SYSTEMS, METHODS, AND KITS FOR DIAGNOSTICS AND TREATMENT OF VIRAL RESPIRATORY INFECTION

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application is related to and claims the benefit of U.S. Provisional Application No. 63/001,629, titled Systems, Methods and Kits for Diagnostics and Treatment of SARS-CoV-2, filed on Mar. 30, 2020, U.S. Provisional Application No. 63/004,171, titled Systems, Methods and Kits for Diagnostics and Treatment of Viral Respiratory Infection, filed on Apr. 2, 2020, U.S. Provisional Application No. 63/004,398, titled Systems, Methods and Kits for Diagnostics and Treatment of Viral Respiratory Infection, filed on Apr. 2, 2020, U.S. Provisional Application No. 62/704,126, titled Systems, Methods and Kits for Diagnostics and Treatment of Viral Respiratory Infection, filed on Apr. 22, 2020, U.S. Provisional Application No. 62/704,416, titled Systems, Methods and Kits for Diagnostics and Treatment of Viral Respiratory Infection, filed on May 8, 2020, and U.S. Provisional Application No. 62/704,531, titled Systems, Methods and Kits for Diagnostics and Treatment of Viral Respiratory Infection, filed on May 14, 2020, the entire contents of each being incorporated herein by reference.

FIELD

[0002] The present invention relates to system, methods, and kits for treating, preventing, and diagnosing viral infection using an androgen mediated pathway. The present invention relates to methods and kits for predicting viral respiratory disease severity. Additionally, the present invention relates to methods and kits for guiding treatment of viral respiratory disease by testing for polymorphisms in the androgen receptor gene or genes under regulatory control of the androgen receptor. Similarly, the following invention relates to systems and methods for treatment of viral respiratory disease with various anti-androgens including, but not limited to, androgen receptor antagonists, androgen synthesis inhibitors, or antigonadotropins. Additionally, the present systems, methods, and kits are useful for treating, preventing, and diagnosing coronavirus, e.g., SARS-CoV-2 (COVID-19).

BACKGROUND

[0003] In late 2019, a novel coronavirus, subsequently named SARS-CoV-2 (COVID-19), was first reported in Hubei province in China. Since it was first reported, a worldwide pandemic has ensued affecting more than 450,000 individuals as of March 2020. In the midst of the pandemic, epidemiological reports unveiled a disproportionate low rate of severe cases among adult females compared to adult males, 42% and 58%, respectively. Similarly, the rate of severe cases among pre-pubescent children was exceptionally low at 0.6% (See Guan W J, Ni Z Y, Hu Y, Liang W H, Ou C Q, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020). An explanation for the skewed prevalence of severe COVID-19 infection in adult males has yet to be elucidated.

[0004] In newborns, it has long been recognized that male infants are more susceptible to respiratory distress syndrome (See Torday J S, Nielsen H C, Fend Mde M, Avery M E. Sex differences in fetal lung maturation. Am Rev Respir Dis. 1981; 123(2): 205-208) and less likely to respond to prenatal glucocorticoid therapy to protect against respiratory distress. Respiratory distress is intimately tied to the production of pulmonary surfactant, e.g., pulmonary surfactant proteins have been demonstrated to protect against influenza A (See Hartshorn K L, Crouch E C, White M R, Eggleton P, Tauber A I, Chang D, Sastry K. Evidence for a Protective Role of Pulmonary Surfactant Protein D (SP-D) Against Influenza A Viruses. J Clin Invest. 1994; 94 (1): 311-319). In animal studies, it was demonstrated that a sexual dimorphism in fetal pulmonary surfactant production is influenced by the androgen receptor (AR) (See Nielsen H C. Androgen receptors influence the production of pulmonary surfactant in the testicular feminization mouse fetus. J Clin Invest. 1985; 76(1): 177-181). For example, in rabbits, dihydrotestosterone was shown to inhibit fetal pulmonary surfactant production in both males and females while an anti-androgen, flutamide, was demonstrated to remove the sexual dimorphism in surfactant production.

[0005] While severe COVID-19 symptoms are primarily manifested in older adults, the similar sexual dimorphism in the severity of respiratory disease is of interest. In addition, AR expression is low prior to pubertal maturation and may contribute to the low incidence of severe COVID-19 infection in children. The lower rate of severe COVID-19 infection in female patients may be attributed to lower androgen receptor expression.

SUMMARY

[0006] Systems, methods, and kits are disclosed herein for diagnosing and treating viral respiratory infection by first measuring polymorphisms in the androgen receptor gene or polymorphisms in genes under regulatory control of the androgen receptor. Identification of polymorphisms in the androgen receptor gene can be used to guide treatments of viral respiratory disease. Treatments for viral respiratory disease may include, but are not limited to, androgen receptor antagonists, androgen synthesis inhibitors, or antigonadotropins. Specifically, the present systems, methods, and kits are useful for treating, preventing, and diagnosing viral respiratory disease as a result of coronavirus infection, e.g., SARS-CoV-2 (COVID-19).

[0007] In an exemplary embodiment, a composition administered to a subject having or suspected of having a viral respiratory infection includes any one or combination of: an androgen receptor antagonists or anti-androgen; an androgen synthesis inhibitor; an agent that counters the effect of androgens; a globulin (SHBG) stimulator; an antigonadotropin; a mineralocorticoid to suppress androgen production in the adrenal gland; a glucocorticoid to suppress androgen production in the adrenal gland; an insulin sensitizing medication; and a vaccine or an immunogen against androstenedione that reduces the level of testosterone or increases estrogen.

[0008] In some embodiments: the anti-androgen is any one or combination of: cyproterone acetate, megestrol acetate, chlormadinone acetate, spironolactone, medrogestone, oxendolone, osaterone, bifluranol acetate, finasteride, dutastride, flutamide, bicalutamide, nilutamide, topilutamide, enzalutamide, apalutamide, dienogest, drospirenone, medrogestone, nomegestrol acetate, promegestone, trimegestone, ketoconazole, abiraterone acetate, seviteronel, aminoglutethimide, epristeride, alfaestradiol, isotretinoin, saw palmetto, marijuana, cannabinoids, darolutamide, EZN-