US 20210277093A1

(19) United States

(12) Patent Application Publication

Mond et al.

(10) Pub. No.: US 2021/0277093 A1

(43) Pub. Date: Sep. 9, 2021

(54) **IMMUNOTHERAPEUTIC COMPOSITIONS AND METHODS OF PRODUCTION FOR CORONAVIRUS**

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(21) Appl. No.: **17/196,846**

(22) Filed: **Mar. 9, 2021**

Related U.S. Application Data

(60) Provisional application No. 62/987,213, filed on Mar. 9, 2020, provisional application No. 62/994,624, filed on Mar. 25, 2020.

Publication Classification

(51) **Int. Cl.**

C07K 16/10	(2006.01)
G01N 33/569	(2006.01)
A61P 31/14	(2006.01)
A61K 45/06	(2006.01)
A61K 39/42	(2006.01)

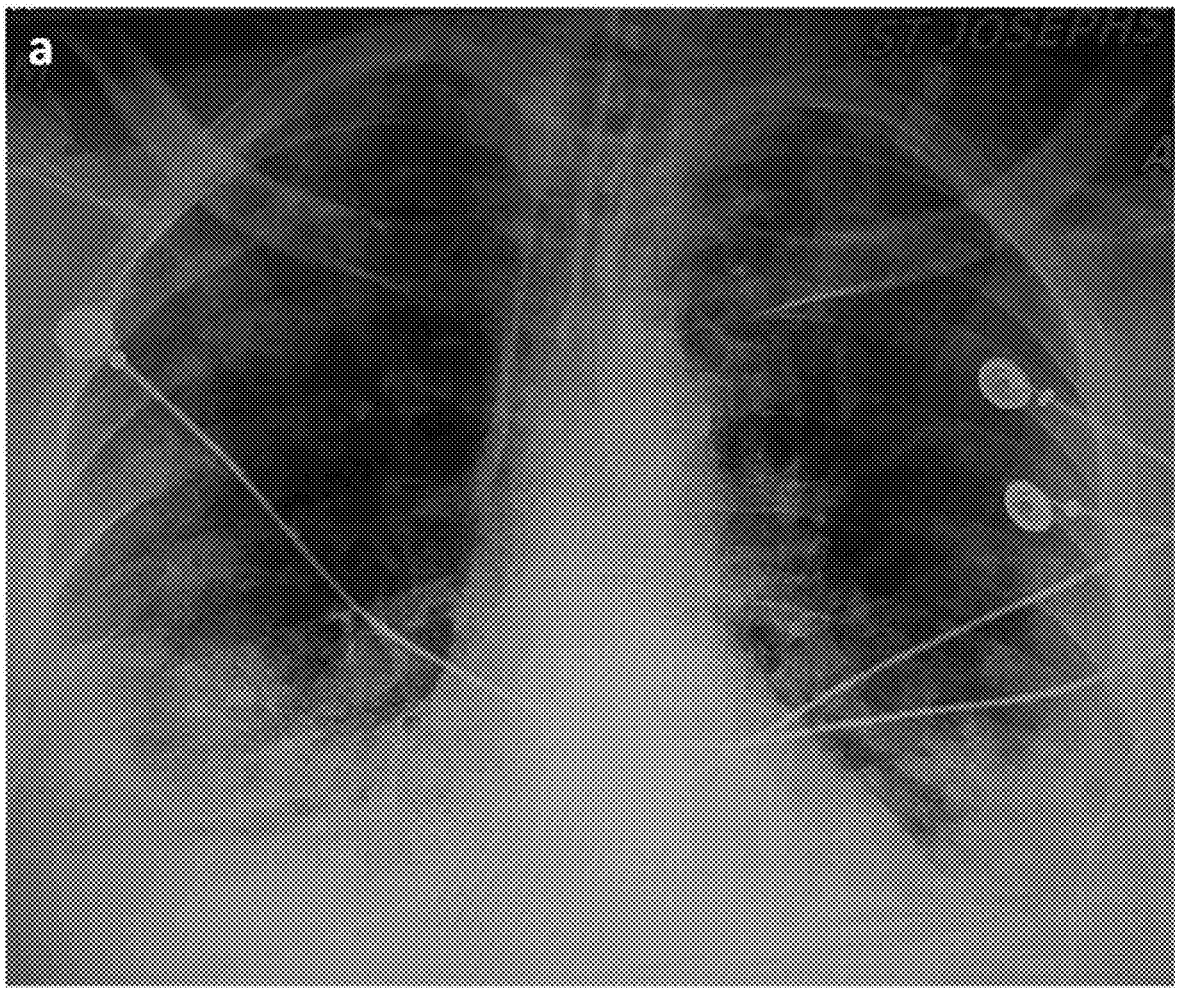
(52) **U.S. Cl.**

CPC ***C07K 16/10*** (2013.01); ***G01N 33/56983*** (2013.01); ***A61P 31/14*** (2018.01); *A61K 2039/505* (2013.01); ***A61K 39/42*** (2013.01); *C07K 2317/10* (2013.01); *G01N 2469/20* (2013.01); ***A61K 45/06*** (2013.01)

(57) **ABSTRACT**

Embodiments of the present disclosure relate generally to compositions and methods for the treatment and/or prevention of pathogenic viral infections, e.g., coronavirus infections. In particular, the present disclosure provides human plasma compositions and immunoglobulin prepared therefrom containing select antibody titers specific for coronavirus (e.g., SARS CoV-2), methods of identifying human donors and donor samples for use in the compositions, methods of manufacturing the compositions, and methods of utilizing the compositions for prophylactic administration and/or therapeutic treatment (e.g., passive immunization or immune-prophylaxis).

Specification includes a Sequence Listing.



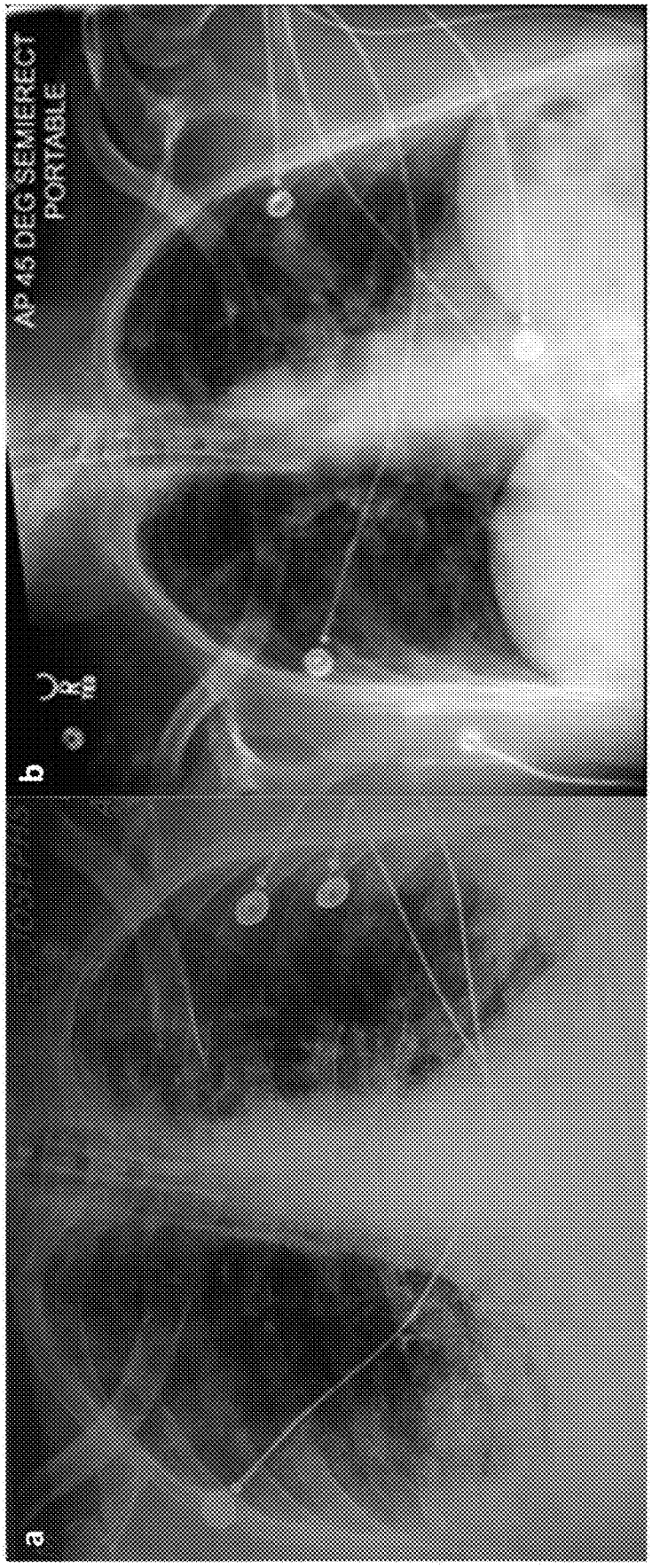


FIG. 1A

FIG. 1B

IMMUNOTHERAPEUTIC COMPOSITIONS AND METHODS OF PRODUCTION FOR CORONAVIRUS

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to and the benefit of U.S. Provisional Application No. 62/987,213, filed Mar. 9, 2020 and U.S. Provisional Application No. 62/994,624, filed Mar. 25, 2020, which are hereby incorporated by reference in their entireties.

FIELD

[0002] The present disclosure relates to compositions and methods for the treatment and/or prevention of pathogenic infections (e.g., coronavirus infections). In particular, the present disclosure provides human plasma compositions and immunoglobulin prepared therefrom containing select antibody titers specific for SARS CoV-2, methods of identifying human plasma donors and donor samples for use in the compositions, and methods of utilizing the compositions for prophylactic administration and/or therapeutic treatment (e.g., passive immunization or immune-prophylaxis).

BACKGROUND

[0003] Commercially available immunoglobulins are derived from pooled human serum, collected, processed, and distributed for sale by the blood and plasma products industry. The first purified human immunoglobulin G (IgG) preparation used clinically was immune serum globulin which was produced in the 1940s (Cohn, E. J., et al. J. Am Chem. Soc., 68:459-475 (1946) and Oncely, J. L. et al., J. Am Chem Soc. 71:541-550 (1949)). The immunoglobulin produced by this method demonstrated a molecular distribution having a high molecular weight, when analyzed by way of high resolution size exclusion chromatography. Immunoglobulin has historically been used primarily to prevent infections in patients who are immune deficient. Immunoglobulin obtained from the plasma of thousands of different donors contains antibodies to many of the pathogens that the donor individuals have encountered in their lifetime and it is these antibodies when infused into patients that prevent them from suffering serious infections.

[0004] However, significant limitations exist with currently available immunoglobulin products. Since immunoglobulin from thousands of random donors are pooled, the antibody titers to the many infectious organisms (e.g., viruses) for which protection is sought varies greatly and very often are not sufficient to meet the immune needs of individuals (e.g., in case of a serious infection with a pathogen).

[0005] In addition, pools of immune globulin contain only antibodies to pathogens to which the person was exposed and not to pathogens to which the individual had no immunological exposure. Thus, pathogens that undergo extensive mutations or pathogens that might be carried by non-human vectors and develop mechanisms to infect humans will be unable to stimulate an immediate anamnestic immunological response that would be required to prevent infection.

SUMMARY

[0006] The present disclosure relates to compositions and methods for the treatment and/or prevention of pathogenic infections such as, for example, coronavirus infections for which standard immune globulin pools will not adequately provide. In particular, the present disclosure provides pooled human plasma compositions and immunoglobulin prepared therefrom, methods of identifying human plasma for use in the compositions, and methods of utilizing the compositions for prophylactic administration and/or therapeutic treatment (e.g., passive immunization or immune-prophylaxis).

[0007] In accordance with the embodiments provided herein, the present disclosure provides pooled plasma compositions and/or immunoglobulin prepared therefrom having increased neutralizing antibody titers against specific viral pathogens, such as for example, coronavirus (coronavirus OC43, coronavirus 229E, coronavirus NL63, coronavirus HKU1, MERS-CoV, SARS-CoV, SARS-CoV-2 (COVID-19)). As described further herein, the compositions include pooled plasma samples and/or immunoglobulin prepared therefrom, which are obtained from a plurality of selected donor human subjects (e.g., 50, 100, 200, 300, 400, 500 or more subjects). In some embodiments, a pooled sample comprising higher neutralizing antibody titers against one virus also has proportionally higher neutralizing antibody titers against other viruses. For example, pooled plasma samples can be obtained from a plurality of selected human donor subjects having increased antibody titers against a coronavirus (e.g., at least 1.2 fold greater than antibody titers from a corresponding control sample and/or an antibody neutralization titer of at least 40 to about 30,000). Additionally, in some embodiments, pooled plasma samples can be obtained from a plurality of selected human donor subjects having increased antibody titers against a respiratory pathogent (e.g., RSV (e.g., at least 1.2 fold greater than antibody titers from a corresponding control sample or an antibody neutralization titer of at least 1000 to 8000)), and these pooled plasma samples can also have proportionally increased antibody titers against a coronavirus (e.g., at least 1.2 fold greater than antibody titers from a corresponding control sample or an antibody neutralization titer of at least 40 to about 30,000).

[0008] In one embodiment, the present disclosure provides a composition comprising pooled plasma samples obtained from a plurality of selected human subjects (e.g., 50, 100, 200, 300, 400, 500 or more human plasma donors), wherein the pooled plasma comprises elevated levels (e.g., selected, consistent and/or standardized levels), compared to the pathogen-specific antibody titers found in a mixture of plasma samples obtained from a plurality random human subjects (e.g., 50, 100, 200, 300, 400, 500 or more human plasma donors), of pathogen-specific antibody titers to one or more (e.g., two, three, four, or more) coronaviruses (e.g., coronavirus OC43, coronavirus 229E, coronavirus NL63, coronavirus HKU1, MERS-CoV, SARS-CoV, and/or SARS-CoV-2 (COVID-19). Embodiments of the present disclosure are not limited by the type of viral pathogens for which the pooled plasma comprises elevated levels of specific antibody titers. For example, the pooled plasma composition may comprise elevated levels of pathogen-specific antibody titers to one or more of coronavirus OC43, coronavirus 229E, coronavirus NL63, coronavirus HKU1, MERS-CoV, SARS-CoV, and/or SARS-CoV-2 (COVID-19)). In another embodiment, the pooled plasma from selected plasma donors comprises elevated levels, compared to the pathogen-specific antibody titers found in a mixture of plasma samples obtained from a plurality of random human sub-

jects, of pathogen-specific antibody titers to two or more non-coronavirus pathogens, for example, respiratory syncytial virus (RSV), influenza A virus, influenza B virus, parainfluenza virus type 1, parainfluenza virus type 2, metapneumovirus, or any other respiratory pathogen known in the art or described herein. In still another embodiment, the pooled plasma comprises elevated levels, compared to the pathogen-specific antibody titers found in a mixture of plasma samples obtained from a plurality of random human subjects, of pathogen-specific antibody titers to three, four, five, six or more viral pathogens described herein. In one embodiment, the pooled plasma comprises a coronavirus-specific antibody titer that is at least 1.2 fold greater (e.g., 1.2 fold, 1.3 fold, 1.4 fold, 1.5 fold, 1.6 fold, 1.7 fold, 1.8 fold, 1.9 fold, 2 fold, 3 fold, 4 fold, 5 fold 6 fold, 7 fold, 8 fold, 9 fold, 10 fold or more) than the corresponding antibody titer found in a mixture of plasma samples obtained from 100 or more random human subjects. In some embodiments, the antibody neutralization titer for a coronavirus is at least 40 to about 30,000. In another embodiment, the pooled plasma comprises pathogen-specific antibody titers to at least a second viral pathogen selected from respiratory syncytial virus (RSV), influenza A virus, influenza B virus, parainfluenza virus type 1, parainfluenza virus type 2, metapneumovirus, coronavirus OC43, coronavirus 229E, coronavirus NL63, coronavirus HKU1, MERS-CoV, SARS-CoV, and SARS-CoV-2 (COVID-19), that is significantly elevated (e.g., at least 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2.0, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3.0, 4.0, 5.0, 6.0, 7.0, 8.0 or more fold) compared to the pathogen-specific antibody titers found in a mixture of plasma samples obtained from a plurality of random human subjects.

[0009] Thus, in one embodiment, the present disclosure provides means for the identification and characterization of plasma and/or immune globulin compositions containing a desired functional, neutralizing coronavirus antibody titer rather than one in which only the total amount of IgG is known.

[0010] In accordance with these embodiments, anti-SARS CoV-2 antibody titer present in a donor plasma sample can be identified by total antibody binding (e.g., using an ELISA). For example, in some embodiments, the present disclosure provides a pooled plasma composition comprising plasma from a plurality of plasma donors wherein each donor's plasma exhibits an SARS CoV-2 antibody titer that is at least 1.2 fold greater (e.g., 1.2, 1.5, 2, 2.5, 3, 3.5, 4.5, 5, 6, 7, 8, 9, 10 fold or greater, or any value therebetween) than the SARS CoV-2-specific antibody titer found in a negative control (e.g., plasma devoid of coronavirus antibodies, or a mixture of plasma samples obtained from a plurality of random, non-convalescent human subjects). In some embodiments, plasma samples are selected based upon the total amount of SARS CoV-2-specific antibody titer (e.g., only those plasma samples that display a threshold (e.g., 2 fold or higher) SARS CoV-2-specific antibody titer are selected). In some embodiments, the selected plasma samples are assayed to characterize SARS CoV-2 neutralizing antibody titer in the samples. In further embodiments, plasma samples are selected based upon the SARS CoV-2 neutralizing antibody titer (e.g., only those plasma samples that display a SARS CoV-2 neutralizing antibody titer in the top 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90% or higher of all plasma samples tested) are selected. In some embodiments, plasma samples are selected based upon both the SARS CoV-2-specific antibody titer and the SARS CoV-2-specific neutralizing titer. For example, as disclosed herein, it was determined that of all convalescent, COVID-19 convalescent plasma analyzed, there exist plasma samples that display a high level of a SARS CoV-2-antibody binding, but lack a corresponding high SARS CoV-2-neutrlizing titer. Compositions and methods disclosed herein are useful at identifying these plasma samples in order to specifically exclude these plasma samples from use in a pooled plasma composition or immune globulin prepared therefrom disclosed herein. The disclosure is not limited to any particular assay for determining neutralizing antibody titer. Indeed, any assay available in the art may be utilized. In some embodiments, a plaque/focus reduction neutralization test (P/FRNT) is performed. In further embodiments, an automated high-throughput antibody neutralization assay based on foci and plaque reduction is used. In other embodiments, a virus reduction neutralization test (VRNT) is utilized (see, e.g., Whiteman et al., Am J Trop Med Hyg. 2018 December; 99(6):1430-1439). In still other embodiments, a pseudovirus neutralization assay is utilized (Creative Diagnostics, Shirley, N.Y.). In some embodiments, a multiplexed bead-based SARS-CoV-2 serological assay is used (NIST, Gaithersburg, Md.).

[0011] The disclosure provides a method of producing an immune globulin comprising obtaining a plurality of plasma samples from a plurality of plasma donors (e.g., COVID-19 convalescent plasma donors or COVID-19 vaccinated donors), conducting a first assay on each plasma sample to measure total anti-SARS CoV-2 antibody titer, selecting, based upon the first assay, plasma samples having a total anti-SARS CoV-2 antibody binding titer that is about two-fold or higher (e.g., 3-, 4-, 5-, 6-, 7-, 8-, 9-, 10-fold or higher) than the amount of total anti-SARS CoV-2 antibody binding titer in a control sample, conducting a second assay on each selected plasma sample from step (3) to measure SARS CoV-2 neutralizing antibody titer, identifying, based upon the second assay, plasma samples having a neutralizing antibody titer in the lower 65% of all plasma samples assayed and excluding the identified plasma samples from further processing, pooling the non-excluded plasma samples, and preparing immune globulin from the pooled plasma samples. In some embodiments, each of the plurality of plasma donors is a COVID-19 convalescent plasma donor. In other embodiments, each of the plurality of plasma donors is a COVID-19 vaccinated plasma donor. In some embodiments, the control sample is a mixture of plasma samples obtained from random human plasma donors (e.g., 50, 100, 150, 200, 250, 500, 1000 or more plasma donors or number therebetween). In other embodiments, the control sample is a commercially available immune globulin. In some embodiments, plasma samples having a neutralizing antibody titer in the lower 70% of all plasma samples assayed are identified and excluded from further processing. In still other embodiments, plasma samples having a neutralizing antibody titer in the lower 75% of all plasma samples assayed are identified and excluded from further processing. In other embodiments, plasma samples having a neutralizing antibody titer in the lower 80% of all plasma samples assayed are identified and excluded from further processing. The disclosure is not limited by the number of non-excluded, pooled plasma samples. In some embodiments, the number of non-excluded, pooled plasma samples is 250-500 or more. In other embodiments, the number of

non-excluded, pooled plasma samples is 500-1000 or more. In some embodiments, the immune globulin is prepared using a cold alcohol fractionation process that isolates the immune globulin fraction from the pooled plasma as a solution. In further embodiments, the immune globulin is combined with a pharmaceutically acceptable carrier.

[0012] In some embodiments, the disclosure provides a method of producing an immune globulin comprising obtaining a plurality of plasma samples from human plasma donors vaccinated with one or more coronavirus vaccines (e.g., one or more vaccines disclosed herein or available in the art); conducting a first assay on each plasma sample to measure total anti-SARS CoV-2 antibody titer, selecting, based upon the first assay, plasma samples having a total anti-SARS CoV-2 antibody binding titer that is about two-fold or higher (e.g., 3-, 4-, 5-, 6-, 7-, 8-, 9-, 10-fold or higher) than the amount of total anti-SARS CoV-2 antibody binding titer in a control sample, conducting a second assay on each selected plasma sample from step (3) to measure SARS CoV-2 neutralizing antibody titer, identifying, based upon the second assay, plasma samples having a neutralizing antibody titer in the lower 65% of all plasma samples assayed and excluding the identified plasma samples from further processing, pooling the non-excluded plasma samples, and preparing immune globulin from the pooled plasma samples. In some embodiments, immunoglobulin is prepared using a cold alcohol fractionation process (e.g., that isolates the immune globulin fraction from the pooled plasma as a solution). In some embodiments, the disclosure provides a pharmaceutical composition comprising an immune globulin obtained by the methods disclosed. In further embodiments, the disclosure provides a method of treating a human patient comprising administering an immune globulin obtained by the disclosed methods to a subject/patient. In some embodiments, the immune globulin reduces viral load in the lung and/or nose of a subject administered the composition compared to a control subject not receiving the composition. In some embodiments, the immune globulin reduces lung histopathology of a subject administered the composition compared to a control subject not receiving the composition. In one embodiment, the pooled plasma comprises plasma samples obtained from 50-3000 or more (e.g., more than 50, 100, 200, 300, 400, 500, 750, 1000, 1250, 1500, 1750, 2000, 2500, 3000, 3500, 4000 or more) human subjects (e.g., COVID-19 convalescent patients, or, vaccinated human plasma donors). In one preferred embodiment, the pooled plasma comprises plasma samples obtained from 100-1000 human subjects. In another preferred embodiment, the pooled plasma comprises plasma samples obtained from at least 1000 human subjects. In one embodiment, the composition comprising pooled plasma samples further comprises a pharmaceutically acceptable carrier (e.g., natural and/or non-naturally occurring carriers). In one embodiment, the pooled plasma composition is utilized to prepare immunoglobulin (e.g., for intravenous administration to a subject). In one embodiment, the pooled plasma composition and/or immunoglobulin provides a therapeutic benefit to a subject administered the composition that is not achievable via administration of a mixture of plasma samples obtained from a plurality of random human subjects and/or immunoglobulin prepared from same. Embodiments of the present disclosure are not limited by the type of therapeutic benefit provided. Indeed, a variety of therapeutic benefits may be attained including those described herein. In one embodiment, the pooled plasma and/or immunoglobulin possesses enhanced viral neutralization properties compared to a mixture of plasma samples obtained from a plurality of random human subjects or immunoglobulin prepared from same. In a further embodiment, the enhanced viral neutralization properties reduce and/or prevent infection in a subject administered the composition for a duration of time that is longer than, and not achievable in, a subject administered a mixture of plasma samples obtained from a plurality of random human subjects. For example, in one embodiment, immunoglobulin prepared from pooled plasma according to the present disclosure (e.g., characterized, selected and blended according to the embodiments of the present disclosure) that is administered to a subject results in a significant, concentration dependent anti-coronavirus neutralization activity, specific neutralization activity that is not achieved or achievable using immunoglobulin prepared from randomly pooled plasma samples (e.g., over a period of hours, days, weeks or longer). While an understanding of a mechanism is not needed to practice aspects of the disclosure, and while the present disclosure is not limited to any particular mechanism, in some embodiments, identification and selection of plasma donors that display both a threshold level of SARS CoV-2 antibody binding and a threshold level of SARS CoV-2 neutralization activity, according to processes and methods disclosed, provides pooled plasma composition and/or immunoglobulin prepared therefrom that possess therapeutic activity and properties superior to and/or absent from conventional convalescent plasma. For example, in some embodiments, plasma samples from convalescent plasma donors (e.g., donors that have recovered from COVID-19) are characterized for SARS CoV-2 antibody binding and SARS CoV-2 neutralization activity, and those samples that display a moderate to high levels of SARS CoV-2 antibody binding but that do not display SARS CoV-2 neutralizing activity (e.g., neutralizing activity that correlates with the total amount of antibody binding) are specifically excluded from use in a pooled plasma composition and/or immunoglobulin prepared therefrom. While an understanding of a mechanism is not needed to practice aspects of the disclosure, and while the present disclosure is not limited to any particular mechanism, in some embodiments, excluding plasma containing moderate to high levels of SARS CoV-2 binding antibodies that lack neutralizing activity from a pooled plasma composition provides a significantly more effective pooled plasma composition and/or immunoglobulin prepared therefrom.

[0013] In one embodiment, the therapeutic benefit of a pooled plasma and/or immunoglobulin of the present disclosure is enhanced viral neutralization properties that reduce or prevent infection (e.g., coronavirus infection) in a subject administered the pooled plasma and/or immunoglobulin for a duration of time that is longer than, and not achievable in, a subject administered a mixture of pooled plasma and/or immunoglobulin prepared from same obtained from a plurality of random human subjects. In one embodiment, the therapeutic benefit is a significant reduction in viral load of a subject administered the pooled plasma and/or immunoglobulin compared to a control subject not receiving same. In a further embodiment, the pooled plasma and/or immunoglobulin significantly reduces lung histopathology in a subject administered the pooled plasma and/or immunoglobulin compared to a control subject not receiving

same. In yet a further embodiment, the pooled plasma and/or immunoglobulin significantly reduces the level of pathogenic viral RNA in a tissue selected from lung, liver and kidney in a subject administered the pooled plasma and/or immunoglobulin compared to a control subject. In one embodiment, a subject administered immunoglobulin prepared from pooled plasma according to the present disclosure displays a mean fold increase in coronavirus neutralization titer that is at least 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2.0, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3.0, 4.0, 5.0, 6.0, 7.0, 8.0 fold or more, or any ranger therebetween, at a time point of at least 1-14 days (e.g., 14 day, 15 days, 16 days, 17 days, 18 days, 19 days or more) post administration of the immunoglobulin. Embodiments of the present disclosure are not limited by the amount of immunoglobulin administered to a subject. In one embodiment, a subject is administered between 250-2500 mg/kg of the immunoglobulin one time, or daily for two or more days (e.g., 2, 3, 4, or more consecutive days). In one embodiment, a subject is administered 1500 mg/kg of immunoglobulin on day one and 750 mg/kg immunoglobulin on day 2. In another embodiment, a subject is administered 750 mg/kg of immunoglobulin on day one and 750 mg/kg immunoglobulin on day 2. In one embodiment, the pooled plasma and/or immunoglobulin prepared from same reduces the incidence of infection in a subject administered the composition. In another embodiment, a pooled plasma and/or immunoglobulin prepared from same reduces the number of days a subject administered the pooled plasma and/or immunoglobulin is required to be administered antibiotics (e.g., to treat infection). In yet another embodiment, a pooled plasma and/or immunoglobulin prepared from the same increases the trough level of circulating anti-SARS CoV-2-specific, functional antibodies in a subject (e.g., increases the level of neutralizing titers specific for SARS CoV-2, thereby providing protective levels of anti-SARS CoV-2-specific antibodies between scheduled dates of administration of the pooled plasma and/or immunoglobulin prepared from same that are not maintained in a subject administered a mixture of plasma samples obtained from a plurality of more random human subjects (e.g., 50, 100, 200, 300, 400, 500 or more subjects) or immunoglobulin prepared from same).

[0014] In another embodiment, the present disclosure provides an immunotherapeutic composition comprising pooled plasma samples obtained from a plurality of selected human subjects, wherein the pooled plasma comprises elevated levels, compared to the pathogen-specific antibody titers found in a mixture of plasma samples obtained from a plurality of random human subjects, of pathogen-specific antibody titers to two or more viral pathogens selected from respiratory syncytial virus (RSV), influenza A virus, influenza B virus, parainfluenza virus type 1, parainfluenza virus type 2, metapneumovirus, coronavirus OC43, coronavirus 229E, coronavirus NL63, coronavirus HKU1, MERS-CoV, SARS-CoV, and SARS-CoV-2 (COVID-19); and a pharmaceutically acceptable carrier. In one embodiment, an immunotherapeutic composition provided herein further comprises one or more biologically active agents. Embodiments of the present disclosure are not limited to the type of biologically active agent/material. Indeed, a variety of biologically active agents/materials may be used including, but not limited to, antibodies, anti-toxin material, anti-inflammatory agent, anti-cancer agent, antimicrobial agent, therapeutic agent, antihistamine, cytokine, chemokine, vitamin, mineral, or the like.

[0015] In one embodiment, the biologically active agent is an anti-toxin agent. In one embodiment, the anti-toxin agent is a mono-specific, bi-specific or multi-specific antibody with specificity toward a viral, bacterial or fungal toxin. In a further embodiment, the bacterial or fungal toxin is selected from Botulinum neurotoxin, Tetanus toxin, *E. coli* toxin, *Clostridium difficile* toxin, *Vibrio* RTX toxin, Staphylococcal toxins, Cyanobacteria toxin, and mycotoxins. In another embodiment, the immunotherapeutic composition further comprises an aliquot of a single or multiple monoclonal antibodies with a single or multiple specificities (e.g., the immunogenic composition may be spiked with one or more antibodies or biologically active material (e.g., a monoclonal antibody of any specificity, an anti-toxin agent, etc.)). Embodiments of the present disclosure are not limited by the type of one or more antibodies that are added to (e.g., spiked into) the immunogenic composition. Indeed, any one or more antibodies (e.g., specific for a pathogen or pathogen product) may be used including, but not limited to standard antibodies, bi-specific antibodies, multi-specific antibodies, or the like known in the art (e.g., specific for one or a multiplicity of antigens).

[0016] In some embodiments, compositions of the present disclosure (e.g., pooled plasma samples and/or immunoglobulin prepared therefrom) are spiked with one or more antibodies that bind to one or more epitope(s) of a target antigen (e.g., epitope of a viral pathogen). The presence of one or more antibodies in the compositions described herein can enhance the therapeutic effects of the compositions, including treating and/or preventing one or more aspects of the viral infection. In some embodiments, the one or more antibodies have been shown to bind a specific target antigen and may also have been shown to have therapeutic efficacy against a given pathogen, such as a virus. In some embodiments, existing antibodies added to the therapeutic compositions of the present disclosure enhance therapeutic efficacy, and include, but are not limited to, antibodies that bind one or more antigenic regions of a virus that are conserved among viruses or viral subtypes, that are unique among viruses or viral subtypes (e.g., variants), and/or are present in a particular virus because of genetic recombination.

[0017] As would be recognized by one of ordinary skill in the art based on the present disclosure, antibodies that bind one or more epitopes of a viral pathogen can be generated and added to the compositions of the present disclosure (e.g., pooled plasma samples and/or immunoglobulin prepared from same). In some embodiments, antibodies are generated against one or more epitopes of a coronavirus antigen (e.g., coronavirus OC43, coronavirus 229E, coronavirus NL63, coronavirus HKU1, MERS-CoV, SARS-CoV, or SARS-CoV-2 (COVID-19)). In accordance with these embodiments, the present disclosure includes any method for generating a coronavirus antibody that binds at least one epitope of a coronavirus antigen. Such antibodies can be generated using amino acid sequence information currently available corresponding to any of the known coronavirus strains, as well as that of any future coronavirus strains identified, by methods known in the art, non-limiting examples of which are described further below. In some embodiments, antibodies are generated that bind an epitope or epitopes present in more than one coronavirus strain (e.g., cross-reactive anti-

bodies that recognize a conserved region of a coronavirus protein). In some embodiments, antibodies are generated that bind an epitope or epitopes present in a single coronavirus strain (e.g., antibodies that recognize a unique region of a coronavirus protein). In accordance with these embodiments, the sequence of SARS-CoV-2 can be accessed via NCBI GenBank accession code MN908947; the sequence of SARS-CoV can be accessed via NCBI GenBank accession code AY274119; the sequence of MERS-CoV can be accessed via NCBI GenBank accession code NC_019843; the sequence of HKU1 (beta coronavirus) can be accessed via NCBI GenBank accession code KF686346; the sequence of OC43 (beta coronavirus) can be accessed via NCBI GenBank accession code NC_006213; the sequence of NL63 (alpha coronavirus) can be accessed via NCBI GenBank accession code NC_005831; and the sequence of 229E (alpha coronavirus) can be accessed via NCBI GenBank accession code NC_002645.

[0018] In some embodiments, one or more coronavirus antigens (e.g., comprising one or more antigenic epitopes of a coronavirus antigen described herein) are used as or in a vaccine to immunize a subject (e.g., to generate a coronavirus-specific immune response). In some embodiments, a subject administered the vaccine is used as a plasma donor (e.g., to generate an immune globulin composition described herein). In some embodiments, the present disclosure includes human plasma immunoglobulin compositions containing antibodies specific for a coronavirus or coronaviruses obtained from human donor samples that have been immunized with a coronavirus vaccine and methods of utilizing the compositions for prophylactic administration and/or therapeutic treatment (e.g., passive immunization or immune-prophylaxis). In some embodiments, immunoglobulin compositions of the present disclosure can be obtained from pooled plasma samples obtained from a plurality of donor human subjects (e.g., 50, 100, 200, 300, 400, 500 or more subjects) that have been immunized with one or more coronavirus antigens (e.g., comprising one or more antigenic epitopes of a coronavirus antigen described herein) derived from a coronavirus (e.g., coronavirus OC43, coronavirus 229E, coronavirus NL63, coronavirus HKU1, MERS-CoV, SARS-CoV, or SARS-CoV-2 (COVID-19)).

[0019] In some embodiments, one or more epitopes of a coronavirus antigen find use in an antibody binding assay (e.g., ELISA) and/or a neutralization assay described herein.

[0020] In another embodiment, the present disclosure provides a method of providing immunotherapy to a subject (e.g., a subject in need thereof (e.g., a subject with disease or at risk for disease)) comprising administering to the subject a therapeutically effective amount of a composition comprising pooled plasma samples or immunoglobulin prepared therefrom obtained from a plurality of selected human subjects (e.g., 50, 100, 200, 300, 400, 500 or more subjects), wherein the pooled plasma comprises elevated levels, compared to the pathogen-specific antibody titers found in a mixture of plasma samples obtained from a plurality of random human subjects (e.g., 50, 100, 200, 300, 400, 500 or more subjects), of pathogen-specific antibody titers to one or more (e.g., two, three, four, five or more) viral pathogens selected from coronavirus (e.g., coronavirus OC43, coronavirus 229E, coronavirus NL63, coronavirus HKU1, MERS-CoV, SARS-CoV, SARS-CoV-2 (COVID-19)), respiratory syncytial virus (RSV), influenza A virus, influenza B virus, parainfluenza virus type 1, parainfluenza virus type 2, and metapneumovirus. In one embodiment, the immunotherapy is used to prophylactically treat infection associated with a microbial pathogen. In another embodiment, the immunotherapy is used to therapeutically treat infection associated with a microbial pathogen.

[0021] An advantage of the compositions and methods described herein is that many embodiments do not require the subject to be given additional drugs to treat their risk of infection, and therefore they are spared adverse side effects or interactions with other therapies. Another advantage of the compositions and methods described herein is that the compositions and methods may be used to treat or prevent disease wherein drugs or other conventional treatments do not exist to treat or prevent the disease (e.g., compositions and methods of the present disclosure can be used to treat and/or prevent infection with coronavirus). Another advantage of the compositions and methods described herein is that immunoglobulin provided by the present disclosure provides protection and therapeutic benefit to a coronavirus infected patient. In one embodiment, compositions and methods of the present disclosure are utilized for prophylactic and/or therapeutic treatment of infection for which there exists no known cure (e.g., various viral illnesses). In some embodiments, compositions and methods of the present disclosure are utilized for prophylactic and/or therapeutic treatment of infections. In some embodiments, compositions and methods of the present disclosure are utilized for prophylactic and/or therapeutic treatment of a subject that harbors a non-competent immune system (e.g., in which treatment with antibiotic or other conventional antimicrobial therapy would have little to no value).

[0022] In other embodiments, compositions and methods of the present disclosure are utilized to reduce the risk of a subject developing an infection (e.g., a respiratory infection). Embodiments of the present disclosure are not limited by the type of subject treated with the compositions and methods provided herein. Indeed, a variety of subjects may be so treated, including, but not limited to, a subject at risk of developing an infection (e.g., respiratory or other type of infection, thereby reducing the risk of developing infection in a subject having an elevated risk of infection). In one embodiment, the immunotherapy provides the subject with prophylactic immunity against one or more pathogens selected from coronavirus (e.g., coronavirus OC43, coronavirus 229E, coronavirus NL63, coronavirus HKU1, MERS-CoV, SARS-CoV, SARS-CoV-2 (COVID-19)), and respiratory syncytial virus (RSV). However, embodiments of the present disclosure are not so limited. Indeed, immunotherapy with the compositions and methods of the present disclosure may provide the subject with prophylactic immunity to any of the microbial pathogens described herein.

[0023] In another embodiment, the present disclosure provides a method of producing a pooled plasma composition, comprising obtaining plasma samples from human subjects; characterizing the pathogen-specific antibody titer, within a subset of the plasma samples, for one or more viral pathogens selected from respiratory syncytial virus (RSV), influenza A virus, influenza B virus, parainfluenza virus type 1, parainfluenza virus type 2, metapneumovirus, coronavirus OC43, coronavirus 229E, coronavirus NL63, coronavirus HKU1, MERS-CoV, SARS-CoV, SARS-CoV-2 (COVID-19); selecting, based upon the antibody titers characterized, plasma samples that have elevated levels, compared to a control value (e.g., the pathogen-specific antibody titers

found in a mixture of plasma samples obtained from a plurality of random human subjects), of pathogen-specific antibody titers to one or more pathogens selected from coronavirus (e.g., coronavirus OC43, coronavirus 229E, coronavirus NL63, coronavirus HKU1, MERS-CoV, SARS-CoV, SARS-CoV-2 (COVID-19)), respiratory syncytial virus (RSV), influenza A virus, influenza B virus, parainfluenza virus type 1, parainfluenza virus type 2, metapneumovirus; pooling the selected plasma samples with other plasma samples to generate the pooled plasma composition, wherein the pooled plasma composition comprises pathogen-specific antibody titers to one or more respiratory pathogens selected from respiratory syncytial virus (RSV), influenza A virus, influenza B virus, parainfluenza virus type 1, parainfluenza virus type 2, metapneumovirus, coronavirus OC43, coronavirus 229E, coronavirus NL63, coronavirus HKU1, MERS-CoV, SARS-CoV, SARS-CoV-2 (COVID-19), the one or more titers being elevated at least 1.1 fold compared to a control value (e.g., the pathogen-specific antibody titers in a mixture of plasma samples obtained from a plurality of random human subjects). In one embodiment, the method comprises selecting, based upon the antibody titers characterized, plasma samples that have elevated levels, compared to the pathogen-specific antibody titers found in a mixture of plasma samples obtained from a plurality of random human subjects, of pathogen-specific antibody titers to two or more viral pathogens selected from respiratory syncytial virus (RSV), influenza A virus, influenza B virus, parainfluenza virus type 1, parainfluenza virus type 2, metapneumovirus, coronavirus OC43, coronavirus 229E, coronavirus NL63, coronavirus HKU1, MERS-CoV, SARS-CoV, and SARS-CoV-2 (COVID-19).

[0024] In a further embodiment, the method comprises selecting, based upon the antibody titers characterized, plasma samples that have elevated levels, compared to the pathogen-specific antibody titers found in a mixture of plasma samples obtained from a plurality of random human subjects, of pathogen-specific antibody titers to two, three, four or more pathogens selected from coronavirus (e.g., coronavirus OC43, coronavirus 229E, coronavirus NL63, coronavirus HKU1, MERS-CoV, SARS-CoV, SARS-CoV-2 (COVID-19)), respiratory syncytial virus (RSV), influenza A virus, influenza B virus, parainfluenza virus type 1, parainfluenza virus type 2, and metapneumovirus. In one embodiment, the pooled plasma composition comprises pathogen-specific antibody titers to at least two or more respiratory pathogens selected from coronavirus (e.g., coronavirus OC43, coronavirus 229E, coronavirus NL63, coronavirus HKU1, MERS-CoV, SARS-CoV, SARS-CoV-2 (COVID-19)), respiratory syncytial virus (RSV), influenza A virus, influenza B virus, parainfluenza virus type 1, parainfluenza virus type 2, and metapneumovirus that are each elevated at least 1.1 fold compared to the pathogen-specific antibody titers found in a mixture of plasma samples obtained from a plurality of random human subjects. In one embodiment, the pooled plasma composition comprises pathogen-specific antibody titers to at least two or more respiratory pathogens selected from coronavirus (e.g., coronavirus OC43, coronavirus 229E, coronavirus NL63, coronavirus HKU1, MERS-CoV, SARS-CoV, SARS-CoV-2 (COVID-19)), respiratory syncytial virus (RSV), influenza A virus, influenza B virus, parainfluenza virus type 1, parainfluenza virus type 2, and metapneumovirus that are each elevated at least 1.2 fold compared to the pathogen-specific antibody titers found in a mixture of plasma samples obtained from a plurality of random human subjects. In another embodiment, the pooled plasma composition comprises a coronavirus-specific antibody titer that is at least 1.2 fold greater (e.g., 1.2, 1.5, 2, 2.5, 3, 3.5, 4.5, 5, 6, 7, 8, 9, 10 fold or more or any value therebetween) than the coronavirus-specific antibody titer found in a mixture of plasma samples obtained from a plurality of random human subjects. For example, in one embodiment, the present disclosure provides a method of producing a pooled plasma composition (e.g., containing a specific, elevated antibody titer for coronavirus and a specific, elevated antibody titer for at least a second viral pathogen), from at least 100 human plasma donors, comprising obtaining plasma samples from selected human plasma donors, wherein the selected human donors are identified via characterizing the specific titer of antibodies to a coronavirus in a plasma sample from a human donor, wherein characterizing the specific titer of antibodies comprises a first, plasma screening assay utilized to determine total SARS CoV-2 antibody binding titer, a second assay of plasma samples selected from the first assay, wherein the second assay determines SARS CoV-2 neutralizing titer, a second selection of plasma samples displaying a desired neutralization titer and exclusion of plasma samples lacking the desired neutralization titer, wherein only those samples that display a desired, threshold total SARS CoV-2 antibody binding titer (e.g., 2 fold or higher compared to a control) and a threshold SARS CoV-2 neutralizing titer (e.g., the top 25%, top 20%, top 15%, top 10%, top 5% or greater, or any value therebetween) are pooled together to generate a pooled plasma composition (e.g., from which immunoglobulin is produced).

[0025] In some embodiments, the present disclosure provides a composition comprising pooled plasma samples (e.g., a therapeutic composition) comprising plasma from a plurality of donors (e.g., 100 or more human donors), that have been clinically diagnosed with an infection by a viral pathogen, such as an infection from one or more of a coronavirus (e.g., coronavirus OC43, coronavirus 229E, coronavirus NL63, coronavirus HKU1, MERS-CoV, SARS-CoV, SARS-CoV-2 (COVID-19)), respiratory syncytial virus (RSV), influenza A virus, influenza B virus, parainfluenza virus type 1, parainfluenza virus type 2, and metapneumovirus. In some embodiments, plurality of donors have recovered or are recovering from the viral infection. In some embodiments, a clinical diagnosis of a viral infection is carried out by a medical or laboratory professional and involves obtaining a sample(s) from the plurality of donors (e.g., blood sample, plasma sample, serum sample, fecal sample, urine sample cheek swab, sputum sample, and the like), and testing the sample using any of a variety of antibody-based and/or molecular (e.g., PCR) and/or clinical chemistry testing protocols to identify the presence of the virus and/or one or more physiological responses from the subject that correlates to the presence/absence of the virus. A clinical diagnosis generally involves a physiological readout based on the sample that indicates whether a subject has recovered or is recovering from the infection. A physiological indication of recovery can include, but is not limited to, presence/absence of an antibody, a nucleic acid, a metabolite, and the like. In some embodiments, a clinical diagnosis can indicate whether a subject has a coronavirus infection (e.g., coronavirus OC43, coronavirus 229E, coronavirus NL63, coronavirus HKU1, MERS-CoV, SARS-CoV, SARS-

CoV-2 (COVID-19)), as well as whether the subject has recovered or is recovering from the coronavirus infection. In some embodiments, the one or more of the plurality of human plasma donors have been clinically diagnosed with infection by the coronavirus and have recovered from the infection. In some embodiments, the one or more of the plurality of human plasma donors have been clinically diagnosed with an infection from the at least a second virus and have recovered from the infection. In some embodiments, the one or more of the plurality of human plasma donors have not been clinically diagnosed with infection by the coronavirus. In some embodiments, the one or more of the plurality of human plasma donors have not been clinically diagnosed with an infection from the at least a second virus. In some embodiments, the one or more of the plurality of human donors have been selected based on at least one pre-preselection criterion, including but not limited to occupation (e.g., teacher, flight attendant, healthcare professional), proximity to an infection hotspot, degree of contact to other humans, and the like.

[0026] In some embodiments, the present disclosure provides a composition comprising pooled plasma samples (e.g., a therapeutic composition) comprising plasma from a plurality of donors (e.g., 100 or more human donors), wherein all or a subset of the plurality of donors possess a high titer of pathogen-specific antibodies to one or more viral pathogens as a result of administration of an immunogenic composition (e.g., viral vaccine) comprising antigens to the plurality of pathogens, which generates an immunogenic response in the subject. In some embodiments, the plurality of human plasma donors have been clinically diagnosed as having or not having a particular viral infection. In some embodiments, the plurality of human plasma donors have not been clinically diagnosed as having or not having a particular viral infection. As described further herein, compositions of the present disclosure include pooled plasma samples from this plurality of donors that have received a coronavirus vaccine (e.g., vaccine for one or more of coronavirus OC43, coronavirus 229E, coronavirus NL63, coronavirus HKU1, MERS-CoV, SARS-CoV, SARS-CoV-2 (COVID-19)).

[0027] In one embodiment, compositions are provided that comprise a plurality of different types of antibodies (e.g., directed to different pathogens (e.g., viral pathogens, bacterial pathogens, eukaryotic pathogens, etc.), recognize different antigens, recognize different epitopes, etc.) and are enriched (e.g., elevated titer) for at least two different antibodies or sets of antibodies (e.g., directed to different pathogens, recognize different antigens, recognize different epitopes, etc.). In particular embodiments, compositions comprise tailored antibody pools. In some embodiments, at least from about 0.01% to about 70% of the total immunoglobulin present in the composition is directed to one or more targeted pathogens, although embodiments of the present disclosure are not so limited (e.g., the composition may comprise less than 0.01% or more than 70% of immunoglobulin directed to targeted pathogens). Immunoglobulin directed to targeted pathogens may comprise >0.1% >2%, >5%, >10%, >20%, >30%, >40%, >50%, >60%, >70%, >80%, or >90% of the total immunoglobulin present in the composition. In certain embodiments, a composition comprises two or more immunoglobulins to targeted pathogens, each present at greater than 1% of total immunoglobulin present in the composition (e.g., two or more immunoglobulins to targeted pathogens present at greater than 1.5%, 2.0%, 3.0%, 4.0%, 5.0% or more of total immunoglobulin, two or more immunoglobulins to targeted pathogens present at greater than 10% of total immunoglobulin, two or more immunoglobulins to targeted pathogens present at greater than 15% of total immunoglobulin, two or more immunoglobulins to targeted pathogens present at greater than 20% of total immunoglobulin, two or more immunoglobulins to targeted pathogens present at greater than 25% of total immunoglobulin, etc.).

[0028] Any suitable method for obtaining plasma, antibody samples, pooled plasma compositions and/or immunoglobulin from same are within the scope of the present disclosure. Further, any suitable method for producing, manufacturing, purifying, fractionating, enriching, etc. antibody samples and/or plasma pools is within the bounds of the present disclosure. Exemplary techniques and procedures for collecting antibody samples and producing plasma pools are provide, for example, in: U.S. Pat. Nos. 4,174,388; 4,346,073; 4,482,483; 4,587,121; 4,617,379; 4,659,563; 4,665,159; 4,717,564; 4,717,766; 4,801,450; 4,863,730; 5,505,945; 5,582,827; 6,692,739; 6,962,700; 6,984,492; 7,045,131; 7,488,486; 7,597,891; 6,372,216; U.S. Patent App. No. 2003/0118591; U.S. Patent App. No. 2003/0133929 U.S. Patent App. No. 2005/0053605; U.S. Patent App. No. 2005/0287146; U.S. Patent App. No. 2006/0110407; U.S. Patent App. No. 2006/0198848; U.S. Patent App. No. 2006/0222651; U.S. Patent App. No. 2007/0037170; U.S. Patent App. No. 2007/0249550; U.S. Patent App. No. 2009/0232798; U.S. Patent App. No. 2009/0269359; U.S. Patent App. No. 2010/0040601; U.S. Patent App. No. 2011/0059085; and U.S. Patent App. No. 2012/0121578; herein incorporated by reference in their entireties. Embodiments of the present disclosure may utilize any suitable combination of techniques, methods, or compositions from the above listed references.

[0029] In some embodiments, plasma and/or antibody samples are obtained from donor subjects in the form of donated or purchased biological material (e.g., blood or plasma). In some embodiments, plasma and/or antibody samples (e.g., blood, plasma, isolated antibodies, etc.) are obtained from a commercial source. In some embodiments, a plasma and/or antibody sample, blood donation, or plasma donation is screened for pathogens, and either cleaned or discarded if particular pathogens are present. In one embodiment, screening occurs prior to pooling a donor sample with other donor samples. In other embodiments, screening occurs after pooling of samples. Antibodies, blood, and/or plasma may be obtained from any suitable subjects. In some embodiments, antibodies, blood, and/or plasma are obtained from a subject who has recently (e.g., within 1 year, within 6 months, within 2 months, within 1 month, within 2 weeks, within 1 week, within 3 days, within 2 days, within 1 day) been vaccinated against or been exposed to one or more specific pathogens. In certain embodiments, a subject positive for antibodies to the pathogen of interest is administered antigens to that pathogen to increase titer of the desired antibodies. In some embodiments, a subject has produced antibodies and/or has elevated titer of antibodies against one or more specific pathogens. In certain embodiments, a subject, whether negative or positive for antibodies to a specific microbial pathogen is administered one or more different viral, bacterial and/or fungal antigens/vaccines in order to increase titer of specific, desired antibodies (e.g.,

viral-, bacterial- and/or fungal-specific antibodies). Pathogens to which a donor may have elevated titer of antibodies include, but are not limited to, respiratory syncytial virus (RSV) and coronavirus (e.g., coronavirus OC43, coronavirus 229E, coronavirus NL63, coronavirus HKU1, MERS-CoV, SARS-CoV, or SARS-CoV-2 (COVID-19)), or other human viral or bacterial pathogens.

[0030] In some embodiments, plasma samples known, identified, and/or selected (e.g., according to methods described herein) to contain elevated titer of a particular antibody (e.g., antibodies directed to coronavirus) or a set of plasma samples are combined (e.g., pooled) to produce a composition comprising pooled plasma samples (e.g., with elevated titer of antibodies directed to a particular pathogen or to a set of pathogens (e.g., coronavirus, and one or more other respiratory pathogens)). For example, a composition comprising pooled plasma samples is produced by pooling plasma samples obtained from selected human subjects, wherein the pooled plasma comprises elevated levels (e.g., elevated by about 20%, 30%, 40%, 50%, 60%, 70%, 85%, 90%, 100%, 125%, 150%, 160%, 170%, 175%, 180%, 200%, 225%, 250%, 275%, 300%, 350%, 400%, 450%, 500%, 550%, 600%, 650%, 700%, 750%, 800%, 850%, 900%, 950%, 1000% or more), compared to a control value (e.g., the pathogen-specific antibody titers found in a mixture of plasma samples obtained from 100 or more random human subjects), of pathogen-specific (e.g., coronavirus specific) antibody titers. In a further embodiment, immune globulin is prepared from the pooled plasma (e.g., according to techniques and methods described herein). In some embodiments, a composition comprising pooled plasma samples is produced by pooling plasma samples obtained from selected human donors and non-selected human donors, wherein the pooled plasma comprises elevated levels, compared to the pathogen-specific antibody titers found in a mixture of plasma samples obtained from 100 or more random human subjects, of coronavirus-specific antibody titers (e.g., individuals recently exposed to one or more of coronavirus OC43, coronavirus 229E, coronavirus NL63, coronavirus HKU1, MERS-CoV, SARS-CoV, or SARS-CoV-2 (COVID-19)), of coronavirus-specific antibody titers individuals recently vaccinated for coronavirus), and other viral pathogen specific titers. In one embodiment, a composition comprising pooled plasma samples and/or immune globulin prepared therefrom is a sterile solution with a pH of about 6.0-7.8 (e.g., 5.0-6.0, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8, or higher). In another embodiment, a composition comprising pooled plasma samples and/or immune globulin prepared therefrom is prepared according US FDA standards for immune globulin preparation (e.g., 37 CFR §§ 640.100; 640.101; 640.102; 640.103; 640.104, Apr. 1, 2013).

[0031] In one embodiment, a composition comprising pooled plasma samples and/or immune globulin prepared therefrom comprises elevated antibody titer levels, compared to a control antibody titer value (e.g., the pathogen-specific antibody titer found in a mixture of plasma samples obtained from 100 or more random human subjects), of pathogen-specific antibodies to respiratory syncytial virus and one or more respiratory pathogens selected from, influenza A virus, influenza B virus, parainfluenza virus type 1, parainfluenza virus type 2, metapneumovirus and coronavirus, wherein the elevated levels of RSV specific, influenza A virus specific, influenza B virus specific, parainfluenza virus type 1 specific, parainfluenza virus type 2 specific, metapneumovirus specific and/or coronavirus (e.g., coronavirus OC43, coronavirus 229E, coronavirus NL63, coronavirus HKU1, MERS-CoV, SARS-CoV, or SARS-CoV-2 (COVID-19) specific antibodies are elevated at least 20%, 30%, 40%, 50%, 60%, 70%, 85%, 90%, 100%, 125%, 150%, 175%, 200%, 225%, 250%, 275%, 300%, 350%, 400%, 450%, 500%, 550%, 600%, 650%, 700%, 750%, 800%, 850%, 900%, 950%, 1000% or more), compared to a control value (e.g., the pathogen-specific antibody titer level found in a mixture of plasma samples obtained from 100 or more random human subjects). The present disclosure provides a method, in one embodiment, of generating the above described composition comprising obtaining plasma samples from selected human donors and non-selected human donors; pooling 100 or more plasma samples from both selected donors and non-selected donors to generate the pooled plasma composition. In one embodiment, the plasma samples from selected human donors and non-selected human donors are screened in order to confirm the absence of bloodborne pathogens (e.g., before or after pooling). In a further embodiment, selected human donors are identified via identifying the specific titer of antibodies to one or more respiratory pathogens selected from respiratory syncytial virus, influenza A virus, influenza B virus, parainfluenza virus type 1, parainfluenza virus type 2, metapneumovirus and coronavirus (e.g., coronavirus OC43, coronavirus 229E, coronavirus NL63, coronavirus HKU1, MERS-CoV, SARS-CoV, or SARS-CoV-2 (COVID-19)). In a preferred embodiment, selected human donors are identified via identifying the specific titer of antibodies to respiratory syncytial virus and/or coronavirus. In a further embodiment, the selected human donors comprise high titer donors and medium titer donors, wherein high titer donors comprise a pathogen specific antibody titer that is 2-5 times, 5-8 times, 8-10 times, 10-14 times, 14 times or greater than a standard value (e.g., the titer of pathogen specific antibodies present in a pool of plasma samples from 100 or more random human subjects), and wherein medium titer donors comprise a pathogen specific antibody titer that is the titer of pathogen specific antibodies present in a pool of plasma samples from 100 or more random human subjects or that is only marginally higher (e.g., 5-20% higher) or marginally lower (e.g., 5-20% lower) than this value. In still a further embodiment, the selected human donors comprise high titer donors, medium titer donors and low titers donors, wherein high titer donors comprise a pathogen specific antibody titer that is 2-5 times, 5-8 times, 8-10 times, 10-14 times, 14 times or greater than a standard value (the titer of pathogen specific antibodies present in a pool of plasma samples from 100 or more random human subjects), wherein medium titer donors comprise a pathogen specific antibody titer that is the titer of pathogen specific antibodies present in a pool of plasma samples from 100 or more random human subjects or that is only marginally higher (e.g., 5-20% higher) or marginally lower (e.g., 5-20% lower) than this value, and wherein low titer donors comprise a pathogen specific antibody titer that is around 20-50 percent the titer of pathogen specific antibodies present in a pool of plasma samples from 100 or more random human subjects.

[0032] In one embodiment, identifying antibody titer comprises a plasma screening assay assessing neutralizing activity in a plasma sample, and screening assay assessing antibody titer. In one embodiment, neutralizing activity in

plasma is measured via the absence of infection by coronavirus. In a further embodiment, the plasma screening assay assessing neutralization activity categorizes plasma samples as high titer, medium titer, or low titer for coronavirus specific antibodies (e.g., titer being calculated and assigned to a donor/donor sample at the dilution that give 50% inhibition of virus growth (that point which is 50% of the two extremes (saline plus virus is 100 growth and no virus added is 0 growth) according to methods described herein. In some embodiments, coronavirus antibody neutralization titers can range from at least 40 to about 30,000, In still a further embodiment, plasma samples identified as displaying the top 20%-30% of neutralizing activity of all donors are processed to produce purified immunoglobulin. In a preferred embodiment, only plasma samples identified as displaying the top 20% of neutralizing activity of all donors are processed to produce purified immunoglobulin. In one embodiment, a screening assay characterizes the coronavirus specific antibody titer of a purified immunoglobulin fraction of the plasma sample. In another embodiment, the pooled plasma composition comprises a coronavirus neutralization antibody titer of 100, 1000, 2000, 5000, 10000, 15000, 20000, 25000 or more. In one embodiment, the pooled plasma composition comprise about 1800-2500 liters (e.g., about 1000, about 1100, about 1200, about 1300, about 1400, about 1500, about 1600, about 1700, about 1800, about 1900, about 2000, about 2100, about 2200, about 2300, about 2400 or about 2500 liters) of plasma from 100 donors (e.g., with a coronavirus neutralization antibody titer of 40 or more). In one embodiment, a pooled plasma composition of the present disclosure comprises about 2200 liters of plasma (e.g., from 100 donors with a coronavirus neutralization antibody titer of 40 or more). The disclosure is not limited by the type of control utilized. In some embodiments, the control is plasma samples obtained from 100 or more random human subjects. In other embodiments, the control is a conventional hyperimmune immune globulin (e.g., hyperimmune immune globulin for rabies (HYPERRAB, Grifols, Clayton, N.C.), hyperimmune globulin for hepatitis (e.g., HYPERHEP B, Talecris Biotherapeutics, Research Triangle Park, N.C.), hyperimmune globulin for RSV (e.g., RESPIGAM, MEDIMMUNE, Inc.)). In still other embodiments, the control is any commercially available immunoglobulin (e.g., non-hyperimmune globulin).

[0033] In one embodiment, the pooled plasma composition comprises a coronavirus-specific antibody titer that is at least 2 fold greater (e.g., 2, 3, 4, 5, 6, 7, 8, 9, 10 fold or more) than the coronavirus-specific antibody titer found in a mixture of plasma samples obtained from 100 or more random human subjects. In one embodiment, the pooled plasma composition provides a therapeutic benefit to a subject administered the composition that is not achievable via administration of a mixture of plasma samples obtained from 100 or more random human subjects. Multiple types of therapeutic benefits are provided including, but not limited to, inhibition of infection caused by coronavirus or other respiratory, viral pathogen in a subject administered the composition for a duration of time that is longer than and not achievable in a subject administered a mixture of plasma samples obtained from 100 or more random human subjects; significant reduction in viral load in the lung and/or nose; significant reduction in lung histopathology; and/or significant reduction in the level of pathogenic viral RNA in lung, liver, kidney and/or other tissue.

[0034] In one embodiment, each individual plasma sample used in a process or composition of the present disclosure is collected only at an FDA approved blood establishments and is tested by serological tests (e.g., FDA approved serological tests). In another embodiment, an individual plasma sample and/or a pooled plasma composition of the present disclosure is tested for the presence of an infectious agent (e.g., viral pathogen) using Nucleic Acid Testing (NAT) and used in a process or composition of the present disclosure only when the absence of the pathogens is confirmed.

[0035] Embodiments of the present disclosure are not limited by the type of subject (e.g., mammal, non-human primate, human, etc.) administered or treated with a composition of the present disclosure (e.g., pooled plasma samples and/or immunotherapeutic composition comprising same). Indeed, the subject may be any subject in need of treatment with a composition of the present disclosure (e.g., a subject infected with or susceptible to infection (e.g., due to an immune deficiency) with an infectious agent (e.g., any one or more infectious agents described herein (e.g., respiratory pathogens))). In some embodiments, the subject is at elevated risk for infection (e.g., by one or multiple specific pathogens (e.g., respiratory pathogens)). The subject may be a neonate. In some embodiments, the subject has an immunodeficiency (e.g., a subject receiving immunosuppressing drugs (e.g., a transplant patient), suffering from a disease of the immune system, suffering from a disease that depresses immune functions, undergoing a therapy (e.g., chemotherapy) that results in a suppressed immune system, experiencing an extended hospital stay, and/or a subject anticipating direct exposure to a pathogen or pathogens. In some embodiments, the subject treated with the compositions and/or methods of the present disclosure include subjects with a healthy or normal immune system (e.g., that has a bacterial, viral and/or fungal infection). In some embodiments, the subject to be treated is one that has a greater than normal risk of being exposed to an agent or material (e.g., a toxin or toxins). In some embodiments, the subject is a soldier, an emergency responder or other subject that has a higher than normal risk of being exposed to a toxin (e.g., biological toxin), wherein treatment with the compositions and/or methods of the present disclosure provide the subject one or more immune response benefits (e.g., administration of an immunotherapeutic composition to a soldier prevents the soldier from showing signs or symptoms of disease or morbidity normally associated with exposure to a toxin).

[0036] The present disclosure thus provides methods and compositions for preventing and/or treating infections associated with viruses (e.g., coronaviruses). In some embodiments, the present disclosure provides compositions (e.g., kits) and methods for identifying subjects useful for providing donor plasma/serum (e.g., with high titers of viral-specific antibodies). In some embodiments, the present disclosure provides new therapeutic compositions for active and passive immunization against infections caused by and/or associated with a viral pathogens. In some embodiments, the present disclosure provides new therapeutic compositions for active and passive immunization against infections caused by and/or associated with a specific virus (e.g., respiratory syncytial virus or coronavirus).

BRIEF DESCRIPTION OF DRAWINGS

[0037] FIGS. **1**A-B: FIG. **1**A: Representative chest X-ray from day 13 post-admission (day 2 post-treatment) of an

adult patient with Severe Acute Respiratory Distress Syndrome and confirmed COVID-19. The patient displayed progression of confluent ground-glass consolidative opacities involving the lung bases, and involvement of the periphery of the upper lobes bilaterally. FIG. 1B: Chest X-ray from day 24 post-admission (day 13 post-treatment) display persistent bilateral patchy pulmonary infiltrates with improved pulmonary ventilation.

DETAILED DESCRIPTION

[0038] Embodiments of the present disclosure relate to compositions and methods for the treatment and/or prevention of pathogenic infections (e.g., coronavirus infections). In particular, the present disclosure provides human plasma immunoglobulin compositions, methods of identifying human donors and donor samples for use in the compositions, and methods of utilizing the compositions for prophylactic administration and/or therapeutic treatment (e.g., passive immunization or immune-prophylaxis).

[0039] Hyperimmune serum globulins (immune serum globulin having high titers of a particular antibody), in distinction to normal immunoglobulin, have been therapeutically useful in treating patients who require immediate infusion of high titer antibodies. For example, tetanus hyperimmune globulin is useful in treating patients who may have suspected tetanus and rabies hyperimmune globulin for treating patients with suspected rabies. Hyperimmune serum globulins can be produced from plasma or serum obtained from a selected donor(s) who have elevated titers for a specific antibody than is normally found in the average population (that is not found at a high titer in the average population). These donors have either been recently immunized with a particular vaccine (See, e.g., U.S. Pat. No. 4,174,388) or else they have recently recovered from an infection or disease (See, e.g., Stiehm, Pediatrics, Vol. 63, No. 1, 301-319 (1979); herein incorporated by reference in its entirety). These high titer sera or plasmas are pooled and subjected to fractionation procedures (Cohn et al, J. Am. Chem. Soc., 68, 459 (1946); Oncley, et al, J. Am. Chem. Soc., 71, 541 (1949); herein incorporated by reference in their entireties). Such procedures have required specific selection of a donor or limited numbers of donors in order to produce hyperimmune globulin with elevated concentrations of the desired antibodies.

[0040] Coronaviruses are named for the crown-like spikes on their surface. There are four main sub-groupings of coronaviruses, known as alpha, beta, gamma, and delta. Human coronaviruses were first identified in the mid-1960s. The seven coronaviruses that can infect people are: 229E (alpha coronavirus;) NL63 (alpha coronavirus); OC43 (beta coronavirus); HKU1 (beta coronavirus); MERS-CoV (the beta coronavirus that causes Middle East Respiratory Syndrome, or MERS); SARS-CoV (the beta coronavirus that causes severe acute respiratory syndrome, or SARS); and SARS-CoV-2 (the novel coronavirus that causes coronavirus disease 2019, or COVID-19). Coronaviruses are a large family of viruses that are common in people and many different species of animals, including camels, cattle, cats, and bats. Rarely, animal coronaviruses can infect people and then spread between people such as with MERS-CoV, SARS-CoV, and SARS-CoV-2 (COVID-19). The SARS-CoV-2 virus is a betacoronavirus, like MERS-CoV and SARS-CoV. All three of these viruses have their origins in bats. MERS-CoV and SARS-CoV have been known to cause severe illness in people. The complete clinical picture with regard to COVID-19 is not fully understood. Reported illnesses have ranged from mild to severe, including illness resulting in death. While information so far suggests that most COVID-19 illness is mild, a report out of China suggests serious illness occurs in 16% of cases. Older people and people with certain underlying health conditions like heart disease, lung disease and diabetes, for example, seem to be at greater risk of serious illness.

[0041] Respiratory syncytial virus (RSV) is considered the most important cause of severe respiratory disease in infants and young children. It can also be an important cause of lower respiratory tract disease in the elderly, hematopoietic stem cell transplant patients and organ transplant patients. In the United States alone it has been reported that this virus causes pneumonia, bronchitis and croup in approximately 4 million children each year, resulting in about 4500 deaths. In the western world it is the major cause for hospitalization of children (National Research Council News Report, 35, 9 (1985); Stott, E. J. et al, Archives of Virology, 84:1-52 (1985); and W. H. O. Scientific Group, World Health Organization Technical Report Series 642 (1980); herein incorporated by reference in their entireties).

[0042] In accordance with the embodiments provided herein, the present disclosure provides hyperimmune globulin compositions comprising pooled plasma samples and/or immunoglobulin prepared therefrom having increased neutralizing antibody titers against specific viral pathogens, such as for example, coronavirus (coronavirus OC43, coronavirus 229E, coronavirus NL63, coronavirus HKU1, MERS-CoV, SARS-CoV, SARS-CoV-2 (COVID-19)). As described further herein, the compositions include pooled plasma samples and/or immunoglobulin prepared therefrom, which are obtained from a plurality of donor human subjects (e.g., 100, 200, 300, 400, 500 or more subjects). In some embodiments, a pooled sample comprising higher neutralizing antibody titers against one virus also has proportionally higher neutralizing antibody titers against other viruses. For example, pooled plasma samples can be obtained from a plurality of donor human subjects having increased antibody titers against a coronavirus (e.g., at least 1.2 fold greater than antibody titers from a corresponding control sample or an antibody neutralization titer of at least 40 to about 30,000), and these pooled plasma samples can also have proportionally increased antibody titers against at least a second virus (e.g., at least 1.2 fold greater than antibody titers from a corresponding control sample), including, but not limited to, respiratory syncytial virus (RSV), influenza A virus, influenza B virus, parainfluenza virus type 1, parainfluenza virus type 2, metapneumovirus, coronavirus OC43, coronavirus 229E, coronavirus NL63, coronavirus HKU1, MERS-CoV, SARS-CoV, and SARS-CoV-2 (COVID-19). Additionally, in some embodiments, pooled plasma samples can be obtained from a plurality of donor human subjects having increased antibody titers against RSV (e.g., at least 1.2 fold greater than antibody titers from a corresponding control sample or an antibody neutralization titer from at least 1000 to 8000), and these pooled plasma samples can also have proportionally increased antibody titers against a coronavirus (e.g., at least 1.2 fold greater than antibody titers from a corresponding control sample or an antibody neutralization titer from at least 40 to about 30,000).

[0043] In one embodiment, the pooled plasma composition comprises a coronavirus-specific antibody titer that is at

least 1.2 fold greater (e.g., 1.2, 1.5, 2, 2.5, 3, 3.5, 4.5, 5, 6, 7, 8, 9, 10 fold or more) than the coronavirus-specific antibody titer found in a mixture of plasma samples obtained from a plurality of random human subjects.

[0044] The present disclosure provides novel hyperimmune globulin compositions (and methods of generating these compositions) containing high titers of coronavirus neutralizing antibodies, which are surprisingly and significantly different than conventional immune globulin preparations as well as other IVIG preparations (e.g., other hyperimmune IVIG preparations prepared from non-selected convalescent plasma from any recovered patient). In one embodiment, it was surprisingly discovered that hyperimmune globulin prepared according to methods of the present disclosure have an elevated titer of coronavirus neutralizing antibodies that are functionally reactive and independent of the total amount of binding antibodies (e.g., as measured by ELISA) that are present in the composition. In one preferred embodiment, the disclosure provides that total coronavirus IgG binding antibodies do not correlate with and are not predictive of the amount of functional, neutralizing antibodies present in immune globulin prepared from the sera/plasma of a convalescent patient and/o a vaccinated donor. For example, in some cases, low levels of binding antibody were associated with high levels of neutralizing antibodies, and vice versa. Thus, measurement of total antibody levels only in plasma and/or immunoglobulin preparations does not predict or correlate with protective efficacy of that preparation. Thus, in one embodiment, the present disclosure provides means for the identification and characterization of plasma and/or immune globulin compositions containing a desired functional, neutralizing coronavirus antibody titer rather than one in which only the total amount of IgG is known.

[0045] In accordance with these embodiments, anti-SARS CoV-2 antibody titer present in a donor plasma sample can be identified by total antibody binding (e.g., using an ELISA). For example, in some embodiments, the present disclosure provides a pooled plasma composition comprising plasma from a plurality of plasma donors wherein each donor's plasma exhibits an SARS CoV-2 antibody titer that is at least 1.2 fold greater (e.g., 1.2, 1.5, 2, 2.5, 3, 3.5, 4.5, 5, 6, 7, 8, 9, 10 fold or greater, or any value therebetween) than the SARS CoV-2-specific antibody titer found in a negative control (e.g., plasma devoid of coronavirus antibodies, or a mixture of plasma samples obtained from a plurality of random, non-convalescent human subjects). In some embodiments, plasma samples are selected based upon the total amount of SARS CoV-2-specific antibody titer (e.g., only those plasma samples that display a threshold (e.g., 2 fold or higher) SARS CoV-2-specific antibody titer are selected). In some embodiments, the selected plasma samples are assayed to characterize SARS CoV-2 neutralizing antibody titer in the samples. In further embodiments, plasma samples are selected based upon the SARS CoV-2 neutralizing antibody titer (e.g., only those plasma samples that display a SARS CoV-2 neutralizing antibody titer in the top 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90% or higher of all plasma samples tested are selected). In some embodiments, plasma samples are selected based upon both the SARS CoV-2-specific antibody titer and the SARS CoV-2-specific neutralizing titer. For example, as disclosed herein, it was determined that of all convalescent, COVID-19 convalescent plasma analyzed, there exist plasma samples that display a high level of a SARS CoV-2-antibody binding, but lack a corresponding high SARS CoV-2-neutrlizing titer. Compositions and methods disclosed herein are useful at identifying these plasma samples in order to specifically exclude these plasma samples from use in a pooled plasma composition or immune globulin prepared therefrom disclosed herein. The disclosure is not limited to any particular assay for determining neutralizing antibody titer. Indeed, any assay available in the art may be utilized. In some embodiments, a plaque/focus reduction neutralization test (P/FRNT) is performed. In further embodiments, an automated high-throughput antibody neutralization assay based on foci and plaque reduction is used. In other embodiments, a virus reduction neutralization test (VRNT) is utilized (see, e.g., Whiteman et al., Am J Trop Med Hyg. 2018 December; 99(6):1430-1439). In still other embodiments, a pseudovirus neutralization assay is utilized (Creative Diagnostics, Shirley, N.Y.). In some embodiments, a multiplexed bead-based SARS-CoV-2 serological assay is used (Gaithersburg, Md.).

[0046] For example, in some embodiments, the disclosure provides a method of producing an immune globulin comprising obtaining a plurality of plasma samples from a plurality of plasma donors (e.g., COVID-19 convalescent plasma donors or COVID-19 vaccinated donors), conducting a first assay on each plasma sample to measure total anti-SARS CoV-2 antibody titer, selecting, based upon the first assay, plasma samples having a total anti-SARS CoV-2 antibody binding titer that is about two-fold or higher (e.g., 3-, 4-, 5-, 6-, 7-, 8-, 9-, 10-fold or higher) than the amount of total anti-SARS CoV-2 antibody binding titer in a control sample, conducting a second assay on each selected plasma sample from step (3) to measure SARS CoV-2 neutralizing antibody titer, identifying, based upon the second assay, plasma samples having a neutralizing antibody titer in the lower 65% of all plasma samples assayed and excluding the identified plasma samples from further processing, pooling the non-excluded plasma samples, and preparing immune globulin from the pooled plasma samples. In some embodiments, each of the plurality of plasma donors is a COVID-19 convalescent plasma donor. In other embodiments, each of the plurality of plasma donors is a COVID-19 vaccinated plasma donor. In some embodiments, the control sample is a mixture of plasma samples obtained from random human plasma donors (e.g., 50, 100, 150, 200, 250, 500, 1000 or more plasma donors or number therebetween). In other embodiments, the control sample is a commercially available immune globulin. In some embodiments, plasma samples having a neutralizing antibody titer in the lower 70% of all plasma samples assayed are identified and excluded from further processing. In still other embodiments, plasma samples having a neutralizing antibody titer in the lower 75% of all plasma samples assayed are identified and excluded from further processing. In other embodiments, plasma samples having a neutralizing antibody titer in the lower 80% of all plasma samples assayed are identified and excluded from further processing. The disclosure is not limited by the number of non-excluded, pooled plasma samples. In some embodiments, the number of non-excluded, pooled plasma samples is 250-500 or more. In some embodiments, the number of non-excluded, pooled plasma samples is 500-1000 or more. In some embodiments, the immune globulin is prepared using a cold alcohol fractionation process that isolates the immune globulin fraction from

the pooled plasma as a solution. In further embodiments, the immune globulin is combined with a pharmaceutically acceptable carrier.

[0047] The disclosure further provides a method of providing immunotherapy to a subject in need thereof, comprising administering to the subject an immunotherapeutic composition comprising an immune globulin disclosed herein and a pharmaceutically acceptable carrier. In some embodiments, the immunotherapeutic composition is administered to the subject so as to provide from about 1.0-3.0 or more grams of immune globulin per kilogram of the subject. In some embodiments, each of the plurality of plasma donors is a COVID-19 convalescent plasma donor. In some embodiments, each of the plurality of plasma donors is a COVID-19 vaccinated plasma donor. In some embodiments, the immunotherapeutic composition further comprises a biologically active agent selected from the group consisting of an anti-inflammatory agent, an anti-cancer agent, an anti-microbial agent, an antihistamine, a cytokine, and a chemokine. In some embodiments, the immunotherapeutic composition further comprises an immunotherapeutic agent selected from the group consisting of a recombinant antibody, an antibody fragment, an antibody-like molecule, a monoclonal antibody, an antiviral, an immunotherapeutic protein and an immunotherapeutic small molecule. In some embodiments, the immunotherapeutic composition further comprises an anti-inflammatory agent selected from the group consisting of a recombinant antibody, an antibody fragment, a monoclonal antibody, an anti-inflammatory protein and an anti-inflammatory small molecule. In some embodiments, the subject treated is diagnosed with an infection or condition (e.g., a viral infection (e.g., SARS CoV-2 infection). In some embodiments, the subject is not diagnosed with an infection or condition. In some embodiments, the subject is age 65 or older.

[0048] The disclosure provides a pharmaceutical composition comprising an immune globulin disclosed herein. The disclosure provides a method of providing immunotherapy to a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a pharmaceutical composition comprising an immune globulin disclosed herein. In some embodiments, the immunotherapy is used to treat and/or prevent infection in the subject. In some embodiments, the immunotherapy is used to treat and/or prevent inflammation in the subject. In some embodiments, the pharmaceutical composition further comprises an anti-toxin agent. In some embodiments, the anti-toxin agent is a mono-specific, bi-specific or multi-specific antibody with specificity toward a bacterial or fungal toxin. In some embodiments, the bacterial or fungal toxin is selected from the group consisting of Botulinum neurotoxin, Tetanus toxin, *E. coli* toxin, *Clostridium difficile* toxin, *Vibrio* RTX toxin, Staphylococcal toxins, Cyanobacteria toxin, and mycotoxins. In some embodiments, the pharmaceutical composition further comprises a biologically active agent selected from the group consisting of an anti-inflammatory agent, an anti-cancer agent, an anti-microbial agent, an antihistamine, a cytokine, and a chemokine. In some embodiments, the pharmaceutical composition further comprises an immunotherapeutic agent selected from the group consisting of a recombinant antibody, an antibody fragment, an antibody-like molecule, a monoclonal antibody, an antiviral, an immunotherapeutic protein and an immunotherapeutic small molecule. In some embodiments, the pharmaceutical composition further comprises an anti-inflammatory agent selected from the group consisting of a recombinant antibody, an antibody fragment, a monoclonal antibody, an anti-inflammatory protein and an anti-inflammatory small molecule. In some embodiments, the immunotherapy is used to treat coronavirus infection in the subject.

[0049] In further embodiments, the disclosure provides a method of treating a human patient comprising administering an immune globulin obtained by the disclosed methods to a subject/patient. In some embodiments, the immune globulin reduces viral load in the lung and/or nose of a subject administered the composition compared to a control subject not receiving the composition. In some embodiments, the immune globulin reduces lung histopathology of a subject administered the composition compared to a control subject not receiving the composition. In one embodiment, the pooled plasma composition provides a therapeutic benefit to a subject administered the composition that is not achievable via administration of a mixture of plasma samples obtained from a plurality of random human subjects. Embodiments of the present disclosure are not limited by the type of therapeutic benefit provided. Indeed, a variety of therapeutic benefits may be attained including those described herein. In one embodiment, the pooled plasma composition possesses enhanced viral neutralization properties compared to a mixture of plasma samples obtained from a plurality of random human subjects. In a further embodiment, the enhanced viral neutralization properties reduce and/or prevent infection in a subject administered the composition for a duration of time that is longer than, and not achievable in, a subject administered a mixture of plasma samples obtained from a plurality of random human subjects.

[0050] The methods and compositions of the present disclosure overcome hurdles of antibody-based therapeutics (e.g., immune globulin treatments). For example, compositions and methods of the disclosure overcome the risk of exacerbating COVID-19 severity via antibody-dependent enhancement (ADE). Although an understanding of a mechanism is not needed to practice the present disclosure, and while the disclosure is not limited to any particular mechanism, in one embodiment, the methods of compositions of the disclosure specifically identify and exclude plasma samples (e.g., prior to pooling plasma samples and immune globulin isolation) containing high levels of SARS CoV-2 specific antibodies that lack neutralizing antibodies or that contain antibodies at sub-neutralizing levels that bind to viral antigens without blocking or clearing infection.

[0051] ADE has been documented to increase the severity of multiple viral infections, including other respiratory viruses such as respiratory syncytial virus (RSV) (See, e.g., Kim et al., Am. J. Epidemiol. 89, 422-434 (1969); and Graham, Vaccine 34, 3535-3541 (2016)) and measles (See, e.g., Nader et al., J. Pediatr. 72, 22-28 (1968); and Polack, Pediatr. Res. 62, 111-115 (2007)). ADE in respiratory infections is included in a broader category named enhanced respiratory disease (ERD), which also includes non-antibody-based mechanisms such as cytokine cascades and cell-mediated immunopathology. ADE caused by enhanced viral replication has been observed for other viruses that infect macrophages, including dengue virus and feline infectious peritonitis virus (FIPV).

[0052] ADE has been documented to occur through two distinct mechanisms in viral infections: by enhanced antibody-mediated virus uptake into Fc gamma receptor IIa (FcγRIIa)-expressing phagocytic cells leading to increased viral infection and replication, or by excessive antibody Fc-mediated effector functions or immune complex formation causing enhanced inflammation and immunopathology. Both ADE pathways can occur when non-neutralizing antibodies or antibodies at sub-neutralizing levels bind to viral antigens without blocking or clearing infection.

[0053] ADE can be measured in several ways, including in vitro assays (which are most common for the first mechanism involving FcγRIIa-mediated enhancement of infection in phagocytes), immunopathology or lung pathology. ADE via FcγRIIa-mediated endocytosis into phagocytic cells can be observed in vitro and has been extensively studied for macrophage-tropic viruses, including dengue virus in humans. In this mechanism, non-neutralizing antibodies bind to the viral surface and traffic virions directly to macrophages, which then internalize the virions and become productively infected. Since many antibodies against different dengue serotypes are cross-reactive but non-neutralizing, secondary infections with heterologous strains can result in increased viral replication and more severe disease, leading to major safety risks. Non-neutralizing antibodies, or antibodies at sub-neutralizing levels, enhanced entry into alveolar and peritoneal macrophages, which are thought to disseminate infection and worsen disease outcome.

[0054] Accordingly, while an understanding of a mechanism is not needed to practice the present disclosure, and while the disclosure is not limited to any particular mechanism, in one embodiment, the methods of compositions of the disclosure provide pooled plasma compositions and immune globulin prepared therefrom that contain high titers of SARS CoV-2 neutralizing antibodies that prevent trafficking of virions to macrophages and infection of the macrophages, and/or that prevent secondary infections and/or that prevent viral entry into alveolar or peritoneal macrophages (e.g., thereby eliminating the risk of ADE or ERD).

[0055] Another described ADE mechanism is best exemplified by respiratory pathogens, Fc-mediated antibody effector functions can enhance respiratory disease by initiating a powerful immune cascade that results in observable lung pathology (See, e.g., Ye et al., Front. Immunol. 8, 317 (2017); and Winarski, et al., Proc. Natl Acad. Sci. USA 116, 15194-15199 (2019)). Fc-mediated activation of local and circulating innate immune cells such as monocytes, macrophages, neutrophils, dendritic cells and natural killer cells can lead to dysregulated immune activation despite their potential effectiveness at clearing virus-infected cells and debris. For non-macrophage tropic respiratory viruses such as RSV and measles, non-neutralizing antibodies have been shown to induce ADE and ERD by forming immune complexes that deposit into airway tissues and activate cytokine and complement pathways, resulting in inflammation, airway obstruction and, in severe cases, leading to acute respiratory distress syndrome.

[0056] Accordingly, while an understanding of a mechanism is not needed to practice the present disclosure, and while the disclosure is not limited to any particular mechanism, in one embodiment, the methods of compositions of the disclosure provide pooled plasma compositions and immune globulin prepared therefrom that contain high titers of SARS CoV-2 neutralizing antibodies that prevent activation of local and circulating innate immune cells (e.g., monocytes, macrophages, neutrophils, dendritic cells and natural killer cells) and prevent dysregulated immune activation, prevent immune cascades that results in observable lung pathology, prevent and/or reduce ADE and ERD by blocking deposit of immune complexes in airway tissue, and/or prevent inflammation, airway obstruction and, acute respiratory distress syndrome. Moreover, in some embodiments, the present disclosure provides methods of providing immunotherapy to a subject comprising administering to the subject an immunotherapeutic composition comprising an immune globulin of the disclosure such that the subject receives a high dose (e.g., from about 1.0-3 grams per kilogram, or any value therebetween) of the immune globulin (e.g., that acts as anti-inflammatory).

[0057] In one embodiment, identifying antibody titer comprises a plasma screening assay assessing neutralizing activity/titer (e.g., SARS CoV-2 neutralizing activity or other coronavirus neutralizing activity) in a plasma sample, and a screening assay assessing antibody titer (e.g., SARS CoV2-specific antibody titer and/or other coronavirus antibody titer). In one embodiment, neutralizing activity in plasma is measured via the absence of infection.

[0058] In another embodiment, the pooled plasma comprises elevated levels, compared to the pathogen-specific antibody titers found in a mixture of plasma samples obtained from 100 or more random human subjects, of pathogen-specific antibody titers to two, three, four or more respiratory pathogens described herein. In one embodiment, the pooled plasma comprises a coronavirus-specific antibody titer that is at least 1.2 fold greater (e.g. 1.2 fold, 1.4 fold, 1.6 fold, 1.8 fold, 2 fold, 3 fold, 4 fold, 5 fold 6 fold, 7 fold, 8 fold, 9 fold, 10 fold, 12 fold, 15 fold or more) than the coronavirus-specific antibody titer found in a mixture of plasma samples obtained from 100 or more random human subjects. In another embodiment, the pooled plasma comprises pathogen-specific antibody titers to at least two or more respiratory pathogens selected from respiratory syncytial virus, influenza A virus, influenza B virus, parainfluenza virus type 1, parainfluenza virus type 2, metapneumovirus, and coronavirus that are each elevated at least 1.2 fold compared to the pathogen-specific antibody titers found in a mixture of plasma samples obtained from 100 or more random human subjects. In another embodiment, the pooled plasma comprises pathogen-specific antibody titers to at least three or more respiratory pathogens selected from respiratory syncytial virus, influenza A virus, influenza B virus, parainfluenza virus type 1, parainfluenza virus type 2, metapneumovirus, and coronavirus that are each elevated at least 1.5 fold compared to the pathogen-specific antibody titers found in a mixture of plasma samples obtained from 100 or more random human subjects. In still another embodiment, the pooled plasma comprises pathogen-specific antibody titers to at least four or more respiratory pathogens selected from respiratory syncytial virus, influenza A virus, influenza B virus, parainfluenza virus type 1, parainfluenza virus type 2, metapneumovirus, and coronavirus that are each elevated at least 1.5 fold compared to the pathogen-specific antibody titers found in a mixture of plasma samples obtained from 100 or more random human subjects. In one embodiment, the pooled plasma comprises plasma samples obtained from 500-3000 or more (e.g., more than 100, 250, 500, 750, 1000, 1250, 1500, 1750, 2000, 2500, 3000, 3500, 4000 or more human subjects). In one

embodiment, the pooled plasma is utilized to prepare immunoglobulin (e.g., for intravenous administration to a subject). In one embodiment, the pooled plasma and/or immunoglobulin provides a therapeutic benefit to a subject administered the pooled plasma and/or immunoglobulin that is not achievable via administration of a mixture of plasma samples (or immunoglobulin prepared from same) obtained from 100 or more random human subjects. Embodiments of the present disclosure are not limited by the type of therapeutic benefit provided. Indeed, a variety of therapeutic benefits may be attained including those described herein. In one embodiment, the pooled plasma and/or immunoglobulin possesses enhanced viral neutralization properties compared to a mixture of plasma samples obtained from 100 or more random human subjects or immunoglobulin prepared from same. For example, in one embodiment, the pooled plasma possesses enhanced viral neutralization properties against one or more (e.g., two, three, four, five or more) respiratory pathogens (e.g., described herein). In a further embodiment, the enhanced viral neutralization properties reduce and/or prevent infection in a subject administered the composition for a duration of time that is longer than, and not achievable in, a subject administered a mixture of plasma samples obtained from 100 or more random human subjects. In one embodiment, the pooled plasma and/or immunoglobulin prepared from same reduces the incidence of infection in a subject administered the composition. In another embodiment, a pooled plasma and/or immunoglobulin prepared from same reduces the number of days a subject administered the pooled plasma and/or immunoglobulin is required to be administered antibiotics (e.g., to treat infection). In yet another embodiment, a pooled plasma and/or immunoglobulin prepared from same increases the trough level of circulating anti-respiratory pathogen specific antibodies in a subject (e.g., increases the level of neutralizing titers specific for respiratory pathogens (e.g., thereby providing protective levels of anti-respiratory pathogen specific antibodies between scheduled dates of administration of the pooled plasma and/or immunoglobulin prepared from same that are not maintained in a subject administered a mixture of plasma samples obtained from 100 or more random human subjects or immunoglobulin prepared from same)). In one embodiment, the composition comprising pooled plasma samples further comprises a pharmaceutically acceptable carrier (e.g., any natural or non-naturally occurring carrier(s) known in the art). In one embodiment, a subject administered immunoglobulin prepared from pooled plasma according to the embodiments of the present disclosure displays a mean fold increase in anti-RSV neutralization titer that is at least 4 fold, at least 5 fold, at least 6 fold, at least 7 fold, at least 8 fold, at least 9 fold or more at a time point of at least 1 to 14 days post administration (e.g., 14 day, 15 days, 16 days, 17 days, 18 days, 19 days or more) of the immunoglobulin. Embodiments of the present disclosure are not limited by the amount of immunoglobulin administered to a subject. In one embodiment, a subject is administered between 100-5000 mg/kg of the immunoglobulin one time, or daily for two or more days (e.g., 2, 3, 4, or more consecutive days). In another embodiment, such doses are administered intermittently, e.g. every week, every two weeks, every three weeks, every four weeks, etc. In one embodiment, a subject is administered between 750-1500 mg/kg of immunoglobulin on day one and between 750-1500 mg/kg immunoglobulin on day 2. In one embodiment, a subject is administered 1500 mg/kg of immunoglobulin on day one and 750 mg/kg immunoglobulin on day 2. In another embodiment, a subject is administered 750 mg/kg of immunoglobulin on day one and 750 mg/kg immunoglobulin on day 2. In one embodiments, a subject is administered immunoglobulin on day one, optionally administered immunoglobulin on day 2, and then re-administered immunoglobulin every 21 days. In one embodiments, a subject is administered immunoglobulin on day one, optionally administered immunoglobulin on day 2, and then re-administered immunoglobulin every 28 days. In one embodiment, the pooled plasma and/or immunoglobulin prepared from same reduces the incidence of infection in a subject administered the composition. In another embodiment, a pooled plasma and/or immunoglobulin prepared from same reduces the number of days a subject administered the pooled plasma and/or immunoglobulin is required to be administered antibiotics (e.g., to treat infection).

[0059] In one embodiment, the composition comprising pooled plasma samples further comprises a pharmaceutically acceptable carrier (e.g., any natural or non-naturally occurring carrier(s) known in the art). In one embodiment, a subject administered immunoglobulin prepared from pooled plasma according to the embodiments of the present disclosure displays a mean fold increase in anti-coronavirus (e.g., coronavirus OC43, coronavirus 229E, coronavirus NL63, coronavirus HKU1, MERS-CoV, SARS-CoV, or SARS-CoV-2 (COVID-19)) neutralization titer that is at least 2 fold, at least 3 fold, at least 4 fold, at least 5 fold, at least 6 fold, at least 7 fold, at least 8 fold, at least 9 fold or more at a time point of at least 1 to 14 days post administration (e.g., 14 day, 15 days, 16 days, 17 days, 18 days, 19 days or more) of the immunoglobulin.

[0060] In certain embodiments, plasma and/or antibody samples comprise donated and/or purchased body fluid samples, for example individual blood or blood component samples (e.g., plasma). These samples may be purified and/or screened for the presence of pathogens or other impurities (e.g., before or after pooling). Multiple donor antibody samples (e.g., donor plasma samples or other antibody-containing samples) can pooled together to create a pooled plasma sample/primary antibody pool (e.g., after identifying or screening for desired antibody titer in the antibody samples). By combining individual antibody samples (e.g., blood or blood component (e.g., plasma) samples) which have higher than normal titers of antibodies to one or more selected antigens, epitopes, extracellular proteins, viral surface proteins, together with plasma taken from donors not selected for high titers, a pooled plasma sample/primary antibody pool is created that exhibits elevated titer for such antibodies. In some embodiments, selected antigens, epitopes, extracellular proteins, viral surface proteins, etc. are administered to subjects to induce the expression of desired antibodies (e.g., from which antibody samples can be harvested). The resulting enhanced high titer antibody sample (e.g., blood, serum, plasma, purified antibodies (e.g., containing higher antibody titer as compared to a control level (e.g., the antibody titer in pooled plasma samples from 100 or more random human subjects)) is recovered and pooled with antibody samples from other subjects exhibiting or anticipated to exhibit elevated titer for the same antibodies (or antibodies directed to the same antigens, extracellular proteins, viral surface proteins, etc.), or with antibody samples from subject that have not been

screened for antibody titer or that possess a low or absent antibody titer to a specific pathogen. In some embodiments, the pooled antibody samples are purified, screened, and/or concentrated. In one embodiment, pooling of samples (e.g., 100 or more samples) occurs in a manner that uses the fewest possible number of samples from high titer donors (e.g., identified by the compositions and methods described herein) but that still maintains a desired, standardized and elevated antibody titer to one or more (e.g., two, three, four or more) respiratory pathogens described herein.

[0061] Certain embodiments of the present disclosure utilize plasma from subjects that have been administered immunogenic substances (e.g., vaccines, antigens, epitopes, extracellular proteins, viral surface proteins, etc.) in order to generate elevated levels of specific neutralizing antibodies within the subject. Embodiments of the present disclosure are not limited by the type of antigen used for administration to a subject (e.g., donor) to induce the expression of specific antibodies. In some embodiments, the antigen is a polysaccharide (e.g., unconjugated or conjugated to a carrier or protein) or a plurality of the same. In some embodiments, a vaccine is a commercially available vaccine. Embodiments of the present disclosure are not limited by the vaccine. Similarly, embodiments of the present disclosure are not limited by the type or route of administration/immunization. Indeed, any route/type of immunization may be utilized including, but not limited to, the methods described in U.S. Patent Publication Nos. US2008026002, US2007009542; US2002094338; US2005070876; US2002010428; US2009047353; US2008066739; and US2002038111), each of which is hereby incorporated by reference in its entirety. In some embodiments, the vaccine is a coronavirus vaccine (e.g., coronavirus mRNA vaccine (e.g., Moderna's mRNA-1273 vaccine (Moderna, Cambridge, Mass.) or adenovirus based vaccine (e.g., Astra Zeneca's AZD1222 (AstraZeneca, Gaithersburg, Mass.).

[0062] Thus, in some embodiments, the present disclosure provides methods of stimulating high antibody levels in a donor, which includes administering to an animal, for example a human, a pharmaceutically-acceptable composition comprising an immunologically effective amount of an antigen composition (e.g., a coronavirus antigen composition). The composition can include partially or significantly purified antigens (e.g., coronavirus antigens (e.g., polysaccharide, protein and/or peptide epitopes, obtained from natural or recombinant sources, which may be obtained naturally or either chemically synthesized, or alternatively produced in vitro from recombinant host cells expressing DNA segments encoding such epitopes)). Methods to determine the efficacy of immunization (e.g., determining the levels of coronavirus-specific antibody titers) are known in the art, and any known method may be utilized to assess the efficacy of immunization. In some embodiments, detection methods for the evaluation of the efficacy of a vaccine (e.g., a coronavirus conjugate vaccine) is used.

