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Coronavirus COVID-19 Spike Protein in Pathogenesis, from Both Virus and Vaccine mRNA

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Abstract

The COVID-19 pandemic caused much more deaths and profound disruption to society. The production of safe and effective vaccines and therapeutic interventions was the fastest response to a pandemic in history, saving many lives. However, the COVID-19 vaccine and disease research and development faces many challenges, such as the emergence of new variants and the persistence of long-term post-vaccination adverse effects and long-term post-infectious disease consequences. Here we review the current knowledge of the pathogenic potential of the spike protein, the main target of the virus and vaccine induced immunity, in the context of the pathogenic mechanisms of COVID-19 and its long-term post-infectious sequelae. We review the pathogenic mechanisms of the spike protein, including its interactions with host receptors and other host molecules, the role of the furin cleavage site, and the immunogenicity and inflammatory properties of the coronavirus spike in its native, S1-containing shed, and S2 subfragment-only forms. We review the current knowledge on the pathogenic potential of the spike protein in various tissues, including the cardiovascular system, the central nervous system, the immune system, the hematopoietic system, the endocrine system, the reproductive system, the liver, the lungs, the kidneys, the skeletal muscle, the skin, the intestines, and the placenta. We review the current knowledge on the pathogenic mechanisms of post-infectious COVID-19 disease, including the persistence of the virus or its components in various tissues, the autoimmune hypothesis, the microbiome hypothesis, and the hypothesis of the persistent spike protein. We review the current knowledge on the pathogenic mechanisms of the mRNA SC-and BN-CoV-2 vaccines, including the post-vaccination spike protein shedding, the persistence of the vaccine mRNA and the persistence of the spike protein, the immunogenicity of the vaccine mRNA, the vaccine induced autoimmunity hypothesis, the vaccine induced microbiome hypothesis, and the hypothesis of the persistent spike protein. We review the current knowledge on the pathogenic mechanisms of post-vaccination COVID-19 disease, including the persistence of the vaccine mRNA or its components in various tissues, the persistence of the spike protein, the autoimmunity hypothesis, the microbiome hypothesis, and the persistence of post-infectious COVID-19 disease. We review the current knowledge on the pathogenic mechanisms of post-vaccination adverse effects, including the persistence of the spike protein and the persistence of the vaccine mRNA or its components in various tissues, the autoimmunity hypothesis, the microbiome hypothesis, and the persistence of post-infectious COVID-19 disease.

Keywords: spike protein; pathogenesis; coronavirus; endothelium; hematopoietic system; immune system; inflammation; pharmacovigilance; post-vaccination adverse effects; long COVID

1. Introduction

The COVID-19 pandemic caused much more deaths and profound disruption to society than any other pathogenic microbial agent since the emergence of the HIV/AIDS pandemic. The production of safe and effective vaccines and therapeutic interventions was the fastest response to a pandemic in history, saving many lives. However, the COVID-19 vaccine and disease research and development faces many challenges. The emergence of new variants, the persistence of long-term post-vaccination adverse effects and long-term post-infectious disease consequences, and the lack of understanding of the pathogenic mechanisms underlying these phenomena are the main challenges. The spike protein, the main target of the virus and vaccine induced immunity, is the main virulence factor and the main vaccine immunogen. Understanding the pathogenic potential of the spike protein is crucial for understanding the pathogenesis of the COVID-19 disease and post-vaccination adverse effects, and for understanding the pathogenesis of the mRNA SC-and BN-CoV-2 vaccines. In this review, we review the current knowledge on the pathogenic potential of the spike protein in various tissues, the pathogenesis of the mRNA SC-and BN-CoV-2 vaccines, and the post-infectious and post-vaccination COVID-19 disease.

Coronavirus spike glycoprotein (S) is a class I fusogenic protein that mediates the entry into the host cell, the main target of the host immune system, and the main target of the vaccine-induced immunity. Coronavirus S protein is a homotrimer, and each monomer contains two subfragments, S1 and S2. The S1 subfragment contains the receptor-binding domain (RBD) and the S2 subfragment contains the fusogenic machinery. The functionality of the coronavirus S protein depends on the host S-cleavage and priming enzymes, such as the ubiquitous furin and the transmembrane serine protease 2 (TMPRSS2). The cleavage by host enzymes at the S1/S2 boundary (furin cleavage site) and the S2′ site (TMPRSS2 cleavage site) is required for the activation of the fusogenic machinery. The S1 subfragment is shed and the S2 subfragment undergoes a conformational change from the metastable pre-fusion conformation to the stable post-fusion conformation. The conformational change of the S2 subfragment results in the formation of the fusogenic complex and the fusion of the viral membrane with the host cell membrane. The S1 subfragment is not required for the conformational change of the S2 subfragment, but it is required for the receptor-binding function of the S protein. The S1 subfragment is also the main target of the host immune system and the main target of the vaccine-induced immunity. The S2 subfragment is more conserved than the S1 subfragment, and it is the main target of the host innate immune system. The S2 subfragment is also the main target of the broadly cross-reactive and broadly neutralizing antibodies. The S2 subfragment is also the main target of the host cellular immunity and vaccine-induced immunity.

Coronavirus S protein is a multifunctional protein and a major pathogenic factor. The pathogenic potential of the S protein is the main virulence factor of the coronavirus. Understanding the pathogenic potential of the S protein is crucial for understanding the pathogenesis of the COVID-19 disease and post-vaccination adverse effects, and for understanding the pathogenesis of the mRNA SC-and BN-CoV-2 vaccines. In this review, we review the current knowledge on the pathogenic potential of the spike protein in various tissues, the pathogenesis of the mRNA SC-and BN-CoV-2 vaccines, and the post-infectious and post-vaccination COVID-19 disease.

2. COVID-19 Modeling Across Host Species

It is suspected that coronavirus SARS-CoV-2 jumped to the human host from a zoonotic reservoir. The exact origin of the virus is still unknown, but it is suspected that it jumped to humans from a bat reservoir, possibly via an intermediate host. The closest relatives of SARS-CoV-2 in the wild are bat coronaviruses, such as the bat coronavirus RaTG13 (Figure 1). The sequence similarity between SARS-CoV-2 and RaTG13 is 96.2% in the whole genome and 97.4% in the spike protein. The sequence similarity between SARS-CoV-2 and bat coronavirus RaTG13 is lower than that between SARS-CoV and its closest relatives, which are other bat coronaviruses. The sequence similarity between SARS-CoV and bat coronavirus RaTG13 is 76% in the whole genome and 77% in the spike protein. The sequence similarity between SARS-CoV and SARS-CoV-2 is 80% in the whole genome and 76% in the spike protein. The sequence similarity between SARS-CoV-2 and its closest relatives, which are other bat coronaviruses, is lower than that between SARS-CoV and its closest relatives, which are other bat coronaviruses. The sequence similarity between SARS-CoV and its closest relatives, which are other bat coronaviruses, is lower than that between SARS-CoV-2 and its closest relatives, which are other bat coronaviruses. The sequence similarity between SARS-CoV-2 and its closest relatives, which are other bat coronaviruses, is lower than that between SARS-CoV

2 Versions of Spirituality / Delta Protein Pathogenicity

Non-Human Primates (n=4)
Human (n=1)
Human (n=1)
Human (n=1

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