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Review Article

The Structure and Mechanism of Spike Protein, as Well as its Role in Numerous Viral Diseases

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ABSTRACT

A spike protein is a protein that builds a huge spike that ejects from an enveloped virus's membrane. The spike protein is the only virus membrane protein that enables the virus to penetrate through the cell. Spike Protein has three potential methods of action. Most common viral illnesses have relatively similar virus structures, which are predominantly made up of dimers or trimers of the spike glycoprotein, as well as analogous mechanisms of host cell invasion. The purpose of this paper is to explore the structure of the spike protein and its cell invasion method. The prevalence of spike protein in distinct viruses, as well as their similar invasion mechanisms, are also highlighted in the paper. We observed that many infectious viruses have very identical structures, predominantly constituted of spike glycoprotein, as well as similar processes of invasion into host cells. There are diverse sorts of pathogenesis that have been identified, especially those relating to host cell contamination and the means wherein the infection spreads and produces disease. The Spike protein must be operational for the virus to penetrate the host organism, and variations in the protein's activation techniques are thought to have an influence in viral pathogenesis. Vaccines struggle to prevent the transmission of all virus variants due to variances in the spike protein in different viral versions, as well as modifications in them. More research into the structure of spike glycoproteins, as well as the creation of more effective vaccines to inhibit spike protein invasion and infection, are required.

Keywords: ACE 2, CD147 receptor, Coronavirus, Omicron variant, Spike protein.

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INTRODUCTION

Viruses must break through the cell membrane barrier to commence an infestation. Membrane merging, governed by specific viral fusion proteins, is how encapsulated viruses accomplish this. The majority of viral fusions proteins begin out as antecedent proteins that are cleaved by biological proteolytic enzymes, resulting in a metastable combination of receptor binding subunits and membrane fusion subunits.[1] Some encapsulated viruses also gain access to their host cells through merging of membranes, which is facilitated by a virus-encoded union, or "spike" protein anchored in the viral envelope.[2] Class I fusion proteins are often prepared for fusion initiation by proteolysis, whereas class II fusion proteins are normally predisposed for fusion stimulation by proteolysis.[3] The objectives of this article are to investigate the structure of the spike protein as well as the technique by which it invades cells. This review article covers the structure of the spike protein, its invasion method, and its prevalence in different viruses' step by step.

A spike protein, is a protein that builds a massive protruding protrusion called a spike that protrudes from an enclosed virus coat. Glycoproteins that form dimers or trimers are the most prevalent proteins. The viral envelope is composed of 3 protein aggregates: the membrane protein (M) and the envelope protein (E) are involved in virus cluster, whereas the spike protein (S) is involved in virus entry into host cells. The spike (S) protein is the only viral membrane protein that allows the virus to enter cells. It attaches to the target cell's receptor and facilitates virus-cell fusion.[4] Two very different cell adhesion and membrane adhesion are facilitated by the big spike protein (S) on the virion interface. The spike (S) protein is a vital aim for antiviral neutralizing antibodies because it promotes infection of receptor-expressing host cells.

STRUCTURE OF SPIKE PROTEIN

Spike protein is a massive type I transmembrane protein that fluctuates in size between 1,160 amino acid residues for avian infectious bronchitis virus to 1,400 amino acid residues for feline coronavirus (FCoV). In between 21 and 35 N-glycosylation spots, this protein is significantly glycosylated. When spike proteins unite into trimers at the virion interface, the "corona," or crown-like image, is developed.

The S glycoprotein is made up of 180-kDa precursors that oligomerize in the endoplasmic reticulum before being integrated into sprouting virions in a pre-Golgi segment.[5] The Spike protein has an external N-terminus, a transmembrane segment embedded in the viral envelope, and a transient internal C-terminal portion with a circumference of with a size of 180–200 kDa.[1] Underneath the electron microscope, spikes appear as distinct, 20-nm-long, bulbous external extensions on the virion envelope. In order to prevent being recognized by the host defenses upon invasion, the spikes are wrapped by polysaccharide molecules.[6] S1 and S2 are two sections of the spike protein, which is a trimeric category I fusion protein. The S1 subunit is thought to produce the globular head, whereas the S2 subunit is thought to constitute the spike's stalk-like portion.[7] S1A, S1B, S1C, and S1D subdomains constitute the S1 subunit (Figure 1). The S1A subunit stated as N transmembrane domain (NTD), detects carbohydrates, such as sialic acid which makes it easier for the virus to adhere, S1B domain, also known as the receptor-binding