[0063] In some embodiments, kits and methods are provided that identify samples and/or pools with specific antibody titers (e.g., antibody titers that are elevated). In one embodiment, a suitable amount of a detection reagent (e.g., antibody specific for antibodies, an antigen, or other reagent known in the art) is immobilized on a solid support and labeled with a detectable agent. Antibodies can be immobilized to a variety of solid substrates by known methods. Suitable solid support substrates include materials having a membrane or coating supported by or attached to sticks, beads, cups, flat packs, or other solid support. Other solid substrates include cell culture plates, ELISA plates, tubes, and polymeric membranes. The antibodies can be labeled with a detectable agent such as a fluorochrome, a radioactive label, biotin, or another enzyme, such as horseradish peroxidase, alkaline phosphatase and 2-galactosidase. If the detection reagent is an enzyme, a means for detecting the detection reagent can be supplied with the kit. A suitable means for detecting a detectable agent employs an enzyme as a detectable agent and an enzyme substrate that changes color upon contact with the enzyme. The kit can also contain a means to evaluate the product of the assay, for example, a color chart, or numerical reference chart. Some suitable methods for characterizing samples and pools are provided in the references incorporated by reference herein. Embodiments of the present disclosure are not limited by the method used to characterize samples and pools as having elevated titer.

[0064] In certain embodiments, compositions are provided (e.g., antibody samples, pooled plasma samples, immunoglobulins, etc.) in which antibodies have been purified and/or isolated from one or more contaminants. Human immunoglobulins were first isolated on a large scale during the 1940's by F. J. Cohn. In some embodiments, the techniques provided by Cohn (Cohn et al., J. Am. Chem. Soc. 1946; 68:459-475; herein incorporated by reference in its entirety) or modified Cohn-techniques are utilized in preparation of immunoglobulins herein. In some embodiments, various purification and isolation methods are utilized to produce substantially unmodified, unaltered, non-denatured and/or native immunoglobulin molecules of high purity. Exemplary techniques are provided, for example, in U.S. Pat. No. 4,482,483, herein incorporated by reference in its entirety. In some embodiments, compositions (e.g., antibody pools) comprise >50% immunoglobulin (e.g., >60%, >70%, >80%, >90%, >95%, >99%). Various methods may be utilized for producing such compositions, including, for example, standard protein purification and isolation techniques as well as fractionation of biological fluids (e.g., plasma). Descriptions of fractionation of antibodies for use in immunotherapeutics are found, for example in U.S. Pat. No. 4,346,073 and other references provided herein, each of which is incorporated by reference in their entireties. In certain embodiments, immunoglobulins are purified by a fractional precipitation method, ion-exchange chromatography, size exclusion chromatography, ultrafiltration, affinity chromatography, or any suitable combinations thereof (See, e.g., U.S. Pat. Nos. 7,597,891; 4,256,631; 4,305,870; Lullau et al., J. Biol. Chem. 1996; 271:16300-16309; Corthesy, Biochem. Soc. Trans. 1997; 25:471-475; and Crottet et al., Biochem. J. 1999; 341:299-306; herein incorporated by reference in their entireties).

[0065] In some embodiments, plasma samples are pooled to produce a large volume of antibodies/immunoglobulins (e.g., for commercial, clinical, therapeutic, and/or research use). In particular embodiments, antibody samples (e.g., plasma samples) exhibiting a certain desired characteristic or characteristics are pooled to result in a primary antibody pool (e.g., pooled plasma samples) enhanced for, exhibiting, and/or enriched in that desired characteristic. In certain embodiments, antibody samples (e.g., plasma) obtained from a plurality of subjects (e.g., >2 subjects, >5 subjects, >10 subjects, >20 subjects, >100 subjects, >200 subjects,

>500 subjects, >1,000 subjects, >2,000 subjects, >5,000 subjects, >10,000 subjects, or more) are pooled. The subjects from which the antibody samples (e.g., blood, plasma, etc.) may be obtained may have had recent exposure to a pathogen, antigen, or epitope, been recently vaccinated with a pathogen, antigen, or epitope, or have been specifically exposed to a pathogen, antigen, or epitope for the purpose of producing specific antibodies.

[0066] In some embodiments, methods are provided for pooling/combining primary antibody pools (e.g., pooled plasma samples) to produce secondary antibody pools or tailored antibody pools. Two or more primary antibody pools, each exhibiting a desired characteristic (e.g., antibodies against RSV, antibodies against coronavirus, etc.), are combined at a desired ratio to produce a tailored antibody pool. In some embodiments, a tailored antibody pool exhibits the relative sum of the characteristics of the primary antibody pools from which it is derived (e.g., tailored pool confers immunity to specific pathogens to an extent that is consistent with the relative amount of the primary pools from which it is derived). In other embodiments, a tailored antibody pool exhibits distinct characteristics from the primary antibody pools from which it is derived (e.g., tailored pool confers immunity to a specific pathogen to a greater extent than the primary pools from which it is derived used individually, provides enhanced general immunity compared to use of individual primary pools, provides enhanced anti-inflammatory benefit compared to use of individual primary pools).

[0067] A composition of the present disclosure (e.g., pooled plasma and/or immunoglobulin prepared from same) can be administered by any suitable means, including parenteral, subcutaneous, intraperitoneal, intrapulmonary, and, if desired for local treatment, intralesional administration. Parenteral infusions include intramuscular, intravenous, intraarterial, intraperitoneal, or subcutaneous administration. In addition, compositions of the present disclosure may be administered by pulse infusion, particularly with declining doses. Dosing can be by any suitable route, e.g. by injections, such as intravenous or subcutaneous injections, depending in part on whether the administration is acute or chronic.

[0068] A composition of the present disclosure may be formulated, dosed, and/or administered in a fashion consistent with good medical practice. Factors for consideration in this context include the particular disorder being treated, the clinical condition of the individual patient, the cause of the disorder, the site of delivery of the agent, the method of administration, the scheduling of administration, and other factors known to medical practitioners. Compositions of the present disclosure need not be, but optionally are formulated with one or more agents currently used to prevent or treat the disorder in question. The effective amount of such other agents depends on the amount of antibody present in the formulation, the type of disorder or treatment, and other factors discussed above. These are generally used in the same dosages and with administration routes as described herein, or about from 1 to 99% of the dosages described herein, or in any dosage and by any route that is empirically/clinically determined to be appropriate.

[0069] For the prevention or treatment of disease, the appropriate dosage of a composition of the present disclosure (when used alone or in combination with one or more other additional therapeutic agents) may depend upon a number of factors including the type of disease to be treated, the type of antibody, the patient's size, body surface area, age, the particular compound to be administered, sex, time and route of administration, general health, interaction with other drugs being concurrently administered, the severity and course of the disease, whether the antibody is administered for preventive or therapeutic purposes, previous therapy, and the patient's clinical history.

[0070] An exact dosage may be determined by the individual physician in view of the patient to be treated. Dosage and administration are adjusted to provide sufficient levels of the active moiety (e.g., plasma pool) or to maintain the desired effect. Additional factors which may be taken into account include the severity of the disease state; age, weight, and gender of the patient; diet, time and frequency of administration, drug combination(s), reaction sensitivities, and tolerance/response to therapy. Long acting pharmaceutical compositions might be administered every 3 to 4 days, every week, or once every two weeks, four weeks, six weeks, eight weeks or more, depending on half-life and clearance rate of the particular formulation.

[0071] A composition of the present disclosure may be administered to the patient at one time or over a series of treatments. Depending on the type and severity of the disease, about 1 μg/kg to 5000 mg/kg (e.g. 0.5 mg/kg-1500 mg/kg) of a composition of the present disclosure can be an initial candidate dosage for administration to the patient, whether, for example, by one or more separate administrations, or by continuous infusion. As described herein, additional drugs or agents (e.g., antibiotics, antivirals, anti-inflammatory and/or healing compounds) may be administered concurrently with a pooled plasma composition of the present disclosure. An exemplary daily dosage of such agent may range from about 1 μg/kg to 100 mg/kg or more. For repeated administrations over several days or longer, depending on the condition, the treatment can generally be sustained until a desired suppression of disease symptoms occurs. One exemplary dosage of a composition of the present disclosure would be in the range from about 0.05 mg/kg to about 10 mg/kg. Thus, one or more doses of about 0.5 mg/kg, 2.0 mg/kg, 4.0 mg/kg or 10 mg/kg (or any combination thereof) may be administered to a patient. Such doses may be administered intermittently, e.g. every week or every two or three weeks. A medical practitioner is readily able to monitor the therapeutic administration of a composition of the present disclosure and can in turn determine if higher or lower doses of the composition is to be administered.

[0072] Compositions of the present disclosure may be administered (e.g., intravenously, orally, intramuscularly, subcutaneously, etc.) to a patient in a pharmaceutically acceptable carrier such as physiological saline. Such methods are well known to those of ordinary skill in the art.

[0073] Accordingly, in some embodiments of the present disclosure, a composition can be administered to a patient alone, or in combination with other drugs or in pharmaceutical compositions where it is mixed with excipient(s) or other pharmaceutically acceptable carriers. In one embodiment of the present disclosure, the pharmaceutically acceptable carrier is pharmaceutically inert. Depending on the condition being treated, pharmaceutical compositions may be formulated and administered systemically or locally. Techniques for formulation and administration may be found in the latest edition of "Remington's Pharmaceutical

Sciences" (Mack Publishing Co, Easton Pa.). Suitable routes may, for example, include oral or transmucosal administration; as well as parenteral delivery, including intramuscular, subcutaneous, intramedullary, intrathecal, intraventricular, intravenous, intraperitoneal, or intranasal administration.

[0074] For injection, a composition of the present disclosure may be formulated in aqueous solutions, preferably in physiologically compatible buffers such as Hanks' solution, Ringer's solution, or physiologically buffered saline. For tissue or cellular administration, penetrants appropriate to the particular barrier to be permeated are used in the formulation. Such penetrants are generally known in the art.

[0075] In other embodiments, the compositions of the present disclosure (e.g., pharmaceutical compositions) can be formulated using pharmaceutically acceptable carriers well known in the art in dosages suitable for oral administration. Such carriers enable the pharmaceutical compositions to be formulated as tablets, pills, capsules, liquids, gels, syrups, slurries, suspensions and the like, for oral or nasal ingestion by a patient to be treated.

[0076] Pharmaceutical compositions suitable for use in embodiments of the present disclosure include compositions wherein the active ingredients are contained in an effective amount to achieve the intended purpose. For example, an effective amount of a composition of the present disclosure may be that amount that results in the inhibition of growth and/or killing of viruses (e.g., coronavirus) in a subject. Determination of effective amounts is well within the capability of those skilled in the art, especially in light of the disclosure provided herein.

[0077] In addition to the active ingredients pharmaceutical compositions may contain suitable pharmaceutically acceptable carriers comprising excipients and auxiliaries that facilitate processing of the compositions of the present disclosure into preparations which can be used pharmaceutically.

[0078] The pharmaceutical compositions of embodiments of the present disclosure may be manufactured in a manner that is itself known (e.g., by means of conventional mixing, dissolving, granulating, dragee-making, levigating, emulsifying, encapsulating, entrapping or lyophilizing processes).

[0079] Pharmaceutical formulations for parenteral administration include aqueous solutions of the compositions in water-soluble form. Additionally, suspensions of the compositions may be prepared as appropriate oily injection suspensions. Suitable lipophilic solvents or vehicles include fatty oils such as sesame oil, or synthetic fatty acid esters, such as ethyl oleate or triglycerides, or liposomes. Aqueous injection suspensions may contain substances that increase the viscosity of the suspension, such as sodium carboxymethyl cellulose, sorbitol, or dextran. Optionally, the suspension may also contain suitable stabilizers or agents that increase the solubility of the compositions to allow for the preparation of highly concentrated solutions.

[0080] Compositions of the present disclosure formulated in a pharmaceutical acceptable carrier may be prepared, placed in an appropriate container, and labeled for treatment of an indicated condition. Conditions indicated on the label may include treatment or prevention of a viral infection.

[0081] The pharmaceutical composition may be provided as a salt and can be formed with many acids, including but not limited to hydrochloric, sulfuric, acetic, lactic, tartaric, malic, succinic, and the like. Salts tend to be more soluble in aqueous or other protonic solvents that are the corresponding free base forms. In other cases, the preferred preparation may be a lyophilized powder in 1 mM-50 mM histidine, 0.1%-2% sucrose, 2%-% mannitol at a pH range of 4.5 to 5.5 that is combined with buffer prior to use.

[0082] Compositions may optionally contain carriers such as preserving, wetting, emulsifying, and dispensing agents. Prevention of the action of microorganisms can be ensured by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, sorbic acid, and the like. It may also be desirable to include isotonic agents, for example, sugars, sodium chloride, and the like. Prolonged absorption of the immunoglobulins can be brought about by the use of agents delaying absorption, for example, aluminum monostearate and gelatin.

[0083] In some embodiments, a composition of the present disclosure is administered to a subject to provide therapeutic, preventative, prophylactic, and/or other benefits.

[0084] In some embodiments, an immunotherapeutic composition of the present disclosure is effective in treating (e.g., therapeutically, preventatively, prophylactically, etc.) a subject and/or bind antigens from, and/or are directed to pathogenic viruses including, but not limited to: adenovirus, coxsackie virus, Epstein-barr virus, BK virus, hepatitis a virus, hepatitis b virus, hepatitis c virus, herpes simplex virus (type 1), herpes simplex virus (type 2), cytomegalovirus, human herpesvirus (type 8), human immunodeficiency virus (HIV), influenza virus, measles virus, mumps virus, human papillomavirus, parainfluenza virus, poliovirus, rabies virus, respiratory syncytial virus, rubella virus, and varicella-zoster virus.

[0085] The use of specific compositions and methods of the present disclosure to treat pathogens or treat/prevent infection may vary depending on the site of infection. For example, immunotherapeutic compositions used for treating and/or preventing respiratory infections (e.g., caused by or associated with coronavirus infection) might include immunoglobulins with antibodies and/or monoclonal antibodies specific for at least two of the following pathogens: respiratory syncytial virus, influenza A virus, influenza B virus, influenza C virus, parainfluenza virus type 1, parainfluenza virus type 2, rhinovirus, metapneumovirus, coronavirus, or any other respiratory or other type of pathogen known by those of ordinary skill in the art or described herein.

[0086] Various diseases (e.g., cancer, AIDS, etc.), infections, and treatments (e.g., antivirals, antirejections medications, chemotherapies, etc.) can result in localized or general inflammation in a subject, which can lead to discomfort, downstream health problems, morbidity, and/or death. In some embodiments, compositions and methods of the present disclosure provide anti-inflammatory benefits when administered to a subject. Pooled immunoglobulins have been shown to provide an anti-inflammatory action when passively administered (See, e.g., Nimmerjahn and Ravetch, Annu. Rev. Immunol. 2008. 26:513-33; Ramakrishna et al. Plos Pathogens. 2011. 7:6:e1002071; herein incorporated by reference in their entireties). In some embodiments, a composition of the present disclosure exerts enhanced anti-inflammatory effect (e.g., 10% enhancement, 20% enhancement, 50% enhancement, 2-fold enhancement 3-fold enhancement, 5-fold enhancement, 10-fold enhancement, or greater) compared to the anti-inflammatory effect of a mixture of plasma samples obtained from random human subjects (e.g., 1000 or more random human subjects). Although an understanding of a mechanism is not necessary to prac-

tice embodiments of the present disclosure and while these embodiments are not limited to any particular mechanism, in one embodiment, a pooled plasma composition of the present disclosure displays significantly enhanced anti-inflammatory effect compared to a conventional IVIG because the pooled plasma composition of the present disclosure comprises plasma from at least 100 donors (e.g., compared to a conventional hyperimmune globulin prepared from a limited number of donors (e.g., in one embodiment, the larger the number of different plasma samples pooled, the more beneficial the anti-inflammatory effect (e.g., the greater the histopathological benefit (e.g., reduction of epithelial cell death)) observed)) and/or because the pooled plasma composition is produced to exclude plasma samples that contain high levels of SARS CoV-2 antibody binding but that lack a corresponding high level of SARS CoV-2 neutralization activity.

[0087] In some embodiments, immunotherapeutic compositions of the present disclosure comprise specific antibody titers against specific pathogens. For example, the antibody titers for specific pathogens in the compositions of the present disclosure may be between 1 and 1000 μg/ml (e.g., 1 μg/ml . . . 2 μg/ml . . . 100 μg/ml . . . 200 μg/ml . . . 500 μg/ml . . . 1000 μg/ml), although higher and lower titers are contemplated.

[0088] In some embodiments, the protective activity of an immunotherapeutic composition disclosed is enhanced by further comprising one or more additional agents, including, but not limited to: antibiotics, antivirals, anti-inflammatory and/or healing compounds. For example, biocides, surfactants, bacterial blocking receptor analogues, cytokines, growth factors, macrophage chemotactic agents, cephalosporins, aminoglycosides, fluoroquinolones, etc., can be provided at therapeutically acceptable levels in the compositions of the present disclosure.

[0089] In some embodiments of the present disclosure, compositions are administered alone, while in other embodiments, the compositions are preferably present in a pharmaceutical formulation comprising at least one active ingredient/agent, as defined above, together with a solid support or alternatively, together with one or more pharmaceutically acceptable carriers and optionally other therapeutic agents. Each carrier must be "acceptable" in the sense that it is compatible with the other ingredients of the formulation and not injurious to the subject.

[0090] Compositions of the present disclosure can be administered via any suitable route of administration (e.g., enteral route, parenteral route, etc.). The term "enteral route" of administration refers to the administration via any part of the gastrointestinal tract. Examples of enteral routes include oral, mucosal, buccal, and rectal route, or intragastric route. "Parenteral route" of administration refers to a route of administration other than enteral route. Examples of parenteral routes of administration include intravenous, intramuscular, intradermal, intraperitoneal, intratumor, intravesical, intraarterial, intrathecal, intracapsular, intraorbital, intracardiac, transtracheal, intraarticular, subcapsular, subarachnoid, intraspinal, epidural and intrasternal, subcutaneous, or topical administration. In typical embodiments, compositions are administered to a subject such that they enter the bloodstream (e.g., intravenous administration). In some embodiments, compositions are administered to devices or instruments that will come into contact with a subject's body (e.g., medical devices, bandages, etc.). The antibodies and compositions of the disclosure can be administered using any suitable method, such as by oral ingestion (e.g., pill, tablet, syrup, liquid, elixir, etc.), nasogastric tube, gastrostomy tube, injection (e.g., intravenous), infusion, implantable infusion pump, and osmotic pump. The suitable route and method of administration may vary depending on a number of factors such as the specific antibody or antibodies being used, the rate of absorption desired, specific formulation or dosage form used, type or severity of the disorder being treated, the specific site of action, and conditions of the patient, and can be readily selected by a person skilled in the art

[0091] The term "therapeutically effective amount" refers to an amount that is effective for an intended therapeutic purpose. For example, in the context of enhancing an immune response, a "therapeutically effective amount" is any amount that is effective in stimulating, evoking, increasing, improving, or augmenting any response of a mammal's immune system. In the context of providing anti-inflammatory action, a "therapeutically effective amount" is any amount that is sufficient to cause any desirable or beneficial reduction in inflammation or prevention of the occurrence of inflammation. The therapeutically effective amount of an antibody usually ranges from about 0.001 to about 5000 mg/kg, and more usually about 0.05 to about 100 mg/kg, of the body weight of the mammal. For example, the amount can be about 0.3 mg/kg, 1 mg/kg, 3 mg/kg, 5 mg/kg, 10 mg/kg, 50 mg/kg, or 100 mg/kg of body weight of the mammal. The precise dosage level to be administered can be readily determined by a person skilled in the art and will depend on a number of factors, such as the type, and severity of the disorder to be treated, the particular binding molecule employed, the route of administration, the time of administration, the duration of the treatment, the particular additional therapy employed, the age, sex, weight, condition, general health and prior medical history of the patient being treated, and like factors well known in the medical arts.

[0092] An immunotherapeutic composition or other composition of the present disclosure is often administered on multiple occasions. Intervals between single doses can be, for example, on the order of hours, days, weeks, months, or years. An exemplary treatment regimen entails administration once per week, once every two weeks, once every three weeks, once every four weeks, once a month, once every 3 months or once every three to 6 months. Example dosage regimens for a immunotherapeutic composition comprising a tailored antibody pool include 1 mg/kg body weight or 3 mg/kg body weight via intravenous administration, using one of the following dosing schedules: (i) every four weeks for six dosages, then every three months; (ii) every three weeks; (iii) 3 mg/kg body weight once followed by 1 mg/kg body weight every three weeks. Other dosages and regimens may be determined by clinicians, researchers, or other practitioners based on embodiments of the present disclosure.

[0093] Compositions of the present disclosure can be combined with additional agents (e.g., antibodies, antibody fragments, antibody-like molecules, monoclonal antibodies, or other proteins or small molecules) to enhance the immunotherapeutic and/or anti-inflammatory affect. Such additional agents may be produced recombinantly, synthetically, in vitro, etc. Embodiments of the present disclosure are not limited by the types of additional agents that a pooled plasma composition or other sample is combined with. In

some embodiments, recombinant or synthetic antibodies (e.g., humanized monoclonals) or antibody fragments (e.g., directed to a specific pathogen or antigen) are added. In addition, antibodies (e.g., monoclonal, polyclonal, etc.) for specified viruses can be added to the compositions. In some embodiments, various therapeutics (e.g., anti-inflammatory agents, chemotherapeutics), stabilizers, buffers, etc. are added to the antibody sample pools, for example, to further enhance the efficacy, stability, administerability, duration of action, range of uses, etc.

[0094] In some embodiments, compositions of the present disclosure (e.g., pooled plasma samples and/or immunoglobulin prepared therefrom) are spiked with one or more antibodies that bind to one or more epitope(s) of a target antigen (e.g., epitope of a viral pathogen (e.g., an epitope of coronavirus)). The presence of one or more antibodies in the compositions described herein can enhance the therapeutic effects of the compositions, including treating and/or preventing one or more aspects of the viral infection. In some embodiments, the one or more antibodies bind a specific target antigen and may also have therapeutic efficacy against a given pathogen, such as a virus. In some embodiments, existing antibodies that can be added to the therapeutic compositions of the present disclosure to enhance therapeutic efficacy include, but are not limited to, antibodies that bind one or more antigenic regions of a virus that are conserved among viruses or viral subtypes, that are unique among viruses or viral subtypes (e.g., variants), and/or are present in a particular virus because of genetic recombination. For example, viral spike proteins are known to elicit potent neutralizing-antibody and T-cell responses. The ability of a virus (e.g., coronavirus OC43, coronavirus 229E, coronavirus NL63, coronavirus HKU1, MERS-CoV, SARS-CoV, or SARS-CoV-2 (COVID-19)) to gain entry into cells and establish infection is mediated by the interactions of its Spike glycoproteins with human cell surface receptors. In the case of coronaviruses, Spike proteins are large type I transmembrane protein trimers that protrude from the surface of coronavirus virions. Each Spike protein comprises a large ectodomain (comprising S1 and S2), a transmembrane anchor, and a short intracellular tail. The 51 subunit of the ectodomain mediates binding of the virion to host cell-surface receptors through its receptor-binding domain (RBD). The S2 subunit fuses with both host and viral membranes, by undergoing structural changes.

[0095] In some embodiments, antibodies added to the compositions of the present disclosure (e.g., pooled plasma samples and/or immunoglobulin prepared therefrom) include antibodies targeting coronavirus Spike proteins. For example, the SARS-CoV-specific human monoclonal antibody, CR3022 (and/or variations and derivatives thereof), are added to the compositions of the present disclosure (see, e.g., Tian, X. et al., *Emerg Microbes Infect.* 2020 December; 9(1):382-385). In some embodiments, antibodies added to the compositions of the present disclosure include antibodies that bind one or more epitopes of coronavirus Spike proteins having amino acid sequences that are unique compared to other coronaviruses. For example, antibodies can be included that bind at least one amino acid variant at positions 455, 486, 493, 494, 501, and 505 of the 51 subunit of coronaviruses. Antibodies can also be included that bind at least one amino acid variant at positions 673, 678, and 686 of the S2 subunit of coronaviruses (see, e.g., Andersen, K. G. et al., *Nature Medicine*. Mar. 17, 2020). In other embodiments, antibodies can be included that bind one or more epitopes of coronavirus proteins that are not known to be naturally present (e.g., not endogenous to a coronavirus), but may have become part of a coronavirus genome due to genetic recombination or engineering. For example, antibodies can be included that bind one or more epitopes of HIV gp120 and/or Gag proteins.

[0096] As would be recognized by one of ordinary skill in the art based on the present disclosure, antibodies that bind one or more epitopes of a viral pathogen can be generated and added to the compositions of the present disclosure (e.g., pooled plasma samples). In some embodiments, antibodies can be generated against one or more epitopes of a coronavirus antigen (e.g., coronavirus OC43, coronavirus 229E, coronavirus NL63, coronavirus HKU1, MERS-CoV, SARS-CoV, or SARS-CoV-2 (COVID-19)). In accordance with these embodiments, the present disclosure includes any methods for generating a coronavirus antibody that binds at least one epitope of a coronavirus antigen. Such antibodies can be generated using amino acid sequence information currently available corresponding to any of the known coronavirus strains, as well as that of any future coronavirus strains identified, by methods known in the art, examples of which are described further below.

[0097] In some embodiments, antibodies can be generated that bind an epitope or epitopes present in more than one coronavirus strain (e.g., antibodies that recognize a conserved region of a coronavirus protein). In some embodiments, antibodies can be generated that bind an epitope or epitopes present in a single coronavirus strain (e.g., antibodies that recognize a unique region of a coronavirus protein). In accordance with these embodiments, the sequence of SARS-CoV-2 can be accessed via NCBI GenBank accession code MN908947 (SEQ ID NO: 1); the sequence of SARS-CoV can be accessed via NCBI GenBank accession code AY274119 (SEQ ID NO: 2); the sequence of MERS-CoV can be accessed via NCBI GenBank accession code NC_019843 (SEQ ID NO: 3); the sequence of HKU1 (beta coronavirus) can be accessed via NCBI GenBank accession code KF686346 (SEQ ID NO: 4); the sequence of OC43 (beta coronavirus) can be accessed via NCBI GenBank accession code NC 006213 (SEQ ID NO: 5); the sequence of NL63 (alpha coronavirus) can be accessed via NCBI GenBank accession code NC_005831 (SEQ ID NO: 6); and the sequence of 229E (alpha coronavirus) can be accessed via NCBI GenBank accession code NC_002645 (SEQ ID NO: 7).

[0098] In some embodiments, the present disclosure provides a coronavirus antigen, epitope, and any fragment thereof useful for generating an immunogenic response in a subject (e.g., a coronavirus vaccine composition), and using that subject as a plasma donor to generate immune globulin compositions, as described further herein. In some embodiments, the present disclosure includes human plasma immunoglobulin compositions containing antibodies specific for a coronavirus or coronaviruses obtained from human donor samples that have been immunized with a coronavirus vaccine and methods of utilizing the compositions for prophylactic administration and/or therapeutic treatment (e.g., passive immunization or immune-prophylaxis). For example, in some embodiments, antigens and epitopes from

SARS-CoV-2 (COVID-19) can be identified based on sequence similarities to epitopes identified other coronaviruses, such as SARS-CoV (e.g., using Immune Epitope Database and Analysis Resource (IEDB), as described in Grifoni, A. et al., *Cell Press* (2020): https://marlin-prod.literatumonline.com/pb-assets/journals/research/cell-host-microbe/PDFs/CHOM_2264_S50.pdf). Table 1 provides SARS-CoV-2 (COVID-19) B cell epitope regions, and Table 2 provides SARS-CoV-2 (COVID-19) T cell epitope regions (below), based on sequence similarities to SARS-CoV (S=surface glycoprotein; M=membrane protein; N=nucleocapsid phosphoprotein).

TABLE 1

Protein	SARS-CoV Sequence	SEQ ID NO:	SARS-CoV-2 Sequence (COVID-19)	SEQ ID NO:	SARS-CoV-2 Region (Start-End)	% Identity
S	DAVDCSQNPLAE LKCSVKSFEIDKG IYQTSNF	8	DAVDCALDPLSE TKCTLKSFTVEK GIYQTSN	9	287-317	69
S	VCGPKLSTDLIKN QCVNFNFNGLTG TGVLTPSSKRFQP FQQFGRDVSDFT DSVRDPKTSEILD ISPCSFGGVSVIT	10	VCGPKKSTNLVK NKCVNFNFNGLT GTGVLTESNKKF LPFQQFGRDIADT TDAVRDPQTLEIL DITPCSFGGVSVI	11	524-598	80
S	GTNASSEVAVLY QDVNCTDVSTAI HADQLTPAWRIY STGNN	12	GTNTSNQVAVLY QDVNCTEVPVAI HADQLTPTWRVY STGS	13	601-640	78
S	FSQILPDPLKPTK RSFIED	14	FSQILPDPSKPSK RSFIE	15	802-819	89
S	FGAGAALQIPFA MQMAYRFNGIG	16	FGAGAALQIPFA MQMAYRFNGI	17	888-909	100
M	MADNGTITVEEL KQLLEQWNLVIG	18	MADSNGTITVEE LKKLLEQWNLVI	19	1-24	92
M	PLMESELVIGAVII RGHLRMA	20	PLLESELVIGAVIL RGHLRI	21	132-151	90
N	PQGLPNNTASWF TALTQHGKEE	22	RPQGLPNNTASW FTALTQHGK	23	42-62	95
N	NNAATVLQLPQG TTLPKGFYA	24	NNNAATVLQLPQ GTTLPKGF	25	153-172	95
N	KHIDAYKTFPPTE PKKDKKKKTDEA QPLPQRQKKQPT VTLLPAADMDD	26	NKHIDAYKTFPPT EPKKDKKKKTDE AQPLPQRQKKQP TVTLLPAADM	27	355-401	90

TABLE 2

Protein	SARS-CoV Sequence	SEQ ID NO:	SARS-CoV-2 Sequence (COVID-19)	SEQ ID NO:	SARS-CoV-2 Region (Start-End)	% Identity
S	VRGWVFGSTMN NKSQSVI	28	IRGWIFGTTLDS KTQSLL	29	101-118	50
S	CTFEYISDAFSL D	30	CTFEYVSQPFLM D	31	166-178	62
S	DAFSLDVSEKSG N	32	QPFLMDLEGKQ GN	33	173-185	38
S	TNFRAILTAFSP AQDIW	34	TRFQTLLALHRS YLTPGDSSSGW	35	236-258	17
S	KSFEIDKGIYQTS NFRVV	36	KSFTVEKGIYQT SNFRVQ	37	304-321	78
S	STFFSTFKCYGV SATKL	38	SASFSTFKCYGV SPTKL	39	371-387	82

TABLE 2-continued

Protein	SARS-CoV Sequence	SEQ ID NO:	SARS-CoV-2 Sequence (COVID-19)	SEQ ID NO:	SARS-CoV-2 Region (Start-End)	% Identity
S	KLPDDFMGCV	40	KLPDDFTGCV	41	424-433	90
S	NIDATSTGNYNY KYRYLR	42	NLDSKVGGNYN YLYRLFR	43	440-457	56
S	YLRHGKLRPFER DISNVP	44	YLYRLFRKSNLK PFERDI	45	451-468	58
S	RPFERDISNVPFS	46	KPFERDISTEIYQ	47	462-474	54
S	KSIVAYTMSLGA DSSIAY	48	QSIIAYTMSLGA ENSVAY	49	690-707	72
S	SIVAYTMSL	50	SIIAYTMSL	51	691-699	89
S	TECANLLLQYGS FCTQL	52	TECSNLLLQYGS FCTQL	53	747-763	94
S	VKQMYKTPTLK YFGGFNF	54	VKQIYKTPPIKD FGGFNF	55	785-802	78
S	ESLTTTSTALGK LQDVV	56	DSLSSTASALGK LQDVV	57	936-952	71
S	ALNTLVKQL	58	ALNTLVKQL	59	958-966	100
S	VLNDILSRL	60	VLNDILSRL	61	976-984	100
S	LITGRLQSL	62	LITGRLQSL	63	996-1004	100
S	QLIRAAEIRASA NLAATK	64	QLIRAAEIRASA NLAATK	65	1011-1028	100
S	SWFITQRNFFSP QII	66	HWFVTQRNFYE PQII	67	1101-1115	73
S	RLNEVAKNL	68	RLNEVAKNL	69	1185-1193	100
S	NLNESLIDL	70	NLNESLIDL	71	1192-1200	100
S	FIAGLIAIV	72	FIAGLIAIV	73	1220-1228	100
Orf 3a	RFFTLGSITAQP VKI	74	RIFTIGTVTLKQ GEI	75	6-20	40
Orf 3a	SITAQPVKI	76	TVTLKQGEI	77	12-20	22
M	TLACFVLAAV	78	TLACFVLAAV	79	61-70	100
M	GLMWLSYFV	80	GLMWLSYFI	81	89-97	89
M	HLRMAGHSL	82	HLRIAGHHL	83	148-156	78
N	ALNTPKDHI	84	ALNTPKDHI	85	138-146	100
N	LQLPQGTTL	86	LQLPQGTTL	87	159-167	100
N	GETALALLLL	88	GDAALALLLL	89	215-224	80
N	LALLLLDRL	90	LALLLLDRL	91	219-227	100
N	LLLDRLNQL	92	LLLDRLNQL	93	222-230	100
N	RLNQLESKV	94	RLNQLESKM	95	226-234	89
N	TKQYNVTQAF	96	TKAYNVTQAF	97	265-274	90
N	GMSRIGMEV	98	GMSRIGMEV	99	316-324	100
N	MEVTPSGTWL	100	MEVTPSGTWL	101	322-331	100
N	QFKDNVILL	102	NFKDQVILL	103	345-353	78

TABLE 2-continued

Protein	SARS-CoV Sequence	SEQ ID NO:	SARS-CoV-2 Sequence (COVID-19)	SEQ ID NO:	SARS-CoV-2 Region (Start-End)	% Identity
Orf 1ab	CLDAGINYV	104	CLEASFNYL	105	2139-2147	56
Orf 1ab	WLMWFIISI	106	WLMWLIINL	107	2292-2300	67
Orf 1ab	ILLLDQVLV	108	ILLLDQALV	109	2498-2506	89
Orf 1ab	LLCVLAALV	110	SACVLAAEC	111	2840-2848	56
Orf 1ab	ALSGVFCGV	112	SLPGVFCGV	113	2942-2950	78
Orf 1ab	TLMNVITLV	114	TLMNVLTLV	115	3639-3647	89
Orf 1ab	SMWALVISV	116	SMWALIISV	117	3661-3669	89

[0099] In some embodiments, monoclonal antibodies can be made using the hybridoma method first described by Kohler et al., *Nature,* 256:495 (1975), and further described, e.g., in Hongo et al., *Hybridoma,* 14 (3): 253-260 (1995), Harlow et al., *Antibodies: A Laboratory Manual*, (Cold Spring Harbor Laboratory Press, 2nd ed. 1988); Hammerling et al., in: *Monoclonal Antibodies and T-Cell Hybridomas* 563-681 (Elsevier, N.Y., 1981), and Ni, *Xiandai Mianyixue,* 26(4):265-268 (2006) regarding human-human hybridomas. Additional methods include those described, for example, in U.S. Pat. No. 7,189,826 regarding production of monoclonal human natural IgM antibodies from hybridoma cell lines. Human hybridoma technology (Trioma technology) is described in Vollmers and Brandlein, *Histology and Histopathology,* 20(3):927-937 (2005) and Vollmers and Brandlein, *Methods and Findings in Experimental and Clinical Pharmacology,* 27(3):185-91 (2005).

[0100] For various other hybridoma techniques, see, e.g., US 2006/258841; US 2006/183887 (fully human antibodies), US 2006/059575; US 2005/287149; US 2005/100546; US 2005/026229; and U.S. Pat. Nos. 7,078,492 and 7,153,507. An exemplary protocol for producing monoclonal antibodies using the hybridoma method is described as follows. In one embodiment, a mouse or other appropriate host animal, such as a hamster, is immunized to elicit lymphocytes that produce or are capable of producing antibodies that will specifically bind to the protein used for immunization. Antibodies are raised in animals by multiple subcutaneous (sc) or intraperitoneal (ip) injections of a polypeptide comprising a coronavirus antigen or a fragment thereof, and an adjuvant, such as monophosphoryl lipid A (MPL)/trehalose dicrynomycolate (TDM) (Ribi Immunochem. Research, Inc., Hamilton, Mont.). A polypeptide comprising a coronavirus antigen or a fragment thereof may be prepared using methods well known in the art, such as recombinant methods, some of which are further described herein. Serum from immunized animals is assayed for anti-coronavirus antibodies, and booster immunizations are optionally administered. Lymphocytes from animals producing anti-coronavirus antibodies are isolated. Alternatively, lymphocytes may be immunized in vitro.

[0101] Lymphocytes are then fused with myeloma cells using a suitable fusing agent, such as polyethylene glycol, to form a hybridoma cell. See, e.g., Goding, *Monoclonal Antibodies: Principles and Practice*, pp. 59-103 (Academic Press, 1986). Myeloma cells may be used that fuse efficiently, support stable high-level production of antibody by the selected antibody-producing cells, and are sensitive to a medium such as HAT medium. Exemplary myeloma cells include, but are not limited to, murine myeloma lines, such as those derived from MOPC-21 and MPC-11 mouse tumors available from the Salk Institute Cell Distribution Center, San Diego, Calif. USA, and SP-2 or X63-Ag8-653 cells available from the American Type Culture Collection, Rockville, Md. USA. Human myeloma and mouse-human heteromyeloma cell lines also have been described for the production of human monoclonal antibodies (Kozbor, *J. Immunol.,* 133:3001 (1984); Brodeur et al., *Monoclonal Antibody Production Techniques and Applications*, pp. 51-63 (Marcel Dekker, Inc., New York, 1987)).

[0102] Antibodies of the present disclosure can be made by using combinatorial libraries to screen for antibodies with the desired activity or activities. For example, a variety of methods are known in the art for generating phage display libraries and screening such libraries for antibodies possessing the desired binding characteristics. Such methods are described generally in Hoogenboom et al. in *Methods in Molecular Biology* 178:1-37 (O'Brien et al., ed., Human Press, Totowa, N.J., 2001). For example, one method of generating antibodies of interest is through the use of a phage antibody library as described in Lee et al., J. Mol. Biol. (2004), 340(5):1073-93. Repertoires of VH and VL genes can be separately cloned by polymerase chain reaction (PCR) and recombined randomly in phage libraries, which can then be searched for antigen-binding clones as described in Winter et al., *Ann. Rev. Immunol.,* 12: 433-455 (1994). Libraries from immunized sources provide high-affinity antibodies to the immunogen without the requirement of constructing hybridomas. Alternatively, the naive repertoire can be cloned to provide a single source of human antibodies to a wide range of non-self and also self antigens without any immunization as described by Griffiths et al., *EMBO J,* 12: 725-734 (1993). Finally, naive libraries can also be made synthetically by cloning the unrearranged V-gene segments from stem cells, and using PCR primers containing random sequence to encode the highly variable CDR3 regions and to accomplish rearrangement in vitro as described by Hoogenboom and Winter, *J Mol. Biol.,* 227: 381-388 (1992).

[0103] In general, nucleic acids encoding antibody gene fragments are obtained from immune cells harvested from humans or animals. If a library biased in favor of anti-coronavirus clones is desired, a subject can be immunized

with one or more epitopes of a coronavirus to generate an antibody response, and spleen cells and/or circulating B cells other peripheral blood lymphocytes (PBLs) are recovered for library construction. In some embodiments, a human antibody gene fragment library biased in favor of anti-coronavirus clones is obtained by generating an antibody response in transgenic mice carrying a functional human immunoglobulin gene array (and lacking a functional endogenous antibody production system) such that coronavirus immunization gives rise to B cells producing human antibodies against one or more epitopes of a coronavirus antigen.

[0104] Alternatively, the use of spleen cells and/or B cells or other PBLs from an unimmunized donor provides a better representation of the possible antibody repertoire, and also permits the construction of an antibody library using any animal (human or non-human) species in which coronavirus is not antigenic. For libraries incorporating in vitro antibody gene construction, stem cells are harvested from the subject to provide nucleic acids encoding unrearranged antibody gene segments. The immune cells of interest can be obtained from a variety of animal species, such as human, mouse, rat, lagomorpha, luprine, canine, feline, porcine, bovine, equine, and avian species, etc. Nucleic acid molecules encoding antibody variable gene segments (including VH and VL segments) can be recovered from the cells of interest and amplified.

[0105] DNA encoding hybridoma-derived monoclonal antibodies or phage display Fv clones is readily isolated and sequenced using conventional procedures (e.g., by using oligonucleotide primers designed to specifically amplify the heavy and light chain coding regions of interest from hybridoma or phage DNA template). Once isolated, the DNA can be placed into expression vectors, which are then transfected into host cells such as *E. coli* cells, simian COS cells, Chinese hamster ovary (CHO) cells, or myeloma cells that do not otherwise produce immunoglobulin protein, to obtain the synthesis of the desired monoclonal antibodies in the recombinant host cells. Review articles on recombinant expression in bacteria of antibody-encoding DNA include Skerra et al., *Curr. Opinion in Immunol.,* 5: 256 (1993) and Pluckthun, *Immunol. Revs,* 130: 151 (1992).

[0106] DNA encoding the Fv clones can be combined with known DNA sequences encoding heavy chain and/or light chain constant regions (e.g., the appropriate DNA sequences can be obtained from Kabat et al.) to form clones encoding full or partial length heavy and/or light chains. It will be appreciated that constant regions of any isotype can be used for this purpose, including IgG, IgM, IgA, IgD, and IgE constant regions, and that such constant regions can be obtained from any human or animal species. An Fv clone derived from the variable domain DNA of one animal (such as human) species and then fused to constant region DNA of another animal species to form coding sequence(s) for "hybrid," full length heavy chain and/or light chain is included in the definition of "chimeric" and "hybrid" antibody as used herein. In certain embodiments, an Fv clone derived from human variable DNA is fused to human constant region DNA to form coding sequence(s) for full- or partial-length human heavy and/or light chains.

[0107] DNA encoding anti-coronavirus antibody derived from a hybridoma can also be modified, for example, by substituting the coding sequence for human heavy- and light-chain constant domains in place of homologous murine sequences derived from the hybridoma clone (e.g. as in the method of Morrison et al., *Proc. Natl. Acad. Sci. USA,* 81: 6851-6855 (1984)). DNA encoding a hybridoma- or Fv clone-derived antibody or fragment can be further modified by covalently joining to the immunoglobulin coding sequence all or part of the coding sequence for a non-immunoglobulin polypeptide. In this manner, "chimeric" or "hybrid" antibodies are prepared that have the binding specificity of the Fv clone or hybridoma clone-derived antibodies of the present disclosure.

[0108] Antibodies may also be produced using recombinant methods. For recombinant production of an anti-coronavirus antibody, nucleic acid encoding the antibody is isolated and inserted into a replicable vector for further cloning (amplification of the DNA) or for expression. DNA encoding the antibody may be readily isolated and sequenced using conventional procedures (e.g., by using oligonucleotide probes that are capable of binding specifically to genes encoding the heavy and light chains of the antibody). Many vectors are available. The vector components generally include, but are not limited to, one or more of the following: a signal sequence, an origin of replication, one or more marker genes, an enhancer element, a promoter, and a transcription termination sequence.

[0109] In some embodiments, one or more coronavirus antigens (e.g., comprising one or more antigenic epitopes of a coronavirus antigen described herein) are used as or in a vaccine that is used to immunize a subject. In some embodiments, the subject can then be used as a plasma donor to generate immune globulin compositions, as described further herein. In some embodiments, the present disclosure includes human plasma immunoglobulin compositions containing antibodies specific for a coronavirus or coronaviruses obtained from human donor samples that have been immunized with a coronavirus vaccine and methods of utilizing the compositions for prophylactic administration and/or therapeutic treatment (e.g., passive immunization or immune-prophylaxis). Hyperimmune serum globulins (immune serum globulin having high titers of a particular coronavirus antibody), in distinction to normal immunoglobulin, have been therapeutically useful in treating patients who require immediate infusion of high titer antibodies. In some embodiments, hyperimmune globulin compositions of the present disclosure can be obtained from pooled plasma samples obtained from a plurality of donor human subjects (e.g., 50, 100, 200, 300, 400, 500 or more subjects) that have been immunized with one or more antigenic epitopes against a coronavirus (e.g., coronavirus OC43, coronavirus 229E, coronavirus NL63, coronavirus HKU1, MERS-CoV, SARS-CoV, or SARS-CoV-2 (COVID-19)).

[0110] In accordance with the embodiments disclosed herein, the compositions and methods of the present disclosure include the characterization and selection of donor human subjects with high antibody titers against a coronavirus (e.g., coronavirus OC43, coronavirus 229E, coronavirus NL63, coronavirus HKU1, MERS-CoV, SARS-CoV, or SARS-CoV-2 (COVID-19)). To aid in the characterization and selection of donor human plasma sufficient to be included in the therapeutic compositions of the present disclosure, various assays can be used to measure and/or quantify the total levels of antibody binding in a sample of donor plasma, as well as the levels of neutralizing antibodies in a sample of donor plasma. Suitable assays include flow

cytometry assays, competitive assays, inhibition assays, immunofluorescence assays, enzyme-linked immunosorbent (ELISA) assays, lateral flow assays, sandwich assays, and neutralization assays. In some embodiments, characterization of a donor plasma sample is performed using an enzyme linked immunosorbent assay (ELISA). ELISA (also referred to in the art as an "enzyme immunoassay" (EIA)) is a plate-based assay technique designed for detecting and quantifying soluble substances such as peptides, proteins, antibodies, and hormones in a sample. In an ELISA, a target macromolecule (e.g., a cell receptor) is immobilized on a solid surface (e.g., a microplate) and then complexed with a binding member specific for the target (e.g., a ligand) that is linked to a reporter enzyme. Detection is accomplished by measuring the activity of the reporter enzyme via incubation with the appropriate substrate to produce a measurable product (e.g., absorbance, chemiluminescence, fluorescence, or other visual signal). In the context of the present disclosure, an ELISA may be performed in either competitive or non-competitive formats. In some embodiments, an ELISA can be used to measure total antibody binding to a given antigen in a donor plasma sample.

[0111] In some embodiments, the ELISA is a competitive inhibition assay (also referred to in the art as "inhibition ELISA" or "competitive immunoassay") which enables the screening of inhibitory proteins by measuring the concentration of a potential inhibitor protein (e.g., a neutralizing antibody) by detection of signal interference. Systems and methods for performing ELISA are known in the art and commercially available (see, e.g., Methods in Immunodiagnosis, 2nd Edition, Rose and Bigazzi, eds., John Wiley and Sons, 1980 and Campbell et al., Methods of Immunology, W. A. Benjamin, Inc., 1964). Assays may be performed in the absence of cells or viruses (i.e., "cell-free" or "virus-free" assays).

[0112] In some embodiments, the disclosed methods desirably include positive and/or negative controls. A control may be analyzed concurrently with the sample from the subject, or a control may be analyzed before or after the sample has been analyzed using the disclosed methods. The results obtained from the sample can be compared to the results obtained from the control(s). Standard curves for the controls may be provided, with which assay results for the sample may be compared. Numerous neutralizing antibodies directed against several types of coronaviruses have been isolated, and any of these neutralizing antibodies may be included as a positive control panel. Exemplary coronavirus neutralizing antibodies that may be included in the positive control panel are disclosed in, for example, Zost et al., Rapid isolation and profiling of a diverse panel of human monoclonal antibodies targeting the SARS-CoV-2 spike protein. Nat Med (2020). In other embodiments, the method further comprises comparing the results obtained from the sample with the results obtained using a negative control. The negative control may comprise at least one antibody that does not neutralize coronavirus infection (i.e., "coronavirus non-neutralizing antibodies"). The negative control may comprise a panel of two or more, three or more, four or more, or at least five coronavirus non-neutralizing antibodies.

[0113] Embodiments of the present disclosure further provide methods of identifying plasma comprising coronavirus neutralizing antibodies. The disclosure is not limited to any particular assay for determining neutralizing antibody titer. Indeed, any assay available in the art may be utilized. In some embodiments, a plaque/focus reduction neutralization test (P/FRNT) is performed. In further embodiments, an automated high-throughput antibody neutralization assay based on foci and plaque reduction is used. In other embodiments, a virus reduction neutralization test (VRNT) is utilized (see, e.g., Whiteman et al., Am J Trop Med Hyg. 2018 December; 99(6):1430-1439). In still other embodiments, a pseudovirus neutralization assay is utilized (Creative Diagnostics, Shirley, N.Y.). In some embodiments, a multiplexed bead-based SARS-CoV-2 serological assay is used (Gaithersburg, Md.).

[0114] Descriptions of the plasma sample, solid support, conjugate, controls, and components thereof set forth above in connection with the methods of detecting coronavirus binding antibodies also are applicable to the methods of identifying plasma comprising coronavirus neutralizing antibodies. The disclosure also provides a method of identifying a subject (e.g., a subject that has been vaccinated with a vaccine specific for the coronavirus or a subject that has recovered from coronavirus infection) harboring coronavirus neutralizing antibodies and/or quantifying the titer of coronavirus neutralizing antibodies in a subject, the method comprising performing any of the above-described methods on a sample obtained from the subject (e.g., a sample comprising plasma).

[0115] The above-described methods may be utilized in a variety of applications, including to determine the efficacy of immunization or vaccination against a coronavirus (e.g., determining the levels of coronavirus-specific antibody titers). In such an embodiment, the disclosed methods are performed on a sample from a subject has been vaccinated with a vaccine specific for the coronavirus. The methods also may be employed to screen plasma for its ability to provide protection from coronavirus infection, as well as for therapeutic applications (e.g., convalescent plasma).

[0116] In some embodiments, the present disclosure provides methods for the characterization of donor plasma from individuals that have recovered from infection with SARS CoV-2, which contain anti-SARS CoV-2 antibodies. Plasma from coronavirus disease 2019 (COVID-19) convalescent patients can be analyzed for specific SARS CoV-2 antibody levels (e.g., using a serological assay such as an ELISA) as well as functional activity (using an assay to detect neutralizing anti-SARS CoV-2 activity).

Definitions

[0117] As used herein, the term "subject" refers to any human or animal (e.g., non-human primate, rodent, feline, canine, bovine, porcine, equine, etc.).

[0118] As used herein, the term "sample" is used in its broadest sense and encompass materials obtained from any source. As used herein, the term "sample" is used to refer to materials obtained from a biological source, for example, obtained from animals (including humans), and encompasses any fluids, solids and tissues. In particular embodiments of the present disclosure, biological samples include blood and blood products such as plasma, serum and the like. However, these examples are not to be construed as limiting the types of samples that find use with the present disclosure.

[0119] As used herein, the term "antibody" refers to an immunoglobulin molecule that is typically composed of two identical pairs of polypeptide chains, each pair having one

"light" (L) chain and one "heavy" (H) chain. Human light chains are classified as kappa and lambda light chains. Heavy chains are classified as mu, delta, gamma, alpha, or epsilon, and define the antibody's isotype as IgM, IgD, IgG, IgA, and IgE, respectively. Within light and heavy chains, the variable and constant regions are joined by a "J" region of about 12 or more amino acids, with the heavy chain also including a "D" region of about 3 or more amino acids. Each heavy chain is comprised of a heavy chain variable region (abbreviated herein as HCVR or V_H) and a heavy chain constant region. The heavy chain constant region is comprised of three domains, C_{H1}, C_{H2} and C_{H3}. Each light chain is comprised of a light chain variable region (abbreviated herein as LCVR or V_L) and a light chain constant region. The light chain constant region is comprised of one domain, CL. The constant regions of the antibodies may mediate the binding of the immunoglobulin to host tissues or factors, including various cells of the immune system (e.g., effector cells) and the first component (C1q) of the classical complement system. The V_H and V_L regions can be further subdivided into regions of hypervariability, termed complementarity determining regions (CDR), interspersed with regions that are more conserved, termed framework regions (FR). Each V_H and V_L is composed of three CDRs and four FRs, arranged from amino-terminus to carboxy-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4. The variable regions of each heavy/light chain pair (V_H and V_L), respectively, form the antibody binding site. The term "antibody" encompasses an antibody that is part of an antibody multimer (a multimeric form of antibodies), such as dimers, trimers, or higher-order multimers of monomeric antibodies. It also encompasses an antibody that is linked or attached to, or otherwise physically or functionally associated with, a non-antibody moiety. Further, the term "antibody" is not limited by any particular method of producing the antibody. For example, it includes, inter alia, recombinant antibodies, synthetic antibodies, monoclonal antibodies, polyclonal antibodies, bi-specific antibodies, and multi-specific antibodies.

[0120] As used herein, the term "antibody derivative" or "derivative" of an antibody refers to a molecule that is capable of binding to the same antigen that the antibody from which it is derived binds to and comprises an amino acid sequence that is the same or similar to the antibody linked to an additional molecular entity. The amino acid sequence of the antibody that is contained in the antibody derivative may be the full-length antibody, or may be any portion or portions of a full-length antibody. The additional molecular entity may be a chemical or biological molecule. Examples of additional molecular entities include chemical groups, amino acids, peptides, proteins (such as enzymes, antibodies), and chemical compounds. The additional molecular entity may have any utility, such as for use as a detection agent, label, marker, pharmaceutical or therapeutic agent. The amino acid sequence of an antibody may be attached or linked to the additional entity by chemical coupling, genetic fusion, noncovalent association or otherwise. The term "antibody derivative" also encompasses chimeric antibodies, humanized antibodies, and molecules that are derived from modifications of the amino acid sequences of an antibody, such as conservation amino acid substitutions, additions, and insertions.

[0121] As used herein, the term "antigen" refers to any substance that is capable of inducing an adaptive immune response. An antigen may be whole cell (e.g. bacterial cell), virus, fungus, or an antigenic portion or component thereof. Examples of antigens include, but are not limited to, microbial pathogens, bacteria, viruses, proteins, glycoproteins, lipoproteins, peptides, glycopeptides, lipopeptides, toxoids, carbohydrates, tumor-specific antigens, and antigenic portions or components thereof.

[0122] As used herein, the term "antigen-binding fragment" of an antibody refers to one or more portions of a full-length antibody that retain the ability to bind to the same antigen that the antibody binds to.

[0123] As used herein, the terms "immunoglobulin," "immunoglobulin molecule" and "IG" encompass (1) antibodies, (2) antigen-binding fragments of an antibody, and (3) derivatives of an antibody, each as defined herein. As described herein, immunoglobulin may be prepared from (e.g., fractionated from, isolated from, purified from, concentrated from, etc.) pooled plasma compositions (e.g., for administration to a subject). As used herein, the term "Intravenous immunoglobulin (IVIG)" refers to conventional immunoglobulin prepared from the plasma of over one thousand random human donors, whereas the term "IVIG of the present disclosure," for example SARS CoV-2-IVIG described herein, and in particular, refers to immune globulin prepared from a plurality of human donors, according to methods of the present disclosure, that contains an elevated SARS CoV-2-specific antibody titer and neutralization titer compared to a control sample (e.g., conventional IVIG prepared from a mixture of plasma samples obtained from 100 or more random human plasma donors). Additionally, for example, coronavirus-IVIG described herein, and in particular, refers to immune globulin prepared from a plurality of human donors, according to methods of the present disclosure, that contains an elevated coronavirus specific antibody titer compared to a control sample (e.g., conventional IVIG prepared from a mixture of plasma samples obtained from 100 or more random human plasma donors). As used herein, the terms "hyperimmune globulin," "hyperimmune serum globulin" and "hyperimmune immune globulin" refer to immune serum globulin having a high titer of antibodies specific for a single organism or antigen (e.g., specific for hepatitis, specific for tetanus, specific for rabies, or specific for varicella zoster) produced from plasma or serum obtained from a donor(s) that has an elevated antibody titer for the single, specific organism or antigen. For example, Varicella Zoster Immune Globulin (VZIG, Massachusetts Public Health Biologic Laboratories, Boston, Mass.; or VARIZIG, Cangene Corporation, Winnipeg, Canada)) is a purified human immune globulin that has a high antibody titer specific for varicella zoster prepared from several hundred plasma donors and lacks significant antibody titers, or has decreased antibody titers, for other organisms or antigens (e.g., measles). Other hyperimmune globulin products are generally produced from donors that have been immunized to the specific pathogen or antigen (e.g., Rabies Immune Globulin, HYPERRAB, Grifols, Clayton, N.C., produced from a few hundred or less donors immunized with rabies vaccine).

[0124] As used herein, the term "antibody sample" refers to an antibody-containing composition (e.g., fluid (e.g., plasma, blood, purified antibodies, blood or plasma fractions, blood or plasma components etc.)) taken from or provided by a donor (e.g., natural source) or obtained from a synthetic, recombinant, other in vitro source, or from a

commercial source. The antibody sample may exhibit elevated titer of a particular antibody or set of antibodies based on the pathogenic/antigenic exposures (e.g., natural exposure or through vaccination) of the donor or the antibodies engineered to be produced in the synthetic, recombinant, or in vitro context. Herein, an antibody sample with elevated titer of antibody X is referred to as an "X-elevated antibody sample." For example, an antibody sample with elevated titer of antibodies against cytomegalovirus is referred to as a "cytomegalovirus-elevated antibody sample.

[0125] As used herein, the term "isolated antibody" or "isolated binding molecule" refers to an antibody or binding molecule that is identified and separated from at least one contaminant with which it is ordinarily associated in its source. Examples of an isolated antibody include: an antibody that: (1) is not associated with one or more naturally associated components that accompany it in its natural state; (2) is substantially free of other proteins from its origin source; or (3) is expressed recombinantly, in vitro, or cell-free, or is produced synthetically and the is removed the environment in which it was produced.

[0126] As used herein, the terms "pooled plasma," "pooled plasma samples" and "pooled plasma composition" refer to a mixture of two or more plasma samples and/or a composition prepared from same (e.g., immunoglobulin). Elevated titer of a particular antibody or set of antibodies in pooled plasma reflects the elevated titers of the antibody samples that make up the pooled plasma. For example, plasma samples may be obtained from subjects that have been vaccinated (e.g., with a vaccine) or that have naturally high titers of antibodies to one or more pathogens as compared to the antibody level(s) found in the population as a whole. Upon pooling of the plasma samples, a pooled plasma composition is produced (e.g., that has elevated titer of antibodies specific to a particular pathogen). Herein, a pooled plasma with elevated titer of antibody X (e.g., wherein "X" is a microbial pathogen) is referred to as "X-elevated antibody pool." For example, a pooled plasma with elevated titer of antibodies against cytomegalovirus is referred to as "cytomegalovirus-elevated antibody pool." Also used herein is the term "primary antibody pool" which refers to a mixture of two or more plasma samples. Elevated titer of a particular antibody or set of antibodies in a primary antibody pool reflects the elevated titers of the antibody samples that make up the primary antibody pool. For example, many plasma donations may be obtained from subjects that have been vaccinated (e.g., with a polyvalent *Pseudomonas aeruginosa* vaccine). Upon pooling of the plasma samples, a primary antibody pool is produced that has elevated titer of antibodies to *Pseudomonas aeruginosa*. Herein, a primary antibody pool with elevated titer of antibody X (e.g., wherein "X" is a microbial pathogen) is referred to as "X-elevated antibody pool." For example, a primary antibody pool with elevated titer of antibodies against cytomegalovirus is referred to as "cytomegalovirus-elevated antibody pool." Pooled plasma compositions can be used to prepare immunoglobulin (e.g., that is subsequently administered to a subject) via methods known in the art (e.g., fractionation, purification, isolation, etc.). The present disclosure provides that both pooled plasma compositions and immunoglobulin prepared from same may be administered to a subject to provide prophylactic and/or therapeutic benefits to the subject. Accordingly, the term pooled plasma composition may refer to immunoglobulin prepared from pooled plasma/pooled plasma samples.

[0127] As used herein, the term "secondary antibody pool" or "tailored antibody pool" refer to a mixture of two or more primary antibody pools. Such a pool for example, may be tailored to exhibit elevated titer of specific antibodies or sets of antibodies by combining primary pools that exhibit such elevated titers. For example, a primary pool with elevated titer of *Pseudomonas aeruginosa* antibodies could be combined with a primary pool with elevated titer of Varicella-zoster virus antibodies to produce a tailored antibody pool with elevated titer of antibodies against *Pseudomonas aeruginosa* and Varicella-zoster virus.

[0128] As used herein, the term, "spiked antibody pool" refers to a pooled plasma sample (e.g., primary or tailored antibody pool) that contains antibodies from at least one natural source spiked or combined with antibodies or other immunoglobulin produced synthetically, recombinantly, or through other in vitro means.

[0129] As used herein, the term "isolated antibody" or "isolated binding molecule" refers to an antibody or binding molecule that is identified and separated from at least one contaminant with which it is ordinarily associated in its source. Examples of an isolated antibody include: an antibody that: (1) is not associated with one or more naturally associated components that accompany it in its natural state; (2) is substantially free of other proteins from its origin source; or (3) is expressed recombinantly, in vitro, or cell-free, or is produced synthetically and the is removed the environment in which it was produced.

[0130] As used herein, the term "purified" or "to purify" means the result of any process that removes some of a contaminant from the component of interest, such as a protein (e.g., antibody) or nucleic acid. The percent of a purified component is thereby increased in the sample.

[0131] As used herein, the term "immunotherapeutic agents" refers to a chemical or biological substance that can enhance an immune response (e.g., specific or general) of a mammal. Examples of immunotherapeutic agents include: passively administered primary antibody pools; tailored antibody pools (e.g., passively administered tailored antibody pools); vaccines, chemokines, antibodies, antibody fragments, *bacillus* Calmette-Guerin (BCG); cytokines such as interferons; vaccines such as MyVax personalized immunotherapy, Onyvax-P, Oncophage, GRNVAC1, Favld, Provenge, GVAX, Lovaxin C, BiovaxID, GMXX, and Neu-Vax; and antibodies such as alemtuzumab (CAMPATH), bevacizumab (AVASTIN), cetuximab (ERBITUX), gemtuzunab ozogamicin (MYLOTARG), ibritumomab tiuxetan (ZEVALIN), panitumumab (VECTIBIX), rituximab (RITUXAN, MABTHERA), trastuzumab (HERCEPTIN), tositumomab (BEXXAR), tremelimumab, CAT-3888, agonist antibodies to CD40 receptor that are disclosed in WO2003/040170, and any immunomodulating substance.

[0132] As used herein, the term "donor" refers to a subject that provides a biological sample (e.g., blood, plasma, etc.). A donor/donor sample may be screened for the presence or absence of specific pathogens (e.g., using U.S. Food and Drug Administration (FDA) guidelines for assessing safety standards for blood products (e.g., issued by the FDA Blood Products Advisory Committee). For example, a donor/donor sample may be screened according to FDA guidelines to verify the absence of one or more bloodborne pathogens (e.g., human immunodeficiency virus (HIV) 1 (HIV-1),

HIV-2; *Treponema pallidum* (syphilis); *Plasmodium falciparum, P. malariae, P. ovale, P. vivax* or *P. knowlesi* (malaria); hepatitis B virus (HBV), hepatitis C virus HCV); prions (Creutzfeldt Jakob disease); West Nile virus; parvovirus; Typanosoma *cruzi*; coronavirus (e.g., coronavirus OC43, coronavirus 229E, coronavirus NL63, coronavirus HKU1, MERS-CoV, SARS-CoV, or SARS-CoV-2 (COVID-19)); vaccinia virus or other pathogen routinely screened or that is recommended to be screed for by a regulatory body such as the FDA). As used herein, the terms "selected donor," "selected human subject" and the like refer to a subject that is chosen and/or identified to provide a biological sample (e.g., blood, plasma, etc.) based on the presence of a desired characteristic of that biological sample (e.g., a specific titer (e.g., high, average or low titer) of antibodies (e.g., determined using one or more screening methods (e.g., neutralization assay or other assay (e.g., ELISA) described herein) specific for one or more pathogens (e.g., one or more respiratory pathogens (e.g., SARS CoV-2))). For example, in one embodiment described herein, a high titer selected donor comprises a pathogen specific antibody titer that is about 1.5-2.0 times, 2-5 times, 5-8 times, 8-10 times, 10-14 times, 14 times or greater than a standard value (the titer of pathogen specific antibodies present in a pool of plasma samples from 100 or more random human subjects), wherein medium titer donors comprise a pathogen specific antibody titer that is the titer of pathogen specific antibodies present in a pool of plasma samples from 100 or more random human subjects or that is only marginally higher (e.g., 5-20% higher) or marginally lower (e.g., 5-20% lower) than this value, and wherein low titer donors comprise a pathogen specific antibody titer that is around 20-50 percent or less than the titer of pathogen specific antibodies present in a pool of plasma samples from 100 or more random human subjects. Thus, a random donor/random donor sample may be a subject/sample that passes FDA bloodborne pathogen screening requirements and is not selected on the basis of antibody titers (e.g., SARS CoV-2 antibody titers).

[0133] As used herein, an "immunostimulatory amount" refers to that amount of a vaccine (e.g., viral, bacterial and/or fungal vaccine) that is able to stimulate the immune response. An immune response includes the set of biological effects leading to the body's production of immunoglobulins, or antibodies, in response to a foreign entity. Accordingly, immune response refers to the activation of B cells, in vivo or in culture, through stimulation of B cell surface Ig receptor molecules. The measurement of the immune response is within the ordinary skill of those in this art and includes the determination of antibody levels using methods described in the series by P. Tijssen, Laboratory Techniques in Biochemistry and Molecular Biology: Practice and Theory of Enzyme Immunoassays, (Burdon & van Knippenberg eds., 3rd ed., 1985) Elsevier, New York; and Antibodies: A Laboratory Manual, (Harlow & Lane eds., 1988), Cold Spring Harbor Laboratory Press; as well as procedures such as countercurrent immuno-electrophoresis (GIEP), radioimmunoassay, radio-immunoprecipitation, enzyme-linked immuno-sorbent assays (ELISA), dot blot assays, and sandwich assays, see U.S. Pat. Nos. 4,376,110 and 4,486,530, all of which are incorporated by reference. Measurement of the immune response also includes detection or determination of B cell activation events that may precede antibody production, or signal an increase in antibody production. Such measurements include, B cell proliferation assays, phosphorylation assays, assays of intracytoplasmic free calcium concentration, and other methods of determining B cell activation known in the art. Representative assays are provided in Mongini et al., J. Immunol. 159:3782-91 (1997); Frade, et al., BBRC 188:833-842 (1992); Tsokos et al., J. Immunol. 144:1640-1645 (1990); Delcayre et al., BBRC 159:1213-1220 (1989); and Nemerow et al., J. Immunol. 135:3068-73 (1985) each of which is incorporated by reference. In preferred embodiments, the practice of the present disclosure includes promoting, enhancing or stimulating an immune response. These actions refer to establishing an immune response that did not previously exist; to optimizing or increasing a desired immune response; to establishing or increasing a secondary response characterized by increased isotype switching, memory response, or both; to providing a statistically increased immunoprotective effect against a pathogen; to generating an equivalent or greater humoral immune response, or other measure of B cell activation, from a reduced or limiting dose of antigen; to generating an increased humoral immune response, or other measure of B cell activation, in response to an equivalent dose of antigen; or to lowering the affinity threshold for B cell activation in vivo or in vitro. Preferably, an immunostimulatory amount refers to that amount of vaccine that is able to stimulate an immune response in a subject (e.g., a donor), and from which subject plasma, serum or other blood component is harvested for use in the compositions and methods of the present disclosure (e.g., for the therapeutic and/or prophylactic treatment of microbial (e.g., viral, bacterial and/or fungal) infection in a subject treated with compositions and methods described herein)).

[0134] The terms "buffer" or "buffering agents" refer to materials, that when added to a solution, cause the solution to resist changes in pH.

[0135] The terms "reducing agent" and "electron donor" refer to a material that donates electrons to a second material to reduce the oxidation state of one or more of the second material's atoms.

[0136] The term "monovalent salt" refers to any salt in which the metal (e.g., Na, K, or Li) has a net 1+ charge in solution (i.e., one more proton than electron).

[0137] The term "divalent salt" refers to any salt in which a metal (e.g., Mg, Ca, or Sr) has a net 2+ charge in solution.

[0138] The terms "chelator" or "chelating agent" refer to any materials having more than one atom with a lone pair of electrons that are available to bond to a metal ion.

[0139] The term "solution" refers to an aqueous or non-aqueous mixture.

[0140] As used herein, the term "adjuvant" refers to any substance that can stimulate an immune response (e.g., a mucosal immune response). Some adjuvants can cause activation of a cell of the immune system (e.g., an adjuvant can cause an immune cell to produce and secrete a cytokine). Examples of adjuvants that can cause activation of a cell of the immune system include, but are not limited to, the nanoemulsion formulations described herein, saponins purified from the bark of the *Q. saponaria* tree, such as QS21 (a glycolipid that elutes in the 21st peak with HPLC fractionation; Aquila Biopharmaceuticals, Inc., Worcester, Mass.); poly(di(carboxylatophenoxy)phosphazene (PCPP polymer; Virus Research Institute, USA); derivatives of lipopolysaccharides such as monophosphoryl lipid A (MPL; Ribi ImmunoChem Research, Inc., Hamilton, Mont.), muramyl dipeptide (MDP; Ribi) and threonyl-muramyl dipeptide (t-MDP;

Ribi); OM-174 (a glucosamine disaccharide related to lipid A; OM Pharma SA, Meyrin, Switzerland); cholera toxin (CT), and *Leishmania* elongation factor (a purified *Leishmania* protein; Corixa Corporation, Seattle, Wash.). Traditional adjuvants are well known in the art and include, for example, aluminum phosphate or hydroxide salts ("alum"). In some embodiments, compositions of the present disclosure are administered with one or more adjuvants (e.g., to skew the immune response towards a Th1 and/or Th2 type response). In some embodiments, an adjuvants described in US2005158329; US2009010964; US2004047882; or U.S. Pat. No. 6,262,029 (each of which is hereby incorporated by reference in its entirety) is utilized.

[0141] As used herein, the term "an amount effective to induce an immune response" (e.g., of a composition for inducing an immune response), refers to the dosage level required (e.g., when administered to a subject) to stimulate, generate and/or elicit an immune response in the subject. An effective amount can be administered in one or more administrations (e.g., via the same or different route), applications or dosages and is not intended to be limited to a particular formulation or administration route.

[0142] As used herein, the term "under conditions such that said subject generates an immune response" refers to any qualitative or quantitative induction, generation, and/or stimulation of an immune response (e.g., innate or acquired).

[0143] A used herein, the term "immune response" refers to a response by the immune system of a subject. For example, immune responses include, but are not limited to, a detectable alteration (e.g., increase) in Toll-like receptor (TLR) activation, lymphokine (e.g., cytokine (e.g., Th1 or Th2 type cytokines) or chemokine) expression and/or secretion, macrophage activation, dendritic cell activation, T cell activation (e.g., CD4+ or CD8+ T cells), NK cell activation, and/or B cell activation (e.g., antibody generation and/or secretion). Additional examples of immune responses include binding of an immunogen (e.g., antigen (e.g., immunogenic polypeptide)) to an MHC molecule and inducing a cytotoxic T lymphocyte ("CTL") response, inducing a B cell response (e.g., antibody production), and/or T-helper lymphocyte response, and/or a delayed type hypersensitivity (DTH) response against the antigen from which the immunogenic polypeptide is derived, expansion (e.g., growth of a population of cells) of cells of the immune system (e.g., T cells, B cells (e.g., of any stage of development (e.g., plasma cells), and increased processing and presentation of antigen by antigen presenting cells. An immune response may be to immunogens that the subject's immune system recognizes as foreign (e.g., non-self antigens from microorganisms (e.g., pathogens), or self-antigens recognized as foreign). Thus, it is to be understood that, as used herein, "immune response" refers to any type of immune response, including, but not limited to, innate immune responses (e.g., activation of Toll receptor signaling cascade) cell-mediated immune responses (e.g., responses mediated by T cells (e.g., antigen-specific T cells) and non-specific cells of the immune system) and humoral immune responses (e.g., responses mediated by B cells (e.g., via generation and secretion of antibodies into the plasma, lymph, and/or tissue fluids). The term "immune response" is meant to encompass all aspects of the capability of a subject's immune system to respond to antigens and/or immunogens (e.g., both the initial response to an immunogen (e.g., a pathogen) as well as acquired (e.g., memory) responses that are a result of an adaptive immune response).

[0144] As used herein, the terms "immunogen" and "antigen" refer to an agent (e.g., a microorganism (e.g., bacterium, virus or fungus) and/or portion or component thereof (e.g., a protein antigen or a polysaccharide)) that is capable of eliciting an immune response in a subject.

[0145] As used herein, the term "pathogen product" refers to any component or product derived from a pathogen including, but not limited to, polypeptides, peptides, proteins, nucleic acids, membrane fractions, and polysaccharides.

[0146] The terms "pharmaceutically acceptable" or "pharmacologically acceptable," as used herein, refer to compositions that do not substantially produce adverse reactions (e.g., toxic, allergic or immunological reactions) when administered to a subject.

[0147] As used herein, the term "pharmaceutically acceptable carrier" refers to any of the standard pharmaceutical carriers including, but not limited to, phosphate buffered saline solution, water, and various types of wetting agents (e.g., sodium lauryl sulfate), any and all solvents, dispersion media, coatings, sodium lauryl sulfate, isotonic and absorption delaying agents, disintrigrants (e.g., potato starch or sodium starch glycolate), polyethyl glycol, other natural and non-naturally occurring carries, and the like. The compositions also can include stabilizers and preservatives. Examples of carriers, stabilizers and adjuvants have been described and are known in the art (See e.g., Martin, Remington's Pharmaceutical Sciences, 15th Ed., Mack Publ. Co., Easton, Pa. (1975), incorporated herein by reference).

[0148] As used herein, the term "pharmaceutically acceptable salt" refers to any salt (e.g., obtained by reaction with an acid or a base) of a composition of the present disclosure that is physiologically tolerated in the target subject. "Salts" of the compositions of the present disclosure may be derived from inorganic or organic acids and bases. Examples of acids include, but are not limited to, hydrochloric, hydrobromic, sulfuric, nitric, perchloric, fumaric, maleic, phosphoric, glycolic, lactic, salicylic, succinic, toluene-p-sulfonic, tartaric, acetic, citric, methanesulfonic, ethanesulfonic, formic, benzoic, malonic, sulfonic, naphthalene-2-sulfonic, benzenesulfonic acid, and the like. Other acids, such as oxalic, while not in themselves pharmaceutically acceptable, may be employed in the preparation of salts useful as intermediates in obtaining the compositions of the present disclosure and their pharmaceutically acceptable acid addition salts. Examples of bases include, but are not limited to, alkali metal (e.g., sodium) hydroxides, alkaline earth metal (e.g., magnesium) hydroxides, ammonia, and compounds of formula $NW4^+$, wherein W is C_{1-4} alkyl, and the like.

[0149] Examples of salts include, but are not limited to: acetate, adipate, alginate, aspartate, benzoate, benzenesulfonate, bisulfate, butyrate, citrate, camphorate, camphorsulfonate, cyclopentanepropionate, digluconate, dodecylsulfate, ethanesulfonate, fumarate, flucoheptanoate, glycerophosphate, hemisulfate, heptanoate, hexanoate, chloride, bromide, iodide, 2-hydroxyethanesulfonate, lactate, maleate, methanesulfonate, 2-naphthalenesulfonate, nicotinate, oxalate, palmoate, pectinate, persulfate, phenylpropionate, picrate, pivalate, propionate, succinate, tartrate, thiocyanate, tosylate, undecanoate, and the like. Other examples of salts include anions of the compounds of the present disclosure compounded with a suitable cation such as Na^+, $NH4^+$, and $NW4^+$ (wherein W is a C_{1-4} alkyl group), and the

like. For therapeutic use, salts of the compounds of the present disclosure are contemplated as being pharmaceutically acceptable. However, salts of acids and bases that are non-pharmaceutically acceptable may also find use, for example, in the preparation or purification of a pharmaceutically acceptable compound.

[0150] For therapeutic use, salts of the compositions of the present disclosure are contemplated as being pharmaceutically acceptable. However, salts of acids and bases that are non-pharmaceutically acceptable may also find use, for example, in the preparation or purification of a pharmaceutically acceptable composition.

[0151] As used herein, the terms "at risk for infection" and "at risk for disease" refer to a subject that is predisposed to experiencing a particular infection or disease (e.g., respiratory infection or disease). This predisposition may be genetic (e.g., a particular genetic tendency to experience the disease, such as heritable disorders), or due to other factors (e.g., immunosuppression, compromised immune system, immunodeficiency, environmental conditions, exposures to detrimental compounds present in the environment, etc.). Thus, it is not intended that embodiments of the present disclosure be limited to any particular risk (e.g., a subject may be "at risk for disease" simply by being exposed to and interacting with other people), nor is it intended that embodiments of the present disclosure be limited to any particular diseaseThe present invention relates to a steam sample concentrator and conditioning (SSCC) system. The SSCC system concentrates impurities carried in steam and facilitates analysis of the impurities. The SSCC system prevents the dissolution of noncondensable gases (NCGs) (e.g., hydrogen sulfide (H_2S) and carbon dioxide (CO_2)) in geothermal steam that interfere with steam analysis. For example, when steam is analyzed, it is often separated into condensate and noncondensable gas phases. The SSCC system of the invention, via prevention of the dissolution of NCGs in a steam sample after separation of condensate and noncondensable gas phases, enables a significantly more accurate measurement of the impurities in the sample compared to conventional systems.

EXAMPLES

[0152] The following examples are provided in order to demonstrate and further illustrate certain preferred embodiments and aspects of the present disclosure and are not to be construed as limiting the scope thereof.

[0153] Studies have shown that the ability of humans to respond to foreign antigens (e.g., microbial pathogens (e.g., naturally occurring or in the form of a vaccine)) is controlled by the major histocompatibility complex (human leukocyte antigen "HLA" type in humans, the major histocompatibility complex of the mouse, H-2, is homologous to HLA in humans). Additional studies have shown that the histocompatibility complex controls the humoral antibody responses generated within a subject against microbial pathogens. Different HLA typing programs have existed for some time and have studied HLA type with regard to various immunological responses in humans (e.g., bone marrow transplant graft and/or rejection, organ transplant, autoimmunity, cancer, and strength of immune response (e.g., humoral immune response) generated by a subject). While HLA typing can be useful in these limited contexts, cost, medical record and other concerns make it unfeasible to HLA type individuals in other contexts.

[0154] Experiments were conducted during development of embodiments of the present disclosure in order to determine if a subset of plasma donors could be identified as strong (e.g., high) humoral immune responders in the absence of HLA typing. For example, the identification of individual subjects, or a population of individuals, that are strong humoral immune responders may itself be useful in order to identify individuals as potential plasma donors (e.g., for the manufacture of immunoglobulin). In addition, experiments were conducted in order to determine if individuals could be identified that were strong responders not only to a single microbial pathogen but to a plurality of microbial pathogens (e.g., such an individual, or population of individuals, may contain high titers due to the strength of humoral immune response in the subject, not just to a single microbial pathogen/antigen but to a plurality of microbial pathogens/antigens (e.g., any or all of the microbial pathogens/antigens to which the individual, or population of individuals, had been exposed in the course of their lifetime (s)). Thus, experiments were conducted in an effort to identify plasma donors as generally high responders in the absence of having to tissue type (e.g., HLA type) the donors for a specific histocompatibility gene complex. To this end, plasma donor samples were studied and characterized for antibody titers for one or a plurality respiratory pathogens in order to characterize the donors (e.g., as a high/strong responder to antigen challenge via generation of elevated levels of antibodies versus donors that are not strong responders/do not generate elevated levels of antibodies (e.g., via determining antibody titers to one or more respiratory pathogens in the subjects)).

[0155] Respiratory pathogens were chosen because individuals are ubiquitously exposed to a plurality of respiratory pathogens. That is, almost all adult and pediatric human populations have been exposed to a plurality of respiratory pathogens and would have therefore generated at some point in their lifetime a humoral antibody response that is measurable. Experiments were conducted in order to determine if high/strong responders could be identified using antibody titers to one or a plurality of respiratory pathogens. In one non-limiting example described below, experiments were conducted in order to determine if antibody titer to respiratory syncytial virus (RSV) in a donor plasma sample could be used to predict the antibody titer to other respiratory pathogens in the donor plasma sample. For example, experiments were performed in order to determine if high antibody titer to a respiratory pathogen (e.g., RSV) could be used as a biomarker to identify a donor as an overall high/strong responder to antigen challenge (e.g., to a plurality of respiratory or other pathogens) via generation of elevated levels of antibodies, versus donors that are not strong responders/do not generate elevated levels of antibodies.

[0156] As shown in Tables 3 and 4 (below), a proportional and positive correlation was found among the observed antibody titers of coronavirus and the observed titers to other non-coronavirus pathogens. Table 3 includes ratios of geometric means (95% CI) from data comparing neutralizing antibody titers for various viral pathogens from commercial IVIG (left number within parentheses) and plasma from subjects administered ASCENIV (right number within parentheses). These data indicated that plasma samples identified as having elevated coronavirus titer value also possessed elevated titers to other non-coronavirus pathogens, such as RSV. Calculated fold changes in antibody titers

are provided in Table 4, and demonstrate a 5.9 fold increase in coronavirus OC43 and a 5.5 fold increase in coronavirus 229E based on administration to a human subject of at least a 500 mg/kg dose of ASCENIV.

TABLE 3

Correlation Between Titers to RSV and Titers to Non-RSV Respiratory Virus.

Virus	Ratio of geometric means (95% CI) (ASCENIV/ commercial IGIV)[a]	p Value[b]
RSV	1.861 (1.249, 2.771)	0.003
PIV1	1.792 (1.282, 2.505)	0.001
OC43	1.610 (1.127, 2.301)	0.010
PIV2	1.601 (1.160, 2.210)	0.005
229E	1.494 (1.144, 1.950)	0.004
Flu A	1.402 (1.067, 1.843)	0.016
Flu B	1.316 (1.026, 1.688)	0.031
hMPV	1.264 (0.990, 1.613)	0.060
PIV 1 and 2	1.694 (1.250, 2.296)	0.001
OC43 and 229E	1.551 (1.237, 1.945)	<0.001
All viruses[c]	1.529 (1.227, 1.907)	<0.001

[a]Three randomly selected RI-002 batches and seven unselected commercial lots of IGIV from four different manufactures/brands
[b]Two-group t-test for null hypothesis of no difference between the groups in geometric means (i.e., ratio of geometric means = 1).
[c]Pooled RSV, respiratory syncytial virus; Flu A, influenza A; FluB, influenza B; hMPV, human metapneumovirus; PIV1, parainfluenza virus serotypes 1; PIV2, parainfluenza virus serotypes 2; OC43, coronavirus CoV OC43; 229E, coronaviruses CoV 229E.

TABLE 4

Calculated fold change in antibody titers after ASCENIV administration.

Virus	Calculated Fold Change Antibody Titers
RSV	6.790
PIV1 and 3	6.538
OC43	5.874
PIV2	5.841
229E	5.451
Flu A	5.115
Flu B	4.802
hMPV	4.612
PIV 1 and 2	6.181
OC43 and 229E	5.659
All viruses[a]	NA

[a]Pooled RSV, respiratory syncytial virus; Flu A, influenza A; FluB, influenza B; hMPV, human metapneumovirus; PIV1, parainfluenza virus serotypes 1; PIV2, parainfluenza virus serotypes 2; OC43, coronavirus CoV OC43; 229E, coronaviruses CoV 229E.

[0157] The above data is based on measured values for RSV neutralizing antibodies in ASCENIV at ≥500 mg/kg in phase 3 manuscript at fold increase of 6.790 and ratio of geometric means. Calculation: Fold change RSV/Ratio of means RSV=Fold change virus/Ratio of means virus. Calculated example for PIV1 and 3: 6.790/1.861=X/1.792; X=6.538 for PIV 1 and 3.

[0158] Together these data demonstrate that hyperimmune globulin compositions comprising pooled plasma samples and/or immunoglobulin prepared therefrom having increased neutralizing antibody titers against RSV, for example, also have elevated neutralizing antibody titers against coronavirus (coronavirus OC43, coronavirus 229E and if measured would have elevated titers to other respiratory viruses including coronavirus NL63, coronavirus HKU1, MERS-CoV, SARS-CoV, SARS-CoV-2 (COVID-19)). The data also suggest that hyperimmune globulin compositions comprising pooled plasma samples and/or immunoglobulin prepared therefrom having increased neutralizing antibody titers against coronavirus (coronavirus OC43, coronavirus 229E, coronavirus NL63, coronavirus HKU1, MERS-CoV, SARS-CoV, SARS-CoV-2 (COVID-19)) also have elevated neutralizing antibody titers against at least a second virus (e.g., RSV).

[0159] As described further herein, the compositions include pooled plasma samples and/or immunoglobulin prepared therefrom, which can be obtained from a plurality of donor human subjects (e.g., 100, 200, 300, 400, 500 or more subjects). In some embodiments, a pooled sample comprising higher neutralizing antibody titers against one virus can also have proportionally higher neutralizing antibody titers against other viruses. For example, as described further herein, pooled plasma samples can be obtained from a plurality of donor human subjects having increased antibody titers against a coronavirus (e.g., at least 1.2 fold greater than antibody titers from a corresponding control sample or an antibody neutralization titer from at least 40 to about 30,000), and these pooled plasma samples can also have proportionally increased antibody titers against at least a second virus (e.g., at least 1.1 fold greater than antibody titers from a corresponding control sample or an antibody neutralization titer from at least 40 to about 30,000), including, but not limited to, respiratory syncytial virus (RSV), influenza A virus, influenza B virus, parainfluenza virus type 1, parainfluenza virus type 2, metapneumovirus, coronavirus OC43, coronavirus 229E, coronavirus NL63, coronavirus HKU1, MERS-CoV, SARS-CoV, and SARS-CoV-2 (COVID-19).

[0160] Accordingly, the present disclosure provides a blending/pooling process that provides a pooled plasma composition or immunoglobulin prepared from same that contains a standardized and reproducible level of respiratory pathogen (e.g., coronavirus) specific antibodies thereby providing a heretofore unavailable, consistent and reproducible immunoglobulin product (e.g., for use as IVIG). Experiments confirmed that a pooled plasma composition or immunoglobulin prepared from the same (e.g., 2500 liters of pooled plasma from 1000 donors with a final RSV neutralization titer of 1800) could be consistently generated from different groups of 1000 donors. Further experiments confirmed that a pooled plasma composition (e.g., 2500 liters of pooled plasma from 1000 donors with a final RSV neutralization titer of 1800) contained antibody levels to tetanus, measles and polio that prevent, or protect from, infection with same, and also contained elevated antibody titer(s) specific for the respiratory pathogens described herein.

[0161] Materials and Methods

[0162] Enzyme immunoassay (EIA) was performed to detect virus-specific serum IgG for nine respiratory viruses: influenza A and B, RSV, parainfluenza (PIV) virus serotypes 1, 2 and 3, human metapneumovirus (hMPV), and coronavirus 229E (CoV 229E) and coronavirus OC43 per published methods (See, e.g., Falsey et al., J Am Geriatr Soc. 1992; 40:115-119; Falsey et al., J Am Geriatr Soc. 1995; 43:30-36; Falsey et al., J Am Geriatr Soc. 1997; 45:706-711; Falsey et al., J Infect Dis. 2003; 187:785-790). Briefly, antigens were produced from virally infected whole cell lysates for all viruses except RSV. Purified viral surface glycoproteins were used as antigen for RSV EIA according to published methods (See, e.g., Falsey et al., J Am Geriatr Soc. 1992; 40:115-119). Serial two-fold dilutions of each sample were tested in duplicate. Data analysis was per-

formed via a paired-data approach. Data pairs were created by matching the donor ID within each ELISA assay run.

[0163] ELISA testing of IVIG was performed blinded to the type of sample. All samples were diluted with sample dilution buffer (PBS with 0.3% Tween 20 and 0.1 M EDTA) to a standard concentration of 50 mg of IgG per ml. Each viral antigen was diluted at previously determined concentration in bicarbonate buffer and coated separately on enzyme immunoassay microtiter plates and stored overnight in humidified chambers at 4° C. The following day, plates were washed and eight serial 2-fold dilutions in duplicate of unknown product were incubated on the antigen plates at room temperature in humidified chambers for 3 hours. The initial dilution of IVIG solution placed on antigen plates was 1:1600. Plates were then washed and bound IgG was detected with alkaline phosphatase conjugated goat anti-human IgG followed by substrate. A standard serum was included on each plate and the IgG titer for a specific virus was defined as the highest dilution with an optical density (OD) of 0.20.

[0164] Statistical Analysis. Titer data was tabulated with descriptive statistics of N (sample size, mean, geometric mean, standard deviation, minimum, median, and maximum). Difference between the RSV-IVIG and commercial IVIG (that is, Group 1 vs Group 2) were presented as the ratio of geometric means (RGM) and 95% Confidence intervals for the RGM was also provided. P-value for testing of the null hypothesis that the RGM equaled to 1 was produced based on 2-sample t-test at significance level of 0.05.

[0165] The properties of the IVIG from 1000 or more samples containing elevated levels of neutralizing antibody titers to one or more respiratory pathogens generated using the compositions and methods of the present disclosure is a significant advancement and improvement over other IVIG available in the art. In particular, the IVIG compositions of the present disclosure do not display or possess a neutralizing antibody titer for only a single pathogen (e.g., dominance for only one type of respiratory pathogens), but rather, through the methods of identifying donors and the blending processes developed and described herein, IVIG is provided that contains significantly elevated neutralizing titers to a plurality of respiratory pathogens and other pathogens, compared to the titers in 1000 randomly mixed plasma samples. The discovery of the use of neutralizing antibody titer to RSV (or other respiratory pathogen) as a biomarker to identify plasma donors that are high-titer selected donors (high/strong responders in general to respiratory pathogens (e.g., influenza A virus, influenza B virus, parainfluenza virus type 1, parainfluenza virus type 2, metapneumovirus, and coronavirus) makes possible the ability to identify donors and plasma that can be blended with non-high titer selected donors and non-selected donor plasma to provide a beneficial pooled plasma product. Thus, while an understanding of a mechanism is not needed to practice the embodiments of the present disclosure, and while these embodiments are not limited to any particular mechanism of action, in some embodiments, the present disclosure provides a heretofore unavailable pooled plasma composition (e.g., prepared according to the above described methods)) that contains a significant amount (e.g., greater than 50%) of non-high titer selected donor plasma (non-high titer RSV plasma) that provide therapeutic benefit not achievable with standard hyperimmune immune globulin (e.g., prepared from a limited number (e.g., 100-300) of plasma donors). In a further embodiment, due to the elevated levels of neutralizing antibody titers to one or a plurality of RSV, influenza A virus, influenza B virus, parainfluenza virus type 1, parainfluenza virus type 2, metapneumovirus, and coronavirus, such pooled plasma compositions provide a significantly improved therapeutic benefit to a subject administered the composition. For example, a pooled composition of the present disclosure, compared to pooled plasma samples obtained from 1000 or more random human subjects, provides viral neutralization properties against one or a plurality of respiratory pathogens or other pathogens that is not provided for by randomly pooled samples. In this way, a subject administered a composition of the present disclosure is able to fight off, or be treated for, infections that are not treatable with a composition of pooled plasma samples obtained from 1000 or more random human subjects or that are not treatable with a conventional hyperimmune immune globulin. For example, a pooled plasma composition according to the present disclosure (e.g., from 1000 or more samples wherein the pooled plasma composition comprises a neutralizing RSV antibody titer of 1800 or above and elevated levels of antibodies to one or more respiratory pathogens) when administered to a subject provides the subject the ability to fight off, or be treated for, infections that are not treatable with a composition of pooled plasma samples obtained from 1000 or more random human subjects and/or that are not treatable with a conventional hyperimmune immune globulin prepared from limited numbers of donors.

[0166] Whole Blood Assay. Automated whole blood analysis was carried out on blood samples collected in EDTA-containing tubes. Total number of white blood cells and lymphocytes was analyzed.

[0167] RSV plaque assay. Lung homogenates were clarified by centrifugation and diluted 1:10 and 1:100 in EMEM. Confluent HEp-2 monolayers in 24-well plates were infected in duplicates with 50 μl of sample per well starting with undiluted (neat) samples followed by diluted homogenates. After one hour incubation at 37° C. in a 5% CO_2 incubator, wells were overlayed with 0.75% methylcellulose medium and plates restored into the 37° C. incubator. After 4 days of incubation the overlay was removed and the cells were fixed with 0.1% crystal violet stain for one hour, then rinsed and air-dried. Plaques were counted and viral titers were expressed as plaque forming units per gram of tissue. Viral titer for a group was calculated as the geometric mean+ standard error for all animals in that group at a given time. Student-t test was applied to determine significance of change in viral replication between vehicle-treated and test groups, with $p<0.05$ indicating a statistically-significant difference.

[0168] Real-time PCR. Total RNA was extracted from homogenized lung, kidney or liver tissue using the RNeasy purification kit (QIAGEN). One μg of total RNA was used to prepare cDNA using QuantiTect Reverse Transcription Kit (Qiagen). For the real-time PCR reactions the QuantiFast SYBR Green PCR Kit (Qiagen) was used in a final volume of 25 μl, with final primer concentrations of 0.5 μM. Reactions were set up in 96-well trays. Amplifications were performed on a Bio-Rad iCycler for 1 cycle of 95° C. for 3 min, followed by 40 cycles of 95° C. for 10 sec, 60° C. for

10 sec, and 72° C. for 15 sec. The baseline cycles and cycle threshold (Ct) were calculated by the iQ5 software in the PCR Base Line Subtracted

[0169] Curve Fit mode. Relative quantification of DNA was applied to all samples. The standard curves were developed using serially-diluted cDNA sample most enriched in the transcript of interest (e.g., lungs from day 4 post-primary RSV infection). The Ct values were plotted against $\log_{10}$ cDNA dilution factor. These curves were used to convert the Ct values obtained for different samples to relative expression units. These relative expression units were then normalized to the level of β-actin mRNA ("housekeeping gene") expressed in the corresponding sample. For animal studies, mRNA levels were expressed as the geometric mean±SEM for all animals in a group at a given time.

[0170] Case Study: Clinical Use of a Hyperimmune Globulin in an Adult with Severe Acute Respiratory Distress Syndrome and Confirmed COVID-19 Disease

[0171] As demonstrated by the following clinical case study, the compositions and methods of the present disclosure are effective for treating a coronavirus infection in a human subject.

[0172] A 70-year-old African American male with bronchiectasis presented to the emergency room with a one week history of increasing dyspnea, dry cough, sudden onset of high-grade fevers and body chills. The patient's condition progressed to severe respiratory compromise and he was admitted to the hospital's intensive care unit (ICU). Initial blood chemistry was unremarkable. A complete blood count revealed a mild shift to the left and lymphopenia. Pan cultures were drawn and a complete viral panel was ordered including a COVID-19 diagnostic, which was later confirmed positive. Patient was empirically initiated on broad-spectrum anti-infectives, and methylprednisolone

[0173] On day 3 post-admission, saturating oxygen (502c) was 94% with pO_2 66 mmHg. A CT scan of the chest indicated progression of pulmonary disease with diffuse, primarily peripheral ground-glass opacities, consistent with COVID-19 pneumonia and atelectatic change in the left lower lobe with traction bronchiectasis. The patient was placed on high-flow nasal cannula (HFNC).

[0174] One week after admission, the patient's respiratory status further deteriorated with PaO_2 of 48 mmHg. A PaO_2/fraction of inspired oxygen (FiO_2; P/F) ratio of 80 was consistent with rapid progression to severe acute respiratory distress syndrome. The patient was intubated and placed on mechanical ventilation. Subsequent CT scans indicated bilateral pulmonary diffuse interstitial and ground-glass opacities with new trace left pleural effusion demonstrating progression of disease. Interleukin-6 serum levels were elevated at 29.3 pg/ml (reference: 0.0-15.5 pg/mL), prompting initiation of tocilizumab. Despite ongoing management and therapeutic interventions, respiratory function further declined during the next 7 days, as evidenced by increased density of ground glass opacities per CT scan and increasing respiratory distress.

