SARS-CoV2 and Poly(A) Polymerase: Natural or Human Selection?

Introduction

To better understand the main topic, a brief introduction to natural selection and how it can influence the evolution of any form of life is necessary. Let's start with a practical example: why is the giraffe the mammal with the longest neck or why does the elephant have a trunk? Let's focus on the first case. After hundreds of years of debate on the subject, science has confirmed that the hypothesis is attributable to two fundamental factors: the change in environmental factors essential for life and the possibility of mutation of the living form itself, i.e. the adaptive capacity. To better explain this, let's consider that the giraffe has a height of around 5 meters, which we define as the current innate factor. On the other hand, among the various heights of the leaves that it feeds on, there are also those within its reach, which relates to the environmental factor mentioned before. In other words, the environmental factor must be compatible with the innate factor, i.e. the giraffe must have the means to feed itself. However, it was not always like this. The giraffe's ancestors, such as the sivatherium or the cantumeris, which existed 15-20 million years ago, had a much lower height according to fossil evidence. Let's suppose that over time there has been a significant change in the environmental factor concerning the position of the nourishment of these species, for various reasons the food was no longer at the same height, but only acacia trees remained, one of the current foods of giraffes. Acacia trees are much taller than simple shrubs. Being herbivorous species, giraffes were left with very few alternatives. The most common could be a migration or the stay of some specimens in the areas where the food was still within reach. This is the case with the okapi, the other living species of the giraffidae family, which feeds on leaves and buds of forests. Another assumption is that there was a giraffe with the third cervical vertebra more slanted (in fact, it was studied that the elongation of the giraffe's neck started from the aforementioned C3 vertebra), large enough to reach some leaves located higher up. In the subsequent progeny of the species, all the new giraffes preserving the longer neck would have had easy access to food, while those born with shorter necks, unable to feed, would have been destined to die. Without delving too much into technical terminology, we can talk about a dominant hereditary trait (i.e. a trait that is more likely to be expressed in the subsequent offspring), or a recessive hereditary trait (i.e. a trait that is less likely to be expressed in the subsequent offspring). Since the environmental factor required only giraffes with long necks to survive, it is evident that only those with the dominant gene for elongated cervical vertebrae have survived, leading to the perpetuation of the elongation, until reaching the current dimensions. Although it is not known exactly whether the height of the trees was the only cause of extinction for all the other species of the giraffidae family, it is certainly a fundamental element for all terrestrial herbivorous species in those regions.

In theory, all of this may seem easy and straightforward, but it is not. Every minimal mutational factor must still adhere to the indispensable physical and chemical laws that govern our universe. Therefore, having cervical vertebrae with a total length of 2 meters upwards implies the vascular need to push blood to the head with greater efficiency than in other mammals. This means that the heart must pump the blood with more pressure. If the giraffe did not have a heart with an average length of 60

centimeters and a weight of about 10 kilos, its blood would not even reach the middle of its neck, in the same way that a network of capillaries prevents excessive blood flow when the giraffe bends its head to the ground, as well as in other somatic and genetic traits, such as legs, tongue, horns, etc.
All the variables that condition and force life forms to adapt to survive are defined as natural selection. We could analyze every single gene of every single plant or animal to be amazed (not more than necessary, given the premises) by how its presence is not random, but dictated by millions of years and billions of reproductive cycles that have allowed every form of life to survive until the present day, in a continuous struggle between the mutation of environmental factors and the adaptive capacity of the species. For example, if we artificially introduce a mutation into any living being, it must first face the health condition of the being itself (if it leads to diseases or deficiencies, it could be fatal), and if the gene carrying such a mutation were superfluous, i.e. not favored in natural selection, it would most likely become recessive or lost.

Getting to the point

The reproductive cycle of a virus is much faster than that of a complex living being. This is not only caused by the frequency of reproductions but also by the number of reproductions that the virus executes in parallel, since the infected cells are thousands at a time. However, the aforementioned arguments about the environment in which the virus must interact to propagate and reproduce, as well as its adaptive capacity, remain valid.
In the specific case of CoVid-19, it has been observed that, in its current evolutionary cycle, despite producing variations (as should occur in any organic form that reproduces), the mutations are not as significant as those of other viruses (primarily HIV), especially if we consider that more than a third of the world's population has been infected, and it is a virus that replicates in estimated times ranging from minutes to hours. If we multiply these times by all the world's infected population, the significant variations that have been generated so far are relatively modest. Another factor that proves this is that the vaccines produced so far, based on the original CoVid strain dating back to 2019, show good overall effectiveness against all variations known so far.
However, there is a "anomaly" that has emerged, much faster than the normal mutation of the original sequence or subsequent variations, i.e. the series of adenines at the end of the genome in 2019 has rapidly weakened, to the point that it no longer exists in some strains. In simpler terms, the final part of the virus is rapidly disappearing, and (more importantly) it is not necessary for the virus's survival or reproduction: we are talking about the Poly(A) Polymerase.