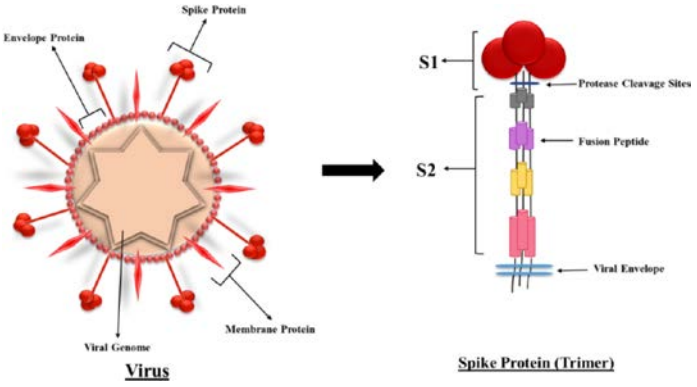

Figure 1: Structure of the Spike Protein.

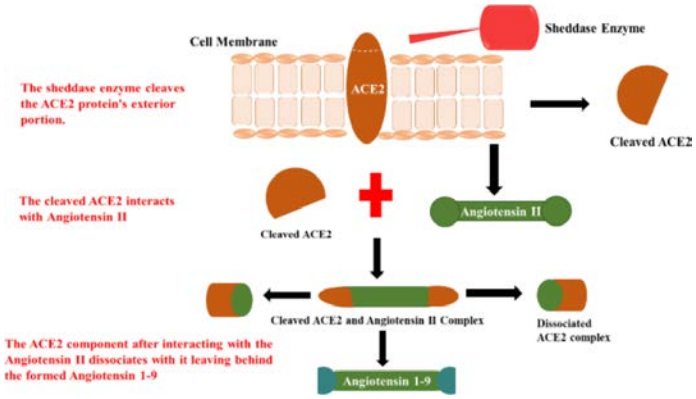

Figure 2a: Interaction of ACE2 with Angiotensin II and its transformation into Angiotensin 1-9.

domain (RBD), binds with the mammalian ACE-2 receptor. While the S2 subunit enables the viral and human cellular membranes to merge.[8] Three elongated α-helices, several α-helical fragments, elongated coiled β-sheets, membrane bridging α-helix, and a within cell cysteine-rich segment constitute up the structural constituents of the S2 sub-unit.[9] Following S protein synthesis in the infected host, a proteolytic site identified by furin-like proteases may dissociate the S1 and S2 domains.

Although splitting of the S protein into the S1 and S2 has already been suggested to facilitate fusogenicity,[10] it is not necessary for fusion.[11] The S2 subunit's ectodomain has two sections with a 4,3 hydrophobic (heptad) repetition, a sequence pattern found in coiled coils. The locations and sequencing of all these two-heptad repeats (HR) segments, called HR1 and HR2, are constant amongst individuals of the three coronavirus antigenic complexes.[12] The HR1 and HR2 domains have also been associated with viral fusion in a lot of researches. First, a putative internal fusion peptide at or even within the HR1 domain has been hypothesized. Second, viruses harboring polymorphisms in the membrane-proximal HR2 locus had spike oligomerization and fusing capability deficiencies.[13]

ACTION MECHANISM OF SPIKE PROTEIN

ACE 2 mediated action mechanism

The S protein mostly on the viral interface has a huge impact in infecting. It's a trimeric group I TM glycoprotein that's involved in viral penetration and can be found in a variety of viruses. The S protein expressed on the surface of the virion is the important element from which the S protein binds with the receptor.[14] SARS-CoV is also reported to utilize the ACE2 receptor. The S1 portion of the SARS-CoV S protein engages with ACE2 to stimulate endosome growth, promoting in virus mating capability at lower pH.[15]

The SARS-CoV-2 Spike protein detects the ACE2 receptor on the host genome and adheres to it. The active form of ACE2 produces sheddase, an additional enzyme. The sheddase enzyme cleaves the ACE2 protein's exterior portion and releases it into the bloodstream. The cleaved ACE2 interacts with Angiotensin II and transforms it to Angiotensin 1-9, a potent antioxidant and vasodilator. The Receptor binding domain of the S1 subunit of the S protein attaches to ACE2, facilitating virus adherence to host tissues in the format of a trimer (Figures 2a and 2b).