[0175] On Day 11, patient was administered a novel immune globulin intravenous (IGIV), human-slra, 10% (ADMA Biologics) liquid therapeutic at 1500 mg/kg. Several broad-spectrum anti-infectives were discontinued and patient continued on hydroxychloroquine. Pulmonary status further declined over the course of several days, with continued progression of pneumonia (FIG. **1***a*). Worsening aeration of the lungs was noted with an associated continuation on mechanical ventilation and a P/F ratio of 200. Patient developed a new fever spike, prompting anti-infective modification and initiation of meropenem and micafungin. The patient received a second dose of the same IGIV, human-slra, 10% liquid on day 14 at 750 mg/kg. Tracheal aspirate swab continued to be negative for the respiratory viral pathogen panel. Four days later post Ig infusion, respiratory function improved with a positive end-expiratory pressure of 6 at 40% FiO_2. The patient was successfully extubated and placed on BIPAP followed by HFNC. Patient remained positive for SARS-CoV-2 infection (FIG. **1***b*). Day 28, 502c was 99% with an improved P/F ratio of 371. Patient showed no signs of dyspnea, fever, and chills, and was transferred to the rehabilitation unit after confirming negative for SARS-CoV-2. Patient was discharged from the hospital on Day 34.

[0176] This case describes the use of a polyclonal hyperimmune globulin composition containing elevated levels of antibodies to multiple respiratory viruses to treat a COVID-positive patient with rapidly progressive respiratory disease who failed multiple medical interventions. Previous research has demonstrated the clinical benefits of polyclonal immune globulin and hyperimmune globulin for treatment of many viral-mediated infection such as polio, measles, mumps, influenza A and B, H1N1, Ebola and coronaviruses including MERS-CoV, severe acute respiratory [SAR] virus, and SARS-CoV-2. However, in this specific case report, the specific Ig administered was unique in its plasma pool composition to standardize antibody concentrations to meet specifications for polio, measles, diphtheria and RSV. Although the anti-infective interventions administered to the patient may have synergized with the infused uniquely formulated Ig composition, it is worthwhile to note that the patient's improved pulmonary distress was not evident until after the administration of the novel immune globulin intravenous (IGIV), human-slra, 10% (ADMA Biologics) liquid therapeutic composition. Despite being administered late in the course of the COVID-19 disease, the high loading dose of this unique Ig composition containing elevated levels of anti-viral antibodies coupled with its anti-inflammatory effects demonstrates its clinical efficacy in treating viral infections.

[0177] Various modification, recombination, and variation of the described features and embodiments will be apparent to those skilled in the art without departing from the scope and spirit of embodiments of the present disclosure. Although specific embodiments have been described, it should be understood that the embodiment of the present disclosure as claimed should not be unduly limited to such specific embodiments. Indeed, various modifications of the described modes and embodiments that are obvious to those skilled in the relevant fields are intended to be within the scope of the following claims. All publications and patents mentioned in the present application and/or listed below are herein incorporated by reference in their entireties.

Sequences

Sequences referenced in the present disclosure are provided below:
SARS-CoV-2 (COVID-19); NCBI GenBank accession code MN908947:
MESLVPGFNEKTHVQLSLPVLQVRDVLVRGFGDSVEEVLSEARQHLKDGTCGLVEVEK
GVLPQLEQPYVFIKRSDARTAPHGHVMVELVAELEGIQYGRSGETLGVLVPHVGEIPVA
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RELNGGAYTRYVDNNFCGPDGYPLECIKDLLARAGKASCTLSEQLDFIDTKRGVYCCRE
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SPLYAFASEAARVVRSIFSRTLETAQNSVRVLQKAAITILDGISQYSLRLIDAMMFTSDLA
TNNLVVMAYITGGVVQLTSQWLTNIFGTVYEKLKPVLDWLEEKFKEGVEFLRDGWEIV
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Sequences
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SARS-CoV; NCBI GenBank accession code AY274119: MESLVLGVNEKTHVQLSLPVLQVRDVLVRGFGDSVEEALSEAREHLKNGTCGLVELEK GVLPQLEQPYVFIKRSDALSTNHGHKVVELVAEMDGIQYGRSGITLGVLVPHVGETPIA YRNVLLRKNGNKGAGGHSYGIDLKSYDLGDELGTDPIEDYEQNWNTKHGSGALRELTR ELNGGAVTRYVDNNFCGPDGYPLDCIKDFLARAGKSMCTLSEQLDYIESKRGVYCCRD HEHEIAWFTERSDKSYEHQTPFEIKSAKKFDTFKGECPKFVFPLNSKVKVIQPRVEKKKT EGFMGRIRSVYPVASPQECNNMHLSTLMKCNHCDEVSWQTCDFLKATCEHCGTENLVI EGPTTCGYLPTNAVVKMPCPACQDPEIGPEHSVADYHNHSNIETRLRKGGRTRCFGGCV FAYVGCYNKRAYWVPRASADIGSGHTGITGDNVETLNEDLLEILSRERVNININVGDFHLN EEVAIILASFSASTSAFIDTIKSLDYKSFKTIVESCGNYKVTKGKPVKGAWNIGQQRSVLT PLCGFPSQAAGVIRSIFARTLDAANHSIPDLQRAAVTILDGISEQSLRLVDAMVYTSDLLT NSVIIMAYVTGGLVQQTSQWLSNLLGTTVEKLRPIFEWIEAKLSAGVEFLKDAWEILKFL ITGVFDIVKGQIQVASDNIKDCVKCFIDVVNKALEMCIDQVTIAGAKLRSLNLGEVFIAQS KGLYRQCIRGKEQLQLLMPLKAPKEVTFLEGDSHDTVLTSEEVVLKNGELEALETPVDS FTNGAIVGTPVCVNGLMLLEIKDKEQYCALSPGLLATNNVFRLKGGAPIKGVTFGEDTV WEVQGYKNVRITFELDERVDKVLNEKCSVYTVESGTEVTEFACVVAEAVVKTLQPVSD LLTNMGIDLDEWSVATFYLFDDAGEENFSSRMYCSFYPPDEEEEDDAECEEEEIDETCEH EYGTEDDYQGLPLEFGASAETVRVEEEEEEDWLDDTTEQSEIEPEPEPTPEEPVNQFTGY LKLTDNVAIKCVDIVKEAQSANPMVIVNAANIHLKHGGGVAGALNKATNGAMQKESD DYIKLNGPLTVGGSCLLSGHNLAKKCLHVVGPNLNAGEDIQLLKAAYENFNSQDILLAP LLSAGIFGAKPLQSLQVCVQTVRTQVYIAVNDKALYEQVVMDYLDNLKPRVEAPKQEE PPNTEDSKTEEKSVVQKPVDVKPKIKACIDEVTTTLEETKFLTNKLLLFADINGKLYHDS QNMLRGEDMSFLEKDAPYMVGDVITSGDITCVVIPSKKAGGTTEMLSRALKKVPVDEYI TTYPGQGCAGYTLEEAKTALKKCKSAFYVLPSEAPNAKEEILGTVSWNLREMLAHAEE TRKLMPICMDVRAIMATIQRKYKGIKIQEGIVDYGVRFFFYTSKEPVASIITKLNSLNEPL VTMPIGYVTHGFNLEEAARCMRSLKAPAVVSVSSPDAVTTYNGYLTSSSKTSEEHFVET

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Sequences
VSLAGSYRDWSYSGQRTELGVEFLKRGDKIVYHTLESPVEFHLDGEVLSLDKLKSLLSL REVKTIKVFTTVDNTNLHTQLVDMSMTYGQQFGPTYLDGADVTKIKPHVNHEGKTFFV LPSDDTLRSEAFEYYHTLDESFLGRYMSALNHTKKWKFPQVGGLTSIKWADNNCYLSS VLLALQQLEVKFNAPALQEAYYRARAGDAANFCALILAYSNKTVGELGDVRETMTHLL QHANLESAKRVLNVVCKHCGQKTTTLTGVEAVMYMGTLSYDNLKTGVSIPCVCGRDA TQYLVQQESSFVMMSAPPAEYKLQQGTFLCANEYTGNYQCGHYTHITAKETLYRIDGA HLTKMSEYKGPVTDVFYKETSYTTTIKPVSYKLDGVTYTEIEPKLDGYYKKDNAYYTEQ PIDLVPTQPLPNASFDNFKLTCSNTKFADDLNQMTGFTKPASRELSVTFFPDLNGDVVAI DYRHYSASFKKGAKLLHKPIVWHINQATTKTTFKPNTWCLRCLWSTKPVDTSNSFEVL AVEDTQGMDNLACESQQPTSEEVVENPTIQKEVIECDVKTTEVVGNVILKPSDEGVKVT QELGHEDLMAAYVENTSITIKKPNELSLALGLKTIATHGIAAINSVPWSKILAYVKPFLGQ AAITTSNCAKRLAQRVFNNYMPYVFTLLFQLCTFTKSTNSRIRASLPTTIAKNSVKSVAK LCLDAGINYVKSPKFSKLFTIAMWLLLLSICLGSLICVTAAFGVLLSNFGAPSYCNGVREL YLNSSNVTTMDFCEGSFPCSICLSGLDSLDSYPALETIQVTISSYKLDLTILGLAAEWVLA YMLFTKFFYLLGLSAIMQVFFGYFASHFISNSWLMWFIISIVQMAPVSAMVRMYIFFASF YYIWKSYVHIMDGCTSSTCMMCYKRNRATRVECTTIVNGMKRSFYVYANGGRGFCKT HNWNCLNCDTFCTGSTFISDEVARDLSLQFKRPINPTDQSSYIVDSVAVKNGALHLYFD KAGQKTYERHPLSHFVNLDNLRANNTKGSLPINVIVFDGKSKCDESASKSASVYYSQLM CQPILLLDQALVSDVGDSTEVSVKMFDAYVDTFSATFSVPMEKLKALVATAHSELAKG VALDGVLSTFVSAARQGVVDTDVDTKDVIECLKLSHHSDLEVTGDSCNNFMLTYNKVE NMTPRDLGACIDCNARHINAQVAKSHNVSLIWNVKDYMSLSEQLRKQIRSAAKKNNIPF RLTCATTRQVVNVITTKISLKGGKIVSTCFKLMLKATLLCVLAALVCYIVMPVHTLSIHD GYTNEIIGYKAIQDGVTRDIISTDDCFANKHAGFDAWFSQRGGSYKNDKSCPVVAAIITR EIGFIVPGLPGTVLRAINGDFLHFLPRVFSAVGNICYTPSKLIEYSDFATSACVLAAECTIF KDAMGKPVPYCYDTNLLEGSISYSELRPDTRYVLMDGSIIQFPNTYLEGSVRVVTTFDAE YCRHGTCERSEVGICLSTSGRWVLNNEHYRALSGVFCGVDAMNLIANIFTPLVQPVGAL DVSASVVAGGIIAILVTCAAYYFMKFRRVFGEYNHVVAANALLFLMSFTILCLVPAYSFL PGVYSVFYLYLTFYFTNDVSFLAHLQWFAMFSPIVPFWITAIYVFCISLKHCHWFFNNYL RKRVMFNGVTFSTFEEAALCTFLLNKEMYLKLRSETLLPLTQYNRYLALYNKYKYFSG ALDTTSYREAACCHLAKALNDFSNSGADVLYQPPQTSITSAVLQSGFRKMAFPSGKVEG CMVQVTCGTTTLNGLWLDDTVYCPRHVICTAEDMLNPNYEDLLIRKSNHSFLVQAGNV QLRVIGHSMQNCLLRLKVDTSNPKTPKYKFVRIQPGQTFSVLACYNGSPSGVYQCAMRP NHTIKGSFLNGSCGSVGFNIDYDCVSFCYMHHMELPTGVHAGTDLEGKFYGPFVDRQT AQAAGTDTTITLNVLAWLYAAVINGDRWFLNRFTTTLNDFNLVAMKYNYEPLTQDHV DILGPLSAQTGIAVLDMCAALKELLQNGMNGRTILGSTILEDEFTPFDVVRQCSGVTFQG KFKKIVKGTHHWMLLTFLTSLLILVQSTQWSLFFFVYENAFLPFTLGIMAIAACAMLLVK HKHAFLCLFLLPSLATVAYFNMVYMPASWVMRIMTWLELADTSLSGYRLKDCVMYAS ALVLLILMTARTVYDDAARRVWTLMNVITLVYKVYYGNALDQAISMWALVISVTSNYS GVVTTIMFLARAIVFVCVEYYPLLFITGNTLQCIMLVYCFLGYCCCCYFGLFCLLNRYFR LTLGVYDYLVSTQEFRYMNSQGLLPPKSSIDAFKLNIKLLGIGGKPCIKVATVQSKMSDV KCTSVVLLSVLQQLRVESSSKLWAQCVQLHNDILLAKDTTEAFEKMVSLLSVLLSMQG AVDINRLCEEMLDNRATLQAIASEFSSLPSYAAYATAQEAYEQAVANGDSEVVLKKLK KSLNVAKSEFDRDAAMQRKLEKMADQAMTQMYKQARSEDKRAKVTSAMQTMLFTM LRKLDNDALNNIINNARDGCVPLNIIPLTTAAKLMVVVPDYGTYKNTCDGNTFTYASAL WEIQQVVDADSKIVQLSEINMDNSPNLAWPLIVTALRANSAVKLQNNELSPVALRQMSC AAGTTQTACTDDNALAYYNNSKGGRFVLALLSDHQDLKWARFPKSDGTGTIYTELEPP CRFVTDTPKGPKVKYLYFIKGLNNLNRGMVLGSLAATVRLQAGNATEVPANSTVLSFC AFAVDPAKAYKDYLASGGQPITNCVKMLCTHTGTGQAITVTPEANMDQESFGGASCCL YCRCHIDHPNPKGFCDLKGKYVQIPTTCANDPVGFTLRNTVCTVCGMWKGYGCSCDQL REPLMQSADASTFFKRVCGVSAARLTPCGTGTSTDVVYRAFDIYNEKVAGFAKFLKTNC CRFQEKDEEGNLLDSYFVVKRHTMSNYQHEETIYNLVKDCPAVAVHDFFKFRVDGDM VPHISRQRLTKYTMADLVYALRHFDEGNCDTLKEILVTYNCCDDDYFNKKDWYDFVEN PDILRVYANLGERVRQSLLKTVQFCDAMIRDAGIVGVLTLDNQDLNGNWYDFGDFVQV APGCGVPIVDSYYSLLMPILTLTRALAAESHMDADLAKPLIKWDLLKYDFTEERLCLFD RYFKYWDQTYHPNCINCLDDRCILHCANFNVLFSTVFPPTSFGPLVRKIFVDGVPFVVST GYHFRELGVVHNQDVNLHSSRLSFKELLVYAADPAMHAASGNLLLDKRTTCFSVAALT NNVAFQTVKPGNFNKDFYDFAVSKGFFKEGSSVELKHFFFAQDGNAAISDYDYYRYNL PTMCDIRQLLFVVEVVDKYFDCYDGGCINANQVIVNNLDKSAGFPFNKWGKARLYYDS MSYEDQDALFAYTKRNVIPTITQMNLKYAISAKNRARTVAGVSICSTMTNRQFHQKLLK SIAATRGATVVIGTSKFYGGWHNMLKTVYSDVETPHLMGWDYPKCDRAMPNMLRIMA SLVLARKHNTCCNLSHRFYRLANECAQVLSEMVMCGGSLYVKPGGTSSGDATTAYAN SVFNICQAVTANVNALLSTDGNKIADKYVRNLQHRLYECLYRNRDVDHEFVDEFYAYL RKHFSMMILSDDAVVCYNSNYAAQGLVASIKNFKAVLYYQNNVFMSEAKCWTETDLT KGPHEFCSQHTMLVKQGDDYVYLPYPDPSRILGAGCFVDDIVKTDGTLMIERFVSLAID AYPLTKHPNQEYADVFHLYLQYIRKLHDELTGHMLDMYSVMLTNDNTSRYWEPEFYE AMYTPHTVLQAVGACVLCNSQTSLRCGACIRRPFLCCKCCYDHVISTSHKLVLSVNPYV CNAPGCDVTDVTQLYLGGMSYYCKSHKPPISFPLCANGQVFGLYKNTCVGSDNVTDFN AIATCDWTNAGDYILANTCTERLKLFAAETLKATEETFKLSYGIATVREVLSDRELHLS WEVGKPRPPLNRNYVFTGYRVTKNSKVQIGEYTFEKGDYGDAVVYRGTTTYKLNVGD YFVLTSHTVMPLSAPTLVPQEHYVRITGLYPTLNISDEFSSNVANYQKVGMQKYSTLQG PPGTGKSHFAIGLALYYPSARIVYTACSHAAVDALCEKALKYLPIDKCSRIIPARARVECF DKFKVNSTLEQYVFCTVNALPETTADIVVFDEISMATNYDLSVVNARLRAKHYVYIGDP AQLPAPRTLLTKGTLEPEYFNSVCRLMKTIGPDMFLGTCRRCPAEIVDTVSALVYDNKL KAHKDKSAQCFKMFYKGVITHDVSSAINRPQIGVVREFLTRNPAWRKAVFISPYNSQNA

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Sequences
VASKILGLPTQTVDSSQGSEYDYVIFTQTTETAHSCNVNRFNVAITRAKIGILCIMSDRDL YDKLQFTSLEIPRRNVATLQAENVTGLFKDCSKIITGLHPTQAPTHLSVDIKFKTEGLCVD IPGIPKDMTYRRLISMMGFKMNYQVNGYPNMFITREEAIRHVRAWIGFDVEGCHATRD AVGTNLPLQLGFSTGVNLVAVPTGYVDTENNTEFTRVNAKPPPGDQFKHLIPLMYKGLP WNVVRIKIVQMLSDTLKGLSDRVVFVLWAHGFELTSMKYFVKIGPERTCCLCDKRATC FSTSSDTYACWNHSVGFDYVYNPFMIDVQQWGFTGNLQSNHDQHCQVHGNAHVASCD AIMTRCLAVHECFVKRVDWSVEYPIIGDELRVNSACRKVQHMVVKSALLADKFPVLHD IGNPKAIKCVPQAEVEWKFYDAQPCSDKAYKIEELFYSYATHHDKFTDGVCLFWNCNV DRYPANAIVCRFDTRVLSNLNLPGCDGGSLYVNKHAFHTPAFDKSAFTNLKQLPFFYYS DSPCESHGKQVVSDIDYVPLKSATCITRCNLGGAVCRHHANEYRQYLDAYNMMISAGF SLWIYKQFDTYNLWNTFTRLQSLENVAYNVVNKGHFDGHAGEAPVSIINNAVYTKVDG IDVEIFENKTTLPVNVAFELWAKRNIKPVPEIKILNNLGVDIAANTVIWDYKREAPAHVS TIGVCTMTDIAKKPTESACSSLTVLFDGRVEGQVDLFRNARNGVLITEGSVKGLTPSKGP AQASVNGVTLIGESVKTQFNYFKKVDGIIQQLPETYFTQSRDLEDFKPRSQMETDFLELA MDEFIQRYKLEGYAFEHIVYGDFSHGQLGGLHLMIGLAKRSQDSPLKLEDFIPMDSTVK NYFITDAQTGSSKCVCSVIDLLLDDFVEIIKSQDLSVISKVVKVTIDYAEISFMLWCKDGH VETFYPKLQASQAWQPGVAMPNLYKMQRMLLEKCDLQNYGENAVIPKGIMMNVAKY TQLCQYLNTLTLAVPYNMRVIHFGAGSDKGVAPGTAVLRQWLPTGTLLVDSDLNDFVS DADSTLIGDCATVHTANKWDLIISDMYDPRTKHVTKENDSKEGFFTYLCGFIKQKLALG GSIAVKITEHSWNADLYKLMGHFSWWTAFVTNVNASSSEAFLIGANYLGKPKEQIDGYT MHANYIFWRNTNPIQLSSYSLFDMSKFPLKLRGTAVMSLKENQINDMIYSLLEKGRLIIR ENNRVVVSSDILVNN (SEQ ID NO: 2)
MERS-CoV; NCBI GenBank accession code NC_019843: MSFVAGVTAQGARGTYRAALNSEKHQDHVSLTVPLCGSGNLVEKLSPWFMDGENAYE VVKAMLLKKEPLLYVPIRLAGHTRHLPGPRVYLVERLIACENPFMVNQLAYSSSANGSL VGTTLQGKPIGMFFPYDIELVTGKQNILLRKYGRGGYHYTPPHYERDNTSCPEWMDDFE ADPKGKYAQNLLKKLIGGDVTPVDQYMCGVDGKPISAYAFLMAKDGITKLADVEADV AARADDEGFITLKNNLYRLVWHVERKDVPYPKQSIFTINSVVQKDGVENTPPHYFTLGC KILTLTPRNKWSGVSDLSLKQKLLYTFYGKESLENPTYIYHSAFIECGSCGNDSWLTGNA IQGFACGCGASYTANDVEVQSSGMIKPNALLCATCPFAKGDSCSSNCKHSVAQLVSYLS ERCNVIADSKSFTLIFGGVAYAYFGCEEGTMYFVPRAKSVVSRIGDSIFTGCTGSWNKVT QIANMFLEQTQHSLNFVGEFVVNDVVLAILSGTTTNVDKIRQLLKGVTLDKLRDYLADY DVAVTAGPFMDNAINVGGTGLQYAAITAPYVVLTGLGESFKKVATIPYKVCNSVKDTL AYYAHSVLYRVFPYDMDSGVSSFSELLFDCVDLSVASTYFLVRILQDKTGDFMSTIITSC QTAVSKLLDTCFEATEATFNFLLDLAGLFRIFLRNAYVYTSQGFVVVNGKVSTLVKQVL DLLNKGMQLLHTKVSWAGSKIIAVIYSGRESLIFPSGTYYCVTTKAKSVQQDLDVILPGE FSKKQLGLLQPTDNSTTVSVTVSSNMVETVVGQLEQTNMHSPDVIVGDYVIISEKLFVRS KEEDGFAFYPACTNGHAVPTLFRLKGGAPVKKVAFGGDQVHEVAAVRSVTVEYNIHA VLDTLLASSSLRTFVVDKSLSIEEFADVVKEQVSDLLVKLLRGMPIPDFDLDDFIDAPCY CFNAEGDASWSSTMIFSLHPVECDEECSEVEASDLEEGESECISETSTEQVDVSHETSDDE WAAAVDEAFPLDEAEDVTESVQEEAQPVEVPVEDIAQVVIADTLQETPVVPDTVEVPPQ VVKLPSAPQTIQPEVKEVAPVYEADTEQTQNVTVKPKRLRKKRNVDPLSNFEHKVITEC VTIVLGDAIQVAKCYGESVLVNAANTHLKHGGGIAGAINAASKGAVQKESDEYILAKGP LQVGDSVLLQGHSLAKNILHVVGPDARAKQDVSLLSKCYKAMNAYPLVVTPLVSAGIF GVKPAVSFDYLIREAKTRVLVVVNSQDVYKSLTIVDIPQSLTFSYDGLRGAIRKAKDYGF TVFVCTDNSANTKVLRNKGVDYTKKFLTVDGVQYYCYTSKDTLDDILQQANKSVGIIS MPLGYVSHGLDLMQAGSVVRRVNVPYVCLLANKEQEAILMSEDVKLNPSEDFIKHVRT NGGYNSWHLVEGELLVQDLRLNKLLHWSDQTICYKDSVFYVVKNSTAFPFETLSACRA YLDSRTTQQLTIEVLVTVDGVNFRTVVLNNKNTYRSQLGCVFFNGADISDTIPDEKQNG HSLYLADNLTADETKALKELYGPVDPTFLHRFYSLKAAVHGWKMVVCDKVRSLKLSD NNCYLNAVIMTLDLLKDIKFVIPALQHAFMKHKGGDSTDFIALIMAYGNCTFGAPDDAS RLLHTVLAKAELCCSARMVWREWCNVCGIKDVVLQGLKACCYVGVQTVEDLRARMT YVCQCGGERHRQLVEHTTPWLLLSGTPNEKLVTTSTAPDFVAFNVFQGIETAVGHYVH ARLKGGLILKFDSGTVSKTSDWKCKVTDVLFPGQKYSSDCNVVRYSLDGNFRTEVDPD LSAFYVKDGKYFTSEPPVTYSPATILAGSVYTNSCLVSSDGQPGGDAISLSFNNLLGFDSS KPVTKKYTYSFLPKEDGDVLLAEFDTYDPIYKNGAMYKGKPILWVNKASYDTNLNKFN RASLRQIFDVAPIELENKFTPLSVESTPVEPPTVDVVALQQEMTIVKCKGLNKPFVKDNV SFVADDSGTPVVEYLSKEDLHTLYVDPKYQVIVLKDNVLSSMLRLHTVESGDINVVAAS GSLTRKVKLLFRASFYFKEFATRTFTATTAVGSCIKSVVRHLGVTKGILTGCFSFAKMLF MLPLAYFSDSKLGTTEVKVSALKTAGVVTGNVVKQCCTAAVDLSMDKLRRVDWKSTL RLLLMLCTTMVLLSSVYHLYVFNQVLSSDVMFEDAQGLKKFYKEVRAYLGISSACDGL ASAYRANSFDVPTFCANRSAMCNWCLISQDSITHYPALKMVQTHLSHYVLNIDWLWFA FETGLAYMLYTSAFNWLLLAGTLHYFFAQTSIFVDWRSYNYAVSSAFWLFTHIPMAGL VRMYNLLACLWLLRKFYQHVINGCKDTACLLCYKRNRLTRVEASTVVCGGKRTFYITA NGGISFCRRHNWNCVDCDTAGVGNTFICEEVANDLTTALRRPINATDRSHYYVDSVTV KETVVQFNYRRDGQPFYERFPLCAFTNLDKLKFKEVCKTTTGIPEYNFIIYDSSDRGQES LARSACVYYSQVLCKSILLVDSSLVTSVGDSSEIATKMFDSFVNSFVSLYNVTRDKLEKL ISTARDGVRRGDNFHSVLTTFIDAARGPAGVESDVETNEIVDSVQYAHKHDIQITNESYN NYVPSYVKPDSVSTSDLGSLIDCNAASVNQIVLRNSNGACIWNAAAYMKLSDALKRQIR IACRKCNLAFRLTTSKLRANDNILSVRFTANKIVGGAPTWFNALRDFTLKGYVLATIIVF LCAVLMYLCLPTFSMAPVEFYEDRILDFKVLDNGIIRDVNPDDKCFANKHRSFTQWYHE HVGGVYDNSITCPLTVAVIAGVAGARIPDVPTTLAWVNNQIIFFVSRVFANTGSVCYTPI DEIPYKSFSDSGCILPSECTMFRDAEGRMTPYCHDPTVLPGAFAYSQMRPHVRYDLYDG

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Sequences
NMFIKFPEVVFESTLRITRTLSTQYCRFGSCEYAQEGVCITTNGSWAIFNDHHLNRPGVY CGSDFIDIVRRLAVSLFQPITYFQLTTSLVLGIGLCAFLTLLFYYINKVKRAFADYTQCAVI AVVAAVLNSLCICFVTSIPLCIVPYTALYYYATFYFTNEPAFIMHVSWYIMFGPIVPIWMT CVYTVAMCFRHFFWVLAYFSKKHVEVFTDGKLNCSFQDAASNIFVINKDTYAALRNSL TNDAYSRFLGLFNKYKYFSGAMETAAYREAAACHLAKALQTYSETGSDLLYQPPNCSIT SGVLQSGLVKMSHPSGDVEACMVQVTCGSMTLNGLWLDNTVWCPRHVMCPADQLSD PNYDALLISMTNHSFSVQKHIGAPANLRVVGHAMQGTLLKLTVDVANPSTPAYTFTTV KPGAAFSVLACYNGRPTGTFTVVMRPNYTIKGSFLCGSCGSVGYTKEGSVINFCYMHQ MELANGTHTGSAFDGTMYGAFMDKQVHQVQLTDKYCSVNVVAWLYAAILNGCAWF VKPNRTSVVSFNEWALANQFTEFVGTQSVDMLAVKTGVAIEQLLYAIQQLYTGFQGKQI LGSTMLEDEFTPEDVNMQIMGVVMQSGVRKVTYGTAHWLFATLVSTYVIILQATKFTL WNYLFETIPTQLFPLLFVTMAFVMLLVKHKHTFLTLFLLPVAICLTYANIVYEPTTPISSA LIAVANWLAPTNAYMRTTHTDIGVYISMSLVLVIVVKRLYNPSLSNFALALCSGVMWL YTYSIGEASSPIAYLVFVTTLTSDYTITVFVTVNLAKVCTYAIFAYSPQLTLVFPEVKMILL LYTCLGFMCTCYFGVFSLLNLKLRAPMGVYDFKVSTQEFRFMTANNLTAPRNSWEAM ALNFKLIGIGGTPCIKVAAMQSKLTDLKCTSVVLLSVLQQLHLEANSRAWAFCVKCHND ILAATDPSEAFEKFVSLFATLMTFSGNVDLDALASDIFDTPSVLQATLSEFSHLATFAELE AAQKAYQEAMDSGDTSPQVLKALQKAVNIAKNAYEKDKAVARKLERMADQAMTSM YKQARAEDKKAKIVSAMQTMLFGMIKKLDNDVLNGIISNARNGCIPLSVIPLCASNKLR VVIPDFTVWNQVVTYPSLNYAGALWDITVINNVDNEIVKSSDVVDSNENLTWPLVLECT RASTSAVKLQNNEIKPSGLKTMVVSAGQEQTNCNTSSLAYYEPVQGRKMLMALLSDNA YLKWARVEGKDGFVSVELQPPCKFLIAGPKGPEIRYLYFVKNLNNLHRGQVLGHIAATV RLQAGSNTEFASNSSVLSLVNFTVDPQKAYLDFVNAGGAPLTNCVKMLTPKTGTGIAIS VKPESTADQETYGGASVCLYCRAHIEHPDVSGVCKYKGKFVQIPAQCVRDPVGFCLSNT PCNVCQYWIGYGCNCDSLRQAALPQSKDSNFLNRVRGSIVNARIEPCSSGLSTDVVFRA FDICNYKAKVAGIGKYYKTNTCRFVELDDQGHHLDSYFVVKRHTMENYELEKHCYDLL RDCDAVAPHDFFIFDVDKVKTPHIVRQRLTEYTMMDLVYALRHFDQNSEVLKAILVKY GCCDVTYFENKLWFDFVENPSVIGVYHKLGERVRQAILNTVKFCDHMVKAGLVGVLTL DNQDLNGKWYDFGDFVITQPGSGVAIVDSYYSYLMPVLSMTDCLAAETHRDCDFNKPL IEWPLTEYDFTDYKVQLFEKYFKYWDQTYHANCVNCTDDRCVLHCANFNVLFAMTMP KTCFGPIVRKIFVDGVPFVVSCGYHYKELGLVMNMDVSLHRHRLSLKELMMYAADPA MHIASSNAFLDLRTSCFSVAALTTGLTFQTVRPGNFNQDFYDFVVSKGFFKEGSSVTLKH FFFAQDGNAAITDYNYYSYNLPTMCDIKQMLFCMEVVNKYFEIYDGGCLNASEVVVNN LDKSAGHPFNKFGKARVYYESMSYQEQDELFAMTKRNVIPTMTQMNLKYAISAKNRA RTVAGVSILSTMTNRQYHQKMLKSMAATRGATCVIGTTKFYGGWDFMLKTLYKDVDN PHLMGWDYPKCDRAMPNMCRIFASLILARKHGTCCTTRDRFYRLANECAQVLSEYVLC GGGYYVKPGGTSSGDATTAYANSVFNILQATTANVSALMGANGNKIVDKEVKDMQFD LYVNVYRSTSPDPKFVDKYYAFLNKHFSMMILSDDGVVCYNSDYAAKGYIAGIQNFKE TLYYQNNVFMSEAKCWVETDLKKGPHEFCSQHTLYIKDGDDGYFLPYPDPSRILSAGCF VDDIVKTDGTLMVERFVSLAIDAYPLTKHEDIEYQNVFWVYLQYIEKLYKDLTGHMLD SYSVMLCGDNSAKFWEEAFYRDLYSSPTTLQAVGSCVVCHSQTSLRCGTCIRRPFLCCK CCYDHVIATPHKMVLSVSPYVCNAPGCGVSDVTKLYLGGMSYFCVDHRPVCSFPLCAN GLVFGLYKNMCTGSPSIVEFNRLATCDWTESGDYTLANTTTEPLKLFAAETLRATEEAS KQSYAIATIKEIVGERQLLLVWEAGKSKPPLNRNYVFTGYHITKNSKVQLGEYIFERIDYS DAVSYKSSTTYKLTVGDIFVLTSHSVATLTAPTIVNQERYVKITGLYPTITVPEEFASHVA NFQKSGYSKYVTVQGPPGTGKSHFAIGLAIYYPTARVVYTACSHAAVDALCEKAFKYL NIAKCSRIIPAKARVECYDRFKVNETNSQYLFSTINALPETSADILVVDEVSMCTNYDLSII NARIKAKHIVYVGDPAQLPAPRTLLTRGTLEPENFNSVTRLMCNLGPDIFLSMCYRCPKE IVSTVSALVYNNKLLAKKELSGQCFKILYKGNVTHDASSAINRPQLTFVKNFITANPAWS KAVFISPYNSQNAVSRSMLGLTTQTVDSSQGSEYQYVIFCQTADTAHANNINRFNVAITR AQKGILCVMTSQALFESLEFTELSFTNYKLQSQIVTGLFKDCSRETSGLSPAYAPTYVSV DDKYKTSDELCVNLNLPANVPYSRVISRMGFKLDATVPGYPKLFITREEAVRQVRSWIG FDVEGAHASRNACGTNVPLQLGFSTGVNFVVQPVGVVDTEWGNMLTGIAARPPPGEQF KHLVPLMHKGAAWPIVRRRIVQMLSDTLDKLSDYCTFVCWAHGFELTSASYFCKIGKE QKCCMCNRRAAAYSSPLQSYACWTHSCGYDYVYNPFFVDVQQWGYVGNLATNHDRY CSVHQGAHVASNDAIMTRCLAIHSCFIERVDWDIEYPYISHEKKLNSCCRIVERNVVRAA LLAGSFDKVYDIGNPKGIPIVDDPVVDWHYFDAQPLTRKVQQLFYTEDMASRFADGLC LFWNCNVPKYPNNAIVCRFDTRVHSEFNLPGCDGGSLYVNKHAFHTPAYDVSAFRDLK PLPFFYYSTTPCEVHGNGSMIEDIDYVPLKSAVCITACNLGGAVCRKHATEYREYMEAY NLVSASGFRLWCYKTFDIYNLWSTFTKVQGLENIAFNVVKQGHFIGVEGELPVAVVND KIFTKSGVNDICMFENKTTLPTNIAFELYAKRAVRSHPDFKLLHNLQADICYKFVLWDYE RSNIYGTATIGVCKYTDIDVNSALNICFDIRDNCSLEKFMSTPNAIFISDRKIKKYPCMVG PDYAYFNGAIIRDSDVVKQPVKFYLYKKVNNEFIDPTECIYTQSRSCSDFLPLSDMEKDF LSFDSDVFIKKYGLENYAFEHVVYGDFSHTTLGGLHLLIGLYKKQQEGHIIMEEMLKGSS TIHNYFITETNTAAFKAVCSVIDLKLDDFVMILKSQDLGVVSKVVKVPIDLTMIEFMLWC KDGQVQTFYPRLQASADWKPGHAMPSLFKVQNVNLERCELANYKQSIPMPRGVHMNI AKYMQLCQYLNTCTLAVPANMRVIHFGAGSDKGIAPGTSVLRQWLPTDAIIIDNDLNEF VSDADITLFGDCVTVRVGQQVDLVISDMYDPTTKNVTGSNESKALFFTYLCNLINNNLA LGGSVAIKITEHSWSVELYELMGKFAWWTVFCTNANASSSEGFLLGINYLGTIKENIDGG AMHANYIFWRNSTPMNLSTYSLFDLSKFQLKLKGTPVLQLKESQINELVISLLSQGKLLI RDNDTLSVSTDVLVNTYRKLR (SEQ ID NO: 3)

HKU1 (beta coronavirus); NCBI GenBank accession code KF686346:
MIKTSKYGLGFKWAPEFRWLLPDAAEELASPMKSDEGGLCPSTGQAMESVGFVYDNH

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Sequences
VKIDCRCILGQEWHVQSNLIRDIFVHEDLHVVEVLTKTAVKSGTAILIKSPLHSLGGFPKG YVMGLFRSYKTKRYVVHHLSMTTSTTNFGEDFLGWIVPFGFMPSYVHKWFQFCRLYIE ESDLIISNFKFDDYDFSVEDVYAEVHAEPKGKYSQKAYALLRQYRGIKPVLFVDQYGCD YSGKLADCLQAYGHYSLQDMRQKQSVWLANCDFDIVVAWHVVRDSRFVMRLQTIATI CGIKYVAQPTEDVVDGDVVIREPVHLLSADAIVLKLPSLMKVMTHMDDFSIKSIYNVDL CDCGFVMQYGYVDCFNDNCDFYGWVSGNMMDGFSCPLCCTVYDSSEVKAQSSGVIPE NPVLFTNSTDTVNHDSFNLYGYSVTPFGSCIYWSPRPGLWIPIIKSSVKSYDDLVYSGVV GCKSIVKETALITHALYLDYVQCKCGNLEQNHILGVNNSWCRQLLLNRGDYNMLLKNI DLFVKRRADFACKFAVCGDGFVPFLLDGLIPRSYYLIQSGIFFTSLMSQFSQEVSDMCLK MCILFMDRVSVATFYIEHYVNRLVTQFKLLGTTLVNKMVNWFNTMLDASAPATGWLL YQLLNGLFVVSQANFNFVALIPDYAKILVNKFYTFFKLLLECVTVDVLKDMPVLKTING LVCIVGNKFYNVSTGLIPGFVLPCNAQEQQIYFFEGVAESVIVEDDVIENVKSSLSSYEYC QPPKSVEKICIIDNMYMGKCGDKFFPIVMNDKNICLLDQAWRFPCAGRKVNFNEKPVV MEIPSLMTVKVMFDLDSTFDDILGKVCSEFEVEKGVTVDDFVAVVCDAIENALNSCKEH PVVGYQVRAFLNKLNDNVVYLFDEAGDEAMASRMYCTFAIEDVEDVISSEAVEDTIDGI VEDTINDDEDVVTGDNDDEDVVTGDNDDEDVVTGDNDDEDVVTGDNDDEDVVTGDN DDEDVVTGDNDDEDVVTGDNDDEDVVTGDNDDEDVVTGDNDDEDVVTGDNDDEDV VTGDNDDEDVVTGDNDDEDVVTGDNDDEDVVTGDNDDEDVVTGDNDDEDVVTGDN DDEDVVTGDNDDEDNNDEEIVTGDNDDQIVVTGDDVDDIESIYDFDTYKALLVFNDVY NDALFVSYGSSVETETYFKVNGLWSPTITHTNCWLRSVLLVMQKLPFKFKDLAIENMW LSYKVGYNQSFVDYLLTTIPKAIVLPQGGFVADFAYWFLNQFDINAYANWCCLKCGFSF DLNGLDALFFYGDIVSHVCKCGHNMTLIAADLPCTLHFSLFDDNFCAFCTPKKIFIAACA VDVNVCHSVAVIGDEQIDGKFVTKFSGDKFDFIVGYGMSFSMSSFELAQLYGLCITPNV CFVKGDIINVARLVKADVIVNPANGHMLHGGGVAKAIAVAAGKKFSKETAAMVKSKG VCQVGDCYVSTGGKLCKTILNIVGPDARQDGRQSYVLLARAYKHLNNYDCCLSTLISA GIFSVPADVSLTYLLGVVDKQVILVSNNKEDFDIIQKCQITSVVGTKALAVRLTANVGRV IKFETDAYKLFLSGDDCFVSNSSVIQEVLLLRHDIQLNNDVRDYLLSKMTSLPKDWRLIN KFDVINGVKTVKYFECPNSIYICSQGKDFGYVCDGSFYKATVNQVCVLLAKKIDVLLTV DGVNFKSISLTVGEVFGKILGNVFCDGIDVTKLKCSDFYADKILYQYENLSLADISAVQS SFGFDQQQLLAYYNFLTVCKWSVVVNGPFFSFEQSHNNCYVNVACLMLQHINLKFNK WQWQEAWYEFRAGRPHRLVALVLAKGHFKFDEPSDATDFIRVVLKQADLSGAICELEL ICDCGIKQESRVGVDAVMHFGTLAKTDLFNGYKIGCNCAGRIVHCTKLNVPFLICSNTPL SKDLPDDVVAANMFMGVGVGHYTHLKCGSPYQHYDACSVKKYTGVSGCLTDCLYLK NLTQTFTSMLTNYFLDDVEMVAYNPDLSQYYCDNGKYYTKPIIKAQFKPFAKVDGVYT NFKLVGHDICAQLNDKLGFNVDLPFVEYKVTVWPVATGDVVLASDDLYVKRYFKGCE TFGKPVIWFCHDEASLNSLTYFNKPSFKSENRYSVLSVDSVSEESQGNVVTPVMESQIST KEVKLKGVRKTVKIEDAIIVNDENSSIKVVKSLSLVDVWDMYLTGCDYVVWVANELSR LVKSPTVREYIRYGIKPITIPIDLLCLRDDNQTLLVPKIFKARAIEFYGFLKWLFIYVFSLLH FTNDKTIFYTTEIASKFTFNLFCLALKNAFQTFRWSIFIKGFLVVATVFLFWFNFLYINVIF SDFYLPNISVFPIFVGRIVMWIKATFGLVTICDFYSKLGVGFTSHFCNGSFICELCHSGFD MLDTYAAIDFVQYEVDRRVLFDYVSLVKLIVELVIGYSLYTVWFYPLFCLIGLQLFTTWL PDLFMLETMHWLIRFIVFVANMLPAFVLLRFYIVVTAMYKVVGFIRHIVYGCNKAGCLF CYKRNCSVRVKCSTIVGGVIRYYDITANGGTGFCVKHQWNCFNCHSFKPGNTFITVEAA IELSKELKRPVNPTDASHYVVTDIKQVGCMMRLFYDRDGQRVYDDVDASLFVDINNLL HSKVKVVPNLYVVVVESDADRANFLNAVVFYAQSLYRPILLVDKKLITTACNGISVTQT MFDVYVDTFMSHFDVDRKSFNNFVNIAHASLREGVQLEKVLDTFVGCVRKCCSIDSDV ETRFITKSMISAVAAGLEFTDENYNNLVPTYLKSDNIVAADLGVLIQNGAKHVQGNVAK AANISCIWFIDAFNQLTADLQHKLKKACVKTGLKLKLTFNKQEASVPILTTPFSLKGGVV LSNLLYILFFVSLICFILLWALLPTYSVYKSDIHLPAYASFKVIDNGVVRDISVNDLCFAN KFFQFDQWYESTFGSVYYHNSMDCPIVVAVMDEDIGSTMFNVPTKVLRHGFHVLHFLT YAFASDSVQCYTPHIQISYNDFYASGCVLSSLCTMFKRGDGTPHPYCYSDGVMKNASLY TSLVPHTRYSLANSNGFIRFPDVISEGIVRIVRTRSMTYCRVGACEYAEEGICFNFNSSWV LNNDYYRSMPGTFCGRDLFDLFYQFFSSLIRPIDFFSLTASSIFGAILAIVVVLVFYYLIKL KRAFGDYTSVVVINVVVWCINFLMLFVFQVYPICACVYACFYFYVTLYFPSEISVIMHLQ WIVMYGAIMPFWFCVTYVAMVIANHVLWLFSYCRKIGVNVCSDSTFEETSLTTFMITKD SYCRLKNSVSDVAYNRYLSLYNKYRYYSGKMDTAAYREAACSQLAKAMETFNHNNG NDVLYQPPTASVSTSFLQSGIVKMVSPTSKIEPCIVSVTYGSMTLNGLWLDDKVYCPRH VICSSSNMNEPDYSALLCRVTLGDFTIMSGRMSLTVVSYQMQGCQLVLTVSLQNPYTPK YTFGNVKPGETFTVLAAYNGRPQGAFHVTMRSSYTIKGSFLCGSCGSVGYVLTGDSVKF VYMHQLELSTGCHTGTDFTGNFYGPYRDAQVVQLPVKDYVQTVNVIAWLYAAILNNC AWFVQNDVCSTEDFNVWAMANGFSQVKADLVLDALASMTGVSIETLLAAIKRLYMGF QGRQILGSCTFEDELAPSDVYQQLAGVKLQSKTKRFIKETIYWILISTFLFSCIISAFVKWT IFMYINTHMIGVTLCVLCFVSFMMLLVKHKHFYLTMYIIPVLCTLFYVNYLVVYKEGFR GFTYVWLSYFVPAVNFTYVYEVFYGCILCVFAIFITMHSINHDIFSLMFLVGRIVTLISMW YFGSNLEEDVLLFITAFLGTYTWTTILSLAIAKIVANWLSVNIFYFTDVPYIKLILLSYLFIG YILSCYWGFFSLLNSVFRMPMGVYNYKISVQELRYMNANGLRPPRNSFEAILLNLKLLGI GGVPVIEVSQIQSKLTDVKCANVVLLNCLQHLHVASNSKLWQYCSVLHNEILSTSDLSV AFDKLAQLLIVLFANPAAVDTKCLASIDEVSDDYVQDSTVLQALQSEFVNMASFVEYEV AKKNLADAKNSGSVNQQQIKQLEKACNIAKSVYERDKAVARKLERMADLALTNMYKE ARINDKKSKVVSALQTMLFSMVRKLDNQALNSILDNAVKGCVPLSAIPALAANTLTIIIP DKQVFDKVVDNVYVTYAGSVWHIQTVQDADGINKQLTDISVDSNWPLVIIANRYNEVA NAVMQNNELMPHKLKIQVVNSGSDMNCNIPTQCYYNNGSSGRIVYAVLSDVDGLKYT KIMKDDGNCVVLELDPPCKFSIQDVKGLKIKYLYFIKGCNTLARGWVVGTLSSTIRLQA GVATEYAANSSILSLCAFSVDPKKTYLDYIQQGGVPIINCVKMLCDHAGTGMAITIKPEA

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Sequences
TINQDSYGGASVCIYCRARVEHPDVDGICKLRGKFVQVPLGIKDPILYVLTHDVCQVCG FWRDGSCSCVGSSVAVQSKDLNFLNRVRGTSVNARLVPCASGLSTDVQLRAFDICNTN RAGIGLYYKVNCCRFQRIDDDGNKLDKFFVVKRTNLEVYNKEKTYYELTKSCGVVAEH DFFTFDIDGSRVPHIVRRNLSKYTMLDLCYALRHFDRNDCSILCEILCEYADCKESYFSK KDWYDFVENPDIINIYKKLGPIFNRALLNTVIFADTLVEVGLVGVLTLDNQDLYGQWYD FGDFIQTAPGFGVAVADSYYSYMMPMLTMCHVLDCELFVNDSYRQFDLVQYDFTDYK LELFNKYFKYWGMKYHPNTVDCDNDRCIIHCANFNILFSMVLPNTCFGPLVRQIFVDGV PFVVSIGYHYKELGVVMNLDVDTHRYRLSLKDLLLYAADPAMHVASASALLDLRTCCF SVAAITSGIKFQTVKPGNFNQDFYEFVKSKGLFKEGSTVDLKHFFFTQDGNAAITDYNY YKYNLPTMVDIKQLLFVLEVVYKYFEIYDGGCIPASQVIVNNYDKSAGYPFNKFGKARL YYEALSFEEQNEIYAYTKRNVLPTLTQMNLKYAISAKNRARTVAGVSILSTMTGRMFHQ KCLKSIAATRGVPVVIGTTKFYGGWDDMLRHLIKDVDNPVLMGWDYPKCDRAMPNIL RIVSSLVLARKHEFCCSHGDRFYRLANECAQVLSEIVMCGGCYYVKPGGTSSGDATTAF ANSVFNICQAVTANVCSLMACNGHKIEDLSIRNLQKRLYSNVYRTDYVDYTFVNEYYE FLCKHFSMMILSDDGVVCYNSDYASKGYIANISVFQQVLYYQNNVFMSESKCWVENDI TNGPHEFCSQHTMLVKIDGDYVYLPYPDPSRILGAGCFVDDLLKTDSVLLIERFVSLAID AYPLVYHENEEYQKVFRVYLEYIKKLYNDLGTQILDSYSVILSTCDGLKFTEESFYKNM YLKSAVMQSVGACVVCSSQTSLRCGSCIRKPLLCCKCCYDHVMATNHKYVLSVSPYVC NAPNCDVSDVTKLYLGGMSYYCENHKPHYSFKLVMNGMVFGLYKQSCTGSPYIDDFN KIASCKWTEVDDYVLANECIERLKLFAAETQKATEEAFKQSYASATIQEIVSDREVILCW ETGKVKPPLNKNYVFTGYHFTSTGKTVLGEYVFDKSELTNGVYYRATTTYKLSIGDVFV LTSHSVASLSAPTLVPQENYASIRFSSVYSVPLVFQNNVANYQHIGMKRYCTVQGPPGT GKSHLAIGLAVYYYTARVVYTAASHAAVDALCEKAYKFLNINDCTRIIPAKVRVDCYD KFKINDTTCKYVFTTINALPELVTDIVVVDEVSMLTNYELSVINARIKAKHYVYIGDPAQ LPAPRVLLSKGSLEPRHFNSITKIMCCLGPDIFLGNCYRCPKEIVETVSALVYDNKLKAK NDNSSLCFKVYFKGQTTHESSSAVNIQQIYLISKFLKANPVWNSAVFISPYNSQNYVAKR VLGVQTQTVDSAQGSEYDYVIYSQTAETAHSVNVNRFNVAITRAKKGIFCVMSNMQLF ESLNFITLPLDKIQNQTLPRLHCTTNLFKDCSKSCLGYHPAHAPSFLAVDDKYKVNENLA VNLNICEPVLTYSRLISLMGFKLDLTLDGYSKLFITKDEAIKRVRGWVGFDVEGAHATRE NIGTNFPLQIGFSTGVDFVVEATGLFAERDCYTFKKTVAKAPPGEKFKHLIPLMSKGQK WDIVRIRIVQMLSDYLLDLSDSVVFITWSASFELTCLRYFAKLGRELNCNVCSNRATCYN SRTGYYGCWRHSYTCDYVYNPLIVDIQQWGYTGSLTSNHDIICNVHKGAHVASADAIM TRCLAIYDCFCKSVNWNLEYPIISNEVSINTSCRLLQRVMLKAAMLCNRYNLCYDIGNP KGLACVKDYEFKFYDAFPVAKFVKQLFYVYDVHKDNFKDGLCMFWNCNVDKYPSNSI VCRFDTRVLNKLNLPGCNGGSLYVNKHAFHTNPFTRTVFENLKPMPFFYYSDTPCVYV DGLESKQVDYVPLRSATCITRCNLGGAVCSKHAEEYCNYLESYNIVTTAGFTFWVYKNF DFYNLWNTFTTLQSLENVIYNLVNVGHYDGRTGELPCAIINDKVVVKINNVDTVIFKNN TSFPTNIAVELFTKRSIRHHPELKILRNLNIDICWKHVLWDYVKDSLFCSSTYGVCKYTDL KFIENLNILFDGRDTGALEAFRKARNGVFISTEKLSRLSMIKGPQRADLNGVIVDKVGEL KVEFWFAMRKDGDDVIFSRTDSLCSSHYWSPQGNLGGNCAGNVIGNDALTRFTIFTQSR VLSSFEPRSDLERDFIDMDDNLFIAKYGLEDYAFDHIVYGSFNHKVIGGLHLLIGLFRRLK KSNLLIQEFLQYDSSIHSYFITDQECGSSKSVCTVIDLLLDDFVSIVKSLNLSCVSKVVNIN VDFKDFQFMLWCNDNKIMTFYPKMQATNDWKPGYSMPVLYKYLNVPLERVSLWNYG KPINLPTGCMMNVAKYTQLCQYLNTTTLAVPVNMRVLHLGAGSDKEVAPGSAVLRQW LPSGSILVDNDLNPFVSDSLVTYFGDCMTLPFDCHWDLIISDMYDPLTKNIGDYNVSKDG FFTYICHLIRDKLSLGGSVAIKITEFSWNADLYKLMSCFAFWTVFCTNVNASSSEGFLIGI NYLGKSSFEIDGNVMHANYLFWRNSTTWNGGAYSLFDMTKFSLKLAGTAVVNLRPDQ LNDLVYSLIERGKLLVRDTRKEIFVGDSLVNTC (SEQ ID NO: 4)
OC43 (beta coronavirus); NCBI GenBank accession code NC_006213: MSKINKYGLELHWAPEFPWMFEDAEEKLDNPSSSEVDMICSTTAQKLETDGICPENHVM VDCRRLLKQECCVQSSLIREIVMNASPYDLEVLLQDALQSREAVLVTTPLGMSLEACYV RGCNPKGWTMGLFRRRSVCNTGRCTVNKHVAYQLYMIDPAGVCLGAGQFVGWVIPLA FMPVQSRKFIVPWVMYLRKRGEKGAYNKDHGRGGFGHVYDFKVEDAYDQVHDEPKG KFSKKAYALIRGYRGVKPLLYVDQYGCDYTGSLADGLEAYADKTLQEMKALFPTWSQ ELLFDVIVAWHVVRDPRYVMRLQSAATIRSVAYVANPTEDLCDGSVVIKEPVHVYADD SIILRQYNLVDIMSHFYMEADTVVNAFYGVALKDCGFVMQFGYIDCEQDSCDFKGWIP GNMIDGFACTTCGHVYEVGDLMAQSSGVLPVNPVLHTKSAAGYGGFGCKDSFTLYGQ TVVYFGGCVYWSPARNIWIPILKSSVKSYDSLVYTGVLGCKAIVKETNLICKALYLDYV QHKCGNLHQRELLGVSDVWHKQLLLNRGVYKPLLENIDYFNMRRAKFSLETFTVCADG FMPFLLDDLVPRAYYLAVSGQAFCDYADKLCHAVVSKSKELLDVSLDSLGAAIHYLNS KIVDLAQHFSDFGTSFVSKIVHFFKTFTTSTALAFAWVLFHVLHGAYIVVESDIYFVKNIP RYASAVAQAFQSVAKVVLDSLRVTFIDGLSCFKIGRRRICLSGRKIYEVERGLLHSSQLPL DVYDLTMPSQVQKAKQKPIYLKGSGSDFSLADSVVEVVTTSLTPCGYSEPPKVAAKICIV DNVYMAKAGDKYYPVVVDDHVGLLDQAWRVPCAGRRVTFKEQPTVKEIISMPKIIKVF YELDNDFNTILNTACGVFEVDDTVDMEEFYAVVIDAIEEKLSPCKELEGVGAKVSAFLQ KLEDNPLFLFDEAGEEVLAPKLYCAFTAPEDDDFLEESDVEEDDVEGEETDLTVTSAGQ PCVASEQEESSEVLEDTLDDGPSVETSDSQVEEDVEMSDFVDLESVIQDYENVCFEFYTT EPEFVKVLGLYVPKATRNNCWLRSVLAVMQKLPCQFKDKNLQDLWVLYKQQYSQLFV DTLVNKIPANIVLPQGGYVADFAYWFLTLCDWQCVAYWKCIKCDLALKLKGLDAMFF YGDVVSHICKCGESMVLIDVDVPFTAHFALKDKLFCAFITKRIVYKAACVVDVNDSHSM AVVDGKQIDDHRITSITSDKFDFIIGHGMSFSMTTFEIAQLYGSCITPNVCFVKGDIIKVSK LVKAEVVVNPANGHMAHGGGVAKAIAVAAGQQFVKETTDMVKSKGVCATGDCYVST GGKLCKTVLNVVGPDARTQGKQSYVLLERVYKHLNNYDCVVTTLISAGIFSVPSDVSLT

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Sequences
YLLGTAKKQVVLVSNNQEDFDLISKCQITAVEGTKKLAARLSFNVGRSIVYETDANKLIL INDVAFVSTFNVLQDVLSLRHDIALDDDARTFVQSNVDVVPEGWRVVNKFYQINGVRT VKYFECTGGIDICSQDKVFGYVQQGIFNKATVAQIKALFLDKVDILLTVDGVNFTNRFVP VGESFGKSLGNVFCDGVNVTKHKCDINYKGKVFFQFDNLSSEDLKAVRSSFNFDQKELL AYYNMLVNCFKWQVVVNGKYFTFKQANNNCFVNVSCLMLQSLHLTFKIVQWQEAWL EFRSGRPARFVALVLAKGGFKFGDPADSRDFLRVVFSQVDLTGAICDFEIACKCGVKQE QRTGLDAVMHFGTLSREDLEIGYTVDCSCGKKLIHCVRFDVPFLICSNTPASVKLPKGVG SANIFIGDKVGHYVHVKCEQSYQLYDASNVKKVTDVTGKLSDCLYLKNLKQTFKSVLT TYYLDDVKKIEYKPDLSQYYCDGGKYYTQRIIKAQFKTFEKVDGVYTNFKLIGHTVCDS LNAKLGFDSSKEFVEYKITEWPTATGDVVLATDDLYVKRYERGCITFGKPVIWLSHEKA SLNSLTYFNRPSLVDDNKFDVLKVDDVDDGGDSSESGAKETKEINIIKLSGVKKPFKVED SVIVNDDTSETKYVKSLSIVDVYDMWLTGCKYVVRTANALSRAVNVPTIRKFIKFGMTL VSIPIDLLNLREIKPAVNVVKAVRNKISVCFNFIKWLFVLLFGWIKISADNKVIYTTETASK LTCKLVALAFKNAFLTFKWSMVARGACIIATIFLLWFNFIYANVIFSDFYLPKIGFLPTFV GKIAQWIKNTFSLVTICDLYSIQDVGFKNQYCNGSIACQFCLAGFDMLDNYKAIDVVQY EADRRAFVDYTGVLKIVIELIVSYALYTAWFYPLFALISIQILTTWLPELFMLSTLHWSFR LLVALANMLPAHVFMRFYIIIASFIKLFSLFRHVAYGCSKSGCLFCYKRNRSLRVKCSTIV GGMIRYYDVMANGGTGFCSKHQWNCIDCDSYKPGNTFITVEAALDLSKELKRPIQPTD VAYHTVTDVKQVGCSMRLFYDRDGQRTYDDVNASLFVDYSNLLHSKVKSVPNMHVV VVENDADKANFLNAAVFYAQSLFRPILMVDKNLITTANTGTSVTETMFDVYVDTFLSM FDVDKKSLNALIATAHSSIKQGTQIYKVLDTFLSCARKSCSIDSDVDTKCLADSVMSAVS AGLELTDESCNNLVPTYLKSDNIVAADLGVLIQNSAKHVQGNVAKIAGVSCIWSVDAFN QFSSDFQHKLKKACCKTGLKLKLTYNKQMANVSVLTTPFSLKGGAVFSYFVYVCFVLS LVCFIGLWCLMPTYTVHKSDFQLPVYASYKVLDNGVIRDVSVEDVCFANKFEQFDQWY ESTFGLSYYSNSMACPIVVAVIDQDFGSTVFNVPTKVLRYGYHVLHFITHALSADGVQC YTPHSQISYSNFYASGCVLSSACTMFTMADGSPQPYCYTEGLMQNASLYSSLVPHVRYN LANAKGFIRFPEVLREGLVRIVRTRSMSYCRVGLCEEADEGICFNFNGSWVLNNDYYRS LPGTFCGRDVFDLIYQLFKGLAQPVDFLALTASSIAGAILAVIVVLVFYYLIKLKRAFGDY TSVVFVNVIVWCVNFMMLFVFQVYPILSCVYAICYFYATLYFPSEISVIMHLQWLVMYG TIMPLWFCLLYIAVVVSNHAFWVFSYCRKLGTSVRSDGTFEEMALTTFMITKDSYCKLK NSLSDVAFNRYLSLYNKYRYYSGKMDTAAYREAACSQLAKAMDTFTNNNGSDVLYQP PTASVSTSFLQSGIVKMVNPTSKVEPCVVSVTYGNMTLNGLWLDDKVYCPRHVICSASD MTNPDYTNLLCRVTSSDFTVLFDRLSLTVMSYQMRGCMLVLTVTLQNSRTPKYTFGVV KPGETFTVLAAYNGKPQGAFHVTMRSSYTIKGSFLCGSCGSVGYVIMGDCVKFVYMHQ LELSTGCHTGTDFNGDFYGPYKDAQVVQLLIQDYIQSVNFVAWLYAAILNNCNWFVQS DKCSVEDFNVWALSNGFSQVKSDLVIDALASMTGVSLETLLAAIKRLKNGFQGRQIMGS CSFEDELTPSDVYQQLAGIKLQSKRTRLFKGTVCWIMASTFLFSCIITAFVKWTMFMYVT TNMFSITFCALCVISLAMLLVKHKHLYLTMYITPVLFTLLYNNYLVVYKHTFRGYVYA WLSYYVPSVEYTYTDEVIYGMLLLVGMVFVTLRSINHDLFSFIMFVGRLISVFSLWYKG SNLEEEILLMLASLFGTYTWTTVLSMAVAKVIAKWVAVNVLYFTDIPQIKIVLLCYLFIG YIISCYWGLFSLMNSLFRMPLGVYNYKISVQELRYMNANGLRPPKNSFEALMLNFKLLG IGGVPIIEVSQFQSKLTDVKCANVVLLNCLQHLHVASNSKLWHYCSTLHNEILATSDLSV AFEKLAQLLIVLFANPAAVDSKCLTSIEEVCDDYAKDNTVLQALQSEFVNMASFVEYEV AKKNLDEARFSGSANQQQLKQLEKACNIAKSAYERDRAVAKKLERMADLALTNMYKE ARINDKKSKVVSALQTMLFSMVRKLDNQALNSILDNAVKGCVPLNAIPSLAANTLNIIVP DKSVYDQVVDNVYVTYAGNVWQIQTIQDSDGTNKQLNEISDDCNWPLVIIANRYNEVS ATVLQNNELMPAKLKIQVVNSGPDQTCNTPTQCYYNNSNNGKIVYAILSDVDGLKYTKI LKDDGNFVVLELDPPCKFTVQDAKGLKIKYLYFVKGCNTLARGWVVGTISSTVRLQAG TATEYASNSSILSLCAFSVDPKKTYLDFIQQGGTPIANCVKMLCDHAGTGMAITVKPDAT TSQDSYGGASVCIYCRARVEHPDVDGLCKLRGKFVQVPVGIKDPVSYVLTHDVCRVCG FWRDGSCSCVSTDTTVQSKDTNFLNRVRGTSVDARLVPCASGLSTDVQLRAFDIYNASV AGIGLHLKVNCCRFQRVDENGDKLDQFFVVKRTDLTIYNREMKCYERVKDCKFVAEH DFFTFDVEGSRVPHIVRKDLTKYTMLDLCYALRHFDRNDCMLLCDILSIYAGCEQSYFT KKDWYDFVENPDIINVYKKLGPIFNRALVSATEFADKLVEVGLVGVLTLDNQDLNGKW YDFGDYVIAAPGCGVAIADSYYSYIMPMLTMCHALDCELYVNNAYRLFDLVQYDFTDY KLELFNKYFKHWSMPYHPNTVDCQDDRCIIHCANFNILFSMVLPNTCFGPLVRQIFVDG VPFVVSIGYHYKELGIVMNMDVDTHRYRLSLKDLLLYAADPALHVASASALYDLRTCC FSVAAITSGVKFQTVKPGNFNQDFYDFVLSKGLLKEGSSVDLKHFFFTQDGNAAITDYN YYKYNLPTMVDIKQLLFVLEVVYKYFEIYDGGCIPASQVIVNNYDKSAGYPFNKFGKAR LYYEALSFEEQDEIYAYTKRNVLPTLTQMNLKYAISAKNRARTVAGVSILSTMTGRMFH QKCLKSIAATRGVPVVIGTTKFYGGWDDMLRRLIKDVDNPVLMGWDYPKCDRAMPNL LRIVSSLVLARKHETCCSQSDRFYRLANECAQVLSEIVMCGGCYYVKPGGTSSGDATTA FANSVFNICQAVSANVCALMSCNGNKIEDLSIRALQKRLYSHVYRSDKVDSTFVTEYYE FLNKHFSMMILSDDGVVCYNSDYASKGYIANISAFQQVLYYQNNVFMSESKCWVEHDI NNGPHEFCSQHTMLVKMDGDDVYLPYPNPSRILGAGCFVDDLLKTDSVLLIERFVSLAI DAYPLVYHENEEYQKVFRVYLAYIKKLYNDLGNQILDSYSVILSTCDGQKFTDESFYKN MYLRSAVMQSVGACVVCSSQTSLRCGSCIRKPLLCCKCCYDHVMATDHKYVLSVSPYV CNAPGCDVNDVTKLYLGGMSYYCEDHKPQYSFKLVMNGLVFGLYKQSCTGSPYIDDF NRIASCKWTDVDDYILANECTERLKLFAAETQKATEEAFKQSYASATIQEIVSERELILS WEIGKVKPPLNKNYVFTGYHFTKNGKTVLGEYVFDKSELTNGVYYRATTTYKLSVGDV FVLTSHSVANLSAPTLVPQENYSSIRFASVYSVLETFQNNVVNYQHIGMKRYCTVQGPP GTGKSHLAIGLAVFYCTARVVYTAASHAAVDALCEKAYKFLNINDCTRIVPAKVRVEC YDKFKINDTTRKYVFTTINALPEMVTDIVVVDEVSMLTNYELSVINARIRAKHYVYIGDP AQLPAPRVLLSKGTLEPKYFNTVTKLMCCLGPDIFLGTCYRCPKEIVDTVSALVYENKL

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Sequences
KAKNESSSLCFKVYYKGVTTHESSSAVNMQQIYLINKFLKANPLWHKAVFISPYNSQNF AAKRVLGLQTQTVDSAQGSEYDYVIYSQTAETAHSVNVNRFNVAITRAKKGILCVMSN MQLFEALQFTTLTLDKVPQAVETKVQCSTNLFKDCSKSYSGYHPAHAPSFLAVDDKYK ATGDLAVCLGIGDSAVTYSRLISLMGFKLDVTLDGYCKLFITKEEAVKRVRAWVGFDAE GAHATRDSIGTNFPLQLGFSTGIDFVVEATGLFADRDGYSFKKAVAKAPPGEQFKHLIPL MTRGHRWDVVRPRIVQMFADHLIDLSDCVVLVTWAANFELTCLRYFAKVGREISCNVC TKRATVYNSRTGYYGCWRHSVTCDYLYNPLIVDIQQWGYIGSLSSNHDLYCSVHKGAH VASSDAIMTRCLAVYDCFCNNINWNVEYPIISNELSINTSCRVLQRVILKAAMLCNRYTL CYDIGNPKAIACVKDFDFKFYDAQPIVKSVKTLLYSFEAHKDSFKDGLCMFWNCNVDK YPPNAVVCRFDTRVLNNLNLPGCNGGSLYVNKHAFHTKPFARAAFEHLKPMPFFYYSD TPCVYMDGMDAKQVDYVPLKSATCITRCNLGGAVCLKHAEEYREYLESYNTATTAGFT FWVYKTFDFYNLWNTFTKLQSLENVVYNLVKTGHYTGQAGEMPCAIINDKVVAKIDKE DVVIFINNTTYPTNVAVELFAKRSVRHHPELKLFRNLNIDVCWKHVIWDYARESIFCSNT YGVCMYTDLKFIDKLNVLFDGRDNGALEAFKRSNNGVYISTTKVKSLSMIRGPPRAELN GVVVDKVGDTDCVFYFAVRKEGQDVIFSQFDSLGVSSNQSPQGNLGSNGKPGNVGGND ALSISTIFTQSRVISSFTCRTDMEKDFIALDQDVFIQKYGLEDYAFEHIVYGNFNQKIIGGL HLLIGLYRRQQTSNLVVQEFVSYDSSIHSYFITDEKSGGSKSVCTVIDILLDDFVALVKSL NLNCVSKVVNVNVDFKDFQFMLWCNDEKVMTFYPRLQAASDWKPGYSMPVLYKYLN SPMERVSLWNYGKPVTLPTGCMMNVAKYTQLCQYLNTTTLAVPVNMRVLHLGAGSE KGVAPGSAVLRQWLPAGTILVDNDLYPFVSDSVATYFGDCITLPFDCQWDLIISDMYDPI TKNIGEYNVSKDGFFTYICHMIRDKLALGGSVAIKITEFSWNAELYKLMGYFAFWTVFC TNANASSSEGFLIGINYLCKPKVEIDGNVMHANYLFWRNSTVWNGGAYSLFDMAKFPL KLAGTAVINLRADQINDMVYSLLEKGKLLIRDTNKEVFVGDSLVNVI (SEQ ID NO: 5)
NL63 (alpha coronavirus); NCBI GenBank accession code NC_005831: MFYNQVTLAVASDSEISGFGFAIPSVAVRTYSEAAAQGFQACRFVAFGLQDCVTGINDD DYVIALTGTNQLCAKILPFSDRPLNLRGWLIFSNSNYVLQDFDVVFGHGAGSVVFVDKY MCGFDGKPVLPKNMWEFRDYFNNNTDSIVIGGVTYQLAWDVIRKDLSYEQQNVLAIESI HYLGTTGHTLKSGCKLTNAKPPKYSSKVVLSGEWNAVYRAFGSPFITNGMSLLDIIVKP VFFNAFVKCNCGSESWSVGAWDGYLSSCCGTPAKKLCVVPGNVVPGDVIITSTSAGCG VKYYAGLVVKHITNITGVSLWRVTAVHSDGMFVASSSYDALLHRNSLDPFCFDVNTLL SNQLRLAFLGASVTEDVKFAASTGVIDISAGMFGLYDDILTNNKPWFVRKASGLFDAIW DAFVAAIKLVPTTTGVLVRFVKSIASTVLTVSNGVIIMCADVPDAFQSVYRTFTQAICAA FDFSLDVFKIGDVKFKRLGDYVLTENALVRLTTEVVRGVRDARIKKAMFTKVVVGPTTE VKFSVIELATVNLRLVDCAPVVCPKGKIVVIAGQAFFYSGGFYRFMVDPTTVLNDPVFT GDLFYTIKFSGFKLDGFNHQFVTASSATDAIIAVELLLLDFKTAVFVYTCVVDGCSVIVR RDATFATHVCFKDCYNVWEQFCIDNCGEPWFLTDYNAILQSNNPQCAIVQASESKVLLE RFLPKCPEILLSIDDGHLWNLFVEKFNFVTDWLKTLKLTLTSNGLLGNCAKRFRRVLVK LLDVYNGFLETVCSVAYTAGVCIKYYAVNVPYVVISGFVSRVIRRERCDMTFPCVSCVT FFYEFLDTCFGVSKPNAIDVEHLELKETVFVEPKDGGQFFVSGDYLWYVVDDIYYPASC NGVLPVAFTKLAGGKISFSDDVIVHDVEPTHKVKLIFEFEDDVVTSLCKKSFGKSIIYTGD WEGLHEVLTSAMNVIGQHIKLPQFYIYDEEGGYDVSKPVMISQWPISNDSNGCVVEAST DFHQLECIVDDSVREEVDIIEQPFEEVEHVLSIKQPFSFSFRDELGVRVLDQSDNNCWIST TLVQLQLTKLLDDSIEMQLFKVGKVDSIVQKCYELSHLISGSLGDSGKLLSELLKEKYTC SITFEMSCDCGKKFDDQVGCLFWIMPYTKLFQKGECCICHKMQTYKLVSMKGTGVFVQ DPAPIDIDAFPVKPICSSVYLGVKGSGHYQTNLYSFNKAIDGFGVFDIKNSSVNTVCFVD VDFHSVEIEAGEVKPFAVYKNVKFYLGDISHLVNCVSFDFVVNAANENLLHGGGVARAI DILTEGQLQSLSKDYISSNGPLKVGAGVMLECEKFNVFNVVGPRTGKHEHSLLVEAYNS ILFENGIPLMPLLSCGIFGVRIENSLKALFSCDINKPLQVFVYSSNEEQAVLKFLDGLDLTP VIDDVDVVKPFRVEGNFSFFDCGVNALDGDIYLLFTNSILMLDKQGQLLDTKLNGILQQ AALDYLATVKTVPAGNLVKLFVESCTIYMCVVPSINDLSFDKNLGRCVRKLNRLKTCVI ANVPAIDVLKKLLSSLTLTVKFVVESNVMDVNDCFKNDNVVLKITEDGINVKDVVVESS KSLGKQLGVVSDGVDSFEGVLPINTDTVLSVAPEVDWVAFYGFEKAALFASLDVKPYG YPNDFVGGFRVLGTTDNNCWVNATCIILQYLKPTFKSKGLNVLWNKFVTGDVGPFVSFI YFITMSSKGQKGDAEEALSKLSEYLISDSIVTLEQYSTCDICKSTVVEVKSAIVCASVLKD GCDVGFCPHRHKLRSRVKFVNGRVVITNVGEPIISQPSKLLNGIAYTTFSGSFDNGHYVV YDAANNAVYDGARLFSSDLSTLAVTAIVVVGGCVTSNVPTIVSEKISVMDKLDTGAQKF FQFGDFVMNNIVLFLTWLLSMFSLLRTSIMKHDIKVIAKAPKRTGVILTRSFKYNIRSALF VIKQKWCVIVTLFKFLLLLYAIYALVFMIVQFSPFNSLLCGDIVSGYEKSTFNKDIYCGNS MVCKMCLFSYQEFNDLDHTSLVWKHIRDPILISLQPFVILVILLIFGNMYLRFGLLYFVAQ FISTFGSFLGFHQKQWFLHFVPFDVLCNEFLATFIVCKIVLFVRHIIVGCNNADCVACSKS ARLKRVPLQTIINGMHKSFYVNANGGTCFCNKHNFFCVNCDSFGPGNTFINGDIARELG NVVKTAVQPTAPAYVIIDKVDFVNGFYRLYSGDTFWRYDFDITESKYSCKEVLKNCNVL ENFIVYNNSGSNITQIKNACVYFSQLLCEPIKLVNSELLSTLSVDFNGVLHKAYVDVLCN SFFKELTANMSMAECKATLGLTVSDDDFVSAVANAHRYDVLLSDLSFNNFFISYAKPED KLSVYDIACCMRAGSKVVNHNVLIKESIPIVWGVKDFNTLSQEGKKYLVKTTKAKGLTF LLTFNDNQAITQVPATSIVAKQGAGFKRTYNFLWYVCLFVVALFIGVSFIDYTTTVTSFH GYDFKYIENGQLKVFEAPLHCVRNVFDNFNQWHEAKFGVVTTNSDKCPIVVGVSERIN VVPGVPTNVYLVGKTLVFTLQAAFGNTGVCYDFDGVTTSDKCIFNSACTRLEGLGGDN VYCYNTDLIEGSKPYSTLQPNAYYKYDAKNYVRFPEILARGFGLRTIRTLATRYCRVGE CRDSHKGVCFGFDKWYVNDGRVDDGYICGDGLIDLLVNVLSIFSSSFSVVAMSGHMLF NFLFAAFITFLCFLVTKFKRVFGDLSYGVFTVVCATLINNISYVVTQNLFFMLLYAILYFV FTRTVRYAWIWHIAYIVAYFLLIPWWLLTWFSFAAFLELLPNVFKLKISTQLFEGDKFIGT FESAAAGTFVLDMRSYERLINTISPEKLKNYAASYNKYKYYSGSASEADYRCACYAHLA

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Sequences
KAMLDYAKDHNDMLYSPPTISYNSTLQSGLKKMAQPSGCVERCVVRVCYGSTVLNGV WLGDTVTCPRHVIAPSTTVLIDYDHAYSTMRLHNFSVSHNGVFLGVVGVTMHGSVLRI KVSQSNVHTPKHVFKTLKPGDSFNILACYEGIASGVFGVNLRTNFTIKGSFINGACGSPG YNVRNDGTVEFCYLHQIELGSGAHVGSDFTGSVYGNFDDQPSLQVESANLMLSDNVVA FLYAALLNGCRWWLCSTRVNVDGFNEWAMANGYTSVSSVECYSILAAKTGVSVEQLL ASIQHLHEGFGGKNILGYSSLCDEFTLAEVVKQMYGVNLQSGKVIFGLKTMFLFSVFFT MFWAELFIYTNTIWINPVILTPIFCLLLFLSLVLTMFLKHKFLFLQVFLLPTVIATALYNCV LDYYIVKFLADHFNYNVSVLQMDVQGLVNVLVCLFVVFLHTWRFSKERFTHWFTYVC SLIAVAYTYFYSGDFLSLLVMFLCAISSDWYIGAIVFRLSRLIVFFSPESVFSVFGDVKLTL VVYLICGYLVCTYWGILYWFNRFFKCTMGVYDFKVSAAEFKYMVANGLHAPHGPFDA LWLSFKLLGIGGDRCIKISTVQSKLTDLKCTNVVLLGCLSSMNIAANSSEWAYCVDLHN KINLCDDPEKAQSMLLALLAFFLSKHSDFGLDGLIDSYFDNSSTLQSVASSFVSMPSYIAY ENARQAYEDAIANGSSSQLIKQLKRAMNIAKSEFDHEISVQKKINRMAEQAATQMYKEA RSVNRKSKVISAMHSLLFGMLRRLDMSSVETVLNLARDGVVPLSVIPATSASKLTIVSPD LESYSKIVCDGSVHYAGVVWTLNDVKDNDGRPVHVKEITKENVETLTWPLILNCERVV KLQNNEIMPGKLKQKPMKAEGDGGVLGDGNALYNTEGGKTFMYAYISNKADLKFVK WEYEGGCNTIELDSPCRFMVETPNGPQVKYLYFVKNLNTLRRGAVLGFIGATIRLQAGK QTELAVNSGLLTACAFSVDPATTYLEAVKHGAKPVSNCIKMLSNGAGNGQAITTSVDA NTNQDSYGGASICLYCRAHVPHPSMDGYCKFKGKCVQVPIGCLDPIRFCLENNVCNVC GCWLGHGCACDRTTIQSVDISYLNRARGSSAARLEPCNGTDIDKCVRAFDIYNKNVSFL GKCLKMNCVRFKNADLKDGYFVIKRCTKSVMEHEQSMYNLLNFSGALAEHDFFTWKD GRVIYGNVSRHNLTKYTMMDLVYAMRNFDEQNCDVLKEVLVLTGCCDNSYFDSKGW YDPVENEDIHRVYASLGKIVARAMLKCVALCDAMVAKGVVGVLTLDNQDLNGNFYDF GDFVVSLPNMGVPCCTSYYSYMMPEVIGLTNCLASECFVKSDIFGSDFKTFDLLKYDFTE HKENLFNKYFKHWSFDYHPNCSDCYDDMCVIHCANFNTLFATTIPGTAFGPLCRKVFID GVPLVTTAGYHFKQLGLVWNKDVNTHSVRLTITELLQFVTDPSLIIASSPALVDQRTICFS VAALSTGLTNQVVKPGHFNEEFYNFLRLRGFFDEGSELTLKHFFFAQNGDAAVKDFDFY RYNKPTILDICQARVTYKIVSRYFDIYEGGCIKACEVVVTNLNKSAGWPLNKFGKASLY YESISYEEQDALFALTKRNVLPTMTQLNLKYAISGKERARTVGGVSLLSTMTTRQYHQK HLKSIVNTRNATVVIGTTKFYGGWNNMLRTLIDGVENPMLMGWDYPKCDRALPNMIR MISAMVLGSKHVNCCTATDRFYRLGNELAQVLTEVVYSNGGFYFKPGGTTSGDASTAY ANSIFNIFQAVSSNINRLLSVPSDSCNNVNVRDLQRRLYDNCYRLTSVEESFIDDYYGYL RKHFSMMILSDDGVVCYNKDYAELGYIADISAFKATLYYQNNVFMSTSKCWVEEDLTK GPHEFCSQHTMQIVDKDGTYYLPYPDPSRILSAGVFVDDVVKTDAVVLLERYVSLAIDA YPLSKHPNSEYRKVFYVLLDWVKHLNKNLNEGVLESFSVTLLDNQEDKFWCEDFYAS MYENSTILQAAGLCVVCGSQTVLRCGDCLRKPMLCTKCAYDHVFGTDHKFILAITPYVC NASGCGVSDVKKLYLGGLNYYCTNHKPQLSFPLCSAGNIFGLYKNSATGSLDVEVFNRL ATSDWTDVRDYKLANDVKDTLRLFAAETIKAKEESVKSSYAFATLKEVVGPKELLLSW ESGKVKPPLNRNSVFTCFQISKDSKFQIGEFIFEKVEYGSDTVTYKSTVTTKLVPGMIFVL TSHNVQPLRAPTIANQEKYSSIYKLHPAFNVSDAYANLVPYYQLIGKQKITTIQGPPGSG KSHCSIGLGLYYPGARIVFVACAHAAVDSLCAKAMTVYSIDKCTRIIPARARVECYSGFK PNNTSAQYIFSTVNALPECNADIVVVDEVSMCTNYDLSVINQRLSYKHIVYVGDPQQLP APRVMITKGVMEPVDYNVVTQRMCAIGPDVFLHKCYRCPAEIVNTVSELVYENKFVPV KPASKQCFKVFFKGNVQVDNGSSINRKQLEIVKLFLVKNPSWSKAVFISPYNSQNYVAS RFLGLQIQTVDSSQGSEYDYVIYAQTSDTAHACNVNRFNVAITRAKKGIFCVMCDKTLF DSLKFFEIKHADLHSSQVCGLFKNCTRTPLNLPPTHAHTFLSLSDQFKTTGDLAVQIGSN NVCTYEHVISFMGFRFDISIPGSHSLFCTRDFAIRNVRGWLGMDVESAHVCGDNIGTNVP LQVGFSNGVNFVVQTEGCVSTNFGDVIKPVCAKSPPGEQFRHLIPLLRKGQPWLIVRRRI VQMISDYLSNLSDILVFVLWAGSLELTTMRYFVKIGPIKYCYCGNSATCYNSVSNEYCCF KHALGCDYVYNPYAFDIQQWGYVGSLSQNHHTFCNIHRNEHDASGDAVMTRCLAVHD CFVKNVDWTVTYPFIANEKFINGCGRNVQGHVVRAALKLYKPSVIHDIGNPKGVRCAV TDAKWYCYDKQPVNSNVKLLDYDYATHGQLDGLCLFWNCNVDMYPEFSIVCRFDTRT RSVFNLEGVNGGSLYVNKHAFHTPAYDKRAFVKLKPMPFFYFDDSDCDVVQEQVNYV PLRASSCVTRCNIGGAVCSKHANLYQKYVEAYNTFTQAGFNIWVPHSFDVYNLWQIFIE TNLQSLENIAFNVVKKGCFTGVDGELPVAVVNDKVFVRYGDVDNLVFTNKTTLPTNVA FELFAKRKMGLTPPLSILKNLGVVATYKFVLWDYEAERPFTSYTKSVCKYTDFNEDVCV CFDNSIQGSYERFTLTTNAVLFSTVVIKNLTPIKLNFGMLNGMPVSSIKGDKGVEKLVNW YIYVRKNGQFQDHYDGFYTQGRNLSDFTPRSDMEYDFLNMDMGVFINKYGLEDFNFEH VVYGDVSKTTLGGLHLLISQFRLSKMGVLKADDFVTASDTTLRCCTVTYLNELSSKVVC TYMDLLLDDFVTILKSLDLGVISKVHEVIIDNKPYRWMLWCKDNHLSTFYPQLQSAEW KCGYAMPQIYKLQRMCLEPCNLYNYGAGIKLPSGIMLNVVKYTQLCQYLNSTTMCVPH NIVIRVLHYGAGSDKGVAPGTTVLKRWLPPDAIIIDNDINDYVSDADFSITGDCATVYLED KFDLLISDMYDGRIKFCDGENVSKDGFFTYLNGVIREKLAIGGSVAIKITEYSWNKYLYE LIQRFAFWTLFCTSVNTSSSEAFLIGINYLGDFIQGPFIAGNTVHANYIFWRNSTIMSLSYN SVLDLSKFECKHKATVVVTLKDSDVNDMVLSLIKSGRLLLRNNGRFGGFSNHLVSTK (SEQ ID NO: 6)
229E (alpha coronavirus); NCBI GenBank accession code NC_002645: MACNRVTLAVASDSEISANGCSTIAQAVRRYSEAASNGFRACRFVSLDLQDCIVGIADD TYVMGLHGNQTLFCNIMKFSDRPFMLHGWLVFSNSNYLLEEFDVVFGKRGGGNVTYT DQYLCGADGKPVMSEDLWQFVDHFGENEEIIINGHTYVCAWLTKRKPLDYKRQNNLAI EEIEYVHGDALHTLRNGSVLEMAKEVKTSSKVVLSDALDKLYKVFGSPVMTNGSNILEA FTKPVFISALVQCTCGTKSWSVGDWTGFKSSCCNVISNKLCVVPGNVKPGDAVITTQQA GAGIKYFCGMTLKFVANIEGVSVWRVIALQSVDCFVASSTFVEEEHVNRMDTFCFNVR

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Sequences
NSVTDECRLAMLGAEMTSNVRRQVASGVIDISTGWFDVYDDIFAESKPWFVRKAEDIFG PCWSALASALKQLKVTTGELVRFVKSICNSAVAVVGGTIQILASVPEKFLNAFDVFVTAI QTVFDCAVETCTIAGKAFDKVFDYVLLDNALVKLVTTKLKGVRERGLNKVKYATVVV GSTEEVKSSRVERSTAVLTIANNYSKLFDEGYTVVIGDVAYFVSDGYFRLMASPNSVLT TAVYKPLFAFNVNVMGTRPEKFPTTVTCENLESAVLFVNDKITEFQLDYSIDVIDNEIIVK PNISLCVPLYVRDYVDKWDDFCRQYSNESWFEDDYRAFISVLDITDAAVKAAESKAFV DTIVPPCPSILKVIDGGKIWNGVIKNVNSVRDWLKSLKLNLTQQGLLGTCAKRFKRWLGI LLEAYNAFLDTVVSTVKIGGLTFKTYAFDKPYIVIRDIVCKVENKTEAEWIELFPHNDRIK SFSTFESAYMPIADPTHFDIEEVELLDAEFVEPGCGGILAVIDEHVFYKKDGVYYPSNGT NILPVAFTKAAGGKVSFSDDVEVKDIEPVYRVKLCFEFEDEKLVDVCEKAIGKKIKHEG DWDSFCKTIQSALSVVSCYVNLPTYYIYDEEGGNDLSLPVMISEWPLSVQQAQQEATLP DIAEDVVDQVEEVNSIFDIETVDVKHDVSPFEMPFEELNGLKILKQLDNNCWVNSVMLQ IQLTGILDGDYAMQFFKMGRVAKMIERCYTAEQCIRGAMGDVGLCMYRLLKDLHTGF MVMDYKCSCTSGRLEESGAVLFCTPTKKAFPYGTCLNCNAPRMCTIRQLQGTIIFVQQK PEPVNPVSFVVKPVCSSIFRGAVSCGHYQTNIYSQNLCVDGFGVNKIQPWTNDALNTICI KDADYNAKVEISVTPIKNTVDTTPKEEFVVKEKLNAFLVHDNVAFYQGDVDTVVNGVD FDFIVNAANENLAHGGGLAKALDVYTKGKLQRLSKEHIGLAGKVKVGTGVMVECDSL RIFNVVGPRKGKHERDLLIKAYNTINNEQGTPLTPILSCGIFGIKLETSLEVLLDVCNTKEV KVFVYTDTEVCKVKDFVSGLVNVQKVEQPKIEPKPVSVIKVAPKPYRVDGKFSYFTEDL LCVADDKPIVLFTDSMLTLDDRGLALDNALSGVLSAAIKDCVDINKAIPSGNLIKFDIGSV VVYMCVVPSEKDKHLDNNVQRCTRKLNRLMCDIVCTIPADYILPLVLSSLTCNVSFVGE LKAAEAKVITIKVTEDGVNVHDVTVTTDKSFEQQVGVIADKDKDLSGAVPSDLNTSELL TKAIDVDWVEFYGFKDAVTFATVDHSAFAYESAVVNGIRVLKTSDNNCWVNAVCIALQ YSKPHFISQGLDAAWNKFVLGDVEIFVAFVYYVARLMKGDKGDAEDTLTKLSKYLANE AQVQLEHYSSCVECDAKFKNSVASINSAIVCASVKRDGVQVGYCVHGIKYYSRVRSVR GRAIIVSVEQLEPCAQSRLLSGVAYTAFSGPVDKGHYTVYDTAKKSMYDGDRFVKHDL SLLSVTSVVMVGGYVAPVNTVKPKPVINQLDEKAQKFFDFGDFLIHNFVIFFTWLLSMF TLCKTAVTTGDVKIMAKAPQRTGVVLKRSLKYNLKASAAVLKSKWWLLAKFTKLLLLI YTLYSVVLLCVRFGPFNFCSETVNGYAKSNFVKDDYCDGSLGCKMCLFGYQELSQFSH LDVVWKHITDPLFSNMQPFIVMVLLLIFGDNYLRCFLLYFVAQMISTVGVFLGYKETNW FLHFIPFDVICDELLVTVIVIKVISFVRHVLFGCENPDCIACSKSARLKRFPVNTIVNGVQR SFYVNANGGSKFCKKHRFFCVDCDSYGYGSTFITPEVSRELGNITKTNVQPTGPAYVMI DKVEFENGFYRLYSCETFWRYNFDITESKYSCKEVFKNCNVLDDFIVFNNNGTNVTQVK NASVYFSQLLCRPIKLVDSELLSTLSVDFNGVLHKAYIDVLRNSFGKDLNANMSLAECK RALGLSISDHEFTSAISNAHRCDVLLSDLSFNNFVSSYAKPEEKLSAYDLACCMRAGAK VVNANVLTKDQTPIVWHAKDFNSLSAEGRKYIVKTSKAKGLTFLLTINENQAVTQIPAT SIVAKQGAGDAGHSLTWLWLLCGLVCLIQFYLCFFMPYFMYDIVSSFEGYDFKYIENGQ LKNFEAPLKCVRNVFENFEDWHYAKFGFTPLNKQSCPIVVGVSEIVNTVAGIPSNVYLV GKTLIFTLQAAFGNAGVCYDIFGVTTPEKCIFTSACTRLEGLGGNNVYCYNTALMEGSLP YSSIQANAYYKYDNGNFIKLPEVIAQGFGFRTVRTIATKYCRVGECVESNAGVCFGFDK WFVNDGRVANGYVCGTGLWNLVFNILSMFSSSFSVAAMSGQILLNCALGAFAIFCCFLV TKFRRMFGDLSVGVCTVVVAVLLNNVSYIVTQNLVTMIAYAILYFFATRSLRYAWIWC AAYLIAYISFAPWWLCAWYFLAMLTGLLPSLLKLKVSTNLFEGDKFVGTFESAAAGTFV IDMRSYEKLANSISPEKLKSYAASYNRYKYYSGNANEADYRCACYAYLAKAMLDFSRD HNDILYTPPTVSYGSTLQAGLRKMAQPSGFVEKCVVRVCYGNTVLNGLWLGDIVYCPR HVIASNTTSAIDYDHEYSIMRLHNFSIISGTAFLGVVGATMHGVTLKIKVSQTNMHTPRH SFRTLKSGEGFNILACYDGCAQGVFGVNMRTNWTIRGSFINGACGSPGYNLKNGEVEFV YMHQIELGSGSHVGSSFDGVMYGGFEDQPNLQVESANQMLTVNVVAFLYAAILNGCT WWLKGEKLFVEHYNEWAQANGFTAMNGEDAFSILAAKTGVCVERLLHAIQVLNNGFG GKQILGYSSLNDEFSINEVVKQMFGVNLQSGKTTSMFKSISLFAGFFVMFWAELFVYTTT IWVNPGFLTPFMILLVALSLCLTFVVKHKVLFLQVFLLPSIIVAAIQNCAWDYHVTKVLA EKFDYNVSVMQMDIQGFVNIFICLFVALLHTWRFAKERCTHWCTYLFSLIAVLYTALYS YDYVSLLVMLLCAISNEWYIGAIIFRICRFGVAFLPVEYVSYFDGVKTVLLFYMLLGFVS CMYYGLLYWINRFCKCTLGVYDFCVSPAEFKYMVANGLNAPNGPFDALFLSFKLMGIG GPRTIKVSTVQSKLTDLKCTNVVLMGILSNMNIASNSKEWAYCVEMHNKINLCDDPETA QELLLALLAFFLSKHSDFGLGDLVDSYFENDSILQSVASSFVGMPSFVAYETARQEYENA VANGSSPQIIKQLKKAMNVAKAEFDRESSVQKKINRMAEQAAAAMYKEARAVNRKSK VVSAMHSLLFGMLRRLDMSSVDTILNMARNGVVPLSVIPATSAARLVVVVPDHDSFVK MMVDGFVHYAGVVWTLQEVKDNDGKNVHLKDVTKENQEILVWPLILTCERVVVKLQN NEIMPGKMKVKATKGEGDGGITSEGNALYNNEGGRAFMYAYVTTKPGMKYVKWEHD SGVVTVELEPPCRFVIDTPTGPQIKYLYFVKNLNNLRRGAVLGYIGATVRLQAGKQTEFV SNSHLLTHCSFAVDPAAAYLDAVKQGAKPVGNCVKMLTNGSGSGQAITCTIDSNTTQD TYGGASVCIYCRAHVAHPTMDGFCQYKGKWVQVPIGTNDPIRFCLENTVCKVCGCWL NHGCTCDRTAIQSFDNSYLNRVRGSSAARLEPCNGTDIDYCVRAFDVYNKDASFIGKNL KSNCVRFKNVDKDDAFYIVKRCIKSVMDHEQSMYNLLKGCNAVAKHDFFTWHEGRTI YGNVSRQDLTKYTMMDLCFALRNFDEKDCEVFKEILVLTGCCSTDYFEMKNWFDPIEN EDIHRVYAALGKVVANAMLKCVAFCDEMVLKGVVGVLTLDNQDLNGNFYDFGDFVL CPPGMGIPYCTSYYSYMMPVMGMTNCLASECFMKSDIFGQDFKTFDLLKYDFTEHKEV LFNKYFKYWGQDYHPDCVDCHDEMCILHCSNFNTLFATTIPNTAFGPLCRKVFIDGVPV VATAGYHFKQLGLVWNKDVNTHSTRLTITELLQFVTDPTLIVASSPALVDKRTVCFSVA ALSTGLTSQTVKPGHFNKEFYDFLRSQGFFDEGSELTLKHFFFTQKGDAAIKDFDYYRY NRPTMLDIGQARVAYQVAARYFDCYEGGCITSREVVVTNLNKSAGWPLNKFGKAGLY YESISYEEQDAIFSLTKRNILPTMTQLNLKYAISGKERARTVGGVSLLATMTTRQFHQKC LKSIVATRNATVVIGTTKFYGGWDNMLKNLMADVDDPKLMGWDYPKCDRAMPSMIR

