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REVIEW ARTICLE **OPEN ACCESS**

General Details of Structural Proteins of Coronaviruses with Special Reference of SARS-COV-2 or COVID-19

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ABSTRACT
The whole world is facing severe crisis due to SARS-COV-2 or COVID-19 pandemic. This review highlights the basic structural details of coronaviruses along with special reference of novel coronavirus that is SARS-COV-2 or COVID-19. They are enveloped, non-segmented, positive sense RNA viruses. The genome is packed inside a helical capsid formed by the nucleocapsid protein (N) and further surrounded by an envelope. Coronaviruses have four main structural proteins: Spike (S), Membrane (M), Envelope (E) and Nucleocapsid (N). Hemagglutinin-esterase (HE) is minor structural protein present in a subset of beta-coronaviruses. In between the S-E-M-N genes, coronaviruses encode species-specific accessory proteins. A notable difference was found in the longer spike protein of COVID-19 when compared with the bat SARS-like coronaviruses and SARS-CoV. COVID-19 appears to have no HE gene same as SARS-CoV and MERS-CoV.
Keywords: SARS-COV-2, Hemagglutinin-esterase, MERS-CoV, *S-E-M-N genes*

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INTRODUCTION

The whole world is facing severe crisis due to SARS-COV-2 or COVID-19 pandemic**.** According to World Health Organization to date (13 April 2020) there are more than 1. 8 million confirmed cases of COVID-19 and more than 113 675 deaths. On the basis of genomic structures and phylogenetic relationship, the subfamily Coronavirinae comprises of four genera Alphacoronavirus, Betacoronavirus, Gammacoronavirus and Deltacoronavirus [1]. There are seven human coronaviruses which cause mild respiratory illness (229 E, NL63, OC43 and HKU1) to severe respiratory syndrome (MERS-COV, SARS-COV and SARS-COV-2 or COVID-19). The current COVID-19 is the newest addition to this family that infects humans and appears to share the same cellular receptor as SARS-CoV, namely the ACE2 (angiotensin converting enzyme 2) [2]. This review highlights the basic structural details of coronaviruses along with special reference of novel coronavirus that is SARS-COV-2 or COVID-19.

GENERAL DETAILS OF STRUCTURAL PROTEINS OF CORONAVIRUSES

They are enveloped, non-segmented, positive sense RNA viruses. They have the largest genome among all RNA viruses, typically ranging from 27 to 32 kb. The genome is packed inside a helical capsid formed by the nucleocapsid protein (N) and further surrounded by an envelope.
The COVID-19 in China is closely related to bat SARS-like Betacoronavirus [3]. The lengths of the COVID-19 encoded proteins were found to be almost similar among COVID-19 and bat SARS-like coronaviruses [3].
Coronaviruses have four main structural proteins (Fig.1 and Fig.2):

(1) Spike (S)
(2) Membrane (M)
(3) Envelope (E)
(4) Nucleocapsid (N)

Minor structural proteins:

(5) Hemagglutinin-esterase (HE)

(1) **Spike (S):** Distinctive structure on the surface of the virus [4], [5] and mediates attachment of the host receptors [6]. The spike glycoproteins composed of two subunits (S1 and S2). Homotrimers of S proteins compose the spikes on the viral surface, guiding the link to host receptors [7]. In some Coronaviruses, the expression of S at the cell membrane can also mediate cell-cell fusion between infected and adjacent, uninfected cells. This formation of giant, multinucleated cells, or syncytia, has been proposed as a strategy to allow direct spreading of the virus between cells, subverting virus-neutralising antibodies [8], [9], [10]. A notable difference was found in the longer spike protein of COVID-19 when compared with the bat SARS-like coronaviruses and SARS-CoV [3]. S protein cleaved into two subunits S1 and S2 where S1 comprises of minimal receptor-binding domain (270–510) that helps in receptor binding and S2 facilitates membrane fusion [11]. Electron microscopy studies revealed that the spike is a clove-shaped trimer with three S1 heads and a trimeric S2 stalk [12], [13], [4], [14]. The S1 domain of COVID-19 spike glycoprotein potentially interacts with the human CD26, a key immunoregulatory factor for hijacking and virulence [15]. S protein is crucial for receptor binding, membrane fusion, internalization of the virus, tissue tropism and host range and therefore is the crucial targets for vaccine development [7]. Spike glycoprotein of COVID-19 exhibits higher sequence similarity with 12.8% of difference with SARS-CoV [16].

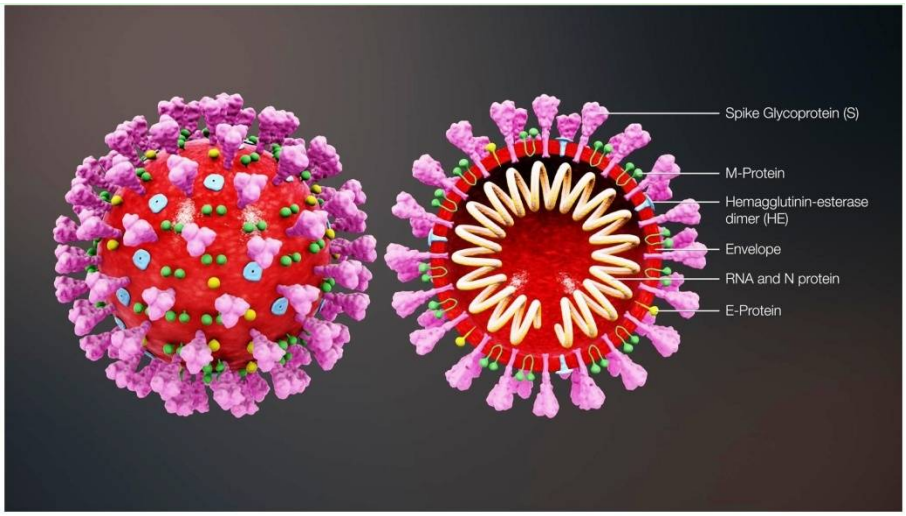

Fig.1 Image shows the major elements including the Spike (S protein), M protein, viral envelope (E protein), HE protein and helical RNA (N protein) of coronaviruses.
Source: https://www.scientificanimations.com/wiki-images/

