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STRUCTURAL DESIGN AND DIVERSITY OF COVID-19

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ABSTRACT:

The topic most talked about in the year 2020 is the Coronavirus. Although this biological agent is invisible to the naked eye, it has made the most horrific effect on the planet. While the structure and biological nature of the virus is being studied by Scientists all across the globe, the microbe, along with affecting the lives of people has caused a great loss in the entire economy. Ever since the outbreak, lifestyle of people has changed dramatically making the usual gatherings and travel look dangerous. The world is adjusting to the "new normal". A different outlook on hygiene, has made us cautious and obligated to sanitize frequently. As this virus is being discussed and proved to be fatal, every man has now turned his attention to the Virus and follow current research like never before. Though the cure to this virus is yet to be found, many findings of the virus is as important and taking us closer to a solution to deal with the Coronavirus.

I. INTRODUCTION:

Novel Corona Virus has wreaked havoc around the world. This pulmonary disease has appeared first in December 2019 in the city of Wuhan, the capital of Hubei province, China and spread wildly causing the entire globe to shut down and put every country in an emergency SOS condition. The virus has first been named by W.H.O as "Severe Acute Respiratory Syndrome – Coronavirus 2" i.e SARS-CoV2 as the RNA genome was found to be 82% identical to SARS-CoV. Coronavirus belongs to the family CoronaviridaeoforderNidoviralesand the genus Betacoronavirus.

In definition "Virus" is an infective agent that typically consists of a nucleic acid molecule in a protein coat, is too small to be seen by light microscopy, and is able to multiply only within the living cells of a host.

SARS-CoV2 has appeared first in 2019, and is known to cause Coronavirus disease, also referred to as "Covid-19". The first occurrence of Coronavirus was associated with Huanan seafood market in Wuhan. After the virus proved to be transmitted by human to human contact ie. Droplets from a sneeze or cough or by touching surfaces contaminated by droplets from infected persons. The number of cases increased exponentially by this mode of

transmission. A pandemic is an epidemic of an infectious disease that has spread across a large region I.e. multiple continents or worldwide, affecting a substantial number of people. The Coronavirus was declared as a pandemic by World Health Organization (W.H.O) on 11th March 2020. Recent studies on the comparative evolution of animal and human coronaviruses have led to the conclusion that HCoV 229E and OC43 (the common cold virus, now globally endemic in humans) crossed species from their animal reservoirs (bats and cattle, respectively) to humans within the last 200 years. This gave rise to a new conclusion that coronaviruses continue to cross species barriers and cause novel diseases.

As of 31st May 2020, there are 1,90,535 cases in India and 6.15 million cases in the world with a current fatality rate of ~ 6%.

II. CLASSIFICATION

Coronaviruses are classified together on the basis of the crown or halo-like appearance of the envelope glycoproteins, and on characteristic features of chemistry and replication. Most human coronaviruses fall into one of two serotypes: OC43-like and 229E-like. These differ in both antigenic determinants and culturing requirements: 229E-like coronaviruses can usually be isolated in human embryonic fibroblast cultures; OC43-like viruses can be isolated, or adapted to growth, in suckling mouse brain.

Another classification of Coronavirus can be done under three groups, based on antigenic relationships of the spike (S), membrane (M) and nucleocapsid (N) proteins. The HCoVs 229E and NL63 are group 1 coronaviruses, while OC43 occurring in humans, HKU-1 and SARS coronaviruses are classified in group 2 also occurring in humans whereas, the Group 3 coronaviruses are found mostly in Avian species. Genetic recombination readily occurs between members of the same and of different coronavirus groups providing opportunity for increased genetic diversity. It has been proposed that bat coronavirus was the ancestor of many mammalian coronaviruses.

Coronavirus can also be classified based on genera:

Alphacoronavirus – infect mammals

Betacoronavirus – infect mammals

Gammacoronavirus - infect avian species and

Deltacoronavirus – infect both mammals and avian species

As of May 2013, GenBank has 46 published complete genomes of the Alpha (group 1), Beta- (group 2), Gamma - (group 3), and Delta- (group 4) CoVs.

ALPHACORONAVIRUS:

Representative alphacoronaviruses include human coronavirus NL63 (HCoV -NL63), porcine transmissible gastroenteritis coronavirus (TGEV), PEDV, and porcine respiratory coronavirus (PRCV).

This genus, like other coronaviruses, has

a spike protein with a type II fusion machine (S2) and a receptor-binding domain (S1). It assembles into a trimer. Unlike beta- and gamma-coronaviruses, this protein is not cleaved into two halves.

Both types of Alphacoronavirus 1, feline coronavirus (FCoV) and canine coronavirus (CCoV), are known to exist in two serotypes. Serotype II targets Aminopeptidase N, while the receptor for Serotype I is unknown. The difference is due to a different spike protein. There is a common ancestor for FCoV and CCoV. This ancestor gradually evolved into FCoV I and CCoV I. An S protein from an unknown virus was recombined into the ancestor and gave rise to CCoV II. CCoV II once again recombined with FCoV to create FCoV II. CCoV II gradually evolved into TGEV. A spike deletion in TGEV creates PRCV. All these viruses are sorted into the subgenus Tegacovirus.

BETACORONAVIRUS:

Alpha- and Betacoronaviruses mainly infect bats, but they also infect other species like humans, camels, and rabbits. Beta-CoVs that have caused epidemics in humans generally induce fever and respiratory symptoms. They include:

SARS-CoV, SARS.