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Sequences
MLSAMILGSKHVTCCTASDKFYRLSNELAQVLTEVVYSNGGFYFKPGGTTSGDATTAY ANSVFNIFQAVSSNINCVLSVNSSNCNNFNVKKLQRQLYDNCYRNSNVDESFVDDFYGY LQKHFSMMILSDDSVVCYNKTYAGLGYIADISAFKATLYYQNGVFMSTAKCWTEEDLSI GPHEFCSQHTMQIVDENGKYYLPYPDPSRIISAGVFVDDITKTDAVILLERYVSLAIDAYP LSKHPKPEYRKVFYALLDWVKHLNKTLNEGVLESFSVTLLDEHESKFWDESFYASMYE KSTVLQAAGLCVVCGSQTVLRCGDCLRRPMLCTKCAYDHVFGTDHKFILAITPYVCNTS GCNVNDVTKLYLGGLNYYCVDHKPHLSFPLCSAGNVFGLYKSSALGSMDIDVFNKLST SDWSDIRDYKLANDAKESLRLFAAETVKAKEESVKSSYAYATLKEIVGPKELLLLWESG KAKPPLNRNSVFTCFQITKDSKFQVGEFVFEKVDYGSDTVTYKSTATTKLVPGMLFILTS HNVAPLRAPTMANQEKYSTIYKLHPSFNVSDAYANLVPYYQLIGKQRITTIQGPPGSGKS HCSIGIGVYYPGARIVFTACSHAAVDSLCAKAVTAYSVDKCTRIIPARARVECYSGFKPN NNSAQYVFSTVNALPEVNADIVVVDEVSMCTNYDLSVINQRISYKHIVYVGDPQQLPAP RVLISKGVMEPIDYNVVTQRMCAIGPDVFLHKCYRCPAEIVNTVSELVYENKFVPVKEA SKQCFKIFERGSVQVDNGSSINRRQLDVVKRFIHKNSTWSKAVFISPYNSQNYVAARLLG LQTQTVDSAQGSEYDYVIFAQTSDTAHACNANRFNVAITRAKKGIFCIMSDRTLFDALK FFEITMTDLQSESSCGLFKDCARNPIDLPPSHATTYLSLSDRFKTSGDLAVQIGNNNVCTY EHVISYMGFRFDVSMPGSHSLFCTRDFAMRHVRGWLGMDVEGAHVTGDNVGTNVPLQ VGFSNGVDFVAQPEGCVLTNTGSVVKPVRARAPPGEQFTHIVPLLRKGQPWSVLRKRIV QMIADFLAGSSDVLVFVLWAGGLELTTMRYFVKIGAVKHCQCGTVATCYNSVSNDYC CFKHALGCDYVYNPYVIDIQQWGYVGSLSTNHHAICNVHRNEHVASGDAIMTRCLAVY DCFVKNVDWSITYPMIANENAINKGGRTVQSHIMRAAIKLYNPKAIHDIGNPKGIRCAVT DAKWYCYDKNPINSNVKTLEYDYMTHGQMDGLCLFWNCNVDMYPEFSIVCRFDTRTR STLNLEGVNGGSLYVNNHAFHTPAYDKRAMAKLKPAPFFYYDDGSCEVVHDQVNYVP LRATNCITKCNIGGAVCSKHANLYRAYVESYNIFTQAGFNIWVPTTFDCYNLWQTFTEV NLQGLENIAFNVVNKGSFVGADGELPVAISGDKVFVRDGNTDNLVFVNKTSLPTNIAFE LFAKRKVGLTPPLSILKNLGVVATYKFVLWDYEAERPLTSFTKSVCGYTDFAEDVCTCY DNSIQGSYERFTLSTNAVLFSATAVKTGGKSLPAIKLNFGMLNGNAIATVKSEDGNIKNI NWFVYVRKDGKPVDHYDGFYTQGRNLQDFLPRSTMEEDFLNMDIGVFIQKYGLEDFNF EHVVYGDVSKTTLGGLHLLISQVRLSKMGILKAEEFVAASDITLKCCTVTYLNDPSSKTV CTYMDLLLDDFVSVLKSLDLTVVSKVHEVIIDNKPWRWMLWCKDNAVATFYPQLQSA EWKCGYSMPGIYKTQRMCLEPCNLYNYGAGLKLPSGIMFNVVKYTQLCQYFNSTTLCV PHNMRVLHLGAGSDYGVAPGTAVLKRWLPHDAIVVDNDVVDYVSDADFSVTGDCAT VYLEDKFDLLISDMYDGRTKAIDGENVSKEGFFTYINGFICEKLAIGGSIAIKVTEYSWNK KLYELVQRFSFWTMFCTSVNTSSSEAFVVGINYLGDFAQGPFIDGNIIHANYVFWRNSTV MSLSYNSVLDLSKFNCKHKATVVVQLKDSDINEMVLSLVRSGKLLVRGNGKCLSFSNH LVSTK (SEQ ID NO: 7)

SEQUENCE LISTING

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<160> NUMBER OF SEQ ID NOS: 117

<210> SEQ ID NO 1
<211> LENGTH: 7096
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 1

Met Glu Ser Leu Val Pro Gly Phe Asn Glu Lys Thr His Val Gln Leu
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Ser Leu Pro Val Leu Gln Val Arg Asp Val Leu Val Arg Gly Phe Gly
            20                  25                  30

Asp Ser Val Glu Glu Val Leu Ser Glu Ala Arg Gln His Leu Lys Asp
        35                  40                  45

Gly Thr Cys Gly Leu Val Glu Val Glu Lys Gly Val Leu Pro Gln Leu
    50                  55                  60

Glu Gln Pro Tyr Val Phe Ile Lys Arg Ser Asp Ala Arg Thr Ala Pro
65                  70                  75                  80

His Gly His Val Met Val Glu Leu Val Ala Glu Leu Glu Gly Ile Gln
                85                  90                  95

Tyr Gly Arg Ser Gly Glu Thr Leu Gly Val Leu Val Pro His Val Gly
            100                 105                 110

Glu Ile Pro Val Ala Tyr Arg Lys Val Leu Leu Arg Lys Asn Gly Asn
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        115                 120                 125

Lys Gly Ala Gly Gly His Ser Tyr Gly Ala Asp Leu Lys Ser Phe Asp
    130                 135                 140

Leu Gly Asp Glu Leu Gly Thr Asp Pro Tyr Glu Asp Phe Gln Glu Asn
145                 150                 155                 160

Trp Asn Thr Lys His Ser Ser Gly Val Thr Arg Glu Leu Met Arg Glu
                165                 170                 175

Leu Asn Gly Gly Ala Tyr Thr Arg Tyr Val Asp Asn Asn Phe Cys Gly
            180                 185                 190

Pro Asp Gly Tyr Pro Leu Glu Cys Ile Lys Asp Leu Leu Ala Arg Ala
        195                 200                 205

Gly Lys Ala Ser Cys Thr Leu Ser Glu Gln Leu Asp Phe Ile Asp Thr
    210                 215                 220

Lys Arg Gly Val Tyr Cys Cys Arg Glu His Glu His Glu Ile Ala Trp
225                 230                 235                 240

Tyr Thr Glu Arg Ser Glu Lys Ser Tyr Glu Leu Gln Thr Pro Phe Glu
                245                 250                 255

Ile Lys Leu Ala Lys Lys Phe Asp Thr Phe Asn Gly Glu Cys Pro Asn
            260                 265                 270

Phe Val Phe Pro Leu Asn Ser Ile Ile Lys Thr Ile Gln Pro Arg Val
        275                 280                 285

Glu Lys Lys Lys Leu Asp Gly Phe Met Gly Arg Ile Arg Ser Val Tyr
    290                 295                 300

Pro Val Ala Ser Pro Asn Glu Cys Asn Gln Met Cys Leu Ser Thr Leu
305                 310                 315                 320

Met Lys Cys Asp His Cys Gly Glu Thr Ser Trp Gln Thr Gly Asp Phe
                325                 330                 335

Val Lys Ala Thr Cys Glu Phe Cys Gly Thr Glu Asn Leu Thr Lys Glu
            340                 345                 350

Gly Ala Thr Thr Cys Gly Tyr Leu Pro Gln Asn Ala Val Val Lys Ile
        355                 360                 365

Tyr Cys Pro Ala Cys His Asn Ser Glu Val Gly Pro Glu His Ser Leu
    370                 375                 380

Ala Glu Tyr His Asn Glu Ser Gly Leu Lys Thr Ile Leu Arg Lys Gly
385                 390                 395                 400

Gly Arg Thr Ile Ala Phe Gly Gly Cys Val Phe Ser Tyr Val Gly Cys
                405                 410                 415

His Asn Lys Cys Ala Tyr Trp Val Pro Arg Ala Ser Ala Asn Ile Gly
            420                 425                 430

Cys Asn His Thr Gly Val Val Gly Glu Gly Ser Glu Gly Leu Asn Asp
        435                 440                 445

Asn Leu Leu Glu Ile Leu Gln Lys Glu Lys Val Asn Ile Asn Ile Val
    450                 455                 460

Gly Asp Phe Lys Leu Asn Glu Glu Ile Ala Ile Ile Leu Ala Ser Phe
465                 470                 475                 480

Ser Ala Ser Thr Ser Ala Phe Val Glu Thr Val Lys Gly Leu Asp Tyr
                485                 490                 495

Lys Ala Phe Lys Gln Ile Val Glu Ser Cys Gly Asn Phe Lys Val Thr
            500                 505                 510

Lys Gly Lys Ala Lys Lys Gly Ala Trp Asn Ile Gly Glu Gln Lys Ser
        515                 520                 525
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Ile Leu Ser Pro Leu Tyr Ala Phe Ala Ser Glu Ala Ala Arg Val Val
    530                 535                 540

Arg Ser Ile Phe Ser Arg Thr Leu Glu Thr Ala Gln Asn Ser Val Arg
545                 550                 555                 560

Val Leu Gln Lys Ala Ala Ile Thr Ile Leu Asp Gly Ile Ser Gln Tyr
                565                 570                 575

Ser Leu Arg Leu Ile Asp Ala Met Met Phe Thr Ser Asp Leu Ala Thr
            580                 585                 590

Asn Asn Leu Val Val Met Ala Tyr Ile Thr Gly Gly Val Val Gln Leu
        595                 600                 605

Thr Ser Gln Trp Leu Thr Asn Ile Phe Gly Thr Val Tyr Glu Lys Leu
    610                 615                 620

Lys Pro Val Leu Asp Trp Leu Glu Glu Lys Phe Lys Glu Gly Val Glu
625                 630                 635                 640

Phe Leu Arg Asp Gly Trp Glu Ile Val Lys Phe Ile Ser Thr Cys Ala
                645                 650                 655

Cys Glu Ile Val Gly Gly Gln Ile Val Thr Cys Ala Lys Glu Ile Lys
            660                 665                 670

Glu Ser Val Gln Thr Phe Phe Lys Leu Val Asn Lys Phe Leu Ala Leu
        675                 680                 685

Cys Ala Asp Ser Ile Ile Ile Gly Gly Ala Lys Leu Lys Ala Leu Asn
    690                 695                 700

Leu Gly Glu Thr Phe Val Thr His Ser Lys Gly Leu Tyr Arg Lys Cys
705                 710                 715                 720

Val Lys Ser Arg Glu Glu Thr Gly Leu Leu Met Pro Leu Lys Ala Pro
                725                 730                 735

Lys Glu Ile Ile Phe Leu Glu Gly Glu Thr Leu Pro Thr Glu Val Leu
            740                 745                 750

Thr Glu Glu Val Val Leu Lys Thr Gly Asp Leu Gln Pro Leu Glu Gln
        755                 760                 765

Pro Thr Ser Glu Ala Val Glu Ala Pro Leu Val Gly Thr Pro Val Cys
    770                 775                 780

Ile Asn Gly Leu Met Leu Leu Glu Ile Lys Asp Thr Glu Lys Tyr Cys
785                 790                 795                 800

Ala Leu Ala Pro Asn Met Met Val Thr Asn Asn Thr Phe Thr Leu Lys
                805                 810                 815

Gly Gly Ala Pro Thr Lys Val Thr Phe Gly Asp Asp Thr Val Ile Glu
            820                 825                 830

Val Gln Gly Tyr Lys Ser Val Asn Ile Thr Phe Glu Leu Asp Glu Arg
        835                 840                 845

Ile Asp Lys Val Leu Asn Glu Lys Cys Ser Ala Tyr Thr Val Glu Leu
    850                 855                 860

Gly Thr Glu Val Asn Glu Phe Ala Cys Val Val Ala Asp Ala Val Ile
865                 870                 875                 880

Lys Thr Leu Gln Pro Val Ser Glu Leu Leu Thr Pro Leu Gly Ile Asp
                885                 890                 895

Leu Asp Glu Trp Ser Met Ala Thr Tyr Tyr Leu Phe Asp Glu Ser Gly
            900                 905                 910

Glu Phe Lys Leu Ala Ser His Met Tyr Cys Ser Phe Tyr Pro Pro Asp
        915                 920                 925
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Glu Asp Glu Glu Glu Gly Asp Cys Glu Glu Glu Glu Phe Glu Pro Ser
    930                 935                 940

Thr Gln Tyr Glu Tyr Gly Thr Glu Asp Asp Tyr Gln Gly Lys Pro Leu
945                 950                 955                 960

Glu Phe Gly Ala Thr Ser Ala Ala Leu Gln Pro Glu Glu Glu Gln Glu
                965                 970                 975

Glu Asp Trp Leu Asp Asp Asp Ser Gln Gln Thr Val Gly Gln Gln Asp
            980                 985                 990

Gly Ser Glu Asp Asn Gln Thr Thr  Thr Ile Gln Thr Ile  Val Glu Val
        995                 1000                1005

Gln Pro  Gln Leu Glu Met Glu  Leu Thr Pro Val Val  Gln Thr Ile
    1010                1015                1020

Glu Val  Asn Ser Phe Ser Gly  Tyr Leu Lys Leu Thr  Asp Asn Val
    1025                1030                1035

Tyr Ile  Lys Asn Ala Asp Ile  Val Glu Glu Ala Lys  Lys Val Lys
    1040                1045                1050

Pro Thr  Val Val Val Asn Ala  Ala Asn Val Tyr Leu  Lys His Gly
    1055                1060                1065

Gly Gly  Val Ala Gly Ala Leu  Asn Lys Ala Thr Asn  Asn Ala Met
    1070                1075                1080

Gln Val  Glu Ser Asp Asp Tyr  Ile Ala Thr Asn Gly  Pro Leu Lys
    1085                1090                1095

Val Gly  Gly Ser Cys Val Leu  Ser Gly His Asn Leu  Ala Lys His
    1100                1105                1110

Cys Leu  His Val Val Gly Pro  Asn Val Asn Lys Gly  Glu Asp Ile
    1115                1120                1125

Gln Leu  Leu Lys Ser Ala Tyr  Glu Asn Phe Asn Gln  His Glu Val
    1130                1135                1140

Leu Leu  Ala Pro Leu Leu Ser  Ala Gly Ile Phe Gly  Ala Asp Pro
    1145                1150                1155

Ile His  Ser Leu Arg Val Cys  Val Asp Thr Val Arg  Thr Asn Val
    1160                1165                1170

Tyr Leu  Ala Val Phe Asp Lys  Asn Leu Tyr Asp Lys  Leu Val Ser
    1175                1180                1185

Ser Phe  Leu Glu Met Lys Ser  Glu Lys Gln Val Glu  Gln Lys Ile
    1190                1195                1200

Ala Glu  Ile Pro Lys Glu Glu  Val Lys Pro Phe Ile  Thr Glu Ser
    1205                1210                1215

Lys Pro  Ser Val Glu Gln Arg  Lys Gln Asp Asp Lys  Lys Ile Lys
    1220                1225                1230

Ala Cys  Val Glu Glu Val Thr  Thr Thr Leu Glu Glu  Thr Lys Phe
    1235                1240                1245

Leu Thr  Glu Asn Leu Leu Leu  Tyr Ile Asp Ile Asn  Gly Asn Leu
    1250                1255                1260

His Pro  Asp Ser Ala Thr Leu  Val Ser Asp Ile Asp  Ile Thr Phe
    1265                1270                1275

Leu Lys  Lys Asp Ala Pro Tyr  Ile Val Gly Asp Val  Val Gln Glu
    1280                1285                1290

Gly Val  Leu Thr Ala Val Val  Ile Pro Thr Lys Lys  Ala Gly Gly
    1295                1300                1305

Thr Thr  Glu Met Leu Ala Lys  Ala Leu Arg Lys Val  Pro Thr Asp
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    1310                1315                1320

Asn Tyr  Ile Thr Thr Tyr Pro  Gly Gln Gly Leu Asn  Gly Tyr Thr
    1325                1330                1335

Val Glu  Glu Ala Lys Thr Val  Leu Lys Lys Cys Lys  Ser Ala Phe
    1340                1345                1350

Tyr Ile  Leu Pro Ser Ile Ile  Ser Asn Glu Lys Gln  Glu Ile Leu
    1355                1360                1365

Gly Thr  Val Ser Trp Asn Leu  Arg Glu Met Leu Ala  His Ala Glu
    1370                1375                1380

Glu Thr  Arg Lys Leu Met Pro  Val Cys Val Glu Thr  Lys Ala Ile
    1385                1390                1395

Val Ser  Thr Ile Gln Arg Lys  Tyr Lys Gly Ile Lys  Ile Gln Glu
    1400                1405                1410

Gly Val  Val Asp Tyr Gly Ala  Arg Phe Tyr Phe Tyr  Thr Ser Lys
    1415                1420                1425

Thr Thr  Val Ala Ser Leu Ile  Asn Thr Leu Asn Asp  Leu Asn Glu
    1430                1435                1440

Thr Leu  Val Thr Met Pro Leu  Gly Tyr Val Thr His  Gly Leu Asn
    1445                1450                1455

Leu Glu  Glu Ala Ala Arg Tyr  Met Arg Ser Leu Lys  Val Pro Ala
    1460                1465                1470

Thr Val  Ser Val Ser Ser Pro  Asp Ala Val Thr Ala  Tyr Asn Gly
    1475                1480                1485

Tyr Leu  Thr Ser Ser Ser Lys  Thr Pro Glu Glu His  Phe Ile Glu
    1490                1495                1500

Thr Ile  Ser Leu Ala Gly Ser  Tyr Lys Asp Trp Ser  Tyr Ser Gly
    1505                1510                1515

Gln Ser  Thr Gln Leu Gly Ile  Glu Phe Leu Lys Arg  Gly Asp Lys
    1520                1525                1530

Ser Val  Tyr Tyr Thr Ser Asn  Pro Thr Thr Phe His  Leu Asp Gly
    1535                1540                1545

Glu Val  Ile Thr Phe Asp Asn  Leu Lys Thr Leu Leu  Ser Leu Arg
    1550                1555                1560

Glu Val  Arg Thr Ile Lys Val  Phe Thr Thr Val Asp  Asn Ile Asn
    1565                1570                1575

Leu His  Thr Gln Val Val Asp  Met Ser Met Thr Tyr  Gly Gln Gln
    1580                1585                1590

Phe Gly  Pro Thr Tyr Leu Asp  Gly Ala Asp Val Thr  Lys Ile Lys
    1595                1600                1605

Pro His  Asn Ser His Glu Gly  Lys Thr Phe Tyr Val  Leu Pro Asn
    1610                1615                1620

Asp Asp  Thr Leu Arg Val Glu  Ala Phe Glu Tyr Tyr  His Thr Thr
    1625                1630                1635

Asp Pro  Ser Phe Leu Gly Arg  Tyr Met Ser Ala Leu  Asn His Thr
    1640                1645                1650

Lys Lys  Trp Lys Tyr Pro Gln  Val Asn Gly Leu Thr  Ser Ile Lys
    1655                1660                1665

Trp Ala  Asp Asn Asn Cys Tyr  Leu Ala Thr Ala Leu  Leu Thr Leu
    1670                1675                1680

Gln Gln  Ile Glu Leu Lys Phe  Asn Pro Pro Ala Leu  Gln Asp Ala
    1685                1690                1695
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Tyr Tyr  Arg Ala Arg Ala Gly  Glu Ala Ala Asn Phe  Cys Ala Leu
    1700                 1705                 1710

Ile Leu  Ala Tyr Cys Asn Lys  Thr Val Gly Glu Leu  Gly Asp Val
    1715                 1720                 1725

Arg Glu  Thr Met Ser Tyr Leu  Phe Gln His Ala Asn  Leu Asp Ser
    1730                 1735                 1740

Cys Lys  Arg Val Leu Asn Val  Val Cys Lys Thr Cys  Gly Gln Gln
    1745                 1750                 1755

Gln Thr  Thr Leu Lys Gly Val  Glu Ala Val Met Tyr  Met Gly Thr
    1760                 1765                 1770

Leu Ser  Tyr Glu Gln Phe Lys  Lys Gly Val Gln Ile  Pro Cys Thr
    1775                 1780                 1785

Cys Gly  Lys Gln Ala Thr Lys  Tyr Leu Val Gln Gln  Glu Ser Pro
    1790                 1795                 1800

Phe Val  Met Met Ser Ala Pro  Pro Ala Gln Tyr Glu  Leu Lys His
    1805                 1810                 1815

Gly Thr  Phe Thr Cys Ala Ser  Glu Tyr Thr Gly Asn  Tyr Gln Cys
    1820                 1825                 1830

Gly His  Tyr Lys His Ile Thr  Ser Lys Glu Thr Leu  Tyr Cys Ile
    1835                 1840                 1845

Asp Gly  Ala Leu Leu Thr Lys  Ser Ser Glu Tyr Lys  Gly Pro Ile
    1850                 1855                 1860

Thr Asp  Val Phe Tyr Lys Glu  Asn Ser Tyr Thr Thr  Thr Ile Lys
    1865                 1870                 1875

Pro Val  Thr Tyr Lys Leu Asp  Gly Val Val Cys Thr  Glu Ile Asp
    1880                 1885                 1890

Pro Lys  Leu Asp Asn Tyr Tyr  Lys Lys Asp Asn Ser  Tyr Phe Thr
    1895                 1900                 1905

Glu Gln  Pro Ile Asp Leu Val  Pro Asn Gln Pro Tyr  Pro Asn Ala
    1910                 1915                 1920

Ser Phe  Asp Asn Phe Lys Phe  Val Cys Asp Asn Ile  Lys Phe Ala
    1925                 1930                 1935

Asp Asp  Leu Asn Gln Leu Thr  Gly Tyr Lys Lys Pro  Ala Ser Arg
    1940                 1945                 1950

Glu Leu  Lys Val Thr Phe Phe  Pro Asp Leu Asn Gly  Asp Val Val
    1955                 1960                 1965

Ala Ile  Asp Tyr Lys His Tyr  Thr Pro Ser Phe Lys  Lys Gly Ala
    1970                 1975                 1980

Lys Leu  Leu His Lys Pro Ile  Val Trp His Val Asn  Asn Ala Thr
    1985                 1990                 1995

Asn Lys  Ala Thr Tyr Lys Pro  Asn Thr Trp Cys Ile  Arg Cys Leu
    2000                 2005                 2010

Trp Ser  Thr Lys Pro Val Glu  Thr Ser Asn Ser Phe  Asp Val Leu
    2015                 2020                 2025

Lys Ser  Glu Asp Ala Gln Gly  Met Asp Asn Leu Ala  Cys Glu Asp
    2030                 2035                 2040

Leu Lys  Pro Val Ser Glu Glu  Val Val Glu Asn Pro  Thr Ile Gln
    2045                 2050                 2055

Lys Asp  Val Leu Glu Cys Asn  Val Lys Thr Thr Glu  Val Val Gly
    2060                 2065                 2070
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Asp Ile  Ile Leu Lys Pro Ala  Asn Asn Ser Leu Lys  Ile Thr Glu
    2075                 2080                 2085

Glu Val  Gly His Thr Asp Leu  Met Ala Ala Tyr Val  Asp Asn Ser
    2090                 2095                 2100

Ser Leu  Thr Ile Lys Lys Pro  Asn Glu Leu Ser Arg  Val Leu Gly
    2105                 2110                 2115

Leu Lys  Thr Leu Ala Thr His  Gly Leu Ala Ala Val  Asn Ser Val
    2120                 2125                 2130

Pro Trp  Asp Thr Ile Ala Asn  Tyr Ala Lys Pro Phe  Leu Asn Lys
    2135                 2140                 2145

Val Val  Ser Thr Thr Thr Asn  Ile Val Thr Arg Cys  Leu Asn Arg
    2150                 2155                 2160

Val Cys  Thr Asn Tyr Met Pro  Tyr Phe Phe Thr Leu  Leu Leu Gln
    2165                 2170                 2175

Leu Cys  Thr Phe Thr Arg Ser  Thr Asn Ser Arg Ile  Lys Ala Ser
    2180                 2185                 2190

Met Pro  Thr Thr Ile Ala Lys  Asn Thr Val Lys Ser  Val Gly Lys
    2195                 2200                 2205

Phe Cys  Leu Glu Ala Ser Phe  Asn Tyr Leu Lys Ser  Pro Asn Phe
    2210                 2215                 2220

Ser Lys  Leu Ile Asn Ile Ile  Ile Trp Phe Leu Leu  Leu Ser Val
    2225                 2230                 2235

Cys Leu  Gly Ser Leu Ile Tyr  Ser Thr Ala Ala Leu  Gly Val Leu
    2240                 2245                 2250

Met Ser  Asn Leu Gly Met Pro  Ser Tyr Cys Thr Gly  Tyr Arg Glu
    2255                 2260                 2265

Gly Tyr  Leu Asn Ser Thr Asn  Val Thr Ile Ala Thr  Tyr Cys Thr
    2270                 2275                 2280

Gly Ser  Ile Pro Cys Ser Val  Cys Leu Ser Gly Leu  Asp Ser Leu
    2285                 2290                 2295

Asp Thr  Tyr Pro Ser Leu Glu  Thr Ile Gln Ile Thr  Ile Ser Ser
    2300                 2305                 2310

Phe Lys  Trp Asp Leu Thr Ala  Phe Gly Leu Val Ala  Glu Trp Phe
    2315                 2320                 2325

Leu Ala  Tyr Ile Leu Phe Thr  Arg Phe Phe Tyr Val  Leu Gly Leu
    2330                 2335                 2340

Ala Ala  Ile Met Gln Leu Phe  Phe Ser Tyr Phe Ala  Val His Phe
    2345                 2350                 2355

Ile Ser  Asn Ser Trp Leu Met  Trp Leu Ile Ile Asn  Leu Val Gln
    2360                 2365                 2370

Met Ala  Pro Ile Ser Ala Met  Val Arg Met Tyr Ile  Phe Phe Ala
    2375                 2380                 2385

Ser Phe  Tyr Tyr Val Trp Lys  Ser Tyr Val His Val  Val Asp Gly
    2390                 2395                 2400

Cys Asn  Ser Ser Thr Cys Met  Met Cys Tyr Lys Arg  Asn Arg Ala
    2405                 2410                 2415

Thr Arg  Val Glu Cys Thr Thr  Ile Val Asn Gly Val  Arg Arg Ser
    2420                 2425                 2430

Phe Tyr  Val Tyr Ala Asn Gly  Gly Lys Gly Phe Cys  Lys Leu His
    2435                 2440                 2445

Asn Trp  Asn Cys Val Asn Cys  Asp Thr Phe Cys Ala  Gly Ser Thr
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    2450                2455                2460

Phe Ile  Ser Asp Glu Val Ala  Arg Asp Leu Ser Leu  Gln Phe Lys
    2465                2470                2475

Arg Pro  Ile Asn Pro Thr Asp  Gln Ser Ser Tyr Ile  Val Asp Ser
    2480                2485                2490

Val Thr  Val Lys Asn Gly Ser  Ile His Leu Tyr Phe  Asp Lys Ala
    2495                2500                2505

Gly Gln  Lys Thr Tyr Glu Arg  His Ser Leu Ser His  Phe Val Asn
    2510                2515                2520

Leu Asp  Asn Leu Arg Ala Asn  Asn Thr Lys Gly Ser  Leu Pro Ile
    2525                2530                2535

Asn Val  Ile Val Phe Asp Gly  Lys Ser Lys Cys Glu  Glu Ser Ser
    2540                2545                2550

Ala Lys  Ser Ala Ser Val Tyr  Tyr Ser Gln Leu Met  Cys Gln Pro
    2555                2560                2565

Ile Leu  Leu Leu Asp Gln Ala  Leu Val Ser Asp Val  Gly Asp Ser
    2570                2575                2580

Ala Glu  Val Ala Val Lys Met  Phe Asp Ala Tyr Val  Asn Thr Phe
    2585                2590                2595

Ser Ser  Thr Phe Asn Val Pro  Met Glu Lys Leu Lys  Thr Leu Val
    2600                2605                2610

Ala Thr  Ala Glu Ala Glu Leu  Ala Lys Asn Val Ser  Leu Asp Asn
    2615                2620                2625

Val Leu  Ser Thr Phe Ile Ser  Ala Ala Arg Gln Gly  Phe Val Asp
    2630                2635                2640

Ser Asp  Val Glu Thr Lys Asp  Val Val Glu Cys Leu  Lys Leu Ser
    2645                2650                2655

His Gln  Ser Asp Ile Glu Val  Thr Gly Asp Ser Cys  Asn Asn Tyr
    2660                2665                2670

Met Leu  Thr Tyr Asn Lys Val  Glu Asn Met Thr Pro  Arg Asp Leu
    2675                2680                2685

Gly Ala  Cys Ile Asp Cys Ser  Ala Arg His Ile Asn  Ala Gln Val
    2690                2695                2700

Ala Lys  Ser His Asn Ile Ala  Leu Ile Trp Asn Val  Lys Asp Phe
    2705                2710                2715

Met Ser  Leu Ser Glu Gln Leu  Arg Lys Gln Ile Arg  Ser Ala Ala
    2720                2725                2730

Lys Lys  Asn Asn Leu Pro Phe  Lys Leu Thr Cys Ala  Thr Thr Arg
    2735                2740                2745

Gln Val  Val Asn Val Val Thr  Thr Lys Ile Ala Leu  Lys Gly Gly
    2750                2755                2760

Lys Ile  Val Asn Asn Trp Leu  Lys Gln Leu Ile Lys  Val Thr Leu
    2765                2770                2775

Val Phe  Leu Phe Val Ala Ala  Ile Phe Tyr Leu Ile  Thr Pro Val
    2780                2785                2790

His Val  Met Ser Lys His Thr  Asp Phe Ser Ser Glu  Ile Ile Gly
    2795                2800                2805

Tyr Lys  Ala Ile Asp Gly Gly  Val Thr Arg Asp Ile  Ala Ser Thr
    2810                2815                2820

Asp Thr  Cys Phe Ala Asn Lys  His Ala Asp Phe Asp  Thr Trp Phe
    2825                2830                2835
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Ser Gln  Arg Gly Gly Ser Tyr  Thr Asn Asp Lys Ala  Cys Pro Leu
    2840                 2845                 2850

Ile Ala  Ala Val Ile Thr Arg  Glu Val Gly Phe Val  Val Pro Gly
    2855                 2860                 2865

Leu Pro  Gly Thr Ile Leu Arg  Thr Thr Asn Gly Asp  Phe Leu His
    2870                 2875                 2880

Phe Leu  Pro Arg Val Phe Ser  Ala Val Gly Asn Ile  Cys Tyr Thr
    2885                 2890                 2895

Pro Ser  Lys Leu Ile Glu Tyr  Thr Asp Phe Ala Thr  Ser Ala Cys
    2900                 2905                 2910

Val Leu  Ala Ala Glu Cys Thr  Ile Phe Lys Asp Ala  Ser Gly Lys
    2915                 2920                 2925

Pro Val  Pro Tyr Cys Tyr Asp  Thr Asn Val Leu Glu  Gly Ser Val
    2930                 2935                 2940

Ala Tyr  Glu Ser Leu Arg Pro  Asp Thr Arg Tyr Val  Leu Met Asp
    2945                 2950                 2955

Gly Ser  Ile Ile Gln Phe Pro  Asn Thr Tyr Leu Glu  Gly Ser Val
    2960                 2965                 2970

Arg Val  Val Thr Thr Phe Asp  Ser Glu Tyr Cys Arg  His Gly Thr
    2975                 2980                 2985

Cys Glu  Arg Ser Glu Ala Gly  Val Cys Val Ser Thr  Ser Gly Arg
    2990                 2995                 3000

Trp Val  Leu Asn Asn Asp Tyr  Tyr Arg Ser Leu Pro  Gly Val Phe
    3005                 3010                 3015

Cys Gly  Val Asp Ala Val Asn  Leu Leu Thr Asn Met  Phe Thr Pro
    3020                 3025                 3030

Leu Ile  Gln Pro Ile Gly Ala  Leu Asp Ile Ser Ala  Ser Ile Val
    3035                 3040                 3045

Ala Gly  Gly Ile Val Ala Ile  Val Val Thr Cys Leu  Ala Tyr Tyr
    3050                 3055                 3060

Phe Met  Arg Phe Arg Arg Ala  Phe Gly Glu Tyr Ser  His Val Val
    3065                 3070                 3075

Ala Phe  Asn Thr Leu Leu Phe  Leu Met Ser Phe Thr  Val Leu Cys
    3080                 3085                 3090

Leu Thr  Pro Val Tyr Ser Phe  Leu Pro Gly Val Tyr  Ser Val Ile
    3095                 3100                 3105

Tyr Leu  Tyr Leu Thr Phe Tyr  Leu Thr Asn Asp Val  Ser Phe Leu
    3110                 3115                 3120

Ala His  Ile Gln Trp Met Val  Met Phe Thr Pro Leu  Val Pro Phe
    3125                 3130                 3135

Trp Ile  Thr Ile Ala Tyr Ile  Ile Cys Ile Ser Thr  Lys His Phe
    3140                 3145                 3150

Tyr Trp  Phe Phe Ser Asn Tyr  Leu Lys Arg Arg Val  Val Phe Asn
    3155                 3160                 3165

Gly Val  Ser Phe Ser Thr Phe  Glu Glu Ala Ala Leu  Cys Thr Phe
    3170                 3175                 3180

Leu Leu  Asn Lys Glu Met Tyr  Leu Lys Leu Arg Ser  Asp Val Leu
    3185                 3190                 3195

Leu Pro  Leu Thr Gln Tyr Asn  Arg Tyr Leu Ala Leu  Tyr Asn Lys
    3200                 3205                 3210
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Tyr Lys  Tyr Phe Ser Gly Ala  Met Asp Thr Thr Ser  Tyr Arg Glu
    3215                 3220                 3225

Ala Ala  Cys Cys His Leu Ala  Lys Ala Leu Asn Asp  Phe Ser Asn
    3230                 3235                 3240

Ser Gly  Ser Asp Val Leu Tyr  Gln Pro Pro Gln Thr  Ser Ile Thr
    3245                 3250                 3255

Ser Ala  Val Leu Gln Ser Gly  Phe Arg Lys Met Ala  Phe Pro Ser
    3260                 3265                 3270

Gly Lys  Val Glu Gly Cys Met  Val Gln Val Thr Cys  Gly Thr Thr
    3275                 3280                 3285

Thr Leu  Asn Gly Leu Trp Leu  Asp Asp Val Val Tyr  Cys Pro Arg
    3290                 3295                 3300

His Val  Ile Cys Thr Ser Glu  Asp Met Leu Asn Pro  Asn Tyr Glu
    3305                 3310                 3315

Asp Leu  Leu Ile Arg Lys Ser  Asn His Asn Phe Leu  Val Gln Ala
    3320                 3325                 3330

Gly Asn  Val Gln Leu Arg Val  Ile Gly His Ser Met  Gln Asn Cys
    3335                 3340                 3345

Val Leu  Lys Leu Lys Val Asp  Thr Ala Asn Pro Lys  Thr Pro Lys
    3350                 3355                 3360

Tyr Lys  Phe Val Arg Ile Gln  Pro Gly Gln Thr Phe  Ser Val Leu
    3365                 3370                 3375

Ala Cys  Tyr Asn Gly Ser Pro  Ser Gly Val Tyr Gln  Cys Ala Met
    3380                 3385                 3390

Arg Pro  Asn Phe Thr Ile Lys  Gly Ser Phe Leu Asn  Gly Ser Cys
    3395                 3400                 3405

Gly Ser  Val Gly Phe Asn Ile  Asp Tyr Asp Cys Val  Ser Phe Cys
    3410                 3415                 3420

Tyr Met  His His Met Glu Leu  Pro Thr Gly Val His  Ala Gly Thr
    3425                 3430                 3435

Asp Leu  Glu Gly Asn Phe Tyr  Gly Pro Phe Val Asp  Arg Gln Thr
    3440                 3445                 3450

Ala Gln  Ala Ala Gly Thr Asp  Thr Thr Ile Thr Val  Asn Val Leu
    3455                 3460                 3465

Ala Trp  Leu Tyr Ala Ala Val  Ile Asn Gly Asp Arg  Trp Phe Leu
    3470                 3475                 3480

Asn Arg  Phe Thr Thr Thr Leu  Asn Asp Phe Asn Leu  Val Ala Met
    3485                 3490                 3495

Lys Tyr  Asn Tyr Glu Pro Leu  Thr Gln Asp His Val  Asp Ile Leu
    3500                 3505                 3510

Gly Pro  Leu Ser Ala Gln Thr  Gly Ile Ala Val Leu  Asp Met Cys
    3515                 3520                 3525

Ala Ser  Leu Lys Glu Leu Leu  Gln Asn Gly Met Asn  Gly Arg Thr
    3530                 3535                 3540

Ile Leu  Gly Ser Ala Leu Leu  Glu Asp Glu Phe Thr  Pro Phe Asp
    3545                 3550                 3555

Val Val  Arg Gln Cys Ser Gly  Val Thr Phe Gln Ser  Ala Val Lys
    3560                 3565                 3570

Arg Thr  Ile Lys Gly Thr His  His Trp Leu Leu Leu  Thr Ile Leu
    3575                 3580                 3585

Thr Ser  Leu Leu Val Leu Val  Gln Ser Thr Gln Trp  Ser Leu Phe
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    3590                3595                3600

Phe Phe  Leu Tyr Glu Asn Ala  Phe Leu Pro Phe Ala  Met Gly Ile
    3605                3610                3615

Ile Ala  Met Ser Ala Phe Ala  Met Met Phe Val Lys  His Lys His
    3620                3625                3630

Ala Phe  Leu Cys Leu Phe Leu  Leu Pro Ser Leu Ala  Thr Val Ala
    3635                3640                3645

Tyr Phe  Asn Met Val Tyr Met  Pro Ala Ser Trp Val  Met Arg Ile
    3650                3655                3660

Met Thr  Trp Leu Asp Met Val  Asp Thr Ser Leu Ser  Gly Phe Lys
    3665                3670                3675

Leu Lys  Asp Cys Val Met Tyr  Ala Ser Ala Val Val  Leu Leu Ile
    3680                3685                3690

Leu Met  Thr Ala Arg Thr Val  Tyr Asp Asp Gly Ala  Arg Arg Val
    3695                3700                3705

Trp Thr  Leu Met Asn Val Leu  Thr Leu Val Tyr Lys  Val Tyr Tyr
    3710                3715                3720

Gly Asn  Ala Leu Asp Gln Ala  Ile Ser Met Trp Ala  Leu Ile Ile
    3725                3730                3735

Ser Val  Thr Ser Asn Tyr Ser  Gly Val Val Thr Thr  Val Met Phe
    3740                3745                3750

Leu Ala  Arg Gly Ile Val Phe  Met Cys Val Glu Tyr  Cys Pro Ile
    3755                3760                3765

Phe Phe  Ile Thr Gly Asn Thr  Leu Gln Cys Ile Met  Leu Val Tyr
    3770                3775                3780

Cys Phe  Leu Gly Tyr Phe Cys  Thr Cys Tyr Phe Gly  Leu Phe Cys
    3785                3790                3795

Leu Leu  Asn Arg Tyr Phe Arg  Leu Thr Leu Gly Val  Tyr Asp Tyr
    3800                3805                3810

Leu Val  Ser Thr Gln Glu Phe  Arg Tyr Met Asn Ser  Gln Gly Leu
    3815                3820                3825

Leu Pro  Pro Lys Asn Ser Ile  Asp Ala Phe Lys Leu  Asn Ile Lys
    3830                3835                3840

Leu Leu  Gly Val Gly Gly Lys  Pro Cys Ile Lys Val  Ala Thr Val
    3845                3850                3855

Gln Ser  Lys Met Ser Asp Val  Lys Cys Thr Ser Val  Val Leu Leu
    3860                3865                3870

Ser Val  Leu Gln Gln Leu Arg  Val Glu Ser Ser Ser  Lys Leu Trp
    3875                3880                3885

Ala Gln  Cys Val Gln Leu His  Asn Asp Ile Leu Leu  Ala Lys Asp
    3890                3895                3900

Thr Thr  Glu Ala Phe Glu Lys  Met Val Ser Leu Leu  Ser Val Leu
    3905                3910                3915

Leu Ser  Met Gln Gly Ala Val  Asp Ile Asn Lys Leu  Cys Glu Glu
    3920                3925                3930

Met Leu  Asp Asn Arg Ala Thr  Leu Gln Ala Ile Ala  Ser Glu Phe
    3935                3940                3945

Ser Ser  Leu Pro Ser Tyr Ala  Ala Phe Ala Thr Ala  Gln Glu Ala
    3950                3955                3960

Tyr Glu  Gln Ala Val Ala Asn  Gly Asp Ser Glu Val  Val Leu Lys
    3965                3970                3975
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Lys Leu  Lys Lys Ser Leu Asn  Val Ala Lys Ser Glu  Phe Asp Arg
    3980                 3985                 3990

Asp Ala  Ala Met Gln Arg Lys  Leu Glu Lys Met Ala  Asp Gln Ala
    3995                 4000                 4005

Met Thr  Gln Met Tyr Lys Gln  Ala Arg Ser Glu Asp  Lys Arg Ala
    4010                 4015                 4020

Lys Val  Thr Ser Ala Met Gln  Thr Met Leu Phe Thr  Met Leu Arg
    4025                 4030                 4035

Lys Leu  Asp Asn Asp Ala Leu  Asn Asn Ile Ile Asn  Asn Ala Arg
    4040                 4045                 4050

Asp Gly  Cys Val Pro Leu Asn  Ile Ile Pro Leu Thr  Thr Ala Ala
    4055                 4060                 4065

Lys Leu  Met Val Val Ile Pro  Asp Tyr Asn Thr Tyr  Lys Asn Thr
    4070                 4075                 4080

Cys Asp  Gly Thr Thr Phe Thr  Tyr Ala Ser Ala Leu  Trp Glu Ile
    4085                 4090                 4095

Gln Gln  Val Val Asp Ala Asp  Ser Lys Ile Val Gln  Leu Ser Glu
    4100                 4105                 4110

Ile Ser  Met Asp Asn Ser Pro  Asn Leu Ala Trp Pro  Leu Ile Val
    4115                 4120                 4125

Thr Ala  Leu Arg Ala Asn Ser  Ala Val Lys Leu Gln  Asn Asn Glu
    4130                 4135                 4140

Leu Ser  Pro Val Ala Leu Arg  Gln Met Ser Cys Ala  Ala Gly Thr
    4145                 4150                 4155

Thr Gln  Thr Ala Cys Thr Asp  Asp Asn Ala Leu Ala  Tyr Tyr Asn
    4160                 4165                 4170

Thr Thr  Lys Gly Gly Arg Phe  Val Leu Ala Leu Leu  Ser Asp Leu
    4175                 4180                 4185

Gln Asp  Leu Lys Trp Ala Arg  Phe Pro Lys Ser Asp  Gly Thr Gly
    4190                 4195                 4200

Thr Ile  Tyr Thr Glu Leu Glu  Pro Pro Cys Arg Phe  Val Thr Asp
    4205                 4210                 4215

Thr Pro  Lys Gly Pro Lys Val  Lys Tyr Leu Tyr Phe  Ile Lys Gly
    4220                 4225                 4230

Leu Asn  Asn Leu Asn Arg Gly  Met Val Leu Gly Ser  Leu Ala Ala
    4235                 4240                 4245

Thr Val  Arg Leu Gln Ala Gly  Asn Ala Thr Glu Val  Pro Ala Asn
    4250                 4255                 4260

Ser Thr  Val Leu Ser Phe Cys  Ala Phe Ala Val Asp  Ala Ala Lys
    4265                 4270                 4275

Ala Tyr  Lys Asp Tyr Leu Ala  Ser Gly Gly Gln Pro  Ile Thr Asn
    4280                 4285                 4290

Cys Val  Lys Met Leu Cys Thr  His Thr Gly Thr Gly  Gln Ala Ile
    4295                 4300                 4305

Thr Val  Thr Pro Glu Ala Asn  Met Asp Gln Glu Ser  Phe Gly Gly
    4310                 4315                 4320

Ala Ser  Cys Cys Leu Tyr Cys  Arg Cys His Ile Asp  His Pro Asn
    4325                 4330                 4335

Pro Lys  Gly Phe Cys Asp Leu  Lys Gly Lys Tyr Val  Gln Ile Pro
    4340                 4345                 4350
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Thr Thr  Cys Ala Asn Asp Pro  Val Gly Phe Thr Leu  Lys Asn Thr
    4355                 4360                 4365

Val Cys  Thr Val Cys Gly Met  Trp Lys Gly Tyr Gly  Cys Ser Cys
    4370                 4375                 4380

Asp Gln  Leu Arg Glu Pro Met  Leu Gln Ser Ala Asp  Ala Gln Ser
    4385                 4390                 4395

Phe Leu  Asn Arg Val Cys Gly  Val Ser Ala Ala Arg  Leu Thr Pro
    4400                 4405                 4410

Cys Gly  Thr Gly Thr Ser Thr  Asp Val Val Tyr Arg  Ala Phe Asp
    4415                 4420                 4425

Ile Tyr  Asn Asp Lys Val Ala  Gly Phe Ala Lys Phe  Leu Lys Thr
    4430                 4435                 4440

Asn Cys  Cys Arg Phe Gln Glu  Lys Asp Glu Asp Asp  Asn Leu Ile
    4445                 4450                 4455

Asp Ser  Tyr Phe Val Val Lys  Arg His Thr Phe Ser  Asn Tyr Gln
    4460                 4465                 4470

His Glu  Glu Thr Ile Tyr Asn  Leu Leu Lys Asp Cys  Pro Ala Val
    4475                 4480                 4485

Ala Lys  His Asp Phe Phe Lys  Phe Arg Ile Asp Gly  Asp Met Val
    4490                 4495                 4500

Pro His  Ile Ser Arg Gln Arg  Leu Thr Lys Tyr Thr  Met Ala Asp
    4505                 4510                 4515

Leu Val  Tyr Ala Leu Arg His  Phe Asp Glu Gly Asn  Cys Asp Thr
    4520                 4525                 4530

Leu Lys  Glu Ile Leu Val Thr  Tyr Asn Cys Cys Asp  Asp Asp Tyr
    4535                 4540                 4545

Phe Asn  Lys Lys Asp Trp Tyr  Asp Phe Val Glu Asn  Pro Asp Ile
    4550                 4555                 4560

Leu Arg  Val Tyr Ala Asn Leu  Gly Glu Arg Val Arg  Gln Ala Leu
    4565                 4570                 4575

Leu Lys  Thr Val Gln Phe Cys  Asp Ala Met Arg Asn  Ala Gly Ile
    4580                 4585                 4590

Val Gly  Val Leu Thr Leu Asp  Asn Gln Asp Leu Asn  Gly Asn Trp
    4595                 4600                 4605

Tyr Asp  Phe Gly Asp Phe Ile  Gln Thr Thr Pro Gly  Ser Gly Val
    4610                 4615                 4620

Pro Val  Val Asp Ser Tyr Tyr  Ser Leu Leu Met Pro  Ile Leu Thr
    4625                 4630                 4635

Leu Thr  Arg Ala Leu Thr Ala  Glu Ser His Val Asp  Thr Asp Leu
    4640                 4645                 4650

Thr Lys  Pro Tyr Ile Lys Trp  Asp Leu Leu Lys Tyr  Asp Phe Thr
    4655                 4660                 4665

Glu Glu  Arg Leu Lys Leu Phe  Asp Arg Tyr Phe Lys  Tyr Trp Asp
    4670                 4675                 4680

Gln Thr  Tyr His Pro Asn Cys  Val Asn Cys Leu Asp  Asp Arg Cys
    4685                 4690                 4695

Ile Leu  His Cys Ala Asn Phe  Asn Val Leu Phe Ser  Thr Val Phe
    4700                 4705                 4710

Pro Pro  Thr Ser Phe Gly Pro  Leu Val Arg Lys Ile  Phe Val Asp
    4715                 4720                 4725

Gly Val  Pro Phe Val Val Ser  Thr Gly Tyr His Phe  Arg Glu Leu
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    4730                4735                4740

Gly Val  Val His Asn Gln Asp  Val Asn Leu His Ser  Ser Arg Leu
    4745                4750                4755

Ser Phe  Lys Glu Leu Leu Val  Tyr Ala Ala Asp Pro  Ala Met His
    4760                4765                4770

Ala Ala  Ser Gly Asn Leu Leu  Leu Asp Lys Arg Thr  Thr Cys Phe
    4775                4780                4785

Ser Val  Ala Ala Leu Thr Asn  Asn Val Ala Phe Gln  Thr Val Lys
    4790                4795                4800

Pro Gly  Asn Phe Asn Lys Asp  Phe Tyr Asp Phe Ala  Val Ser Lys
    4805                4810                4815

Gly Phe  Phe Lys Glu Gly Ser  Ser Val Glu Leu Lys  His Phe Phe
    4820                4825                4830

Phe Ala  Gln Asp Gly Asn Ala  Ala Ile Ser Asp Tyr  Asp Tyr Tyr
    4835                4840                4845

Arg Tyr  Asn Leu Pro Thr Met  Cys Asp Ile Arg Gln  Leu Leu Phe
    4850                4855                4860

Val Val  Glu Val Val Asp Lys  Tyr Phe Asp Cys Tyr  Asp Gly Gly
    4865                4870                4875

Cys Ile  Asn Ala Asn Gln Val  Ile Val Asn Asn Leu  Asp Lys Ser
    4880                4885                4890

Ala Gly  Phe Pro Phe Asn Lys  Trp Gly Lys Ala Arg  Leu Tyr Tyr
    4895                4900                4905

Asp Ser  Met Ser Tyr Glu Asp  Gln Asp Ala Leu Phe  Ala Tyr Thr
    4910                4915                4920

Lys Arg  Asn Val Ile Pro Thr  Ile Thr Gln Met Asn  Leu Lys Tyr
    4925                4930                4935

Ala Ile  Ser Ala Lys Asn Arg  Ala Arg Thr Val Ala  Gly Val Ser
    4940                4945                4950

Ile Cys  Ser Thr Met Thr Asn  Arg Gln Phe His Gln  Lys Leu Leu
    4955                4960                4965

Lys Ser  Ile Ala Ala Thr Arg  Gly Ala Thr Val Val  Ile Gly Thr
    4970                4975                4980

Ser Lys  Phe Tyr Gly Gly Trp  His Asn Met Leu Lys  Thr Val Tyr
    4985                4990                4995

Ser Asp  Val Glu Asn Pro His  Leu Met Gly Trp Asp  Tyr Pro Lys
    5000                5005                5010

Cys Asp  Arg Ala Met Pro Asn  Met Leu Arg Ile Met  Ala Ser Leu
    5015                5020                5025

Val Leu  Ala Arg Lys His Thr  Thr Cys Cys Ser Leu  Ser His Arg
    5030                5035                5040

Phe Tyr  Arg Leu Ala Asn Glu  Cys Ala Gln Val Leu  Ser Glu Met
    5045                5050                5055

Val Met  Cys Gly Gly Ser Leu  Tyr Val Lys Pro Gly  Gly Thr Ser
    5060                5065                5070

Ser Gly  Asp Ala Thr Thr Ala  Tyr Ala Asn Ser Val  Phe Asn Ile
    5075                5080                5085

Cys Gln  Ala Val Thr Ala Asn  Val Asn Ala Leu Leu  Ser Thr Asp
    5090                5095                5100

Gly Asn  Lys Ile Ala Asp Lys  Tyr Val Arg Asn Leu  Gln His Arg
    5105                5110                5115
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Leu Tyr  Glu Cys Leu Tyr Arg  Asn Arg Asp Val Asp  Thr Asp Phe
    5120                 5125                 5130

Val Asn  Glu Phe Tyr Ala Tyr  Leu Arg Lys His Phe  Ser Met Met
    5135                 5140                 5145

Ile Leu  Ser Asp Asp Ala Val  Val Cys Phe Asn Ser  Thr Tyr Ala
    5150                 5155                 5160

Ser Gln  Gly Leu Val Ala Ser  Ile Lys Asn Phe Lys  Ser Val Leu
    5165                 5170                 5175

Tyr Tyr  Gln Asn Asn Val Phe  Met Ser Glu Ala Lys  Cys Trp Thr
    5180                 5185                 5190

Glu Thr  Asp Leu Thr Lys Gly  Pro His Glu Phe Cys  Ser Gln His
    5195                 5200                 5205

Thr Met  Leu Val Lys Gln Gly  Asp Asp Tyr Val Tyr  Leu Pro Tyr
    5210                 5215                 5220

Pro Asp  Pro Ser Arg Ile Leu  Gly Ala Gly Cys Phe  Val Asp Asp
    5225                 5230                 5235

Ile Val  Lys Thr Asp Gly Thr  Leu Met Ile Glu Arg  Phe Val Ser
    5240                 5245                 5250

Leu Ala  Ile Asp Ala Tyr Pro  Leu Thr Lys His Pro  Asn Gln Glu
    5255                 5260                 5265

Tyr Ala  Asp Val Phe His Leu  Tyr Leu Gln Tyr Ile  Arg Lys Leu
    5270                 5275                 5280

His Asp  Glu Leu Thr Gly His  Met Leu Asp Met Tyr  Ser Val Met
    5285                 5290                 5295

Leu Thr  Asn Asp Asn Thr Ser  Arg Tyr Trp Glu Pro  Glu Phe Tyr
    5300                 5305                 5310

Glu Ala  Met Tyr Thr Pro His  Thr Val Leu Gln Ala  Val Gly Ala
    5315                 5320                 5325

Cys Val  Leu Cys Asn Ser Gln  Thr Ser Leu Arg Cys  Gly Ala Cys
    5330                 5335                 5340

Ile Arg  Arg Pro Phe Leu Cys  Cys Lys Cys Cys Tyr  Asp His Val
    5345                 5350                 5355

Ile Ser  Thr Ser His Lys Leu  Val Leu Ser Val Asn  Pro Tyr Val
    5360                 5365                 5370

Cys Asn  Ala Pro Gly Cys Asp  Val Thr Asp Val Thr  Gln Leu Tyr
    5375                 5380                 5385

Leu Gly  Gly Met Ser Tyr Tyr  Cys Lys Ser His Lys  Pro Pro Ile
    5390                 5395                 5400

Ser Phe  Pro Leu Cys Ala Asn  Gly Gln Val Phe Gly  Leu Tyr Lys
    5405                 5410                 5415

Asn Thr  Cys Val Gly Ser Asp  Asn Val Thr Asp Phe  Asn Ala Ile
    5420                 5425                 5430

Ala Thr  Cys Asp Trp Thr Asn  Ala Gly Asp Tyr Ile  Leu Ala Asn
    5435                 5440                 5445

Thr Cys  Thr Glu Arg Leu Lys  Leu Phe Ala Ala Glu  Thr Leu Lys
    5450                 5455                 5460

Ala Thr  Glu Glu Thr Phe Lys  Leu Ser Tyr Gly Ile  Ala Thr Val
    5465                 5470                 5475

Arg Glu  Val Leu Ser Asp Arg  Glu Leu His Leu Ser  Trp Glu Val
    5480                 5485                 5490
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Gly Lys  Pro Arg Pro Pro Leu  Asn Arg Asn Tyr Val  Phe Thr Gly
    5495                 5500                 5505

Tyr Arg  Val Thr Lys Asn Ser  Lys Val Gln Ile Gly  Glu Tyr Thr
    5510                 5515                 5520

Phe Glu  Lys Gly Asp Tyr Gly  Asp Ala Val Val Tyr  Arg Gly Thr
    5525                 5530                 5535

Thr Thr  Tyr Lys Leu Asn Val  Gly Asp Tyr Phe Val  Leu Thr Ser
    5540                 5545                 5550

His Thr  Val Met Pro Leu Ser  Ala Pro Thr Leu Val  Pro Gln Glu
    5555                 5560                 5565

His Tyr  Val Arg Ile Thr Gly  Leu Tyr Pro Thr Leu  Asn Ile Ser
    5570                 5575                 5580

Asp Glu  Phe Ser Ser Asn Val  Ala Asn Tyr Gln Lys  Val Gly Met
    5585                 5590                 5595

Gln Lys  Tyr Ser Thr Leu Gln  Gly Pro Pro Gly Thr  Gly Lys Ser
    5600                 5605                 5610

His Phe  Ala Ile Gly Leu Ala  Leu Tyr Tyr Pro Ser  Ala Arg Ile
    5615                 5620                 5625

Val Tyr  Thr Ala Cys Ser His  Ala Ala Val Asp Ala  Leu Cys Glu
    5630                 5635                 5640

Lys Ala  Leu Lys Tyr Leu Pro  Ile Asp Lys Cys Ser  Arg Ile Ile
    5645                 5650                 5655

Pro Ala  Arg Ala Arg Val Glu  Cys Phe Asp Lys Phe  Lys Val Asn
    5660                 5665                 5670

Ser Thr  Leu Glu Gln Tyr Val  Phe Cys Thr Val Asn  Ala Leu Pro
    5675                 5680                 5685

Glu Thr  Thr Ala Asp Ile Val  Val Phe Asp Glu Ile  Ser Met Ala
    5690                 5695                 5700

Thr Asn  Tyr Asp Leu Ser Val  Val Asn Ala Arg Leu  Arg Ala Lys
    5705                 5710                 5715

His Tyr  Val Tyr Ile Gly Asp  Pro Ala Gln Leu Pro  Ala Pro Arg
    5720                 5725                 5730

Thr Leu  Leu Thr Lys Gly Thr  Leu Glu Pro Glu Tyr  Phe Asn Ser
    5735                 5740                 5745

Val Cys  Arg Leu Met Lys Thr  Ile Gly Pro Asp Met  Phe Leu Gly
    5750                 5755                 5760

Thr Cys  Arg Arg Cys Pro Ala  Glu Ile Val Asp Thr  Val Ser Ala
    5765                 5770                 5775

Leu Val  Tyr Asp Asn Lys Leu  Lys Ala His Lys Asp  Lys Ser Ala
    5780                 5785                 5790

Gln Cys  Phe Lys Met Phe Tyr  Lys Gly Val Ile Thr  His Asp Val
    5795                 5800                 5805

Ser Ser  Ala Ile Asn Arg Pro  Gln Ile Gly Val Val  Arg Glu Phe
    5810                 5815                 5820

Leu Thr  Arg Asn Pro Ala Trp  Arg Lys Ala Val Phe  Ile Ser Pro
    5825                 5830                 5835

Tyr Asn  Ser Gln Asn Ala Val  Ala Ser Lys Ile Leu  Gly Leu Pro
    5840                 5845                 5850

Thr Gln  Thr Val Asp Ser Ser  Gln Gly Ser Glu Tyr  Asp Tyr Val
    5855                 5860                 5865

Ile Phe  Thr Gln Thr Thr Glu  Thr Ala His Ser Cys  Asn Val Asn
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    5870                5875                5880

Arg Phe  Asn Val Ala Ile Thr  Arg Ala Lys Val Gly  Ile Leu Cys
    5885                5890                5895

Ile Met  Ser Asp Arg Asp Leu  Tyr Asp Lys Leu Gln  Phe Thr Ser
    5900                5905                5910

Leu Glu  Ile Pro Arg Arg Asn  Val Ala Thr Leu Gln  Ala Glu Asn
    5915                5920                5925

Val Thr  Gly Leu Phe Lys Asp  Cys Ser Lys Val Ile  Thr Gly Leu
    5930                5935                5940

His Pro  Thr Gln Ala Pro Thr  His Leu Ser Val Asp  Thr Lys Phe
    5945                5950                5955

Lys Thr  Glu Gly Leu Cys Val  Asp Ile Pro Gly Ile  Pro Lys Asp
    5960                5965                5970

Met Thr  Tyr Arg Arg Leu Ile  Ser Met Met Gly Phe  Lys Met Asn
    5975                5980                5985

Tyr Gln  Val Asn Gly Tyr Pro  Asn Met Phe Ile Thr  Arg Glu Glu
    5990                5995                6000

Ala Ile  Arg His Val Arg Ala  Trp Ile Gly Phe Asp  Val Glu Gly
    6005                6010                6015

Cys His  Ala Thr Arg Glu Ala  Val Gly Thr Asn Leu  Pro Leu Gln
    6020                6025                6030

Leu Gly  Phe Ser Thr Gly Val  Asn Leu Val Ala Val  Pro Thr Gly
    6035                6040                6045

Tyr Val  Asp Thr Pro Asn Asn  Thr Asp Phe Ser Arg  Val Ser Ala
    6050                6055                6060

Lys Pro  Pro Pro Gly Asp Gln  Phe Lys His Leu Ile  Pro Leu Met
    6065                6070                6075

Tyr Lys  Gly Leu Pro Trp Asn  Val Val Arg Ile Lys  Ile Val Gln
    6080                6085                6090

Met Leu  Ser Asp Thr Leu Lys  Asn Leu Ser Asp Arg  Val Val Phe
    6095                6100                6105

Val Leu  Trp Ala His Gly Phe  Glu Leu Thr Ser Met  Lys Tyr Phe
    6110                6115                6120

Val Lys  Ile Gly Pro Glu Arg  Thr Cys Cys Leu Cys  Asp Arg Arg
    6125                6130                6135

Ala Thr  Cys Phe Ser Thr Ala  Ser Asp Thr Tyr Ala  Cys Trp His
    6140                6145                6150

His Ser  Ile Gly Phe Asp Tyr  Val Tyr Asn Pro Phe  Met Ile Asp
    6155                6160                6165

Val Gln  Gln Trp Gly Phe Thr  Gly Asn Leu Gln Ser  Asn His Asp
    6170                6175                6180

Leu Tyr  Cys Gln Val His Gly  Asn Ala His Val Ala  Ser Cys Asp
    6185                6190                6195

Ala Ile  Met Thr Arg Cys Leu  Ala Val His Glu Cys  Phe Val Lys
    6200                6205                6210

Arg Val  Asp Trp Thr Ile Glu  Tyr Pro Ile Ile Gly  Asp Glu Leu
    6215                6220                6225

Lys Ile  Asn Ala Ala Cys Arg  Lys Val Gln His Met  Val Val Lys
    6230                6235                6240

Ala Ala  Leu Leu Ala Asp Lys  Phe Pro Val Leu His  Asp Ile Gly
    6245                6250                6255
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Asn Pro  Lys Ala Ile Lys Cys  Val Pro Gln Ala Asp  Val Glu Trp
    6260                 6265                 6270

Lys Phe  Tyr Asp Ala Gln Pro  Cys Ser Asp Lys Ala  Tyr Lys Ile
    6275                 6280                 6285

Glu Glu  Leu Phe Tyr Ser Tyr  Ala Thr His Ser Asp  Lys Phe Thr
    6290                 6295                 6300

Asp Gly  Val Cys Leu Phe Trp  Asn Cys Asn Val Asp  Arg Tyr Pro
    6305                 6310                 6315

Ala Asn  Ser Ile Val Cys Arg  Phe Asp Thr Arg Val  Leu Ser Asn
    6320                 6325                 6330

Leu Asn  Leu Pro Gly Cys Asp  Gly Gly Ser Leu Tyr  Val Asn Lys
    6335                 6340                 6345

His Ala  Phe His Thr Pro Ala  Phe Asp Lys Ser Ala  Phe Val Asn
    6350                 6355                 6360

Leu Lys  Gln Leu Pro Phe Phe  Tyr Tyr Ser Asp Ser  Pro Cys Glu
    6365                 6370                 6375

Ser His  Gly Lys Gln Val Val  Ser Asp Ile Asp Tyr  Val Pro Leu
    6380                 6385                 6390

Lys Ser  Ala Thr Cys Ile Thr  Arg Cys Asn Leu Gly  Gly Ala Val
    6395                 6400                 6405

Cys Arg  His His Ala Asn Glu  Tyr Arg Leu Tyr Leu  Asp Ala Tyr
    6410                 6415                 6420

Asn Met  Met Ile Ser Ala Gly  Phe Ser Leu Trp Val  Tyr Lys Gln
    6425                 6430                 6435

Phe Asp  Thr Tyr Asn Leu Trp  Asn Thr Phe Thr Arg  Leu Gln Ser
    6440                 6445                 6450

Leu Glu  Asn Val Ala Phe Asn  Val Val Asn Lys Gly  His Phe Asp
    6455                 6460                 6465

Gly Gln  Gln Gly Glu Val Pro  Val Ser Ile Ile Asn  Asn Thr Val
    6470                 6475                 6480

Tyr Thr  Lys Val Asp Gly Val  Asp Val Glu Leu Phe  Glu Asn Lys
    6485                 6490                 6495

Thr Thr  Leu Pro Val Asn Val  Ala Phe Glu Leu Trp  Ala Lys Arg
    6500                 6505                 6510

Asn Ile  Lys Pro Val Pro Glu  Val Lys Ile Leu Asn  Asn Leu Gly
    6515                 6520                 6525

Val Asp  Ile Ala Ala Asn Thr  Val Ile Trp Asp Tyr  Lys Arg Asp
    6530                 6535                 6540

Ala Pro  Ala His Ile Ser Thr  Ile Gly Val Cys Ser  Met Thr Asp
    6545                 6550                 6555

Ile Ala  Lys Lys Pro Thr Glu  Thr Ile Cys Ala Pro  Leu Thr Val
    6560                 6565                 6570

Phe Phe  Asp Gly Arg Val Asp  Gly Gln Val Asp Leu  Phe Arg Asn
    6575                 6580                 6585

Ala Arg  Asn Gly Val Leu Ile  Thr Glu Gly Ser Val  Lys Gly Leu
    6590                 6595                 6600

Gln Pro  Ser Val Gly Pro Lys  Gln Ala Ser Leu Asn  Gly Val Thr
    6605                 6610                 6615

Leu Ile  Gly Glu Ala Val Lys  Thr Gln Phe Asn Tyr  Tyr Lys Lys
    6620                 6625                 6630
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Val Asp  Gly Val Val Gln Gln  Leu Pro Glu Thr Tyr  Phe Thr Gln
    6635                 6640                 6645

Ser Arg  Asn Leu Gln Glu Phe  Lys Pro Arg Ser Gln  Met Glu Ile
    6650                 6655                 6660

Asp Phe  Leu Glu Leu Ala Met  Asp Glu Phe Ile Glu  Arg Tyr Lys
    6665                 6670                 6675

Leu Glu  Gly Tyr Ala Phe Glu  His Ile Val Tyr Gly  Asp Phe Ser
    6680                 6685                 6690

His Ser  Gln Leu Gly Gly Leu  His Leu Leu Ile Gly  Leu Ala Lys
    6695                 6700                 6705

Arg Phe  Lys Glu Ser Pro Phe  Glu Leu Glu Asp Phe  Ile Pro Met
    6710                 6715                 6720

Asp Ser  Thr Val Lys Asn Tyr  Phe Ile Thr Asp Ala  Gln Thr Gly
    6725                 6730                 6735

Ser Ser  Lys Cys Val Cys Ser  Val Ile Asp Leu Leu  Leu Asp Asp
    6740                 6745                 6750

Phe Val  Glu Ile Ile Lys Ser  Gln Asp Leu Ser Val  Val Ser Lys
    6755                 6760                 6765

Val Val  Lys Val Thr Ile Asp  Tyr Thr Glu Ile Ser  Phe Met Leu
    6770                 6775                 6780

Trp Cys  Lys Asp Gly His Val  Glu Thr Phe Tyr Pro  Lys Leu Gln
    6785                 6790                 6795

Ser Ser  Gln Ala Trp Gln Pro  Gly Val Ala Met Pro  Asn Leu Tyr
    6800                 6805                 6810

Lys Met  Gln Arg Met Leu Leu  Glu Lys Cys Asp Leu  Gln Asn Tyr
    6815                 6820                 6825

Gly Asp  Ser Ala Thr Leu Pro  Lys Gly Ile Met Met  Asn Val Ala
    6830                 6835                 6840

Lys Tyr  Thr Gln Leu Cys Gln  Tyr Leu Asn Thr Leu  Thr Leu Ala
    6845                 6850                 6855

Val Pro  Tyr Asn Met Arg Val  Ile His Phe Gly Ala  Gly Ser Asp
    6860                 6865                 6870

Lys Gly  Val Ala Pro Gly Thr  Ala Val Leu Arg Gln  Trp Leu Pro
    6875                 6880                 6885

Thr Gly  Thr Leu Leu Val Asp  Ser Asp Leu Asn Asp  Phe Val Ser
    6890                 6895                 6900

Asp Ala  Asp Ser Thr Leu Ile  Gly Asp Cys Ala Thr  Val His Thr
    6905                 6910                 6915

Ala Asn  Lys Trp Asp Leu Ile  Ile Ser Asp Met Tyr  Asp Pro Lys
    6920                 6925                 6930

Thr Lys  Asn Val Thr Lys Glu  Asn Asp Ser Lys Glu  Gly Phe Phe
    6935                 6940                 6945

Thr Tyr  Ile Cys Gly Phe Ile  Gln Gln Lys Leu Ala  Leu Gly Gly
    6950                 6955                 6960

Ser Val  Ala Ile Lys Ile Thr  Glu His Ser Trp Asn  Ala Asp Leu
    6965                 6970                 6975

Tyr Lys  Leu Met Gly His Phe  Ala Trp Trp Thr Ala  Phe Val Thr
    6980                 6985                 6990

Asn Val  Asn Ala Ser Ser Ser  Glu Ala Phe Leu Ile  Gly Cys Asn
    6995                 7000                 7005

Tyr Leu  Gly Lys Pro Arg Glu  Gln Ile Asp Gly Tyr  Val Met His
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    7010                7015                7020

Ala Asn  Tyr Ile Phe Trp Arg  Asn Thr Asn Pro Ile  Gln Leu Ser
    7025                7030                7035

Ser Tyr  Ser Leu Phe Asp Met  Ser Lys Phe Pro Leu  Lys Leu Arg
    7040                7045                7050

Gly Thr  Ala Val Met Ser Leu  Lys Glu Gly Gln Ile  Asn Asp Met
    7055                7060                7065

Ile Leu  Ser Leu Leu Ser Lys  Gly Arg Leu Ile Ile  Arg Glu Asn
    7070                7075                7080

Asn Arg  Val Val Ile Ser Ser  Asp Val Leu Val Asn  Asn
    7085                7090                7095


<210> SEQ ID NO 2
<211> LENGTH: 7073
<212> TYPE: PRT
<213> ORGANISM: SARS coronavirus Tor2

<400> SEQUENCE: 2

Met Glu Ser Leu Val Leu Gly Val Asn Glu Lys Thr His Val Gln Leu
1               5                   10                  15

Ser Leu Pro Val Leu Gln Val Arg Asp Val Leu Val Arg Gly Phe Gly
            20                  25                  30

Asp Ser Val Glu Glu Ala Leu Ser Glu Ala Arg Glu His Leu Lys Asn
        35                  40                  45

Gly Thr Cys Gly Leu Val Glu Leu Glu Lys Gly Val Leu Pro Gln Leu
    50                  55                  60

Glu Gln Pro Tyr Val Phe Ile Lys Arg Ser Asp Ala Leu Ser Thr Asn
65                  70                  75                  80

His Gly His Lys Val Val Glu Leu Val Ala Glu Met Asp Gly Ile Gln
                85                  90                  95

Tyr Gly Arg Ser Gly Ile Thr Leu Gly Val Leu Val Pro His Val Gly
            100                 105                 110

Glu Thr Pro Ile Ala Tyr Arg Asn Val Leu Leu Arg Lys Asn Gly Asn
        115                 120                 125

Lys Gly Ala Gly Gly His Ser Tyr Gly Ile Asp Leu Lys Ser Tyr Asp
    130                 135                 140

Leu Gly Asp Glu Leu Gly Thr Asp Pro Ile Glu Asp Tyr Glu Gln Asn
145                 150                 155                 160

Trp Asn Thr Lys His Gly Ser Gly Ala Leu Arg Glu Leu Thr Arg Glu
                165                 170                 175

Leu Asn Gly Gly Ala Val Thr Arg Tyr Val Asp Asn Asn Phe Cys Gly
            180                 185                 190

Pro Asp Gly Tyr Pro Leu Asp Cys Ile Lys Asp Phe Leu Ala Arg Ala
        195                 200                 205

Gly Lys Ser Met Cys Thr Leu Ser Glu Gln Leu Asp Tyr Ile Glu Ser
    210                 215                 220

Lys Arg Gly Val Tyr Cys Cys Arg Asp His Glu His Glu Ile Ala Trp
225                 230                 235                 240

Phe Thr Glu Arg Ser Asp Lys Ser Tyr Glu His Gln Thr Pro Phe Glu
                245                 250                 255

Ile Lys Ser Ala Lys Lys Phe Asp Thr Phe Lys Gly Glu Cys Pro Lys
            260                 265                 270
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Phe Val Phe Pro Leu Asn Ser Lys Val Lys Val Ile Gln Pro Arg Val
        275                 280                 285

Glu Lys Lys Lys Thr Glu Gly Phe Met Gly Arg Ile Arg Ser Val Tyr
    290                 295                 300

Pro Val Ala Ser Pro Gln Glu Cys Asn Asn Met His Leu Ser Thr Leu
305                 310                 315                 320

Met Lys Cys Asn His Cys Asp Glu Val Ser Trp Gln Thr Cys Asp Phe
                325                 330                 335

Leu Lys Ala Thr Cys Glu His Cys Gly Thr Glu Asn Leu Val Ile Glu
            340                 345                 350

Gly Pro Thr Thr Cys Gly Tyr Leu Pro Thr Asn Ala Val Val Lys Met
        355                 360                 365

Pro Cys Pro Ala Cys Gln Asp Pro Glu Ile Gly Pro Glu His Ser Val
    370                 375                 380

Ala Asp Tyr His Asn His Ser Asn Ile Glu Thr Arg Leu Arg Lys Gly
385                 390                 395                 400

Gly Arg Thr Arg Cys Phe Gly Gly Cys Val Phe Ala Tyr Val Gly Cys
                405                 410                 415

Tyr Asn Lys Arg Ala Tyr Trp Val Pro Arg Ala Ser Ala Asp Ile Gly
            420                 425                 430

Ser Gly His Thr Gly Ile Thr Gly Asp Asn Val Glu Thr Leu Asn Glu
        435                 440                 445

Asp Leu Leu Glu Ile Leu Ser Arg Glu Arg Val Asn Ile Asn Ile Val
    450                 455                 460

Gly Asp Phe His Leu Asn Glu Glu Val Ala Ile Ile Leu Ala Ser Phe
465                 470                 475                 480

Ser Ala Ser Thr Ser Ala Phe Ile Asp Thr Ile Lys Ser Leu Asp Tyr
                485                 490                 495

Lys Ser Phe Lys Thr Ile Val Glu Ser Cys Gly Asn Tyr Lys Val Thr
            500                 505                 510

Lys Gly Lys Pro Val Lys Gly Ala Trp Asn Ile Gly Gln Gln Arg Ser
        515                 520                 525

Val Leu Thr Pro Leu Cys Gly Phe Pro Ser Gln Ala Ala Gly Val Ile
    530                 535                 540

Arg Ser Ile Phe Ala Arg Thr Leu Asp Ala Ala Asn His Ser Ile Pro
545                 550                 555                 560

Asp Leu Gln Arg Ala Ala Val Thr Ile Leu Asp Gly Ile Ser Glu Gln
                565                 570                 575

Ser Leu Arg Leu Val Asp Ala Met Val Tyr Thr Ser Asp Leu Leu Thr
            580                 585                 590

Asn Ser Val Ile Ile Met Ala Tyr Val Thr Gly Gly Leu Val Gln Gln
        595                 600                 605

Thr Ser Gln Trp Leu Ser Asn Leu Leu Gly Thr Thr Val Glu Lys Leu
    610                 615                 620

Arg Pro Ile Phe Glu Trp Ile Glu Ala Lys Leu Ser Ala Gly Val Glu
625                 630                 635                 640

Phe Leu Lys Asp Ala Trp Glu Ile Leu Lys Phe Leu Ile Thr Gly Val
                645                 650                 655

Phe Asp Ile Val Lys Gly Gln Ile Gln Val Ala Ser Asp Asn Ile Lys
            660                 665                 670

Asp Cys Val Lys Cys Phe Ile Asp Val Val Asn Lys Ala Leu Glu Met
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        675                 680                 685

Cys Ile Asp Gln Val Thr Ile Ala Gly Ala Lys Leu Arg Ser Leu Asn
    690                 695                 700

Leu Gly Glu Val Phe Ile Ala Gln Ser Lys Gly Leu Tyr Arg Gln Cys
705                 710                 715                 720

Ile Arg Gly Lys Glu Gln Leu Gln Leu Leu Met Pro Leu Lys Ala Pro
                725                 730                 735

Lys Glu Val Thr Phe Leu Glu Gly Asp Ser His Asp Thr Val Leu Thr
            740                 745                 750

Ser Glu Glu Val Val Leu Lys Asn Gly Glu Leu Glu Ala Leu Glu Thr
        755                 760                 765

Pro Val Asp Ser Phe Thr Asn Gly Ala Ile Val Gly Thr Pro Val Cys
    770                 775                 780

Val Asn Gly Leu Met Leu Leu Glu Ile Lys Asp Lys Glu Gln Tyr Cys
785                 790                 795                 800

Ala Leu Ser Pro Gly Leu Leu Ala Thr Asn Asn Val Phe Arg Leu Lys
                805                 810                 815

Gly Gly Ala Pro Ile Lys Gly Val Thr Phe Gly Glu Asp Thr Val Trp
            820                 825                 830

Glu Val Gln Gly Tyr Lys Asn Val Arg Ile Thr Phe Glu Leu Asp Glu
        835                 840                 845

Arg Val Asp Lys Val Leu Asn Glu Lys Cys Ser Val Tyr Thr Val Glu
    850                 855                 860

Ser Gly Thr Glu Val Thr Glu Phe Ala Cys Val Val Ala Glu Ala Val
865                 870                 875                 880

Val Lys Thr Leu Gln Pro Val Ser Asp Leu Leu Thr Asn Met Gly Ile
                885                 890                 895

Asp Leu Asp Glu Trp Ser Val Ala Thr Phe Tyr Leu Phe Asp Asp Ala
            900                 905                 910

Gly Glu Glu Asn Phe Ser Ser Arg Met Tyr Cys Ser Phe Tyr Pro Pro
        915                 920                 925

Asp Glu Glu Glu Glu Asp Asp Ala Glu Cys Glu Glu Glu Glu Ile Asp
    930                 935                 940

Glu Thr Cys Glu His Glu Tyr Gly Thr Glu Asp Asp Tyr Gln Gly Leu
945                 950                 955                 960

Pro Leu Glu Phe Gly Ala Ser Ala Glu Thr Val Arg Val Glu Glu Glu
                965                 970                 975

Glu Glu Glu Asp Trp Leu Asp Asp Thr Thr Glu Gln Ser Glu Ile Glu
            980                 985                 990

Pro Glu Pro Glu Pro Thr Pro Glu  Glu Pro Val Asn Gln  Phe Thr Gly
        995                 1000                 1005

Tyr Leu  Lys Leu Thr Asp Asn  Val Ala Ile Lys Cys  Val Asp Ile
    1010                 1015                 1020

Val Lys  Glu Ala Gln Ser Ala  Asn Pro Met Val Ile  Val Asn Ala
    1025                 1030                 1035

Ala Asn  Ile His Leu Lys His  Gly Gly Gly Val Ala  Gly Ala Leu
    1040                 1045                 1050

Asn Lys  Ala Thr Asn Gly Ala  Met Gln Lys Glu Ser  Asp Asp Tyr
    1055                 1060                 1065

Ile Lys  Leu Asn Gly Pro Leu  Thr Val Gly Gly Ser  Cys Leu Leu
    1070                 1075                 1080
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Ser Gly  His Asn Leu Ala Lys  Lys Cys Leu His Val  Val Gly Pro
    1085                 1090                 1095

Asn Leu  Asn Ala Gly Glu Asp  Ile Gln Leu Leu Lys  Ala Ala Tyr
    1100                 1105                 1110

Glu Asn  Phe Asn Ser Gln Asp  Ile Leu Leu Ala Pro  Leu Leu Ser
    1115                 1120                 1125

Ala Gly  Ile Phe Gly Ala Lys  Pro Leu Gln Ser Leu  Gln Val Cys
    1130                 1135                 1140

Val Gln  Thr Val Arg Thr Gln  Val Tyr Ile Ala Val  Asn Asp Lys
    1145                 1150                 1155

Ala Leu  Tyr Glu Gln Val Val  Met Asp Tyr Leu Asp  Asn Leu Lys
    1160                 1165                 1170

Pro Arg  Val Glu Ala Pro Lys  Gln Glu Glu Pro Pro  Asn Thr Glu
    1175                 1180                 1185

Asp Ser  Lys Thr Glu Glu Lys  Ser Val Val Gln Lys  Pro Val Asp
    1190                 1195                 1200

Val Lys  Pro Lys Ile Lys Ala  Cys Ile Asp Glu Val  Thr Thr Thr
    1205                 1210                 1215

Leu Glu  Glu Thr Lys Phe Leu  Thr Asn Lys Leu Leu  Leu Phe Ala
    1220                 1225                 1230

Asp Ile  Asn Gly Lys Leu Tyr  His Asp Ser Gln Asn  Met Leu Arg
    1235                 1240                 1245

Gly Glu  Asp Met Ser Phe Leu  Glu Lys Asp Ala Pro  Tyr Met Val
    1250                 1255                 1260

Gly Asp  Val Ile Thr Ser Gly  Asp Ile Thr Cys Val  Val Ile Pro
    1265                 1270                 1275

Ser Lys  Lys Ala Gly Gly Thr  Thr Glu Met Leu Ser  Arg Ala Leu
    1280                 1285                 1290

Lys Lys  Val Pro Val Asp Glu  Tyr Ile Thr Thr Tyr  Pro Gly Gln
    1295                 1300                 1305

Gly Cys  Ala Gly Tyr Thr Leu  Glu Glu Ala Lys Thr  Ala Leu Lys
    1310                 1315                 1320

Lys Cys  Lys Ser Ala Phe Tyr  Val Leu Pro Ser Glu  Ala Pro Asn
    1325                 1330                 1335

Ala Lys  Glu Glu Ile Leu Gly  Thr Val Ser Trp Asn  Leu Arg Glu
    1340                 1345                 1350

Met Leu  Ala His Ala Glu Glu  Thr Arg Lys Leu Met  Pro Ile Cys
    1355                 1360                 1365

Met Asp  Val Arg Ala Ile Met  Ala Thr Ile Gln Arg  Lys Tyr Lys
    1370                 1375                 1380

Gly Ile  Lys Ile Gln Glu Gly  Ile Val Asp Tyr Gly  Val Arg Phe
    1385                 1390                 1395

Phe Phe  Tyr Thr Ser Lys Glu  Pro Val Ala Ser Ile  Ile Thr Lys
    1400                 1405                 1410

Leu Asn  Ser Leu Asn Glu Pro  Leu Val Thr Met Pro  Ile Gly Tyr
    1415                 1420                 1425

Val Thr  His Gly Phe Asn Leu  Glu Glu Ala Ala Arg  Cys Met Arg
    1430                 1435                 1440

Ser Leu  Lys Ala Pro Ala Val  Val Ser Val Ser Ser  Pro Asp Ala
    1445                 1450                 1455
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Val Thr  Thr Tyr Asn Gly Tyr  Leu Thr Ser Ser Ser  Lys Thr Ser
    1460                 1465                 1470

Glu Glu  His Phe Val Glu Thr  Val Ser Leu Ala Gly  Ser Tyr Arg
    1475                 1480                 1485

Asp Trp  Ser Tyr Ser Gly Gln  Arg Thr Glu Leu Gly  Val Glu Phe
    1490                 1495                 1500

Leu Lys  Arg Gly Asp Lys Ile  Val Tyr His Thr Leu  Glu Ser Pro
    1505                 1510                 1515

Val Glu  Phe His Leu Asp Gly  Glu Val Leu Ser Leu  Asp Lys Leu
    1520                 1525                 1530

Lys Ser  Leu Leu Ser Leu Arg  Glu Val Lys Thr Ile  Lys Val Phe
    1535                 1540                 1545

Thr Thr  Val Asp Asn Thr Asn  Leu His Thr Gln Leu  Val Asp Met
    1550                 1555                 1560

Ser Met  Thr Tyr Gly Gln Gln  Phe Gly Pro Thr Tyr  Leu Asp Gly
    1565                 1570                 1575

Ala Asp  Val Thr Lys Ile Lys  Pro His Val Asn His  Glu Gly Lys
    1580                 1585                 1590

Thr Phe  Phe Val Leu Pro Ser  Asp Asp Thr Leu Arg  Ser Glu Ala
    1595                 1600                 1605

Phe Glu  Tyr Tyr His Thr Leu  Asp Glu Ser Phe Leu  Gly Arg Tyr
    1610                 1615                 1620

Met Ser  Ala Leu Asn His Thr  Lys Lys Trp Lys Phe  Pro Gln Val
    1625                 1630                 1635

Gly Gly  Leu Thr Ser Ile Lys  Trp Ala Asp Asn Asn  Cys Tyr Leu
    1640                 1645                 1650

Ser Ser  Val Leu Leu Ala Leu  Gln Gln Leu Glu Val  Lys Phe Asn
    1655                 1660                 1665

Ala Pro  Ala Leu Gln Glu Ala  Tyr Tyr Arg Ala Arg  Ala Gly Asp
    1670                 1675                 1680

Ala Ala  Asn Phe Cys Ala Leu  Ile Leu Ala Tyr Ser  Asn Lys Thr
    1685                 1690                 1695

Val Gly  Glu Leu Gly Asp Val  Arg Glu Thr Met Thr  His Leu Leu
    1700                 1705                 1710

Gln His  Ala Asn Leu Glu Ser  Ala Lys Arg Val Leu  Asn Val Val
    1715                 1720                 1725

Cys Lys  His Cys Gly Gln Lys  Thr Thr Thr Leu Thr  Gly Val Glu
    1730                 1735                 1740

Ala Val  Met Tyr Met Gly Thr  Leu Ser Tyr Asp Asn  Leu Lys Thr
    1745                 1750                 1755

Gly Val  Ser Ile Pro Cys Val  Cys Gly Arg Asp Ala  Thr Gln Tyr
    1760                 1765                 1770

Leu Val  Gln Gln Glu Ser Ser  Phe Val Met Met Ser  Ala Pro Pro
    1775                 1780                 1785

Ala Glu  Tyr Lys Leu Gln Gln  Gly Thr Phe Leu Cys  Ala Asn Glu
    1790                 1795                 1800

Tyr Thr  Gly Asn Tyr Gln Cys  Gly His Tyr Thr His  Ile Thr Ala
    1805                 1810                 1815

Lys Glu  Thr Leu Tyr Arg Ile  Asp Gly Ala His Leu  Thr Lys Met
    1820                 1825                 1830

Ser Glu  Tyr Lys Gly Pro Val  Thr Asp Val Phe Tyr  Lys Glu Thr
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    1835                1840                1845

Ser Tyr  Thr Thr Thr Ile Lys  Pro Val Ser Tyr Lys  Leu Asp Gly
    1850                1855                1860

Val Thr  Tyr Thr Glu Ile Glu  Pro Lys Leu Asp Gly  Tyr Tyr Lys
    1865                1870                1875

Lys Asp  Asn Ala Tyr Tyr Thr  Glu Gln Pro Ile Asp  Leu Val Pro
    1880                1885                1890

Thr Gln  Pro Leu Pro Asn Ala  Ser Phe Asp Asn Phe  Lys Leu Thr
    1895                1900                1905

Cys Ser  Asn Thr Lys Phe Ala  Asp Asp Leu Asn Gln  Met Thr Gly
    1910                1915                1920

Phe Thr  Lys Pro Ala Ser Arg  Glu Leu Ser Val Thr  Phe Phe Pro
    1925                1930                1935

Asp Leu  Asn Gly Asp Val Val  Ala Ile Asp Tyr Arg  His Tyr Ser
    1940                1945                1950

Ala Ser  Phe Lys Lys Gly Ala  Lys Leu Leu His Lys  Pro Ile Val
    1955                1960                1965

Trp His  Ile Asn Gln Ala Thr  Thr Lys Thr Thr Phe  Lys Pro Asn
    1970                1975                1980

Thr Trp  Cys Leu Arg Cys Leu  Trp Ser Thr Lys Pro  Val Asp Thr
    1985                1990                1995

Ser Asn  Ser Phe Glu Val Leu  Ala Val Glu Asp Thr  Gln Gly Met
    2000                2005                2010

Asp Asn  Leu Ala Cys Glu Ser  Gln Gln Pro Thr Ser  Glu Glu Val
    2015                2020                2025

Val Glu  Asn Pro Thr Ile Gln  Lys Glu Val Ile Glu  Cys Asp Val
    2030                2035                2040

Lys Thr  Thr Glu Val Val Gly  Asn Val Ile Leu Lys  Pro Ser Asp
    2045                2050                2055

Glu Gly  Val Lys Val Thr Gln  Glu Leu Gly His Glu  Asp Leu Met
    2060                2065                2070

Ala Ala  Tyr Val Glu Asn Thr  Ser Ile Thr Ile Lys  Lys Pro Asn
    2075                2080                2085

Glu Leu  Ser Leu Ala Leu Gly  Leu Lys Thr Ile Ala  Thr His Gly
    2090                2095                2100

Ile Ala  Ala Ile Asn Ser Val  Pro Trp Ser Lys Ile  Leu Ala Tyr
    2105                2110                2115

Val Lys  Pro Phe Leu Gly Gln  Ala Ala Ile Thr Thr  Ser Asn Cys
    2120                2125                2130

Ala Lys  Arg Leu Ala Gln Arg  Val Phe Asn Asn Tyr  Met Pro Tyr
    2135                2140                2145

Val Phe  Thr Leu Leu Phe Gln  Leu Cys Thr Phe Thr  Lys Ser Thr
    2150                2155                2160

Asn Ser  Arg Ile Arg Ala Ser  Leu Pro Thr Thr Ile  Ala Lys Asn
    2165                2170                2175

Ser Val  Lys Ser Val Ala Lys  Leu Cys Leu Asp Ala  Gly Ile Asn
    2180                2185                2190

Tyr Val  Lys Ser Pro Lys Phe  Ser Lys Leu Phe Thr  Ile Ala Met
    2195                2200                2205

Trp Leu  Leu Leu Leu Ser Ile  Cys Leu Gly Ser Leu  Ile Cys Val
    2210                2215                2220
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Thr Ala  Ala Phe Gly Val Leu  Leu Ser Asn Phe Gly  Ala Pro Ser
    2225                 2230                 2235

Tyr Cys  Asn Gly Val Arg Glu  Leu Tyr Leu Asn Ser  Ser Asn Val
    2240                 2245                 2250

Thr Thr  Met Asp Phe Cys Glu  Gly Ser Phe Pro Cys  Ser Ile Cys
    2255                 2260                 2265

Leu Ser  Gly Leu Asp Ser Leu  Asp Ser Tyr Pro Ala  Leu Glu Thr
    2270                 2275                 2280

Ile Gln  Val Thr Ile Ser Ser  Tyr Lys Leu Asp Leu  Thr Ile Leu
    2285                 2290                 2295

Gly Leu  Ala Ala Glu Trp Val  Leu Ala Tyr Met Leu  Phe Thr Lys
    2300                 2305                 2310

Phe Phe  Tyr Leu Leu Gly Leu  Ser Ala Ile Met Gln  Val Phe Phe
    2315                 2320                 2325

Gly Tyr  Phe Ala Ser His Phe  Ile Ser Asn Ser Trp  Leu Met Trp
    2330                 2335                 2340

Phe Ile  Ile Ser Ile Val Gln  Met Ala Pro Val Ser  Ala Met Val
    2345                 2350                 2355

Arg Met  Tyr Ile Phe Phe Ala  Ser Phe Tyr Tyr Ile  Trp Lys Ser
    2360                 2365                 2370

Tyr Val  His Ile Met Asp Gly  Cys Thr Ser Ser Thr  Cys Met Met
    2375                 2380                 2385

Cys Tyr  Lys Arg Asn Arg Ala  Thr Arg Val Glu Cys  Thr Thr Ile
    2390                 2395                 2400

Val Asn  Gly Met Lys Arg Ser  Phe Tyr Val Tyr Ala  Asn Gly Gly
    2405                 2410                 2415

Arg Gly  Phe Cys Lys Thr His  Asn Trp Asn Cys Leu  Asn Cys Asp
    2420                 2425                 2430

Thr Phe  Cys Thr Gly Ser Thr  Phe Ile Ser Asp Glu  Val Ala Arg
    2435                 2440                 2445

Asp Leu  Ser Leu Gln Phe Lys  Arg Pro Ile Asn Pro  Thr Asp Gln
    2450                 2455                 2460

Ser Ser  Tyr Ile Val Asp Ser  Val Ala Val Lys Asn  Gly Ala Leu
    2465                 2470                 2475

His Leu  Tyr Phe Asp Lys Ala  Gly Gln Lys Thr Tyr  Glu Arg His
    2480                 2485                 2490

Pro Leu  Ser His Phe Val Asn  Leu Asp Asn Leu Arg  Ala Asn Asn
    2495                 2500                 2505

Thr Lys  Gly Ser Leu Pro Ile  Asn Val Ile Val Phe  Asp Gly Lys
    2510                 2515                 2520

Ser Lys  Cys Asp Glu Ser Ala  Ser Lys Ser Ala Ser  Val Tyr Tyr
    2525                 2530                 2535

Ser Gln  Leu Met Cys Gln Pro  Ile Leu Leu Leu Asp  Gln Ala Leu
    2540                 2545                 2550

Val Ser  Asp Val Gly Asp Ser  Thr Glu Val Ser Val  Lys Met Phe
    2555                 2560                 2565

Asp Ala  Tyr Val Asp Thr Phe  Ser Ala Thr Phe Ser  Val Pro Met
    2570                 2575                 2580

Glu Lys  Leu Lys Ala Leu Val  Ala Thr Ala His Ser  Glu Leu Ala
    2585                 2590                 2595
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Lys Gly  Val Ala Leu Asp Gly  Val Leu Ser Thr Phe  Val Ser Ala
    2600                 2605                 2610

Ala Arg  Gln Gly Val Val Asp  Thr Asp Val Asp Thr  Lys Asp Val
    2615                 2620                 2625

Ile Glu  Cys Leu Lys Leu Ser  His His Ser Asp Leu  Glu Val Thr
    2630                 2635                 2640

Gly Asp  Ser Cys Asn Asn Phe  Met Leu Thr Tyr Asn  Lys Val Glu
    2645                 2650                 2655

Asn Met  Thr Pro Arg Asp Leu  Gly Ala Cys Ile Asp  Cys Asn Ala
    2660                 2665                 2670

Arg His  Ile Asn Ala Gln Val  Ala Lys Ser His Asn  Val Ser Leu
    2675                 2680                 2685

Ile Trp  Asn Val Lys Asp Tyr  Met Ser Leu Ser Glu  Gln Leu Arg
    2690                 2695                 2700

Lys Gln  Ile Arg Ser Ala Ala  Lys Lys Asn Asn Ile  Pro Phe Arg
    2705                 2710                 2715

Leu Thr  Cys Ala Thr Thr Arg  Gln Val Val Asn Val  Ile Thr Thr
    2720                 2725                 2730

Lys Ile  Ser Leu Lys Gly Gly  Lys Ile Val Ser Thr  Cys Phe Lys
    2735                 2740                 2745

Leu Met  Leu Lys Ala Thr Leu  Leu Cys Val Leu Ala  Ala Leu Val
    2750                 2755                 2760

Cys Tyr  Ile Val Met Pro Val  His Thr Leu Ser Ile  His Asp Gly
    2765                 2770                 2775

Tyr Thr  Asn Glu Ile Ile Gly  Tyr Lys Ala Ile Gln  Asp Gly Val
    2780                 2785                 2790

Thr Arg  Asp Ile Ile Ser Thr  Asp Asp Cys Phe Ala  Asn Lys His
    2795                 2800                 2805

Ala Gly  Phe Asp Ala Trp Phe  Ser Gln Arg Gly Gly  Ser Tyr Lys
    2810                 2815                 2820

Asn Asp  Lys Ser Cys Pro Val  Val Ala Ala Ile Ile  Thr Arg Glu
    2825                 2830                 2835

Ile Gly  Phe Ile Val Pro Gly  Leu Pro Gly Thr Val  Leu Arg Ala
    2840                 2845                 2850

Ile Asn  Gly Asp Phe Leu His  Phe Leu Pro Arg Val  Phe Ser Ala
    2855                 2860                 2865

Val Gly  Asn Ile Cys Tyr Thr  Pro Ser Lys Leu Ile  Glu Tyr Ser
    2870                 2875                 2880

Asp Phe  Ala Thr Ser Ala Cys  Val Leu Ala Ala Glu  Cys Thr Ile
    2885                 2890                 2895

Phe Lys  Asp Ala Met Gly Lys  Pro Val Pro Tyr Cys  Tyr Asp Thr
    2900                 2905                 2910

Asn Leu  Leu Glu Gly Ser Ile  Ser Tyr Ser Glu Leu  Arg Pro Asp
    2915                 2920                 2925

Thr Arg  Tyr Val Leu Met Asp  Gly Ser Ile Ile Gln  Phe Pro Asn
    2930                 2935                 2940

Thr Tyr  Leu Glu Gly Ser Val  Arg Val Val Thr Thr  Phe Asp Ala
    2945                 2950                 2955

Glu Tyr  Cys Arg His Gly Thr  Cys Glu Arg Ser Glu  Val Gly Ile
    2960                 2965                 2970

Cys Leu  Ser Thr Ser Gly Arg  Trp Val Leu Asn Asn  Glu His Tyr
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    2975                2980                2985

Arg Ala  Leu Ser Gly Val Phe  Cys Gly Val Asp Ala  Met Asn Leu
    2990                2995                3000

Ile Ala  Asn Ile Phe Thr Pro  Leu Val Gln Pro Val  Gly Ala Leu
    3005                3010                3015

Asp Val  Ser Ala Ser Val Val  Ala Gly Gly Ile Ile  Ala Ile Leu
    3020                3025                3030