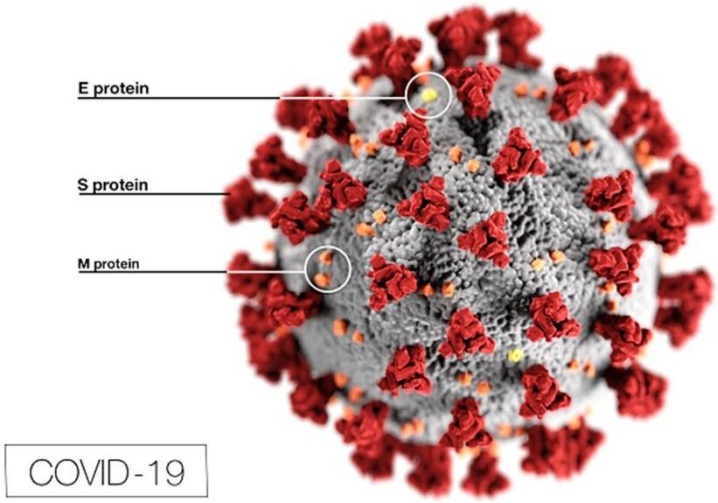

Fig.2 Image reveals ultrastructural morphology exhibited by coronaviruses (COVID-19).
Source: https://health.mil/News/Articles/2020/01/24/Coronavirus?type=Presentations

(2) **Membrane (M):** It is most abundant structural protein in the virion and is thought to give the virion its shape [17], [18]. Recent studies suggest the M protein exists as a dimer in the virion, and may adopt two different conformations allowing it to promote membrane curvature as well as bind to the nucleocapsid [19]. The M protein comprises of short N-terminal glycosylated ectodomain with three transmembrane domains (TM) and a long C-terminal CT domain [20]. It is also regarded as the central organiser of coronavirus assembly, interacting with all other major coronaviral structural proteins [21].

(3) **Envelope (E):** It is found in small quantities within the virion. E-protein from coronaviruses are highly divergent but have a common architecture [22]. E-protein facilitates assembly and release of the virus but also has other functions (such as ion channel activity in SARS-CoV E-protein is not required for viral replication but is required for pathogenesis [8]. The E protein is the smallest of the major structural proteins, but also the most enigmatic. During the replication cycle, E is abundantly expressed inside the infected cell, but only a small portion is incorporated into the virion envelope [23]. Recombinant coronaviruses have lacking E exhibit significantly reduced viral titres, crippled viral maturation, or yield propagation incompetent progeny, demonstrating the importance of E in virus production and maturation [24], [25], [26], [27], [28]. The coronavirus E protein is unique in that it can form homotypic interactions, which allows it to oligomerise and generate an ion-channel protein known as a viroporin [29], [30].

(4) **Nucleocapsid (N):** Only protein present in nucleocapsid. N protein binds the viral genome in a beads-on-a-string type conformation [8]. Although N is largely involved in processes relating to the viral genome, it is also involved in other aspects of the coronavirus replication cycle and the host cellular response to viral infection [31]. Interestingly, localisation of N to the endoplasmic reticulum (ER)-Golgi region has proposed a function for it in assembly and budding [32], [33]. However, transient expression of N was shown to substantially increase the production of virus-like particles (VLPs) in some coronaviruses, suggesting that it might not be required for envelope formation, but for complete virion formation instead [34], [35],[36], [37].

These four proteins occur in the order S-E-M-N in every known coronavirus lineage [38]. The M and E proteins are required for virus morphogenesis, assembly and budding. S glycoprotein is a type 1 fusion viral protein that comprises of two heptad repeat regions known as HR-C and HR-N which forms the coiled-coil structures surrounded by protein ectodomain [39].

(5) **Hemagglutinin-esterase (HE):** It is present in a subset of beta-coronaviruses. The protein acts as a hemagglutinin, binds sialic acids on surface glycoproteins and contains acetyl-esterase activity [40]. These activities are thought to enhance S protein–mediated cell entry and virus spread through the mucosa [8]. COVID-19 appears to have no HE gene same as SARS-CoV and MERS-CoV [41].

Accessory proteins or non structural proteins (NSPs): In between the S-E-M-N genes, coronaviruses encode species-specific accessory proteins, many of which appear to be incorporated in virions at low levels, ranging from one accessory in alpha coronaviruses including human coronavirus NL63 [42] to a predicted nine accessories in gamma coronavirus HKU22 [38]. The genomic position of these accessory genes varies, with accessories encoded before S in some beta coronaviruses and gamma coronaviruses and commonly in deltacoronaviruses [43].

FUTURE PERSPECTIVES AND CONCLUSION

The Structural Proteins of Coronaviruses with Special Reference of SARS-COV-2 or COVID-19 will help better understanding of infection, transmission, pathogenesis of Viruses. Development of Vaccine for SARS-COV-2 or COVID-19 is strongly needed today to control the infection, as S (spike) protein is crucial binding of receptor, membrane fusion, internalization of the virus, tissue tropism and host range and therefore is the crucial targets for vaccine development. It is hoped that present review will help researcher engaged in study of different strains of Coronaviruses along with SARS-COV-2 or COVID-19.

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