Viral fusion is yet another proposed pathway. The merging of the viral membrane with the recipient cellular membranes leads to the emission of the viral DNA into the host genome, which is termed viral fusion. Fusion is dependent on the splitting of the SARS-CoV-2 S1 and S2 subunits. Host proteases cleave the S protein into two subunits, the S1, and S2, and the fragments formed reside in a noncovalent state till viral fusion takes place.[16] SARS-CoV-2 S comprises numerous furin cleavage sites,

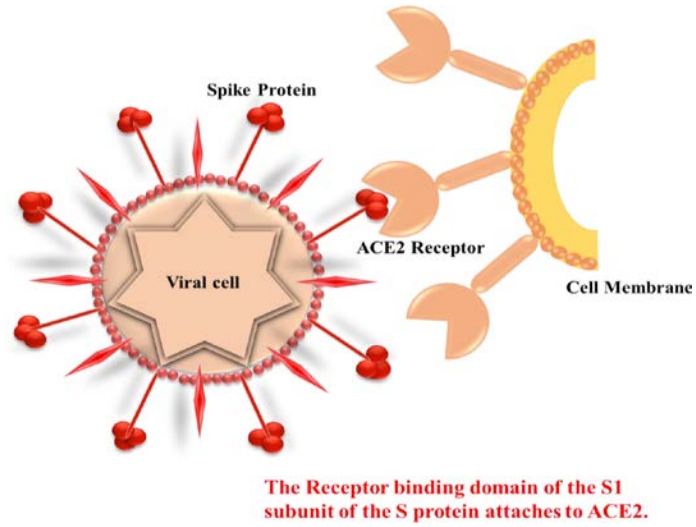

Figure 2b: The S1 subunit of the S protein attaches to ACE2, enabling the virus to adhere to host tissues.

that boost its infection rate by increasing the likelihood of becoming split by furin-like proteases. The furin-like disintegration site is also prevalent in extremely virulent influenza viruses and is linked to their virulence.[17] Trypsin is the other host tissue protease that has been shown to split viral S protein. The generation of 6 helix bundles is needed for viral fusion to take effect. The fusion peptide in the SARS-CoV-2 N-terminus, including the two heptad repeats domains on S2, are crucial for virus union.[18] The fusion peptide of novel coronavirus is revealed after the Spike protein is fragmented, facilitating viral blending. The fusion protein changes its shape and subsequently penetrates the cellular membrane underneath the influence of some specific ligands.[19]

CD147 receptor mediated action mechanism

The viruses have indeed been known to relate effectively with group of differentiating 147 (CD147), a type 1 transmembrane protein that pertains to the immune-globulin class and is implicated in malignant transformation, plasmodium invasion, and virus attack.[20,21] Whenever the virus's spike protein interacts to CD147 on the host genome, the virus infects, and then multiplies. Recently, it was realized that, in furthermore to ACE-2, the SARS-CoV-2 virus attach to it and reaches the cell wall through CD147. Figure 3. Meplazumab was used in combination with ELISA, to illustrate the novel pathway of viral attachment via CD147-spike protein in an investigation. The S protein in the host genome

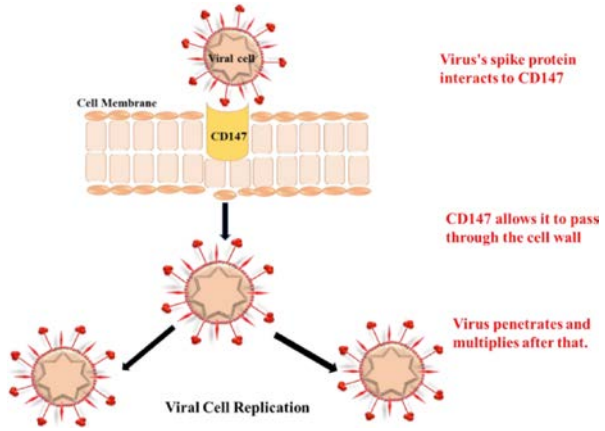

Figure 3: Explains the CD147 mediated action mechanism of the Spike Protein.

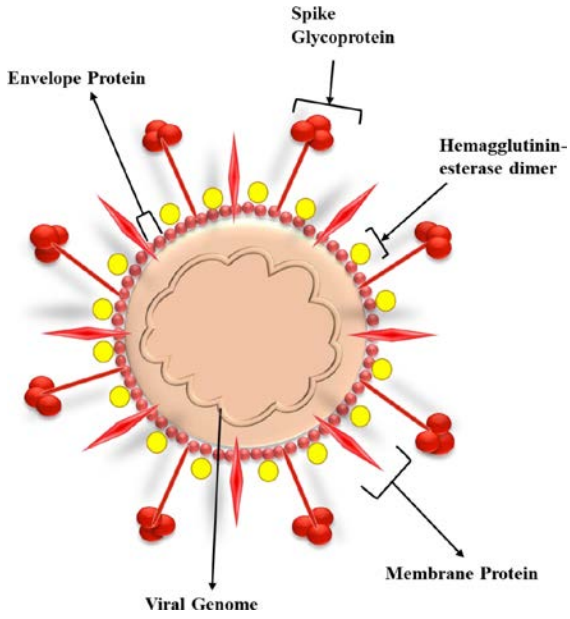

Figure 4: Highlights the structure of the Corona virus.