Val Thr  Cys Ala Ala Tyr Tyr  Phe Met Lys Phe Arg  Arg Val Phe
    3035                3040                3045

Gly Glu  Tyr Asn His Val Val  Ala Ala Asn Ala Leu  Leu Phe Leu
    3050                3055                3060

Met Ser  Phe Thr Ile Leu Cys  Leu Val Pro Ala Tyr  Ser Phe Leu
    3065                3070                3075

Pro Gly  Val Tyr Ser Val Phe  Tyr Leu Tyr Leu Thr  Phe Tyr Phe
    3080                3085                3090

Thr Asn  Asp Val Ser Phe Leu  Ala His Leu Gln Trp  Phe Ala Met
    3095                3100                3105

Phe Ser  Pro Ile Val Pro Phe  Trp Ile Thr Ala Ile  Tyr Val Phe
    3110                3115                3120

Cys Ile  Ser Leu Lys His Cys  His Trp Phe Phe Asn  Asn Tyr Leu
    3125                3130                3135

Arg Lys  Arg Val Met Phe Asn  Gly Val Thr Phe Ser  Thr Phe Glu
    3140                3145                3150

Glu Ala  Ala Leu Cys Thr Phe  Leu Leu Asn Lys Glu  Met Tyr Leu
    3155                3160                3165

Lys Leu  Arg Ser Glu Thr Leu  Leu Pro Leu Thr Gln  Tyr Asn Arg
    3170                3175                3180

Tyr Leu  Ala Leu Tyr Asn Lys  Tyr Lys Tyr Phe Ser  Gly Ala Leu
    3185                3190                3195

Asp Thr  Thr Ser Tyr Arg Glu  Ala Ala Cys Cys His  Leu Ala Lys
    3200                3205                3210

Ala Leu  Asn Asp Phe Ser Asn  Ser Gly Ala Asp Val  Leu Tyr Gln
    3215                3220                3225

Pro Pro  Gln Thr Ser Ile Thr  Ser Ala Val Leu Gln  Ser Gly Phe
    3230                3235                3240

Arg Lys  Met Ala Phe Pro Ser  Gly Lys Val Glu Gly  Cys Met Val
    3245                3250                3255

Gln Val  Thr Cys Gly Thr Thr  Thr Leu Asn Gly Leu  Trp Leu Asp
    3260                3265                3270

Asp Thr  Val Tyr Cys Pro Arg  His Val Ile Cys Thr  Ala Glu Asp
    3275                3280                3285

Met Leu  Asn Pro Asn Tyr Glu  Asp Leu Leu Ile Arg  Lys Ser Asn
    3290                3295                3300

His Ser  Phe Leu Val Gln Ala  Gly Asn Val Gln Leu  Arg Val Ile
    3305                3310                3315

Gly His  Ser Met Gln Asn Cys  Leu Leu Arg Leu Lys  Val Asp Thr
    3320                3325                3330

Ser Asn  Pro Lys Thr Pro Lys  Tyr Lys Phe Val Arg  Ile Gln Pro
    3335                3340                3345

Gly Gln  Thr Phe Ser Val Leu  Ala Cys Tyr Asn Gly  Ser Pro Ser
    3350                3355                3360
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Gly Val  Tyr Gln Cys Ala Met  Arg Pro Asn His Thr  Ile Lys Gly
    3365                 3370                 3375

Ser Phe  Leu Asn Gly Ser Cys  Gly Ser Val Gly Phe  Asn Ile Asp
    3380                 3385                 3390

Tyr Asp  Cys Val Ser Phe Cys  Tyr Met His His Met  Glu Leu Pro
    3395                 3400                 3405

Thr Gly  Val His Ala Gly Thr  Asp Leu Glu Gly Lys  Phe Tyr Gly
    3410                 3415                 3420

Pro Phe  Val Asp Arg Gln Thr  Ala Gln Ala Ala Gly  Thr Asp Thr
    3425                 3430                 3435

Thr Ile  Thr Leu Asn Val Leu  Ala Trp Leu Tyr Ala  Ala Val Ile
    3440                 3445                 3450

Asn Gly  Asp Arg Trp Phe Leu  Asn Arg Phe Thr Thr  Thr Leu Asn
    3455                 3460                 3465

Asp Phe  Asn Leu Val Ala Met  Lys Tyr Asn Tyr Glu  Pro Leu Thr
    3470                 3475                 3480

Gln Asp  His Val Asp Ile Leu  Gly Pro Leu Ser Ala  Gln Thr Gly
    3485                 3490                 3495

Ile Ala  Val Leu Asp Met Cys  Ala Ala Leu Lys Glu  Leu Leu Gln
    3500                 3505                 3510

Asn Gly  Met Asn Gly Arg Thr  Ile Leu Gly Ser Thr  Ile Leu Glu
    3515                 3520                 3525

Asp Glu  Phe Thr Pro Phe Asp  Val Val Arg Gln Cys  Ser Gly Val
    3530                 3535                 3540

Thr Phe  Gln Gly Lys Phe Lys  Lys Ile Val Lys Gly  Thr His His
    3545                 3550                 3555

Trp Met  Leu Leu Thr Phe Leu  Thr Ser Leu Leu Ile  Leu Val Gln
    3560                 3565                 3570

Ser Thr  Gln Trp Ser Leu Phe  Phe Phe Val Tyr Glu  Asn Ala Phe
    3575                 3580                 3585

Leu Pro  Phe Thr Leu Gly Ile  Met Ala Ile Ala Ala  Cys Ala Met
    3590                 3595                 3600

Leu Leu  Val Lys His Lys His  Ala Phe Leu Cys Leu  Phe Leu Leu
    3605                 3610                 3615

Pro Ser  Leu Ala Thr Val Ala  Tyr Phe Asn Met Val  Tyr Met Pro
    3620                 3625                 3630

Ala Ser  Trp Val Met Arg Ile  Met Thr Trp Leu Glu  Leu Ala Asp
    3635                 3640                 3645

Thr Ser  Leu Ser Gly Tyr Arg  Leu Lys Asp Cys Val  Met Tyr Ala
    3650                 3655                 3660

Ser Ala  Leu Val Leu Leu Ile  Leu Met Thr Ala Arg  Thr Val Tyr
    3665                 3670                 3675

Asp Asp  Ala Ala Arg Arg Val  Trp Thr Leu Met Asn  Val Ile Thr
    3680                 3685                 3690

Leu Val  Tyr Lys Val Tyr Tyr  Gly Asn Ala Leu Asp  Gln Ala Ile
    3695                 3700                 3705

Ser Met  Trp Ala Leu Val Ile  Ser Val Thr Ser Asn  Tyr Ser Gly
    3710                 3715                 3720

Val Val  Thr Thr Ile Met Phe  Leu Ala Arg Ala Ile  Val Phe Val
    3725                 3730                 3735
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Cys Val  Glu Tyr Tyr Pro Leu  Leu Phe Ile Thr Gly  Asn Thr Leu
    3740                 3745                 3750

Gln Cys  Ile Met Leu Val Tyr  Cys Phe Leu Gly Tyr  Cys Cys Cys
    3755                 3760                 3765

Cys Tyr  Phe Gly Leu Phe Cys  Leu Leu Asn Arg Tyr  Phe Arg Leu
    3770                 3775                 3780

Thr Leu  Gly Val Tyr Asp Tyr  Leu Val Ser Thr Gln  Glu Phe Arg
    3785                 3790                 3795

Tyr Met  Asn Ser Gln Gly Leu  Leu Pro Pro Lys Ser  Ser Ile Asp
    3800                 3805                 3810

Ala Phe  Lys Leu Asn Ile Lys  Leu Leu Gly Ile Gly  Gly Lys Pro
    3815                 3820                 3825

Cys Ile  Lys Val Ala Thr Val  Gln Ser Lys Met Ser  Asp Val Lys
    3830                 3835                 3840

Cys Thr  Ser Val Val Leu Leu  Ser Val Leu Gln Gln  Leu Arg Val
    3845                 3850                 3855

Glu Ser  Ser Ser Lys Leu Trp  Ala Gln Cys Val Gln  Leu His Asn
    3860                 3865                 3870

Asp Ile  Leu Leu Ala Lys Asp  Thr Thr Glu Ala Phe  Glu Lys Met
    3875                 3880                 3885

Val Ser  Leu Leu Ser Val Leu  Leu Ser Met Gln Gly  Ala Val Asp
    3890                 3895                 3900

Ile Asn  Arg Leu Cys Glu Glu  Met Leu Asp Asn Arg  Ala Thr Leu
    3905                 3910                 3915

Gln Ala  Ile Ala Ser Glu Phe  Ser Ser Leu Pro Ser  Tyr Ala Ala
    3920                 3925                 3930

Tyr Ala  Thr Ala Gln Glu Ala  Tyr Glu Gln Ala Val  Ala Asn Gly
    3935                 3940                 3945

Asp Ser  Glu Val Val Leu Lys  Lys Leu Lys Lys Ser  Leu Asn Val
    3950                 3955                 3960

Ala Lys  Ser Glu Phe Asp Arg  Asp Ala Ala Met Gln  Arg Lys Leu
    3965                 3970                 3975

Glu Lys  Met Ala Asp Gln Ala  Met Thr Gln Met Tyr  Lys Gln Ala
    3980                 3985                 3990

Arg Ser  Glu Asp Lys Arg Ala  Lys Val Thr Ser Ala  Met Gln Thr
    3995                 4000                 4005

Met Leu  Phe Thr Met Leu Arg  Lys Leu Asp Asn Asp  Ala Leu Asn
    4010                 4015                 4020

Asn Ile  Ile Asn Asn Ala Arg  Asp Gly Cys Val Pro  Leu Asn Ile
    4025                 4030                 4035

Ile Pro  Leu Thr Thr Ala Ala  Lys Leu Met Val Val  Val Pro Asp
    4040                 4045                 4050

Tyr Gly  Thr Tyr Lys Asn Thr  Cys Asp Gly Asn Thr  Phe Thr Tyr
    4055                 4060                 4065

Ala Ser  Ala Leu Trp Glu Ile  Gln Gln Val Val Asp  Ala Asp Ser
    4070                 4075                 4080

Lys Ile  Val Gln Leu Ser Glu  Ile Asn Met Asp Asn  Ser Pro Asn
    4085                 4090                 4095

Leu Ala  Trp Pro Leu Ile Val  Thr Ala Leu Arg Ala  Asn Ser Ala
    4100                 4105                 4110

Val Lys  Leu Gln Asn Asn Glu  Leu Ser Pro Val Ala  Leu Arg Gln
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    4115                4120                4125

Met Ser  Cys Ala Ala Gly Thr  Thr Gln Thr Ala Cys  Thr Asp Asp
    4130                4135                4140

Asn Ala  Leu Ala Tyr Tyr Asn  Asn Ser Lys Gly Gly  Arg Phe Val
    4145                4150                4155

Leu Ala  Leu Leu Ser Asp His  Gln Asp Leu Lys Trp  Ala Arg Phe
    4160                4165                4170

Pro Lys  Ser Asp Gly Thr Gly  Thr Ile Tyr Thr Glu  Leu Glu Pro
    4175                4180                4185

Pro Cys  Arg Phe Val Thr Asp  Thr Pro Lys Gly Pro  Lys Val Lys
    4190                4195                4200

Tyr Leu  Tyr Phe Ile Lys Gly  Leu Asn Asn Leu Asn  Arg Gly Met
    4205                4210                4215

Val Leu  Gly Ser Leu Ala Ala  Thr Val Arg Leu Gln  Ala Gly Asn
    4220                4225                4230

Ala Thr  Glu Val Pro Ala Asn  Ser Thr Val Leu Ser  Phe Cys Ala
    4235                4240                4245

Phe Ala  Val Asp Pro Ala Lys  Ala Tyr Lys Asp Tyr  Leu Ala Ser
    4250                4255                4260

Gly Gly  Gln Pro Ile Thr Asn  Cys Val Lys Met Leu  Cys Thr His
    4265                4270                4275

Thr Gly  Thr Gly Gln Ala Ile  Thr Val Thr Pro Glu  Ala Asn Met
    4280                4285                4290

Asp Gln  Glu Ser Phe Gly Gly  Ala Ser Cys Cys Leu  Tyr Cys Arg
    4295                4300                4305

Cys His  Ile Asp His Pro Asn  Pro Lys Gly Phe Cys  Asp Leu Lys
    4310                4315                4320

Gly Lys  Tyr Val Gln Ile Pro  Thr Thr Cys Ala Asn  Asp Pro Val
    4325                4330                4335

Gly Phe  Thr Leu Arg Asn Thr  Val Cys Thr Val Cys  Gly Met Trp
    4340                4345                4350

Lys Gly  Tyr Gly Cys Ser Cys  Asp Gln Leu Arg Glu  Pro Leu Met
    4355                4360                4365

Gln Ser  Ala Asp Ala Ser Thr  Phe Phe Lys Arg Val  Cys Gly Val
    4370                4375                4380

Ser Ala  Ala Arg Leu Thr Pro  Cys Gly Thr Gly Thr  Ser Thr Asp
    4385                4390                4395

Val Val  Tyr Arg Ala Phe Asp  Ile Tyr Asn Glu Lys  Val Ala Gly
    4400                4405                4410

Phe Ala  Lys Phe Leu Lys Thr  Asn Cys Cys Arg Phe  Gln Glu Lys
    4415                4420                4425

Asp Glu  Glu Gly Asn Leu Leu  Asp Ser Tyr Phe Val  Val Lys Arg
    4430                4435                4440

His Thr  Met Ser Asn Tyr Gln  His Glu Glu Thr Ile  Tyr Asn Leu
    4445                4450                4455

Val Lys  Asp Cys Pro Ala Val  Ala Val His Asp Phe  Phe Lys Phe
    4460                4465                4470

Arg Val  Asp Gly Asp Met Val  Pro His Ile Ser Arg  Gln Arg Leu
    4475                4480                4485

Thr Lys  Tyr Thr Met Ala Asp  Leu Val Tyr Ala Leu  Arg His Phe
    4490                4495                4500
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Asp Glu  Gly Asn Cys Asp Thr  Leu Lys Glu Ile Leu  Val Thr Tyr
    4505                 4510                 4515

Asn Cys  Cys Asp Asp Asp Tyr  Phe Asn Lys Lys Asp  Trp Tyr Asp
    4520                 4525                 4530

Phe Val  Glu Asn Pro Asp Ile  Leu Arg Val Tyr Ala  Asn Leu Gly
    4535                 4540                 4545

Glu Arg  Val Arg Gln Ser Leu  Leu Lys Thr Val Gln  Phe Cys Asp
    4550                 4555                 4560

Ala Met  Arg Asp Ala Gly Ile  Val Gly Val Leu Thr  Leu Asp Asn
    4565                 4570                 4575

Gln Asp  Leu Asn Gly Asn Trp  Tyr Asp Phe Gly Asp  Phe Val Gln
    4580                 4585                 4590

Val Ala  Pro Gly Cys Gly Val  Pro Ile Val Asp Ser  Tyr Tyr Ser
    4595                 4600                 4605

Leu Leu  Met Pro Ile Leu Thr  Leu Thr Arg Ala Leu  Ala Ala Glu
    4610                 4615                 4620

Ser His  Met Asp Ala Asp Leu  Ala Lys Pro Leu Ile  Lys Trp Asp
    4625                 4630                 4635

Leu Leu  Lys Tyr Asp Phe Thr  Glu Glu Arg Leu Cys  Leu Phe Asp
    4640                 4645                 4650

Arg Tyr  Phe Lys Tyr Trp Asp  Gln Thr Tyr His Pro  Asn Cys Ile
    4655                 4660                 4665

Asn Cys  Leu Asp Asp Arg Cys  Ile Leu His Cys Ala  Asn Phe Asn
    4670                 4675                 4680

Val Leu  Phe Ser Thr Val Phe  Pro Pro Thr Ser Phe  Gly Pro Leu
    4685                 4690                 4695

Val Arg  Lys Ile Phe Val Asp  Gly Val Pro Phe Val  Val Ser Thr
    4700                 4705                 4710

Gly Tyr  His Phe Arg Glu Leu  Gly Val Val His Asn  Gln Asp Val
    4715                 4720                 4725

Asn Leu  His Ser Ser Arg Leu  Ser Phe Lys Glu Leu  Leu Val Tyr
    4730                 4735                 4740

Ala Ala  Asp Pro Ala Met His  Ala Ala Ser Gly Asn  Leu Leu Leu
    4745                 4750                 4755

Asp Lys  Arg Thr Thr Cys Phe  Ser Val Ala Ala Leu  Thr Asn Asn
    4760                 4765                 4770

Val Ala  Phe Gln Thr Val Lys  Pro Gly Asn Phe Asn  Lys Asp Phe
    4775                 4780                 4785

Tyr Asp  Phe Ala Val Ser Lys  Gly Phe Phe Lys Glu  Gly Ser Ser
    4790                 4795                 4800

Val Glu  Leu Lys His Phe Phe  Phe Ala Gln Asp Gly  Asn Ala Ala
    4805                 4810                 4815

Ile Ser  Asp Tyr Asp Tyr Tyr  Arg Tyr Asn Leu Pro  Thr Met Cys
    4820                 4825                 4830

Asp Ile  Arg Gln Leu Leu Phe  Val Val Glu Val Val  Asp Lys Tyr
    4835                 4840                 4845

Phe Asp  Cys Tyr Asp Gly Gly  Cys Ile Asn Ala Asn  Gln Val Ile
    4850                 4855                 4860

Val Asn  Asn Leu Asp Lys Ser  Ala Gly Phe Pro Phe  Asn Lys Trp
    4865                 4870                 4875
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Gly Lys  Ala Arg Leu Tyr Tyr  Asp Ser Met Ser Tyr  Glu Asp Gln
    4880                 4885                 4890

Asp Ala  Leu Phe Ala Tyr Thr  Lys Arg Asn Val Ile  Pro Thr Ile
    4895                 4900                 4905

Thr Gln  Met Asn Leu Lys Tyr  Ala Ile Ser Ala Lys  Asn Arg Ala
    4910                 4915                 4920

Arg Thr  Val Ala Gly Val Ser  Ile Cys Ser Thr Met  Thr Asn Arg
    4925                 4930                 4935

Gln Phe  His Gln Lys Leu Leu  Lys Ser Ile Ala Ala  Thr Arg Gly
    4940                 4945                 4950

Ala Thr  Val Val Ile Gly Thr  Ser Lys Phe Tyr Gly  Gly Trp His
    4955                 4960                 4965

Asn Met  Leu Lys Thr Val Tyr  Ser Asp Val Glu Thr  Pro His Leu
    4970                 4975                 4980

Met Gly  Trp Asp Tyr Pro Lys  Cys Asp Arg Ala Met  Pro Asn Met
    4985                 4990                 4995

Leu Arg  Ile Met Ala Ser Leu  Val Leu Ala Arg Lys  His Asn Thr
    5000                 5005                 5010

Cys Cys  Asn Leu Ser His Arg  Phe Tyr Arg Leu Ala  Asn Glu Cys
    5015                 5020                 5025

Ala Gln  Val Leu Ser Glu Met  Val Met Cys Gly Gly  Ser Leu Tyr
    5030                 5035                 5040

Val Lys  Pro Gly Gly Thr Ser  Ser Gly Asp Ala Thr  Thr Ala Tyr
    5045                 5050                 5055

Ala Asn  Ser Val Phe Asn Ile  Cys Gln Ala Val Thr  Ala Asn Val
    5060                 5065                 5070

Asn Ala  Leu Leu Ser Thr Asp  Gly Asn Lys Ile Ala  Asp Lys Tyr
    5075                 5080                 5085

Val Arg  Asn Leu Gln His Arg  Leu Tyr Glu Cys Leu  Tyr Arg Asn
    5090                 5095                 5100

Arg Asp  Val Asp His Glu Phe  Val Asp Glu Phe Tyr  Ala Tyr Leu
    5105                 5110                 5115

Arg Lys  His Phe Ser Met Met  Ile Leu Ser Asp Asp  Ala Val Val
    5120                 5125                 5130

Cys Tyr  Asn Ser Asn Tyr Ala  Ala Gln Gly Leu Val  Ala Ser Ile
    5135                 5140                 5145

Lys Asn  Phe Lys Ala Val Leu  Tyr Tyr Gln Asn Asn  Val Phe Met
    5150                 5155                 5160

Ser Glu  Ala Lys Cys Trp Thr  Glu Thr Asp Leu Thr  Lys Gly Pro
    5165                 5170                 5175

His Glu  Phe Cys Ser Gln His  Thr Met Leu Val Lys  Gln Gly Asp
    5180                 5185                 5190

Asp Tyr  Val Tyr Leu Pro Tyr  Pro Asp Pro Ser Arg  Ile Leu Gly
    5195                 5200                 5205

Ala Gly  Cys Phe Val Asp Asp  Ile Val Lys Thr Asp  Gly Thr Leu
    5210                 5215                 5220

Met Ile  Glu Arg Phe Val Ser  Leu Ala Ile Asp Ala  Tyr Pro Leu
    5225                 5230                 5235

Thr Lys  His Pro Asn Gln Glu  Tyr Ala Asp Val Phe  His Leu Tyr
    5240                 5245                 5250

Leu Gln  Tyr Ile Arg Lys Leu  His Asp Glu Leu Thr  Gly His Met
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    5255                5260                5265

Leu Asp  Met Tyr Ser Val Met  Leu Thr Asn Asp Asn  Thr Ser Arg
    5270                5275                5280

Tyr Trp  Glu Pro Glu Phe Tyr  Glu Ala Met Tyr Thr  Pro His Thr
    5285                5290                5295

Val Leu  Gln Ala Val Gly Ala  Cys Val Leu Cys Asn  Ser Gln Thr
    5300                5305                5310

Ser Leu  Arg Cys Gly Ala Cys  Ile Arg Arg Pro Phe  Leu Cys Cys
    5315                5320                5325

Lys Cys  Cys Tyr Asp His Val  Ile Ser Thr Ser His  Lys Leu Val
    5330                5335                5340

Leu Ser  Val Asn Pro Tyr Val  Cys Asn Ala Pro Gly  Cys Asp Val
    5345                5350                5355

Thr Asp  Val Thr Gln Leu Tyr  Leu Gly Gly Met Ser  Tyr Tyr Cys
    5360                5365                5370

Lys Ser  His Lys Pro Pro Ile  Ser Phe Pro Leu Cys  Ala Asn Gly
    5375                5380                5385

Gln Val  Phe Gly Leu Tyr Lys  Asn Thr Cys Val Gly  Ser Asp Asn
    5390                5395                5400

Val Thr  Asp Phe Asn Ala Ile  Ala Thr Cys Asp Trp  Thr Asn Ala
    5405                5410                5415

Gly Asp  Tyr Ile Leu Ala Asn  Thr Cys Thr Glu Arg  Leu Lys Leu
    5420                5425                5430

Phe Ala  Ala Glu Thr Leu Lys  Ala Thr Glu Glu Thr  Phe Lys Leu
    5435                5440                5445

Ser Tyr  Gly Ile Ala Thr Val  Arg Glu Val Leu Ser  Asp Arg Glu
    5450                5455                5460

Leu His  Leu Ser Trp Glu Val  Gly Lys Pro Arg Pro  Pro Leu Asn
    5465                5470                5475

Arg Asn  Tyr Val Phe Thr Gly  Tyr Arg Val Thr Lys  Asn Ser Lys
    5480                5485                5490

Val Gln  Ile Gly Glu Tyr Thr  Phe Glu Lys Gly Asp  Tyr Gly Asp
    5495                5500                5505

Ala Val  Val Tyr Arg Gly Thr  Thr Thr Tyr Lys Leu  Asn Val Gly
    5510                5515                5520

Asp Tyr  Phe Val Leu Thr Ser  His Thr Val Met Pro  Leu Ser Ala
    5525                5530                5535

Pro Thr  Leu Val Pro Gln Glu  His Tyr Val Arg Ile  Thr Gly Leu
    5540                5545                5550

Tyr Pro  Thr Leu Asn Ile Ser  Asp Glu Phe Ser Ser  Asn Val Ala
    5555                5560                5565

Asn Tyr  Gln Lys Val Gly Met  Gln Lys Tyr Ser Thr  Leu Gln Gly
    5570                5575                5580

Pro Pro  Gly Thr Gly Lys Ser  His Phe Ala Ile Gly  Leu Ala Leu
    5585                5590                5595

Tyr Tyr  Pro Ser Ala Arg Ile  Val Tyr Thr Ala Cys  Ser His Ala
    5600                5605                5610

Ala Val  Asp Ala Leu Cys Glu  Lys Ala Leu Lys Tyr  Leu Pro Ile
    5615                5620                5625

Asp Lys  Cys Ser Arg Ile Ile  Pro Ala Arg Ala Arg  Val Glu Cys
    5630                5635                5640
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Phe Asp  Lys Phe Lys Val Asn  Ser Thr Leu Glu Gln  Tyr Val Phe
    5645                 5650                 5655

Cys Thr  Val Asn Ala Leu Pro  Glu Thr Thr Ala Asp  Ile Val Val
    5660                 5665                 5670

Phe Asp  Glu Ile Ser Met Ala  Thr Asn Tyr Asp Leu  Ser Val Val
    5675                 5680                 5685

Asn Ala  Arg Leu Arg Ala Lys  His Tyr Val Tyr Ile  Gly Asp Pro
    5690                 5695                 5700

Ala Gln  Leu Pro Ala Pro Arg  Thr Leu Leu Thr Lys  Gly Thr Leu
    5705                 5710                 5715

Glu Pro  Glu Tyr Phe Asn Ser  Val Cys Arg Leu Met  Lys Thr Ile
    5720                 5725                 5730

Gly Pro  Asp Met Phe Leu Gly  Thr Cys Arg Arg Cys  Pro Ala Glu
    5735                 5740                 5745

Ile Val  Asp Thr Val Ser Ala  Leu Val Tyr Asp Asn  Lys Leu Lys
    5750                 5755                 5760

Ala His  Lys Asp Lys Ser Ala  Gln Cys Phe Lys Met  Phe Tyr Lys
    5765                 5770                 5775

Gly Val  Ile Thr His Asp Val  Ser Ser Ala Ile Asn  Arg Pro Gln
    5780                 5785                 5790

Ile Gly  Val Val Arg Glu Phe  Leu Thr Arg Asn Pro  Ala Trp Arg
    5795                 5800                 5805

Lys Ala  Val Phe Ile Ser Pro  Tyr Asn Ser Gln Asn  Ala Val Ala
    5810                 5815                 5820

Ser Lys  Ile Leu Gly Leu Pro  Thr Gln Thr Val Asp  Ser Ser Gln
    5825                 5830                 5835

Gly Ser  Glu Tyr Asp Tyr Val  Ile Phe Thr Gln Thr  Thr Glu Thr
    5840                 5845                 5850

Ala His  Ser Cys Asn Val Asn  Arg Phe Asn Val Ala  Ile Thr Arg
    5855                 5860                 5865

Ala Lys  Ile Gly Ile Leu Cys  Ile Met Ser Asp Arg  Asp Leu Tyr
    5870                 5875                 5880

Asp Lys  Leu Gln Phe Thr Ser  Leu Glu Ile Pro Arg  Arg Asn Val
    5885                 5890                 5895

Ala Thr  Leu Gln Ala Glu Asn  Val Thr Gly Leu Phe  Lys Asp Cys
    5900                 5905                 5910

Ser Lys  Ile Ile Thr Gly Leu  His Pro Thr Gln Ala  Pro Thr His
    5915                 5920                 5925

Leu Ser  Val Asp Ile Lys Phe  Lys Thr Glu Gly Leu  Cys Val Asp
    5930                 5935                 5940

Ile Pro  Gly Ile Pro Lys Asp  Met Thr Tyr Arg Arg  Leu Ile Ser
    5945                 5950                 5955

Met Met  Gly Phe Lys Met Asn  Tyr Gln Val Asn Gly  Tyr Pro Asn
    5960                 5965                 5970

Met Phe  Ile Thr Arg Glu Glu  Ala Ile Arg His Val  Arg Ala Trp
    5975                 5980                 5985

Ile Gly  Phe Asp Val Glu Gly  Cys His Ala Thr Arg  Asp Ala Val
    5990                 5995                 6000

Gly Thr  Asn Leu Pro Leu Gln  Leu Gly Phe Ser Thr  Gly Val Asn
    6005                 6010                 6015
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Leu Val  Ala Val Pro Thr Gly  Tyr Val Asp Thr Glu  Asn Asn Thr
    6020                 6025                 6030

Glu Phe  Thr Arg Val Asn Ala  Lys Pro Pro Pro Gly  Asp Gln Phe
    6035                 6040                 6045

Lys His  Leu Ile Pro Leu Met  Tyr Lys Gly Leu Pro  Trp Asn Val
    6050                 6055                 6060

Val Arg  Ile Lys Ile Val Gln  Met Leu Ser Asp Thr  Leu Lys Gly
    6065                 6070                 6075

Leu Ser  Asp Arg Val Val Phe  Val Leu Trp Ala His  Gly Phe Glu
    6080                 6085                 6090

Leu Thr  Ser Met Lys Tyr Phe  Val Lys Ile Gly Pro  Glu Arg Thr
    6095                 6100                 6105

Cys Cys  Leu Cys Asp Lys Arg  Ala Thr Cys Phe Ser  Thr Ser Ser
    6110                 6115                 6120

Asp Thr  Tyr Ala Cys Trp Asn  His Ser Val Gly Phe  Asp Tyr Val
    6125                 6130                 6135

Tyr Asn  Pro Phe Met Ile Asp  Val Gln Gln Trp Gly  Phe Thr Gly
    6140                 6145                 6150

Asn Leu  Gln Ser Asn His Asp  Gln His Cys Gln Val  His Gly Asn
    6155                 6160                 6165

Ala His  Val Ala Ser Cys Asp  Ala Ile Met Thr Arg  Cys Leu Ala
    6170                 6175                 6180

Val His  Glu Cys Phe Val Lys  Arg Val Asp Trp Ser  Val Glu Tyr
    6185                 6190                 6195

Pro Ile  Ile Gly Asp Glu Leu  Arg Val Asn Ser Ala  Cys Arg Lys
    6200                 6205                 6210

Val Gln  His Met Val Val Lys  Ser Ala Leu Leu Ala  Asp Lys Phe
    6215                 6220                 6225

Pro Val  Leu His Asp Ile Gly  Asn Pro Lys Ala Ile  Lys Cys Val
    6230                 6235                 6240

Pro Gln  Ala Glu Val Glu Trp  Lys Phe Tyr Asp Ala  Gln Pro Cys
    6245                 6250                 6255

Ser Asp  Lys Ala Tyr Lys Ile  Glu Glu Leu Phe Tyr  Ser Tyr Ala
    6260                 6265                 6270

Thr His  His Asp Lys Phe Thr  Asp Gly Val Cys Leu  Phe Trp Asn
    6275                 6280                 6285

Cys Asn  Val Asp Arg Tyr Pro  Ala Asn Ala Ile Val  Cys Arg Phe
    6290                 6295                 6300

Asp Thr  Arg Val Leu Ser Asn  Leu Asn Leu Pro Gly  Cys Asp Gly
    6305                 6310                 6315

Gly Ser  Leu Tyr Val Asn Lys  His Ala Phe His Thr  Pro Ala Phe
    6320                 6325                 6330

Asp Lys  Ser Ala Phe Thr Asn  Leu Lys Gln Leu Pro  Phe Phe Tyr
    6335                 6340                 6345

Tyr Ser  Asp Ser Pro Cys Glu  Ser His Gly Lys Gln  Val Val Ser
    6350                 6355                 6360

Asp Ile  Asp Tyr Val Pro Leu  Lys Ser Ala Thr Cys  Ile Thr Arg
    6365                 6370                 6375

Cys Asn  Leu Gly Gly Ala Val  Cys Arg His His Ala  Asn Glu Tyr
    6380                 6385                 6390

Arg Gln  Tyr Leu Asp Ala Tyr  Asn Met Met Ile Ser  Ala Gly Phe
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    6395                6400                6405

Ser Leu  Trp Ile Tyr Lys Gln  Phe Asp Thr Tyr Asn  Leu Trp Asn
    6410                6415                6420

Thr Phe  Thr Arg Leu Gln Ser  Leu Glu Asn Val Ala  Tyr Asn Val
    6425                6430                6435

Val Asn  Lys Gly His Phe Asp  Gly His Ala Gly Glu  Ala Pro Val
    6440                6445                6450

Ser Ile  Ile Asn Asn Ala Val  Tyr Thr Lys Val Asp  Gly Ile Asp
    6455                6460                6465

Val Glu  Ile Phe Glu Asn Lys  Thr Thr Leu Pro Val  Asn Val Ala
    6470                6475                6480

Phe Glu  Leu Trp Ala Lys Arg  Asn Ile Lys Pro Val  Pro Glu Ile
    6485                6490                6495

Lys Ile  Leu Asn Asn Leu Gly  Val Asp Ile Ala Ala  Asn Thr Val
    6500                6505                6510

Ile Trp  Asp Tyr Lys Arg Glu  Ala Pro Ala His Val  Ser Thr Ile
    6515                6520                6525

Gly Val  Cys Thr Met Thr Asp  Ile Ala Lys Lys Pro  Thr Glu Ser
    6530                6535                6540

Ala Cys  Ser Ser Leu Thr Val  Leu Phe Asp Gly Arg  Val Glu Gly
    6545                6550                6555

Gln Val  Asp Leu Phe Arg Asn  Ala Arg Asn Gly Val  Leu Ile Thr
    6560                6565                6570

Glu Gly  Ser Val Lys Gly Leu  Thr Pro Ser Lys Gly  Pro Ala Gln
    6575                6580                6585

Ala Ser  Val Asn Gly Val Thr  Leu Ile Gly Glu Ser  Val Lys Thr
    6590                6595                6600

Gln Phe  Asn Tyr Phe Lys Lys  Val Asp Gly Ile Ile  Gln Gln Leu
    6605                6610                6615

Pro Glu  Thr Tyr Phe Thr Gln  Ser Arg Asp Leu Glu  Asp Phe Lys
    6620                6625                6630

Pro Arg  Ser Gln Met Glu Thr  Asp Phe Leu Glu Leu  Ala Met Asp
    6635                6640                6645

Glu Phe  Ile Gln Arg Tyr Lys  Leu Glu Gly Tyr Ala  Phe Glu His
    6650                6655                6660

Ile Val  Tyr Gly Asp Phe Ser  His Gly Gln Leu Gly  Gly Leu His
    6665                6670                6675

Leu Met  Ile Gly Leu Ala Lys  Arg Ser Gln Asp Ser  Pro Leu Lys
    6680                6685                6690

Leu Glu  Asp Phe Ile Pro Met  Asp Ser Thr Val Lys  Asn Tyr Phe
    6695                6700                6705

Ile Thr  Asp Ala Gln Thr Gly  Ser Ser Lys Cys Val  Cys Ser Val
    6710                6715                6720

Ile Asp  Leu Leu Leu Asp Asp  Phe Val Glu Ile Ile  Lys Ser Gln
    6725                6730                6735

Asp Leu  Ser Val Ile Ser Lys  Val Val Lys Val Thr  Ile Asp Tyr
    6740                6745                6750

Ala Glu  Ile Ser Phe Met Leu  Trp Cys Lys Asp Gly  His Val Glu
    6755                6760                6765

Thr Phe  Tyr Pro Lys Leu Gln  Ala Ser Gln Ala Trp  Gln Pro Gly
    6770                6775                6780
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Val Ala  Met Pro Asn Leu Tyr  Lys Met Gln Arg Met  Leu Leu Glu
    6785                 6790                 6795

Lys Cys  Asp Leu Gln Asn Tyr  Gly Glu Asn Ala Val  Ile Pro Lys
    6800                 6805                 6810

Gly Ile  Met Met Asn Val Ala  Lys Tyr Thr Gln Leu  Cys Gln Tyr
    6815                 6820                 6825

Leu Asn  Thr Leu Thr Leu Ala  Val Pro Tyr Asn Met  Arg Val Ile
    6830                 6835                 6840

His Phe  Gly Ala Gly Ser Asp  Lys Gly Val Ala Pro  Gly Thr Ala
    6845                 6850                 6855

Val Leu  Arg Gln Trp Leu Pro  Thr Gly Thr Leu Leu  Val Asp Ser
    6860                 6865                 6870

Asp Leu  Asn Asp Phe Val Ser  Asp Ala Asp Ser Thr  Leu Ile Gly
    6875                 6880                 6885

Asp Cys  Ala Thr Val His Thr  Ala Asn Lys Trp Asp  Leu Ile Ile
    6890                 6895                 6900

Ser Asp  Met Tyr Asp Pro Arg  Thr Lys His Val Thr  Lys Glu Asn
    6905                 6910                 6915

Asp Ser  Lys Glu Gly Phe Phe  Thr Tyr Leu Cys Gly  Phe Ile Lys
    6920                 6925                 6930

Gln Lys  Leu Ala Leu Gly Gly  Ser Ile Ala Val Lys  Ile Thr Glu
    6935                 6940                 6945

His Ser  Trp Asn Ala Asp Leu  Tyr Lys Leu Met Gly  His Phe Ser
    6950                 6955                 6960

Trp Trp  Thr Ala Phe Val Thr  Asn Val Asn Ala Ser  Ser Ser Glu
    6965                 6970                 6975

Ala Phe  Leu Ile Gly Ala Asn  Tyr Leu Gly Lys Pro  Lys Glu Gln
    6980                 6985                 6990

Ile Asp  Gly Tyr Thr Met His  Ala Asn Tyr Ile Phe  Trp Arg Asn
    6995                 7000                 7005

Thr Asn  Pro Ile Gln Leu Ser  Ser Tyr Ser Leu Phe  Asp Met Ser
    7010                 7015                 7020

Lys Phe  Pro Leu Lys Leu Arg  Gly Thr Ala Val Met  Ser Leu Lys
    7025                 7030                 7035

Glu Asn  Gln Ile Asn Asp Met  Ile Tyr Ser Leu Leu  Glu Lys Gly
    7040                 7045                 7050

Arg Leu  Ile Ile Arg Glu Asn  Asn Arg Val Val Val  Ser Ser Asp
    7055                 7060                 7065

Ile Leu  Val Asn Asn
    7070


<210> SEQ ID NO 3
<211> LENGTH: 7078
<212> TYPE: PRT
<213> ORGANISM: Middle East respiratory syndrome-related coronavirus

<400> SEQUENCE: 3

Met Ser Phe Val Ala Gly Val Thr Ala Gln Gly Ala Arg Gly Thr Tyr
1               5                   10                  15

Arg Ala Ala Leu Asn Ser Glu Lys His Gln Asp His Val Ser Leu Thr
            20                  25                  30

Val Pro Leu Cys Gly Ser Gly Asn Leu Val Glu Lys Leu Ser Pro Trp
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        35                  40                  45

Phe Met Asp Gly Glu Asn Ala Tyr Glu Val Val Lys Ala Met Leu Leu
    50                  55                  60

Lys Lys Glu Pro Leu Leu Tyr Val Pro Ile Arg Leu Ala Gly His Thr
65                  70                  75                  80

Arg His Leu Pro Gly Pro Arg Val Tyr Leu Val Glu Arg Leu Ile Ala
                85                  90                  95

Cys Glu Asn Pro Phe Met Val Asn Gln Leu Ala Tyr Ser Ser Ser Ala
            100                 105                 110

Asn Gly Ser Leu Val Gly Thr Thr Leu Gln Gly Lys Pro Ile Gly Met
        115                 120                 125

Phe Phe Pro Tyr Asp Ile Glu Leu Val Thr Gly Lys Gln Asn Ile Leu
    130                 135                 140

Leu Arg Lys Tyr Gly Arg Gly Gly Tyr His Tyr Thr Pro Phe His Tyr
145                 150                 155                 160

Glu Arg Asp Asn Thr Ser Cys Pro Glu Trp Met Asp Asp Phe Glu Ala
                165                 170                 175

Asp Pro Lys Gly Lys Tyr Ala Gln Asn Leu Leu Lys Lys Leu Ile Gly
            180                 185                 190

Gly Asp Val Thr Pro Val Asp Gln Tyr Met Cys Gly Val Asp Gly Lys
        195                 200                 205

Pro Ile Ser Ala Tyr Ala Phe Leu Met Ala Lys Asp Gly Ile Thr Lys
    210                 215                 220

Leu Ala Asp Val Glu Ala Asp Val Ala Ala Arg Ala Asp Asp Glu Gly
225                 230                 235                 240

Phe Ile Thr Leu Lys Asn Asn Leu Tyr Arg Leu Val Trp His Val Glu
                245                 250                 255

Arg Lys Asp Val Pro Tyr Pro Lys Gln Ser Ile Phe Thr Ile Asn Ser
            260                 265                 270

Val Val Gln Lys Asp Gly Val Glu Asn Thr Pro Pro His Tyr Phe Thr
        275                 280                 285

Leu Gly Cys Lys Ile Leu Thr Leu Thr Pro Arg Asn Lys Trp Ser Gly
    290                 295                 300

Val Ser Asp Leu Ser Leu Lys Gln Lys Leu Leu Tyr Thr Phe Tyr Gly
305                 310                 315                 320

Lys Glu Ser Leu Glu Asn Pro Thr Tyr Ile Tyr His Ser Ala Phe Ile
                325                 330                 335

Glu Cys Gly Ser Cys Gly Asn Asp Ser Trp Leu Thr Gly Asn Ala Ile
            340                 345                 350

Gln Gly Phe Ala Cys Gly Cys Gly Ala Ser Tyr Thr Ala Asn Asp Val
        355                 360                 365

Glu Val Gln Ser Ser Gly Met Ile Lys Pro Asn Ala Leu Leu Cys Ala
    370                 375                 380

Thr Cys Pro Phe Ala Lys Gly Asp Ser Cys Ser Ser Asn Cys Lys His
385                 390                 395                 400

Ser Val Ala Gln Leu Val Ser Tyr Leu Ser Glu Arg Cys Asn Val Ile
                405                 410                 415

Ala Asp Ser Lys Ser Phe Thr Leu Ile Phe Gly Gly Val Ala Tyr Ala
            420                 425                 430

Tyr Phe Gly Cys Glu Glu Gly Thr Met Tyr Phe Val Pro Arg Ala Lys
        435                 440                 445
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Ser Val Val Ser Arg Ile Gly Asp Ser Ile Phe Thr Gly Cys Thr Gly
    450                 455                 460

Ser Trp Asn Lys Val Thr Gln Ile Ala Asn Met Phe Leu Glu Gln Thr
465                 470                 475                 480

Gln His Ser Leu Asn Phe Val Gly Glu Phe Val Val Asn Asp Val Val
                485                 490                 495

Leu Ala Ile Leu Ser Gly Thr Thr Thr Asn Val Asp Lys Ile Arg Gln
            500                 505                 510

Leu Leu Lys Gly Val Thr Leu Asp Lys Leu Arg Asp Tyr Leu Ala Asp
        515                 520                 525

Tyr Asp Val Ala Val Thr Ala Gly Pro Phe Met Asp Asn Ala Ile Asn
    530                 535                 540

Val Gly Gly Thr Gly Leu Gln Tyr Ala Ala Ile Thr Ala Pro Tyr Val
545                 550                 555                 560

Val Leu Thr Gly Leu Gly Glu Ser Phe Lys Lys Val Ala Thr Ile Pro
                565                 570                 575

Tyr Lys Val Cys Asn Ser Val Lys Asp Thr Leu Ala Tyr Tyr Ala His
            580                 585                 590

Ser Val Leu Tyr Arg Val Phe Pro Tyr Asp Met Asp Ser Gly Val Ser
        595                 600                 605

Ser Phe Ser Glu Leu Leu Phe Asp Cys Val Asp Leu Ser Val Ala Ser
    610                 615                 620

Thr Tyr Phe Leu Val Arg Ile Leu Gln Asp Lys Thr Gly Asp Phe Met
625                 630                 635                 640

Ser Thr Ile Ile Thr Ser Cys Gln Thr Ala Val Ser Lys Leu Leu Asp
                645                 650                 655

Thr Cys Phe Glu Ala Thr Glu Ala Thr Phe Asn Phe Leu Leu Asp Leu
            660                 665                 670

Ala Gly Leu Phe Arg Ile Phe Leu Arg Asn Ala Tyr Val Tyr Thr Ser
        675                 680                 685

Gln Gly Phe Val Val Val Asn Gly Lys Val Ser Thr Leu Val Lys Gln
    690                 695                 700

Val Leu Asp Leu Leu Asn Lys Gly Met Gln Leu Leu His Thr Lys Val
705                 710                 715                 720

Ser Trp Ala Gly Ser Lys Ile Ile Ala Val Ile Tyr Ser Gly Arg Glu
                725                 730                 735

Ser Leu Ile Phe Pro Ser Gly Thr Tyr Tyr Cys Val Thr Thr Lys Ala
            740                 745                 750

Lys Ser Val Gln Gln Asp Leu Asp Val Ile Leu Pro Gly Glu Phe Ser
        755                 760                 765

Lys Lys Gln Leu Gly Leu Leu Gln Pro Thr Asp Asn Ser Thr Thr Val
    770                 775                 780

Ser Val Thr Val Ser Ser Asn Met Val Glu Thr Val Val Gly Gln Leu
785                 790                 795                 800

Glu Gln Thr Asn Met His Ser Pro Asp Val Ile Val Gly Asp Tyr Val
                805                 810                 815

Ile Ile Ser Glu Lys Leu Phe Val Arg Ser Lys Glu Glu Asp Gly Phe
            820                 825                 830

Ala Phe Tyr Pro Ala Cys Thr Asn Gly His Ala Val Pro Thr Leu Phe
        835                 840                 845
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Arg Leu Lys Gly Gly Ala Pro Val Lys Lys Val Ala Phe Gly Gly Asp
    850                 855                 860

Gln Val His Glu Val Ala Ala Val Arg Ser Val Thr Val Glu Tyr Asn
865                 870                 875                 880

Ile His Ala Val Leu Asp Thr Leu Leu Ala Ser Ser Ser Leu Arg Thr
                885                 890                 895

Phe Val Val Asp Lys Ser Leu Ser Ile Glu Glu Phe Ala Asp Val Val
            900                 905                 910

Lys Glu Gln Val Ser Asp Leu Leu Val Lys Leu Leu Arg Gly Met Pro
        915                 920                 925

Ile Pro Asp Phe Asp Leu Asp Asp Phe Ile Asp Ala Pro Cys Tyr Cys
    930                 935                 940

Phe Asn Ala Glu Gly Asp Ala Ser Trp Ser Ser Thr Met Ile Phe Ser
945                 950                 955                 960

Leu His Pro Val Glu Cys Asp Glu Glu Cys Ser Glu Val Glu Ala Ser
                965                 970                 975

Asp Leu Glu Glu Gly Glu Ser Glu Cys Ile Ser Glu Thr Ser Thr Glu
            980                 985                 990

Gln Val Asp Val Ser His Glu Thr  Ser Asp Asp Glu Trp  Ala Ala Ala
        995                 1000                1005

Val Asp  Glu Ala Phe Pro Leu  Asp Glu Ala Glu Asp  Val Thr Glu
    1010                1015                1020

Ser Val  Gln Glu Glu Ala Gln  Pro Val Glu Val Pro  Val Glu Asp
    1025                1030                1035

Ile Ala  Gln Val Val Ile Ala  Asp Thr Leu Gln Glu  Thr Pro Val
    1040                1045                1050

Val Pro  Asp Thr Val Glu Val  Pro Pro Gln Val Val  Lys Leu Pro
    1055                1060                1065

Ser Ala  Pro Gln Thr Ile Gln  Pro Glu Val Lys Glu  Val Ala Pro
    1070                1075                1080

Val Tyr  Glu Ala Asp Thr Glu  Gln Thr Gln Asn Val  Thr Val Lys
    1085                1090                1095

Pro Lys  Arg Leu Arg Lys Lys  Arg Asn Val Asp Pro  Leu Ser Asn
    1100                1105                1110

Phe Glu  His Lys Val Ile Thr  Glu Cys Val Thr Ile  Val Leu Gly
    1115                1120                1125

Asp Ala  Ile Gln Val Ala Lys  Cys Tyr Gly Glu Ser  Val Leu Val
    1130                1135                1140

Asn Ala  Ala Asn Thr His Leu  Lys His Gly Gly Gly  Ile Ala Gly
    1145                1150                1155

Ala Ile  Asn Ala Ala Ser Lys  Gly Ala Val Gln Lys  Glu Ser Asp
    1160                1165                1170

Glu Tyr  Ile Leu Ala Lys Gly  Pro Leu Gln Val Gly  Asp Ser Val
    1175                1180                1185

Leu Leu  Gln Gly His Ser Leu  Ala Lys Asn Ile Leu  His Val Val
    1190                1195                1200

Gly Pro  Asp Ala Arg Ala Lys  Gln Asp Val Ser Leu  Leu Ser Lys
    1205                1210                1215

Cys Tyr  Lys Ala Met Asn Ala  Tyr Pro Leu Val Val  Thr Pro Leu
    1220                1225                1230

Val Ser  Ala Gly Ile Phe Gly  Val Lys Pro Ala Val  Ser Phe Asp
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    1235                1240                1245

Tyr Leu  Ile Arg Glu Ala Lys  Thr Arg Val Leu Val  Val Val Asn
    1250                1255                1260

Ser Gln  Asp Val Tyr Lys Ser  Leu Thr Ile Val Asp  Ile Pro Gln
    1265                1270                1275

Ser Leu  Thr Phe Ser Tyr Asp  Gly Leu Arg Gly Ala  Ile Arg Lys
    1280                1285                1290

Ala Lys  Asp Tyr Gly Phe Thr  Val Phe Val Cys Thr  Asp Asn Ser
    1295                1300                1305

Ala Asn  Thr Lys Val Leu Arg  Asn Lys Gly Val Asp  Tyr Thr Lys
    1310                1315                1320

Lys Phe  Leu Thr Val Asp Gly  Val Gln Tyr Tyr Cys  Tyr Thr Ser
    1325                1330                1335

Lys Asp  Thr Leu Asp Asp Ile  Leu Gln Gln Ala Asn  Lys Ser Val
    1340                1345                1350

Gly Ile  Ile Ser Met Pro Leu  Gly Tyr Val Ser His  Gly Leu Asp
    1355                1360                1365

Leu Met  Gln Ala Gly Ser Val  Val Arg Arg Val Asn  Val Pro Tyr
    1370                1375                1380

Val Cys  Leu Leu Ala Asn Lys  Glu Gln Glu Ala Ile  Leu Met Ser
    1385                1390                1395

Glu Asp  Val Lys Leu Asn Pro  Ser Glu Asp Phe Ile  Lys His Val
    1400                1405                1410

Arg Thr  Asn Gly Gly Tyr Asn  Ser Trp His Leu Val  Glu Gly Glu
    1415                1420                1425

Leu Leu  Val Gln Asp Leu Arg  Leu Asn Lys Leu Leu  His Trp Ser
    1430                1435                1440

Asp Gln  Thr Ile Cys Tyr Lys  Asp Ser Val Phe Tyr  Val Val Lys
    1445                1450                1455

Asn Ser  Thr Ala Phe Pro Phe  Glu Thr Leu Ser Ala  Cys Arg Ala
    1460                1465                1470

Tyr Leu  Asp Ser Arg Thr Thr  Gln Gln Leu Thr Ile  Glu Val Leu
    1475                1480                1485

Val Thr  Val Asp Gly Val Asn  Phe Arg Thr Val Val  Leu Asn Asn
    1490                1495                1500

Lys Asn  Thr Tyr Arg Ser Gln  Leu Gly Cys Val Phe  Phe Asn Gly
    1505                1510                1515

Ala Asp  Ile Ser Asp Thr Ile  Pro Asp Glu Lys Gln  Asn Gly His
    1520                1525                1530

Ser Leu  Tyr Leu Ala Asp Asn  Leu Thr Ala Asp Glu  Thr Lys Ala
    1535                1540                1545

Leu Lys  Glu Leu Tyr Gly Pro  Val Asp Pro Thr Phe  Leu His Arg
    1550                1555                1560

Phe Tyr  Ser Leu Lys Ala Ala  Val His Gly Trp Lys  Met Val Val
    1565                1570                1575

Cys Asp  Lys Val Arg Ser Leu  Lys Leu Ser Asp Asn  Asn Cys Tyr
    1580                1585                1590

Leu Asn  Ala Val Ile Met Thr  Leu Asp Leu Leu Lys  Asp Ile Lys
    1595                1600                1605

Phe Val  Ile Pro Ala Leu Gln  His Ala Phe Met Lys  His Lys Gly
    1610                1615                1620
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Gly Asp  Ser Thr Asp Phe Ile  Ala Leu Ile Met Ala  Tyr Gly Asn
    1625                 1630                 1635

Cys Thr  Phe Gly Ala Pro Asp  Asp Ala Ser Arg Leu  Leu His Thr
    1640                 1645                 1650

Val Leu  Ala Lys Ala Glu Leu  Cys Cys Ser Ala Arg  Met Val Trp
    1655                 1660                 1665

Arg Glu  Trp Cys Asn Val Cys  Gly Ile Lys Asp Val  Val Leu Gln
    1670                 1675                 1680

Gly Leu  Lys Ala Cys Cys Tyr  Val Gly Val Gln Thr  Val Glu Asp
    1685                 1690                 1695

Leu Arg  Ala Arg Met Thr Tyr  Val Cys Gln Cys Gly  Gly Glu Arg
    1700                 1705                 1710

His Arg  Gln Leu Val Glu His  Thr Thr Pro Trp Leu  Leu Leu Ser
    1715                 1720                 1725

Gly Thr  Pro Asn Glu Lys Leu  Val Thr Thr Ser Thr  Ala Pro Asp
    1730                 1735                 1740

Phe Val  Ala Phe Asn Val Phe  Gln Gly Ile Glu Thr  Ala Val Gly
    1745                 1750                 1755

His Tyr  Val His Ala Arg Leu  Lys Gly Gly Leu Ile  Leu Lys Phe
    1760                 1765                 1770

Asp Ser  Gly Thr Val Ser Lys  Thr Ser Asp Trp Lys  Cys Lys Val
    1775                 1780                 1785

Thr Asp  Val Leu Phe Pro Gly  Gln Lys Tyr Ser Ser  Asp Cys Asn
    1790                 1795                 1800

Val Val  Arg Tyr Ser Leu Asp  Gly Asn Phe Arg Thr  Glu Val Asp
    1805                 1810                 1815

Pro Asp  Leu Ser Ala Phe Tyr  Val Lys Asp Gly Lys  Tyr Phe Thr
    1820                 1825                 1830

Ser Glu  Pro Pro Val Thr Tyr  Ser Pro Ala Thr Ile  Leu Ala Gly
    1835                 1840                 1845

Ser Val  Tyr Thr Asn Ser Cys  Leu Val Ser Ser Asp  Gly Gln Pro
    1850                 1855                 1860

Gly Gly  Asp Ala Ile Ser Leu  Ser Phe Asn Asn Leu  Leu Gly Phe
    1865                 1870                 1875

Asp Ser  Ser Lys Pro Val Thr  Lys Lys Tyr Thr Tyr  Ser Phe Leu
    1880                 1885                 1890

Pro Lys  Glu Asp Gly Asp Val  Leu Leu Ala Glu Phe  Asp Thr Tyr
    1895                 1900                 1905

Asp Pro  Ile Tyr Lys Asn Gly  Ala Met Tyr Lys Gly  Lys Pro Ile
    1910                 1915                 1920

Leu Trp  Val Asn Lys Ala Ser  Tyr Asp Thr Asn Leu  Asn Lys Phe
    1925                 1930                 1935

Asn Arg  Ala Ser Leu Arg Gln  Ile Phe Asp Val Ala  Pro Ile Glu
    1940                 1945                 1950

Leu Glu  Asn Lys Phe Thr Pro  Leu Ser Val Glu Ser  Thr Pro Val
    1955                 1960                 1965

Glu Pro  Pro Thr Val Asp Val  Val Ala Leu Gln Gln  Glu Met Thr
    1970                 1975                 1980

Ile Val  Lys Cys Lys Gly Leu  Asn Lys Pro Phe Val  Lys Asp Asn
    1985                 1990                 1995
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Val Ser  Phe Val Ala Asp Asp  Ser Gly Thr Pro Val  Val Glu Tyr
    2000                 2005                 2010

Leu Ser  Lys Glu Asp Leu His  Thr Leu Tyr Val Asp  Pro Lys Tyr
    2015                 2020                 2025

Gln Val  Ile Val Leu Lys Asp  Asn Val Leu Ser Ser  Met Leu Arg
    2030                 2035                 2040

Leu His  Thr Val Glu Ser Gly  Asp Ile Asn Val Val  Ala Ala Ser
    2045                 2050                 2055

Gly Ser  Leu Thr Arg Lys Val  Lys Leu Leu Phe Arg  Ala Ser Phe
    2060                 2065                 2070

Tyr Phe  Lys Glu Phe Ala Thr  Arg Thr Phe Thr Ala  Thr Thr Ala
    2075                 2080                 2085

Val Gly  Ser Cys Ile Lys Ser  Val Val Arg His Leu  Gly Val Thr
    2090                 2095                 2100

Lys Gly  Ile Leu Thr Gly Cys  Phe Ser Phe Ala Lys  Met Leu Phe
    2105                 2110                 2115

Met Leu  Pro Leu Ala Tyr Phe  Ser Asp Ser Lys Leu  Gly Thr Thr
    2120                 2125                 2130

Glu Val  Lys Val Ser Ala Leu  Lys Thr Ala Gly Val  Val Thr Gly
    2135                 2140                 2145

Asn Val  Val Lys Gln Cys Cys  Thr Ala Ala Val Asp  Leu Ser Met
    2150                 2155                 2160

Asp Lys  Leu Arg Arg Val Asp  Trp Lys Ser Thr Leu  Arg Leu Leu
    2165                 2170                 2175

Leu Met  Leu Cys Thr Thr Met  Val Leu Leu Ser Ser  Val Tyr His
    2180                 2185                 2190

Leu Tyr  Val Phe Asn Gln Val  Leu Ser Ser Asp Val  Met Phe Glu
    2195                 2200                 2205

Asp Ala  Gln Gly Leu Lys Lys  Phe Tyr Lys Glu Val  Arg Ala Tyr
    2210                 2215                 2220

Leu Gly  Ile Ser Ser Ala Cys  Asp Gly Leu Ala Ser  Ala Tyr Arg
    2225                 2230                 2235

Ala Asn  Ser Phe Asp Val Pro  Thr Phe Cys Ala Asn  Arg Ser Ala
    2240                 2245                 2250

Met Cys  Asn Trp Cys Leu Ile  Ser Gln Asp Ser Ile  Thr His Tyr
    2255                 2260                 2265

Pro Ala  Leu Lys Met Val Gln  Thr His Leu Ser His  Tyr Val Leu
    2270                 2275                 2280

Asn Ile  Asp Trp Leu Trp Phe  Ala Phe Glu Thr Gly  Leu Ala Tyr
    2285                 2290                 2295

Met Leu  Tyr Thr Ser Ala Phe  Asn Trp Leu Leu Leu  Ala Gly Thr
    2300                 2305                 2310

Leu His  Tyr Phe Phe Ala Gln  Thr Ser Ile Phe Val  Asp Trp Arg
    2315                 2320                 2325

Ser Tyr  Asn Tyr Ala Val Ser  Ser Ala Phe Trp Leu  Phe Thr His
    2330                 2335                 2340

Ile Pro  Met Ala Gly Leu Val  Arg Met Tyr Asn Leu  Leu Ala Cys
    2345                 2350                 2355

Leu Trp  Leu Leu Arg Lys Phe  Tyr Gln His Val Ile  Asn Gly Cys
    2360                 2365                 2370

Lys Asp  Thr Ala Cys Leu Leu  Cys Tyr Lys Arg Asn  Arg Leu Thr
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    2375                2380                2385

Arg Val  Glu Ala Ser Thr Val  Val Cys Gly Gly Lys  Arg Thr Phe
    2390                2395                2400

Tyr Ile  Thr Ala Asn Gly Gly  Ile Ser Phe Cys Arg  Arg His Asn
    2405                2410                2415

Trp Asn  Cys Val Asp Cys Asp  Thr Ala Gly Val Gly  Asn Thr Phe
    2420                2425                2430

Ile Cys  Glu Glu Val Ala Asn  Asp Leu Thr Thr Ala  Leu Arg Arg
    2435                2440                2445

Pro Ile  Asn Ala Thr Asp Arg  Ser His Tyr Tyr Val  Asp Ser Val
    2450                2455                2460

Thr Val  Lys Glu Thr Val Val  Gln Phe Asn Tyr Arg  Arg Asp Gly
    2465                2470                2475

Gln Pro  Phe Tyr Glu Arg Phe  Pro Leu Cys Ala Phe  Thr Asn Leu
    2480                2485                2490

Asp Lys  Leu Lys Phe Lys Glu  Val Cys Lys Thr Thr  Thr Gly Ile
    2495                2500                2505

Pro Glu  Tyr Asn Phe Ile Ile  Tyr Asp Ser Ser Asp  Arg Gly Gln
    2510                2515                2520

Glu Ser  Leu Ala Arg Ser Ala  Cys Val Tyr Tyr Ser  Gln Val Leu
    2525                2530                2535

Cys Lys  Ser Ile Leu Leu Val  Asp Ser Ser Leu Val  Thr Ser Val
    2540                2545                2550

Gly Asp  Ser Ser Glu Ile Ala  Thr Lys Met Phe Asp  Ser Phe Val
    2555                2560                2565

Asn Ser  Phe Val Ser Leu Tyr  Asn Val Thr Arg Asp  Lys Leu Glu
    2570                2575                2580

Lys Leu  Ile Ser Thr Ala Arg  Asp Gly Val Arg Arg  Gly Asp Asn
    2585                2590                2595

Phe His  Ser Val Leu Thr Thr  Phe Ile Asp Ala Ala  Arg Gly Pro
    2600                2605                2610

Ala Gly  Val Glu Ser Asp Val  Glu Thr Asn Glu Ile  Val Asp Ser
    2615                2620                2625

Val Gln  Tyr Ala His Lys His  Asp Ile Gln Ile Thr  Asn Glu Ser
    2630                2635                2640

Tyr Asn  Asn Tyr Val Pro Ser  Tyr Val Lys Pro Asp  Ser Val Ser
    2645                2650                2655

Thr Ser  Asp Leu Gly Ser Leu  Ile Asp Cys Asn Ala  Ala Ser Val
    2660                2665                2670

Asn Gln  Ile Val Leu Arg Asn  Ser Asn Gly Ala Cys  Ile Trp Asn
    2675                2680                2685

Ala Ala  Ala Tyr Met Lys Leu  Ser Asp Ala Leu Lys  Arg Gln Ile
    2690                2695                2700

Arg Ile  Ala Cys Arg Lys Cys  Asn Leu Ala Phe Arg  Leu Thr Thr
    2705                2710                2715

Ser Lys  Leu Arg Ala Asn Asp  Asn Ile Leu Ser Val  Arg Phe Thr
    2720                2725                2730

Ala Asn  Lys Ile Val Gly Gly  Ala Pro Thr Trp Phe  Asn Ala Leu
    2735                2740                2745

Arg Asp  Phe Thr Leu Lys Gly  Tyr Val Leu Ala Thr  Ile Ile Val
    2750                2755                2760
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Phe Leu  Cys Ala Val Leu Met  Tyr Leu Cys Leu Pro  Thr Phe Ser
    2765                 2770                 2775

Met Ala  Pro Val Glu Phe Tyr  Glu Asp Arg Ile Leu  Asp Phe Lys
    2780                 2785                 2790

Val Leu  Asp Asn Gly Ile Ile  Arg Asp Val Asn Pro  Asp Asp Lys
    2795                 2800                 2805

Cys Phe  Ala Asn Lys His Arg  Ser Phe Thr Gln Trp  Tyr His Glu
    2810                 2815                 2820

His Val  Gly Gly Val Tyr Asp  Asn Ser Ile Thr Cys  Pro Leu Thr
    2825                 2830                 2835

Val Ala  Val Ile Ala Gly Val  Ala Gly Ala Arg Ile  Pro Asp Val
    2840                 2845                 2850

Pro Thr  Thr Leu Ala Trp Val  Asn Asn Gln Ile Ile  Phe Phe Val
    2855                 2860                 2865

Ser Arg  Val Phe Ala Asn Thr  Gly Ser Val Cys Tyr  Thr Pro Ile
    2870                 2875                 2880

Asp Glu  Ile Pro Tyr Lys Ser  Phe Ser Asp Ser Gly  Cys Ile Leu
    2885                 2890                 2895

Pro Ser  Glu Cys Thr Met Phe  Arg Asp Ala Glu Gly  Arg Met Thr
    2900                 2905                 2910

Pro Tyr  Cys His Asp Pro Thr  Val Leu Pro Gly Ala  Phe Ala Tyr
    2915                 2920                 2925

Ser Gln  Met Arg Pro His Val  Arg Tyr Asp Leu Tyr  Asp Gly Asn
    2930                 2935                 2940

Met Phe  Ile Lys Phe Pro Glu  Val Val Phe Glu Ser  Thr Leu Arg
    2945                 2950                 2955

Ile Thr  Arg Thr Leu Ser Thr  Gln Tyr Cys Arg Phe  Gly Ser Cys
    2960                 2965                 2970

Glu Tyr  Ala Gln Glu Gly Val  Cys Ile Thr Thr Asn  Gly Ser Trp
    2975                 2980                 2985

Ala Ile  Phe Asn Asp His His  Leu Asn Arg Pro Gly  Val Tyr Cys
    2990                 2995                 3000

Gly Ser  Asp Phe Ile Asp Ile  Val Arg Arg Leu Ala  Val Ser Leu
    3005                 3010                 3015

Phe Gln  Pro Ile Thr Tyr Phe  Gln Leu Thr Thr Ser  Leu Val Leu
    3020                 3025                 3030

Gly Ile  Gly Leu Cys Ala Phe  Leu Thr Leu Leu Phe  Tyr Tyr Ile
    3035                 3040                 3045

Asn Lys  Val Lys Arg Ala Phe  Ala Asp Tyr Thr Gln  Cys Ala Val
    3050                 3055                 3060

Ile Ala  Val Val Ala Ala Val  Leu Asn Ser Leu Cys  Ile Cys Phe
    3065                 3070                 3075

Val Thr  Ser Ile Pro Leu Cys  Ile Val Pro Tyr Thr  Ala Leu Tyr
    3080                 3085                 3090

Tyr Tyr  Ala Thr Phe Tyr Phe  Thr Asn Glu Pro Ala  Phe Ile Met
    3095                 3100                 3105

His Val  Ser Trp Tyr Ile Met  Phe Gly Pro Ile Val  Pro Ile Trp
    3110                 3115                 3120

Met Thr  Cys Val Tyr Thr Val  Ala Met Cys Phe Arg  His Phe Phe
    3125                 3130                 3135
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Trp Val  Leu Ala Tyr Phe Ser  Lys Lys His Val Glu  Val Phe Thr
    3140                 3145                 3150

Asp Gly  Lys Leu Asn Cys Ser  Phe Gln Asp Ala Ala  Ser Asn Ile
    3155                 3160                 3165

Phe Val  Ile Asn Lys Asp Thr  Tyr Ala Ala Leu Arg  Asn Ser Leu
    3170                 3175                 3180

Thr Asn  Asp Ala Tyr Ser Arg  Phe Leu Gly Leu Phe  Asn Lys Tyr
    3185                 3190                 3195

Lys Tyr  Phe Ser Gly Ala Met  Glu Thr Ala Ala Tyr  Arg Glu Ala
    3200                 3205                 3210

Ala Ala  Cys His Leu Ala Lys  Ala Leu Gln Thr Tyr  Ser Glu Thr
    3215                 3220                 3225

Gly Ser  Asp Leu Leu Tyr Gln  Pro Pro Asn Cys Ser  Ile Thr Ser
    3230                 3235                 3240

Gly Val  Leu Gln Ser Gly Leu  Val Lys Met Ser His  Pro Ser Gly
    3245                 3250                 3255

Asp Val  Glu Ala Cys Met Val  Gln Val Thr Cys Gly  Ser Met Thr
    3260                 3265                 3270

Leu Asn  Gly Leu Trp Leu Asp  Asn Thr Val Trp Cys  Pro Arg His
    3275                 3280                 3285

Val Met  Cys Pro Ala Asp Gln  Leu Ser Asp Pro Asn  Tyr Asp Ala
    3290                 3295                 3300

Leu Leu  Ile Ser Met Thr Asn  His Ser Phe Ser Val  Gln Lys His
    3305                 3310                 3315

Ile Gly  Ala Pro Ala Asn Leu  Arg Val Val Gly His  Ala Met Gln
    3320                 3325                 3330

Gly Thr  Leu Leu Lys Leu Thr  Val Asp Val Ala Asn  Pro Ser Thr
    3335                 3340                 3345

Pro Ala  Tyr Thr Phe Thr Thr  Val Lys Pro Gly Ala  Ala Phe Ser
    3350                 3355                 3360

Val Leu  Ala Cys Tyr Asn Gly  Arg Pro Thr Gly Thr  Phe Thr Val
    3365                 3370                 3375

Val Met  Arg Pro Asn Tyr Thr  Ile Lys Gly Ser Phe  Leu Cys Gly
    3380                 3385                 3390

Ser Cys  Gly Ser Val Gly Tyr  Thr Lys Glu Gly Ser  Val Ile Asn
    3395                 3400                 3405

Phe Cys  Tyr Met His Gln Met  Glu Leu Ala Asn Gly  Thr His Thr
    3410                 3415                 3420

Gly Ser  Ala Phe Asp Gly Thr  Met Tyr Gly Ala Phe  Met Asp Lys
    3425                 3430                 3435

Gln Val  His Gln Val Gln Leu  Thr Asp Lys Tyr Cys  Ser Val Asn
    3440                 3445                 3450

Val Val  Ala Trp Leu Tyr Ala  Ala Ile Leu Asn Gly  Cys Ala Trp
    3455                 3460                 3465

Phe Val  Lys Pro Asn Arg Thr  Ser Val Val Ser Phe  Asn Glu Trp
    3470                 3475                 3480

Ala Leu  Ala Asn Gln Phe Thr  Glu Phe Val Gly Thr  Gln Ser Val
    3485                 3490                 3495

Asp Met  Leu Ala Val Lys Thr  Gly Val Ala Ile Glu  Gln Leu Leu
    3500                 3505                 3510

Tyr Ala  Ile Gln Gln Leu Tyr  Thr Gly Phe Gln Gly  Lys Gln Ile
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    3515                3520                3525

Leu Gly  Ser Thr Met Leu Glu  Asp Glu Phe Thr Pro  Glu Asp Val
    3530                3535                3540

Asn Met  Gln Ile Met Gly Val  Val Met Gln Ser Gly  Val Arg Lys
    3545                3550                3555

Val Thr  Tyr Gly Thr Ala His  Trp Leu Phe Ala Thr  Leu Val Ser
    3560                3565                3570

Thr Tyr  Val Ile Ile Leu Gln  Ala Thr Lys Phe Thr  Leu Trp Asn
    3575                3580                3585

Tyr Leu  Phe Glu Thr Ile Pro  Thr Gln Leu Phe Pro  Leu Leu Phe
    3590                3595                3600

Val Thr  Met Ala Phe Val Met  Leu Leu Val Lys His  Lys His Thr
    3605                3610                3615

Phe Leu  Thr Leu Phe Leu Leu  Pro Val Ala Ile Cys  Leu Thr Tyr
    3620                3625                3630

Ala Asn  Ile Val Tyr Glu Pro  Thr Thr Pro Ile Ser  Ser Ala Leu
    3635                3640                3645

Ile Ala  Val Ala Asn Trp Leu  Ala Pro Thr Asn Ala  Tyr Met Arg
    3650                3655                3660

Thr Thr  His Thr Asp Ile Gly  Val Tyr Ile Ser Met  Ser Leu Val
    3665                3670                3675

Leu Val  Ile Val Val Lys Arg  Leu Tyr Asn Pro Ser  Leu Ser Asn
    3680                3685                3690

Phe Ala  Leu Ala Leu Cys Ser  Gly Val Met Trp Leu  Tyr Thr Tyr
    3695                3700                3705

Ser Ile  Gly Glu Ala Ser Ser  Pro Ile Ala Tyr Leu  Val Phe Val
    3710                3715                3720

Thr Thr  Leu Thr Ser Asp Tyr  Thr Ile Thr Val Phe  Val Thr Val
    3725                3730                3735

Asn Leu  Ala Lys Val Cys Thr  Tyr Ala Ile Phe Ala  Tyr Ser Pro
    3740                3745                3750

Gln Leu  Thr Leu Val Phe Pro  Glu Val Lys Met Ile  Leu Leu Leu
    3755                3760                3765

Tyr Thr  Cys Leu Gly Phe Met  Cys Thr Cys Tyr Phe  Gly Val Phe
    3770                3775                3780

Ser Leu  Leu Asn Leu Lys Leu  Arg Ala Pro Met Gly  Val Tyr Asp
    3785                3790                3795

Phe Lys  Val Ser Thr Gln Glu  Phe Arg Phe Met Thr  Ala Asn Asn
    3800                3805                3810

Leu Thr  Ala Pro Arg Asn Ser  Trp Glu Ala Met Ala  Leu Asn Phe
    3815                3820                3825

Lys Leu  Ile Gly Ile Gly Gly  Thr Pro Cys Ile Lys  Val Ala Ala
    3830                3835                3840

Met Gln  Ser Lys Leu Thr Asp  Leu Lys Cys Thr Ser  Val Val Leu
    3845                3850                3855

Leu Ser  Val Leu Gln Gln Leu  His Leu Glu Ala Asn  Ser Arg Ala
    3860                3865                3870

Trp Ala  Phe Cys Val Lys Cys  His Asn Asp Ile Leu  Ala Ala Thr
    3875                3880                3885

Asp Pro  Ser Glu Ala Phe Glu  Lys Phe Val Ser Leu  Phe Ala Thr
    3890                3895                3900
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Leu Met  Thr Phe Ser Gly Asn  Val Asp Leu Asp Ala  Leu Ala Ser
    3905                 3910                 3915

Asp Ile  Phe Asp Thr Pro Ser  Val Leu Gln Ala Thr  Leu Ser Glu
    3920                 3925                 3930

Phe Ser  His Leu Ala Thr Phe  Ala Glu Leu Glu Ala  Ala Gln Lys
    3935                 3940                 3945

Ala Tyr  Gln Glu Ala Met Asp  Ser Gly Asp Thr Ser  Pro Gln Val
    3950                 3955                 3960

Leu Lys  Ala Leu Gln Lys Ala  Val Asn Ile Ala Lys  Asn Ala Tyr
    3965                 3970                 3975

Glu Lys  Asp Lys Ala Val Ala  Arg Lys Leu Glu Arg  Met Ala Asp
    3980                 3985                 3990

Gln Ala  Met Thr Ser Met Tyr  Lys Gln Ala Arg Ala  Glu Asp Lys
    3995                 4000                 4005

Lys Ala  Lys Ile Val Ser Ala  Met Gln Thr Met Leu  Phe Gly Met
    4010                 4015                 4020

Ile Lys  Lys Leu Asp Asn Asp  Val Leu Asn Gly Ile  Ile Ser Asn
    4025                 4030                 4035

Ala Arg  Asn Gly Cys Ile Pro  Leu Ser Val Ile Pro  Leu Cys Ala
    4040                 4045                 4050

Ser Asn  Lys Leu Arg Val Val  Ile Pro Asp Phe Thr  Val Trp Asn
    4055                 4060                 4065

Gln Val  Val Thr Tyr Pro Ser  Leu Asn Tyr Ala Gly  Ala Leu Trp
    4070                 4075                 4080

Asp Ile  Thr Val Ile Asn Asn  Val Asp Asn Glu Ile  Val Lys Ser
    4085                 4090                 4095

Ser Asp  Val Val Asp Ser Asn  Glu Asn Leu Thr Trp  Pro Leu Val
    4100                 4105                 4110

Leu Glu  Cys Thr Arg Ala Ser  Thr Ser Ala Val Lys  Leu Gln Asn
    4115                 4120                 4125

Asn Glu  Ile Lys Pro Ser Gly  Leu Lys Thr Met Val  Val Ser Ala
    4130                 4135                 4140

Gly Gln  Glu Gln Thr Asn Cys  Asn Thr Ser Ser Leu  Ala Tyr Tyr
    4145                 4150                 4155

Glu Pro  Val Gln Gly Arg Lys  Met Leu Met Ala Leu  Leu Ser Asp
    4160                 4165                 4170

Asn Ala  Tyr Leu Lys Trp Ala  Arg Val Glu Gly Lys  Asp Gly Phe
    4175                 4180                 4185

Val Ser  Val Glu Leu Gln Pro  Pro Cys Lys Phe Leu  Ile Ala Gly
    4190                 4195                 4200

Pro Lys  Gly Pro Glu Ile Arg  Tyr Leu Tyr Phe Val  Lys Asn Leu
    4205                 4210                 4215

Asn Asn  Leu His Arg Gly Gln  Val Leu Gly His Ile  Ala Ala Thr
    4220                 4225                 4230

Val Arg  Leu Gln Ala Gly Ser  Asn Thr Glu Phe Ala  Ser Asn Ser
    4235                 4240                 4245

Ser Val  Leu Ser Leu Val Asn  Phe Thr Val Asp Pro  Gln Lys Ala
    4250                 4255                 4260

Tyr Leu  Asp Phe Val Asn Ala  Gly Gly Ala Pro Leu  Thr Asn Cys
    4265                 4270                 4275
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Val Lys  Met Leu Thr Pro Lys  Thr Gly Thr Gly Ile  Ala Ile Ser
    4280                 4285                 4290

Val Lys  Pro Glu Ser Thr Ala  Asp Gln Glu Thr Tyr  Gly Gly Ala
    4295                 4300                 4305

Ser Val  Cys Leu Tyr Cys Arg  Ala His Ile Glu His  Pro Asp Val
    4310                 4315                 4320

Ser Gly  Val Cys Lys Tyr Lys  Gly Lys Phe Val Gln  Ile Pro Ala
    4325                 4330                 4335

Gln Cys  Val Arg Asp Pro Val  Gly Phe Cys Leu Ser  Asn Thr Pro
    4340                 4345                 4350

Cys Asn  Val Cys Gln Tyr Trp  Ile Gly Tyr Gly Cys  Asn Cys Asp
    4355                 4360                 4365

Ser Leu  Arg Gln Ala Ala Leu  Pro Gln Ser Lys Asp  Ser Asn Phe
    4370                 4375                 4380

Leu Asn  Arg Val Arg Gly Ser  Ile Val Asn Ala Arg  Ile Glu Pro
    4385                 4390                 4395

Cys Ser  Ser Gly Leu Ser Thr  Asp Val Val Phe Arg  Ala Phe Asp
    4400                 4405                 4410

Ile Cys  Asn Tyr Lys Ala Lys  Val Ala Gly Ile Gly  Lys Tyr Tyr
    4415                 4420                 4425

Lys Thr  Asn Thr Cys Arg Phe  Val Glu Leu Asp Asp  Gln Gly His
    4430                 4435                 4440

His Leu  Asp Ser Tyr Phe Val  Val Lys Arg His Thr  Met Glu Asn
    4445                 4450                 4455

Tyr Glu  Leu Glu Lys His Cys  Tyr Asp Leu Leu Arg  Asp Cys Asp
    4460                 4465                 4470

Ala Val  Ala Pro His Asp Phe  Phe Ile Phe Asp Val  Asp Lys Val
    4475                 4480                 4485

Lys Thr  Pro His Ile Val Arg  Gln Arg Leu Thr Glu  Tyr Thr Met
    4490                 4495                 4500

Met Asp  Leu Val Tyr Ala Leu  Arg His Phe Asp Gln  Asn Ser Glu
    4505                 4510                 4515

Val Leu  Lys Ala Ile Leu Val  Lys Tyr Gly Cys Cys  Asp Val Thr
    4520                 4525                 4530

Tyr Phe  Glu Asn Lys Leu Trp  Phe Asp Phe Val Glu  Asn Pro Ser
    4535                 4540                 4545

Val Ile  Gly Val Tyr His Lys  Leu Gly Glu Arg Val  Arg Gln Ala
    4550                 4555                 4560

Ile Leu  Asn Thr Val Lys Phe  Cys Asp His Met Val  Lys Ala Gly
    4565                 4570                 4575

Leu Val  Gly Val Leu Thr Leu  Asp Asn Gln Asp Leu  Asn Gly Lys
    4580                 4585                 4590

Trp Tyr  Asp Phe Gly Asp Phe  Val Ile Thr Gln Pro  Gly Ser Gly
    4595                 4600                 4605

Val Ala  Ile Val Asp Ser Tyr  Tyr Ser Tyr Leu Met  Pro Val Leu
    4610                 4615                 4620

Ser Met  Thr Asp Cys Leu Ala  Ala Glu Thr His Arg  Asp Cys Asp
    4625                 4630                 4635

Phe Asn  Lys Pro Leu Ile Glu  Trp Pro Leu Thr Glu  Tyr Asp Phe
    4640                 4645                 4650

Thr Asp  Tyr Lys Val Gln Leu  Phe Glu Lys Tyr Phe  Lys Tyr Trp
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    4655                4660                4665

Asp Gln  Thr Tyr His Ala Asn  Cys Val Asn Cys Thr  Asp Asp Arg
    4670                4675                4680

Cys Val  Leu His Cys Ala Asn  Phe Asn Val Leu Phe  Ala Met Thr
    4685                4690                4695

Met Pro  Lys Thr Cys Phe Gly  Pro Ile Val Arg Lys  Ile Phe Val
    4700                4705                4710

Asp Gly  Val Pro Phe Val Val  Ser Cys Gly Tyr His  Tyr Lys Glu
    4715                4720                4725

Leu Gly  Leu Val Met Asn Met  Asp Val Ser Leu His  Arg His Arg
    4730                4735                4740

Leu Ser  Leu Lys Glu Leu Met  Met Tyr Ala Ala Asp  Pro Ala Met
    4745                4750                4755

His Ile  Ala Ser Ser Asn Ala  Phe Leu Asp Leu Arg  Thr Ser Cys
    4760                4765                4770

Phe Ser  Val Ala Ala Leu Thr  Thr Gly Leu Thr Phe  Gln Thr Val
    4775                4780                4785

Arg Pro  Gly Asn Phe Asn Gln  Asp Phe Tyr Asp Phe  Val Val Ser
    4790                4795                4800

Lys Gly  Phe Phe Lys Glu Gly  Ser Ser Val Thr Leu  Lys His Phe
    4805                4810                4815

Phe Phe  Ala Gln Asp Gly Asn  Ala Ala Ile Thr Asp  Tyr Asn Tyr
    4820                4825                4830

Tyr Ser  Tyr Asn Leu Pro Thr  Met Cys Asp Ile Lys  Gln Met Leu
    4835                4840                4845

Phe Cys  Met Glu Val Val Asn  Lys Tyr Phe Glu Ile  Tyr Asp Gly
    4850                4855                4860

Gly Cys  Leu Asn Ala Ser Glu  Val Val Val Asn Asn  Leu Asp Lys
    4865                4870                4875

Ser Ala  Gly His Pro Phe Asn  Lys Phe Gly Lys Ala  Arg Val Tyr
    4880                4885                4890

Tyr Glu  Ser Met Ser Tyr Gln  Glu Gln Asp Glu Leu  Phe Ala Met
    4895                4900                4905

Thr Lys  Arg Asn Val Ile Pro  Thr Met Thr Gln Met  Asn Leu Lys
    4910                4915                4920

Tyr Ala  Ile Ser Ala Lys Asn  Arg Ala Arg Thr Val  Ala Gly Val
    4925                4930                4935

Ser Ile  Leu Ser Thr Met Thr  Asn Arg Gln Tyr His  Gln Lys Met
    4940                4945                4950

Leu Lys  Ser Met Ala Ala Thr  Arg Gly Ala Thr Cys  Val Ile Gly
    4955                4960                4965

Thr Thr  Lys Phe Tyr Gly Gly  Trp Asp Phe Met Leu  Lys Thr Leu
    4970                4975                4980

Tyr Lys  Asp Val Asp Asn Pro  His Leu Met Gly Trp  Asp Tyr Pro
    4985                4990                4995

Lys Cys  Asp Arg Ala Met Pro  Asn Met Cys Arg Ile  Phe Ala Ser
    5000                5005                5010

Leu Ile  Leu Ala Arg Lys His  Gly Thr Cys Cys Thr  Thr Arg Asp
    5015                5020                5025

Arg Phe  Tyr Arg Leu Ala Asn  Glu Cys Ala Gln Val  Leu Ser Glu
    5030                5035                5040
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Tyr Val  Leu Cys Gly Gly Gly  Tyr Tyr Val Lys Pro  Gly Gly Thr
    5045                 5050                 5055

Ser Ser  Gly Asp Ala Thr Thr  Ala Tyr Ala Asn Ser  Val Phe Asn
    5060                 5065                 5070

Ile Leu  Gln Ala Thr Thr Ala  Asn Val Ser Ala Leu  Met Gly Ala
    5075                 5080                 5085

Asn Gly  Asn Lys Ile Val Asp  Lys Glu Val Lys Asp  Met Gln Phe
    5090                 5095                 5100

Asp Leu  Tyr Val Asn Val Tyr  Arg Ser Thr Ser Pro  Asp Pro Lys
    5105                 5110                 5115

Phe Val  Asp Lys Tyr Tyr Ala  Phe Leu Asn Lys His  Phe Ser Met
    5120                 5125                 5130

Met Ile  Leu Ser Asp Asp Gly  Val Val Cys Tyr Asn  Ser Asp Tyr
    5135                 5140                 5145

Ala Ala  Lys Gly Tyr Ile Ala  Gly Ile Gln Asn Phe  Lys Glu Thr
    5150                 5155                 5160

Leu Tyr  Tyr Gln Asn Asn Val  Phe Met Ser Glu Ala  Lys Cys Trp
    5165                 5170                 5175

Val Glu  Thr Asp Leu Lys Lys  Gly Pro His Glu Phe  Cys Ser Gln
    5180                 5185                 5190

His Thr  Leu Tyr Ile Lys Asp  Gly Asp Asp Gly Tyr  Phe Leu Pro
    5195                 5200                 5205

Tyr Pro  Asp Pro Ser Arg Ile  Leu Ser Ala Gly Cys  Phe Val Asp
    5210                 5215                 5220

Asp Ile  Val Lys Thr Asp Gly  Thr Leu Met Val Glu  Arg Phe Val
    5225                 5230                 5235

Ser Leu  Ala Ile Asp Ala Tyr  Pro Leu Thr Lys His  Glu Asp Ile
    5240                 5245                 5250

Glu Tyr  Gln Asn Val Phe Trp  Val Tyr Leu Gln Tyr  Ile Glu Lys
    5255                 5260                 5265

Leu Tyr  Lys Asp Leu Thr Gly  His Met Leu Asp Ser  Tyr Ser Val
    5270                 5275                 5280

Met Leu  Cys Gly Asp Asn Ser  Ala Lys Phe Trp Glu  Glu Ala Phe
    5285                 5290                 5295

Tyr Arg  Asp Leu Tyr Ser Ser  Pro Thr Thr Leu Gln  Ala Val Gly
    5300                 5305                 5310

Ser Cys  Val Val Cys His Ser  Gln Thr Ser Leu Arg  Cys Gly Thr
    5315                 5320                 5325

Cys Ile  Arg Arg Pro Phe Leu  Cys Cys Lys Cys Cys  Tyr Asp His
    5330                 5335                 5340

Val Ile  Ala Thr Pro His Lys  Met Val Leu Ser Val  Ser Pro Tyr
    5345                 5350                 5355

Val Cys  Asn Ala Pro Gly Cys  Gly Val Ser Asp Val  Thr Lys Leu
    5360                 5365                 5370

Tyr Leu  Gly Gly Met Ser Tyr  Phe Cys Val Asp His  Arg Pro Val
    5375                 5380                 5385

Cys Ser  Phe Pro Leu Cys Ala  Asn Gly Leu Val Phe  Gly Leu Tyr
    5390                 5395                 5400

Lys Asn  Met Cys Thr Gly Ser  Pro Ser Ile Val Glu  Phe Asn Arg
    5405                 5410                 5415
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Leu Ala  Thr Cys Asp Trp Thr  Glu Ser Gly Asp Tyr  Thr Leu Ala
    5420                 5425                 5430

Asn Thr  Thr Thr Glu Pro Leu  Lys Leu Phe Ala Ala  Glu Thr Leu
    5435                 5440                 5445

Arg Ala  Thr Glu Glu Ala Ser  Lys Gln Ser Tyr Ala  Ile Ala Thr
    5450                 5455                 5460

Ile Lys  Glu Ile Val Gly Glu  Arg Gln Leu Leu Leu  Val Trp Glu
    5465                 5470                 5475

Ala Gly  Lys Ser Lys Pro Pro  Leu Asn Arg Asn Tyr  Val Phe Thr
    5480                 5485                 5490

Gly Tyr  His Ile Thr Lys Asn  Ser Lys Val Gln Leu  Gly Glu Tyr
    5495                 5500                 5505

Ile Phe  Glu Arg Ile Asp Tyr  Ser Asp Ala Val Ser  Tyr Lys Ser
    5510                 5515                 5520

Ser Thr  Thr Tyr Lys Leu Thr  Val Gly Asp Ile Phe  Val Leu Thr
    5525                 5530                 5535

Ser His  Ser Val Ala Thr Leu  Thr Ala Pro Thr Ile  Val Asn Gln
    5540                 5545                 5550

Glu Arg  Tyr Val Lys Ile Thr  Gly Leu Tyr Pro Thr  Ile Thr Val
    5555                 5560                 5565

Pro Glu  Glu Phe Ala Ser His  Val Ala Asn Phe Gln  Lys Ser Gly
    5570                 5575                 5580

Tyr Ser  Lys Tyr Val Thr Val  Gln Gly Pro Pro Gly  Thr Gly Lys
    5585                 5590                 5595

Ser His  Phe Ala Ile Gly Leu  Ala Ile Tyr Tyr Pro  Thr Ala Arg
    5600                 5605                 5610

Val Val  Tyr Thr Ala Cys Ser  His Ala Ala Val Asp  Ala Leu Cys
    5615                 5620                 5625

Glu Lys  Ala Phe Lys Tyr Leu  Asn Ile Ala Lys Cys  Ser Arg Ile
    5630                 5635                 5640

Ile Pro  Ala Lys Ala Arg Val  Glu Cys Tyr Asp Arg  Phe Lys Val
    5645                 5650                 5655

Asn Glu  Thr Asn Ser Gln Tyr  Leu Phe Ser Thr Ile  Asn Ala Leu
    5660                 5665                 5670

Pro Glu  Thr Ser Ala Asp Ile  Leu Val Val Asp Glu  Val Ser Met
    5675                 5680                 5685

Cys Thr  Asn Tyr Asp Leu Ser  Ile Ile Asn Ala Arg  Ile Lys Ala
    5690                 5695                 5700

Lys His  Ile Val Tyr Val Gly  Asp Pro Ala Gln Leu  Pro Ala Pro
    5705                 5710                 5715

Arg Thr  Leu Leu Thr Arg Gly  Thr Leu Glu Pro Glu  Asn Phe Asn
    5720                 5725                 5730

Ser Val  Thr Arg Leu Met Cys  Asn Leu Gly Pro Asp  Ile Phe Leu
    5735                 5740                 5745

Ser Met  Cys Tyr Arg Cys Pro  Lys Glu Ile Val Ser  Thr Val Ser
    5750                 5755                 5760

Ala Leu  Val Tyr Asn Asn Lys  Leu Leu Ala Lys Lys  Glu Leu Ser
    5765                 5770                 5775

Gly Gln  Cys Phe Lys Ile Leu  Tyr Lys Gly Asn Val  Thr His Asp
    5780                 5785                 5790

Ala Ser  Ser Ala Ile Asn Arg  Pro Gln Leu Thr Phe  Val Lys Asn
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    5795                5800                5805

Phe Ile  Thr Ala Asn Pro Ala  Trp Ser Lys Ala Val  Phe Ile Ser
    5810                5815                5820

Pro Tyr  Asn Ser Gln Asn Ala  Val Ser Arg Ser Met  Leu Gly Leu
    5825                5830                5835

Thr Thr  Gln Thr Val Asp Ser  Ser Gln Gly Ser Glu  Tyr Gln Tyr
    5840                5845                5850

Val Ile  Phe Cys Gln Thr Ala  Asp Thr Ala His Ala  Asn Asn Ile
    5855                5860                5865

Asn Arg  Phe Asn Val Ala Ile  Thr Arg Ala Gln Lys  Gly Ile Leu
    5870                5875                5880

Cys Val  Met Thr Ser Gln Ala  Leu Phe Glu Ser Leu  Glu Phe Thr
    5885                5890                5895

Glu Leu  Ser Phe Thr Asn Tyr  Lys Leu Gln Ser Gln  Ile Val Thr
    5900                5905                5910

Gly Leu  Phe Lys Asp Cys Ser  Arg Glu Thr Ser Gly  Leu Ser Pro
    5915                5920                5925

Ala Tyr  Ala Pro Thr Tyr Val  Ser Val Asp Asp Lys  Tyr Lys Thr
    5930                5935                5940

Ser Asp  Glu Leu Cys Val Asn  Leu Asn Leu Pro Ala  Asn Val Pro
    5945                5950                5955

Tyr Ser  Arg Val Ile Ser Arg  Met Gly Phe Lys Leu  Asp Ala Thr
    5960                5965                5970

Val Pro  Gly Tyr Pro Lys Leu  Phe Ile Thr Arg Glu  Glu Ala Val
    5975                5980                5985

Arg Gln  Val Arg Ser Trp Ile  Gly Phe Asp Val Glu  Gly Ala His
    5990                5995                6000

Ala Ser  Arg Asn Ala Cys Gly  Thr Asn Val Pro Leu  Gln Leu Gly
    6005                6010                6015

Phe Ser  Thr Gly Val Asn Phe  Val Val Gln Pro Val  Gly Val Val
    6020                6025                6030

Asp Thr  Glu Trp Gly Asn Met  Leu Thr Gly Ile Ala  Ala Arg Pro
    6035                6040                6045

Pro Pro  Gly Glu Gln Phe Lys  His Leu Val Pro Leu  Met His Lys
    6050                6055                6060

Gly Ala  Ala Trp Pro Ile Val  Arg Arg Arg Ile Val  Gln Met Leu
    6065                6070                6075

Ser Asp  Thr Leu Asp Lys Leu  Ser Asp Tyr Cys Thr  Phe Val Cys
    6080                6085                6090

Trp Ala  His Gly Phe Glu Leu  Thr Ser Ala Ser Tyr  Phe Cys Lys
    6095                6100                6105

Ile Gly  Lys Glu Gln Lys Cys  Cys Met Cys Asn Arg  Arg Ala Ala
    6110                6115                6120

Ala Tyr  Ser Ser Pro Leu Gln  Ser Tyr Ala Cys Trp  Thr His Ser
    6125                6130                6135

Cys Gly  Tyr Asp Tyr Val Tyr  Asn Pro Phe Phe Val  Asp Val Gln
    6140                6145                6150

Gln Trp  Gly Tyr Val Gly Asn  Leu Ala Thr Asn His  Asp Arg Tyr
    6155                6160                6165

Cys Ser  Val His Gln Gly Ala  His Val Ala Ser Asn  Asp Ala Ile
    6170                6175                6180
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Met Thr  Arg Cys Leu Ala Ile  His Ser Cys Phe Ile  Glu Arg Val
    6185                 6190                 6195

Asp Trp  Asp Ile Glu Tyr Pro  Tyr Ile Ser His Glu  Lys Lys Leu
    6200                 6205                 6210

Asn Ser  Cys Cys Arg Ile Val  Glu Arg Asn Val Val  Arg Ala Ala
    6215                 6220                 6225

Leu Leu  Ala Gly Ser Phe Asp  Lys Val Tyr Asp Ile  Gly Asn Pro
    6230                 6235                 6240

Lys Gly  Ile Pro Ile Val Asp  Asp Pro Val Val Asp  Trp His Tyr
    6245                 6250                 6255

Phe Asp  Ala Gln Pro Leu Thr  Arg Lys Val Gln Gln  Leu Phe Tyr
    6260                 6265                 6270

Thr Glu  Asp Met Ala Ser Arg  Phe Ala Asp Gly Leu  Cys Leu Phe
    6275                 6280                 6285

Trp Asn  Cys Asn Val Pro Lys  Tyr Pro Asn Asn Ala  Ile Val Cys
    6290                 6295                 6300

Arg Phe  Asp Thr Arg Val His  Ser Glu Phe Asn Leu  Pro Gly Cys
    6305                 6310                 6315

Asp Gly  Gly Ser Leu Tyr Val  Asn Lys His Ala Phe  His Thr Pro
    6320                 6325                 6330