MERS-CoV, MERS.

SARS-CoV-2, COVID-19.

Coronaviruses have a large genome size that ranges from 26 to 32 kilobases. The overall structure of β-CoV genome is similar to that of other CoVs, with an ORF1ab replicase polyprotein (rep, pp1ab) preceding other elements. This polyprotein is cleaved into many nonstructural proteins.

Within the genus Betacoronavirus (Group 2 CoV), four lineages (A, B, C, and D) are commonly recognized.

Lineage A (subgenus Embecovirus) includes HCoV-OC43 and HCoV-HKU1 (various species)

Lineage B (subgenus Sarbecovirus) includes SARSr-CoV (which includes all its strains such as SARS-CoV, SARS-CoV -2, and Bat SL-CoV-WIV1)

Lineage C (subgenus Merbecovirus) includes Tylonycteris bat coronavirus HKU4 (BtCoV-HKU4), Pipistrellus bat coronavirus HKU5 (BtCoV-HKU5), and MERS-CoV (various species)

Lineage D (subgenus Nobecovirus) includes Rousettus bat coronavirus HKU9.

III. STRUCTURE OF CORONAVIRUS:

Coronavirus is a large RNA-virus with a diameter of 125nm and protein spikes projecting 20nm long. The large size of the virus could be the reason for its tendency to settle down on inanimate objects and surfaces rather than to get blown away with the wind. The viral envelope is made up of lipid bilayer consisting of membrane (M), Spike (S) and envelope (E) proteins. The ratio of these proteins E: S: M is 1:20:300. The viral genome codes for four main proteins, S- Spike, M- Membrane, E- Envelope and N- Nucleocapsid proteins.

Coronavirus is spherical, sometimes pleomorphic (changing structure). Interestingly, the virus acquired the name “corona” meaning “crown” due to the crown-like shape of the spikes in the surface of the virus. The virus finds receptors once it is transmitted to a sensitive human (host). The transmission occurs easily when the virus is deposited on a surface by a sneeze or a cough and is touched or somehow inhaled by another sensitive host. The spikes on the surface of the virus helps it latch on to receptors on human cell surface. It was found that SARS-CoV-2 spikes bind to receptors on the human cell surface are called angiotensin-converting enzyme 2 (ACE2). Similar to many viruses and bacteriophages, they undergo structural change if necessary and fuse with the cell membrane of the human host cell allowing the viral genome to enter into the cell. The genome consists of positive-sense, single stranded RNA ranging from 26.6kb to 31.7kb of zoonotic origin. Once the viral genome has entered the cell it is now capable of using host cell machinery to synthesize viral proteins and produce numerous new virions that are able to infect adjacent cells and the infect spreads amongst the cells.

Specific to Betacoronavirus shorter spike-like surface protein called hemagglutinin esterase (HE) are found which is believed to be acquired from Influenza C. The coronavirus surface spikes are homotrimers of the S protein, which is composed of an S1 and S2 subunit. The homotrimeric S protein is a class I fusion protein which mediates the receptor binding and membrane fusion between the virus and host cell. The S1 subunit forms the head of the spike and has the receptor binding domain (RBD). The S2 subunit forms the stem which anchors the spike in the viral envelope and on protease activation enable fusion. The E and M protein are important in forming the viral envelope and maintaining its structural shape.

Inside the envelope, there is the nucleocapsid, which is formed from multiple copies of the nucleocapsid (N) protein, which are bound to the positive-sense single-stranded RNA genome in a continuous beads-on-a-string type conformation. The lipid bilayer envelope, membrane proteins, and nucleocapsid protect the virus when it is outside the host cell.

The SARS-CoV2 spike is 20 times more likely to attach to human cells than SARS (2002). Despite similarities in sequence and structure between the spikes of the two viruses, three different antibodies against the 2002 SARS virus could not successfully bind to the SARS-CoV-2 spike protein. This suggests that potential vaccine and antibody-based treatment strategies will need to be unique to the new virus.

IV. CHALLENGES WITH DRUG DESIGNING:

The structural variations of SARS-CoV2 are studied in detail in order to recognize drug targets and receptors.One of the best-characterized

drug targets among coronaviruses is the main protease (Mpro, also called 3CLpro). Along with the papain-like protease, this enzyme is essential for processing the polyproteins that are translated from the viral RNA. The Mpro operates at no fewer than 11 cleavage sites on the large polyprotein 1ab, the recognition sequence at most sites is Leu-Gln,(Ser, Ala, Gly) with cleavage site at Gln. Inhibiting the activity of this enzyme would block viral replication. Because no human proteases with a similar cleavage specificity are known, such inhibitors are unlikely to be toxic. Coronaviruses demonstrate a complex pattern for receptor recognition. For example, the alphacoronavirus HCoV-NL63 and the betacoronavirus SARS-CoV both recognize a zinc peptidase angiotensin-converting enzyme 2 (ACE2).

V. CONCLUSION:

The pandemic has made most of us unclear about the future. The world has seen pandemics namely, The Plague (1855), The Flu (1918), The Cholera Pandemic (1961-75), The Swine flu (2009-10).

Although there have been previous pandemics, The Coronavirus pandemic stands out due to its ease of transmission. The present research is promising as we move closer to the cure. Measures taken by governments all over the world of “Social Distancing” and Nation-wide lockdown norms should be followed in order to contain the spread of the virus. Hopefully the world will regain its normalcy. Until then, following norms and staying safe is the best way to help heal the world.

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