regulates the Raf/MEK/ERK signaling cascade. Modification of the ERK1/2 mediated signaling in the host boosts virus proliferation as well as the induction of cyclooxygenase-2 (COX-2) and swelling.[22]

VIRAL INFECTIONS AIDED BY SPIKE PROTEIN

Spike protein is involved in viral entry and can be found in all types of human coronaviruses as well as other viruses like ebola virus, human immunodeficiency virus, herpes virus, influenza virus, and others. This paper aims to focus on the involvement of spike protein in a variety of different viral infections.

Coronavirus

The Novel Coronavirus 2019 (SARS-CoV-2) that induces COVID-19 was recently discovered to be a newly identified infection from the coronavirus family. A coronavirus is a virus group that can transmit diseases like the common cold, SARS, and MERS.[23] Coughing, spitting, sneezing, and touching a contaminated material are the chief sources of contamination. The genome of the coronavirus is 30000 nucleotides in length. Nucleocapsid (N) protein, Spike (S) protein, Envelope (E) protein, Membrane (M) protein are four structural components encoded, as well as several non-structural proteins. The M-protein is perhaps highly prevalent on the viral envelope and is assumed to be the coronavirus's key coordinator. The S-protein is packaged into the virus's membrane and facilitates viral invasion into the host genome by regulating virus adherence to host cell surface membrane and membrane junction around the viral genome's cell membranes. Figure 4. E-protein is indeed a very minute membrane protein that is a small aspect of the viral particles. It is implicated in virus construction, host cell membrane porosity, and virus-host cell interface.[24]

In the human cell, the method of viral entrance, multiplication, and RNA packaging, the spike (S) protein of the coronavirus adheres to angiotensin-converting enzyme 2 (ACE2) receptors on the exterior of numerous human cells, such as those in the lungs, facilitating virus invasion. The coronavirus spike protein is broken by host proteases (trypsin and furin) in two sites near the S1 and S2 subunits. The S2 domain is cleaved at a subsequent stage to ensure to liberate the fusion peptide. The membrane fusion mechanism will be activated as a result of this event. The procedure by which a human cell receives a virus is considered endocytosis. COVID-19 is assumed to use a distinctive three-step procedure for membrane fusion once it joins the cytoplasm, encompassing receptor-binding and triggered structural modifications in Spike (S) glycoprotein, accompanied by cathepsin L proteolytic cleavage by cytoplasmic proteases as well as further stimulation of the membrane fusion pathway within endosomes.[25]

Coronavirus variants

Alpha variant (Lineage B.1.1.7): Lineage B.1.1.7, commonly known as 20I/501Y, is a SARS-CoV-2 subtype. The V1 or alpha variant became the most widely circulated. In the Spike protein receptor-binding domain, B.1.1.7 has several genetic mutations, the most prominent of these is N501Y. N501 engages hydrophobically with the side chains of the ACE2 receptor domains Y41 and K353. The molecular orientation of the receptor-binding domain, and therefore the binding affinity for ACE2, is anticipated to be impacted by this mutation.[26] The B.1.17 variation was observed to have a 5-fold stronger affinity for the ACE2 receptor. Additionally, the B.1.1.7 receptor binding domain has a 2-fold stronger affinity for ACE2 than that of the wild-type S receptor binding domain.[27] This polymorphism, like others reported in the SARS-CoV-2 S glycoprotein receptor binding domain, may impede antibody neutralization by impairing antibody attachment. A deletion at regions 69 and 70 is one of the known mutations in the S protein. This mutation may boost the viral risk of transmission and pathogenicity.[28] Furthermore, when compared to the wild-type strain, the B.1.1.7 variation is assessed to be 75 percent higher transmittable.

Beta variant (Lineage B.1.351): Eight genetics polymorphisms in the Spike protein distinguish the beta variation, comprising three changes of key receptor binding domain residues- K417N, E484K, and N501Y- that influence ACE2 attachment efficiency.[29] The B.1.351 receptor binding domain has a 4.62-fold stronger attraction for ACE2 than that of the wild-type S receptor binding domain.[30] The improved binding affinity is due to the influence of two additional substitution mutations in the RBD.