Ala Tyr  Asp Val Ser Ala Phe  Arg Asp Leu Lys Pro  Leu Pro Phe
    6335                 6340                 6345

Phe Tyr  Tyr Ser Thr Thr Pro  Cys Glu Val His Gly  Asn Gly Ser
    6350                 6355                 6360

Met Ile  Glu Asp Ile Asp Tyr  Val Pro Leu Lys Ser  Ala Val Cys
    6365                 6370                 6375

Ile Thr  Ala Cys Asn Leu Gly  Gly Ala Val Cys Arg  Lys His Ala
    6380                 6385                 6390

Thr Glu  Tyr Arg Glu Tyr Met  Glu Ala Tyr Asn Leu  Val Ser Ala
    6395                 6400                 6405

Ser Gly  Phe Arg Leu Trp Cys  Tyr Lys Thr Phe Asp  Ile Tyr Asn
    6410                 6415                 6420

Leu Trp  Ser Thr Phe Thr Lys  Val Gln Gly Leu Glu  Asn Ile Ala
    6425                 6430                 6435

Phe Asn  Val Val Lys Gln Gly  His Phe Ile Gly Val  Glu Gly Glu
    6440                 6445                 6450

Leu Pro  Val Ala Val Val Asn  Asp Lys Ile Phe Thr  Lys Ser Gly
    6455                 6460                 6465

Val Asn  Asp Ile Cys Met Phe  Glu Asn Lys Thr Thr  Leu Pro Thr
    6470                 6475                 6480

Asn Ile  Ala Phe Glu Leu Tyr  Ala Lys Arg Ala Val  Arg Ser His
    6485                 6490                 6495

Pro Asp  Phe Lys Leu Leu His  Asn Leu Gln Ala Asp  Ile Cys Tyr
    6500                 6505                 6510

Lys Phe  Val Leu Trp Asp Tyr  Glu Arg Ser Asn Ile  Tyr Gly Thr
    6515                 6520                 6525

Ala Thr  Ile Gly Val Cys Lys  Tyr Thr Asp Ile Asp  Val Asn Ser
    6530                 6535                 6540

Ala Leu  Asn Ile Cys Phe Asp  Ile Arg Asp Asn Cys  Ser Leu Glu
    6545                 6550                 6555
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Lys Phe  Met Ser Thr Pro Asn  Ala Ile Phe Ile Ser  Asp Arg Lys
    6560                 6565                 6570

Ile Lys  Lys Tyr Pro Cys Met  Val Gly Pro Asp Tyr  Ala Tyr Phe
    6575                 6580                 6585

Asn Gly  Ala Ile Ile Arg Asp  Ser Asp Val Val Lys  Gln Pro Val
    6590                 6595                 6600

Lys Phe  Tyr Leu Tyr Lys Lys  Val Asn Asn Glu Phe  Ile Asp Pro
    6605                 6610                 6615

Thr Glu  Cys Ile Tyr Thr Gln  Ser Arg Ser Cys Ser  Asp Phe Leu
    6620                 6625                 6630

Pro Leu  Ser Asp Met Glu Lys  Asp Phe Leu Ser Phe  Asp Ser Asp
    6635                 6640                 6645

Val Phe  Ile Lys Lys Tyr Gly  Leu Glu Asn Tyr Ala  Phe Glu His
    6650                 6655                 6660

Val Val  Tyr Gly Asp Phe Ser  His Thr Thr Leu Gly  Gly Leu His
    6665                 6670                 6675

Leu Leu  Ile Gly Leu Tyr Lys  Lys Gln Gln Glu Gly  His Ile Ile
    6680                 6685                 6690

Met Glu  Glu Met Leu Lys Gly  Ser Ser Thr Ile His  Asn Tyr Phe
    6695                 6700                 6705

Ile Thr  Glu Thr Asn Thr Ala  Ala Phe Lys Ala Val  Cys Ser Val
    6710                 6715                 6720

Ile Asp  Leu Lys Leu Asp Asp  Phe Val Met Ile Leu  Lys Ser Gln
    6725                 6730                 6735

Asp Leu  Gly Val Val Ser Lys  Val Val Lys Val Pro  Ile Asp Leu
    6740                 6745                 6750

Thr Met  Ile Glu Phe Met Leu  Trp Cys Lys Asp Gly  Gln Val Gln
    6755                 6760                 6765

Thr Phe  Tyr Pro Arg Leu Gln  Ala Ser Ala Asp Trp  Lys Pro Gly
    6770                 6775                 6780

His Ala  Met Pro Ser Leu Phe  Lys Val Gln Asn Val  Asn Leu Glu
    6785                 6790                 6795

Arg Cys  Glu Leu Ala Asn Tyr  Lys Gln Ser Ile Pro  Met Pro Arg
    6800                 6805                 6810

Gly Val  His Met Asn Ile Ala  Lys Tyr Met Gln Leu  Cys Gln Tyr
    6815                 6820                 6825

Leu Asn  Thr Cys Thr Leu Ala  Val Pro Ala Asn Met  Arg Val Ile
    6830                 6835                 6840

His Phe  Gly Ala Gly Ser Asp  Lys Gly Ile Ala Pro  Gly Thr Ser
    6845                 6850                 6855

Val Leu  Arg Gln Trp Leu Pro  Thr Asp Ala Ile Ile  Ile Asp Asn
    6860                 6865                 6870

Asp Leu  Asn Glu Phe Val Ser  Asp Ala Asp Ile Thr  Leu Phe Gly
    6875                 6880                 6885

Asp Cys  Val Thr Val Arg Val  Gly Gln Gln Val Asp  Leu Val Ile
    6890                 6895                 6900

Ser Asp  Met Tyr Asp Pro Thr  Thr Lys Asn Val Thr  Gly Ser Asn
    6905                 6910                 6915

Glu Ser  Lys Ala Leu Phe Phe  Thr Tyr Leu Cys Asn  Leu Ile Asn
    6920                 6925                 6930

Asn Asn  Leu Ala Leu Gly Gly  Ser Val Ala Ile Lys  Ile Thr Glu
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    6935                6940                6945

His Ser  Trp Ser Val Glu Leu  Tyr Glu Leu Met Gly  Lys Phe Ala
    6950                6955                6960

Trp Trp  Thr Val Phe Cys Thr  Asn Ala Asn Ala Ser  Ser Ser Glu
    6965                6970                6975

Gly Phe  Leu Leu Gly Ile Asn  Tyr Leu Gly Thr Ile  Lys Glu Asn
    6980                6985                6990

Ile Asp  Gly Gly Ala Met His  Ala Asn Tyr Ile Phe  Trp Arg Asn
    6995                7000                7005

Ser Thr  Pro Met Asn Leu Ser  Thr Tyr Ser Leu Phe  Asp Leu Ser
    7010                7015                7020

Lys Phe  Gln Leu Lys Leu Lys  Gly Thr Pro Val Leu  Gln Leu Lys
    7025                7030                7035

Glu Ser  Gln Ile Asn Glu Leu  Val Ile Ser Leu Leu  Ser Gln Gly
    7040                7045                7050

Lys Leu  Leu Ile Arg Asp Asn  Asp Thr Leu Ser Val  Ser Thr Asp
    7055                7060                7065

Val Leu  Val Asn Thr Tyr Arg  Lys Leu Arg
    7070                7075


<210> SEQ ID NO 4
<211> LENGTH: 7217
<212> TYPE: PRT
<213> ORGANISM: Human coronavirus HKU1

<400> SEQUENCE: 4

Met Ile Lys Thr Ser Lys Tyr Gly Leu Gly Phe Lys Trp Ala Pro Glu
1               5                   10                  15

Phe Arg Trp Leu Leu Pro Asp Ala Ala Glu Glu Leu Ala Ser Pro Met
            20                  25                  30

Lys Ser Asp Glu Gly Gly Leu Cys Pro Ser Thr Gly Gln Ala Met Glu
        35                  40                  45

Ser Val Gly Phe Val Tyr Asp Asn His Val Lys Ile Asp Cys Arg Cys
    50                  55                  60

Ile Leu Gly Gln Glu Trp His Val Gln Ser Asn Leu Ile Arg Asp Ile
65                  70                  75                  80

Phe Val His Glu Asp Leu His Val Val Glu Val Leu Thr Lys Thr Ala
                85                  90                  95

Val Lys Ser Gly Thr Ala Ile Leu Ile Lys Ser Pro Leu His Ser Leu
            100                 105                 110

Gly Gly Phe Pro Lys Gly Tyr Val Met Gly Leu Phe Arg Ser Tyr Lys
        115                 120                 125

Thr Lys Arg Tyr Val Val His His Leu Ser Met Thr Thr Ser Thr Thr
    130                 135                 140

Asn Phe Gly Glu Asp Phe Leu Gly Trp Ile Val Pro Phe Gly Phe Met
145                 150                 155                 160

Pro Ser Tyr Val His Lys Trp Phe Gln Phe Cys Arg Leu Tyr Ile Glu
                165                 170                 175

Glu Ser Asp Leu Ile Ile Ser Asn Phe Lys Phe Asp Asp Tyr Asp Phe
            180                 185                 190

Ser Val Glu Asp Val Tyr Ala Glu Val His Ala Glu Pro Lys Gly Lys
        195                 200                 205
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Tyr Ser Gln Lys Ala Tyr Ala Leu Leu Arg Gln Tyr Arg Gly Ile Lys
    210                 215                 220

Pro Val Leu Phe Val Asp Gln Tyr Gly Cys Asp Tyr Ser Gly Lys Leu
225                 230                 235                 240

Ala Asp Cys Leu Gln Ala Tyr Gly His Tyr Ser Leu Gln Asp Met Arg
                245                 250                 255

Gln Lys Gln Ser Val Trp Leu Ala Asn Cys Asp Phe Asp Ile Val Val
            260                 265                 270

Ala Trp His Val Val Arg Asp Ser Arg Phe Val Met Arg Leu Gln Thr
        275                 280                 285

Ile Ala Thr Ile Cys Gly Ile Lys Tyr Val Ala Gln Pro Thr Glu Asp
    290                 295                 300

Val Val Asp Gly Asp Val Val Ile Arg Glu Pro Val His Leu Leu Ser
305                 310                 315                 320

Ala Asp Ala Ile Val Leu Lys Leu Pro Ser Leu Met Lys Val Met Thr
                325                 330                 335

His Met Asp Asp Phe Ser Ile Lys Ser Ile Tyr Asn Val Asp Leu Cys
            340                 345                 350

Asp Cys Gly Phe Val Met Gln Tyr Gly Tyr Val Asp Cys Phe Asn Asp
        355                 360                 365

Asn Cys Asp Phe Tyr Gly Trp Val Ser Gly Asn Met Met Asp Gly Phe
    370                 375                 380

Ser Cys Pro Leu Cys Cys Thr Val Tyr Asp Ser Ser Glu Val Lys Ala
385                 390                 395                 400

Gln Ser Ser Gly Val Ile Pro Glu Asn Pro Val Leu Phe Thr Asn Ser
                405                 410                 415

Thr Asp Thr Val Asn His Asp Ser Phe Asn Leu Tyr Gly Tyr Ser Val
            420                 425                 430

Thr Pro Phe Gly Ser Cys Ile Tyr Trp Ser Pro Arg Pro Gly Leu Trp
        435                 440                 445

Ile Pro Ile Ile Lys Ser Ser Val Lys Ser Tyr Asp Asp Leu Val Tyr
    450                 455                 460

Ser Gly Val Val Gly Cys Lys Ser Ile Val Lys Glu Thr Ala Leu Ile
465                 470                 475                 480

Thr His Ala Leu Tyr Leu Asp Tyr Val Gln Cys Lys Cys Gly Asn Leu
                485                 490                 495

Glu Gln Asn His Ile Leu Gly Val Asn Asn Ser Trp Cys Arg Gln Leu
            500                 505                 510

Leu Leu Asn Arg Gly Asp Tyr Asn Met Leu Leu Lys Asn Ile Asp Leu
        515                 520                 525

Phe Val Lys Arg Arg Ala Asp Phe Ala Cys Lys Phe Ala Val Cys Gly
    530                 535                 540

Asp Gly Phe Val Pro Phe Leu Leu Asp Gly Leu Ile Pro Arg Ser Tyr
545                 550                 555                 560

Tyr Leu Ile Gln Ser Gly Ile Phe Phe Thr Ser Leu Met Ser Gln Phe
                565                 570                 575

Ser Gln Glu Val Ser Asp Met Cys Leu Lys Met Cys Ile Leu Phe Met
            580                 585                 590

Asp Arg Val Ser Val Ala Thr Phe Tyr Ile Glu His Tyr Val Asn Arg
        595                 600                 605

Leu Val Thr Gln Phe Lys Leu Leu Gly Thr Thr Leu Val Asn Lys Met
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    610                 615                 620

Val Asn Trp Phe Asn Thr Met Leu Asp Ala Ser Ala Pro Ala Thr Gly
625                 630                 635                 640

Trp Leu Leu Tyr Gln Leu Leu Asn Gly Leu Phe Val Val Ser Gln Ala
                645                 650                 655

Asn Phe Asn Phe Val Ala Leu Ile Pro Asp Tyr Ala Lys Ile Leu Val
            660                 665                 670

Asn Lys Phe Tyr Thr Phe Phe Lys Leu Leu Leu Glu Cys Val Thr Val
        675                 680                 685

Asp Val Leu Lys Asp Met Pro Val Leu Lys Thr Ile Asn Gly Leu Val
    690                 695                 700

Cys Ile Val Gly Asn Lys Phe Tyr Asn Val Ser Thr Gly Leu Ile Pro
705                 710                 715                 720

Gly Phe Val Leu Pro Cys Asn Ala Gln Glu Gln Gln Ile Tyr Phe Phe
                725                 730                 735

Glu Gly Val Ala Glu Ser Val Ile Val Glu Asp Asp Val Ile Glu Asn
            740                 745                 750

Val Lys Ser Ser Leu Ser Ser Tyr Glu Tyr Cys Gln Pro Pro Lys Ser
        755                 760                 765

Val Glu Lys Ile Cys Ile Ile Asp Asn Met Tyr Met Gly Lys Cys Gly
    770                 775                 780

Asp Lys Phe Phe Pro Ile Val Met Asn Asp Lys Asn Ile Cys Leu Leu
785                 790                 795                 800

Asp Gln Ala Trp Arg Phe Pro Cys Ala Gly Arg Lys Val Asn Phe Asn
                805                 810                 815

Glu Lys Pro Val Val Met Glu Ile Pro Ser Leu Met Thr Val Lys Val
            820                 825                 830

Met Phe Asp Leu Asp Ser Thr Phe Asp Asp Ile Leu Gly Lys Val Cys
        835                 840                 845

Ser Glu Phe Glu Val Glu Lys Gly Val Thr Val Asp Asp Phe Val Ala
    850                 855                 860

Val Val Cys Asp Ala Ile Glu Asn Ala Leu Asn Ser Cys Lys Glu His
865                 870                 875                 880

Pro Val Val Gly Tyr Gln Val Arg Ala Phe Leu Asn Lys Leu Asn Asp
                885                 890                 895

Asn Val Val Tyr Leu Phe Asp Glu Ala Gly Asp Glu Ala Met Ala Ser
            900                 905                 910

Arg Met Tyr Cys Thr Phe Ala Ile Glu Asp Val Glu Asp Val Ile Ser
        915                 920                 925

Ser Glu Ala Val Glu Asp Thr Ile Asp Gly Ile Val Glu Asp Thr Ile
    930                 935                 940

Asn Asp Asp Glu Asp Val Val Thr Gly Asp Asn Asp Asp Glu Asp Val
945                 950                 955                 960

Val Thr Gly Asp Asn Asp Asp Glu Asp Val Val Thr Gly Asp Asn Asp
                965                 970                 975

Asp Glu Asp Val Val Thr Gly Asp Asn Asp Asp Glu Asp Val Val Thr
            980                 985                 990

Gly Asp Asn Asp Asp Glu Asp Val  Val Thr Gly Asp Asn  Asp Asp Glu
        995                 1000                1005

Asp Val  Val Thr Gly Asp Asn  Asp Asp Glu Asp Val  Val Thr Gly
    1010                1015                1020
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Asp Asn  Asp Asp Glu Asp Val  Val Thr Gly Asp Asn  Asp Asp Glu
    1025                 1030                 1035

Asp Val  Val Thr Gly Asp Asn  Asp Asp Glu Asp Val  Val Thr Gly
    1040                 1045                 1050

Asp Asn  Asp Asp Glu Asp Val  Val Thr Gly Asp Asn  Asp Asp Glu
    1055                 1060                 1065

Asp Val  Val Thr Gly Asp Asn  Asp Asp Glu Asp Val  Val Thr Gly
    1070                 1075                 1080

Asp Asn  Asp Asp Glu Asp Val  Val Thr Gly Asp Asn  Asp Asp Glu
    1085                 1090                 1095

Asp Val  Val Thr Gly Asp Asn  Asp Asp Glu Asp Val  Val Thr Gly
    1100                 1105                 1110

Asp Asn  Asp Asp Glu Asp Asn  Asn Asp Glu Glu Ile  Val Thr Gly
    1115                 1120                 1125

Asp Asn  Asp Asp Gln Ile Val  Val Thr Gly Asp Asp  Val Asp Asp
    1130                 1135                 1140

Ile Glu  Ser Ile Tyr Asp Phe  Asp Thr Tyr Lys Ala  Leu Leu Val
    1145                 1150                 1155

Phe Asn  Asp Val Tyr Asn Asp  Ala Leu Phe Val Ser  Tyr Gly Ser
    1160                 1165                 1170

Ser Val  Glu Thr Glu Thr Tyr  Phe Lys Val Asn Gly  Leu Trp Ser
    1175                 1180                 1185

Pro Thr  Ile Thr His Thr Asn  Cys Trp Leu Arg Ser  Val Leu Leu
    1190                 1195                 1200

Val Met  Gln Lys Leu Pro Phe  Lys Phe Lys Asp Leu  Ala Ile Glu
    1205                 1210                 1215

Asn Met  Trp Leu Ser Tyr Lys  Val Gly Tyr Asn Gln  Ser Phe Val
    1220                 1225                 1230

Asp Tyr  Leu Leu Thr Thr Ile  Pro Lys Ala Ile Val  Leu Pro Gln
    1235                 1240                 1245

Gly Gly  Phe Val Ala Asp Phe  Ala Tyr Trp Phe Leu  Asn Gln Phe
    1250                 1255                 1260

Asp Ile  Asn Ala Tyr Ala Asn  Trp Cys Cys Leu Lys  Cys Gly Phe
    1265                 1270                 1275

Ser Phe  Asp Leu Asn Gly Leu  Asp Ala Leu Phe Phe  Tyr Gly Asp
    1280                 1285                 1290

Ile Val  Ser His Val Cys Lys  Cys Gly His Asn Met  Thr Leu Ile
    1295                 1300                 1305

Ala Ala  Asp Leu Pro Cys Thr  Leu His Phe Ser Leu  Phe Asp Asp
    1310                 1315                 1320

Asn Phe  Cys Ala Phe Cys Thr  Pro Lys Lys Ile Phe  Ile Ala Ala
    1325                 1330                 1335

Cys Ala  Val Asp Val Asn Val  Cys His Ser Val Ala  Val Ile Gly
    1340                 1345                 1350

Asp Glu  Gln Ile Asp Gly Lys  Phe Val Thr Lys Phe  Ser Gly Asp
    1355                 1360                 1365

Lys Phe  Asp Phe Ile Val Gly  Tyr Gly Met Ser Phe  Ser Met Ser
    1370                 1375                 1380

Ser Phe  Glu Leu Ala Gln Leu  Tyr Gly Leu Cys Ile  Thr Pro Asn
    1385                 1390                 1395
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Val Cys  Phe Val Lys Gly Asp  Ile Ile Asn Val Ala  Arg Leu Val
    1400                 1405                 1410

Lys Ala  Asp Val Ile Val Asn  Pro Ala Asn Gly His  Met Leu His
    1415                 1420                 1425

Gly Gly  Gly Val Ala Lys Ala  Ile Ala Val Ala Ala  Gly Lys Lys
    1430                 1435                 1440

Phe Ser  Lys Glu Thr Ala Ala  Met Val Lys Ser Lys  Gly Val Cys
    1445                 1450                 1455

Gln Val  Gly Asp Cys Tyr Val  Ser Thr Gly Gly Lys  Leu Cys Lys
    1460                 1465                 1470

Thr Ile  Leu Asn Ile Val Gly  Pro Asp Ala Arg Gln  Asp Gly Arg
    1475                 1480                 1485

Gln Ser  Tyr Val Leu Leu Ala  Arg Ala Tyr Lys His  Leu Asn Asn
    1490                 1495                 1500

Tyr Asp  Cys Cys Leu Ser Thr  Leu Ile Ser Ala Gly  Ile Phe Ser
    1505                 1510                 1515

Val Pro  Ala Asp Val Ser Leu  Thr Tyr Leu Leu Gly  Val Val Asp
    1520                 1525                 1530

Lys Gln  Val Ile Leu Val Ser  Asn Asn Lys Glu Asp  Phe Asp Ile
    1535                 1540                 1545

Ile Gln  Lys Cys Gln Ile Thr  Ser Val Val Gly Thr  Lys Ala Leu
    1550                 1555                 1560

Ala Val  Arg Leu Thr Ala Asn  Val Gly Arg Val Ile  Lys Phe Glu
    1565                 1570                 1575

Thr Asp  Ala Tyr Lys Leu Phe  Leu Ser Gly Asp Asp  Cys Phe Val
    1580                 1585                 1590

Ser Asn  Ser Ser Val Ile Gln  Glu Val Leu Leu Leu  Arg His Asp
    1595                 1600                 1605

Ile Gln  Leu Asn Asn Asp Val  Arg Asp Tyr Leu Leu  Ser Lys Met
    1610                 1615                 1620

Thr Ser  Leu Pro Lys Asp Trp  Arg Leu Ile Asn Lys  Phe Asp Val
    1625                 1630                 1635

Ile Asn  Gly Val Lys Thr Val  Lys Tyr Phe Glu Cys  Pro Asn Ser
    1640                 1645                 1650

Ile Tyr  Ile Cys Ser Gln Gly  Lys Asp Phe Gly Tyr  Val Cys Asp
    1655                 1660                 1665

Gly Ser  Phe Tyr Lys Ala Thr  Val Asn Gln Val Cys  Val Leu Leu
    1670                 1675                 1680

Ala Lys  Lys Ile Asp Val Leu  Leu Thr Val Asp Gly  Val Asn Phe
    1685                 1690                 1695

Lys Ser  Ile Ser Leu Thr Val  Gly Glu Val Phe Gly  Lys Ile Leu
    1700                 1705                 1710

Gly Asn  Val Phe Cys Asp Gly  Ile Asp Val Thr Lys  Leu Lys Cys
    1715                 1720                 1725

Ser Asp  Phe Tyr Ala Asp Lys  Ile Leu Tyr Gln Tyr  Glu Asn Leu
    1730                 1735                 1740

Ser Leu  Ala Asp Ile Ser Ala  Val Gln Ser Ser Phe  Gly Phe Asp
    1745                 1750                 1755

Gln Gln  Gln Leu Leu Ala Tyr  Tyr Asn Phe Leu Thr  Val Cys Lys
    1760                 1765                 1770

Trp Ser  Val Val Val Asn Gly  Pro Phe Phe Ser Phe  Glu Gln Ser
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    1775                1780                1785

His Asn  Asn Cys Tyr Val Asn  Val Ala Cys Leu Met  Leu Gln His
    1790                1795                1800

Ile Asn  Leu Lys Phe Asn Lys  Trp Gln Trp Gln Glu  Ala Trp Tyr
    1805                1810                1815

Glu Phe  Arg Ala Gly Arg Pro  His Arg Leu Val Ala  Leu Val Leu
    1820                1825                1830

Ala Lys  Gly His Phe Lys Phe  Asp Glu Pro Ser Asp  Ala Thr Asp
    1835                1840                1845

Phe Ile  Arg Val Val Leu Lys  Gln Ala Asp Leu Ser  Gly Ala Ile
    1850                1855                1860

Cys Glu  Leu Glu Leu Ile Cys  Asp Cys Gly Ile Lys  Gln Glu Ser
    1865                1870                1875

Arg Val  Gly Val Asp Ala Val  Met His Phe Gly Thr  Leu Ala Lys
    1880                1885                1890

Thr Asp  Leu Phe Asn Gly Tyr  Lys Ile Gly Cys Asn  Cys Ala Gly
    1895                1900                1905

Arg Ile  Val His Cys Thr Lys  Leu Asn Val Pro Phe  Leu Ile Cys
    1910                1915                1920

Ser Asn  Thr Pro Leu Ser Lys  Asp Leu Pro Asp Asp  Val Val Ala
    1925                1930                1935

Ala Asn  Met Phe Met Gly Val  Gly Val Gly His Tyr  Thr His Leu
    1940                1945                1950

Lys Cys  Gly Ser Pro Tyr Gln  His Tyr Asp Ala Cys  Ser Val Lys
    1955                1960                1965

Lys Tyr  Thr Gly Val Ser Gly  Cys Leu Thr Asp Cys  Leu Tyr Leu
    1970                1975                1980

Lys Asn  Leu Thr Gln Thr Phe  Thr Ser Met Leu Thr  Asn Tyr Phe
    1985                1990                1995

Leu Asp  Asp Val Glu Met Val  Ala Tyr Asn Pro Asp  Leu Ser Gln
    2000                2005                2010

Tyr Tyr  Cys Asp Asn Gly Lys  Tyr Tyr Thr Lys Pro  Ile Ile Lys
    2015                2020                2025

Ala Gln  Phe Lys Pro Phe Ala  Lys Val Asp Gly Val  Tyr Thr Asn
    2030                2035                2040

Phe Lys  Leu Val Gly His Asp  Ile Cys Ala Gln Leu  Asn Asp Lys
    2045                2050                2055

Leu Gly  Phe Asn Val Asp Leu  Pro Phe Val Glu Tyr  Lys Val Thr
    2060                2065                2070

Val Trp  Pro Val Ala Thr Gly  Asp Val Val Leu Ala  Ser Asp Asp
    2075                2080                2085

Leu Tyr  Val Lys Arg Tyr Phe  Lys Gly Cys Glu Thr  Phe Gly Lys
    2090                2095                2100

Pro Val  Ile Trp Phe Cys His  Asp Glu Ala Ser Leu  Asn Ser Leu
    2105                2110                2115

Thr Tyr  Phe Asn Lys Pro Ser  Phe Lys Ser Glu Asn  Arg Tyr Ser
    2120                2125                2130

Val Leu  Ser Val Asp Ser Val  Ser Glu Glu Ser Gln  Gly Asn Val
    2135                2140                2145

Val Thr  Pro Val Met Glu Ser  Gln Ile Ser Thr Lys  Glu Val Lys
    2150                2155                2160
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Leu Lys  Gly Val Arg Lys Thr  Val Lys Ile Glu Asp  Ala Ile Ile
    2165                 2170                 2175

Val Asn  Asp Glu Asn Ser Ser  Ile Lys Val Val Lys  Ser Leu Ser
    2180                 2185                 2190

Leu Val  Asp Val Trp Asp Met  Tyr Leu Thr Gly Cys  Asp Tyr Val
    2195                 2200                 2205

Val Trp  Val Ala Asn Glu Leu  Ser Arg Leu Val Lys  Ser Pro Thr
    2210                 2215                 2220

Val Arg  Glu Tyr Ile Arg Tyr  Gly Ile Lys Pro Ile  Thr Ile Pro
    2225                 2230                 2235

Ile Asp  Leu Leu Cys Leu Arg  Asp Asp Asn Gln Thr  Leu Leu Val
    2240                 2245                 2250

Pro Lys  Ile Phe Lys Ala Arg  Ala Ile Glu Phe Tyr  Gly Phe Leu
    2255                 2260                 2265

Lys Trp  Leu Phe Ile Tyr Val  Phe Ser Leu Leu His  Phe Thr Asn
    2270                 2275                 2280

Asp Lys  Thr Ile Phe Tyr Thr  Thr Glu Ile Ala Ser  Lys Phe Thr
    2285                 2290                 2295

Phe Asn  Leu Phe Cys Leu Ala  Leu Lys Asn Ala Phe  Gln Thr Phe
    2300                 2305                 2310

Arg Trp  Ser Ile Phe Ile Lys  Gly Phe Leu Val Val  Ala Thr Val
    2315                 2320                 2325

Phe Leu  Phe Trp Phe Asn Phe  Leu Tyr Ile Asn Val  Ile Phe Ser
    2330                 2335                 2340

Asp Phe  Tyr Leu Pro Asn Ile  Ser Val Phe Pro Ile  Phe Val Gly
    2345                 2350                 2355

Arg Ile  Val Met Trp Ile Lys  Ala Thr Phe Gly Leu  Val Thr Ile
    2360                 2365                 2370

Cys Asp  Phe Tyr Ser Lys Leu  Gly Val Gly Phe Thr  Ser His Phe
    2375                 2380                 2385

Cys Asn  Gly Ser Phe Ile Cys  Glu Leu Cys His Ser  Gly Phe Asp
    2390                 2395                 2400

Met Leu  Asp Thr Tyr Ala Ala  Ile Asp Phe Val Gln  Tyr Glu Val
    2405                 2410                 2415

Asp Arg  Arg Val Leu Phe Asp  Tyr Val Ser Leu Val  Lys Leu Ile
    2420                 2425                 2430

Val Glu  Leu Val Ile Gly Tyr  Ser Leu Tyr Thr Val  Trp Phe Tyr
    2435                 2440                 2445

Pro Leu  Phe Cys Leu Ile Gly  Leu Gln Leu Phe Thr  Thr Trp Leu
    2450                 2455                 2460

Pro Asp  Leu Phe Met Leu Glu  Thr Met His Trp Leu  Ile Arg Phe
    2465                 2470                 2475

Ile Val  Phe Val Ala Asn Met  Leu Pro Ala Phe Val  Leu Leu Arg
    2480                 2485                 2490

Phe Tyr  Ile Val Val Thr Ala  Met Tyr Lys Val Val  Gly Phe Ile
    2495                 2500                 2505

Arg His  Ile Val Tyr Gly Cys  Asn Lys Ala Gly Cys  Leu Phe Cys
    2510                 2515                 2520

Tyr Lys  Arg Asn Cys Ser Val  Arg Val Lys Cys Ser  Thr Ile Val
    2525                 2530                 2535
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Gly Gly  Val Ile Arg Tyr Tyr  Asp Ile Thr Ala Asn  Gly Gly Thr
    2540                 2545                 2550

Gly Phe  Cys Val Lys His Gln  Trp Asn Cys Phe Asn  Cys His Ser
    2555                 2560                 2565

Phe Lys  Pro Gly Asn Thr Phe  Ile Thr Val Glu Ala  Ala Ile Glu
    2570                 2575                 2580

Leu Ser  Lys Glu Leu Lys Arg  Pro Val Asn Pro Thr  Asp Ala Ser
    2585                 2590                 2595

His Tyr  Val Val Thr Asp Ile  Lys Gln Val Gly Cys  Met Met Arg
    2600                 2605                 2610

Leu Phe  Tyr Asp Arg Asp Gly  Gln Arg Val Tyr Asp  Asp Val Asp
    2615                 2620                 2625

Ala Ser  Leu Phe Val Asp Ile  Asn Asn Leu Leu His  Ser Lys Val
    2630                 2635                 2640

Lys Val  Val Pro Asn Leu Tyr  Val Val Val Val Glu  Ser Asp Ala
    2645                 2650                 2655

Asp Arg  Ala Asn Phe Leu Asn  Ala Val Val Phe Tyr  Ala Gln Ser
    2660                 2665                 2670

Leu Tyr  Arg Pro Ile Leu Leu  Val Asp Lys Lys Leu  Ile Thr Thr
    2675                 2680                 2685

Ala Cys  Asn Gly Ile Ser Val  Thr Gln Thr Met Phe  Asp Val Tyr
    2690                 2695                 2700

Val Asp  Thr Phe Met Ser His  Phe Asp Val Asp Arg  Lys Ser Phe
    2705                 2710                 2715

Asn Asn  Phe Val Asn Ile Ala  His Ala Ser Leu Arg  Glu Gly Val
    2720                 2725                 2730

Gln Leu  Glu Lys Val Leu Asp  Thr Phe Val Gly Cys  Val Arg Lys
    2735                 2740                 2745

Cys Cys  Ser Ile Asp Ser Asp  Val Glu Thr Arg Phe  Ile Thr Lys
    2750                 2755                 2760

Ser Met  Ile Ser Ala Val Ala  Ala Gly Leu Glu Phe  Thr Asp Glu
    2765                 2770                 2775

Asn Tyr  Asn Asn Leu Val Pro  Thr Tyr Leu Lys Ser  Asp Asn Ile
    2780                 2785                 2790

Val Ala  Ala Asp Leu Gly Val  Leu Ile Gln Asn Gly  Ala Lys His
    2795                 2800                 2805

Val Gln  Gly Asn Val Ala Lys  Ala Ala Asn Ile Ser  Cys Ile Trp
    2810                 2815                 2820

Phe Ile  Asp Ala Phe Asn Gln  Leu Thr Ala Asp Leu  Gln His Lys
    2825                 2830                 2835

Leu Lys  Lys Ala Cys Val Lys  Thr Gly Leu Lys Leu  Lys Leu Thr
    2840                 2845                 2850

Phe Asn  Lys Gln Glu Ala Ser  Val Pro Ile Leu Thr  Thr Pro Phe
    2855                 2860                 2865

Ser Leu  Lys Gly Gly Val Val  Leu Ser Asn Leu Leu  Tyr Ile Leu
    2870                 2875                 2880

Phe Phe  Val Ser Leu Ile Cys  Phe Ile Leu Leu Trp  Ala Leu Leu
    2885                 2890                 2895

Pro Thr  Tyr Ser Val Tyr Lys  Ser Asp Ile His Leu  Pro Ala Tyr
    2900                 2905                 2910

Ala Ser  Phe Lys Val Ile Asp  Asn Gly Val Val Arg  Asp Ile Ser
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    2915                2920                2925

Val Asn  Asp Leu Cys Phe Ala  Asn Lys Phe Phe Gln  Phe Asp Gln
    2930                2935                2940

Trp Tyr  Glu Ser Thr Phe Gly  Ser Val Tyr Tyr His  Asn Ser Met
    2945                2950                2955

Asp Cys  Pro Ile Val Val Ala  Val Met Asp Glu Asp  Ile Gly Ser
    2960                2965                2970

Thr Met  Phe Asn Val Pro Thr  Lys Val Leu Arg His  Gly Phe His
    2975                2980                2985

Val Leu  His Phe Leu Thr Tyr  Ala Phe Ala Ser Asp  Ser Val Gln
    2990                2995                3000

Cys Tyr  Thr Pro His Ile Gln  Ile Ser Tyr Asn Asp  Phe Tyr Ala
    3005                3010                3015

Ser Gly  Cys Val Leu Ser Ser  Leu Cys Thr Met Phe  Lys Arg Gly
    3020                3025                3030

Asp Gly  Thr Pro His Pro Tyr  Cys Tyr Ser Asp Gly  Val Met Lys
    3035                3040                3045

Asn Ala  Ser Leu Tyr Thr Ser  Leu Val Pro His Thr  Arg Tyr Ser
    3050                3055                3060

Leu Ala  Asn Ser Asn Gly Phe  Ile Arg Phe Pro Asp  Val Ile Ser
    3065                3070                3075

Glu Gly  Ile Val Arg Ile Val  Arg Thr Arg Ser Met  Thr Tyr Cys
    3080                3085                3090

Arg Val  Gly Ala Cys Glu Tyr  Ala Glu Glu Gly Ile  Cys Phe Asn
    3095                3100                3105

Phe Asn  Ser Ser Trp Val Leu  Asn Asn Asp Tyr Tyr  Arg Ser Met
    3110                3115                3120

Pro Gly  Thr Phe Cys Gly Arg  Asp Leu Phe Asp Leu  Phe Tyr Gln
    3125                3130                3135

Phe Phe  Ser Ser Leu Ile Arg  Pro Ile Asp Phe Phe  Ser Leu Thr
    3140                3145                3150

Ala Ser  Ser Ile Phe Gly Ala  Ile Leu Ala Ile Val  Val Val Leu
    3155                3160                3165

Val Phe  Tyr Tyr Leu Ile Lys  Leu Lys Arg Ala Phe  Gly Asp Tyr
    3170                3175                3180

Thr Ser  Val Val Val Ile Asn  Val Val Val Trp Cys  Ile Asn Phe
    3185                3190                3195

Leu Met  Leu Phe Val Phe Gln  Val Tyr Pro Ile Cys  Ala Cys Val
    3200                3205                3210

Tyr Ala  Cys Phe Tyr Phe Tyr  Val Thr Leu Tyr Phe  Pro Ser Glu
    3215                3220                3225

Ile Ser  Val Ile Met His Leu  Gln Trp Ile Val Met  Tyr Gly Ala
    3230                3235                3240

Ile Met  Pro Phe Trp Phe Cys  Val Thr Tyr Val Ala  Met Val Ile
    3245                3250                3255

Ala Asn  His Val Leu Trp Leu  Phe Ser Tyr Cys Arg  Lys Ile Gly
    3260                3265                3270

Val Asn  Val Cys Ser Asp Ser  Thr Phe Glu Glu Thr  Ser Leu Thr
    3275                3280                3285

Thr Phe  Met Ile Thr Lys Asp  Ser Tyr Cys Arg Leu  Lys Asn Ser
    3290                3295                3300
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Val Ser  Asp Val Ala Tyr Asn  Arg Tyr Leu Ser Leu  Tyr Asn Lys
    3305                 3310                 3315

Tyr Arg  Tyr Tyr Ser Gly Lys  Met Asp Thr Ala Ala  Tyr Arg Glu
    3320                 3325                 3330

Ala Ala  Cys Ser Gln Leu Ala  Lys Ala Met Glu Thr  Phe Asn His
    3335                 3340                 3345

Asn Asn  Gly Asn Asp Val Leu  Tyr Gln Pro Pro Thr  Ala Ser Val
    3350                 3355                 3360

Ser Thr  Ser Phe Leu Gln Ser  Gly Ile Val Lys Met  Val Ser Pro
    3365                 3370                 3375

Thr Ser  Lys Ile Glu Pro Cys  Ile Val Ser Val Thr  Tyr Gly Ser
    3380                 3385                 3390

Met Thr  Leu Asn Gly Leu Trp  Leu Asp Asp Lys Val  Tyr Cys Pro
    3395                 3400                 3405

Arg His  Val Ile Cys Ser Ser  Ser Asn Met Asn Glu  Pro Asp Tyr
    3410                 3415                 3420

Ser Ala  Leu Leu Cys Arg Val  Thr Leu Gly Asp Phe  Thr Ile Met
    3425                 3430                 3435

Ser Gly  Arg Met Ser Leu Thr  Val Val Ser Tyr Gln  Met Gln Gly
    3440                 3445                 3450

Cys Gln  Leu Val Leu Thr Val  Ser Leu Gln Asn Pro  Tyr Thr Pro
    3455                 3460                 3465

Lys Tyr  Thr Phe Gly Asn Val  Lys Pro Gly Glu Thr  Phe Thr Val
    3470                 3475                 3480

Leu Ala  Ala Tyr Asn Gly Arg  Pro Gln Gly Ala Phe  His Val Thr
    3485                 3490                 3495

Met Arg  Ser Ser Tyr Thr Ile  Lys Gly Ser Phe Leu  Cys Gly Ser
    3500                 3505                 3510

Cys Gly  Ser Val Gly Tyr Val  Leu Thr Gly Asp Ser  Val Lys Phe
    3515                 3520                 3525

Val Tyr  Met His Gln Leu Glu  Leu Ser Thr Gly Cys  His Thr Gly
    3530                 3535                 3540

Thr Asp  Phe Thr Gly Asn Phe  Tyr Gly Pro Tyr Arg  Asp Ala Gln
    3545                 3550                 3555

Val Val  Gln Leu Pro Val Lys  Asp Tyr Val Gln Thr  Val Asn Val
    3560                 3565                 3570

Ile Ala  Trp Leu Tyr Ala Ala  Ile Leu Asn Asn Cys  Ala Trp Phe
    3575                 3580                 3585

Val Gln  Asn Asp Val Cys Ser  Thr Glu Asp Phe Asn  Val Trp Ala
    3590                 3595                 3600

Met Ala  Asn Gly Phe Ser Gln  Val Lys Ala Asp Leu  Val Leu Asp
    3605                 3610                 3615

Ala Leu  Ala Ser Met Thr Gly  Val Ser Ile Glu Thr  Leu Leu Ala
    3620                 3625                 3630

Ala Ile  Lys Arg Leu Tyr Met  Gly Phe Gln Gly Arg  Gln Ile Leu
    3635                 3640                 3645

Gly Ser  Cys Thr Phe Glu Asp  Glu Leu Ala Pro Ser  Asp Val Tyr
    3650                 3655                 3660

Gln Gln  Leu Ala Gly Val Lys  Leu Gln Ser Lys Thr  Lys Arg Phe
    3665                 3670                 3675
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Ile Lys  Glu Thr Ile Tyr Trp  Ile Leu Ile Ser Thr  Phe Leu Phe
    3680                 3685                 3690

Ser Cys  Ile Ile Ser Ala Phe  Val Lys Trp Thr Ile  Phe Met Tyr
    3695                 3700                 3705

Ile Asn  Thr His Met Ile Gly  Val Thr Leu Cys Val  Leu Cys Phe
    3710                 3715                 3720

Val Ser  Phe Met Met Leu Leu  Val Lys His Lys His  Phe Tyr Leu
    3725                 3730                 3735

Thr Met  Tyr Ile Ile Pro Val  Leu Cys Thr Leu Phe  Tyr Val Asn
    3740                 3745                 3750

Tyr Leu  Val Val Tyr Lys Glu  Gly Phe Arg Gly Phe  Thr Tyr Val
    3755                 3760                 3765

Trp Leu  Ser Tyr Phe Val Pro  Ala Val Asn Phe Thr  Tyr Val Tyr
    3770                 3775                 3780

Glu Val  Phe Tyr Gly Cys Ile  Leu Cys Val Phe Ala  Ile Phe Ile
    3785                 3790                 3795

Thr Met  His Ser Ile Asn His  Asp Ile Phe Ser Leu  Met Phe Leu
    3800                 3805                 3810

Val Gly  Arg Ile Val Thr Leu  Ile Ser Met Trp Tyr  Phe Gly Ser
    3815                 3820                 3825

Asn Leu  Glu Glu Asp Val Leu  Leu Phe Ile Thr Ala  Phe Leu Gly
    3830                 3835                 3840

Thr Tyr  Thr Trp Thr Thr Ile  Leu Ser Leu Ala Ile  Ala Lys Ile
    3845                 3850                 3855

Val Ala  Asn Trp Leu Ser Val  Asn Ile Phe Tyr Phe  Thr Asp Val
    3860                 3865                 3870

Pro Tyr  Ile Lys Leu Ile Leu  Leu Ser Tyr Leu Phe  Ile Gly Tyr
    3875                 3880                 3885

Ile Leu  Ser Cys Tyr Trp Gly  Phe Phe Ser Leu Leu  Asn Ser Val
    3890                 3895                 3900

Phe Arg  Met Pro Met Gly Val  Tyr Asn Tyr Lys Ile  Ser Val Gln
    3905                 3910                 3915

Glu Leu  Arg Tyr Met Asn Ala  Asn Gly Leu Arg Pro  Pro Arg Asn
    3920                 3925                 3930

Ser Phe  Glu Ala Ile Leu Leu  Asn Leu Lys Leu Leu  Gly Ile Gly
    3935                 3940                 3945

Gly Val  Pro Val Ile Glu Val  Ser Gln Ile Gln Ser  Lys Leu Thr
    3950                 3955                 3960

Asp Val  Lys Cys Ala Asn Val  Val Leu Leu Asn Cys  Leu Gln His
    3965                 3970                 3975

Leu His  Val Ala Ser Asn Ser  Lys Leu Trp Gln Tyr  Cys Ser Val
    3980                 3985                 3990

Leu His  Asn Glu Ile Leu Ser  Thr Ser Asp Leu Ser  Val Ala Phe
    3995                 4000                 4005

Asp Lys  Leu Ala Gln Leu Leu  Ile Val Leu Phe Ala  Asn Pro Ala
    4010                 4015                 4020

Ala Val  Asp Thr Lys Cys Leu  Ala Ser Ile Asp Glu  Val Ser Asp
    4025                 4030                 4035

Asp Tyr  Val Gln Asp Ser Thr  Val Leu Gln Ala Leu  Gln Ser Glu
    4040                 4045                 4050

Phe Val  Asn Met Ala Ser Phe  Val Glu Tyr Glu Val  Ala Lys Lys
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    4055                4060                4065

Asn Leu  Ala Asp Ala Lys Asn  Ser Gly Ser Val Asn  Gln Gln Gln
    4070                4075                4080

Ile Lys  Gln Leu Glu Lys Ala  Cys Asn Ile Ala Lys  Ser Val Tyr
    4085                4090                4095

Glu Arg  Asp Lys Ala Val Ala  Arg Lys Leu Glu Arg  Met Ala Asp
    4100                4105                4110

Leu Ala  Leu Thr Asn Met Tyr  Lys Glu Ala Arg Ile  Asn Asp Lys
    4115                4120                4125

Lys Ser  Lys Val Val Ser Ala  Leu Gln Thr Met Leu  Phe Ser Met
    4130                4135                4140

Val Arg  Lys Leu Asp Asn Gln  Ala Leu Asn Ser Ile  Leu Asp Asn
    4145                4150                4155

Ala Val  Lys Gly Cys Val Pro  Leu Ser Ala Ile Pro  Ala Leu Ala
    4160                4165                4170

Ala Asn  Thr Leu Thr Ile Ile  Ile Pro Asp Lys Gln  Val Phe Asp
    4175                4180                4185

Lys Val  Val Asp Asn Val Tyr  Val Thr Tyr Ala Gly  Ser Val Trp
    4190                4195                4200

His Ile  Gln Thr Val Gln Asp  Ala Asp Gly Ile Asn  Lys Gln Leu
    4205                4210                4215

Thr Asp  Ile Ser Val Asp Ser  Asn Trp Pro Leu Val  Ile Ile Ala
    4220                4225                4230

Asn Arg  Tyr Asn Glu Val Ala  Asn Ala Val Met Gln  Asn Asn Glu
    4235                4240                4245

Leu Met  Pro His Lys Leu Lys  Ile Gln Val Val Asn  Ser Gly Ser
    4250                4255                4260

Asp Met  Asn Cys Asn Ile Pro  Thr Gln Cys Tyr Tyr  Asn Asn Gly
    4265                4270                4275

Ser Ser  Gly Arg Ile Val Tyr  Ala Val Leu Ser Asp  Val Asp Gly
    4280                4285                4290

Leu Lys  Tyr Thr Lys Ile Met  Lys Asp Asp Gly Asn  Cys Val Val
    4295                4300                4305

Leu Glu  Leu Asp Pro Pro Cys  Lys Phe Ser Ile Gln  Asp Val Lys
    4310                4315                4320

Gly Leu  Lys Ile Lys Tyr Leu  Tyr Phe Ile Lys Gly  Cys Asn Thr
    4325                4330                4335

Leu Ala  Arg Gly Trp Val Val  Gly Thr Leu Ser Ser  Thr Ile Arg
    4340                4345                4350

Leu Gln  Ala Gly Val Ala Thr  Glu Tyr Ala Ala Asn  Ser Ser Ile
    4355                4360                4365

Leu Ser  Leu Cys Ala Phe Ser  Val Asp Pro Lys Lys  Thr Tyr Leu
    4370                4375                4380

Asp Tyr  Ile Gln Gln Gly Gly  Val Pro Ile Ile Asn  Cys Val Lys
    4385                4390                4395

Met Leu  Cys Asp His Ala Gly  Thr Gly Met Ala Ile  Thr Ile Lys
    4400                4405                4410

Pro Glu  Ala Thr Ile Asn Gln  Asp Ser Tyr Gly Gly  Ala Ser Val
    4415                4420                4425

Cys Ile  Tyr Cys Arg Ala Arg  Val Glu His Pro Asp  Val Asp Gly
    4430                4435                4440
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Ile Cys  Lys Leu Arg Gly Lys  Phe Val Gln Val Pro  Leu Gly Ile
    4445                 4450                 4455

Lys Asp  Pro Ile Leu Tyr Val  Leu Thr His Asp Val  Cys Gln Val
    4460                 4465                 4470

Cys Gly  Phe Trp Arg Asp Gly  Ser Cys Ser Cys Val  Gly Ser Ser
    4475                 4480                 4485

Val Ala  Val Gln Ser Lys Asp  Leu Asn Phe Leu Asn  Arg Val Arg
    4490                 4495                 4500

Gly Thr  Ser Val Asn Ala Arg  Leu Val Pro Cys Ala  Ser Gly Leu
    4505                 4510                 4515

Ser Thr  Asp Val Gln Leu Arg  Ala Phe Asp Ile Cys  Asn Thr Asn
    4520                 4525                 4530

Arg Ala  Gly Ile Gly Leu Tyr  Tyr Lys Val Asn Cys  Cys Arg Phe
    4535                 4540                 4545

Gln Arg  Ile Asp Asp Asp Gly  Asn Lys Leu Asp Lys  Phe Phe Val
    4550                 4555                 4560

Val Lys  Arg Thr Asn Leu Glu  Val Tyr Asn Lys Glu  Lys Thr Tyr
    4565                 4570                 4575

Tyr Glu  Leu Thr Lys Ser Cys  Gly Val Val Ala Glu  His Asp Phe
    4580                 4585                 4590

Phe Thr  Phe Asp Ile Asp Gly  Ser Arg Val Pro His  Ile Val Arg
    4595                 4600                 4605

Arg Asn  Leu Ser Lys Tyr Thr  Met Leu Asp Leu Cys  Tyr Ala Leu
    4610                 4615                 4620

Arg His  Phe Asp Arg Asn Asp  Cys Ser Ile Leu Cys  Glu Ile Leu
    4625                 4630                 4635

Cys Glu  Tyr Ala Asp Cys Lys  Glu Ser Tyr Phe Ser  Lys Lys Asp
    4640                 4645                 4650

Trp Tyr  Asp Phe Val Glu Asn  Pro Asp Ile Ile Asn  Ile Tyr Lys
    4655                 4660                 4665

Lys Leu  Gly Pro Ile Phe Asn  Arg Ala Leu Leu Asn  Thr Val Ile
    4670                 4675                 4680

Phe Ala  Asp Thr Leu Val Glu  Val Gly Leu Val Gly  Val Leu Thr
    4685                 4690                 4695

Leu Asp  Asn Gln Asp Leu Tyr  Gly Gln Trp Tyr Asp  Phe Gly Asp
    4700                 4705                 4710

Phe Ile  Gln Thr Ala Pro Gly  Phe Gly Val Ala Val  Ala Asp Ser
    4715                 4720                 4725

Tyr Tyr  Ser Tyr Met Met Pro  Met Leu Thr Met Cys  His Val Leu
    4730                 4735                 4740

Asp Cys  Glu Leu Phe Val Asn  Asp Ser Tyr Arg Gln  Phe Asp Leu
    4745                 4750                 4755

Val Gln  Tyr Asp Phe Thr Asp  Tyr Lys Leu Glu Leu  Phe Asn Lys
    4760                 4765                 4770

Tyr Phe  Lys Tyr Trp Gly Met  Lys Tyr His Pro Asn  Thr Val Asp
    4775                 4780                 4785

Cys Asp  Asn Asp Arg Cys Ile  Ile His Cys Ala Asn  Phe Asn Ile
    4790                 4795                 4800

Leu Phe  Ser Met Val Leu Pro  Asn Thr Cys Phe Gly  Pro Leu Val
    4805                 4810                 4815
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Arg Gln  Ile Phe Val Asp Gly  Val Pro Phe Val Val  Ser Ile Gly
    4820                 4825                 4830

Tyr His  Tyr Lys Glu Leu Gly  Val Val Met Asn Leu  Asp Val Asp
    4835                 4840                 4845

Thr His  Arg Tyr Arg Leu Ser  Leu Lys Asp Leu Leu  Leu Tyr Ala
    4850                 4855                 4860

Ala Asp  Pro Ala Met His Val  Ala Ser Ala Ser Ala  Leu Leu Asp
    4865                 4870                 4875

Leu Arg  Thr Cys Cys Phe Ser  Val Ala Ala Ile Thr  Ser Gly Ile
    4880                 4885                 4890

Lys Phe  Gln Thr Val Lys Pro  Gly Asn Phe Asn Gln  Asp Phe Tyr
    4895                 4900                 4905

Glu Phe  Val Lys Ser Lys Gly  Leu Phe Lys Glu Gly  Ser Thr Val
    4910                 4915                 4920

Asp Leu  Lys His Phe Phe Phe  Thr Gln Asp Gly Asn  Ala Ala Ile
    4925                 4930                 4935

Thr Asp  Tyr Asn Tyr Tyr Lys  Tyr Asn Leu Pro Thr  Met Val Asp
    4940                 4945                 4950

Ile Lys  Gln Leu Leu Phe Val  Leu Glu Val Val Tyr  Lys Tyr Phe
    4955                 4960                 4965

Glu Ile  Tyr Asp Gly Gly Cys  Ile Pro Ala Ser Gln  Val Ile Val
    4970                 4975                 4980

Asn Asn  Tyr Asp Lys Ser Ala  Gly Tyr Pro Phe Asn  Lys Phe Gly
    4985                 4990                 4995

Lys Ala  Arg Leu Tyr Tyr Glu  Ala Leu Ser Phe Glu  Glu Gln Asn
    5000                 5005                 5010

Glu Ile  Tyr Ala Tyr Thr Lys  Arg Asn Val Leu Pro  Thr Leu Thr
    5015                 5020                 5025

Gln Met  Asn Leu Lys Tyr Ala  Ile Ser Ala Lys Asn  Arg Ala Arg
    5030                 5035                 5040

Thr Val  Ala Gly Val Ser Ile  Leu Ser Thr Met Thr  Gly Arg Met
    5045                 5050                 5055

Phe His  Gln Lys Cys Leu Lys  Ser Ile Ala Ala Thr  Arg Gly Val
    5060                 5065                 5070

Pro Val  Val Ile Gly Thr Thr  Lys Phe Tyr Gly Gly  Trp Asp Asp
    5075                 5080                 5085

Met Leu  Arg His Leu Ile Lys  Asp Val Asp Asn Pro  Val Leu Met
    5090                 5095                 5100

Gly Trp  Asp Tyr Pro Lys Cys  Asp Arg Ala Met Pro  Asn Ile Leu
    5105                 5110                 5115

Arg Ile  Val Ser Ser Leu Val  Leu Ala Arg Lys His  Glu Phe Cys
    5120                 5125                 5130

Cys Ser  His Gly Asp Arg Phe  Tyr Arg Leu Ala Asn  Glu Cys Ala
    5135                 5140                 5145

Gln Val  Leu Ser Glu Ile Val  Met Cys Gly Gly Cys  Tyr Tyr Val
    5150                 5155                 5160

Lys Pro  Gly Gly Thr Ser Ser  Gly Asp Ala Thr Thr  Ala Phe Ala
    5165                 5170                 5175

Asn Ser  Val Phe Asn Ile Cys  Gln Ala Val Thr Ala  Asn Val Cys
    5180                 5185                 5190

Ser Leu  Met Ala Cys Asn Gly  His Lys Ile Glu Asp  Leu Ser Ile
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    5195                5200                5205

Arg Asn  Leu Gln Lys Arg Leu  Tyr Ser Asn Val Tyr  Arg Thr Asp
    5210                5215                5220

Tyr Val  Asp Tyr Thr Phe Val  Asn Glu Tyr Tyr Glu  Phe Leu Cys
    5225                5230                5235

Lys His  Phe Ser Met Met Ile  Leu Ser Asp Asp Gly  Val Val Cys
    5240                5245                5250

Tyr Asn  Ser Asp Tyr Ala Ser  Lys Gly Tyr Ile Ala  Asn Ile Ser
    5255                5260                5265

Val Phe  Gln Gln Val Leu Tyr  Tyr Gln Asn Asn Val  Phe Met Ser
    5270                5275                5280

Glu Ser  Lys Cys Trp Val Glu  Asn Asp Ile Thr Asn  Gly Pro His
    5285                5290                5295

Glu Phe  Cys Ser Gln His Thr  Met Leu Val Lys Ile  Asp Gly Asp
    5300                5305                5310

Tyr Val  Tyr Leu Pro Tyr Pro  Asp Pro Ser Arg Ile  Leu Gly Ala
    5315                5320                5325

Gly Cys  Phe Val Asp Asp Leu  Leu Lys Thr Asp Ser  Val Leu Leu
    5330                5335                5340

Ile Glu  Arg Phe Val Ser Leu  Ala Ile Asp Ala Tyr  Pro Leu Val
    5345                5350                5355

Tyr His  Glu Asn Glu Glu Tyr  Gln Lys Val Phe Arg  Val Tyr Leu
    5360                5365                5370

Glu Tyr  Ile Lys Lys Leu Tyr  Asn Asp Leu Gly Thr  Gln Ile Leu
    5375                5380                5385

Asp Ser  Tyr Ser Val Ile Leu  Ser Thr Cys Asp Gly  Leu Lys Phe
    5390                5395                5400

Thr Glu  Glu Ser Phe Tyr Lys  Asn Met Tyr Leu Lys  Ser Ala Val
    5405                5410                5415

Met Gln  Ser Val Gly Ala Cys  Val Val Cys Ser Ser  Gln Thr Ser
    5420                5425                5430

Leu Arg  Cys Gly Ser Cys Ile  Arg Lys Pro Leu Leu  Cys Cys Lys
    5435                5440                5445

Cys Cys  Tyr Asp His Val Met  Ala Thr Asn His Lys  Tyr Val Leu
    5450                5455                5460

Ser Val  Ser Pro Tyr Val Cys  Asn Ala Pro Asn Cys  Asp Val Ser
    5465                5470                5475

Asp Val  Thr Lys Leu Tyr Leu  Gly Gly Met Ser Tyr  Tyr Cys Glu
    5480                5485                5490

Asn His  Lys Pro His Tyr Ser  Phe Lys Leu Val Met  Asn Gly Met
    5495                5500                5505

Val Phe  Gly Leu Tyr Lys Gln  Ser Cys Thr Gly Ser  Pro Tyr Ile
    5510                5515                5520

Asp Asp  Phe Asn Lys Ile Ala  Ser Cys Lys Trp Thr  Glu Val Asp
    5525                5530                5535

Asp Tyr  Val Leu Ala Asn Glu  Cys Ile Glu Arg Leu  Lys Leu Phe
    5540                5545                5550

Ala Ala  Glu Thr Gln Lys Ala  Thr Glu Glu Ala Phe  Lys Gln Ser
    5555                5560                5565

Tyr Ala  Ser Ala Thr Ile Gln  Glu Ile Val Ser Asp  Arg Glu Val
    5570                5575                5580
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Ile Leu  Cys Trp Glu Thr Gly  Lys Val Lys Pro Pro  Leu Asn Lys
    5585                 5590                 5595

Asn Tyr  Val Phe Thr Gly Tyr  His Phe Thr Ser Thr  Gly Lys Thr
    5600                 5605                 5610

Val Leu  Gly Glu Tyr Val Phe  Asp Lys Ser Glu Leu  Thr Asn Gly
    5615                 5620                 5625

Val Tyr  Tyr Arg Ala Thr Thr  Thr Tyr Lys Leu Ser  Ile Gly Asp
    5630                 5635                 5640

Val Phe  Val Leu Thr Ser His  Ser Val Ala Ser Leu  Ser Ala Pro
    5645                 5650                 5655

Thr Leu  Val Pro Gln Glu Asn  Tyr Ala Ser Ile Arg  Phe Ser Ser
    5660                 5665                 5670

Val Tyr  Ser Val Pro Leu Val  Phe Gln Asn Asn Val  Ala Asn Tyr
    5675                 5680                 5685

Gln His  Ile Gly Met Lys Arg  Tyr Cys Thr Val Gln  Gly Pro Pro
    5690                 5695                 5700

Gly Thr  Gly Lys Ser His Leu  Ala Ile Gly Leu Ala  Val Tyr Tyr
    5705                 5710                 5715

Tyr Thr  Ala Arg Val Val Tyr  Thr Ala Ala Ser His  Ala Ala Val
    5720                 5725                 5730

Asp Ala  Leu Cys Glu Lys Ala  Tyr Lys Phe Leu Asn  Ile Asn Asp
    5735                 5740                 5745

Cys Thr  Arg Ile Ile Pro Ala  Lys Val Arg Val Asp  Cys Tyr Asp
    5750                 5755                 5760

Lys Phe  Lys Ile Asn Asp Thr  Thr Cys Lys Tyr Val  Phe Thr Thr
    5765                 5770                 5775

Ile Asn  Ala Leu Pro Glu Leu  Val Thr Asp Ile Val  Val Val Asp
    5780                 5785                 5790

Glu Val  Ser Met Leu Thr Asn  Tyr Glu Leu Ser Val  Ile Asn Ala
    5795                 5800                 5805

Arg Ile  Lys Ala Lys His Tyr  Val Tyr Ile Gly Asp  Pro Ala Gln
    5810                 5815                 5820

Leu Pro  Ala Pro Arg Val Leu  Leu Ser Lys Gly Ser  Leu Glu Pro
    5825                 5830                 5835

Arg His  Phe Asn Ser Ile Thr  Lys Ile Met Cys Cys  Leu Gly Pro
    5840                 5845                 5850

Asp Ile  Phe Leu Gly Asn Cys  Tyr Arg Cys Pro Lys  Glu Ile Val
    5855                 5860                 5865

Glu Thr  Val Ser Ala Leu Val  Tyr Asp Asn Lys Leu  Lys Ala Lys
    5870                 5875                 5880

Asn Asp  Asn Ser Ser Leu Cys  Phe Lys Val Tyr Phe  Lys Gly Gln
    5885                 5890                 5895

Thr Thr  His Glu Ser Ser Ser  Ala Val Asn Ile Gln  Gln Ile Tyr
    5900                 5905                 5910

Leu Ile  Ser Lys Phe Leu Lys  Ala Asn Pro Val Trp  Asn Ser Ala
    5915                 5920                 5925

Val Phe  Ile Ser Pro Tyr Asn  Ser Gln Asn Tyr Val  Ala Lys Arg
    5930                 5935                 5940

Val Leu  Gly Val Gln Thr Gln  Thr Val Asp Ser Ala  Gln Gly Ser
    5945                 5950                 5955
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Glu Tyr  Asp Tyr Val Ile Tyr  Ser Gln Thr Ala Glu  Thr Ala His
    5960                 5965                 5970

Ser Val  Asn Val Asn Arg Phe  Asn Val Ala Ile Thr  Arg Ala Lys
    5975                 5980                 5985

Lys Gly  Ile Phe Cys Val Met  Ser Asn Met Gln Leu  Phe Glu Ser
    5990                 5995                 6000

Leu Asn  Phe Ile Thr Leu Pro  Leu Asp Lys Ile Gln  Asn Gln Thr
    6005                 6010                 6015

Leu Pro  Arg Leu His Cys Thr  Thr Asn Leu Phe Lys  Asp Cys Ser
    6020                 6025                 6030

Lys Ser  Cys Leu Gly Tyr His  Pro Ala His Ala Pro  Ser Phe Leu
    6035                 6040                 6045

Ala Val  Asp Asp Lys Tyr Lys  Val Asn Glu Asn Leu  Ala Val Asn
    6050                 6055                 6060

Leu Asn  Ile Cys Glu Pro Val  Leu Thr Tyr Ser Arg  Leu Ile Ser
    6065                 6070                 6075

Leu Met  Gly Phe Lys Leu Asp  Leu Thr Leu Asp Gly  Tyr Ser Lys
    6080                 6085                 6090

Leu Phe  Ile Thr Lys Asp Glu  Ala Ile Lys Arg Val  Arg Gly Trp
    6095                 6100                 6105

Val Gly  Phe Asp Val Glu Gly  Ala His Ala Thr Arg  Glu Asn Ile
    6110                 6115                 6120

Gly Thr  Asn Phe Pro Leu Gln  Ile Gly Phe Ser Thr  Gly Val Asp
    6125                 6130                 6135

Phe Val  Val Glu Ala Thr Gly  Leu Phe Ala Glu Arg  Asp Cys Tyr
    6140                 6145                 6150

Thr Phe  Lys Lys Thr Val Ala  Lys Ala Pro Pro Gly  Glu Lys Phe
    6155                 6160                 6165

Lys His  Leu Ile Pro Leu Met  Ser Lys Gly Gln Lys  Trp Asp Ile
    6170                 6175                 6180

Val Arg  Ile Arg Ile Val Gln  Met Leu Ser Asp Tyr  Leu Leu Asp
    6185                 6190                 6195

Leu Ser  Asp Ser Val Val Phe  Ile Thr Trp Ser Ala  Ser Phe Glu
    6200                 6205                 6210

Leu Thr  Cys Leu Arg Tyr Phe  Ala Lys Leu Gly Arg  Glu Leu Asn
    6215                 6220                 6225

Cys Asn  Val Cys Ser Asn Arg  Ala Thr Cys Tyr Asn  Ser Arg Thr
    6230                 6235                 6240

Gly Tyr  Tyr Gly Cys Trp Arg  His Ser Tyr Thr Cys  Asp Tyr Val
    6245                 6250                 6255

Tyr Asn  Pro Leu Ile Val Asp  Ile Gln Gln Trp Gly  Tyr Thr Gly
    6260                 6265                 6270

Ser Leu  Thr Ser Asn His Asp  Ile Ile Cys Asn Val  His Lys Gly
    6275                 6280                 6285

Ala His  Val Ala Ser Ala Asp  Ala Ile Met Thr Arg  Cys Leu Ala
    6290                 6295                 6300

Ile Tyr  Asp Cys Phe Cys Lys  Ser Val Asn Trp Asn  Leu Glu Tyr
    6305                 6310                 6315

Pro Ile  Ile Ser Asn Glu Val  Ser Ile Asn Thr Ser  Cys Arg Leu
    6320                 6325                 6330

Leu Gln  Arg Val Met Leu Lys  Ala Ala Met Leu Cys  Asn Arg Tyr
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    6335                6340                6345

Asn Leu  Cys Tyr Asp Ile Gly  Asn Pro Lys Gly Leu  Ala Cys Val
    6350                6355                6360

Lys Asp  Tyr Glu Phe Lys Phe  Tyr Asp Ala Phe Pro  Val Ala Lys
    6365                6370                6375

Phe Val  Lys Gln Leu Phe Tyr  Val Tyr Asp Val His  Lys Asp Asn
    6380                6385                6390

Phe Lys  Asp Gly Leu Cys Met  Phe Trp Asn Cys Asn  Val Asp Lys
    6395                6400                6405

Tyr Pro  Ser Asn Ser Ile Val  Cys Arg Phe Asp Thr  Arg Val Leu
    6410                6415                6420

Asn Lys  Leu Asn Leu Pro Gly  Cys Asn Gly Gly Ser  Leu Tyr Val
    6425                6430                6435

Asn Lys  His Ala Phe His Thr  Asn Pro Phe Thr Arg  Thr Val Phe
    6440                6445                6450

Glu Asn  Leu Lys Pro Met Pro  Phe Phe Tyr Tyr Ser  Asp Thr Pro
    6455                6460                6465

Cys Val  Tyr Val Asp Gly Leu  Glu Ser Lys Gln Val  Asp Tyr Val
    6470                6475                6480

Pro Leu  Arg Ser Ala Thr Cys  Ile Thr Arg Cys Asn  Leu Gly Gly
    6485                6490                6495

Ala Val  Cys Ser Lys His Ala  Glu Glu Tyr Cys Asn  Tyr Leu Glu
    6500                6505                6510

Ser Tyr  Asn Ile Val Thr Thr  Ala Gly Phe Thr Phe  Trp Val Tyr
    6515                6520                6525

Lys Asn  Phe Asp Phe Tyr Asn  Leu Trp Asn Thr Phe  Thr Thr Leu
    6530                6535                6540

Gln Ser  Leu Glu Asn Val Ile  Tyr Asn Leu Val Asn  Val Gly His
    6545                6550                6555

Tyr Asp  Gly Arg Thr Gly Glu  Leu Pro Cys Ala Ile  Ile Asn Asp
    6560                6565                6570

Lys Val  Val Val Lys Ile Asn  Asn Val Asp Thr Val  Ile Phe Lys
    6575                6580                6585

Asn Asn  Thr Ser Phe Pro Thr  Asn Ile Ala Val Glu  Leu Phe Thr
    6590                6595                6600

Lys Arg  Ser Ile Arg His His  Pro Glu Leu Lys Ile  Leu Arg Asn
    6605                6610                6615

Leu Asn  Ile Asp Ile Cys Trp  Lys His Val Leu Trp  Asp Tyr Val
    6620                6625                6630

Lys Asp  Ser Leu Phe Cys Ser  Ser Thr Tyr Gly Val  Cys Lys Tyr
    6635                6640                6645

Thr Asp  Leu Lys Phe Ile Glu  Asn Leu Asn Ile Leu  Phe Asp Gly
    6650                6655                6660

Arg Asp  Thr Gly Ala Leu Glu  Ala Phe Arg Lys Ala  Arg Asn Gly
    6665                6670                6675

Val Phe  Ile Ser Thr Glu Lys  Leu Ser Arg Leu Ser  Met Ile Lys
    6680                6685                6690

Gly Pro  Gln Arg Ala Asp Leu  Asn Gly Val Ile Val  Asp Lys Val
    6695                6700                6705

Gly Glu  Leu Lys Val Glu Phe  Trp Phe Ala Met Arg  Lys Asp Gly
    6710                6715                6720
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Asp Asp  Val Ile Phe Ser Arg  Thr Asp Ser Leu Cys  Ser Ser His
    6725                 6730                 6735

Tyr Trp  Ser Pro Gln Gly Asn  Leu Gly Gly Asn Cys  Ala Gly Asn
    6740                 6745                 6750

Val Ile  Gly Asn Asp Ala Leu  Thr Arg Phe Thr Ile  Phe Thr Gln
    6755                 6760                 6765

Ser Arg  Val Leu Ser Ser Phe  Glu Pro Arg Ser Asp  Leu Glu Arg
    6770                 6775                 6780

Asp Phe  Ile Asp Met Asp Asp  Asn Leu Phe Ile Ala  Lys Tyr Gly
    6785                 6790                 6795

Leu Glu  Asp Tyr Ala Phe Asp  His Ile Val Tyr Gly  Ser Phe Asn
    6800                 6805                 6810

His Lys  Val Ile Gly Gly Leu  His Leu Leu Ile Gly  Leu Phe Arg
    6815                 6820                 6825

Arg Leu  Lys Lys Ser Asn Leu  Leu Ile Gln Glu Phe  Leu Gln Tyr
    6830                 6835                 6840

Asp Ser  Ser Ile His Ser Tyr  Phe Ile Thr Asp Gln  Glu Cys Gly
    6845                 6850                 6855

Ser Ser  Lys Ser Val Cys Thr  Val Ile Asp Leu Leu  Leu Asp Asp
    6860                 6865                 6870

Phe Val  Ser Ile Val Lys Ser  Leu Asn Leu Ser Cys  Val Ser Lys
    6875                 6880                 6885

Val Val  Asn Ile Asn Val Asp  Phe Lys Asp Phe Gln  Phe Met Leu
    6890                 6895                 6900

Trp Cys  Asn Asp Asn Lys Ile  Met Thr Phe Tyr Pro  Lys Met Gln
    6905                 6910                 6915

Ala Thr  Asn Asp Trp Lys Pro  Gly Tyr Ser Met Pro  Val Leu Tyr
    6920                 6925                 6930

Lys Tyr  Leu Asn Val Pro Leu  Glu Arg Val Ser Leu  Trp Asn Tyr
    6935                 6940                 6945

Gly Lys  Pro Ile Asn Leu Pro  Thr Gly Cys Met Met  Asn Val Ala
    6950                 6955                 6960

Lys Tyr  Thr Gln Leu Cys Gln  Tyr Leu Asn Thr Thr  Thr Leu Ala
    6965                 6970                 6975

Val Pro  Val Asn Met Arg Val  Leu His Leu Gly Ala  Gly Ser Asp
    6980                 6985                 6990

Lys Glu  Val Ala Pro Gly Ser  Ala Val Leu Arg Gln  Trp Leu Pro
    6995                 7000                 7005

Ser Gly  Ser Ile Leu Val Asp  Asn Asp Leu Asn Pro  Phe Val Ser
    7010                 7015                 7020

Asp Ser  Leu Val Thr Tyr Phe  Gly Asp Cys Met Thr  Leu Pro Phe
    7025                 7030                 7035

Asp Cys  His Trp Asp Leu Ile  Ile Ser Asp Met Tyr  Asp Pro Leu
    7040                 7045                 7050

Thr Lys  Asn Ile Gly Asp Tyr  Asn Val Ser Lys Asp  Gly Phe Phe
    7055                 7060                 7065

Thr Tyr  Ile Cys His Leu Ile  Arg Asp Lys Leu Ser  Leu Gly Gly
    7070                 7075                 7080

Ser Val  Ala Ile Lys Ile Thr  Glu Phe Ser Trp Asn  Ala Asp Leu
    7085                 7090                 7095
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Tyr Lys  Leu Met Ser Cys Phe  Ala Phe Trp Thr Val  Phe Cys Thr
    7100                 7105                 7110

Asn Val  Asn Ala Ser Ser Ser  Glu Gly Phe Leu Ile  Gly Ile Asn
    7115                 7120                 7125

Tyr Leu  Gly Lys Ser Ser Phe  Glu Ile Asp Gly Asn  Val Met His
    7130                 7135                 7140

Ala Asn  Tyr Leu Phe Trp Arg  Asn Ser Thr Thr Trp  Asn Gly Gly
    7145                 7150                 7155

Ala Tyr  Ser Leu Phe Asp Met  Thr Lys Phe Ser Leu  Lys Leu Ala
    7160                 7165                 7170

Gly Thr  Ala Val Val Asn Leu  Arg Pro Asp Gln Leu  Asn Asp Leu
    7175                 7180                 7185

Val Tyr  Ser Leu Ile Glu Arg  Gly Lys Leu Leu Val  Arg Asp Thr
    7190                 7195                 7200

Arg Lys  Glu Ile Phe Val Gly  Asp Ser Leu Val Asn  Thr Cys
    7205                 7210                 7215


<210> SEQ ID NO 5
<211> LENGTH: 7095
<212> TYPE: PRT
<213> ORGANISM: Human coronavirus OC43

<400> SEQUENCE: 5

Met Ser Lys Ile Asn Lys Tyr Gly Leu Glu Leu His Trp Ala Pro Glu
1               5                   10                  15

Phe Pro Trp Met Phe Glu Asp Ala Glu Glu Lys Leu Asp Asn Pro Ser
            20                  25                  30

Ser Ser Glu Val Asp Met Ile Cys Ser Thr Thr Ala Gln Lys Leu Glu
        35                  40                  45

Thr Asp Gly Ile Cys Pro Glu Asn His Val Met Val Asp Cys Arg Arg
    50                  55                  60

Leu Leu Lys Gln Glu Cys Cys Val Gln Ser Ser Leu Ile Arg Glu Ile
65                  70                  75                  80

Val Met Asn Ala Ser Pro Tyr Asp Leu Glu Val Leu Leu Gln Asp Ala
                85                  90                  95

Leu Gln Ser Arg Glu Ala Val Leu Val Thr Thr Pro Leu Gly Met Ser
            100                 105                 110

Leu Glu Ala Cys Tyr Val Arg Gly Cys Asn Pro Lys Gly Trp Thr Met
        115                 120                 125

Gly Leu Phe Arg Arg Arg Ser Val Cys Asn Thr Gly Arg Cys Thr Val
    130                 135                 140

Asn Lys His Val Ala Tyr Gln Leu Tyr Met Ile Asp Pro Ala Gly Val
145                 150                 155                 160

Cys Leu Gly Ala Gly Gln Phe Val Gly Trp Val Ile Pro Leu Ala Phe
                165                 170                 175

Met Pro Val Gln Ser Arg Lys Phe Ile Val Pro Trp Val Met Tyr Leu
            180                 185                 190

Arg Lys Arg Gly Glu Lys Gly Ala Tyr Asn Lys Asp His Gly Arg Gly
        195                 200                 205

Gly Phe Gly His Val Tyr Asp Phe Lys Val Glu Asp Ala Tyr Asp Gln
    210                 215                 220

Val His Asp Glu Pro Lys Gly Lys Phe Ser Lys Lys Ala Tyr Ala Leu
225                 230                 235                 240
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Ile Arg Gly Tyr Arg Gly Val Lys Pro Leu Leu Tyr Val Asp Gln Tyr
                245                 250                 255

Gly Cys Asp Tyr Thr Gly Ser Leu Ala Asp Gly Leu Glu Ala Tyr Ala
            260                 265                 270

Asp Lys Thr Leu Gln Glu Met Lys Ala Leu Phe Pro Thr Trp Ser Gln
        275                 280                 285

Glu Leu Leu Phe Asp Val Ile Val Ala Trp His Val Val Arg Asp Pro
    290                 295                 300

Arg Tyr Val Met Arg Leu Gln Ser Ala Ala Thr Ile Arg Ser Val Ala
305                 310                 315                 320

Tyr Val Ala Asn Pro Thr Glu Asp Leu Cys Asp Gly Ser Val Val Ile
                325                 330                 335

Lys Glu Pro Val His Val Tyr Ala Asp Asp Ser Ile Ile Leu Arg Gln
            340                 345                 350

Tyr Asn Leu Val Asp Ile Met Ser His Phe Tyr Met Glu Ala Asp Thr
        355                 360                 365

Val Val Asn Ala Phe Tyr Gly Val Ala Leu Lys Asp Cys Gly Phe Val
    370                 375                 380

Met Gln Phe Gly Tyr Ile Asp Cys Glu Gln Asp Ser Cys Asp Phe Lys
385                 390                 395                 400

Gly Trp Ile Pro Gly Asn Met Ile Asp Gly Phe Ala Cys Thr Thr Cys
                405                 410                 415

Gly His Val Tyr Glu Val Gly Asp Leu Met Ala Gln Ser Ser Gly Val
            420                 425                 430

Leu Pro Val Asn Pro Val Leu His Thr Lys Ser Ala Ala Gly Tyr Gly
        435                 440                 445

Gly Phe Gly Cys Lys Asp Ser Phe Thr Leu Tyr Gly Gln Thr Val Val
    450                 455                 460

Tyr Phe Gly Gly Cys Val Tyr Trp Ser Pro Ala Arg Asn Ile Trp Ile
465                 470                 475                 480

Pro Ile Leu Lys Ser Ser Val Lys Ser Tyr Asp Ser Leu Val Tyr Thr
                485                 490                 495

Gly Val Leu Gly Cys Lys Ala Ile Val Lys Glu Thr Asn Leu Ile Cys
            500                 505                 510

Lys Ala Leu Tyr Leu Asp Tyr Val Gln His Lys Cys Gly Asn Leu His
        515                 520                 525

Gln Arg Glu Leu Leu Gly Val Ser Asp Val Trp His Lys Gln Leu Leu
    530                 535                 540

Leu Asn Arg Gly Val Tyr Lys Pro Leu Leu Glu Asn Ile Asp Tyr Phe
545                 550                 555                 560

Asn Met Arg Arg Ala Lys Phe Ser Leu Glu Thr Phe Thr Val Cys Ala
                565                 570                 575

Asp Gly Phe Met Pro Phe Leu Leu Asp Asp Leu Val Pro Arg Ala Tyr
            580                 585                 590

Tyr Leu Ala Val Ser Gly Gln Ala Phe Cys Asp Tyr Ala Asp Lys Leu
        595                 600                 605

Cys His Ala Val Val Ser Lys Ser Lys Glu Leu Leu Asp Val Ser Leu
    610                 615                 620

Asp Ser Leu Gly Ala Ala Ile His Tyr Leu Asn Ser Lys Ile Val Asp
625                 630                 635                 640
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Leu Ala Gln His Phe Ser Asp Phe Gly Thr Ser Phe Val Ser Lys Ile
                645                 650                 655

Val His Phe Phe Lys Thr Phe Thr Thr Ser Thr Ala Leu Ala Phe Ala
            660                 665                 670

Trp Val Leu Phe His Val Leu His Gly Ala Tyr Ile Val Val Glu Ser
        675                 680                 685

Asp Ile Tyr Phe Val Lys Asn Ile Pro Arg Tyr Ala Ser Ala Val Ala
    690                 695                 700

Gln Ala Phe Gln Ser Val Ala Lys Val Val Leu Asp Ser Leu Arg Val
705                 710                 715                 720

Thr Phe Ile Asp Gly Leu Ser Cys Phe Lys Ile Gly Arg Arg Arg Ile
                725                 730                 735

Cys Leu Ser Gly Arg Lys Ile Tyr Glu Val Glu Arg Gly Leu Leu His
            740                 745                 750

Ser Ser Gln Leu Pro Leu Asp Val Tyr Asp Leu Thr Met Pro Ser Gln
        755                 760                 765

Val Gln Lys Ala Lys Gln Lys Pro Ile Tyr Leu Lys Gly Ser Gly Ser
    770                 775                 780

Asp Phe Ser Leu Ala Asp Ser Val Val Glu Val Val Thr Thr Ser Leu
785                 790                 795                 800

Thr Pro Cys Gly Tyr Ser Glu Pro Pro Lys Val Ala Ala Lys Ile Cys
                805                 810                 815

Ile Val Asp Asn Val Tyr Met Ala Lys Ala Gly Asp Lys Tyr Tyr Pro
            820                 825                 830

Val Val Val Asp Asp His Val Gly Leu Leu Asp Gln Ala Trp Arg Val
        835                 840                 845

Pro Cys Ala Gly Arg Arg Val Thr Phe Lys Glu Gln Pro Thr Val Lys
    850                 855                 860

Glu Ile Ile Ser Met Pro Lys Ile Ile Lys Val Phe Tyr Glu Leu Asp
865                 870                 875                 880

Asn Asp Phe Asn Thr Ile Leu Asn Thr Ala Cys Gly Val Phe Glu Val
                885                 890                 895

Asp Asp Thr Val Asp Met Glu Glu Phe Tyr Ala Val Val Ile Asp Ala
            900                 905                 910

Ile Glu Glu Lys Leu Ser Pro Cys Lys Glu Leu Glu Gly Val Gly Ala
        915                 920                 925

Lys Val Ser Ala Phe Leu Gln Lys Leu Glu Asp Asn Pro Leu Phe Leu
    930                 935                 940

Phe Asp Glu Ala Gly Glu Glu Val Leu Ala Pro Lys Leu Tyr Cys Ala
945                 950                 955                 960

Phe Thr Ala Pro Glu Asp Asp Asp Phe Leu Glu Glu Ser Asp Val Glu
                965                 970                 975

Glu Asp Asp Val Glu Gly Glu Glu Thr Asp Leu Thr Val Thr Ser Ala
            980                 985                 990

Gly Gln Pro Cys Val Ala Ser Glu  Gln Glu Glu Ser Ser  Glu Val Leu
        995                 1000                 1005

Glu Asp  Thr Leu Asp Asp Gly  Pro Ser Val Glu Thr  Ser Asp Ser
    1010                 1015                 1020

Gln Val  Glu Glu Asp Val Glu  Met Ser Asp Phe Val  Asp Leu Glu
    1025                 1030                 1035

Ser Val  Ile Gln Asp Tyr Glu  Asn Val Cys Phe Glu  Phe Tyr Thr
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    1040                1045                1050

Thr Glu  Pro Glu Phe Val Lys  Val Leu Gly Leu Tyr  Val Pro Lys
    1055                1060                1065

Ala Thr  Arg Asn Asn Cys Trp  Leu Arg Ser Val Leu  Ala Val Met
    1070                1075                1080

Gln Lys  Leu Pro Cys Gln Phe  Lys Asp Lys Asn Leu  Gln Asp Leu
    1085                1090                1095

Trp Val  Leu Tyr Lys Gln Gln  Tyr Ser Gln Leu Phe  Val Asp Thr
    1100                1105                1110

Leu Val  Asn Lys Ile Pro Ala  Asn Ile Val Leu Pro  Gln Gly Gly
    1115                1120                1125

Tyr Val  Ala Asp Phe Ala Tyr  Trp Phe Leu Thr Leu  Cys Asp Trp
    1130                1135                1140

Gln Cys  Val Ala Tyr Trp Lys  Cys Ile Lys Cys Asp  Leu Ala Leu
    1145                1150                1155

Lys Leu  Lys Gly Leu Asp Ala  Met Phe Phe Tyr Gly  Asp Val Val
    1160                1165                1170

Ser His  Ile Cys Lys Cys Gly  Glu Ser Met Val Leu  Ile Asp Val
    1175                1180                1185

Asp Val  Pro Phe Thr Ala His  Phe Ala Leu Lys Asp  Lys Leu Phe
    1190                1195                1200

Cys Ala  Phe Ile Thr Lys Arg  Ile Val Tyr Lys Ala  Ala Cys Val
    1205                1210                1215

Val Asp  Val Asn Asp Ser His  Ser Met Ala Val Val  Asp Gly Lys
    1220                1225                1230

Gln Ile  Asp Asp His Arg Ile  Thr Ser Ile Thr Ser  Asp Lys Phe
    1235                1240                1245

Asp Phe  Ile Ile Gly His Gly  Met Ser Phe Ser Met  Thr Thr Phe
    1250                1255                1260

Glu Ile  Ala Gln Leu Tyr Gly  Ser Cys Ile Thr Pro  Asn Val Cys
    1265                1270                1275

Phe Val  Lys Gly Asp Ile Ile  Lys Val Ser Lys Leu  Val Lys Ala
    1280                1285                1290

Glu Val  Val Val Asn Pro Ala  Asn Gly His Met Ala  His Gly Gly
    1295                1300                1305

Gly Val  Ala Lys Ala Ile Ala  Val Ala Ala Gly Gln  Gln Phe Val
    1310                1315                1320

Lys Glu  Thr Thr Asp Met Val  Lys Ser Lys Gly Val  Cys Ala Thr
    1325                1330                1335

Gly Asp  Cys Tyr Val Ser Thr  Gly Gly Lys Leu Cys  Lys Thr Val
    1340                1345                1350

Leu Asn  Val Val Gly Pro Asp  Ala Arg Thr Gln Gly  Lys Gln Ser
    1355                1360                1365

Tyr Val  Leu Leu Glu Arg Val  Tyr Lys His Leu Asn  Asn Tyr Asp
    1370                1375                1380

Cys Val  Val Thr Thr Leu Ile  Ser Ala Gly Ile Phe  Ser Val Pro
    1385                1390                1395

Ser Asp  Val Ser Leu Thr Tyr  Leu Leu Gly Thr Ala  Lys Lys Gln
    1400                1405                1410

Val Val  Leu Val Ser Asn Asn  Gln Glu Asp Phe Asp  Leu Ile Ser
    1415                1420                1425
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Lys Cys  Gln Ile Thr Ala Val  Glu Gly Thr Lys Lys  Leu Ala Ala
    1430                 1435                 1440

Arg Leu  Ser Phe Asn Val Gly  Arg Ser Ile Val Tyr  Glu Thr Asp
    1445                 1450                 1455

Ala Asn  Lys Leu Ile Leu Ile  Asn Asp Val Ala Phe  Val Ser Thr
    1460                 1465                 1470

Phe Asn  Val Leu Gln Asp Val  Leu Ser Leu Arg His  Asp Ile Ala
    1475                 1480                 1485

Leu Asp  Asp Asp Ala Arg Thr  Phe Val Gln Ser Asn  Val Asp Val
    1490                 1495                 1500

Val Pro  Glu Gly Trp Arg Val  Val Asn Lys Phe Tyr  Gln Ile Asn
    1505                 1510                 1515

Gly Val  Arg Thr Val Lys Tyr  Phe Glu Cys Thr Gly  Gly Ile Asp
    1520                 1525                 1530

Ile Cys  Ser Gln Asp Lys Val  Phe Gly Tyr Val Gln  Gln Gly Ile
    1535                 1540                 1545

Phe Asn  Lys Ala Thr Val Ala  Gln Ile Lys Ala Leu  Phe Leu Asp
    1550                 1555                 1560

Lys Val  Asp Ile Leu Leu Thr  Val Asp Gly Val Asn  Phe Thr Asn
    1565                 1570                 1575

Arg Phe  Val Pro Val Gly Glu  Ser Phe Gly Lys Ser  Leu Gly Asn
    1580                 1585                 1590

Val Phe  Cys Asp Gly Val Asn  Val Thr Lys His Lys  Cys Asp Ile
    1595                 1600                 1605

Asn Tyr  Lys Gly Lys Val Phe  Phe Gln Phe Asp Asn  Leu Ser Ser
    1610                 1615                 1620

Glu Asp  Leu Lys Ala Val Arg  Ser Ser Phe Asn Phe  Asp Gln Lys
    1625                 1630                 1635

Glu Leu  Leu Ala Tyr Tyr Asn  Met Leu Val Asn Cys  Phe Lys Trp
    1640                 1645                 1650

Gln Val  Val Val Asn Gly Lys  Tyr Phe Thr Phe Lys  Gln Ala Asn
    1655                 1660                 1665

Asn Asn  Cys Phe Val Asn Val  Ser Cys Leu Met Leu  Gln Ser Leu
    1670                 1675                 1680

His Leu  Thr Phe Lys Ile Val  Gln Trp Gln Glu Ala  Trp Leu Glu
    1685                 1690                 1695

Phe Arg  Ser Gly Arg Pro Ala  Arg Phe Val Ala Leu  Val Leu Ala
    1700                 1705                 1710

Lys Gly  Gly Phe Lys Phe Gly  Asp Pro Ala Asp Ser  Arg Asp Phe
    1715                 1720                 1725

Leu Arg  Val Val Phe Ser Gln  Val Asp Leu Thr Gly  Ala Ile Cys
    1730                 1735                 1740

Asp Phe  Glu Ile Ala Cys Lys  Cys Gly Val Lys Gln  Glu Gln Arg
    1745                 1750                 1755

Thr Gly  Leu Asp Ala Val Met  His Phe Gly Thr Leu  Ser Arg Glu
    1760                 1765                 1770

Asp Leu  Glu Ile Gly Tyr Thr  Val Asp Cys Ser Cys  Gly Lys Lys
    1775                 1780                 1785

Leu Ile  His Cys Val Arg Phe  Asp Val Pro Phe Leu  Ile Cys Ser
    1790                 1795                 1800
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Asn Thr  Pro Ala Ser Val Lys  Leu Pro Lys Gly Val  Gly Ser Ala
    1805                 1810                 1815

Asn Ile  Phe Ile Gly Asp Lys  Val Gly His Tyr Val  His Val Lys
    1820                 1825                 1830

Cys Glu  Gln Ser Tyr Gln Leu  Tyr Asp Ala Ser Asn  Val Lys Lys
    1835                 1840                 1845

Val Thr  Asp Val Thr Gly Lys  Leu Ser Asp Cys Leu  Tyr Leu Lys
    1850                 1855                 1860

Asn Leu  Lys Gln Thr Phe Lys  Ser Val Leu Thr Thr  Tyr Tyr Leu
    1865                 1870                 1875

Asp Asp  Val Lys Lys Ile Glu  Tyr Lys Pro Asp Leu  Ser Gln Tyr
    1880                 1885                 1890

Tyr Cys  Asp Gly Gly Lys Tyr  Tyr Thr Gln Arg Ile  Ile Lys Ala
    1895                 1900                 1905

Gln Phe  Lys Thr Phe Glu Lys  Val Asp Gly Val Tyr  Thr Asn Phe
    1910                 1915                 1920

Lys Leu  Ile Gly His Thr Val  Cys Asp Ser Leu Asn  Ala Lys Leu
    1925                 1930                 1935

Gly Phe  Asp Ser Ser Lys Glu  Phe Val Glu Tyr Lys  Ile Thr Glu
    1940                 1945                 1950

Trp Pro  Thr Ala Thr Gly Asp  Val Val Leu Ala Thr  Asp Asp Leu
    1955                 1960                 1965

Tyr Val  Lys Arg Tyr Glu Arg  Gly Cys Ile Thr Phe  Gly Lys Pro
    1970                 1975                 1980

Val Ile  Trp Leu Ser His Glu  Lys Ala Ser Leu Asn  Ser Leu Thr
    1985                 1990                 1995

Tyr Phe  Asn Arg Pro Ser Leu  Val Asp Asp Asn Lys  Phe Asp Val
    2000                 2005                 2010

Leu Lys  Val Asp Asp Val Asp  Asp Gly Gly Asp Ser  Ser Glu Ser
    2015                 2020                 2025

Gly Ala  Lys Glu Thr Lys Glu  Ile Asn Ile Ile Lys  Leu Ser Gly
    2030                 2035                 2040

Val Lys  Lys Pro Phe Lys Val  Glu Asp Ser Val Ile  Val Asn Asp
    2045                 2050                 2055

Asp Thr  Ser Glu Thr Lys Tyr  Val Lys Ser Leu Ser  Ile Val Asp
    2060                 2065                 2070

Val Tyr  Asp Met Trp Leu Thr  Gly Cys Lys Tyr Val  Val Arg Thr
    2075                 2080                 2085

Ala Asn  Ala Leu Ser Arg Ala  Val Asn Val Pro Thr  Ile Arg Lys
    2090                 2095                 2100

Phe Ile  Lys Phe Gly Met Thr  Leu Val Ser Ile Pro  Ile Asp Leu
    2105                 2110                 2115

Leu Asn  Leu Arg Glu Ile Lys  Pro Ala Val Asn Val  Val Lys Ala
    2120                 2125                 2130

Val Arg  Asn Lys Ile Ser Val  Cys Phe Asn Phe Ile  Lys Trp Leu
    2135                 2140                 2145

Phe Val  Leu Leu Phe Gly Trp  Ile Lys Ile Ser Ala  Asp Asn Lys
    2150                 2155                 2160

Val Ile  Tyr Thr Thr Glu Ile  Ala Ser Lys Leu Thr  Cys Lys Leu
    2165                 2170                 2175

Val Ala  Leu Ala Phe Lys Asn  Ala Phe Leu Thr Phe  Lys Trp Ser
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    2180                2185                2190

Met Val  Ala Arg Gly Ala Cys  Ile Ile Ala Thr Ile  Phe Leu Leu
    2195                2200                2205

Trp Phe  Asn Phe Ile Tyr Ala  Asn Val Ile Phe Ser  Asp Phe Tyr
    2210                2215                2220

Leu Pro  Lys Ile Gly Phe Leu  Pro Thr Phe Val Gly  Lys Ile Ala
    2225                2230                2235

Gln Trp  Ile Lys Asn Thr Phe  Ser Leu Val Thr Ile  Cys Asp Leu
    2240                2245                2250

Tyr Ser  Ile Gln Asp Val Gly  Phe Lys Asn Gln Tyr  Cys Asn Gly
    2255                2260                2265

Ser Ile  Ala Cys Gln Phe Cys  Leu Ala Gly Phe Asp  Met Leu Asp
    2270                2275                2280

Asn Tyr  Lys Ala Ile Asp Val  Val Gln Tyr Glu Ala  Asp Arg Arg
    2285                2290                2295

Ala Phe  Val Asp Tyr Thr Gly  Val Leu Lys Ile Val  Ile Glu Leu
    2300                2305                2310

Ile Val  Ser Tyr Ala Leu Tyr  Thr Ala Trp Phe Tyr  Pro Leu Phe
    2315                2320                2325

Ala Leu  Ile Ser Ile Gln Ile  Leu Thr Thr Trp Leu  Pro Glu Leu
    2330                2335                2340

Phe Met  Leu Ser Thr Leu His  Trp Ser Phe Arg Leu  Leu Val Ala
    2345                2350                2355

Leu Ala  Asn Met Leu Pro Ala  His Val Phe Met Arg  Phe Tyr Ile
    2360                2365                2370

Ile Ile  Ala Ser Phe Ile Lys  Leu Phe Ser Leu Phe  Arg His Val
    2375                2380                2385

Ala Tyr  Gly Cys Ser Lys Ser  Gly Cys Leu Phe Cys  Tyr Lys Arg
    2390                2395                2400

Asn Arg  Ser Leu Arg Val Lys  Cys Ser Thr Ile Val  Gly Gly Met
    2405                2410                2415

Ile Arg  Tyr Tyr Asp Val Met  Ala Asn Gly Gly Thr  Gly Phe Cys
    2420                2425                2430

Ser Lys  His Gln Trp Asn Cys  Ile Asp Cys Asp Ser  Tyr Lys Pro
    2435                2440                2445

