

RBD Protein Vaccine is Safer

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Human genome contains 8% or more retrotransposons acquired in the past from RNA viral infections. Any mRNA or cDNA antigenic vaccines have the opportunity to enter into the vaccine recipients' somatic as well as germline cells. The SARS (severe acute respiratory syndrome)-CoV (Coronavirus)-2 S(spike)-protein mRNA/cDNA antigenic vaccines, currently being used, are only antigenic. They have to go through the human recipients' cellular processes to produce antigens that will stimulate antibody production against SARS-CoV-2, responsible for COVID (Coronavirus Disease) -19. There are scientific evidence supporting mRNA and cDNA antigenic vaccines to cause homologous and heterologous recombination into the somatic cell DNA of the vaccine recipients. On the contrary, the SARS-CoV-2 RBD-protein (antigen) vaccine, will directly stimulate antibody production against SARS-CoV-2, and thus against COVID-19. Hence, the SARS-CoV-2 RBD-protein vaccine is a safer, fast acting, and effective vaccine against COVID-19. It can be applied to immune compromised individuals.

Keywords: RBD = receptor binding protein ; SARS-CoV-2 = severe respiratory syndrome coronavirus 2 ; RBD protein vaccine

The adenoviruses and adeno-associated viruses (AAV) have been used as a vehicle for antigenic vaccines, gene transfer, and human gene therapy for some time. However, they also pose multiple risks and dangers to the recipients of such applications. Unfortunately, these vectors have been found integrate into the recipient's genome. Although rare, it was demonstrated that genes carried by AAV vectors integrate in a site-specific manner into the *q* arm of human *Chromosome 19* which may also express when the virus enters the lytic cycle, induced by a helper virus, as recorded in AAV virus therapy.

In an *in vivo* experiment using mice, the median frequency of chromosomal integrations of adenoviral vector DNA into mice chromosomes were found to be 6.72×10^{-5} as heterologous recombination and 3.88×10^{-7} as homologous recombination. Furthermore, recipients who were previously exposed to the adenoviral vector (which is very common in human) might have pre-existing immunities for the vector, and hence the efficacy of the COVID-19 cDNA vaccines using the adenoviral vector may not be effective as expected. This phenomenon indicates the potential risks associated with SARS-CoV-2 cDNA antigenic vaccines carried by the adenovirus or other viral vectors.

The RBD (Receptor Binding Domain) is a small segment of the S-protein of the SARS-CoV-2 virion. The RBD is highly critical for binding of the virus to the ACE-2 (Angiotensin Converting Enzyme-2) receptors on human mucosal nasal or other epithelial cells. This binding leads to the infection, followed by the disease COVID-19. Hence, using RBD protein as an antigen vaccine to protect humans from SARS-CoV-2 or COVID-19 infections will be highly specific, and thus highly effective.

After the RBD of the SARS-CoV-2 virion binds to ACE-2, two enzymes (furin and TMPRSS2) from the human mucosal cells cleave the S1 domain (RBD) from the S2 domain of the Spike (S) protein. (The S-protein has S1 and S2 domains). The free S2 domain protein then fuses with the human mucosal cell membrane allowing the entry of the SARS-CoV-2 virus into human cells followed by the release of the viral mRNA into the cell cytoplasm, causing the disease. The mRNA antigenic vaccines currently being used encode the entire S-protein carrying both the S1 and S2 domains. After the antigen binds to ACE-2 receptors, the S1 domain is cleaved leaving the S2 domain free. The free S2 domain retains its ability to bind to human mucosal cells opening the pathway for any free-floating SARS-CoV-2 virus to enter into the cells of the vaccine recipient.

The RBD protein of SARS-CoV-2 is an excellent choice for developing vaccines to prevent COVID-19. The RBD itself is an antigen, and hence it will be direct and quick in stimulating the recipients' immune system to produce antibodies against SARS-CoV-2 virions quickly. Furthermore, since RBD is not composed of any nucleotides or nucleic acids, it has no potential for homologous recombination into the recipient's genome. The vaccines composed of antigenic mRNA have

a short life in the recipients' cells, hence it is possible that some recipients of the mRNA vaccines may develop limited immunity against SARS-CoV-2. Furthermore, both the antigenic mRNA and cDNA have the potential for homologous recombination through reverse transcriptase when present and active in the recipients' system.

On the other hand, protein vaccines, like the SARS-CoV-2 RBD, can generate a strong immune response and can be used by almost everyone who needs them, including people with weakened immune systems and long-term health problems. Furthermore, the RBD protein vaccines cannot cause the COVID-19 disease. However, booster shots may be necessary to have a full protection against the ongoing SARS-CoV-2 infections.

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