Gamma variant (B.1.1.28): Lineage P.1, also known as B.1.1.28, or Gamma variant. However, there is little documentation on the P.1 variant's disease transmission; it bears numerous mutations in the S glycoprotein's receptor-binding domain. At residue 417, Thr substitutes Lys in P.1, however, Asn substitutes Lys in B.1.351. Both polymorphisms have been reported to enhance the interactions of the B.1.351 S glycoprotein to ACE2, and the N501Y mutation is anticipated to play a major role in this increase.[31] Five substitution alterations (L18F, T20N, P26S, D138Y,

and R190S) in the N terminal domain and three substitution mutations (D655Y, T1027I, and V1176F) in the S2 subunit characterize the P.1 variation. Despite having higher alterations in the S protein than the B.1.351 variety, P.1 is much less susceptible to nAb neutralization, either inherited spontaneously or as an outcome of immunizations.

Delta variant (B.1.617.2): B.1.617.2, a delta variant, is highly ramping up infections all over. The delta variant is 60 percent highly communicable than the alpha variant, according to one study. When compared to the alpha variation, the delta variant replicates twice as fast. In the delta variation, rising incidence of transmission can increase the incidence of mutation and the rise of new strains. Monoclonal antibodies opposing the receptor linking region as well as the amino-terminal section of B.1.617.2 spike pseudo typed viruses showed reduced sensitivity. B.1.617.2 had a greater replicating frequency than B.1.1.7 in both domains.[32] When compared to wild-type B.1.617.2 spike protein, the B.1.617.2 spike protein showed to induce incredibly efficient syncytium generation which was less susceptible to neutralization antibody restriction. B.1.617.2 also demonstrated a greater proliferation and spike-mediated penetration rate.

Omicron variant (B.1.1.529): Omicron (B.1.1.529) has already been recognized as a variant of concern across the world. In comparison to the Delta variant, there has been a significant rise in transmission and subsequent infection.[33] The Omicron Spike protein seemed to have the highest developmental distance compared to the other variants. The Omicron S protein possesses thirty-four amino acid (AA) mutations, according to a multiple sequence alignment of the current variant of concern variations. The Omicron S1 N terminal domain structures vary markedly from the initial strain, which could contribute to reduced antibody identification, resulting in immune escape and diminished vaccine potency. Omicron is associated to Alpha in aspects of genomic phylogeny. However, Omicron is intimately linked to Beta and Gamma in the receptor-binding domain zone. Together, the Spike protein polymorphisms may boost the Omicron variant's immune escape and infectivity.[34] The receptor-binding domain of Omicron has 15 mutations, neither of which are deletions or insertions. Several altered regions in the Omicron RBD-hACE2 complex limit the binding interactions among receptor-binding domain and hACE2, whereas others improve it. Also, the structure of the Omicron spike protein has yet to be determined experimentally.[35]

Ebola Virus

The Ebola virus (EBOV) is a negative-sense RNA virus that belongs to the Filoviridae class. The Ebola virus produces hemorrhagic fever with a high death rate, and there are presently no curative drugs available for clinical application. Viral particles infect dendritic cells, macrophages, and liver cells, causing infection.[36] The proliferation of the virus within those cells is assumed to be essential for the onset of severe infections, which proceed to virus dissemination to other locations and infection of other cell populations. The nucleoprotein (NP), the transmembrane glycoprotein (GP) virion proteins (VP), polymerase protein (L), and soluble glycoprotein (sGP) are among the eight proteins aggregates transcribed by EBOV's single-stranded negative-sense 19-kb RNA genome1. The Glycoprotein spike is the sole surface protein seen on EBOVs.[37] The glycoprotein (GP) trimer is present in spikes on the viral membrane. Figure 5. Adhesion to host cell lines, endosomal invasion, and membrane fusion are all facilitated by this Glycoprotein molecule.[38] The fully grown glycoprotein is made up of multiple subunits, GP1 and GP2, which heterodimerize and generate trimers by disulfide linkages.