What is Poly(A) Polymerase, and what is it used for?

It is normal at the end of the codons or the end of the genome that one sequence out of "n" reproductive sequences is lost (slightly), causing replication errors and making the messenger RNA and consequently, the resulting DNA unusable. This is, in fact, what determines our own aging. Obviously, the human genome is immensely larger and more complex than the few thousand or tens of thousands of bases that make up a virus, and any direct comparison would be inappropriate. The final adenines are, in fact, essentially superfluous to protein synthesis (meaning "the sequence can do without it"), and they represent a "shield" that gradually wears off, thus preserving the remaining genome intact. In natural

selection, such a sequence can spontaneously generate at the end of certain codons or in the tail of the genome itself, as it helps the viral strain to survive. However, in the case of CoVid, it is strange that all new strains have lost the abovementioned sequence in less than a year, a very singular fact. Furthermore, RNA viruses do not necessarily need this sequence to reproduce correctly. Indeed, errors in duplication are normal in this type of virus, and their survival force does not rely on the accuracy of the copy but on the high number of duplicates that statistically produce valid copies.

For example, the comparison of 32 samples has shown the gradual attenuation of the Poly(A) Polymerase sequence, present in the terminal part of the RNA genome. In fact, the code of the first Covid strain identified in WuHan (containing 29,903 nitrogenous bases) in December 2019 ends with the series ACAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA. The sequence is reduced in the subsequent sequence isolated in France in mid-2020 (derived from the Wuhan strain without significant mutations), which ends with the series ACAAAAAAAAAAA, while it is not even present in some subsequent strains, such as the sequence isolated in India in the early months of 2021 (which, incidentally, starts to contain other mutations compared to the original Chinese strain) that ends with the series ATTTTAGTAGTGCTATCCCCATGT.

Analyzing the Pfizer vaccine, on the other hand, the final sequence contains a Poly-adenylation specifically placed at the end of the genome (precisely for the reasons expressed before), containing a linker of 10 nucleotides GCAΨAΨGACΨ, here is the relative coding:

GAGCΨAGCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAGCAΨAΨGACΨAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

A small clarification regarding the Psy letter in the sequence. This stands for Methyl-Pseudo-Uridine (full chemical name N1-Methylpseudouridine) and is a substitute compound for uridine, which replaces uracil, which in turn replaces thymine in RNA. It is a natural component of transport RNA (tRNA), and the reason why it was put in place of uracil is that it partly activates the innate immune system, which would eliminate the vaccine before the specific T-lymphocytes are generated to counter the Spike protein. Thus, it favors subsequent protein synthesis, due to which Spike proteins will be produced. These will, therefore, be used as a reference by the immune system in case it should be attacked by the Spikes of CoVid during a hypothetical subsequent infection.

Conclusions

Without excluding any alternatives, Poly-adenylation in CoVid strains could also be natural. Even though Bat-CoVid (i.e. CoVid isolated in bats in the Wuhan region, which have become famous as the presumed culprits of the disease's spread to humans) has less of it than the first human isolated strain, a spontaneous process can still be hypothesized, or one cannot eliminate the hypothesis that it was created in the process of species transfer. However, why is it still present in the placental mammalian strains and not in humans? There could be many answers: minor mutations, less radiation, etc.

However, for each additional adenine, there always remains a legitimate doubt as to whether it would have been easier to add it manually. Indeed, modifying a virus is obviously easier than modifying an entire organism, i.e. artificially manipulating its genomic sequence and thus with its nitrogenous bases, thanks to current technologies and equipment, is within the reach of any government agency. This practice falls within the branch of genetic engineering, whose purposes can obviously be both humanitarian (the creation of vaccines) and warlike (biological weapons).

In this case, i.e. in the hypothesis of human engineering of the CoVid virus, we return to the initial discourse. Modifications, not being calculated to integrate with the countless reproductive variables and natural environmental factors, tend spontaneously to extinguish, just as the poly-adenization could have been lost in the past year. Obviously, it remains a hypothesis.

Adeninically yours... Mike Yoshi