Possible Origins of COVID-19

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Abstract

Coronaviridae is a family of enveloped, positive sense, ssRNA viruses. Corona is Latin for the word “crown” and is an apt name for the virus, as it is surrounded by surface projections called peplomers (Figure 1) [2]. The genome of the virus is typically between 26-36 kilobases, which makes it one of the largest RNA based virus family on the planet.

Introduction

COVID-19, also called SARS-CoV-2, is a strain of coronavirus first discovered in December of 2019 in the city of Wuhan, China. Many proposed explanations for the emergence of the virus were volunteered, from the virus originating in bats that were being sold in the market to the virus being genetically engineered in a laboratory from its 2003 SARS predecessor. Although there are varying levels of credibility to these claims, the genome of the virus can offer clues to deduce the origins of the virus. Although genomic characterization of the virus has become available, the origins of the virus are still under debate to this day. This analysis will explain why two theories have a greater validity than initial speculation regarding the virus. [1]

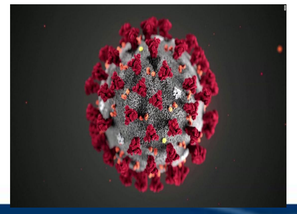

Figure 1: Coronavirus structure.

Methods and Results

Coronaviruses in general utilize positive sense RNA to function as mRNA, which helps them assemble the viral proteins needed for replication and infection. The virus contains three structural proteins, S (spike), E (envelope) and M (membrane) which are translated and migrate to the endoplasmic reticulum. From here, the full virion is assembled and transported to the cell surface using vesicles and is then released into the environment by exocytosis. [3]

There are two main theories for the emergence of the recently discovered SARS-CoV-2:

- Evolution in animal hosts before cross-species transmission
- Evolution in human hosts following zoonotic transfer

The spike protein of the virus contains the receptor-binding domain (RBD). Key residues of the spike protein associated with SARS-CoV-2 responsible for ACE2 receptor contact were analyzed using the NCBI database (Figure 2) [1]. This receptor is specific to humans and helps explain the infectivity of the virus and spread of the disease. In the same figure, polybasic cleavage sites were isolated that come about through insertions and substitutions in the genome, or through recombination of genetic information. This establishes the species as a novel strain of the virus, differing from the previously categorized genus of betacoronaviruses.

References

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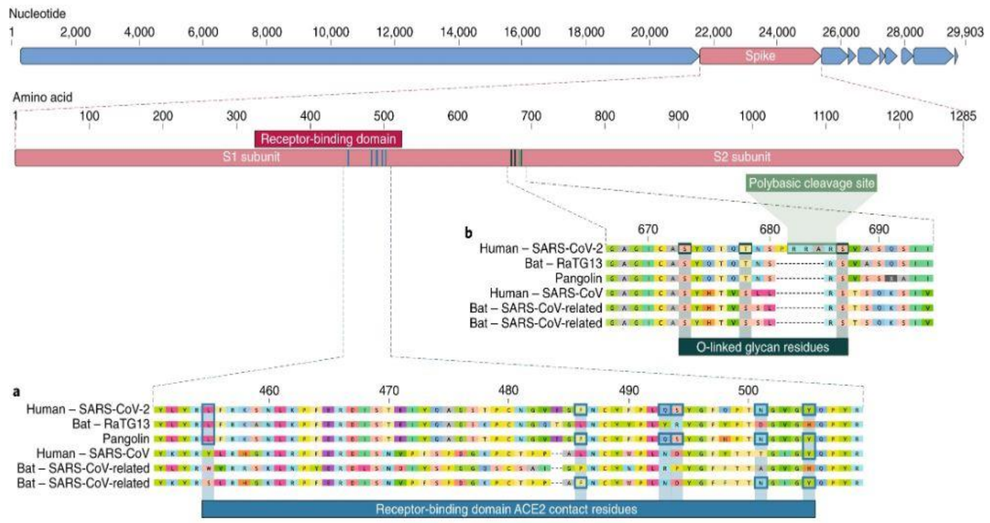

Figure 2: Genomic sequencing of SARS-CoV-2 and other coronavirus species

Discussion

Genomic and computational analyses of the RBD sequence present in SARS-CoV-2 shows that interaction is not ideal and that the sequence is different from that of the SARS virus. [4] Despite this, the affinity of the spike protein in SARS-CoV-2 is very high for the human ACE2 receptor. This shows that the affinity is likely a result of natural selection of human or human-like ACE2 binding sites that permitted another mechanism for binding to arise. [1] Also, collection of the virus from cell culture would have required prior isolation of an extremely genetically similar progenitor virus, which has never been described. Finally, the generation of O-linked glycans is very unlikely to occur in cell to cell passage, because such features suggest the involvement of an immune response. [1] These observations suggest that there is a very low likelihood that SARS-CoV-2 was engineered within a laboratory. An adaptation leading to increased specificity to the ACE2 receptor in animals would have required a large population density and an ACE2-encoding gene like the human analogue. Although bats are a reservoir of various antigens, the specificity of binding in SARS-CoV-2 suggests that at some point, a human host would have been needed to prompt a change in binding mechanism. Therefore, it is more likely that a progenitor form of SARS-CoV-2 was acquired by humans via an animal host and mutated into an infectious form within the human body itself.

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Figures by CNN and Proximal Origins of SARS-CoV-2 article listed in references

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