The crystalline structure of the Ebola virus glycoprotein reveals that this trimer has the appearance of a chalice, with GP2 acting as the bottom and GP1 as the cup.[39] The N-glycan-comprising cap domain and a highly

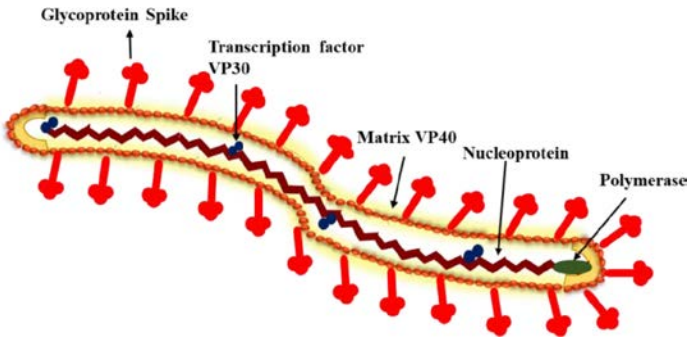

Figure 5: Highlights the structure of the Ebola virus.

N- and O-glycosylated mucin-like domain of GP1 wrap and preserve this chalice. The glycoprotein is shielded from specific antibodies by glycans in these areas.[40] The fusion prompt exposes a hydrophobic GP2 fusion cycle that is ordinarily hidden behind an adjacent GP1 monomer.[41] Crystal structures modifications inside the fusion loop that stimulate fusion require a low pH condition. Membrane fusion mechanisms of Ebola virus are assumed to be analogous to those in other viral glycoproteins described above.[42]

Influenza Virus

Influenza viruses are one-of-a-kind physiologically and molecularly. They generate annual epidemics that have significant health and economic consequences. Influenza viruses are negative-sense RNA viruses that are encapsulated and belong to the Orthomyxoviridae family. Negative-stranded RNA genotypes with eight RNA segments synthesize 10 viral proteins are identified within them.[43]

Influenza virus variants have a diameter of 80-120 nm and are generally spherical. Glycoproteins protrude like spikes from the virus envelope, which is constituted of a layer. The virus's segmented helical ribonucleoprotein (nucleocapsid) is encapsulated inside the covering. Rod-shaped spikes, made up of the hemagglutinin (HA) protein, and mushroom-shaped spikes, made up of the neuraminidase (NA) protein, are the two main forms of surface glycoproteins.[44] Figure 6. The hemagglutinin protein is vital in the virus's adherence to neuraminic acid-containing receptor molecules including its entry into the cell. Neuraminic acid is dissociated off cell surface receptors.

For influenza to invade a cell, the virus must first adhere to its cell surface receptors, then endocytose, and merge the viral and endosomal membranes. The merging method enables the viral genome to be discharged inside the cytoplasm, where it then flows to the nucleus, where viral transcription and multiplication occur.

Rubella Virus

The rubella virus is the presumed cause of German measles. RuV is the only part of the Rubivirus genus, which itself is part of the Togaviridae family. RUBV is a highly communicable virus that transmits through the air. Humans are the only known hosts.[45] RUBV infections are commonly associated with minor symptoms like fever and rash. Contamination in expectant mothers, during the early stages of pregnancy, can culminate in unexpected miscarriage or congenital rubella syndrome. RuV has a spherical morphology but is pleomorphic, with diameters varying from 60 to 80 nanometers.[46] The capping protein and genetic RNA constitute the nucleocapsid core (NC).[47] The RuV core is encased in a bilayer membrane obtained from the host that contains 5- to 6-nm-long spikes that protrude from the edge of the virion; the spikes are made up of E2 and E1 glycoproteins. Figure 7. Clathrin-mediated endocytosis

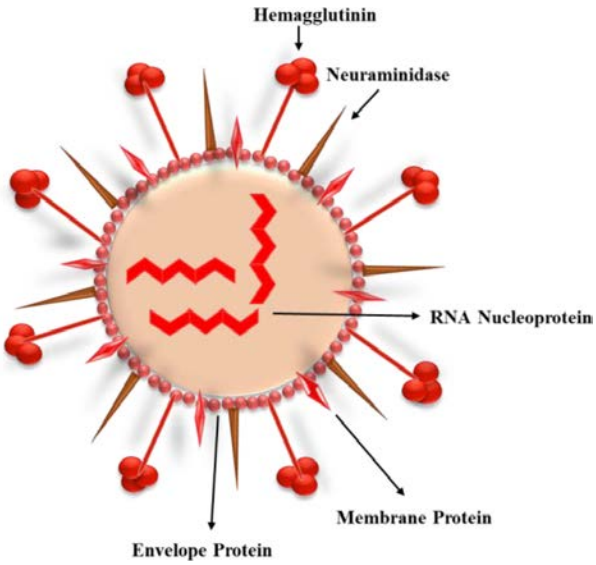

Figure 6: Highlights the structure of the Influenza virus.

