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The Enigma of COVID-19

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Animal viruses, by definition, are a cellular in structure containing nucleic acid protected by a protein covering [1]. While it can be considered that their structure is extremely simple, the genome that they carry is very complex and far more efficient than the genome of a human, who is considered to be the most complex organism on the planet. Viruses are host specific and have been observed to have ascended the throne in clinical setups, more often than not. Although it is not concrete, the possible reason behind this observation is the emergence of new strains. We can safely assume that these new strains of viruses make their entries while being decked out with all forms of molecular weapons. Now, a bunch of these new strains do not always survive, owing to their inconsistent genome stability, but the rest of them are outrageously resilient. These viral genomes boast of enough potential to express their proteins and pathogenicity, almost exclusively, as and when required. They are also capable of evading host immunological responses, owing to the comparatively faster gene rearrangement technique, than that of the vertebrate body's immunoglobulin rearrangement events.

The aspects of the origin and evolution of novel strains of viruses have been debatable. Carters and Saunders (2007) opined that viruses have evolved from their molecular ancestors, which indicates that eukaryotic viruses are evolved versions of prokaryotic viruses. A different theory suggests that RNA viruses were 1st generation viruses, which in due course of continuous "Parasitization", evolved to DNA viruses at a later time due to transposons, repeat, and plasmids [2].

However, in this context, if we were to analyze the degree of complexity of viruses, 2 basic theories will need to be adapted. One informs us of the origin of small viruses like Picorna viruses from molecular ancestors. The other tells us about the cellular origin of larger viruses. In recent times, though, newer strains of viruses have emerged, whose origins are still under debate [3]. Now, per Darwin's theory of natural selection, organisms have inherent abilities to adapt to new niches or habitats, thereby emphasizing the age-old quote "survival of the fittest". Newer viruses follow this rule of thumb, rather strictly. Owing to genome plasticity, viruses can undergo a series of mutations, in a very spontaneous and random manner. This allows them to be in a state of genomic dynamism, thereby adhering to the above theory. This makes it pertinent to mention that viruses are under constant and tremendous pressure from the hosts' immunological effector cells and molecules, leading to genome plasticity are prominent amongst viral genomes' traits. While this is true, there exist pieces of evidence that DNA viruses have more stability with a slower mutation rate, compared to RNA viruses [4-8].

RNA viruses undergo frequent mutations, resulting in varied strains. Interestingly enough, these viruses can and do mutate, while residing in an immune-compromised patient. We can safely say that exit RNA viruses may be different from the ones that entered. This also opens up the possibilities of evolution to a hybrid virus with a reasserted gene, if and when a patient is co-infected with 2 different types of viruses. RNA viruses are also known to be thieving agents, which steal host cellular genes [9], while they were branded as "Cap snatchers" by Herbert KM, et al. [10], given their modus operandi of taking out caps of mRNA from host cells and degrading the recapped mRNA, almost instantaneously.

It is commonly perceived that RNA viruses are very prompt candidates of "Template/Frame shifting" [11]. Along similar lines, the process of "Re-assortment" of genes is quite a feasible mechanism, which is offered by RNA viruses, especially those endowed with segmented genomes [12,13]. Moving on, membrane association is a hallmark of the genome replication of positive-strand RNA (+ RNA viruses) [14]. It has also been suggested that (+) RNA viruses remodel host membranes and lipid metabolisms, by orchestrating virus-host interactions, to create a suitable microenvironment to survive and flourish in host cells.

In addition to all of these, a "passage" concept has also been agreed upon, which aims to decipher the mechanism of the evolution of viruses, in vitro. The concept of passage is that; while being maintained under laboratory conditions, a virus is said to have been "passaged", each time the virus is "sub-cultured". After several such passages, the virus may be genetically different from the original wild strain, thereby leading to the emergence of a novel virus. A scenario presented by Hu NZ, et al. [15] that virus of strain H2 at passage 7 was consecutively passaged in KBM17 cells for 22 passages. Further, it was inferred that H2K7 was an attenuated strain, but further rapid replication adaptation was observed after passages. This observation was well explained by Woo HZ, et al. [16] that the evolutionary dynamics of adaptation are strongly affected, not only by the tendency toward increasing fitness values but also by the accessibility of pathways between genotypes constrained by the genetic code.

Serial passages of the chikungunya virus in the presence of nucleoside analogs favored the appearance of substitution G641D in the RNA helicase nsP [17]. These are the few assertions that can be made regarding the emergence of a novel strain of the Corona virus, better known as the COVID-19, which has taken over and plagued multitudes of countries across the globe. Having said this, it is obligatory to talk about the origin of Covid-19, or rather Corona viruses as a whole. Corona viruses were first identified as human respiratory pathogens, in the year 1965, and were known to demonstrate very high rates of mutation [18]. Coronaviruses are enveloped (+) RNAs, that replicate in the cytoplasm. To deliver their nucleocapsid into the host cell, they rely on the fusion of their envelope with the host cell membrane. The spike glycoprotein (S) mediates this entry of the virus and acts as the primary determinant of cell tropism and pathogenesis. Glycoprotein (S) is classified as a class I fusion protein and is responsible for binding to the receptor on the host cell, whilst mediating the fusion of the host and viral membranes. This is a process driven by major conformational changes of the S protein. On more technical terms, Corona viruses are the containers of the largest ssRNA genome of 33kb. Structurally, coronaviruses are enveloped viruses (as previously discussed) with round, and at times, pleomorphic virions which are 80 to 120 nm in diameter [19].

Coming back on track, it is acknowledged that this so-called 1st generation of corona viruses could not survive for long, owing to host resistance and/or lack of alternate hosts. A few decades later, in the year 2002, new strains of these coronaviruses emerged. It was reported that these strains of coronaviruses had very similar genome sequences, and had been isolated from animals sold at markets, in the region of China, where the first SARS cases had appeared. While none of the workers of these markets had any history of SARS, antibodies to these corona viruses were found in them [20]. A similar virus was also isolated from several bat species. This gave rise to the speculation that coronaviruses had repeatedly crossed into humans from other mammalian species. This rather small outbreak of Corona can be considered as one due to the 2nd generation of corona viruses.

Finally, the corona virus outbreak of 2020- this outbreak had presented itself in the form of pneumonia of an unknown etiology, in Wuhan, China, during the closing stages of the year 2019. The etiology was then confirmed to be a new strain of Corona Virus (CoV), thanks to extensive deep sequencing studies and lab investigations. Aptly, this virus was designated as 2019-nCoV. This name was furthered modified to SARS-CoV-2, by the International Committee on Taxonomy of Viruses. On the 11th of February, 2020, the World Health Organization (WHO) announced that the disease caused by this novel strain as COrona VIrus Disease-2019, better known as COVID-19.

Now, on an ending note, Andersen KG, et al. [21], stated that the proximal origin of the novel strain of COVID-19 is natural. Although the source of emergence is yet to be defined, based on the knowledge that we have gained through past outbreaks, it can be implied that recombination could have occurred, either by viral-viral or viral-host genes committing acts of "molecular piracy" to invade vertebrates and in so doing, render them immune-compromised. Needless to say, this entire pandemic begets an extensive line of investigative and preventive research by the world's brightest to solve this enigma, consequently putting an end to it.

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