Gly Asn  Thr Phe Ile Thr Val  Glu Ala Ala Leu Asp  Leu Ser Lys
    2450                2455                2460

Glu Leu  Lys Arg Pro Ile Gln  Pro Thr Asp Val Ala  Tyr His Thr
    2465                2470                2475

Val Thr  Asp Val Lys Gln Val  Gly Cys Ser Met Arg  Leu Phe Tyr
    2480                2485                2490

Asp Arg  Asp Gly Gln Arg Thr  Tyr Asp Asp Val Asn  Ala Ser Leu
    2495                2500                2505

Phe Val  Asp Tyr Ser Asn Leu  Leu His Ser Lys Val  Lys Ser Val
    2510                2515                2520

Pro Asn  Met His Val Val Val  Val Glu Asn Asp Ala  Asp Lys Ala
    2525                2530                2535

Asn Phe  Leu Asn Ala Ala Val  Phe Tyr Ala Gln Ser  Leu Phe Arg
    2540                2545                2550

Pro Ile  Leu Met Val Asp Lys  Asn Leu Ile Thr Thr  Ala Asn Thr
    2555                2560                2565
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Gly Thr  Ser Val Thr Glu Thr  Met Phe Asp Val Tyr  Val Asp Thr
    2570                 2575                 2580

Phe Leu  Ser Met Phe Asp Val  Asp Lys Lys Ser Leu  Asn Ala Leu
    2585                 2590                 2595

Ile Ala  Thr Ala His Ser Ser  Ile Lys Gln Gly Thr  Gln Ile Tyr
    2600                 2605                 2610

Lys Val  Leu Asp Thr Phe Leu  Ser Cys Ala Arg Lys  Ser Cys Ser
    2615                 2620                 2625

Ile Asp  Ser Asp Val Asp Thr  Lys Cys Leu Ala Asp  Ser Val Met
    2630                 2635                 2640

Ser Ala  Val Ser Ala Gly Leu  Glu Leu Thr Asp Glu  Ser Cys Asn
    2645                 2650                 2655

Asn Leu  Val Pro Thr Tyr Leu  Lys Ser Asp Asn Ile  Val Ala Ala
    2660                 2665                 2670

Asp Leu  Gly Val Leu Ile Gln  Asn Ser Ala Lys His  Val Gln Gly
    2675                 2680                 2685

Asn Val  Ala Lys Ile Ala Gly  Val Ser Cys Ile Trp  Ser Val Asp
    2690                 2695                 2700

Ala Phe  Asn Gln Phe Ser Ser  Asp Phe Gln His Lys  Leu Lys Lys
    2705                 2710                 2715

Ala Cys  Cys Lys Thr Gly Leu  Lys Leu Lys Leu Thr  Tyr Asn Lys
    2720                 2725                 2730

Gln Met  Ala Asn Val Ser Val  Leu Thr Thr Pro Phe  Ser Leu Lys
    2735                 2740                 2745

Gly Gly  Ala Val Phe Ser Tyr  Phe Val Tyr Val Cys  Phe Val Leu
    2750                 2755                 2760

Ser Leu  Val Cys Phe Ile Gly  Leu Trp Cys Leu Met  Pro Thr Tyr
    2765                 2770                 2775

Thr Val  His Lys Ser Asp Phe  Gln Leu Pro Val Tyr  Ala Ser Tyr
    2780                 2785                 2790

Lys Val  Leu Asp Asn Gly Val  Ile Arg Asp Val Ser  Val Glu Asp
    2795                 2800                 2805

Val Cys  Phe Ala Asn Lys Phe  Glu Gln Phe Asp Gln  Trp Tyr Glu
    2810                 2815                 2820

Ser Thr  Phe Gly Leu Ser Tyr  Tyr Ser Asn Ser Met  Ala Cys Pro
    2825                 2830                 2835

Ile Val  Val Ala Val Ile Asp  Gln Asp Phe Gly Ser  Thr Val Phe
    2840                 2845                 2850

Asn Val  Pro Thr Lys Val Leu  Arg Tyr Gly Tyr His  Val Leu His
    2855                 2860                 2865

Phe Ile  Thr His Ala Leu Ser  Ala Asp Gly Val Gln  Cys Tyr Thr
    2870                 2875                 2880

Pro His  Ser Gln Ile Ser Tyr  Ser Asn Phe Tyr Ala  Ser Gly Cys
    2885                 2890                 2895

Val Leu  Ser Ser Ala Cys Thr  Met Phe Thr Met Ala  Asp Gly Ser
    2900                 2905                 2910

Pro Gln  Pro Tyr Cys Tyr Thr  Glu Gly Leu Met Gln  Asn Ala Ser
    2915                 2920                 2925

Leu Tyr  Ser Ser Leu Val Pro  His Val Arg Tyr Asn  Leu Ala Asn
    2930                 2935                 2940
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Ala Lys  Gly Phe Ile Arg Phe  Pro Glu Val Leu Arg  Glu Gly Leu
    2945                 2950                 2955

Val Arg  Ile Val Arg Thr Arg  Ser Met Ser Tyr Cys  Arg Val Gly
    2960                 2965                 2970

Leu Cys  Glu Glu Ala Asp Glu  Gly Ile Cys Phe Asn  Phe Asn Gly
    2975                 2980                 2985

Ser Trp  Val Leu Asn Asn Asp  Tyr Tyr Arg Ser Leu  Pro Gly Thr
    2990                 2995                 3000

Phe Cys  Gly Arg Asp Val Phe  Asp Leu Ile Tyr Gln  Leu Phe Lys
    3005                 3010                 3015

Gly Leu  Ala Gln Pro Val Asp  Phe Leu Ala Leu Thr  Ala Ser Ser
    3020                 3025                 3030

Ile Ala  Gly Ala Ile Leu Ala  Val Ile Val Val Leu  Val Phe Tyr
    3035                 3040                 3045

Tyr Leu  Ile Lys Leu Lys Arg  Ala Phe Gly Asp Tyr  Thr Ser Val
    3050                 3055                 3060

Val Phe  Val Asn Val Ile Val  Trp Cys Val Asn Phe  Met Met Leu
    3065                 3070                 3075

Phe Val  Phe Gln Val Tyr Pro  Ile Leu Ser Cys Val  Tyr Ala Ile
    3080                 3085                 3090

Cys Tyr  Phe Tyr Ala Thr Leu  Tyr Phe Pro Ser Glu  Ile Ser Val
    3095                 3100                 3105

Ile Met  His Leu Gln Trp Leu  Val Met Tyr Gly Thr  Ile Met Pro
    3110                 3115                 3120

Leu Trp  Phe Cys Leu Leu Tyr  Ile Ala Val Val Val  Ser Asn His
    3125                 3130                 3135

Ala Phe  Trp Val Phe Ser Tyr  Cys Arg Lys Leu Gly  Thr Ser Val
    3140                 3145                 3150

Arg Ser  Asp Gly Thr Phe Glu  Glu Met Ala Leu Thr  Thr Phe Met
    3155                 3160                 3165

Ile Thr  Lys Asp Ser Tyr Cys  Lys Leu Lys Asn Ser  Leu Ser Asp
    3170                 3175                 3180

Val Ala  Phe Asn Arg Tyr Leu  Ser Leu Tyr Asn Lys  Tyr Arg Tyr
    3185                 3190                 3195

Tyr Ser  Gly Lys Met Asp Thr  Ala Ala Tyr Arg Glu  Ala Ala Cys
    3200                 3205                 3210

Ser Gln  Leu Ala Lys Ala Met  Asp Thr Phe Thr Asn  Asn Asn Gly
    3215                 3220                 3225

Ser Asp  Val Leu Tyr Gln Pro  Pro Thr Ala Ser Val  Ser Thr Ser
    3230                 3235                 3240

Phe Leu  Gln Ser Gly Ile Val  Lys Met Val Asn Pro  Thr Ser Lys
    3245                 3250                 3255

Val Glu  Pro Cys Val Val Ser  Val Thr Tyr Gly Asn  Met Thr Leu
    3260                 3265                 3270

Asn Gly  Leu Trp Leu Asp Asp  Lys Val Tyr Cys Pro  Arg His Val
    3275                 3280                 3285

Ile Cys  Ser Ala Ser Asp Met  Thr Asn Pro Asp Tyr  Thr Asn Leu
    3290                 3295                 3300

Leu Cys  Arg Val Thr Ser Ser  Asp Phe Thr Val Leu  Phe Asp Arg
    3305                 3310                 3315

Leu Ser  Leu Thr Val Met Ser  Tyr Gln Met Arg Gly  Cys Met Leu
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    3320                3325                3330

Val Leu  Thr Val Thr Leu Gln  Asn Ser Arg Thr Pro  Lys Tyr Thr
    3335                3340                3345

Phe Gly  Val Val Lys Pro Gly  Glu Thr Phe Thr Val  Leu Ala Ala
    3350                3355                3360

Tyr Asn  Gly Lys Pro Gln Gly  Ala Phe His Val Thr  Met Arg Ser
    3365                3370                3375

Ser Tyr  Thr Ile Lys Gly Ser  Phe Leu Cys Gly Ser  Cys Gly Ser
    3380                3385                3390

Val Gly  Tyr Val Ile Met Gly  Asp Cys Val Lys Phe  Val Tyr Met
    3395                3400                3405

His Gln  Leu Glu Leu Ser Thr  Gly Cys His Thr Gly  Thr Asp Phe
    3410                3415                3420

Asn Gly  Asp Phe Tyr Gly Pro  Tyr Lys Asp Ala Gln  Val Val Gln
    3425                3430                3435

Leu Leu  Ile Gln Asp Tyr Ile  Gln Ser Val Asn Phe  Val Ala Trp
    3440                3445                3450

Leu Tyr  Ala Ala Ile Leu Asn  Asn Cys Asn Trp Phe  Val Gln Ser
    3455                3460                3465

Asp Lys  Cys Ser Val Glu Asp  Phe Asn Val Trp Ala  Leu Ser Asn
    3470                3475                3480

Gly Phe  Ser Gln Val Lys Ser  Asp Leu Val Ile Asp  Ala Leu Ala
    3485                3490                3495

Ser Met  Thr Gly Val Ser Leu  Glu Thr Leu Leu Ala  Ala Ile Lys
    3500                3505                3510

Arg Leu  Lys Asn Gly Phe Gln  Gly Arg Gln Ile Met  Gly Ser Cys
    3515                3520                3525

Ser Phe  Glu Asp Glu Leu Thr  Pro Ser Asp Val Tyr  Gln Gln Leu
    3530                3535                3540

Ala Gly  Ile Lys Leu Gln Ser  Lys Arg Thr Arg Leu  Phe Lys Gly
    3545                3550                3555

Thr Val  Cys Trp Ile Met Ala  Ser Thr Phe Leu Phe  Ser Cys Ile
    3560                3565                3570

Ile Thr  Ala Phe Val Lys Trp  Thr Met Phe Met Tyr  Val Thr Thr
    3575                3580                3585

Asn Met  Phe Ser Ile Thr Phe  Cys Ala Leu Cys Val  Ile Ser Leu
    3590                3595                3600

Ala Met  Leu Leu Val Lys His  Lys His Leu Tyr Leu  Thr Met Tyr
    3605                3610                3615

Ile Thr  Pro Val Leu Phe Thr  Leu Leu Tyr Asn Asn  Tyr Leu Val
    3620                3625                3630

Val Tyr  Lys His Thr Phe Arg  Gly Tyr Val Tyr Ala  Trp Leu Ser
    3635                3640                3645

Tyr Tyr  Val Pro Ser Val Glu  Tyr Thr Tyr Thr Asp  Glu Val Ile
    3650                3655                3660

Tyr Gly  Met Leu Leu Leu Val  Gly Met Val Phe Val  Thr Leu Arg
    3665                3670                3675

Ser Ile  Asn His Asp Leu Phe  Ser Phe Ile Met Phe  Val Gly Arg
    3680                3685                3690

Leu Ile  Ser Val Phe Ser Leu  Trp Tyr Lys Gly Ser  Asn Leu Glu
    3695                3700                3705
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Glu Glu  Ile Leu Leu Met Leu  Ala Ser Leu Phe Gly  Thr Tyr Thr
    3710                 3715                 3720

Trp Thr  Thr Val Leu Ser Met  Ala Val Ala Lys Val  Ile Ala Lys
    3725                 3730                 3735

Trp Val  Ala Val Asn Val Leu  Tyr Phe Thr Asp Ile  Pro Gln Ile
    3740                 3745                 3750

Lys Ile  Val Leu Leu Cys Tyr  Leu Phe Ile Gly Tyr  Ile Ile Ser
    3755                 3760                 3765

Cys Tyr  Trp Gly Leu Phe Ser  Leu Met Asn Ser Leu  Phe Arg Met
    3770                 3775                 3780

Pro Leu  Gly Val Tyr Asn Tyr  Lys Ile Ser Val Gln  Glu Leu Arg
    3785                 3790                 3795

Tyr Met  Asn Ala Asn Gly Leu  Arg Pro Pro Lys Asn  Ser Phe Glu
    3800                 3805                 3810

Ala Leu  Met Leu Asn Phe Lys  Leu Leu Gly Ile Gly  Gly Val Pro
    3815                 3820                 3825

Ile Ile  Glu Val Ser Gln Phe  Gln Ser Lys Leu Thr  Asp Val Lys
    3830                 3835                 3840

Cys Ala  Asn Val Val Leu Leu  Asn Cys Leu Gln His  Leu His Val
    3845                 3850                 3855

Ala Ser  Asn Ser Lys Leu Trp  His Tyr Cys Ser Thr  Leu His Asn
    3860                 3865                 3870

Glu Ile  Leu Ala Thr Ser Asp  Leu Ser Val Ala Phe  Glu Lys Leu
    3875                 3880                 3885

Ala Gln  Leu Leu Ile Val Leu  Phe Ala Asn Pro Ala  Ala Val Asp
    3890                 3895                 3900

Ser Lys  Cys Leu Thr Ser Ile  Glu Glu Val Cys Asp  Asp Tyr Ala
    3905                 3910                 3915

Lys Asp  Asn Thr Val Leu Gln  Ala Leu Gln Ser Glu  Phe Val Asn
    3920                 3925                 3930

Met Ala  Ser Phe Val Glu Tyr  Glu Val Ala Lys Lys  Asn Leu Asp
    3935                 3940                 3945

Glu Ala  Arg Phe Ser Gly Ser  Ala Asn Gln Gln Gln  Leu Lys Gln
    3950                 3955                 3960

Leu Glu  Lys Ala Cys Asn Ile  Ala Lys Ser Ala Tyr  Glu Arg Asp
    3965                 3970                 3975

Arg Ala  Val Ala Lys Lys Leu  Glu Arg Met Ala Asp  Leu Ala Leu
    3980                 3985                 3990

Thr Asn  Met Tyr Lys Glu Ala  Arg Ile Asn Asp Lys  Lys Ser Lys
    3995                 4000                 4005

Val Val  Ser Ala Leu Gln Thr  Met Leu Phe Ser Met  Val Arg Lys
    4010                 4015                 4020

Leu Asp  Asn Gln Ala Leu Asn  Ser Ile Leu Asp Asn  Ala Val Lys
    4025                 4030                 4035

Gly Cys  Val Pro Leu Asn Ala  Ile Pro Ser Leu Ala  Ala Asn Thr
    4040                 4045                 4050

Leu Asn  Ile Ile Val Pro Asp  Lys Ser Val Tyr Asp  Gln Val Val
    4055                 4060                 4065

Asp Asn  Val Tyr Val Thr Tyr  Ala Gly Asn Val Trp  Gln Ile Gln
    4070                 4075                 4080
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Thr Ile  Gln Asp Ser Asp Gly  Thr Asn Lys Gln Leu  Asn Glu Ile
    4085                 4090                 4095

Ser Asp  Asp Cys Asn Trp Pro  Leu Val Ile Ile Ala  Asn Arg Tyr
    4100                 4105                 4110

Asn Glu  Val Ser Ala Thr Val  Leu Gln Asn Asn Glu  Leu Met Pro
    4115                 4120                 4125

Ala Lys  Leu Lys Ile Gln Val  Val Asn Ser Gly Pro  Asp Gln Thr
    4130                 4135                 4140

Cys Asn  Thr Pro Thr Gln Cys  Tyr Tyr Asn Asn Ser  Asn Asn Gly
    4145                 4150                 4155

Lys Ile  Val Tyr Ala Ile Leu  Ser Asp Val Asp Gly  Leu Lys Tyr
    4160                 4165                 4170

Thr Lys  Ile Leu Lys Asp Asp  Gly Asn Phe Val Val  Leu Glu Leu
    4175                 4180                 4185

Asp Pro  Pro Cys Lys Phe Thr  Val Gln Asp Ala Lys  Gly Leu Lys
    4190                 4195                 4200

Ile Lys  Tyr Leu Tyr Phe Val  Lys Gly Cys Asn Thr  Leu Ala Arg
    4205                 4210                 4215

Gly Trp  Val Val Gly Thr Ile  Ser Ser Thr Val Arg  Leu Gln Ala
    4220                 4225                 4230

Gly Thr  Ala Thr Glu Tyr Ala  Ser Asn Ser Ser Ile  Leu Ser Leu
    4235                 4240                 4245

Cys Ala  Phe Ser Val Asp Pro  Lys Lys Thr Tyr Leu  Asp Phe Ile
    4250                 4255                 4260

Gln Gln  Gly Gly Thr Pro Ile  Ala Asn Cys Val Lys  Met Leu Cys
    4265                 4270                 4275

Asp His  Ala Gly Thr Gly Met  Ala Ile Thr Val Lys  Pro Asp Ala
    4280                 4285                 4290

Thr Thr  Ser Gln Asp Ser Tyr  Gly Gly Ala Ser Val  Cys Ile Tyr
    4295                 4300                 4305

Cys Arg  Ala Arg Val Glu His  Pro Asp Val Asp Gly  Leu Cys Lys
    4310                 4315                 4320

Leu Arg  Gly Lys Phe Val Gln  Val Pro Val Gly Ile  Lys Asp Pro
    4325                 4330                 4335

Val Ser  Tyr Val Leu Thr His  Asp Val Cys Arg Val  Cys Gly Phe
    4340                 4345                 4350

Trp Arg  Asp Gly Ser Cys Ser  Cys Val Ser Thr Asp  Thr Thr Val
    4355                 4360                 4365

Gln Ser  Lys Asp Thr Asn Phe  Leu Asn Arg Val Arg  Gly Thr Ser
    4370                 4375                 4380

Val Asp  Ala Arg Leu Val Pro  Cys Ala Ser Gly Leu  Ser Thr Asp
    4385                 4390                 4395

Val Gln  Leu Arg Ala Phe Asp  Ile Tyr Asn Ala Ser  Val Ala Gly
    4400                 4405                 4410

Ile Gly  Leu His Leu Lys Val  Asn Cys Cys Arg Phe  Gln Arg Val
    4415                 4420                 4425

Asp Glu  Asn Gly Asp Lys Leu  Asp Gln Phe Phe Val  Val Lys Arg
    4430                 4435                 4440

Thr Asp  Leu Thr Ile Tyr Asn  Arg Glu Met Lys Cys  Tyr Glu Arg
    4445                 4450                 4455

Val Lys  Asp Cys Lys Phe Val  Ala Glu His Asp Phe  Phe Thr Phe
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    4460                4465                4470

Asp Val  Glu Gly Ser Arg Val  Pro His Ile Val Arg  Lys Asp Leu
    4475                4480                4485

Thr Lys  Tyr Thr Met Leu Asp  Leu Cys Tyr Ala Leu  Arg His Phe
    4490                4495                4500

Asp Arg  Asn Asp Cys Met Leu  Leu Cys Asp Ile Leu  Ser Ile Tyr
    4505                4510                4515

Ala Gly  Cys Glu Gln Ser Tyr  Phe Thr Lys Lys Asp  Trp Tyr Asp
    4520                4525                4530

Phe Val  Glu Asn Pro Asp Ile  Ile Asn Val Tyr Lys  Lys Leu Gly
    4535                4540                4545

Pro Ile  Phe Asn Arg Ala Leu  Val Ser Ala Thr Glu  Phe Ala Asp
    4550                4555                4560

Lys Leu  Val Glu Val Gly Leu  Val Gly Val Leu Thr  Leu Asp Asn
    4565                4570                4575

Gln Asp  Leu Asn Gly Lys Trp  Tyr Asp Phe Gly Asp  Tyr Val Ile
    4580                4585                4590

Ala Ala  Pro Gly Cys Gly Val  Ala Ile Ala Asp Ser  Tyr Tyr Ser
    4595                4600                4605

Tyr Ile  Met Pro Met Leu Thr  Met Cys His Ala Leu  Asp Cys Glu
    4610                4615                4620

Leu Tyr  Val Asn Asn Ala Tyr  Arg Leu Phe Asp Leu  Val Gln Tyr
    4625                4630                4635

Asp Phe  Thr Asp Tyr Lys Leu  Glu Leu Phe Asn Lys  Tyr Phe Lys
    4640                4645                4650

His Trp  Ser Met Pro Tyr His  Pro Asn Thr Val Asp  Cys Gln Asp
    4655                4660                4665

Asp Arg  Cys Ile Ile His Cys  Ala Asn Phe Asn Ile  Leu Phe Ser
    4670                4675                4680

Met Val  Leu Pro Asn Thr Cys  Phe Gly Pro Leu Val  Arg Gln Ile
    4685                4690                4695

Phe Val  Asp Gly Val Pro Phe  Val Val Ser Ile Gly  Tyr His Tyr
    4700                4705                4710

Lys Glu  Leu Gly Ile Val Met  Asn Met Asp Val Asp  Thr His Arg
    4715                4720                4725

Tyr Arg  Leu Ser Leu Lys Asp  Leu Leu Leu Tyr Ala  Ala Asp Pro
    4730                4735                4740

Ala Leu  His Val Ala Ser Ala  Ser Ala Leu Tyr Asp  Leu Arg Thr
    4745                4750                4755

Cys Cys  Phe Ser Val Ala Ala  Ile Thr Ser Gly Val  Lys Phe Gln
    4760                4765                4770

Thr Val  Lys Pro Gly Asn Phe  Asn Gln Asp Phe Tyr  Asp Phe Val
    4775                4780                4785

Leu Ser  Lys Gly Leu Leu Lys  Glu Gly Ser Ser Val  Asp Leu Lys
    4790                4795                4800

His Phe  Phe Phe Thr Gln Asp  Gly Asn Ala Ala Ile  Thr Asp Tyr
    4805                4810                4815

Asn Tyr  Tyr Lys Tyr Asn Leu  Pro Thr Met Val Asp  Ile Lys Gln
    4820                4825                4830

Leu Leu  Phe Val Leu Glu Val  Val Tyr Lys Tyr Phe  Glu Ile Tyr
    4835                4840                4845
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Asp Gly  Gly Cys Ile Pro Ala  Ser Gln Val Ile Val  Asn Asn Tyr
    4850                 4855                 4860

Asp Lys  Ser Ala Gly Tyr Pro  Phe Asn Lys Phe Gly  Lys Ala Arg
    4865                 4870                 4875

Leu Tyr  Tyr Glu Ala Leu Ser  Phe Glu Glu Gln Asp  Glu Ile Tyr
    4880                 4885                 4890

Ala Tyr  Thr Lys Arg Asn Val  Leu Pro Thr Leu Thr  Gln Met Asn
    4895                 4900                 4905

Leu Lys  Tyr Ala Ile Ser Ala  Lys Asn Arg Ala Arg  Thr Val Ala
    4910                 4915                 4920

Gly Val  Ser Ile Leu Ser Thr  Met Thr Gly Arg Met  Phe His Gln
    4925                 4930                 4935

Lys Cys  Leu Lys Ser Ile Ala  Ala Thr Arg Gly Val  Pro Val Val
    4940                 4945                 4950

Ile Gly  Thr Thr Lys Phe Tyr  Gly Gly Trp Asp Asp  Met Leu Arg
    4955                 4960                 4965

Arg Leu  Ile Lys Asp Val Asp  Asn Pro Val Leu Met  Gly Trp Asp
    4970                 4975                 4980

Tyr Pro  Lys Cys Asp Arg Ala  Met Pro Asn Leu Leu  Arg Ile Val
    4985                 4990                 4995

Ser Ser  Leu Val Leu Ala Arg  Lys His Glu Thr Cys  Cys Ser Gln
    5000                 5005                 5010

Ser Asp  Arg Phe Tyr Arg Leu  Ala Asn Glu Cys Ala  Gln Val Leu
    5015                 5020                 5025

Ser Glu  Ile Val Met Cys Gly  Gly Cys Tyr Tyr Val  Lys Pro Gly
    5030                 5035                 5040

Gly Thr  Ser Ser Gly Asp Ala  Thr Thr Ala Phe Ala  Asn Ser Val
    5045                 5050                 5055

Phe Asn  Ile Cys Gln Ala Val  Ser Ala Asn Val Cys  Ala Leu Met
    5060                 5065                 5070

Ser Cys  Asn Gly Asn Lys Ile  Glu Asp Leu Ser Ile  Arg Ala Leu
    5075                 5080                 5085

Gln Lys  Arg Leu Tyr Ser His  Val Tyr Arg Ser Asp  Lys Val Asp
    5090                 5095                 5100

Ser Thr  Phe Val Thr Glu Tyr  Tyr Glu Phe Leu Asn  Lys His Phe
    5105                 5110                 5115

Ser Met  Met Ile Leu Ser Asp  Asp Gly Val Val Cys  Tyr Asn Ser
    5120                 5125                 5130

Asp Tyr  Ala Ser Lys Gly Tyr  Ile Ala Asn Ile Ser  Ala Phe Gln
    5135                 5140                 5145

Gln Val  Leu Tyr Tyr Gln Asn  Asn Val Phe Met Ser  Glu Ser Lys
    5150                 5155                 5160

Cys Trp  Val Glu His Asp Ile  Asn Asn Gly Pro His  Glu Phe Cys
    5165                 5170                 5175

Ser Gln  His Thr Met Leu Val  Lys Met Asp Gly Asp  Asp Val Tyr
    5180                 5185                 5190

Leu Pro  Tyr Pro Asn Pro Ser  Arg Ile Leu Gly Ala  Gly Cys Phe
    5195                 5200                 5205

Val Asp  Asp Leu Leu Lys Thr  Asp Ser Val Leu Leu  Ile Glu Arg
    5210                 5215                 5220
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Phe Val  Ser Leu Ala Ile Asp  Ala Tyr Pro Leu Val  Tyr His Glu
    5225                 5230                 5235

Asn Glu  Glu Tyr Gln Lys Val  Phe Arg Val Tyr Leu  Ala Tyr Ile
    5240                 5245                 5250

Lys Lys  Leu Tyr Asn Asp Leu  Gly Asn Gln Ile Leu  Asp Ser Tyr
    5255                 5260                 5265

Ser Val  Ile Leu Ser Thr Cys  Asp Gly Gln Lys Phe  Thr Asp Glu
    5270                 5275                 5280

Ser Phe  Tyr Lys Asn Met Tyr  Leu Arg Ser Ala Val  Met Gln Ser
    5285                 5290                 5295

Val Gly  Ala Cys Val Val Cys  Ser Ser Gln Thr Ser  Leu Arg Cys
    5300                 5305                 5310

Gly Ser  Cys Ile Arg Lys Pro  Leu Leu Cys Cys Lys  Cys Cys Tyr
    5315                 5320                 5325

Asp His  Val Met Ala Thr Asp  His Lys Tyr Val Leu  Ser Val Ser
    5330                 5335                 5340

Pro Tyr  Val Cys Asn Ala Pro  Gly Cys Asp Val Asn  Asp Val Thr
    5345                 5350                 5355

Lys Leu  Tyr Leu Gly Gly Met  Ser Tyr Tyr Cys Glu  Asp His Lys
    5360                 5365                 5370

Pro Gln  Tyr Ser Phe Lys Leu  Val Met Asn Gly Leu  Val Phe Gly
    5375                 5380                 5385

Leu Tyr  Lys Gln Ser Cys Thr  Gly Ser Pro Tyr Ile  Asp Asp Phe
    5390                 5395                 5400

Asn Arg  Ile Ala Ser Cys Lys  Trp Thr Asp Val Asp  Asp Tyr Ile
    5405                 5410                 5415

Leu Ala  Asn Glu Cys Thr Glu  Arg Leu Lys Leu Phe  Ala Ala Glu
    5420                 5425                 5430

Thr Gln  Lys Ala Thr Glu Glu  Ala Phe Lys Gln Ser  Tyr Ala Ser
    5435                 5440                 5445

Ala Thr  Ile Gln Glu Ile Val  Ser Glu Arg Glu Leu  Ile Leu Ser
    5450                 5455                 5460

Trp Glu  Ile Gly Lys Val Lys  Pro Pro Leu Asn Lys  Asn Tyr Val
    5465                 5470                 5475

Phe Thr  Gly Tyr His Phe Thr  Lys Asn Gly Lys Thr  Val Leu Gly
    5480                 5485                 5490

Glu Tyr  Val Phe Asp Lys Ser  Glu Leu Thr Asn Gly  Val Tyr Tyr
    5495                 5500                 5505

Arg Ala  Thr Thr Thr Tyr Lys  Leu Ser Val Gly Asp  Val Phe Val
    5510                 5515                 5520

Leu Thr  Ser His Ser Val Ala  Asn Leu Ser Ala Pro  Thr Leu Val
    5525                 5530                 5535

Pro Gln  Glu Asn Tyr Ser Ser  Ile Arg Phe Ala Ser  Val Tyr Ser
    5540                 5545                 5550

Val Leu  Glu Thr Phe Gln Asn  Asn Val Val Asn Tyr  Gln His Ile
    5555                 5560                 5565

Gly Met  Lys Arg Tyr Cys Thr  Val Gln Gly Pro Pro  Gly Thr Gly
    5570                 5575                 5580

Lys Ser  His Leu Ala Ile Gly  Leu Ala Val Phe Tyr  Cys Thr Ala
    5585                 5590                 5595

Arg Val  Val Tyr Thr Ala Ala  Ser His Ala Ala Val  Asp Ala Leu
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    5600                5605                5610

Cys Glu  Lys Ala Tyr Lys Phe  Leu Asn Ile Asn Asp  Cys Thr Arg
    5615                5620                5625

Ile Val  Pro Ala Lys Val Arg  Val Glu Cys Tyr Asp  Lys Phe Lys
    5630                5635                5640

Ile Asn  Asp Thr Thr Arg Lys  Tyr Val Phe Thr Thr  Ile Asn Ala
    5645                5650                5655

Leu Pro  Glu Met Val Thr Asp  Ile Val Val Val Asp  Glu Val Ser
    5660                5665                5670

Met Leu  Thr Asn Tyr Glu Leu  Ser Val Ile Asn Ala  Arg Ile Arg
    5675                5680                5685

Ala Lys  His Tyr Val Tyr Ile  Gly Asp Pro Ala Gln  Leu Pro Ala
    5690                5695                5700

Pro Arg  Val Leu Leu Ser Lys  Gly Thr Leu Glu Pro  Lys Tyr Phe
    5705                5710                5715

Asn Thr  Val Thr Lys Leu Met  Cys Cys Leu Gly Pro  Asp Ile Phe
    5720                5725                5730

Leu Gly  Thr Cys Tyr Arg Cys  Pro Lys Glu Ile Val  Asp Thr Val
    5735                5740                5745

Ser Ala  Leu Val Tyr Glu Asn  Lys Leu Lys Ala Lys  Asn Glu Ser
    5750                5755                5760

Ser Ser  Leu Cys Phe Lys Val  Tyr Tyr Lys Gly Val  Thr Thr His
    5765                5770                5775

Glu Ser  Ser Ser Ala Val Asn  Met Gln Gln Ile Tyr  Leu Ile Asn
    5780                5785                5790

Lys Phe  Leu Lys Ala Asn Pro  Leu Trp His Lys Ala  Val Phe Ile
    5795                5800                5805

Ser Pro  Tyr Asn Ser Gln Asn  Phe Ala Ala Lys Arg  Val Leu Gly
    5810                5815                5820

Leu Gln  Thr Gln Thr Val Asp  Ser Ala Gln Gly Ser  Glu Tyr Asp
    5825                5830                5835

Tyr Val  Ile Tyr Ser Gln Thr  Ala Glu Thr Ala His  Ser Val Asn
    5840                5845                5850

Val Asn  Arg Phe Asn Val Ala  Ile Thr Arg Ala Lys  Lys Gly Ile
    5855                5860                5865

Leu Cys  Val Met Ser Asn Met  Gln Leu Phe Glu Ala  Leu Gln Phe
    5870                5875                5880

Thr Thr  Leu Thr Leu Asp Lys  Val Pro Gln Ala Val  Glu Thr Lys
    5885                5890                5895

Val Gln  Cys Ser Thr Asn Leu  Phe Lys Asp Cys Ser  Lys Ser Tyr
    5900                5905                5910

Ser Gly  Tyr His Pro Ala His  Ala Pro Ser Phe Leu  Ala Val Asp
    5915                5920                5925

Asp Lys  Tyr Lys Ala Thr Gly  Asp Leu Ala Val Cys  Leu Gly Ile
    5930                5935                5940

Gly Asp  Ser Ala Val Thr Tyr  Ser Arg Leu Ile Ser  Leu Met Gly
    5945                5950                5955

Phe Lys  Leu Asp Val Thr Leu  Asp Gly Tyr Cys Lys  Leu Phe Ile
    5960                5965                5970

Thr Lys  Glu Glu Ala Val Lys  Arg Val Arg Ala Trp  Val Gly Phe
    5975                5980                5985
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Asp Ala  Glu Gly Ala His Ala  Thr Arg Asp Ser Ile  Gly Thr Asn
    5990                 5995                 6000

Phe Pro  Leu Gln Leu Gly Phe  Ser Thr Gly Ile Asp  Phe Val Val
    6005                 6010                 6015

Glu Ala  Thr Gly Leu Phe Ala  Asp Arg Asp Gly Tyr  Ser Phe Lys
    6020                 6025                 6030

Lys Ala  Val Ala Lys Ala Pro  Pro Gly Glu Gln Phe  Lys His Leu
    6035                 6040                 6045

Ile Pro  Leu Met Thr Arg Gly  His Arg Trp Asp Val  Val Arg Pro
    6050                 6055                 6060

Arg Ile  Val Gln Met Phe Ala  Asp His Leu Ile Asp  Leu Ser Asp
    6065                 6070                 6075

Cys Val  Val Leu Val Thr Trp  Ala Ala Asn Phe Glu  Leu Thr Cys
    6080                 6085                 6090

Leu Arg  Tyr Phe Ala Lys Val  Gly Arg Glu Ile Ser  Cys Asn Val
    6095                 6100                 6105

Cys Thr  Lys Arg Ala Thr Val  Tyr Asn Ser Arg Thr  Gly Tyr Tyr
    6110                 6115                 6120

Gly Cys  Trp Arg His Ser Val  Thr Cys Asp Tyr Leu  Tyr Asn Pro
    6125                 6130                 6135

Leu Ile  Val Asp Ile Gln Gln  Trp Gly Tyr Ile Gly  Ser Leu Ser
    6140                 6145                 6150

Ser Asn  His Asp Leu Tyr Cys  Ser Val His Lys Gly  Ala His Val
    6155                 6160                 6165

Ala Ser  Ser Asp Ala Ile Met  Thr Arg Cys Leu Ala  Val Tyr Asp
    6170                 6175                 6180

Cys Phe  Cys Asn Asn Ile Asn  Trp Asn Val Glu Tyr  Pro Ile Ile
    6185                 6190                 6195

Ser Asn  Glu Leu Ser Ile Asn  Thr Ser Cys Arg Val  Leu Gln Arg
    6200                 6205                 6210

Val Ile  Leu Lys Ala Ala Met  Leu Cys Asn Arg Tyr  Thr Leu Cys
    6215                 6220                 6225

Tyr Asp  Ile Gly Asn Pro Lys  Ala Ile Ala Cys Val  Lys Asp Phe
    6230                 6235                 6240

Asp Phe  Lys Phe Tyr Asp Ala  Gln Pro Ile Val Lys  Ser Val Lys
    6245                 6250                 6255

Thr Leu  Leu Tyr Ser Phe Glu  Ala His Lys Asp Ser  Phe Lys Asp
    6260                 6265                 6270

Gly Leu  Cys Met Phe Trp Asn  Cys Asn Val Asp Lys  Tyr Pro Pro
    6275                 6280                 6285

Asn Ala  Val Val Cys Arg Phe  Asp Thr Arg Val Leu  Asn Asn Leu
    6290                 6295                 6300

Asn Leu  Pro Gly Cys Asn Gly  Gly Ser Leu Tyr Val  Asn Lys His
    6305                 6310                 6315

Ala Phe  His Thr Lys Pro Phe  Ala Arg Ala Ala Phe  Glu His Leu
    6320                 6325                 6330

Lys Pro  Met Pro Phe Phe Tyr  Tyr Ser Asp Thr Pro  Cys Val Tyr
    6335                 6340                 6345

Met Asp  Gly Met Asp Ala Lys  Gln Val Asp Tyr Val  Pro Leu Lys
    6350                 6355                 6360
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Ser Ala  Thr Cys Ile Thr Arg  Cys Asn Leu Gly Gly  Ala Val Cys
    6365                 6370                 6375

Leu Lys  His Ala Glu Glu Tyr  Arg Glu Tyr Leu Glu  Ser Tyr Asn
    6380                 6385                 6390

Thr Ala  Thr Thr Ala Gly Phe  Thr Phe Trp Val Tyr  Lys Thr Phe
    6395                 6400                 6405

Asp Phe  Tyr Asn Leu Trp Asn  Thr Phe Thr Lys Leu  Gln Ser Leu
    6410                 6415                 6420

Glu Asn  Val Val Tyr Asn Leu  Val Lys Thr Gly His  Tyr Thr Gly
    6425                 6430                 6435

Gln Ala  Gly Glu Met Pro Cys  Ala Ile Ile Asn Asp  Lys Val Val
    6440                 6445                 6450

Ala Lys  Ile Asp Lys Glu Asp  Val Val Ile Phe Ile  Asn Asn Thr
    6455                 6460                 6465

Thr Tyr  Pro Thr Asn Val Ala  Val Glu Leu Phe Ala  Lys Arg Ser
    6470                 6475                 6480

Val Arg  His His Pro Glu Leu  Lys Leu Phe Arg Asn  Leu Asn Ile
    6485                 6490                 6495

Asp Val  Cys Trp Lys His Val  Ile Trp Asp Tyr Ala  Arg Glu Ser
    6500                 6505                 6510

Ile Phe  Cys Ser Asn Thr Tyr  Gly Val Cys Met Tyr  Thr Asp Leu
    6515                 6520                 6525

Lys Phe  Ile Asp Lys Leu Asn  Val Leu Phe Asp Gly  Arg Asp Asn
    6530                 6535                 6540

Gly Ala  Leu Glu Ala Phe Lys  Arg Ser Asn Asn Gly  Val Tyr Ile
    6545                 6550                 6555

Ser Thr  Thr Lys Val Lys Ser  Leu Ser Met Ile Arg  Gly Pro Pro
    6560                 6565                 6570

Arg Ala  Glu Leu Asn Gly Val  Val Val Asp Lys Val  Gly Asp Thr
    6575                 6580                 6585

Asp Cys  Val Phe Tyr Phe Ala  Val Arg Lys Glu Gly  Gln Asp Val
    6590                 6595                 6600

Ile Phe  Ser Gln Phe Asp Ser  Leu Gly Val Ser Ser  Asn Gln Ser
    6605                 6610                 6615

Pro Gln  Gly Asn Leu Gly Ser  Asn Gly Lys Pro Gly  Asn Val Gly
    6620                 6625                 6630

Gly Asn  Asp Ala Leu Ser Ile  Ser Thr Ile Phe Thr  Gln Ser Arg
    6635                 6640                 6645

Val Ile  Ser Ser Phe Thr Cys  Arg Thr Asp Met Glu  Lys Asp Phe
    6650                 6655                 6660

Ile Ala  Leu Asp Gln Asp Val  Phe Ile Gln Lys Tyr  Gly Leu Glu
    6665                 6670                 6675

Asp Tyr  Ala Phe Glu His Ile  Val Tyr Gly Asn Phe  Asn Gln Lys
    6680                 6685                 6690

Ile Ile  Gly Gly Leu His Leu  Leu Ile Gly Leu Tyr  Arg Arg Gln
    6695                 6700                 6705

Gln Thr  Ser Asn Leu Val Val  Gln Glu Phe Val Ser  Tyr Asp Ser
    6710                 6715                 6720

Ser Ile  His Ser Tyr Phe Ile  Thr Asp Glu Lys Ser  Gly Gly Ser
    6725                 6730                 6735

Lys Ser  Val Cys Thr Val Ile  Asp Ile Leu Leu Asp  Asp Phe Val
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    6740                6745                6750

Ala Leu  Val Lys Ser Leu Asn  Leu Asn Cys Val Ser  Lys Val Val
    6755                6760                6765

Asn Val  Asn Val Asp Phe Lys  Asp Phe Gln Phe Met  Leu Trp Cys
    6770                6775                6780

Asn Asp  Glu Lys Val Met Thr  Phe Tyr Pro Arg Leu  Gln Ala Ala
    6785                6790                6795

Ser Asp  Trp Lys Pro Gly Tyr  Ser Met Pro Val Leu  Tyr Lys Tyr
    6800                6805                6810

Leu Asn  Ser Pro Met Glu Arg  Val Ser Leu Trp Asn  Tyr Gly Lys
    6815                6820                6825

Pro Val  Thr Leu Pro Thr Gly  Cys Met Met Asn Val  Ala Lys Tyr
    6830                6835                6840

Thr Gln  Leu Cys Gln Tyr Leu  Asn Thr Thr Thr Leu  Ala Val Pro
    6845                6850                6855

Val Asn  Met Arg Val Leu His  Leu Gly Ala Gly Ser  Glu Lys Gly
    6860                6865                6870

Val Ala  Pro Gly Ser Ala Val  Leu Arg Gln Trp Leu  Pro Ala Gly
    6875                6880                6885

Thr Ile  Leu Val Asp Asn Asp  Leu Tyr Pro Phe Val  Ser Asp Ser
    6890                6895                6900

Val Ala  Thr Tyr Phe Gly Asp  Cys Ile Thr Leu Pro  Phe Asp Cys
    6905                6910                6915

Gln Trp  Asp Leu Ile Ile Ser  Asp Met Tyr Asp Pro  Ile Thr Lys
    6920                6925                6930

Asn Ile  Gly Glu Tyr Asn Val  Ser Lys Asp Gly Phe  Phe Thr Tyr
    6935                6940                6945

Ile Cys  His Met Ile Arg Asp  Lys Leu Ala Leu Gly  Gly Ser Val
    6950                6955                6960

Ala Ile  Lys Ile Thr Glu Phe  Ser Trp Asn Ala Glu  Leu Tyr Lys
    6965                6970                6975

Leu Met  Gly Tyr Phe Ala Phe  Trp Thr Val Phe Cys  Thr Asn Ala
    6980                6985                6990

Asn Ala  Ser Ser Ser Glu Gly  Phe Leu Ile Gly Ile  Asn Tyr Leu
    6995                7000                7005

Cys Lys  Pro Lys Val Glu Ile  Asp Gly Asn Val Met  His Ala Asn
    7010                7015                7020

Tyr Leu  Phe Trp Arg Asn Ser  Thr Val Trp Asn Gly  Gly Ala Tyr
    7025                7030                7035

Ser Leu  Phe Asp Met Ala Lys  Phe Pro Leu Lys Leu  Ala Gly Thr
    7040                7045                7050

Ala Val  Ile Asn Leu Arg Ala  Asp Gln Ile Asn Asp  Met Val Tyr
    7055                7060                7065

Ser Leu  Leu Glu Lys Gly Lys  Leu Leu Ile Arg Asp  Thr Asn Lys
    7070                7075                7080

Glu Val  Phe Val Gly Asp Ser  Leu Val Asn Val Ile
    7085                7090                7095
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<210> SEQ ID NO 6
<211> LENGTH: 6729
<212> TYPE: PRT
<213> ORGANISM: Human coronavirus NL63

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<400> SEQUENCE: 6

Met Phe Tyr Asn Gln Val Thr Leu Ala Val Ala Ser Asp Ser Glu Ile
1 5 10 15

Ser Gly Phe Gly Phe Ala Ile Pro Ser Val Ala Val Arg Thr Tyr Ser
20 25 30

Glu Ala Ala Ala Gln Gly Phe Gln Ala Cys Arg Phe Val Ala Phe Gly
35 40 45

Leu Gln Asp Cys Val Thr Gly Ile Asn Asp Asp Asp Tyr Val Ile Ala
50 55 60

Leu Thr Gly Thr Asn Gln Leu Cys Ala Lys Ile Leu Pro Phe Ser Asp
65 70 75 80

Arg Pro Leu Asn Leu Arg Gly Trp Leu Ile Phe Ser Asn Ser Asn Tyr
85 90 95

Val Leu Gln Asp Phe Asp Val Val Phe Gly His Gly Ala Gly Ser Val
100 105 110

Val Phe Val Asp Lys Tyr Met Cys Gly Phe Asp Gly Lys Pro Val Leu
115 120 125

Pro Lys Asn Met Trp Glu Phe Arg Asp Tyr Phe Asn Asn Asn Thr Asp
130 135 140

Ser Ile Val Ile Gly Gly Val Thr Tyr Gln Leu Ala Trp Asp Val Ile
145 150 155 160

Arg Lys Asp Leu Ser Tyr Glu Gln Gln Asn Val Leu Ala Ile Glu Ser
165 170 175

Ile His Tyr Leu Gly Thr Thr Gly His Thr Leu Lys Ser Gly Cys Lys
180 185 190

Leu Thr Asn Ala Lys Pro Pro Lys Tyr Ser Ser Lys Val Val Leu Ser
195 200 205

Gly Glu Trp Asn Ala Val Tyr Arg Ala Phe Gly Ser Pro Phe Ile Thr
210 215 220

Asn Gly Met Ser Leu Leu Asp Ile Ile Val Lys Pro Val Phe Phe Asn
225 230 235 240

Ala Phe Val Lys Cys Asn Cys Gly Ser Glu Ser Trp Ser Val Gly Ala
245 250 255

Trp Asp Gly Tyr Leu Ser Ser Cys Cys Gly Thr Pro Ala Lys Lys Leu
260 265 270

Cys Val Val Pro Gly Asn Val Val Pro Gly Asp Val Ile Ile Thr Ser
275 280 285

Thr Ser Ala Gly Cys Gly Val Lys Tyr Tyr Ala Gly Leu Val Val Lys
290 295 300

His Ile Thr Asn Ile Thr Gly Val Ser Leu Trp Arg Val Thr Ala Val
305 310 315 320

His Ser Asp Gly Met Phe Val Ala Ser Ser Ser Tyr Asp Ala Leu Leu
325 330 335

His Arg Asn Ser Leu Asp Pro Phe Cys Phe Asp Val Asn Thr Leu Leu
340 345 350

Ser Asn Gln Leu Arg Leu Ala Phe Leu Gly Ala Ser Val Thr Glu Asp
355 360 365

Val Lys Phe Ala Ala Ser Thr Gly Val Ile Asp Ile Ser Ala Gly Met
370 375 380

Phe Gly Leu Tyr Asp Asp Ile Leu Thr Asn Asn Lys Pro Trp Phe Val

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385                 390                 395                 400

Arg Lys Ala Ser Gly Leu Phe Asp Ala Ile Trp Asp Ala Phe Val Ala
                405                 410                 415

Ala Ile Lys Leu Val Pro Thr Thr Thr Gly Val Leu Val Arg Phe Val
            420                 425                 430

Lys Ser Ile Ala Ser Thr Val Leu Thr Val Ser Asn Gly Val Ile Ile
        435                 440                 445

Met Cys Ala Asp Val Pro Asp Ala Phe Gln Ser Val Tyr Arg Thr Phe
    450                 455                 460

Thr Gln Ala Ile Cys Ala Ala Phe Asp Phe Ser Leu Asp Val Phe Lys
465                 470                 475                 480

Ile Gly Asp Val Lys Phe Lys Arg Leu Gly Asp Tyr Val Leu Thr Glu
                485                 490                 495

Asn Ala Leu Val Arg Leu Thr Thr Glu Val Val Arg Gly Val Arg Asp
            500                 505                 510

Ala Arg Ile Lys Lys Ala Met Phe Thr Lys Val Val Val Gly Pro Thr
        515                 520                 525

Thr Glu Val Lys Phe Ser Val Ile Glu Leu Ala Thr Val Asn Leu Arg
    530                 535                 540

Leu Val Asp Cys Ala Pro Val Val Cys Pro Lys Gly Lys Ile Val Val
545                 550                 555                 560

Ile Ala Gly Gln Ala Phe Phe Tyr Ser Gly Gly Phe Tyr Arg Phe Met
                565                 570                 575

Val Asp Pro Thr Thr Val Leu Asn Asp Pro Val Phe Thr Gly Asp Leu
            580                 585                 590

Phe Tyr Thr Ile Lys Phe Ser Gly Phe Lys Leu Asp Gly Phe Asn His
        595                 600                 605

Gln Phe Val Thr Ala Ser Ser Ala Thr Asp Ala Ile Ile Ala Val Glu
    610                 615                 620

Leu Leu Leu Leu Asp Phe Lys Thr Ala Val Phe Val Tyr Thr Cys Val
625                 630                 635                 640

Val Asp Gly Cys Ser Val Ile Val Arg Arg Asp Ala Thr Phe Ala Thr
                645                 650                 655

His Val Cys Phe Lys Asp Cys Tyr Asn Val Trp Glu Gln Phe Cys Ile
            660                 665                 670

Asp Asn Cys Gly Glu Pro Trp Phe Leu Thr Asp Tyr Asn Ala Ile Leu
        675                 680                 685

Gln Ser Asn Asn Pro Gln Cys Ala Ile Val Gln Ala Ser Glu Ser Lys
    690                 695                 700

Val Leu Leu Glu Arg Phe Leu Pro Lys Cys Pro Glu Ile Leu Leu Ser
705                 710                 715                 720

Ile Asp Asp Gly His Leu Trp Asn Leu Phe Val Glu Lys Phe Asn Phe
                725                 730                 735

Val Thr Asp Trp Leu Lys Thr Leu Lys Leu Thr Leu Thr Ser Asn Gly
            740                 745                 750

Leu Leu Gly Asn Cys Ala Lys Arg Phe Arg Arg Val Leu Val Lys Leu
        755                 760                 765

Leu Asp Val Tyr Asn Gly Phe Leu Glu Thr Val Cys Ser Val Ala Tyr
    770                 775                 780

Thr Ala Gly Val Cys Ile Lys Tyr Tyr Ala Val Asn Val Pro Tyr Val
785                 790                 795                 800
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Val Ile Ser Gly Phe Val Ser Arg Val Ile Arg Arg Glu Arg Cys Asp
                805                 810                 815

Met Thr Phe Pro Cys Val Ser Cys Val Thr Phe Phe Tyr Glu Phe Leu
            820                 825                 830

Asp Thr Cys Phe Gly Val Ser Lys Pro Asn Ala Ile Asp Val Glu His
        835                 840                 845

Leu Glu Leu Lys Glu Thr Val Phe Val Glu Pro Lys Asp Gly Gly Gln
    850                 855                 860

Phe Phe Val Ser Gly Asp Tyr Leu Trp Tyr Val Val Asp Asp Ile Tyr
865                 870                 875                 880

Tyr Pro Ala Ser Cys Asn Gly Val Leu Pro Val Ala Phe Thr Lys Leu
                885                 890                 895

Ala Gly Gly Lys Ile Ser Phe Ser Asp Asp Val Ile Val His Asp Val
            900                 905                 910

Glu Pro Thr His Lys Val Lys Leu Ile Phe Glu Phe Glu Asp Asp Val
        915                 920                 925

Val Thr Ser Leu Cys Lys Lys Ser Phe Gly Lys Ser Ile Ile Tyr Thr
    930                 935                 940

Gly Asp Trp Glu Gly Leu His Glu Val Leu Thr Ser Ala Met Asn Val
945                 950                 955                 960

Ile Gly Gln His Ile Lys Leu Pro Gln Phe Tyr Ile Tyr Asp Glu Glu
                965                 970                 975

Gly Gly Tyr Asp Val Ser Lys Pro Val Met Ile Ser Gln Trp Pro Ile
            980                 985                 990

Ser Asn Asp Ser Asn Gly Cys Val  Val Glu Ala Ser Thr  Asp Phe His
        995                 1000                1005

Gln Leu  Glu Cys Ile Val Asp  Asp Ser Val Arg Glu  Glu Val Asp
    1010                1015                1020

Ile Ile  Glu Gln Pro Phe Glu  Glu Val Glu His Val  Leu Ser Ile
    1025                1030                1035

Lys Gln  Pro Phe Ser Phe Ser  Phe Arg Asp Glu Leu  Gly Val Arg
    1040                1045                1050

Val Leu  Asp Gln Ser Asp Asn  Asn Cys Trp Ile Ser  Thr Thr Leu
    1055                1060                1065

Val Gln  Leu Gln Leu Thr Lys  Leu Leu Asp Asp Ser  Ile Glu Met
    1070                1075                1080

Gln Leu  Phe Lys Val Gly Lys  Val Asp Ser Ile Val  Gln Lys Cys
    1085                1090                1095

Tyr Glu  Leu Ser His Leu Ile  Ser Gly Ser Leu Gly  Asp Ser Gly
    1100                1105                1110

Lys Leu  Leu Ser Glu Leu Leu  Lys Glu Lys Tyr Thr  Cys Ser Ile
    1115                1120                1125

Thr Phe  Glu Met Ser Cys Asp  Cys Gly Lys Lys Phe  Asp Asp Gln
    1130                1135                1140

Val Gly  Cys Leu Phe Trp Ile  Met Pro Tyr Thr Lys  Leu Phe Gln
    1145                1150                1155

Lys Gly  Glu Cys Cys Ile Cys  His Lys Met Gln Thr  Tyr Lys Leu
    1160                1165                1170

Val Ser  Met Lys Gly Thr Gly  Val Phe Val Gln Asp  Pro Ala Pro
    1175                1180                1185
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Ile Asp  Ile Asp Ala Phe Pro  Val Lys Pro Ile Cys  Ser Ser Val
    1190                 1195                 1200

Tyr Leu  Gly Val Lys Gly Ser  Gly His Tyr Gln Thr  Asn Leu Tyr
    1205                 1210                 1215

Ser Phe  Asn Lys Ala Ile Asp  Gly Phe Gly Val Phe  Asp Ile Lys
    1220                 1225                 1230

Asn Ser  Ser Val Asn Thr Val  Cys Phe Val Asp Val  Asp Phe His
    1235                 1240                 1245

Ser Val  Glu Ile Glu Ala Gly  Glu Val Lys Pro Phe  Ala Val Tyr
    1250                 1255                 1260

Lys Asn  Val Lys Phe Tyr Leu  Gly Asp Ile Ser His  Leu Val Asn
    1265                 1270                 1275

Cys Val  Ser Phe Asp Phe Val  Val Asn Ala Ala Asn  Glu Asn Leu
    1280                 1285                 1290

Leu His  Gly Gly Gly Val Ala  Arg Ala Ile Asp Ile  Leu Thr Glu
    1295                 1300                 1305

Gly Gln  Leu Gln Ser Leu Ser  Lys Asp Tyr Ile Ser  Ser Asn Gly
    1310                 1315                 1320

Pro Leu  Lys Val Gly Ala Gly  Val Met Leu Glu Cys  Glu Lys Phe
    1325                 1330                 1335

Asn Val  Phe Asn Val Val Gly  Pro Arg Thr Gly Lys  His Glu His
    1340                 1345                 1350

Ser Leu  Leu Val Glu Ala Tyr  Asn Ser Ile Leu Phe  Glu Asn Gly
    1355                 1360                 1365

Ile Pro  Leu Met Pro Leu Leu  Ser Cys Gly Ile Phe  Gly Val Arg
    1370                 1375                 1380

Ile Glu  Asn Ser Leu Lys Ala  Leu Phe Ser Cys Asp  Ile Asn Lys
    1385                 1390                 1395

Pro Leu  Gln Val Phe Val Tyr  Ser Ser Asn Glu Glu  Gln Ala Val
    1400                 1405                 1410

Leu Lys  Phe Leu Asp Gly Leu  Asp Leu Thr Pro Val  Ile Asp Asp
    1415                 1420                 1425

Val Asp  Val Val Lys Pro Phe  Arg Val Glu Gly Asn  Phe Ser Phe
    1430                 1435                 1440

Phe Asp  Cys Gly Val Asn Ala  Leu Asp Gly Asp Ile  Tyr Leu Leu
    1445                 1450                 1455

Phe Thr  Asn Ser Ile Leu Met  Leu Asp Lys Gln Gly  Gln Leu Leu
    1460                 1465                 1470

Asp Thr  Lys Leu Asn Gly Ile  Leu Gln Gln Ala Ala  Leu Asp Tyr
    1475                 1480                 1485

Leu Ala  Thr Val Lys Thr Val  Pro Ala Gly Asn Leu  Val Lys Leu
    1490                 1495                 1500

Phe Val  Glu Ser Cys Thr Ile  Tyr Met Cys Val Val  Pro Ser Ile
    1505                 1510                 1515

Asn Asp  Leu Ser Phe Asp Lys  Asn Leu Gly Arg Cys  Val Arg Lys
    1520                 1525                 1530

Leu Asn  Arg Leu Lys Thr Cys  Val Ile Ala Asn Val  Pro Ala Ile
    1535                 1540                 1545

Asp Val  Leu Lys Lys Leu Leu  Ser Ser Leu Thr Leu  Thr Val Lys
    1550                 1555                 1560

Phe Val  Val Glu Ser Asn Val  Met Asp Val Asn Asp  Cys Phe Lys
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    1565                1570                1575

Asn Asp  Asn Val Val Leu Lys  Ile Thr Glu Asp Gly  Ile Asn Val
    1580                1585                1590

Lys Asp  Val Val Val Glu Ser  Ser Lys Ser Leu Gly  Lys Gln Leu
    1595                1600                1605

Gly Val  Val Ser Asp Gly Val  Asp Ser Phe Glu Gly  Val Leu Pro
    1610                1615                1620

Ile Asn  Thr Asp Thr Val Leu  Ser Val Ala Pro Glu  Val Asp Trp
    1625                1630                1635

Val Ala  Phe Tyr Gly Phe Glu  Lys Ala Ala Leu Phe  Ala Ser Leu
    1640                1645                1650

Asp Val  Lys Pro Tyr Gly Tyr  Pro Asn Asp Phe Val  Gly Gly Phe
    1655                1660                1665

Arg Val  Leu Gly Thr Thr Asp  Asn Asn Cys Trp Val  Asn Ala Thr
    1670                1675                1680

Cys Ile  Ile Leu Gln Tyr Leu  Lys Pro Thr Phe Lys  Ser Lys Gly
    1685                1690                1695

Leu Asn  Val Leu Trp Asn Lys  Phe Val Thr Gly Asp  Val Gly Pro
    1700                1705                1710

Phe Val  Ser Phe Ile Tyr Phe  Ile Thr Met Ser Ser  Lys Gly Gln
    1715                1720                1725

Lys Gly  Asp Ala Glu Glu Ala  Leu Ser Lys Leu Ser  Glu Tyr Leu
    1730                1735                1740

Ile Ser  Asp Ser Ile Val Thr  Leu Glu Gln Tyr Ser  Thr Cys Asp
    1745                1750                1755

Ile Cys  Lys Ser Thr Val Val  Glu Val Lys Ser Ala  Ile Val Cys
    1760                1765                1770

Ala Ser  Val Leu Lys Asp Gly  Cys Asp Val Gly Phe  Cys Pro His
    1775                1780                1785

Arg His  Lys Leu Arg Ser Arg  Val Lys Phe Val Asn  Gly Arg Val
    1790                1795                1800

Val Ile  Thr Asn Val Gly Glu  Pro Ile Ile Ser Gln  Pro Ser Lys
    1805                1810                1815

Leu Leu  Asn Gly Ile Ala Tyr  Thr Thr Phe Ser Gly  Ser Phe Asp
    1820                1825                1830

Asn Gly  His Tyr Val Val Tyr  Asp Ala Ala Asn Asn  Ala Val Tyr
    1835                1840                1845

Asp Gly  Ala Arg Leu Phe Ser  Ser Asp Leu Ser Thr  Leu Ala Val
    1850                1855                1860

Thr Ala  Ile Val Val Val Gly  Gly Cys Val Thr Ser  Asn Val Pro
    1865                1870                1875

Thr Ile  Val Ser Glu Lys Ile  Ser Val Met Asp Lys  Leu Asp Thr
    1880                1885                1890

Gly Ala  Gln Lys Phe Phe Gln  Phe Gly Asp Phe Val  Met Asn Asn
    1895                1900                1905

Ile Val  Leu Phe Leu Thr Trp  Leu Leu Ser Met Phe  Ser Leu Leu
    1910                1915                1920

Arg Thr  Ser Ile Met Lys His  Asp Ile Lys Val Ile  Ala Lys Ala
    1925                1930                1935

Pro Lys  Arg Thr Gly Val Ile  Leu Thr Arg Ser Phe  Lys Tyr Asn
    1940                1945                1950
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Ile Arg  Ser Ala Leu Phe Val  Ile Lys Gln Lys Trp  Cys Val Ile
    1955                 1960                 1965

Val Thr  Leu Phe Lys Phe Leu  Leu Leu Leu Tyr Ala  Ile Tyr Ala
    1970                 1975                 1980

Leu Val  Phe Met Ile Val Gln  Phe Ser Pro Phe Asn  Ser Leu Leu
    1985                 1990                 1995

Cys Gly  Asp Ile Val Ser Gly  Tyr Glu Lys Ser Thr  Phe Asn Lys
    2000                 2005                 2010

Asp Ile  Tyr Cys Gly Asn Ser  Met Val Cys Lys Met  Cys Leu Phe
    2015                 2020                 2025

Ser Tyr  Gln Glu Phe Asn Asp  Leu Asp His Thr Ser  Leu Val Trp
    2030                 2035                 2040

Lys His  Ile Arg Asp Pro Ile  Leu Ile Ser Leu Gln  Pro Phe Val
    2045                 2050                 2055

Ile Leu  Val Ile Leu Leu Ile  Phe Gly Asn Met Tyr  Leu Arg Phe
    2060                 2065                 2070

Gly Leu  Leu Tyr Phe Val Ala  Gln Phe Ile Ser Thr  Phe Gly Ser
    2075                 2080                 2085

Phe Leu  Gly Phe His Gln Lys  Gln Trp Phe Leu His  Phe Val Pro
    2090                 2095                 2100

Phe Asp  Val Leu Cys Asn Glu  Phe Leu Ala Thr Phe  Ile Val Cys
    2105                 2110                 2115

Lys Ile  Val Leu Phe Val Arg  His Ile Ile Val Gly  Cys Asn Asn
    2120                 2125                 2130

Ala Asp  Cys Val Ala Cys Ser  Lys Ser Ala Arg Leu  Lys Arg Val
    2135                 2140                 2145

Pro Leu  Gln Thr Ile Ile Asn  Gly Met His Lys Ser  Phe Tyr Val
    2150                 2155                 2160

Asn Ala  Asn Gly Gly Thr Cys  Phe Cys Asn Lys His  Asn Phe Phe
    2165                 2170                 2175

Cys Val  Asn Cys Asp Ser Phe  Gly Pro Gly Asn Thr  Phe Ile Asn
    2180                 2185                 2190

Gly Asp  Ile Ala Arg Glu Leu  Gly Asn Val Val Lys  Thr Ala Val
    2195                 2200                 2205

Gln Pro  Thr Ala Pro Ala Tyr  Val Ile Ile Asp Lys  Val Asp Phe
    2210                 2215                 2220

Val Asn  Gly Phe Tyr Arg Leu  Tyr Ser Gly Asp Thr  Phe Trp Arg
    2225                 2230                 2235

Tyr Asp  Phe Asp Ile Thr Glu  Ser Lys Tyr Ser Cys  Lys Glu Val
    2240                 2245                 2250

Leu Lys  Asn Cys Asn Val Leu  Glu Asn Phe Ile Val  Tyr Asn Asn
    2255                 2260                 2265

Ser Gly  Ser Asn Ile Thr Gln  Ile Lys Asn Ala Cys  Val Tyr Phe
    2270                 2275                 2280

Ser Gln  Leu Leu Cys Glu Pro  Ile Lys Leu Val Asn  Ser Glu Leu
    2285                 2290                 2295

Leu Ser  Thr Leu Ser Val Asp  Phe Asn Gly Val Leu  His Lys Ala
    2300                 2305                 2310

Tyr Val  Asp Val Leu Cys Asn  Ser Phe Phe Lys Glu  Leu Thr Ala
    2315                 2320                 2325
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Asn Met  Ser Met Ala Glu Cys  Lys Ala Thr Leu Gly  Leu Thr Val
    2330                 2335                 2340

Ser Asp  Asp Asp Phe Val Ser  Ala Val Ala Asn Ala  His Arg Tyr
    2345                 2350                 2355

Asp Val  Leu Leu Ser Asp Leu  Ser Phe Asn Asn Phe  Phe Ile Ser
    2360                 2365                 2370

Tyr Ala  Lys Pro Glu Asp Lys  Leu Ser Val Tyr Asp  Ile Ala Cys
    2375                 2380                 2385

Cys Met  Arg Ala Gly Ser Lys  Val Val Asn His Asn  Val Leu Ile
    2390                 2395                 2400

Lys Glu  Ser Ile Pro Ile Val  Trp Gly Val Lys Asp  Phe Asn Thr
    2405                 2410                 2415

Leu Ser  Gln Glu Gly Lys Lys  Tyr Leu Val Lys Thr  Thr Lys Ala
    2420                 2425                 2430

Lys Gly  Leu Thr Phe Leu Leu  Thr Phe Asn Asp Asn  Gln Ala Ile
    2435                 2440                 2445

Thr Gln  Val Pro Ala Thr Ser  Ile Val Ala Lys Gln  Gly Ala Gly
    2450                 2455                 2460

Phe Lys  Arg Thr Tyr Asn Phe  Leu Trp Tyr Val Cys  Leu Phe Val
    2465                 2470                 2475

Val Ala  Leu Phe Ile Gly Val  Ser Phe Ile Asp Tyr  Thr Thr Thr
    2480                 2485                 2490

Val Thr  Ser Phe His Gly Tyr  Asp Phe Lys Tyr Ile  Glu Asn Gly
    2495                 2500                 2505

Gln Leu  Lys Val Phe Glu Ala  Pro Leu His Cys Val  Arg Asn Val
    2510                 2515                 2520

Phe Asp  Asn Phe Asn Gln Trp  His Glu Ala Lys Phe  Gly Val Val
    2525                 2530                 2535

Thr Thr  Asn Ser Asp Lys Cys  Pro Ile Val Val Gly  Val Ser Glu
    2540                 2545                 2550

Arg Ile  Asn Val Val Pro Gly  Val Pro Thr Asn Val  Tyr Leu Val
    2555                 2560                 2565

Gly Lys  Thr Leu Val Phe Thr  Leu Gln Ala Ala Phe  Gly Asn Thr
    2570                 2575                 2580

Gly Val  Cys Tyr Asp Phe Asp  Gly Val Thr Thr Ser  Asp Lys Cys
    2585                 2590                 2595

Ile Phe  Asn Ser Ala Cys Thr  Arg Leu Glu Gly Leu  Gly Gly Asp
    2600                 2605                 2610

Asn Val  Tyr Cys Tyr Asn Thr  Asp Leu Ile Glu Gly  Ser Lys Pro
    2615                 2620                 2625

Tyr Ser  Thr Leu Gln Pro Asn  Ala Tyr Tyr Lys Tyr  Asp Ala Lys
    2630                 2635                 2640

Asn Tyr  Val Arg Phe Pro Glu  Ile Leu Ala Arg Gly  Phe Gly Leu
    2645                 2650                 2655

Arg Thr  Ile Arg Thr Leu Ala  Thr Arg Tyr Cys Arg  Val Gly Glu
    2660                 2665                 2670

Cys Arg  Asp Ser His Lys Gly  Val Cys Phe Gly Phe  Asp Lys Trp
    2675                 2680                 2685

Tyr Val  Asn Asp Gly Arg Val  Asp Asp Gly Tyr Ile  Cys Gly Asp
    2690                 2695                 2700

Gly Leu  Ile Asp Leu Leu Val  Asn Val Leu Ser Ile  Phe Ser Ser
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    2705                2710                2715

Ser Phe  Ser Val Val Ala Met  Ser Gly His Met Leu  Phe Asn Phe
    2720                2725                2730

Leu Phe  Ala Ala Phe Ile Thr  Phe Leu Cys Phe Leu  Val Thr Lys
    2735                2740                2745

Phe Lys  Arg Val Phe Gly Asp  Leu Ser Tyr Gly Val  Phe Thr Val
    2750                2755                2760

Val Cys  Ala Thr Leu Ile Asn  Asn Ile Ser Tyr Val  Val Thr Gln
    2765                2770                2775

Asn Leu  Phe Phe Met Leu Leu  Tyr Ala Ile Leu Tyr  Phe Val Phe
    2780                2785                2790

Thr Arg  Thr Val Arg Tyr Ala  Trp Ile Trp His Ile  Ala Tyr Ile
    2795                2800                2805

Val Ala  Tyr Phe Leu Leu Ile  Pro Trp Trp Leu Leu  Thr Trp Phe
    2810                2815                2820

Ser Phe  Ala Ala Phe Leu Glu  Leu Leu Pro Asn Val  Phe Lys Leu
    2825                2830                2835

Lys Ile  Ser Thr Gln Leu Phe  Glu Gly Asp Lys Phe  Ile Gly Thr
    2840                2845                2850

Phe Glu  Ser Ala Ala Ala Gly  Thr Phe Val Leu Asp  Met Arg Ser
    2855                2860                2865

Tyr Glu  Arg Leu Ile Asn Thr  Ile Ser Pro Glu Lys  Leu Lys Asn
    2870                2875                2880

Tyr Ala  Ala Ser Tyr Asn Lys  Tyr Lys Tyr Tyr Ser  Gly Ser Ala
    2885                2890                2895

Ser Glu  Ala Asp Tyr Arg Cys  Ala Cys Tyr Ala His  Leu Ala Lys
    2900                2905                2910

Ala Met  Leu Asp Tyr Ala Lys  Asp His Asn Asp Met  Leu Tyr Ser
    2915                2920                2925

Pro Pro  Thr Ile Ser Tyr Asn  Ser Thr Leu Gln Ser  Gly Leu Lys
    2930                2935                2940

Lys Met  Ala Gln Pro Ser Gly  Cys Val Glu Arg Cys  Val Val Arg
    2945                2950                2955

Val Cys  Tyr Gly Ser Thr Val  Leu Asn Gly Val Trp  Leu Gly Asp
    2960                2965                2970

Thr Val  Thr Cys Pro Arg His  Val Ile Ala Pro Ser  Thr Thr Val
    2975                2980                2985

Leu Ile  Asp Tyr Asp His Ala  Tyr Ser Thr Met Arg  Leu His Asn
    2990                2995                3000

Phe Ser  Val Ser His Asn Gly  Val Phe Leu Gly Val  Val Gly Val
    3005                3010                3015

Thr Met  His Gly Ser Val Leu  Arg Ile Lys Val Ser  Gln Ser Asn
    3020                3025                3030

Val His  Thr Pro Lys His Val  Phe Lys Thr Leu Lys  Pro Gly Asp
    3035                3040                3045

Ser Phe  Asn Ile Leu Ala Cys  Tyr Glu Gly Ile Ala  Ser Gly Val
    3050                3055                3060

Phe Gly  Val Asn Leu Arg Thr  Asn Phe Thr Ile Lys  Gly Ser Phe
    3065                3070                3075

Ile Asn  Gly Ala Cys Gly Ser  Pro Gly Tyr Asn Val  Arg Asn Asp
    3080                3085                3090
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Gly Thr  Val Glu Phe Cys Tyr  Leu His Gln Ile Glu  Leu Gly Ser
    3095                 3100                 3105

Gly Ala  His Val Gly Ser Asp  Phe Thr Gly Ser Val  Tyr Gly Asn
    3110                 3115                 3120

Phe Asp  Asp Gln Pro Ser Leu  Gln Val Glu Ser Ala  Asn Leu Met
    3125                 3130                 3135

Leu Ser  Asp Asn Val Val Ala  Phe Leu Tyr Ala Ala  Leu Leu Asn
    3140                 3145                 3150

Gly Cys  Arg Trp Trp Leu Cys  Ser Thr Arg Val Asn  Val Asp Gly
    3155                 3160                 3165

Phe Asn  Glu Trp Ala Met Ala  Asn Gly Tyr Thr Ser  Val Ser Ser
    3170                 3175                 3180

Val Glu  Cys Tyr Ser Ile Leu  Ala Ala Lys Thr Gly  Val Ser Val
    3185                 3190                 3195

Glu Gln  Leu Leu Ala Ser Ile  Gln His Leu His Glu  Gly Phe Gly
    3200                 3205                 3210

Gly Lys  Asn Ile Leu Gly Tyr  Ser Ser Leu Cys Asp  Glu Phe Thr
    3215                 3220                 3225

Leu Ala  Glu Val Val Lys Gln  Met Tyr Gly Val Asn  Leu Gln Ser
    3230                 3235                 3240

Gly Lys  Val Ile Phe Gly Leu  Lys Thr Met Phe Leu  Phe Ser Val
    3245                 3250                 3255

Phe Phe  Thr Met Phe Trp Ala  Glu Leu Phe Ile Tyr  Thr Asn Thr
    3260                 3265                 3270

Ile Trp  Ile Asn Pro Val Ile  Leu Thr Pro Ile Phe  Cys Leu Leu
    3275                 3280                 3285

Leu Phe  Leu Ser Leu Val Leu  Thr Met Phe Leu Lys  His Lys Phe
    3290                 3295                 3300

Leu Phe  Leu Gln Val Phe Leu  Leu Pro Thr Val Ile  Ala Thr Ala
    3305                 3310                 3315

Leu Tyr  Asn Cys Val Leu Asp  Tyr Tyr Ile Val Lys  Phe Leu Ala
    3320                 3325                 3330

Asp His  Phe Asn Tyr Asn Val  Ser Val Leu Gln Met  Asp Val Gln
    3335                 3340                 3345

Gly Leu  Val Asn Val Leu Val  Cys Leu Phe Val Val  Phe Leu His
    3350                 3355                 3360

Thr Trp  Arg Phe Ser Lys Glu  Arg Phe Thr His Trp  Phe Thr Tyr
    3365                 3370                 3375

Val Cys  Ser Leu Ile Ala Val  Ala Tyr Thr Tyr Phe  Tyr Ser Gly
    3380                 3385                 3390

Asp Phe  Leu Ser Leu Leu Val  Met Phe Leu Cys Ala  Ile Ser Ser
    3395                 3400                 3405

Asp Trp  Tyr Ile Gly Ala Ile  Val Phe Arg Leu Ser  Arg Leu Ile
    3410                 3415                 3420

Val Phe  Phe Ser Pro Glu Ser  Val Phe Ser Val Phe  Gly Asp Val
    3425                 3430                 3435

Lys Leu  Thr Leu Val Val Tyr  Leu Ile Cys Gly Tyr  Leu Val Cys
    3440                 3445                 3450

Thr Tyr  Trp Gly Ile Leu Tyr  Trp Phe Asn Arg Phe  Phe Lys Cys
    3455                 3460                 3465
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Thr Met  Gly Val Tyr Asp Phe  Lys Val Ser Ala Ala  Glu Phe Lys
    3470                 3475                 3480

Tyr Met  Val Ala Asn Gly Leu  His Ala Pro His Gly  Pro Phe Asp
    3485                 3490                 3495

Ala Leu  Trp Leu Ser Phe Lys  Leu Leu Gly Ile Gly  Gly Asp Arg
    3500                 3505                 3510

Cys Ile  Lys Ile Ser Thr Val  Gln Ser Lys Leu Thr  Asp Leu Lys
    3515                 3520                 3525

Cys Thr  Asn Val Val Leu Leu  Gly Cys Leu Ser Ser  Met Asn Ile
    3530                 3535                 3540

Ala Ala  Asn Ser Ser Glu Trp  Ala Tyr Cys Val Asp  Leu His Asn
    3545                 3550                 3555

Lys Ile  Asn Leu Cys Asp Asp  Pro Glu Lys Ala Gln  Ser Met Leu
    3560                 3565                 3570

Leu Ala  Leu Leu Ala Phe Phe  Leu Ser Lys His Ser  Asp Phe Gly
    3575                 3580                 3585

Leu Asp  Gly Leu Ile Asp Ser  Tyr Phe Asp Asn Ser  Ser Thr Leu
    3590                 3595                 3600

Gln Ser  Val Ala Ser Ser Phe  Val Ser Met Pro Ser  Tyr Ile Ala
    3605                 3610                 3615

Tyr Glu  Asn Ala Arg Gln Ala  Tyr Glu Asp Ala Ile  Ala Asn Gly
    3620                 3625                 3630

Ser Ser  Ser Gln Leu Ile Lys  Gln Leu Lys Arg Ala  Met Asn Ile
    3635                 3640                 3645

Ala Lys  Ser Glu Phe Asp His  Glu Ile Ser Val Gln  Lys Lys Ile
    3650                 3655                 3660

Asn Arg  Met Ala Glu Gln Ala  Ala Thr Gln Met Tyr  Lys Glu Ala
    3665                 3670                 3675

Arg Ser  Val Asn Arg Lys Ser  Lys Val Ile Ser Ala  Met His Ser
    3680                 3685                 3690

Leu Leu  Phe Gly Met Leu Arg  Arg Leu Asp Met Ser  Ser Val Glu
    3695                 3700                 3705

Thr Val  Leu Asn Leu Ala Arg  Asp Gly Val Val Pro  Leu Ser Val
    3710                 3715                 3720

Ile Pro  Ala Thr Ser Ala Ser  Lys Leu Thr Ile Val  Ser Pro Asp
    3725                 3730                 3735

Leu Glu  Ser Tyr Ser Lys Ile  Val Cys Asp Gly Ser  Val His Tyr
    3740                 3745                 3750

Ala Gly  Val Val Trp Thr Leu  Asn Asp Val Lys Asp  Asn Asp Gly
    3755                 3760                 3765

Arg Pro  Val His Val Lys Glu  Ile Thr Lys Glu Asn  Val Glu Thr
    3770                 3775                 3780

Leu Thr  Trp Pro Leu Ile Leu  Asn Cys Glu Arg Val  Val Lys Leu
    3785                 3790                 3795

Gln Asn  Asn Glu Ile Met Pro  Gly Lys Leu Lys Gln  Lys Pro Met
    3800                 3805                 3810

Lys Ala  Glu Gly Asp Gly Gly  Val Leu Gly Asp Gly  Asn Ala Leu
    3815                 3820                 3825

Tyr Asn  Thr Glu Gly Gly Lys  Thr Phe Met Tyr Ala  Tyr Ile Ser
    3830                 3835                 3840

Asn Lys  Ala Asp Leu Lys Phe  Val Lys Trp Glu Tyr  Glu Gly Gly
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    3845                3850                3855

Cys Asn  Thr Ile Glu Leu Asp  Ser Pro Cys Arg Phe  Met Val Glu
    3860                3865                3870

Thr Pro  Asn Gly Pro Gln Val  Lys Tyr Leu Tyr Phe  Val Lys Asn
    3875                3880                3885

Leu Asn  Thr Leu Arg Arg Gly  Ala Val Leu Gly Phe  Ile Gly Ala
    3890                3895                3900

Thr Ile  Arg Leu Gln Ala Gly  Lys Gln Thr Glu Leu  Ala Val Asn
    3905                3910                3915

Ser Gly  Leu Leu Thr Ala Cys  Ala Phe Ser Val Asp  Pro Ala Thr
    3920                3925                3930

Thr Tyr  Leu Glu Ala Val Lys  His Gly Ala Lys Pro  Val Ser Asn
    3935                3940                3945

Cys Ile  Lys Met Leu Ser Asn  Gly Ala Gly Asn Gly  Gln Ala Ile
    3950                3955                3960

Thr Thr  Ser Val Asp Ala Asn  Thr Asn Gln Asp Ser  Tyr Gly Gly
    3965                3970                3975

Ala Ser  Ile Cys Leu Tyr Cys  Arg Ala His Val Pro  His Pro Ser
    3980                3985                3990

Met Asp  Gly Tyr Cys Lys Phe  Lys Gly Lys Cys Val  Gln Val Pro
    3995                4000                4005

Ile Gly  Cys Leu Asp Pro Ile  Arg Phe Cys Leu Glu  Asn Asn Val
    4010                4015                4020

Cys Asn  Val Cys Gly Cys Trp  Leu Gly His Gly Cys  Ala Cys Asp
    4025                4030                4035

Arg Thr  Thr Ile Gln Ser Val  Asp Ile Ser Tyr Leu  Asn Arg Ala
    4040                4045                4050

Arg Gly  Ser Ser Ala Ala Arg  Leu Glu Pro Cys Asn  Gly Thr Asp
    4055                4060                4065

Ile Asp  Lys Cys Val Arg Ala  Phe Asp Ile Tyr Asn  Lys Asn Val
    4070                4075                4080

Ser Phe  Leu Gly Lys Cys Leu  Lys Met Asn Cys Val  Arg Phe Lys
    4085                4090                4095

Asn Ala  Asp Leu Lys Asp Gly  Tyr Phe Val Ile Lys  Arg Cys Thr
    4100                4105                4110

Lys Ser  Val Met Glu His Glu  Gln Ser Met Tyr Asn  Leu Leu Asn
    4115                4120                4125

Phe Ser  Gly Ala Leu Ala Glu  His Asp Phe Phe Thr  Trp Lys Asp
    4130                4135                4140

Gly Arg  Val Ile Tyr Gly Asn  Val Ser Arg His Asn  Leu Thr Lys
    4145                4150                4155

Tyr Thr  Met Met Asp Leu Val  Tyr Ala Met Arg Asn  Phe Asp Glu
    4160                4165                4170

Gln Asn  Cys Asp Val Leu Lys  Glu Val Leu Val Leu  Thr Gly Cys
    4175                4180                4185

Cys Asp  Asn Ser Tyr Phe Asp  Ser Lys Gly Trp Tyr  Asp Pro Val
    4190                4195                4200

Glu Asn  Glu Asp Ile His Arg  Val Tyr Ala Ser Leu  Gly Lys Ile
    4205                4210                4215

Val Ala  Arg Ala Met Leu Lys  Cys Val Ala Leu Cys  Asp Ala Met
    4220                4225                4230
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Val Ala  Lys Gly Val Val Gly  Val Leu Thr Leu Asp  Asn Gln Asp
    4235                 4240                 4245

Leu Asn  Gly Asn Phe Tyr Asp  Phe Gly Asp Phe Val  Val Ser Leu
    4250                 4255                 4260

Pro Asn  Met Gly Val Pro Cys  Cys Thr Ser Tyr Tyr  Ser Tyr Met
    4265                 4270                 4275

Met Pro  Ile Met Gly Leu Thr  Asn Cys Leu Ala Ser  Glu Cys Phe
    4280                 4285                 4290

Val Lys  Ser Asp Ile Phe Gly  Ser Asp Phe Lys Thr  Phe Asp Leu
    4295                 4300                 4305

Leu Lys  Tyr Asp Phe Thr Glu  His Lys Glu Asn Leu  Phe Asn Lys
    4310                 4315                 4320

Tyr Phe  Lys His Trp Ser Phe  Asp Tyr His Pro Asn  Cys Ser Asp
    4325                 4330                 4335

Cys Tyr  Asp Asp Met Cys Val  Ile His Cys Ala Asn  Phe Asn Thr
    4340                 4345                 4350

Leu Phe  Ala Thr Thr Ile Pro  Gly Thr Ala Phe Gly  Pro Leu Cys
    4355                 4360                 4365

Arg Lys  Val Phe Ile Asp Gly  Val Pro Leu Val Thr  Thr Ala Gly
    4370                 4375                 4380

Tyr His  Phe Lys Gln Leu Gly  Leu Val Trp Asn Lys  Asp Val Asn
    4385                 4390                 4395

Thr His  Ser Val Arg Leu Thr  Ile Thr Glu Leu Leu  Gln Phe Val
    4400                 4405                 4410

Thr Asp  Pro Ser Leu Ile Ile  Ala Ser Ser Pro Ala  Leu Val Asp
    4415                 4420                 4425

Gln Arg  Thr Ile Cys Phe Ser  Val Ala Ala Leu Ser  Thr Gly Leu
    4430                 4435                 4440

Thr Asn  Gln Val Val Lys Pro  Gly His Phe Asn Glu  Glu Phe Tyr
    4445                 4450                 4455

Asn Phe  Leu Arg Leu Arg Gly  Phe Phe Asp Glu Gly  Ser Glu Leu
    4460                 4465                 4470

Thr Leu  Lys His Phe Phe Phe  Ala Gln Asn Gly Asp  Ala Ala Val
    4475                 4480                 4485

Lys Asp  Phe Asp Phe Tyr Arg  Tyr Asn Lys Pro Thr  Ile Leu Asp
    4490                 4495                 4500

Ile Cys  Gln Ala Arg Val Thr  Tyr Lys Ile Val Ser  Arg Tyr Phe
    4505                 4510                 4515

Asp Ile  Tyr Glu Gly Gly Cys  Ile Lys Ala Cys Glu  Val Val Val
    4520                 4525                 4530

Thr Asn  Leu Asn Lys Ser Ala  Gly Trp Pro Leu Asn  Lys Phe Gly
    4535                 4540                 4545

Lys Ala  Ser Leu Tyr Tyr Glu  Ser Ile Ser Tyr Glu  Glu Gln Asp
    4550                 4555                 4560

Ala Leu  Phe Ala Leu Thr Lys  Arg Asn Val Leu Pro  Thr Met Thr
    4565                 4570                 4575

Gln Leu  Asn Leu Lys Tyr Ala  Ile Ser Gly Lys Glu  Arg Ala Arg
    4580                 4585                 4590

Thr Val  Gly Gly Val Ser Leu  Leu Ser Thr Met Thr  Thr Arg Gln
    4595                 4600                 4605
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Tyr His  Gln Lys His Leu Lys  Ser Ile Val Asn Thr  Arg Asn Ala
    4610                 4615                 4620

Thr Val  Val Ile Gly Thr Thr  Lys Phe Tyr Gly Gly  Trp Asn Asn
    4625                 4630                 4635

Met Leu  Arg Thr Leu Ile Asp  Gly Val Glu Asn Pro  Met Leu Met
    4640                 4645                 4650

Gly Trp  Asp Tyr Pro Lys Cys  Asp Arg Ala Leu Pro  Asn Met Ile
    4655                 4660                 4665

Arg Met  Ile Ser Ala Met Val  Leu Gly Ser Lys His  Val Asn Cys
    4670                 4675                 4680

Cys Thr  Ala Thr Asp Arg Phe  Tyr Arg Leu Gly Asn  Glu Leu Ala
    4685                 4690                 4695

Gln Val  Leu Thr Glu Val Val  Tyr Ser Asn Gly Gly  Phe Tyr Phe
    4700                 4705                 4710

Lys Pro  Gly Gly Thr Thr Ser  Gly Asp Ala Ser Thr  Ala Tyr Ala
    4715                 4720                 4725

Asn Ser  Ile Phe Asn Ile Phe  Gln Ala Val Ser Ser  Asn Ile Asn
    4730                 4735                 4740

Arg Leu  Leu Ser Val Pro Ser  Asp Ser Cys Asn Asn  Val Asn Val
    4745                 4750                 4755

Arg Asp  Leu Gln Arg Arg Leu  Tyr Asp Asn Cys Tyr  Arg Leu Thr
    4760                 4765                 4770

Ser Val  Glu Glu Ser Phe Ile  Asp Asp Tyr Tyr Gly  Tyr Leu Arg
    4775                 4780                 4785

Lys His  Phe Ser Met Met Ile  Leu Ser Asp Asp Gly  Val Val Cys
    4790                 4795                 4800

Tyr Asn  Lys Asp Tyr Ala Glu  Leu Gly Tyr Ile Ala  Asp Ile Ser
    4805                 4810                 4815

Ala Phe  Lys Ala Thr Leu Tyr  Tyr Gln Asn Asn Val  Phe Met Ser
    4820                 4825                 4830

Thr Ser  Lys Cys Trp Val Glu  Glu Asp Leu Thr Lys  Gly Pro His
    4835                 4840                 4845

Glu Phe  Cys Ser Gln His Thr  Met Gln Ile Val Asp  Lys Asp Gly
    4850                 4855                 4860

Thr Tyr  Tyr Leu Pro Tyr Pro  Asp Pro Ser Arg Ile  Leu Ser Ala
    4865                 4870                 4875

Gly Val  Phe Val Asp Asp Val  Val Lys Thr Asp Ala  Val Val Leu
    4880                 4885                 4890

Leu Glu  Arg Tyr Val Ser Leu  Ala Ile Asp Ala Tyr  Pro Leu Ser
    4895                 4900                 4905

Lys His  Pro Asn Ser Glu Tyr  Arg Lys Val Phe Tyr  Val Leu Leu
    4910                 4915                 4920

Asp Trp  Val Lys His Leu Asn  Lys Asn Leu Asn Glu  Gly Val Leu
    4925                 4930                 4935

Glu Ser  Phe Ser Val Thr Leu  Leu Asp Asn Gln Glu  Asp Lys Phe
    4940                 4945                 4950

Trp Cys  Glu Asp Phe Tyr Ala  Ser Met Tyr Glu Asn  Ser Thr Ile
    4955                 4960                 4965

Leu Gln  Ala Ala Gly Leu Cys  Val Val Cys Gly Ser  Gln Thr Val
    4970                 4975                 4980

Leu Arg  Cys Gly Asp Cys Leu  Arg Lys Pro Met Leu  Cys Thr Lys
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    4985                4990                4995

Cys Ala  Tyr Asp His Val Phe  Gly Thr Asp His Lys  Phe Ile Leu
    5000                5005                5010

Ala Ile  Thr Pro Tyr Val Cys  Asn Ala Ser Gly Cys  Gly Val Ser
    5015                5020                5025

Asp Val  Lys Lys Leu Tyr Leu  Gly Gly Leu Asn Tyr  Tyr Cys Thr
    5030                5035                5040

Asn His  Lys Pro Gln Leu Ser  Phe Pro Leu Cys Ser  Ala Gly Asn
    5045                5050                5055

Ile Phe  Gly Leu Tyr Lys Asn  Ser Ala Thr Gly Ser  Leu Asp Val
    5060                5065                5070

Glu Val  Phe Asn Arg Leu Ala  Thr Ser Asp Trp Thr  Asp Val Arg
    5075                5080                5085

Asp Tyr  Lys Leu Ala Asn Asp  Val Lys Asp Thr Leu  Arg Leu Phe
    5090                5095                5100

Ala Ala  Glu Thr Ile Lys Ala  Lys Glu Glu Ser Val  Lys Ser Ser
    5105                5110                5115

Tyr Ala  Phe Ala Thr Leu Lys  Glu Val Val Gly Pro  Lys Glu Leu
    5120                5125                5130

Leu Leu  Ser Trp Glu Ser Gly  Lys Val Lys Pro Pro  Leu Asn Arg
    5135                5140                5145

Asn Ser  Val Phe Thr Cys Phe  Gln Ile Ser Lys Asp  Ser Lys Phe
    5150                5155                5160

Gln Ile  Gly Glu Phe Ile Phe  Glu Lys Val Glu Tyr  Gly Ser Asp
    5165                5170                5175

Thr Val  Thr Tyr Lys Ser Thr  Val Thr Thr Lys Leu  Val Pro Gly
    5180                5185                5190

Met Ile  Phe Val Leu Thr Ser  His Asn Val Gln Pro  Leu Arg Ala
    5195                5200                5205

Pro Thr  Ile Ala Asn Gln Glu  Lys Tyr Ser Ser Ile  Tyr Lys Leu
    5210                5215                5220

His Pro  Ala Phe Asn Val Ser  Asp Ala Tyr Ala Asn  Leu Val Pro
    5225                5230                5235

Tyr Tyr  Gln Leu Ile Gly Lys  Gln Lys Ile Thr Thr  Ile Gln Gly
    5240                5245                5250

Pro Pro  Gly Ser Gly Lys Ser  His Cys Ser Ile Gly  Leu Gly Leu
    5255                5260                5265

Tyr Tyr  Pro Gly Ala Arg Ile  Val Phe Val Ala Cys  Ala His Ala
    5270                5275                5280

Ala Val  Asp Ser Leu Cys Ala  Lys Ala Met Thr Val  Tyr Ser Ile
    5285                5290                5295

Asp Lys  Cys Thr Arg Ile Ile  Pro Ala Arg Ala Arg  Val Glu Cys
    5300                5305                5310

Tyr Ser  Gly Phe Lys Pro Asn  Asn Thr Ser Ala Gln  Tyr Ile Phe
    5315                5320                5325

Ser Thr  Val Asn Ala Leu Pro  Glu Cys Asn Ala Asp  Ile Val Val
    5330                5335                5340

Val Asp  Glu Val Ser Met Cys  Thr Asn Tyr Asp Leu  Ser Val Ile
    5345                5350                5355

Asn Gln  Arg Leu Ser Tyr Lys  His Ile Val Tyr Val  Gly Asp Pro
    5360                5365                5370
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Gln Gln  Leu Pro Ala Pro Arg  Val Met Ile Thr Lys  Gly Val Met
    5375                 5380                 5385

Glu Pro  Val Asp Tyr Asn Val  Val Thr Gln Arg Met  Cys Ala Ile
    5390                 5395                 5400

Gly Pro  Asp Val Phe Leu His  Lys Cys Tyr Arg Cys  Pro Ala Glu
    5405                 5410                 5415

Ile Val  Asn Thr Val Ser Glu  Leu Val Tyr Glu Asn  Lys Phe Val
    5420                 5425                 5430

Pro Val  Lys Pro Ala Ser Lys  Gln Cys Phe Lys Val  Phe Phe Lys
    5435                 5440                 5445

Gly Asn  Val Gln Val Asp Asn  Gly Ser Ser Ile Asn  Arg Lys Gln
    5450                 5455                 5460

Leu Glu  Ile Val Lys Leu Phe  Leu Val Lys Asn Pro  Ser Trp Ser
    5465                 5470                 5475

Lys Ala  Val Phe Ile Ser Pro  Tyr Asn Ser Gln Asn  Tyr Val Ala
    5480                 5485                 5490

Ser Arg  Phe Leu Gly Leu Gln  Ile Gln Thr Val Asp  Ser Ser Gln
    5495                 5500                 5505

Gly Ser  Glu Tyr Asp Tyr Val  Ile Tyr Ala Gln Thr  Ser Asp Thr
    5510                 5515                 5520

Ala His  Ala Cys Asn Val Asn  Arg Phe Asn Val Ala  Ile Thr Arg
    5525                 5530                 5535

Ala Lys  Lys Gly Ile Phe Cys  Val Met Cys Asp Lys  Thr Leu Phe
    5540                 5545                 5550

Asp Ser  Leu Lys Phe Phe Glu  Ile Lys His Ala Asp  Leu His Ser
    5555                 5560                 5565

Ser Gln  Val Cys Gly Leu Phe  Lys Asn Cys Thr Arg  Thr Pro Leu
    5570                 5575                 5580

Asn Leu  Pro Pro Thr His Ala  His Thr Phe Leu Ser  Leu Ser Asp
    5585                 5590                 5595

Gln Phe  Lys Thr Thr Gly Asp  Leu Ala Val Gln Ile  Gly Ser Asn
    5600                 5605                 5610

Asn Val  Cys Thr Tyr Glu His  Val Ile Ser Phe Met  Gly Phe Arg
    5615                 5620                 5625

Phe Asp  Ile Ser Ile Pro Gly  Ser His Ser Leu Phe  Cys Thr Arg
    5630                 5635                 5640

Asp Phe  Ala Ile Arg Asn Val  Arg Gly Trp Leu Gly  Met Asp Val
    5645                 5650                 5655

Glu Ser  Ala His Val Cys Gly  Asp Asn Ile Gly Thr  Asn Val Pro
    5660                 5665                 5670

Leu Gln  Val Gly Phe Ser Asn  Gly Val Asn Phe Val  Val Gln Thr
    5675                 5680                 5685

Glu Gly  Cys Val Ser Thr Asn  Phe Gly Asp Val Ile  Lys Pro Val
    5690                 5695                 5700

Cys Ala  Lys Ser Pro Pro Gly  Glu Gln Phe Arg His  Leu Ile Pro
    5705                 5710                 5715

Leu Leu  Arg Lys Gly Gln Pro  Trp Leu Ile Val Arg  Arg Arg Ile
    5720                 5725                 5730