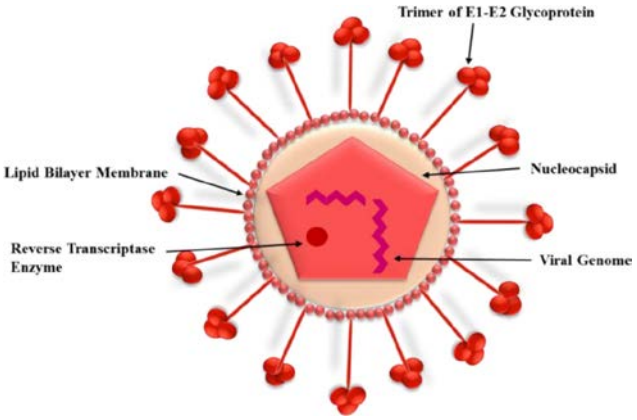

Figure 7: Highlights the structure of the Rubella virus.

permits RUBV particles to invade target cells.[48] The E1 membrane fusion protein facilitates the merging of the virus and endosomal membrane membranes via a low pH and calcium-dependent event.[49] Both of the E1 and E2 proteins have a putative transmembrane (TM) domain with 22 and 39 residues, respectively.[50]

The pathway through which the Rubella virus enters the host cell is unclear. RuV may pass through the cell via the endocytic pathway, per some findings. Initial biochemical studies revealed that exposing the RuV E1 and E2 glycoproteins induced a shape change inside the glycoproteins, facilitating viral envelope fusion with the endosome.[51]

Arena Virus

Arenaviridae is a viral protein family that comprises various evolving pathogens from the Bunyavirales order. Arenaviruses are a family of encapsulated RNA viruses that encompasses 13 multiple individuals. The family name originates from the appearance of fine granules inside virions, that are assumed to constitute host-cell ribosomes. The club-shaped exterior projections incorporated in the extracellular domain measure about 7 nanometers in length.

The virion glycoproteins are absent from spike-less particles obtained after protease treatment, implying that they are structural units of the

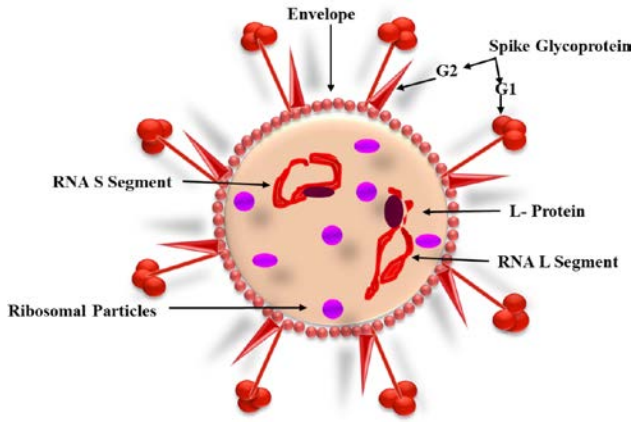

Figure 8: Highlights the structure of the Arena virus.

surface projections. However, it is still unknown how they combine to form discrete spikes. The exterior spike is a simplified cluster of the glycoproteins G1 and G2, that is obtained from a prevalent forerunner via proteolytic cleavage. The transmembrane regions of G2 are expected to interact with the underneath nucleoprotein, whereas G1 is more externally situated. Figure 8. In connection with viral RNA, the nucleoprotein (NP) is found to be made up of a linear array of N molecules. Every genomic section, L (large) and S (small), implements an ambisense coding method to regulate the production of two opposing polypeptides split by a non-coding intergenic sequence.[52]

Vaccine effect on Spike protein

Due to the general Spike protein's methodology in specific receptor binding and membrane fusion, vaccines modeled on it may induce antibodies that inhibit virus binding and fusion or neutralize virus infection. Since the immune response would be too delayed to react at the post-fusion step, when the virus is acquiring access into an uninfected cell, the immune system needs to fight the pathogen at the prefusion step. In a conclusion, the objective underlying vaccine development is to develop a spike protein that is steady in the prefusion state as a target for the immune cells to adapt to fight against.[53] SARS-CoV-1 and MERS-CoV vaccinations are built on the Spike glycoprotein and elicit therapeutic neutralizing antibodies (nAbs). Spike protein is perhaps the most antigenic constituent of SARS-CoV, so it is key for triggering host immunological responses, antibody responses, and/or protective resistance towards viral disease. As a result, the Spike protein has now been considered as a leading focus for vaccine development. Various vaccines built on the SARS-CoV entire length Spike protein have now been developed. African green primates were inoculated with an attenuated parainfluenza virus carrying the full-length S protein of SARS-CoV.[54] Almost all SARS-CoV-2 vaccination options are centered on the spike protein, which is transcribed by mRNA and is preserved through its prefusion state. To sustain the perfusion orientation, two amino acids in the S2 subunit were modified to proline.

