

with the target, or may be one constructed using sequences obtained from an organism which has been exposed to the antigen of interest (or a fragment thereof).

[0081] It is possible to take antibodies and use the techniques of recombinant DNA technology to produce other antibodies or chimeric molecules which retain the specificity of the original antibody. Such techniques may involve introducing DNA encoding the immunoglobulin variable region, or the complementarity determining regions (CDRs), of an antibody to the constant regions, or constant regions plus framework regions, of a different immunoglobulin. See, for instance, EP-A-184187, GB 2188638A or EP-A-239400. A hybridoma producing a monoclonal antibody may be subject to genetic mutation or other changes, which may or may not alter the binding specificity of antibodies produced.

[0082] It may be desirable to humanize non-human (eg murine) antibodies to provide antibodies having the antigen binding properties of the non-human antibody, while minimizing the immunogenic response of the antibodies, e.g. when they are used in human therapy. Thus, humanized antibodies comprise framework regions derived from human immunoglobulins (acceptor antibody) in which residues from one or more complementary determining regions (CDR's) are replaced by residues from CDR's of a non-human species (donor antibody) such as mouse, rat or rabbit antibody having the desired properties, eg specificity, affinity or capacity. Some of the framework residues of the human antibody may also be replaced by corresponding non-human residues, or by residues not present in either donor or acceptor antibodies. These modifications are made to the further refine and optimize the properties of the antibody.

[0083] So-called phage display may also be used in humanizing antibodies; see e.g. WO93/06213.

Example 1

[0084] We immunized Balb/c and ICR mice with either the recombinant protein adjuvanted with MONTANIDE ISA-720™ (A.L.A. Intermountain, 3725 E. Washington Street, Phoenix, Ariz. 85034), or with a pCI-TPA plasmid encoding the *P. berghei* CelTOS using an epidermal delivery by gene-gun to characterize their abilities to induce protective responses against a homologous *P. berghei* challenge. Humoral and cellular immune responses induced by either protein or plasmid immunizations were assessed in an effort to establish immune correlates. Results of the studies are shown in FIGS. 1 through 3. The finding of arrested hepatocytic invasion by inducing immunity to target antigens involved in sporozoite traversal or motility shows the enablement of the embodiment of the invention wherein CelTOS is utilized as a vaccine component.

[0085] Vaccination with PfCelTOS induced responses that protected mice against heterologous challenge (*P. berghei*). The MONTANIDE ISA 720™ adjuvant used for induction of immune responses is commercially available from Seppic, Inc. (A.L.A. Intermountain, 3725 E. Washington Street, Phoenix, Ariz. 85034). The recombinant protein *P. falciparum* CelTOS was developed solely by investigators in Division of MVD at WRAIR through funding from U.S. Agency for International Development (Project Number 936-6001, Award Number AAG-P-00-98-00006, Award Number AAG-P-00-98-00005), and by the United States Army Medical Research and Materiel Command. This malaria vaccine antigen can be used with other for human use adjuvants to induce appropriate immune responses.

[0086] As shown in FIG. 4, the nucleotide sequence of the *Plasmodium* CelTOS is re-coded by the codon harmonization disclosed in published U.S. patent application Ser. No. 10/677,641 to Kincaid et al. The codons are harmonized to optimize for high levels of soluble protein expression in the heterologous system, i.e. *E. coli*—see FIGS. 14A and 14B. The FASTA sequence for wild-type *Plasmodium* CelTOS is: >gil23496693|gb|AAN36249.1| CelTOS, putative [*Plasmodium falciparum* 3D7] MNALRRLPVICSFVFLVFSNVLCFRGNNGHNSSSSLYNGSQFIEQLNNSFTSA FLESQSMNKIGDDLAETISNELVSV-LQKNSPTFLESSFDIKSEVKKHAKSMLKEL IKVGLPS-FENLVAENVKPPKVDPATYGIIVPV-LTSLFNKVVETAVGAKVSDEIWNVY NSPDVSESEESLSDDFFD (SEQ. ID. NO. 4).

[0087] The CelTOS antigen was constructed in recombinant plasmids as shown in FIGS. 7-10. Both PbCelTOS and PfCelTOS recombinants demonstrated expression of the CelTOS antigen as shown in FIGS. 11A and 11B. As the antigen is expressed in prokaryotic cells, i.e. *E. coli* no post-translational modification of N-glycosylation on the expressed protein which occurs such as in eukaryotic expression systems. It is known that *P. falciparum* malaria proteins are not N-glycosylated. N-glycosylation may lead to changes in the protein folding and thus structure and may affect the induction of appropriate immune responses. It is known that the *P. falciparum* CelTOS protein has 2 likely N-glycosylation sites and a third probable N-glycosylation site. Accordingly, the present invention overcomes the above-described shortcomings of the prior art.

[0088] We conclude from Study #1 that recombinant protein PfCelTOS is able to induce a protective response against heterologous challenge with *P. berghei* sporozoites (4000 subcutaneous). At the same time, the PbCelTOS model antigen protected against homologous challenge as well (see Table 1 at FIG. 1). Protective responses were also induced in out-bred ICR mice vaccinated with PfCelTOS (Table 2, ICR mice at FIG. 2) and challenged with 15000 *P. berghei* sporozoites. Repeat dosing in BalbC mice (see Table 2—BalbC at FIG. 3), with PbCelTOS again showed that in this mouse model, CelTOS protected mice against a virulent challenge. These results support the use of PfCelTOS as a transmission blocking (anti-ookinetestage) and anti-infectivity (anti-sporozoite stage) malaria vaccine candidate.

Example 2

Supporting Data Provided for the Ability of Recombinant PfCelTOS Vaccine to Induce a Functional Activity Against Sporozoites

[0089] Motility assays: IFA slides (Cell Point, Gaithersburg, Md.) were pre-coated with RPMI-1640 (Invitrogen, Carlsbad, Calif.) containing 3% BSA (Sigma) for 15 min at 37° C. After removing the media, 10,000 sporozoites/well were added and incubated for 1 hr in a humidified chamber at 37° C. Slides and the deposited protein trails were fixed using 4% paraformaldehyde (10 min, RT). Spots were blocked with PBS containing 10% FBS for 45 min at 37° C. and then incubated with anti-PfCSP mAb (216.5G10 or 8C10 or 2G3 strains) for 45 min at 37° C. Goat-anti-mouse-IgG-FITC was added (1:100 dilution, Southern Biotech) to visualize the trails. Finally, slides were coverslipped using Fluoromount mounting media and microscopy performed (Olympus BX41, 1000× magnification).