Val Gln  Met Ile Ser Asp Tyr  Leu Ser Asn Leu Ser  Asp Ile Leu
    5735                 5740                 5745
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Val Phe  Val Leu Trp Ala Gly  Ser Leu Glu Leu Thr  Thr Met Arg
    5750                 5755                 5760

Tyr Phe  Val Lys Ile Gly Pro  Ile Lys Tyr Cys Tyr  Cys Gly Asn
    5765                 5770                 5775

Ser Ala  Thr Cys Tyr Asn Ser  Val Ser Asn Glu Tyr  Cys Cys Phe
    5780                 5785                 5790

Lys His  Ala Leu Gly Cys Asp  Tyr Val Tyr Asn Pro  Tyr Ala Phe
    5795                 5800                 5805

Asp Ile  Gln Gln Trp Gly Tyr  Val Gly Ser Leu Ser  Gln Asn His
    5810                 5815                 5820

His Thr  Phe Cys Asn Ile His  Arg Asn Glu His Asp  Ala Ser Gly
    5825                 5830                 5835

Asp Ala  Val Met Thr Arg Cys  Leu Ala Val His Asp  Cys Phe Val
    5840                 5845                 5850

Lys Asn  Val Asp Trp Thr Val  Thr Tyr Pro Phe Ile  Ala Asn Glu
    5855                 5860                 5865

Lys Phe  Ile Asn Gly Cys Gly  Arg Asn Val Gln Gly  His Val Val
    5870                 5875                 5880

Arg Ala  Ala Leu Lys Leu Tyr  Lys Pro Ser Val Ile  His Asp Ile
    5885                 5890                 5895

Gly Asn  Pro Lys Gly Val Arg  Cys Ala Val Thr Asp  Ala Lys Trp
    5900                 5905                 5910

Tyr Cys  Tyr Asp Lys Gln Pro  Val Asn Ser Asn Val  Lys Leu Leu
    5915                 5920                 5925

Asp Tyr  Asp Tyr Ala Thr His  Gly Gln Leu Asp Gly  Leu Cys Leu
    5930                 5935                 5940

Phe Trp  Asn Cys Asn Val Asp  Met Tyr Pro Glu Phe  Ser Ile Val
    5945                 5950                 5955

Cys Arg  Phe Asp Thr Arg Thr  Arg Ser Val Phe Asn  Leu Glu Gly
    5960                 5965                 5970

Val Asn  Gly Gly Ser Leu Tyr  Val Asn Lys His Ala  Phe His Thr
    5975                 5980                 5985

Pro Ala  Tyr Asp Lys Arg Ala  Phe Val Lys Leu Lys  Pro Met Pro
    5990                 5995                 6000

Phe Phe  Tyr Phe Asp Asp Ser  Asp Cys Asp Val Val  Gln Glu Gln
    6005                 6010                 6015

Val Asn  Tyr Val Pro Leu Arg  Ala Ser Ser Cys Val  Thr Arg Cys
    6020                 6025                 6030

Asn Ile  Gly Gly Ala Val Cys  Ser Lys His Ala Asn  Leu Tyr Gln
    6035                 6040                 6045

Lys Tyr  Val Glu Ala Tyr Asn  Thr Phe Thr Gln Ala  Gly Phe Asn
    6050                 6055                 6060

Ile Trp  Val Pro His Ser Phe  Asp Val Tyr Asn Leu  Trp Gln Ile
    6065                 6070                 6075

Phe Ile  Glu Thr Asn Leu Gln  Ser Leu Glu Asn Ile  Ala Phe Asn
    6080                 6085                 6090

Val Val  Lys Lys Gly Cys Phe  Thr Gly Val Asp Gly  Glu Leu Pro
    6095                 6100                 6105

Val Ala  Val Val Asn Asp Lys  Val Phe Val Arg Tyr  Gly Asp Val
    6110                 6115                 6120

Asp Asn  Leu Val Phe Thr Asn  Lys Thr Thr Leu Pro  Thr Asn Val
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    6125                6130                6135

Ala Phe  Glu Leu Phe Ala Lys  Arg Lys Met Gly Leu  Thr Pro Pro
    6140                6145                6150

Leu Ser  Ile Leu Lys Asn Leu  Gly Val Val Ala Thr  Tyr Lys Phe
    6155                6160                6165

Val Leu  Trp Asp Tyr Glu Ala  Glu Arg Pro Phe Thr  Ser Tyr Thr
    6170                6175                6180

Lys Ser  Val Cys Lys Tyr Thr  Asp Phe Asn Glu Asp  Val Cys Val
    6185                6190                6195

Cys Phe  Asp Asn Ser Ile Gln  Gly Ser Tyr Glu Arg  Phe Thr Leu
    6200                6205                6210

Thr Thr  Asn Ala Val Leu Phe  Ser Thr Val Val Ile  Lys Asn Leu
    6215                6220                6225

Thr Pro  Ile Lys Leu Asn Phe  Gly Met Leu Asn Gly  Met Pro Val
    6230                6235                6240

Ser Ser  Ile Lys Gly Asp Lys  Gly Val Glu Lys Leu  Val Asn Trp
    6245                6250                6255

Tyr Ile  Tyr Val Arg Lys Asn  Gly Gln Phe Gln Asp  His Tyr Asp
    6260                6265                6270

Gly Phe  Tyr Thr Gln Gly Arg  Asn Leu Ser Asp Phe  Thr Pro Arg
    6275                6280                6285

Ser Asp  Met Glu Tyr Asp Phe  Leu Asn Met Asp Met  Gly Val Phe
    6290                6295                6300

Ile Asn  Lys Tyr Gly Leu Glu  Asp Phe Asn Phe Glu  His Val Val
    6305                6310                6315

Tyr Gly  Asp Val Ser Lys Thr  Thr Leu Gly Gly Leu  His Leu Leu
    6320                6325                6330

Ile Ser  Gln Phe Arg Leu Ser  Lys Met Gly Val Leu  Lys Ala Asp
    6335                6340                6345

Asp Phe  Val Thr Ala Ser Asp  Thr Thr Leu Arg Cys  Cys Thr Val
    6350                6355                6360

Thr Tyr  Leu Asn Glu Leu Ser  Ser Lys Val Val Cys  Thr Tyr Met
    6365                6370                6375

Asp Leu  Leu Leu Asp Asp Phe  Val Thr Ile Leu Lys  Ser Leu Asp
    6380                6385                6390

Leu Gly  Val Ile Ser Lys Val  His Glu Val Ile Ile  Asp Asn Lys
    6395                6400                6405

Pro Tyr  Arg Trp Met Leu Trp  Cys Lys Asp Asn His  Leu Ser Thr
    6410                6415                6420

Phe Tyr  Pro Gln Leu Gln Ser  Ala Glu Trp Lys Cys  Gly Tyr Ala
    6425                6430                6435

Met Pro  Gln Ile Tyr Lys Leu  Gln Arg Met Cys Leu  Glu Pro Cys
    6440                6445                6450

Asn Leu  Tyr Asn Tyr Gly Ala  Gly Ile Lys Leu Pro  Ser Gly Ile
    6455                6460                6465

Met Leu  Asn Val Val Lys Tyr  Thr Gln Leu Cys Gln  Tyr Leu Asn
    6470                6475                6480

Ser Thr  Thr Met Cys Val Pro  His Asn Met Arg Val  Leu His Tyr
    6485                6490                6495

Gly Ala  Gly Ser Asp Lys Gly  Val Ala Pro Gly Thr  Thr Val Leu
    6500                6505                6510
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Lys Arg  Trp Leu Pro Pro Asp  Ala Ile Ile Ile Asp  Asn Asp Ile
    6515                 6520                 6525

Asn Asp  Tyr Val Ser Asp Ala  Asp Phe Ser Ile Thr  Gly Asp Cys
    6530                 6535                 6540

Ala Thr  Val Tyr Leu Glu Asp  Lys Phe Asp Leu Leu  Ile Ser Asp
    6545                 6550                 6555

Met Tyr  Asp Gly Arg Ile Lys  Phe Cys Asp Gly Glu  Asn Val Ser
    6560                 6565                 6570

Lys Asp  Gly Phe Phe Thr Tyr  Leu Asn Gly Val Ile  Arg Glu Lys
    6575                 6580                 6585

Leu Ala  Ile Gly Gly Ser Val  Ala Ile Lys Ile Thr  Glu Tyr Ser
    6590                 6595                 6600

Trp Asn  Lys Tyr Leu Tyr Glu  Leu Ile Gln Arg Phe  Ala Phe Trp
    6605                 6610                 6615

Thr Leu  Phe Cys Thr Ser Val  Asn Thr Ser Ser Ser  Glu Ala Phe
    6620                 6625                 6630

Leu Ile  Gly Ile Asn Tyr Leu  Gly Asp Phe Ile Gln  Gly Pro Phe
    6635                 6640                 6645

Ile Ala  Gly Asn Thr Val His  Ala Asn Tyr Ile Phe  Trp Arg Asn
    6650                 6655                 6660

Ser Thr  Ile Met Ser Leu Ser  Tyr Asn Ser Val Leu  Asp Leu Ser
    6665                 6670                 6675

Lys Phe  Glu Cys Lys His Lys  Ala Thr Val Val Val  Thr Leu Lys
    6680                 6685                 6690

Asp Ser  Asp Val Asn Asp Met  Val Leu Ser Leu Ile  Lys Ser Gly
    6695                 6700                 6705

Arg Leu  Leu Leu Arg Asn Asn  Gly Arg Phe Gly Gly  Phe Ser Asn
    6710                 6715                 6720

His Leu  Val Ser Thr Lys
    6725


<210> SEQ ID NO 7
<211> LENGTH: 6758
<212> TYPE: PRT
<213> ORGANISM: Human coronavirus 229E

<400> SEQUENCE: 7

Met Ala Cys Asn Arg Val Thr Leu Ala Val Ala Ser Asp Ser Glu Ile
1               5                   10                  15

Ser Ala Asn Gly Cys Ser Thr Ile Ala Gln Ala Val Arg Arg Tyr Ser
            20                  25                  30

Glu Ala Ala Ser Asn Gly Phe Arg Ala Cys Arg Phe Val Ser Leu Asp
        35                  40                  45

Leu Gln Asp Cys Ile Val Gly Ile Ala Asp Asp Thr Tyr Val Met Gly
    50                  55                  60

Leu His Gly Asn Gln Thr Leu Phe Cys Asn Ile Met Lys Phe Ser Asp
65                  70                  75                  80

Arg Pro Phe Met Leu His Gly Trp Leu Val Phe Ser Asn Ser Asn Tyr
                85                  90                  95

Leu Leu Glu Glu Phe Asp Val Val Phe Gly Lys Arg Gly Gly Gly Asn
            100                 105                 110

Val Thr Tyr Thr Asp Gln Tyr Leu Cys Gly Ala Asp Gly Lys Pro Val
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        115                 120                 125

Met Ser Glu Asp Leu Trp Gln Phe Val Asp His Phe Gly Glu Asn Glu
    130                 135                 140

Glu Ile Ile Ile Asn Gly His Thr Tyr Val Cys Ala Trp Leu Thr Lys
145                 150                 155                 160

Arg Lys Pro Leu Asp Tyr Lys Arg Gln Asn Asn Leu Ala Ile Glu Glu
                165                 170                 175

Ile Glu Tyr Val His Gly Asp Ala Leu His Thr Leu Arg Asn Gly Ser
            180                 185                 190

Val Leu Glu Met Ala Lys Glu Val Lys Thr Ser Ser Lys Val Val Leu
        195                 200                 205

Ser Asp Ala Leu Asp Lys Leu Tyr Lys Val Phe Gly Ser Pro Val Met
    210                 215                 220

Thr Asn Gly Ser Asn Ile Leu Glu Ala Phe Thr Lys Pro Val Phe Ile
225                 230                 235                 240

Ser Ala Leu Val Gln Cys Thr Cys Gly Thr Lys Ser Trp Ser Val Gly
                245                 250                 255

Asp Trp Thr Gly Phe Lys Ser Ser Cys Cys Asn Val Ile Ser Asn Lys
            260                 265                 270

Leu Cys Val Val Pro Gly Asn Val Lys Pro Gly Asp Ala Val Ile Thr
        275                 280                 285

Thr Gln Gln Ala Gly Ala Gly Ile Lys Tyr Phe Cys Gly Met Thr Leu
    290                 295                 300

Lys Phe Val Ala Asn Ile Glu Gly Val Ser Val Trp Arg Val Ile Ala
305                 310                 315                 320

Leu Gln Ser Val Asp Cys Phe Val Ala Ser Ser Thr Phe Val Glu Glu
                325                 330                 335

Glu His Val Asn Arg Met Asp Thr Phe Cys Phe Asn Val Arg Asn Ser
            340                 345                 350

Val Thr Asp Glu Cys Arg Leu Ala Met Leu Gly Ala Glu Met Thr Ser
        355                 360                 365

Asn Val Arg Arg Gln Val Ala Ser Gly Val Ile Asp Ile Ser Thr Gly
    370                 375                 380

Trp Phe Asp Val Tyr Asp Asp Ile Phe Ala Glu Ser Lys Pro Trp Phe
385                 390                 395                 400

Val Arg Lys Ala Glu Asp Ile Phe Gly Pro Cys Trp Ser Ala Leu Ala
                405                 410                 415

Ser Ala Leu Lys Gln Leu Lys Val Thr Thr Gly Glu Leu Val Arg Phe
            420                 425                 430

Val Lys Ser Ile Cys Asn Ser Ala Val Ala Val Val Gly Gly Thr Ile
        435                 440                 445

Gln Ile Leu Ala Ser Val Pro Glu Lys Phe Leu Asn Ala Phe Asp Val
    450                 455                 460

Phe Val Thr Ala Ile Gln Thr Val Phe Asp Cys Ala Val Glu Thr Cys
465                 470                 475                 480

Thr Ile Ala Gly Lys Ala Phe Asp Lys Val Phe Asp Tyr Val Leu Leu
                485                 490                 495

Asp Asn Ala Leu Val Lys Leu Val Thr Thr Lys Leu Lys Gly Val Arg
            500                 505                 510

Glu Arg Gly Leu Asn Lys Val Lys Tyr Ala Thr Val Val Val Gly Ser
        515                 520                 525
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Thr Glu Glu Val Lys Ser Ser Arg Val Glu Arg Ser Thr Ala Val Leu
    530                 535                 540

Thr Ile Ala Asn Asn Tyr Ser Lys Leu Phe Asp Glu Gly Tyr Thr Val
545                 550                 555                 560

Val Ile Gly Asp Val Ala Tyr Phe Val Ser Asp Gly Tyr Phe Arg Leu
                565                 570                 575

Met Ala Ser Pro Asn Ser Val Leu Thr Thr Ala Val Tyr Lys Pro Leu
            580                 585                 590

Phe Ala Phe Asn Val Asn Val Met Gly Thr Arg Pro Glu Lys Phe Pro
        595                 600                 605

Thr Thr Val Thr Cys Glu Asn Leu Glu Ser Ala Val Leu Phe Val Asn
    610                 615                 620

Asp Lys Ile Thr Glu Phe Gln Leu Asp Tyr Ser Ile Asp Val Ile Asp
625                 630                 635                 640

Asn Glu Ile Ile Val Lys Pro Asn Ile Ser Leu Cys Val Pro Leu Tyr
                645                 650                 655

Val Arg Asp Tyr Val Asp Lys Trp Asp Asp Phe Cys Arg Gln Tyr Ser
            660                 665                 670

Asn Glu Ser Trp Phe Glu Asp Asp Tyr Arg Ala Phe Ile Ser Val Leu
        675                 680                 685

Asp Ile Thr Asp Ala Ala Val Lys Ala Ala Glu Ser Lys Ala Phe Val
    690                 695                 700

Asp Thr Ile Val Pro Pro Cys Pro Ser Ile Leu Lys Val Ile Asp Gly
705                 710                 715                 720

Gly Lys Ile Trp Asn Gly Val Ile Lys Asn Val Asn Ser Val Arg Asp
                725                 730                 735

Trp Leu Lys Ser Leu Lys Leu Asn Leu Thr Gln Gln Gly Leu Leu Gly
            740                 745                 750

Thr Cys Ala Lys Arg Phe Lys Arg Trp Leu Gly Ile Leu Leu Glu Ala
        755                 760                 765

Tyr Asn Ala Phe Leu Asp Thr Val Val Ser Thr Val Lys Ile Gly Gly
    770                 775                 780

Leu Thr Phe Lys Thr Tyr Ala Phe Asp Lys Pro Tyr Ile Val Ile Arg
785                 790                 795                 800

Asp Ile Val Cys Lys Val Glu Asn Lys Thr Glu Ala Glu Trp Ile Glu
                805                 810                 815

Leu Phe Pro His Asn Asp Arg Ile Lys Ser Phe Ser Thr Phe Glu Ser
            820                 825                 830

Ala Tyr Met Pro Ile Ala Asp Pro Thr His Phe Asp Ile Glu Glu Val
        835                 840                 845

Glu Leu Leu Asp Ala Glu Phe Val Glu Pro Gly Cys Gly Gly Ile Leu
    850                 855                 860

Ala Val Ile Asp Glu His Val Phe Tyr Lys Lys Asp Gly Val Tyr Tyr
865                 870                 875                 880

Pro Ser Asn Gly Thr Asn Ile Leu Pro Val Ala Phe Thr Lys Ala Ala
                885                 890                 895

Gly Gly Lys Val Ser Phe Ser Asp Asp Val Glu Val Lys Asp Ile Glu
            900                 905                 910

Pro Val Tyr Arg Val Lys Leu Cys Phe Glu Phe Glu Asp Glu Lys Leu
        915                 920                 925
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Val Asp Val Cys Glu Lys Ala Ile Gly Lys Lys Ile Lys His Glu Gly
    930                 935                 940

Asp Trp Asp Ser Phe Cys Lys Thr Ile Gln Ser Ala Leu Ser Val Val
945                 950                 955                 960

Ser Cys Tyr Val Asn Leu Pro Thr Tyr Tyr Ile Tyr Asp Glu Glu Gly
                965                 970                 975

Gly Asn Asp Leu Ser Leu Pro Val Met Ile Ser Glu Trp Pro Leu Ser
            980                 985                 990

Val Gln Gln Ala Gln Gln Glu Ala  Thr Leu Pro Asp Ile  Ala Glu Asp
        995                 1000                1005

Val Val  Asp Gln Val Glu Glu  Val Asn Ser Ile Phe  Asp Ile Glu
    1010                1015                1020

Thr Val  Asp Val Lys His Asp  Val Ser Pro Phe Glu  Met Pro Phe
    1025                1030                1035

Glu Glu  Leu Asn Gly Leu Lys  Ile Leu Lys Gln Leu  Asp Asn Asn
    1040                1045                1050

Cys Trp  Val Asn Ser Val Met  Leu Gln Ile Gln Leu  Thr Gly Ile
    1055                1060                1065

Leu Asp  Gly Asp Tyr Ala Met  Gln Phe Phe Lys Met  Gly Arg Val
    1070                1075                1080

Ala Lys  Met Ile Glu Arg Cys  Tyr Thr Ala Glu Gln  Cys Ile Arg
    1085                1090                1095

Gly Ala  Met Gly Asp Val Gly  Leu Cys Met Tyr Arg  Leu Leu Lys
    1100                1105                1110

Asp Leu  His Thr Gly Phe Met  Val Met Asp Tyr Lys  Cys Ser Cys
    1115                1120                1125

Thr Ser  Gly Arg Leu Glu Glu  Ser Gly Ala Val Leu  Phe Cys Thr
    1130                1135                1140

Pro Thr  Lys Lys Ala Phe Pro  Tyr Gly Thr Cys Leu  Asn Cys Asn
    1145                1150                1155

Ala Pro  Arg Met Cys Thr Ile  Arg Gln Leu Gln Gly  Thr Ile Ile
    1160                1165                1170

Phe Val  Gln Gln Lys Pro Glu  Pro Val Asn Pro Val  Ser Phe Val
    1175                1180                1185

Val Lys  Pro Val Cys Ser Ser  Ile Phe Arg Gly Ala  Val Ser Cys
    1190                1195                1200

Gly His  Tyr Gln Thr Asn Ile  Tyr Ser Gln Asn Leu  Cys Val Asp
    1205                1210                1215

Gly Phe  Gly Val Asn Lys Ile  Gln Pro Trp Thr Asn  Asp Ala Leu
    1220                1225                1230

Asn Thr  Ile Cys Ile Lys Asp  Ala Asp Tyr Asn Ala  Lys Val Glu
    1235                1240                1245

Ile Ser  Val Thr Pro Ile Lys  Asn Thr Val Asp Thr  Thr Pro Lys
    1250                1255                1260

Glu Glu  Phe Val Val Lys Glu  Lys Leu Asn Ala Phe  Leu Val His
    1265                1270                1275

Asp Asn  Val Ala Phe Tyr Gln  Gly Asp Val Asp Thr  Val Val Asn
    1280                1285                1290

Gly Val  Asp Phe Asp Phe Ile  Val Asn Ala Ala Asn  Glu Asn Leu
    1295                1300                1305

Ala His  Gly Gly Gly Leu Ala  Lys Ala Leu Asp Val  Tyr Thr Lys
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    1310                1315                1320

Gly Lys  Leu Gln Arg Leu Ser  Lys Glu His Ile Gly  Leu Ala Gly
    1325                1330                1335

Lys Val  Lys Val Gly Thr Gly  Val Met Val Glu Cys  Asp Ser Leu
    1340                1345                1350

Arg Ile  Phe Asn Val Val Gly  Pro Arg Lys Gly Lys  His Glu Arg
    1355                1360                1365

Asp Leu  Leu Ile Lys Ala Tyr  Asn Thr Ile Asn Asn  Glu Gln Gly
    1370                1375                1380

Thr Pro  Leu Thr Pro Ile Leu  Ser Cys Gly Ile Phe  Gly Ile Lys
    1385                1390                1395

Leu Glu  Thr Ser Leu Glu Val  Leu Leu Asp Val Cys  Asn Thr Lys
    1400                1405                1410

Glu Val  Lys Val Phe Val Tyr  Thr Asp Thr Glu Val  Cys Lys Val
    1415                1420                1425

Lys Asp  Phe Val Ser Gly Leu  Val Asn Val Gln Lys  Val Glu Gln
    1430                1435                1440

Pro Lys  Ile Glu Pro Lys Pro  Val Ser Val Ile Lys  Val Ala Pro
    1445                1450                1455

Lys Pro  Tyr Arg Val Asp Gly  Lys Phe Ser Tyr Phe  Thr Glu Asp
    1460                1465                1470

Leu Leu  Cys Val Ala Asp Asp  Lys Pro Ile Val Leu  Phe Thr Asp
    1475                1480                1485

Ser Met  Leu Thr Leu Asp Asp  Arg Gly Leu Ala Leu  Asp Asn Ala
    1490                1495                1500

Leu Ser  Gly Val Leu Ser Ala  Ala Ile Lys Asp Cys  Val Asp Ile
    1505                1510                1515

Asn Lys  Ala Ile Pro Ser Gly  Asn Leu Ile Lys Phe  Asp Ile Gly
    1520                1525                1530

Ser Val  Val Val Tyr Met Cys  Val Val Pro Ser Glu  Lys Asp Lys
    1535                1540                1545

His Leu  Asp Asn Asn Val Gln  Arg Cys Thr Arg Lys  Leu Asn Arg
    1550                1555                1560

Leu Met  Cys Asp Ile Val Cys  Thr Ile Pro Ala Asp  Tyr Ile Leu
    1565                1570                1575

Pro Leu  Val Leu Ser Ser Leu  Thr Cys Asn Val Ser  Phe Val Gly
    1580                1585                1590

Glu Leu  Lys Ala Ala Glu Ala  Lys Val Ile Thr Ile  Lys Val Thr
    1595                1600                1605

Glu Asp  Gly Val Asn Val His  Asp Val Thr Val Thr  Thr Asp Lys
    1610                1615                1620

Ser Phe  Glu Gln Gln Val Gly  Val Ile Ala Asp Lys  Asp Lys Asp
    1625                1630                1635

Leu Ser  Gly Ala Val Pro Ser  Asp Leu Asn Thr Ser  Glu Leu Leu
    1640                1645                1650

Thr Lys  Ala Ile Asp Val Asp  Trp Val Glu Phe Tyr  Gly Phe Lys
    1655                1660                1665

Asp Ala  Val Thr Phe Ala Thr  Val Asp His Ser Ala  Phe Ala Tyr
    1670                1675                1680

Glu Ser  Ala Val Val Asn Gly  Ile Arg Val Leu Lys  Thr Ser Asp
    1685                1690                1695
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Asn Asn  Cys Trp Val Asn Ala  Val Cys Ile Ala Leu  Gln Tyr Ser
    1700                 1705                 1710

Lys Pro  His Phe Ile Ser Gln  Gly Leu Asp Ala Ala  Trp Asn Lys
    1715                 1720                 1725

Phe Val  Leu Gly Asp Val Glu  Ile Phe Val Ala Phe  Val Tyr Tyr
    1730                 1735                 1740

Val Ala  Arg Leu Met Lys Gly  Asp Lys Gly Asp Ala  Glu Asp Thr
    1745                 1750                 1755

Leu Thr  Lys Leu Ser Lys Tyr  Leu Ala Asn Glu Ala  Gln Val Gln
    1760                 1765                 1770

Leu Glu  His Tyr Ser Ser Cys  Val Glu Cys Asp Ala  Lys Phe Lys
    1775                 1780                 1785

Asn Ser  Val Ala Ser Ile Asn  Ser Ala Ile Val Cys  Ala Ser Val
    1790                 1795                 1800

Lys Arg  Asp Gly Val Gln Val  Gly Tyr Cys Val His  Gly Ile Lys
    1805                 1810                 1815

Tyr Tyr  Ser Arg Val Arg Ser  Val Arg Gly Arg Ala  Ile Ile Val
    1820                 1825                 1830

Ser Val  Glu Gln Leu Glu Pro  Cys Ala Gln Ser Arg  Leu Leu Ser
    1835                 1840                 1845

Gly Val  Ala Tyr Thr Ala Phe  Ser Gly Pro Val Asp  Lys Gly His
    1850                 1855                 1860

Tyr Thr  Val Tyr Asp Thr Ala  Lys Lys Ser Met Tyr  Asp Gly Asp
    1865                 1870                 1875

Arg Phe  Val Lys His Asp Leu  Ser Leu Leu Ser Val  Thr Ser Val
    1880                 1885                 1890

Val Met  Val Gly Gly Tyr Val  Ala Pro Val Asn Thr  Val Lys Pro
    1895                 1900                 1905

Lys Pro  Val Ile Asn Gln Leu  Asp Glu Lys Ala Gln  Lys Phe Phe
    1910                 1915                 1920

Asp Phe  Gly Asp Phe Leu Ile  His Asn Phe Val Ile  Phe Phe Thr
    1925                 1930                 1935

Trp Leu  Leu Ser Met Phe Thr  Leu Cys Lys Thr Ala  Val Thr Thr
    1940                 1945                 1950

Gly Asp  Val Lys Ile Met Ala  Lys Ala Pro Gln Arg  Thr Gly Val
    1955                 1960                 1965

Val Leu  Lys Arg Ser Leu Lys  Tyr Asn Leu Lys Ala  Ser Ala Ala
    1970                 1975                 1980

Val Leu  Lys Ser Lys Trp Trp  Leu Leu Ala Lys Phe  Thr Lys Leu
    1985                 1990                 1995

Leu Leu  Leu Ile Tyr Thr Leu  Tyr Ser Val Val Leu  Leu Cys Val
    2000                 2005                 2010

Arg Phe  Gly Pro Phe Asn Phe  Cys Ser Glu Thr Val  Asn Gly Tyr
    2015                 2020                 2025

Ala Lys  Ser Asn Phe Val Lys  Asp Asp Tyr Cys Asp  Gly Ser Leu
    2030                 2035                 2040

Gly Cys  Lys Met Cys Leu Phe  Gly Tyr Gln Glu Leu  Ser Gln Phe
    2045                 2050                 2055

Ser His  Leu Asp Val Val Trp  Lys His Ile Thr Asp  Pro Leu Phe
    2060                 2065                 2070
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Ser Asn  Met Gln Pro Phe Ile  Val Met Val Leu Leu  Leu Ile Phe
    2075                 2080                 2085

Gly Asp  Asn Tyr Leu Arg Cys  Phe Leu Leu Tyr Phe  Val Ala Gln
    2090                 2095                 2100

Met Ile  Ser Thr Val Gly Val  Phe Leu Gly Tyr Lys  Glu Thr Asn
    2105                 2110                 2115

Trp Phe  Leu His Phe Ile Pro  Phe Asp Val Ile Cys  Asp Glu Leu
    2120                 2125                 2130

Leu Val  Thr Val Ile Val Ile  Lys Val Ile Ser Phe  Val Arg His
    2135                 2140                 2145

Val Leu  Phe Gly Cys Glu Asn  Pro Asp Cys Ile Ala  Cys Ser Lys
    2150                 2155                 2160

Ser Ala  Arg Leu Lys Arg Phe  Pro Val Asn Thr Ile  Val Asn Gly
    2165                 2170                 2175

Val Gln  Arg Ser Phe Tyr Val  Asn Ala Asn Gly Gly  Ser Lys Phe
    2180                 2185                 2190

Cys Lys  Lys His Arg Phe Phe  Cys Val Asp Cys Asp  Ser Tyr Gly
    2195                 2200                 2205

Tyr Gly  Ser Thr Phe Ile Thr  Pro Glu Val Ser Arg  Glu Leu Gly
    2210                 2215                 2220

Asn Ile  Thr Lys Thr Asn Val  Gln Pro Thr Gly Pro  Ala Tyr Val
    2225                 2230                 2235

Met Ile  Asp Lys Val Glu Phe  Glu Asn Gly Phe Tyr  Arg Leu Tyr
    2240                 2245                 2250

Ser Cys  Glu Thr Phe Trp Arg  Tyr Asn Phe Asp Ile  Thr Glu Ser
    2255                 2260                 2265

Lys Tyr  Ser Cys Lys Glu Val  Phe Lys Asn Cys Asn  Val Leu Asp
    2270                 2275                 2280

Asp Phe  Ile Val Phe Asn Asn  Asn Gly Thr Asn Val  Thr Gln Val
    2285                 2290                 2295

Lys Asn  Ala Ser Val Tyr Phe  Ser Gln Leu Leu Cys  Arg Pro Ile
    2300                 2305                 2310

Lys Leu  Val Asp Ser Glu Leu  Leu Ser Thr Leu Ser  Val Asp Phe
    2315                 2320                 2325

Asn Gly  Val Leu His Lys Ala  Tyr Ile Asp Val Leu  Arg Asn Ser
    2330                 2335                 2340

Phe Gly  Lys Asp Leu Asn Ala  Asn Met Ser Leu Ala  Glu Cys Lys
    2345                 2350                 2355

Arg Ala  Leu Gly Leu Ser Ile  Ser Asp His Glu Phe  Thr Ser Ala
    2360                 2365                 2370

Ile Ser  Asn Ala His Arg Cys  Asp Val Leu Leu Ser  Asp Leu Ser
    2375                 2380                 2385

Phe Asn  Asn Phe Val Ser Ser  Tyr Ala Lys Pro Glu  Glu Lys Leu
    2390                 2395                 2400

Ser Ala  Tyr Asp Leu Ala Cys  Cys Met Arg Ala Gly  Ala Lys Val
    2405                 2410                 2415

Val Asn  Ala Asn Val Leu Thr  Lys Asp Gln Thr Pro  Ile Val Trp
    2420                 2425                 2430

His Ala  Lys Asp Phe Asn Ser  Leu Ser Ala Glu Gly  Arg Lys Tyr
    2435                 2440                 2445

Ile Val  Lys Thr Ser Lys Ala  Lys Gly Leu Thr Phe  Leu Leu Thr
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    2450                2455                2460

Ile Asn  Glu Asn Gln Ala Val  Thr Gln Ile Pro Ala  Thr Ser Ile
    2465                2470                2475

Val Ala  Lys Gln Gly Ala Gly  Asp Ala Gly His Ser  Leu Thr Trp
    2480                2485                2490

Leu Trp  Leu Leu Cys Gly Leu  Val Cys Leu Ile Gln  Phe Tyr Leu
    2495                2500                2505

Cys Phe  Phe Met Pro Tyr Phe  Met Tyr Asp Ile Val  Ser Ser Phe
    2510                2515                2520

Glu Gly  Tyr Asp Phe Lys Tyr  Ile Glu Asn Gly Gln  Leu Lys Asn
    2525                2530                2535

Phe Glu  Ala Pro Leu Lys Cys  Val Arg Asn Val Phe  Glu Asn Phe
    2540                2545                2550

Glu Asp  Trp His Tyr Ala Lys  Phe Gly Phe Thr Pro  Leu Asn Lys
    2555                2560                2565

Gln Ser  Cys Pro Ile Val Val  Gly Val Ser Glu Ile  Val Asn Thr
    2570                2575                2580

Val Ala  Gly Ile Pro Ser Asn  Val Tyr Leu Val Gly  Lys Thr Leu
    2585                2590                2595

Ile Phe  Thr Leu Gln Ala Ala  Phe Gly Asn Ala Gly  Val Cys Tyr
    2600                2605                2610

Asp Ile  Phe Gly Val Thr Thr  Pro Glu Lys Cys Ile  Phe Thr Ser
    2615                2620                2625

Ala Cys  Thr Arg Leu Glu Gly  Leu Gly Gly Asn Asn  Val Tyr Cys
    2630                2635                2640

Tyr Asn  Thr Ala Leu Met Glu  Gly Ser Leu Pro Tyr  Ser Ser Ile
    2645                2650                2655

Gln Ala  Asn Ala Tyr Tyr Lys  Tyr Asp Asn Gly Asn  Phe Ile Lys
    2660                2665                2670

Leu Pro  Glu Val Ile Ala Gln  Gly Phe Gly Phe Arg  Thr Val Arg
    2675                2680                2685

Thr Ile  Ala Thr Lys Tyr Cys  Arg Val Gly Glu Cys  Val Glu Ser
    2690                2695                2700

Asn Ala  Gly Val Cys Phe Gly  Phe Asp Lys Trp Phe  Val Asn Asp
    2705                2710                2715

Gly Arg  Val Ala Asn Gly Tyr  Val Cys Gly Thr Gly  Leu Trp Asn
    2720                2725                2730

Leu Val  Phe Asn Ile Leu Ser  Met Phe Ser Ser Ser  Phe Ser Val
    2735                2740                2745

Ala Ala  Met Ser Gly Gln Ile  Leu Leu Asn Cys Ala  Leu Gly Ala
    2750                2755                2760

Phe Ala  Ile Phe Cys Cys Phe  Leu Val Thr Lys Phe  Arg Arg Met
    2765                2770                2775

Phe Gly  Asp Leu Ser Val Gly  Val Cys Thr Val Val  Val Ala Val
    2780                2785                2790

Leu Leu  Asn Asn Val Ser Tyr  Ile Val Thr Gln Asn  Leu Val Thr
    2795                2800                2805

Met Ile  Ala Tyr Ala Ile Leu  Tyr Phe Phe Ala Thr  Arg Ser Leu
    2810                2815                2820

Arg Tyr  Ala Trp Ile Trp Cys  Ala Ala Tyr Leu Ile  Ala Tyr Ile
    2825                2830                2835
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Ser Phe  Ala Pro Trp Trp Leu  Cys Ala Trp Tyr Phe  Leu Ala Met
    2840                 2845                 2850

Leu Thr  Gly Leu Leu Pro Ser  Leu Leu Lys Leu Lys  Val Ser Thr
    2855                 2860                 2865

Asn Leu  Phe Glu Gly Asp Lys  Phe Val Gly Thr Phe  Glu Ser Ala
    2870                 2875                 2880

Ala Ala  Gly Thr Phe Val Ile  Asp Met Arg Ser Tyr  Glu Lys Leu
    2885                 2890                 2895

Ala Asn  Ser Ile Ser Pro Glu  Lys Leu Lys Ser Tyr  Ala Ala Ser
    2900                 2905                 2910

Tyr Asn  Arg Tyr Lys Tyr Tyr  Ser Gly Asn Ala Asn  Glu Ala Asp
    2915                 2920                 2925

Tyr Arg  Cys Ala Cys Tyr Ala  Tyr Leu Ala Lys Ala  Met Leu Asp
    2930                 2935                 2940

Phe Ser  Arg Asp His Asn Asp  Ile Leu Tyr Thr Pro  Pro Thr Val
    2945                 2950                 2955

Ser Tyr  Gly Ser Thr Leu Gln  Ala Gly Leu Arg Lys  Met Ala Gln
    2960                 2965                 2970

Pro Ser  Gly Phe Val Glu Lys  Cys Val Val Arg Val  Cys Tyr Gly
    2975                 2980                 2985

Asn Thr  Val Leu Asn Gly Leu  Trp Leu Gly Asp Ile  Val Tyr Cys
    2990                 2995                 3000

Pro Arg  His Val Ile Ala Ser  Asn Thr Thr Ser Ala  Ile Asp Tyr
    3005                 3010                 3015

Asp His  Glu Tyr Ser Ile Met  Arg Leu His Asn Phe  Ser Ile Ile
    3020                 3025                 3030

Ser Gly  Thr Ala Phe Leu Gly  Val Val Gly Ala Thr  Met His Gly
    3035                 3040                 3045

Val Thr  Leu Lys Ile Lys Val  Ser Gln Thr Asn Met  His Thr Pro
    3050                 3055                 3060

Arg His  Ser Phe Arg Thr Leu  Lys Ser Gly Glu Gly  Phe Asn Ile
    3065                 3070                 3075

Leu Ala  Cys Tyr Asp Gly Cys  Ala Gln Gly Val Phe  Gly Val Asn
    3080                 3085                 3090

Met Arg  Thr Asn Trp Thr Ile  Arg Gly Ser Phe Ile  Asn Gly Ala
    3095                 3100                 3105

Cys Gly  Ser Pro Gly Tyr Asn  Leu Lys Asn Gly Glu  Val Glu Phe
    3110                 3115                 3120

Val Tyr  Met His Gln Ile Glu  Leu Gly Ser Gly Ser  His Val Gly
    3125                 3130                 3135

Ser Ser  Phe Asp Gly Val Met  Tyr Gly Gly Phe Glu  Asp Gln Pro
    3140                 3145                 3150

Asn Leu  Gln Val Glu Ser Ala  Asn Gln Met Leu Thr  Val Asn Val
    3155                 3160                 3165

Val Ala  Phe Leu Tyr Ala Ala  Ile Leu Asn Gly Cys  Thr Trp Trp
    3170                 3175                 3180

Leu Lys  Gly Glu Lys Leu Phe  Val Glu His Tyr Asn  Glu Trp Ala
    3185                 3190                 3195

Gln Ala  Asn Gly Phe Thr Ala  Met Asn Gly Glu Asp  Ala Phe Ser
    3200                 3205                 3210
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Ile Leu  Ala Ala Lys Thr Gly  Val Cys Val Glu Arg  Leu Leu His
    3215                 3220                 3225

Ala Ile  Gln Val Leu Asn Asn  Gly Phe Gly Gly Lys  Gln Ile Leu
    3230                 3235                 3240

Gly Tyr  Ser Ser Leu Asn Asp  Glu Phe Ser Ile Asn  Glu Val Val
    3245                 3250                 3255

Lys Gln  Met Phe Gly Val Asn  Leu Gln Ser Gly Lys  Thr Thr Ser
    3260                 3265                 3270

Met Phe  Lys Ser Ile Ser Leu  Phe Ala Gly Phe Phe  Val Met Phe
    3275                 3280                 3285

Trp Ala  Glu Leu Phe Val Tyr  Thr Thr Thr Ile Trp  Val Asn Pro
    3290                 3295                 3300

Gly Phe  Leu Thr Pro Phe Met  Ile Leu Leu Val Ala  Leu Ser Leu
    3305                 3310                 3315

Cys Leu  Thr Phe Val Val Lys  His Lys Val Leu Phe  Leu Gln Val
    3320                 3325                 3330

Phe Leu  Leu Pro Ser Ile Ile  Val Ala Ala Ile Gln  Asn Cys Ala
    3335                 3340                 3345

Trp Asp  Tyr His Val Thr Lys  Val Leu Ala Glu Lys  Phe Asp Tyr
    3350                 3355                 3360

Asn Val  Ser Val Met Gln Met  Asp Ile Gln Gly Phe  Val Asn Ile
    3365                 3370                 3375

Phe Ile  Cys Leu Phe Val Ala  Leu Leu His Thr Trp  Arg Phe Ala
    3380                 3385                 3390

Lys Glu  Arg Cys Thr His Trp  Cys Thr Tyr Leu Phe  Ser Leu Ile
    3395                 3400                 3405

Ala Val  Leu Tyr Thr Ala Leu  Tyr Ser Tyr Asp Tyr  Val Ser Leu
    3410                 3415                 3420

Leu Val  Met Leu Leu Cys Ala  Ile Ser Asn Glu Trp  Tyr Ile Gly
    3425                 3430                 3435

Ala Ile  Ile Phe Arg Ile Cys  Arg Phe Gly Val Ala  Phe Leu Pro
    3440                 3445                 3450

Val Glu  Tyr Val Ser Tyr Phe  Asp Gly Val Lys Thr  Val Leu Leu
    3455                 3460                 3465

Phe Tyr  Met Leu Leu Gly Phe  Val Ser Cys Met Tyr  Tyr Gly Leu
    3470                 3475                 3480

Leu Tyr  Trp Ile Asn Arg Phe  Cys Lys Cys Thr Leu  Gly Val Tyr
    3485                 3490                 3495

Asp Phe  Cys Val Ser Pro Ala  Glu Phe Lys Tyr Met  Val Ala Asn
    3500                 3505                 3510

Gly Leu  Asn Ala Pro Asn Gly  Pro Phe Asp Ala Leu  Phe Leu Ser
    3515                 3520                 3525

Phe Lys  Leu Met Gly Ile Gly  Gly Pro Arg Thr Ile  Lys Val Ser
    3530                 3535                 3540

Thr Val  Gln Ser Lys Leu Thr  Asp Leu Lys Cys Thr  Asn Val Val
    3545                 3550                 3555

Leu Met  Gly Ile Leu Ser Asn  Met Asn Ile Ala Ser  Asn Ser Lys
    3560                 3565                 3570

Glu Trp  Ala Tyr Cys Val Glu  Met His Asn Lys Ile  Asn Leu Cys
    3575                 3580                 3585

Asp Asp  Pro Glu Thr Ala Gln  Glu Leu Leu Leu Ala  Leu Leu Ala
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    3590                3595                3600

Phe Phe  Leu Ser Lys His Ser  Asp Phe Gly Leu Gly  Asp Leu Val
    3605                3610                3615

Asp Ser  Tyr Phe Glu Asn Asp  Ser Ile Leu Gln Ser  Val Ala Ser
    3620                3625                3630

Ser Phe  Val Gly Met Pro Ser  Phe Val Ala Tyr Glu  Thr Ala Arg
    3635                3640                3645

Gln Glu  Tyr Glu Asn Ala Val  Ala Asn Gly Ser Ser  Pro Gln Ile
    3650                3655                3660

Ile Lys  Gln Leu Lys Lys Ala  Met Asn Val Ala Lys  Ala Glu Phe
    3665                3670                3675

Asp Arg  Glu Ser Ser Val Gln  Lys Lys Ile Asn Arg  Met Ala Glu
    3680                3685                3690

Gln Ala  Ala Ala Ala Met Tyr  Lys Glu Ala Arg Ala  Val Asn Arg
    3695                3700                3705

Lys Ser  Lys Val Val Ser Ala  Met His Ser Leu Leu  Phe Gly Met
    3710                3715                3720

Leu Arg  Arg Leu Asp Met Ser  Ser Val Asp Thr Ile  Leu Asn Met
    3725                3730                3735

Ala Arg  Asn Gly Val Val Pro  Leu Ser Val Ile Pro  Ala Thr Ser
    3740                3745                3750

Ala Ala  Arg Leu Val Val Val  Val Pro Asp His Asp  Ser Phe Val
    3755                3760                3765

Lys Met  Met Val Asp Gly Phe  Val His Tyr Ala Gly  Val Val Trp
    3770                3775                3780

Thr Leu  Gln Glu Val Lys Asp  Asn Asp Gly Lys Asn  Val His Leu
    3785                3790                3795

Lys Asp  Val Thr Lys Glu Asn  Gln Glu Ile Leu Val  Trp Pro Leu
    3800                3805                3810

Ile Leu  Thr Cys Glu Arg Val  Val Lys Leu Gln Asn  Asn Glu Ile
    3815                3820                3825

Met Pro  Gly Lys Met Lys Val  Lys Ala Thr Lys Gly  Glu Gly Asp
    3830                3835                3840

Gly Gly  Ile Thr Ser Glu Gly  Asn Ala Leu Tyr Asn  Asn Glu Gly
    3845                3850                3855

Gly Arg  Ala Phe Met Tyr Ala  Tyr Val Thr Thr Lys  Pro Gly Met
    3860                3865                3870

Lys Tyr  Val Lys Trp Glu His  Asp Ser Gly Val Val  Thr Val Glu
    3875                3880                3885

Leu Glu  Pro Pro Cys Arg Phe  Val Ile Asp Thr Pro  Thr Gly Pro
    3890                3895                3900

Gln Ile  Lys Tyr Leu Tyr Phe  Val Lys Asn Leu Asn  Asn Leu Arg
    3905                3910                3915

Arg Gly  Ala Val Leu Gly Tyr  Ile Gly Ala Thr Val  Arg Leu Gln
    3920                3925                3930

Ala Gly  Lys Gln Thr Glu Phe  Val Ser Asn Ser His  Leu Leu Thr
    3935                3940                3945

His Cys  Ser Phe Ala Val Asp  Pro Ala Ala Ala Tyr  Leu Asp Ala
    3950                3955                3960

Val Lys  Gln Gly Ala Lys Pro  Val Gly Asn Cys Val  Lys Met Leu
    3965                3970                3975
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Thr Asn  Gly Ser Gly Ser Gly  Gln Ala Ile Thr Cys  Thr Ile Asp
    3980                 3985                 3990

Ser Asn  Thr Thr Gln Asp Thr  Tyr Gly Gly Ala Ser  Val Cys Ile
    3995                 4000                 4005

Tyr Cys  Arg Ala His Val Ala  His Pro Thr Met Asp  Gly Phe Cys
    4010                 4015                 4020

Gln Tyr  Lys Gly Lys Trp Val  Gln Val Pro Ile Gly  Thr Asn Asp
    4025                 4030                 4035

Pro Ile  Arg Phe Cys Leu Glu  Asn Thr Val Cys Lys  Val Cys Gly
    4040                 4045                 4050

Cys Trp  Leu Asn His Gly Cys  Thr Cys Asp Arg Thr  Ala Ile Gln
    4055                 4060                 4065

Ser Phe  Asp Asn Ser Tyr Leu  Asn Arg Val Arg Gly  Ser Ser Ala
    4070                 4075                 4080

Ala Arg  Leu Glu Pro Cys Asn  Gly Thr Asp Ile Asp  Tyr Cys Val
    4085                 4090                 4095

Arg Ala  Phe Asp Val Tyr Asn  Lys Asp Ala Ser Phe  Ile Gly Lys
    4100                 4105                 4110

Asn Leu  Lys Ser Asn Cys Val  Arg Phe Lys Asn Val  Asp Lys Asp
    4115                 4120                 4125

Asp Ala  Phe Tyr Ile Val Lys  Arg Cys Ile Lys Ser  Val Met Asp
    4130                 4135                 4140

His Glu  Gln Ser Met Tyr Asn  Leu Leu Lys Gly Cys  Asn Ala Val
    4145                 4150                 4155

Ala Lys  His Asp Phe Phe Thr  Trp His Glu Gly Arg  Thr Ile Tyr
    4160                 4165                 4170

Gly Asn  Val Ser Arg Gln Asp  Leu Thr Lys Tyr Thr  Met Met Asp
    4175                 4180                 4185

Leu Cys  Phe Ala Leu Arg Asn  Phe Asp Glu Lys Asp  Cys Glu Val
    4190                 4195                 4200

Phe Lys  Glu Ile Leu Val Leu  Thr Gly Cys Cys Ser  Thr Asp Tyr
    4205                 4210                 4215

Phe Glu  Met Lys Asn Trp Phe  Asp Pro Ile Glu Asn  Glu Asp Ile
    4220                 4225                 4230

His Arg  Val Tyr Ala Ala Leu  Gly Lys Val Val Ala  Asn Ala Met
    4235                 4240                 4245

Leu Lys  Cys Val Ala Phe Cys  Asp Glu Met Val Leu  Lys Gly Val
    4250                 4255                 4260

Val Gly  Val Leu Thr Leu Asp  Asn Gln Asp Leu Asn  Gly Asn Phe
    4265                 4270                 4275

Tyr Asp  Phe Gly Asp Phe Val  Leu Cys Pro Pro Gly  Met Gly Ile
    4280                 4285                 4290

Pro Tyr  Cys Thr Ser Tyr Tyr  Ser Tyr Met Met Pro  Val Met Gly
    4295                 4300                 4305

Met Thr  Asn Cys Leu Ala Ser  Glu Cys Phe Met Lys  Ser Asp Ile
    4310                 4315                 4320

Phe Gly  Gln Asp Phe Lys Thr  Phe Asp Leu Leu Lys  Tyr Asp Phe
    4325                 4330                 4335

Thr Glu  His Lys Glu Val Leu  Phe Asn Lys Tyr Phe  Lys Tyr Trp
    4340                 4345                 4350
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Gly Gln  Asp Tyr His Pro Asp  Cys Val Asp Cys His  Asp Glu Met
    4355                 4360                 4365

Cys Ile  Leu His Cys Ser Asn  Phe Asn Thr Leu Phe  Ala Thr Thr
    4370                 4375                 4380

Ile Pro  Asn Thr Ala Phe Gly  Pro Leu Cys Arg Lys  Val Phe Ile
    4385                 4390                 4395

Asp Gly  Val Pro Val Val Ala  Thr Ala Gly Tyr His  Phe Lys Gln
    4400                 4405                 4410

Leu Gly  Leu Val Trp Asn Lys  Asp Val Asn Thr His  Ser Thr Arg
    4415                 4420                 4425

Leu Thr  Ile Thr Glu Leu Leu  Gln Phe Val Thr Asp  Pro Thr Leu
    4430                 4435                 4440

Ile Val  Ala Ser Ser Pro Ala  Leu Val Asp Lys Arg  Thr Val Cys
    4445                 4450                 4455

Phe Ser  Val Ala Ala Leu Ser  Thr Gly Leu Thr Ser  Gln Thr Val
    4460                 4465                 4470

Lys Pro  Gly His Phe Asn Lys  Glu Phe Tyr Asp Phe  Leu Arg Ser
    4475                 4480                 4485

Gln Gly  Phe Phe Asp Glu Gly  Ser Glu Leu Thr Leu  Lys His Phe
    4490                 4495                 4500

Phe Phe  Thr Gln Lys Gly Asp  Ala Ala Ile Lys Asp  Phe Asp Tyr
    4505                 4510                 4515

Tyr Arg  Tyr Asn Arg Pro Thr  Met Leu Asp Ile Gly  Gln Ala Arg
    4520                 4525                 4530

Val Ala  Tyr Gln Val Ala Ala  Arg Tyr Phe Asp Cys  Tyr Glu Gly
    4535                 4540                 4545

Gly Cys  Ile Thr Ser Arg Glu  Val Val Val Thr Asn  Leu Asn Lys
    4550                 4555                 4560

Ser Ala  Gly Trp Pro Leu Asn  Lys Phe Gly Lys Ala  Gly Leu Tyr
    4565                 4570                 4575

Tyr Glu  Ser Ile Ser Tyr Glu  Glu Gln Asp Ala Ile  Phe Ser Leu
    4580                 4585                 4590

Thr Lys  Arg Asn Ile Leu Pro  Thr Met Thr Gln Leu  Asn Leu Lys
    4595                 4600                 4605

Tyr Ala  Ile Ser Gly Lys Glu  Arg Ala Arg Thr Val  Gly Gly Val
    4610                 4615                 4620

Ser Leu  Leu Ala Thr Met Thr  Thr Arg Gln Phe His  Gln Lys Cys
    4625                 4630                 4635

Leu Lys  Ser Ile Val Ala Thr  Arg Asn Ala Thr Val  Val Ile Gly
    4640                 4645                 4650

Thr Thr  Lys Phe Tyr Gly Gly  Trp Asp Asn Met Leu  Lys Asn Leu
    4655                 4660                 4665

Met Ala  Asp Val Asp Asp Pro  Lys Leu Met Gly Trp  Asp Tyr Pro
    4670                 4675                 4680

Lys Cys  Asp Arg Ala Met Pro  Ser Met Ile Arg Met  Leu Ser Ala
    4685                 4690                 4695

Met Ile  Leu Gly Ser Lys His  Val Thr Cys Cys Thr  Ala Ser Asp
    4700                 4705                 4710

Lys Phe  Tyr Arg Leu Ser Asn  Glu Leu Ala Gln Val  Leu Thr Glu
    4715                 4720                 4725

Val Val  Tyr Ser Asn Gly Gly  Phe Tyr Phe Lys Pro  Gly Gly Thr
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    4730                4735                4740

Thr Ser  Gly Asp Ala Thr Thr  Ala Tyr Ala Asn Ser  Val Phe Asn
    4745                4750                4755

Ile Phe  Gln Ala Val Ser Ser  Asn Ile Asn Cys Val  Leu Ser Val
    4760                4765                4770

Asn Ser  Ser Asn Cys Asn Asn  Phe Asn Val Lys Lys  Leu Gln Arg
    4775                4780                4785

Gln Leu  Tyr Asp Asn Cys Tyr  Arg Asn Ser Asn Val  Asp Glu Ser
    4790                4795                4800

Phe Val  Asp Asp Phe Tyr Gly  Tyr Leu Gln Lys His  Phe Ser Met
    4805                4810                4815

Met Ile  Leu Ser Asp Asp Ser  Val Val Cys Tyr Asn  Lys Thr Tyr
    4820                4825                4830

Ala Gly  Leu Gly Tyr Ile Ala  Asp Ile Ser Ala Phe  Lys Ala Thr
    4835                4840                4845

Leu Tyr  Tyr Gln Asn Gly Val  Phe Met Ser Thr Ala  Lys Cys Trp
    4850                4855                4860

Thr Glu  Glu Asp Leu Ser Ile  Gly Pro His Glu Phe  Cys Ser Gln
    4865                4870                4875

His Thr  Met Gln Ile Val Asp  Glu Asn Gly Lys Tyr  Tyr Leu Pro
    4880                4885                4890

Tyr Pro  Asp Pro Ser Arg Ile  Ile Ser Ala Gly Val  Phe Val Asp
    4895                4900                4905

Asp Ile  Thr Lys Thr Asp Ala  Val Ile Leu Leu Glu  Arg Tyr Val
    4910                4915                4920

Ser Leu  Ala Ile Asp Ala Tyr  Pro Leu Ser Lys His  Pro Lys Pro
    4925                4930                4935

Glu Tyr  Arg Lys Val Phe Tyr  Ala Leu Leu Asp Trp  Val Lys His
    4940                4945                4950

Leu Asn  Lys Thr Leu Asn Glu  Gly Val Leu Glu Ser  Phe Ser Val
    4955                4960                4965

Thr Leu  Leu Asp Glu His Glu  Ser Lys Phe Trp Asp  Glu Ser Phe
    4970                4975                4980

Tyr Ala  Ser Met Tyr Glu Lys  Ser Thr Val Leu Gln  Ala Ala Gly
    4985                4990                4995

Leu Cys  Val Val Cys Gly Ser  Gln Thr Val Leu Arg  Cys Gly Asp
    5000                5005                5010

Cys Leu  Arg Arg Pro Met Leu  Cys Thr Lys Cys Ala  Tyr Asp His
    5015                5020                5025

Val Phe  Gly Thr Asp His Lys  Phe Ile Leu Ala Ile  Thr Pro Tyr
    5030                5035                5040

Val Cys  Asn Thr Ser Gly Cys  Asn Val Asn Asp Val  Thr Lys Leu
    5045                5050                5055

Tyr Leu  Gly Gly Leu Asn Tyr  Tyr Cys Val Asp His  Lys Pro His
    5060                5065                5070

Leu Ser  Phe Pro Leu Cys Ser  Ala Gly Asn Val Phe  Gly Leu Tyr
    5075                5080                5085

Lys Ser  Ser Ala Leu Gly Ser  Met Asp Ile Asp Val  Phe Asn Lys
    5090                5095                5100

Leu Ser  Thr Ser Asp Trp Ser  Asp Ile Arg Asp Tyr  Lys Leu Ala
    5105                5110                5115
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Asn Asp  Ala Lys Glu Ser Leu  Arg Leu Phe Ala Ala  Glu Thr Val
    5120                 5125                 5130

Lys Ala  Lys Glu Glu Ser Val  Lys Ser Ser Tyr Ala  Tyr Ala Thr
    5135                 5140                 5145

Leu Lys  Glu Ile Val Gly Pro  Lys Glu Leu Leu Leu  Leu Trp Glu
    5150                 5155                 5160

Ser Gly  Lys Ala Lys Pro Pro  Leu Asn Arg Asn Ser  Val Phe Thr
    5165                 5170                 5175

Cys Phe  Gln Ile Thr Lys Asp  Ser Lys Phe Gln Val  Gly Glu Phe
    5180                 5185                 5190

Val Phe  Glu Lys Val Asp Tyr  Gly Ser Asp Thr Val  Thr Tyr Lys
    5195                 5200                 5205

Ser Thr  Ala Thr Thr Lys Leu  Val Pro Gly Met Leu  Phe Ile Leu
    5210                 5215                 5220

Thr Ser  His Asn Val Ala Pro  Leu Arg Ala Pro Thr  Met Ala Asn
    5225                 5230                 5235

Gln Glu  Lys Tyr Ser Thr Ile  Tyr Lys Leu His Pro  Ser Phe Asn
    5240                 5245                 5250

Val Ser  Asp Ala Tyr Ala Asn  Leu Val Pro Tyr Tyr  Gln Leu Ile
    5255                 5260                 5265

Gly Lys  Gln Arg Ile Thr Thr  Ile Gln Gly Pro Pro  Gly Ser Gly
    5270                 5275                 5280

Lys Ser  His Cys Ser Ile Gly  Ile Gly Val Tyr Tyr  Pro Gly Ala
    5285                 5290                 5295

Arg Ile  Val Phe Thr Ala Cys  Ser His Ala Ala Val  Asp Ser Leu
    5300                 5305                 5310

Cys Ala  Lys Ala Val Thr Ala  Tyr Ser Val Asp Lys  Cys Thr Arg
    5315                 5320                 5325

Ile Ile  Pro Ala Arg Ala Arg  Val Glu Cys Tyr Ser  Gly Phe Lys
    5330                 5335                 5340

Pro Asn  Asn Asn Ser Ala Gln  Tyr Val Phe Ser Thr  Val Asn Ala
    5345                 5350                 5355

Leu Pro  Glu Val Asn Ala Asp  Ile Val Val Val Asp  Glu Val Ser
    5360                 5365                 5370

Met Cys  Thr Asn Tyr Asp Leu  Ser Val Ile Asn Gln  Arg Ile Ser
    5375                 5380                 5385

Tyr Lys  His Ile Val Tyr Val  Gly Asp Pro Gln Gln  Leu Pro Ala
    5390                 5395                 5400

Pro Arg  Val Leu Ile Ser Lys  Gly Val Met Glu Pro  Ile Asp Tyr
    5405                 5410                 5415

Asn Val  Val Thr Gln Arg Met  Cys Ala Ile Gly Pro  Asp Val Phe
    5420                 5425                 5430

Leu His  Lys Cys Tyr Arg Cys  Pro Ala Glu Ile Val  Asn Thr Val
    5435                 5440                 5445

Ser Glu  Leu Val Tyr Glu Asn  Lys Phe Val Pro Val  Lys Glu Ala
    5450                 5455                 5460

Ser Lys  Gln Cys Phe Lys Ile  Phe Glu Arg Gly Ser  Val Gln Val
    5465                 5470                 5475

Asp Asn  Gly Ser Ser Ile Asn  Arg Arg Gln Leu Asp  Val Val Lys
    5480                 5485                 5490
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Arg Phe  Ile His Lys Asn Ser  Thr Trp Ser Lys Ala  Val Phe Ile
    5495                 5500                 5505

Ser Pro  Tyr Asn Ser Gln Asn  Tyr Val Ala Ala Arg  Leu Leu Gly
    5510                 5515                 5520

Leu Gln  Thr Gln Thr Val Asp  Ser Ala Gln Gly Ser  Glu Tyr Asp
    5525                 5530                 5535

Tyr Val  Ile Phe Ala Gln Thr  Ser Asp Thr Ala His  Ala Cys Asn
    5540                 5545                 5550

Ala Asn  Arg Phe Asn Val Ala  Ile Thr Arg Ala Lys  Lys Gly Ile
    5555                 5560                 5565

Phe Cys  Ile Met Ser Asp Arg  Thr Leu Phe Asp Ala  Leu Lys Phe
    5570                 5575                 5580

Phe Glu  Ile Thr Met Thr Asp  Leu Gln Ser Glu Ser  Ser Cys Gly
    5585                 5590                 5595

Leu Phe  Lys Asp Cys Ala Arg  Asn Pro Ile Asp Leu  Pro Pro Ser
    5600                 5605                 5610

His Ala  Thr Thr Tyr Leu Ser  Leu Ser Asp Arg Phe  Lys Thr Ser
    5615                 5620                 5625

Gly Asp  Leu Ala Val Gln Ile  Gly Asn Asn Asn Val  Cys Thr Tyr
    5630                 5635                 5640

Glu His  Val Ile Ser Tyr Met  Gly Phe Arg Phe Asp  Val Ser Met
    5645                 5650                 5655

Pro Gly  Ser His Ser Leu Phe  Cys Thr Arg Asp Phe  Ala Met Arg
    5660                 5665                 5670

His Val  Arg Gly Trp Leu Gly  Met Asp Val Glu Gly  Ala His Val
    5675                 5680                 5685

Thr Gly  Asp Asn Val Gly Thr  Asn Val Pro Leu Gln  Val Gly Phe
    5690                 5695                 5700

Ser Asn  Gly Val Asp Phe Val  Ala Gln Pro Glu Gly  Cys Val Leu
    5705                 5710                 5715

Thr Asn  Thr Gly Ser Val Val  Lys Pro Val Arg Ala  Arg Ala Pro
    5720                 5725                 5730

Pro Gly  Glu Gln Phe Thr His  Ile Val Pro Leu Leu  Arg Lys Gly
    5735                 5740                 5745

Gln Pro  Trp Ser Val Leu Arg  Lys Arg Ile Val Gln  Met Ile Ala
    5750                 5755                 5760

Asp Phe  Leu Ala Gly Ser Ser  Asp Val Leu Val Phe  Val Leu Trp
    5765                 5770                 5775

Ala Gly  Gly Leu Glu Leu Thr  Thr Met Arg Tyr Phe  Val Lys Ile
    5780                 5785                 5790

Gly Ala  Val Lys His Cys Gln  Cys Gly Thr Val Ala  Thr Cys Tyr
    5795                 5800                 5805

Asn Ser  Val Ser Asn Asp Tyr  Cys Cys Phe Lys His  Ala Leu Gly
    5810                 5815                 5820

Cys Asp  Tyr Val Tyr Asn Pro  Tyr Val Ile Asp Ile  Gln Gln Trp
    5825                 5830                 5835

Gly Tyr  Val Gly Ser Leu Ser  Thr Asn His His Ala  Ile Cys Asn
    5840                 5845                 5850

Val His  Arg Asn Glu His Val  Ala Ser Gly Asp Ala  Ile Met Thr
    5855                 5860                 5865

Arg Cys  Leu Ala Val Tyr Asp  Cys Phe Val Lys Asn  Val Asp Trp
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    5870                5875                5880

Ser Ile  Thr Tyr Pro Met Ile  Ala Asn Glu Asn Ala  Ile Asn Lys
    5885                5890                5895

Gly Gly  Arg Thr Val Gln Ser  His Ile Met Arg Ala  Ala Ile Lys
    5900                5905                5910

Leu Tyr  Asn Pro Lys Ala Ile  His Asp Ile Gly Asn  Pro Lys Gly
    5915                5920                5925

Ile Arg  Cys Ala Val Thr Asp  Ala Lys Trp Tyr Cys  Tyr Asp Lys
    5930                5935                5940

Asn Pro  Ile Asn Ser Asn Val  Lys Thr Leu Glu Tyr  Asp Tyr Met
    5945                5950                5955

Thr His  Gly Gln Met Asp Gly  Leu Cys Leu Phe Trp  Asn Cys Asn
    5960                5965                5970

Val Asp  Met Tyr Pro Glu Phe  Ser Ile Val Cys Arg  Phe Asp Thr
    5975                5980                5985

Arg Thr  Arg Ser Thr Leu Asn  Leu Glu Gly Val Asn  Gly Gly Ser
    5990                5995                6000

Leu Tyr  Val Asn Asn His Ala  Phe His Thr Pro Ala  Tyr Asp Lys
    6005                6010                6015

Arg Ala  Met Ala Lys Leu Lys  Pro Ala Pro Phe Phe  Tyr Tyr Asp
    6020                6025                6030

Asp Gly  Ser Cys Glu Val Val  His Asp Gln Val Asn  Tyr Val Pro
    6035                6040                6045

Leu Arg  Ala Thr Asn Cys Ile  Thr Lys Cys Asn Ile  Gly Gly Ala
    6050                6055                6060

Val Cys  Ser Lys His Ala Asn  Leu Tyr Arg Ala Tyr  Val Glu Ser
    6065                6070                6075

Tyr Asn  Ile Phe Thr Gln Ala  Gly Phe Asn Ile Trp  Val Pro Thr
    6080                6085                6090

Thr Phe  Asp Cys Tyr Asn Leu  Trp Gln Thr Phe Thr  Glu Val Asn
    6095                6100                6105

Leu Gln  Gly Leu Glu Asn Ile  Ala Phe Asn Val Val  Asn Lys Gly
    6110                6115                6120

Ser Phe  Val Gly Ala Asp Gly  Glu Leu Pro Val Ala  Ile Ser Gly
    6125                6130                6135

Asp Lys  Val Phe Val Arg Asp  Gly Asn Thr Asp Asn  Leu Val Phe
    6140                6145                6150

Val Asn  Lys Thr Ser Leu Pro  Thr Asn Ile Ala Phe  Glu Leu Phe
    6155                6160                6165

Ala Lys  Arg Lys Val Gly Leu  Thr Pro Pro Leu Ser  Ile Leu Lys
    6170                6175                6180

Asn Leu  Gly Val Val Ala Thr  Tyr Lys Phe Val Leu  Trp Asp Tyr
    6185                6190                6195

Glu Ala  Glu Arg Pro Leu Thr  Ser Phe Thr Lys Ser  Val Cys Gly
    6200                6205                6210

Tyr Thr  Asp Phe Ala Glu Asp  Val Cys Thr Cys Tyr  Asp Asn Ser
    6215                6220                6225

Ile Gln  Gly Ser Tyr Glu Arg  Phe Thr Leu Ser Thr  Asn Ala Val
    6230                6235                6240

Leu Phe  Ser Ala Thr Ala Val  Lys Thr Gly Gly Lys  Ser Leu Pro
    6245                6250                6255
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Ala Ile  Lys Leu Asn Phe Gly  Met Leu Asn Gly Asn  Ala Ile Ala
    6260                 6265                 6270

Thr Val  Lys Ser Glu Asp Gly  Asn Ile Lys Asn Ile  Asn Trp Phe
    6275                 6280                 6285

Val Tyr  Val Arg Lys Asp Gly  Lys Pro Val Asp His  Tyr Asp Gly
    6290                 6295                 6300

Phe Tyr  Thr Gln Gly Arg Asn  Leu Gln Asp Phe Leu  Pro Arg Ser
    6305                 6310                 6315

Thr Met  Glu Glu Asp Phe Leu  Asn Met Asp Ile Gly  Val Phe Ile
    6320                 6325                 6330

Gln Lys  Tyr Gly Leu Glu Asp  Phe Asn Phe Glu His  Val Val Tyr
    6335                 6340                 6345

Gly Asp  Val Ser Lys Thr Thr  Leu Gly Gly Leu His  Leu Leu Ile
    6350                 6355                 6360

Ser Gln  Val Arg Leu Ser Lys  Met Gly Ile Leu Lys  Ala Glu Glu
    6365                 6370                 6375

Phe Val  Ala Ala Ser Asp Ile  Thr Leu Lys Cys Cys  Thr Val Thr
    6380                 6385                 6390

Tyr Leu  Asn Asp Pro Ser Ser  Lys Thr Val Cys Thr  Tyr Met Asp
    6395                 6400                 6405

Leu Leu  Leu Asp Asp Phe Val  Ser Val Leu Lys Ser  Leu Asp Leu
    6410                 6415                 6420

Thr Val  Val Ser Lys Val His  Glu Val Ile Ile Asp  Asn Lys Pro
    6425                 6430                 6435

Trp Arg  Trp Met Leu Trp Cys  Lys Asp Asn Ala Val  Ala Thr Phe
    6440                 6445                 6450

Tyr Pro  Gln Leu Gln Ser Ala  Glu Trp Lys Cys Gly  Tyr Ser Met
    6455                 6460                 6465

Pro Gly  Ile Tyr Lys Thr Gln  Arg Met Cys Leu Glu  Pro Cys Asn
    6470                 6475                 6480

Leu Tyr  Asn Tyr Gly Ala Gly  Leu Lys Leu Pro Ser  Gly Ile Met
    6485                 6490                 6495

Phe Asn  Val Val Lys Tyr Thr  Gln Leu Cys Gln Tyr  Phe Asn Ser
    6500                 6505                 6510

Thr Thr  Leu Cys Val Pro His  Asn Met Arg Val Leu  His Leu Gly
    6515                 6520                 6525

Ala Gly  Ser Asp Tyr Gly Val  Ala Pro Gly Thr Ala  Val Leu Lys
    6530                 6535                 6540

Arg Trp  Leu Pro His Asp Ala  Ile Val Val Asp Asn  Asp Val Val
    6545                 6550                 6555

Asp Tyr  Val Ser Asp Ala Asp  Phe Ser Val Thr Gly  Asp Cys Ala
    6560                 6565                 6570

Thr Val  Tyr Leu Glu Asp Lys  Phe Asp Leu Leu Ile  Ser Asp Met
    6575                 6580                 6585

Tyr Asp  Gly Arg Thr Lys Ala  Ile Asp Gly Glu Asn  Val Ser Lys
    6590                 6595                 6600

Glu Gly  Phe Phe Thr Tyr Ile  Asn Gly Phe Ile Cys  Glu Lys Leu
    6605                 6610                 6615

Ala Ile  Gly Gly Ser Ile Ala  Ile Lys Val Thr Glu  Tyr Ser Trp
    6620                 6625                 6630
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Asn Lys  Lys Leu Tyr Glu Leu  Val Gln Arg Phe Ser  Phe Trp Thr
    6635                 6640                 6645

Met Phe  Cys Thr Ser Val Asn  Thr Ser Ser Ser Glu  Ala Phe Val
    6650                 6655                 6660

Val Gly  Ile Asn Tyr Leu Gly  Asp Phe Ala Gln Gly  Pro Phe Ile
    6665                 6670                 6675

Asp Gly  Asn Ile Ile His Ala  Asn Tyr Val Phe Trp  Arg Asn Ser
    6680                 6685                 6690

Thr Val  Met Ser Leu Ser Tyr  Asn Ser Val Leu Asp  Leu Ser Lys
    6695                 6700                 6705

Phe Asn  Cys Lys His Lys Ala  Thr Val Val Val Gln  Leu Lys Asp
    6710                 6715                 6720

Ser Asp  Ile Asn Glu Met Val  Leu Ser Leu Val Arg  Ser Gly Lys
    6725                 6730                 6735

Leu Leu  Val Arg Gly Asn Gly  Lys Cys Leu Ser Phe  Ser Asn His
    6740                 6745                 6750

Leu Val  Ser Thr Lys
    6755


<210> SEQ ID NO 8
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 8

Asp Ala Val Asp Cys Ser Gln Asn Pro Leu Ala Glu Leu Lys Cys Ser
1               5                   10                  15

Val Lys Ser Phe Glu Ile Asp Lys Gly Ile Tyr Gln Thr Ser Asn Phe
            20                  25                  30


<210> SEQ ID NO 9
<211> LENGTH: 31
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 9

Asp Ala Val Asp Cys Ala Leu Asp Pro Leu Ser Glu Thr Lys Cys Thr
1               5                   10                  15

Leu Lys Ser Phe Thr Val Glu Lys Gly Ile Tyr Gln Thr Ser Asn
            20                  25                  30


<210> SEQ ID NO 10
<211> LENGTH: 76
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 10

Val Cys Gly Pro Lys Leu Ser Thr Asp Leu Ile Lys Asn Gln Cys Val
1               5                   10                  15

Asn Phe Asn Phe Asn Gly Leu Thr Gly Thr Gly Val Leu Thr Pro Ser
            20                  25                  30

Ser Lys Arg Phe Gln Pro Phe Gln Gln Phe Gly Arg Asp Val Ser Asp
        35                  40                  45

Phe Thr Asp Ser Val Arg Asp Pro Lys Thr Ser Glu Ile Leu Asp Ile
    50                  55                  60

Ser Pro Cys Ser Phe Gly Gly Val Ser Val Ile Thr
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65 70 75

<210> SEQ ID NO 11
<211> LENGTH: 75
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 11

Val Cys Gly Pro Lys Lys Ser Thr Asn Leu Val Lys Asn Lys Cys Val
1 5 10 15

Asn Phe Asn Phe Asn Gly Leu Thr Gly Thr Gly Val Leu Thr Glu Ser
20 25 30

Asn Lys Lys Phe Leu Pro Phe Gln Gln Phe Gly Arg Asp Ile Ala Asp
35 40 45

Thr Thr Asp Ala Val Arg Asp Pro Gln Thr Leu Glu Ile Leu Asp Ile
50 55 60

Thr Pro Cys Ser Phe Gly Gly Val Ser Val Ile
65 70 75

<210> SEQ ID NO 12
<211> LENGTH: 41
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 12

Gly Thr Asn Ala Ser Ser Glu Val Ala Val Leu Tyr Gln Asp Val Asn
1 5 10 15

Cys Thr Asp Val Ser Thr Ala Ile His Ala Asp Gln Leu Thr Pro Ala
20 25 30

Trp Arg Ile Tyr Ser Thr Gly Asn Asn
35 40

<210> SEQ ID NO 13
<211> LENGTH: 40
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 13

Gly Thr Asn Thr Ser Asn Gln Val Ala Val Leu Tyr Gln Asp Val Asn
1 5 10 15

Cys Thr Glu Val Pro Val Ala Ile His Ala Asp Gln Leu Thr Pro Thr
20 25 30

Trp Arg Val Tyr Ser Thr Gly Ser
35 40

<210> SEQ ID NO 14
<211> LENGTH: 19
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 14

Phe Ser Gln Ile Leu Pro Asp Pro Leu Lys Pro Thr Lys Arg Ser Phe
1 5 10 15

Ile Glu Asp

<210> SEQ ID NO 15
<211> LENGTH: 18
<212> TYPE: PRT

-continued

<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 15

Phe Ser Gln Ile Leu Pro Asp Pro Ser Lys Pro Ser Lys Arg Ser Phe
1 5 10 15

Ile Glu

<210> SEQ ID NO 16
<211> LENGTH: 23
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 16

Phe Gly Ala Gly Ala Ala Leu Gln Ile Pro Phe Ala Met Gln Met Ala
1 5 10 15

Tyr Arg Phe Asn Gly Ile Gly
20

<210> SEQ ID NO 17
<211> LENGTH: 22
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 17

Phe Gly Ala Gly Ala Ala Leu Gln Ile Pro Phe Ala Met Gln Met Ala
1 5 10 15

Tyr Arg Phe Asn Gly Ile
20

<210> SEQ ID NO 18
<211> LENGTH: 24
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 18

Met Ala Asp Asn Gly Thr Ile Thr Val Glu Glu Leu Lys Gln Leu Leu
1 5 10 15

Glu Gln Trp Asn Leu Val Ile Gly
20

<210> SEQ ID NO 19
<211> LENGTH: 24
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 19

Met Ala Asp Ser Asn Gly Thr Ile Thr Val Glu Glu Leu Lys Lys Leu
1 5 10 15

Leu Glu Gln Trp Asn Leu Val Ile
20

<210> SEQ ID NO 20
<211> LENGTH: 21
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 20

Pro Leu Met Glu Ser Glu Leu Val Ile Gly Ala Val Ile Ile Arg Gly
1 5 10 15

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His Leu Arg Met Ala
20

<210> SEQ ID NO 21
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 21

Pro Leu Leu Glu Ser Glu Leu Val Ile Gly Ala Val Ile Leu Arg Gly
1 5 10 15

His Leu Arg Ile
20

<210> SEQ ID NO 22
<211> LENGTH: 22
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 22

Pro Gln Gly Leu Pro Asn Asn Thr Ala Ser Trp Phe Thr Ala Leu Thr
1 5 10 15

Gln His Gly Lys Glu Glu
20

<210> SEQ ID NO 23
<211> LENGTH: 21
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 23

Arg Pro Gln Gly Leu Pro Asn Asn Thr Ala Ser Trp Phe Thr Ala Leu
1 5 10 15

Thr Gln His Gly Lys
20

<210> SEQ ID NO 24
<211> LENGTH: 21
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 24

Asn Asn Ala Ala Thr Val Leu Gln Leu Pro Gln Gly Thr Thr Leu Pro
1 5 10 15

Lys Gly Phe Tyr Ala
20

<210> SEQ ID NO 25
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 25

Asn Asn Asn Ala Ala Thr Val Leu Gln Leu Pro Gln Gly Thr Thr Leu
1 5 10 15

Pro Lys Gly Phe
20

<210> SEQ ID NO 26
<211> LENGTH: 48

-continued

<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 26

Lys His Ile Asp Ala Tyr Lys Thr Phe Pro Pro Thr Glu Pro Lys Lys
1 5 10 15

Asp Lys Lys Lys Lys Thr Asp Glu Ala Gln Pro Leu Pro Gln Arg Gln
20 25 30

Lys Lys Gln Pro Thr Val Thr Leu Leu Pro Ala Ala Asp Met Asp Asp
35 40 45

<210> SEQ ID NO 27
<211> LENGTH: 47
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 27

Asn Lys His Ile Asp Ala Tyr Lys Thr Phe Pro Pro Thr Glu Pro Lys
1 5 10 15

Lys Asp Lys Lys Lys Lys Thr Asp Glu Ala Gln Pro Leu Pro Gln Arg
20 25 30

Gln Lys Lys Gln Pro Thr Val Thr Leu Leu Pro Ala Ala Asp Met
35 40 45

<210> SEQ ID NO 28
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 28

Val Arg Gly Trp Val Phe Gly Ser Thr Met Asn Asn Lys Ser Gln Ser
1 5 10 15

Val Ile

<210> SEQ ID NO 29
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 29

Ile Arg Gly Trp Ile Phe Gly Thr Thr Leu Asp Ser Lys Thr Gln Ser
1 5 10 15

Leu Leu

<210> SEQ ID NO 30
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 30

Cys Thr Phe Glu Tyr Ile Ser Asp Ala Phe Ser Leu Asp
1 5 10

<210> SEQ ID NO 31
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 31

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```
Cys Thr Phe Glu Tyr Val Ser Gln Pro Phe Leu Met Asp
1               5                   10


<210> SEQ ID NO 32
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 32

Asp Ala Phe Ser Leu Asp Val Ser Glu Lys Ser Gly Asn
1               5                   10


<210> SEQ ID NO 33
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 33

Gln Pro Phe Leu Met Asp Leu Glu Gly Lys Gln Gly Asn
1               5                   10


<210> SEQ ID NO 34
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 34

Thr Asn Phe Arg Ala Ile Leu Thr Ala Phe Ser Pro Ala Gln Asp Ile
1               5                   10                  15

Trp


<210> SEQ ID NO 35
<211> LENGTH: 23
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 35

Thr Arg Phe Gln Thr Leu Leu Ala Leu His Arg Ser Tyr Leu Thr Pro
1               5                   10                  15

Gly Asp Ser Ser Ser Gly Trp
            20


<210> SEQ ID NO 36
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 36

Lys Ser Phe Glu Ile Asp Lys Gly Ile Tyr Gln Thr Ser Asn Phe Arg
1               5                   10                  15

Val Val


<210> SEQ ID NO 37
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 37

Lys Ser Phe Thr Val Glu Lys Gly Ile Tyr Gln Thr Ser Asn Phe Arg
1               5                   10                  15
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Val Gln

<210> SEQ ID NO 38
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 38

Ser Thr Phe Phe Ser Thr Phe Lys Cys Tyr Gly Val Ser Ala Thr Lys
1 5 10 15

Leu

<210> SEQ ID NO 39
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 39

Ser Ala Ser Phe Ser Thr Phe Lys Cys Tyr Gly Val Ser Pro Thr Lys
1 5 10 15

Leu

<210> SEQ ID NO 40
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 40

Lys Leu Pro Asp Asp Phe Met Gly Cys Val
1 5 10

<210> SEQ ID NO 41
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 41

Lys Leu Pro Asp Asp Phe Thr Gly Cys Val
1 5 10

<210> SEQ ID NO 42
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 42

Asn Ile Asp Ala Thr Ser Thr Gly Asn Tyr Asn Tyr Lys Tyr Arg Tyr
1 5 10 15

Leu Arg

<210> SEQ ID NO 43
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 43

Asn Leu Asp Ser Lys Val Gly Gly Asn Tyr Asn Tyr Leu Tyr Arg Leu
1 5 10 15

Phe Arg

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<210> SEQ ID NO 44
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 44

Tyr Leu Arg His Gly Lys Leu Arg Pro Phe Glu Arg Asp Ile Ser Asn
1 5 10 15

Val Pro

<210> SEQ ID NO 45
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 45

Tyr Leu Tyr Arg Leu Phe Arg Lys Ser Asn Leu Lys Pro Phe Glu Arg
1 5 10 15

Asp Ile

<210> SEQ ID NO 46
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 46

Arg Pro Phe Glu Arg Asp Ile Ser Asn Val Pro Phe Ser
1 5 10

<210> SEQ ID NO 47
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 47

Lys Pro Phe Glu Arg Asp Ile Ser Thr Glu Ile Tyr Gln
1 5 10

<210> SEQ ID NO 48
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 48

Lys Ser Ile Val Ala Tyr Thr Met Ser Leu Gly Ala Asp Ser Ser Ile
1 5 10 15

Ala Tyr

<210> SEQ ID NO 49
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 49

Gln Ser Ile Ile Ala Tyr Thr Met Ser Leu Gly Ala Glu Asn Ser Val
1 5 10 15

Ala Tyr

<210> SEQ ID NO 50

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<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 50

Ser Ile Val Ala Tyr Thr Met Ser Leu
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<210> SEQ ID NO 51
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 51

Ser Ile Ile Ala Tyr Thr Met Ser Leu
1 5

<210> SEQ ID NO 52
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 52

Thr Glu Cys Ala Asn Leu Leu Leu Gln Tyr Gly Ser Phe Cys Thr Gln
1 5 10 15

Leu

<210> SEQ ID NO 53
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 53

Thr Glu Cys Ser Asn Leu Leu Leu Gln Tyr Gly Ser Phe Cys Thr Gln
1 5 10 15

Leu

<210> SEQ ID NO 54
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 54

Val Lys Gln Met Tyr Lys Thr Pro Thr Leu Lys Tyr Phe Gly Gly Phe
1 5 10 15

Asn Phe

<210> SEQ ID NO 55
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 55

Val Lys Gln Ile Tyr Lys Thr Pro Pro Ile Lys Asp Phe Gly Gly Phe
1 5 10 15

Asn Phe

<210> SEQ ID NO 56
<211> LENGTH: 17
<212> TYPE: PRT

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<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 56

Glu Ser Leu Thr Thr Thr Ser Thr Ala Leu Gly Lys Leu Gln Asp Val
1 5 10 15

Val

<210> SEQ ID NO 57
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 57

Asp Ser Leu Ser Ser Thr Ala Ser Ala Leu Gly Lys Leu Gln Asp Val
1 5 10 15

Val

<210> SEQ ID NO 58
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 58

Ala Leu Asn Thr Leu Val Lys Gln Leu
1 5

<210> SEQ ID NO 59
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 59

Ala Leu Asn Thr Leu Val Lys Gln Leu
1 5

<210> SEQ ID NO 60
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 60

Val Leu Asn Asp Ile Leu Ser Arg Leu
1 5

<210> SEQ ID NO 61
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 61

Val Leu Asn Asp Ile Leu Ser Arg Leu
1 5

<210> SEQ ID NO 62
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 62

Leu Ile Thr Gly Arg Leu Gln Ser Leu
1 5

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<210> SEQ ID NO 63
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 63

Leu Ile Thr Gly Arg Leu Gln Ser Leu
1 5

<210> SEQ ID NO 64
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 64

Gln Leu Ile Arg Ala Ala Glu Ile Arg Ala Ser Ala Asn Leu Ala Ala
1 5 10 15

Thr Lys

<210> SEQ ID NO 65
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 65

Gln Leu Ile Arg Ala Ala Glu Ile Arg Ala Ser Ala Asn Leu Ala Ala
1 5 10 15

Thr Lys

<210> SEQ ID NO 66
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 66

Ser Trp Phe Ile Thr Gln Arg Asn Phe Phe Ser Pro Gln Ile Ile
1 5 10 15

<210> SEQ ID NO 67
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 67

His Trp Phe Val Thr Gln Arg Asn Phe Tyr Glu Pro Gln Ile Ile
1 5 10 15

<210> SEQ ID NO 68
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 68

Arg Leu Asn Glu Val Ala Lys Asn Leu
1 5

<210> SEQ ID NO 69
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

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<400> SEQUENCE: 69

Arg Leu Asn Glu Val Ala Lys Asn Leu
1 5

<210> SEQ ID NO 70
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 70

Asn Leu Asn Glu Ser Leu Ile Asp Leu
1 5

<210> SEQ ID NO 71
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 71

Asn Leu Asn Glu Ser Leu Ile Asp Leu
1 5

<210> SEQ ID NO 72
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 72

Phe Ile Ala Gly Leu Ile Ala Ile Val
1 5

<210> SEQ ID NO 73
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 73

Phe Ile Ala Gly Leu Ile Ala Ile Val
1 5

<210> SEQ ID NO 74
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 74

Arg Phe Phe Thr Leu Gly Ser Ile Thr Ala Gln Pro Val Lys Ile
1 5 10 15

<210> SEQ ID NO 75
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 75

Arg Ile Phe Thr Ile Gly Thr Val Thr Leu Lys Gln Gly Glu Ile
1 5 10 15

<210> SEQ ID NO 76
<211> LENGTH: 9
<212> TYPE: PRT

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<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 76

Ser Ile Thr Ala Gln Pro Val Lys Ile
1 5

<210> SEQ ID NO 77
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 77

Thr Val Thr Leu Lys Gln Gly Glu Ile
1 5

<210> SEQ ID NO 78
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 78

Thr Leu Ala Cys Phe Val Leu Ala Ala Val
1 5 10

<210> SEQ ID NO 79
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 79

Thr Leu Ala Cys Phe Val Leu Ala Ala Val
1 5 10

<210> SEQ ID NO 80
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 80

Gly Leu Met Trp Leu Ser Tyr Phe Val
1 5

<210> SEQ ID NO 81
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 81

Gly Leu Met Trp Leu Ser Tyr Phe Ile
1 5

<210> SEQ ID NO 82
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 82

His Leu Arg Met Ala Gly His Ser Leu
1 5

<210> SEQ ID NO 83
<211> LENGTH: 9

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<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 83

His Leu Arg Ile Ala Gly His His Leu
1 5

<210> SEQ ID NO 84
<211> LENGTH: 9
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<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 84

Ala Leu Asn Thr Pro Lys Asp His Ile
1 5

<210> SEQ ID NO 85
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 85

Ala Leu Asn Thr Pro Lys Asp His Ile
1 5

<210> SEQ ID NO 86
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 86

Leu Gln Leu Pro Gln Gly Thr Thr Leu
1 5

<210> SEQ ID NO 87
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 87

Leu Gln Leu Pro Gln Gly Thr Thr Leu
1 5

<210> SEQ ID NO 88
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 88

Gly Glu Thr Ala Leu Ala Leu Leu Leu Leu
1 5 10

<210> SEQ ID NO 89
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 89

Gly Asp Ala Ala Leu Ala Leu Leu Leu Leu
1 5 10

<210> SEQ ID NO 90

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<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 90

Leu Ala Leu Leu Leu Leu Asp Arg Leu
1 5

<210> SEQ ID NO 91
<211> LENGTH: 9
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<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 91

Leu Ala Leu Leu Leu Leu Asp Arg Leu
1 5

<210> SEQ ID NO 92
<211> LENGTH: 9
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<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 92

Leu Leu Leu Asp Arg Leu Asn Gln Leu
1 5

<210> SEQ ID NO 93
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 93

Leu Leu Leu Asp Arg Leu Asn Gln Leu
1 5

<210> SEQ ID NO 94
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 94

Arg Leu Asn Gln Leu Glu Ser Lys Val
1 5

<210> SEQ ID NO 95
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 95

Arg Leu Asn Gln Leu Glu Ser Lys Met
1 5

<210> SEQ ID NO 96
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 96

Thr Lys Gln Tyr Asn Val Thr Gln Ala Phe
1 5 10

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<210> SEQ ID NO 97
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 97

Thr Lys Ala Tyr Asn Val Thr Gln Ala Phe
1 5 10

<210> SEQ ID NO 98
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 98

Gly Met Ser Arg Ile Gly Met Glu Val
1 5

<210> SEQ ID NO 99
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 99

Gly Met Ser Arg Ile Gly Met Glu Val
1 5

<210> SEQ ID NO 100
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 100

Met Glu Val Thr Pro Ser Gly Thr Trp Leu
1 5 10

<210> SEQ ID NO 101
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 101

Met Glu Val Thr Pro Ser Gly Thr Trp Leu
1 5 10

<210> SEQ ID NO 102
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 102

Gln Phe Lys Asp Asn Val Ile Leu Leu
1 5

<210> SEQ ID NO 103
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 103

Asn Phe Lys Asp Gln Val Ile Leu Leu
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<210> SEQ ID NO 104
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 104

Cys Leu Asp Ala Gly Ile Asn Tyr Val
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<210> SEQ ID NO 105
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 105

Cys Leu Glu Ala Ser Phe Asn Tyr Leu
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<210> SEQ ID NO 106
<211> LENGTH: 9
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<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 106

Trp Leu Met Trp Phe Ile Ile Ser Ile
1 5

<210> SEQ ID NO 107
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 107

Trp Leu Met Trp Leu Ile Ile Asn Leu
1 5

<210> SEQ ID NO 108
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 108

Ile Leu Leu Leu Asp Gln Val Leu Val
1 5

<210> SEQ ID NO 109
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 109

Ile Leu Leu Leu Asp Gln Ala Leu Val
1 5

<210> SEQ ID NO 110
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 110

Leu Leu Cys Val Leu Ala Ala Leu Val
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<210> SEQ ID NO 111
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 111

Ser Ala Cys Val Leu Ala Ala Glu Cys
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<210> SEQ ID NO 112
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 112

Ala Leu Ser Gly Val Phe Cys Gly Val
1 5

<210> SEQ ID NO 113
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 113

Ser Leu Pro Gly Val Phe Cys Gly Val
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<210> SEQ ID NO 114
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 114

Thr Leu Met Asn Val Ile Thr Leu Val
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<210> SEQ ID NO 115
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 115

Thr Leu Met Asn Val Leu Thr Leu Val
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<210> SEQ ID NO 116
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome-related coronavirus

<400> SEQUENCE: 116

Ser Met Trp Ala Leu Val Ile Ser Val
1 5

<210> SEQ ID NO 117

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<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Severe acute respiratory syndrome coronavirus 2

<400> SEQUENCE: 117

Ser Met Trp Ala Leu Ile Ile Ser Val
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What is claimed:

1. A method of producing an immune globulin comprising:

1) obtaining a plurality of plasma samples from a plurality of plasma donors;
2) conducting a first assay on each plasma sample to measure total anti-SARS CoV-2 antibody titer;
3) selecting, based upon the first assay, plasma samples having a total anti-SARS CoV-2 antibody binding titer that is at least two-fold higher than the amount of total anti-SARS CoV-2 antibody binding titer in a control sample;
4) conducting a second assay on each selected plasma sample from step (3) to measure SARS CoV-2 neutralizing antibody titer;
5) identifying, based upon the second assay, plasma samples having a neutralizing antibody titer in the lower 65% of all plasma samples assayed and excluding the identified plasma samples from further processing;
6) pooling the non-excluded plasma samples from step (5); and
7) preparing immune globulin from the pooled plasma samples of step (6).

2. The method of claim **1**, wherein each of the plurality of plasma donors is a COVID-19 convalescent plasma donor.

3. The method of claim **1**, wherein each of the plurality of plasma donors is a COVID-19 vaccinated plasma donor.

4. The method of claim **1**, wherein the control sample is a mixture of plasma samples obtained from 100 or more random human plasma donors.

5. The method of claim **1**, wherein the control sample is a commercially available immune globulin.

6. The method of claim **1**, wherein step (5) comprises identifying, based upon the second assay, plasma samples having a neutralizing antibody titer in the lower 70% of all plasma samples assayed and excluding the identified plasma samples from further processing.

7. The method of claim **1**, wherein step (5) comprises identifying, based upon the second assay, plasma samples having a neutralizing antibody titer in the lower 75% of all plasma samples assayed and excluding the identified plasma samples from further processing.

8. The method of claim **1**, wherein the number of non-excluded, pooled plasma samples is 250 or more.

9. The method of claim **1**, wherein the number of non-excluded, pooled plasma samples is 500 or more.

10. The method of claim **1**, wherein the immune globulin is prepared using a cold alcohol fractionation process that isolates the immune globulin fraction from the pooled plasma as a solution.

11. The method of claim **1**, wherein the immune globulin is combined with a pharmaceutically acceptable carrier.

12. A method of providing immunotherapy to a subject in need thereof, comprising administering to the subject an immunotherapeutic composition comprising:

A) an immune globulin prepared from pooled plasma samples, wherein the pooled plasma samples are obtained by:
   1) obtaining a plurality of plasma samples from a plurality of plasma donors;
   2) conducting a first assay on each plasma sample to measure total anti-SARS CoV-2 antibody titer;
   3) selecting, based upon the first assay, plasma samples having a total anti-SARS CoV-2 antibody binding titer that is at least two-fold higher than the amount of total anti-SARS CoV-2 antibody binding titer in a control sample, wherein the control sample is a mixture of plasma samples obtained from 100 or more random human plasma donors;
   4) conducting a second assay on each selected plasma sample from step (3) to measure SARS CoV-2 neutralizing antibody titer;
   5) identifying, based upon the second assay, plasma samples having a neutralizing antibody titer in the lower 65% of all plasma samples assayed and excluding the identified plasma samples from further processing; and
   6) pooling the non-excluded plasma samples from step (5) to generate the pooled plasma samples; and

B) a pharmaceutically acceptable carrier;

wherein the immunotherapeutic composition is administered to the subject so as to provide from about 1.5-2.0 grams of immune globulin per kilogram of the subject.

13. The method of claim **12**, wherein each of the plurality of plasma donors is a COVID-19 convalescent plasma donor.

14. The method of claim **12**, wherein each of the plurality of plasma donors is a COVID-19 vaccinated plasma donor.

15. The method of claim **12**, wherein the immunotherapeutic composition further comprises a biologically active agent selected from the group consisting of an anti-inflammatory agent, an anti-cancer agent, an anti-microbial agent, an antihistamine, a cytokine, and a chemokine.

16. The method of claim **12**, wherein the immunotherapeutic composition further comprises an immunotherapeutic agent selected from the group consisting of a recombinant antibody, an antibody fragment, an antibody-like molecule, a monoclonal antibody, an antiviral, an immunotherapeutic protein and an immunotherapeutic small molecule.

17. The method of claim **12**, wherein the immunotherapeutic composition further comprises an anti-inflammatory agent selected from the group consisting of a recombinant antibody, an antibody fragment, a monoclonal antibody, an anti-inflammatory protein and an anti-inflammatory small molecule.

18. The method of claim **12**, wherein the subject is diagnosed with COVID-19.

19. The method of claim **12**, wherein the subject is age 65 or older.

20. A pharmaceutical composition comprising an immune globulin obtained by the method of claim **1**.

* * * * *