HCoVs are RNA viruses that have a faster mutation rate than DNA viruses.[55] Such alterations are particularly prevalent in transmembrane proteins, such as the spike protein. The above mutations boost the HCoVs' long-term survivability by permitting them to escape both cell-mediated and humoral immune responses.[56] Spike proteins, nevertheless, possess the most possibilities as a vaccine target because they can elicit a stronger and long-lasting mucosal immune reaction than most of the other proteins.[57] Any invasive particulate can resist the antibody memory reaction over time due to antigenic drift; however, the T cell immune

reaction frequently gives long-lasting protection. Antibodies targeting Spike glycoprotein were developed in SARS patients, and multiple investigations have shown that such vaccinations confer defense against SARS-CoV-1.[58]

The two major groups of vaccines that target spike protein have been developed. The first is aimed at Spike protein in full length. It stimulates protective immune responses, as well as potent neutralizing antibody and T-cell reactions. It may trigger damaging immune reactions that injure the liver. The second one is Based on recombinant S protein. It generates high levels of neutralizing antibodies and preventive antibodies are induced. Usually, humoral reactions are generated by it.[59]

DISCUSSION

Spike protein has been investigated for years, and some of the most relevant clinical and pathological features have been uncovered. Numerous components of pathophysiology, particularly those related to host cell infestation and the methods by which the virus spreads and causes illness, are documented. Spike protein is considered to be a crucial regulator in viral infection. In this paper, we focused on the major viral diseases as well as the role of the Spike protein as a viral pathophysiology regulation. The primary design of Spike proteins is practically identical to those of several viral diseases. For the virus to infiltrate the host cell, the Spike protein should be active, and changes in the protein's activation methods are considered to have a role in viral pathogenesis. Because of the general Spike protein's involvement in particular membrane fission and receptor adhesion, the immune system must combat the pathogen at the phase of prefusion because the immune response would be too delayed to react at the post-fusion stage when the virus gains access to an uninfected cell. To summaries, the goal of vaccine development is to create a spike protein that is stable in the prefusion stage and serves as a target for immune cells to adapt to fight against.

CONCLUSION

A spike protein, is a protein that constitutes a large spike or peplomer that ejects from the surface of an enclosed virus. The most ubiquitous proteins are glycoproteins that construct dimers or trimers. The only virus membrane protein that enables the virus to pass through the cell is the spike (S) protein. It binds to the receptors on the host cell and facilitates virus-cell fusion. Spike Protein has three different action mechanisms: ACE 2 mediated action, viral fusion mediated action and CD147 receptor-mediated action. Spike protein is present in all forms of human coronaviruses, as well as other viruses, and is involved in the viral invasion. Most prevalent viral diseases have very identical virus structures, primarily consisting of dimers or trimers of the spike glycoprotein, as well as similar mechanisms of invasion into host cells. Virus activity can be altered as a result of mutations in viral cells. Several vaccines have been developed to target the spike glycoprotein and boost the host's protection. Due to differences in the spike protein in different viral versions, as well as changes in them, vaccines find it difficult to prevent the spread of all variants of viruses. As a result, greater research into the structure of spike glycoproteins is needed, as well as the development of more effective immunizations to prevent spike protein invasion and infection.

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ABBREVIATIONS

ACE 2: Angiotensin-converting enzyme 2; **COX 2:** Cyclooxygenase-2; **DNA:** Deoxyribonucleic acid; **EBOV:** Ebola virus; **FCoV:** Feline coronavirus; **GP:** Glycoprotein; **HCoV:** Human coronavirus; **HR:** Heptad repeat; **MERS:** Middle East respiratory syndrome; **NA:** Neuraminidase; **NC:** Nucleocapsid core; **NTD:** N terminal domain; **Raf/MEK/ERK:** Ras/Raf/Mitogen-activated protein kinase/ERK kinase/extracellular-signal-regulated kinase; **RBD:** Receptor binding domain; **RNA:** Ribonucleic acid; **RUBV:** Rubella virus; **S protein:** Spike protein; **SARS:** Severe acute respiratory syndrome; **TM:** Transmembrane; **VP:** Virion proteins.

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