SARS-CoV-2 and COVID-19: Questions about a world ethical governance for a societal and environmental responsibility in health science research.

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Abstract

Why did a new coronavirus, SARS-CoV-2, emerge without anybody being able to identify neither the reservoir nor the vector? Why did it trigger a multi-faced pandemic disease COVID-19? Why does it look like other human infecting viruses? Is this the result of an accidental similarity, an evolutionary convergence or a technological artefact? What is the origin of the virus? Why the released coronavirus couldn't be a HIV candidate vaccine? What technology is needed to built a HIV biomimetic coronavirus? What can we learn from the study of the scientific and social story of the virus and disease? What lesson could we learn?

Keywords: COVID-19, evolution, genetic engineering, HIV, SARS-CoV-2, vaccine.

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1 Introduction: questions.

Coronaviruses are responsible for cold, a common mild disease. But in 2003, a coronavirus from a bat (a wild animal reservoir) was transmitted to humans (the definitive host) via a civet (a wild animal vector). The viral infection triggered a Severe Acute Respiratory Syndrome or SARS. In 2012, another coronavirus, also of wild origin and from a bat, but transmitted by another animal vector, a domestic camel, infected humans. The infection triggered a SARS-like syndrome or MERS, as lethal as SARS. Coronaviruses are highly studied because they infect domestic animals. In December 2019, in Wuhan, Mainland China, a new coronavirus, 2019-nCoV, then renamed SARS-CoV-2, emerged without anybody was able to identify neither the reservoir nor the vector. Everything was as if the virus was totally humanized at the beginning of the outbreak. Depending on the affected person, the new human disease, COVID-19, is both a-symptomatic and may go unnoticed, or multi-symptomatic and very severe, or even lethal. What is the origin of this virus? **Why does the disease express a multi-factor changing face?** What can we learn from the emergence of this new pandemic?

2 The scientific story of the emergence of an unknown uncanny virus

2.1 From 2019-nCoV to SARS-CoV-2 ...

In February 2020, a French mathematician, inter-disciplinary expert, emeritus engineer at the IBM Center for Research in Artificial Intelligence, identified into the 2019-nCoV genome patterns that broke the genetic organization symmetry (Perez, 2020). They were inserted into the gene encoding the envelope protein (protein S) and those encoding the poly-protein which is at the origin of the viral protease and polymerase, enzymes present in every coronavirus.[2] These insertions were identical to the same patterns found in the genome sequences of the similar proteins of another RNA virus, the HIV. Is this an accidental similarity? Is this an evolutionary curiosity or is the virus a synthetic, artificial one? Using software tools, its genome was compared with those of coronaviruses isolated since 2003. The result highlighted a phylogeny in which the new virus, the most recent one, was older, in terms of genetic distance, than those that appeared before it. Everything happens as if it was less evolved than the oldest. Just as if, in a family tree, the grandfather was to be born after the grandson! What was the origin of 2019-nCoV? The 2019-nCoV genome sequencing indicated that it looked like another coronavirus that was issued from a bat and isolated in 2013. What would be the vector? The genome appeared to be located outside all the clades of humanized coronaviruses, whose reservoirs and vectors were known. Did everything happen as if the virus had passed directly from bat to man without any vector, or even **directly from man to man?** Assuming that the origin could be a bat, various vectors were proposed, first a species of reptile (Zhang et al., 2020), finally a pangolin species. Yet, the phylogenies showed that the 2019-nCoV genome was as close (or as far) in terms of genetic distance, to genomes of bat coronaviruses as it is to those of domestic animals. How could this genome then be very different from the genomes of its previous ancestors and coming from the same reservoir without a known vector? With the registration of the viral strain RaGT13, other phylogenies were proposed which placed the virus in an evolutionary position more fitting with the expected one. Why was this alleged ancestral strain, isolated in 2013, not registered in the genetic data banks before 2020? After the registration, 2019-nCoV was **renamed** as SARS-CoV-2.

2.2 A story of many troubles and mess... Why?

A team of young computer scientists, from the Indian Institute of Technology in New Delhi, uploaded a work in bioRXiv, the open online archive, showing an unknown and totally uncanny similarity between the genomes of 2109-nCoV and HIV (Pradhan et al., 2020). The 2019-nCoV genome contained patterns similar to some found in the HIV genome, in the envelope protein and in the poly protease-polymerase genes, validating the work of Perez! How to explain the presence of identical genetic sequences in so different viruses? Was this an adaptive evolutionary convergence phenomenon? How in nature could a set of similar mutations have come to the same functional result in genetic systems evolving within very different hosts? If it was a genetic transfer, how were such targeted genetic recombinations possible? In what host could the invasion of the same host cells by both viruses have arisen? The article was withdrawn, without any specific comment! Simultaneously, the previous work of Perez was framed as a fake news. And 2019-nCoV became SARS-CoV-2. What did the work of the Indian team show? If we compare the 2019-nCoV proteins S with those of coronaviruses, we observe very different amino acid islands in the protein sequence. Could they result from point mutations in the nucleotide coding sequences? These inserts, present in all the first analyzed viruses, as a whole represent less than 1% of the genome. This is much less than the expected genetic divergence with every coronaviruses which are known. With **an astonishing similarity**, the sites of cutting by the proteases looks the same as those present in the HIV proteins and are different from those of the coronaviruses found either in wild reservoirs or wild or domestic vectors. How a natural change of such magnitude by viable and specific mutations could have affected only the cut-off sites, which represent less than 3% of the protein sequence. How to envisage a series of targeted and repeated mutations, which simultaneously creates a new structure of the binding protein at its receptor site? Isn't it highly unlikely that a wild virus has acquired in so few years such similar insertions as those present in the HIV-1 gp120 and Gag proteins? None of these 4 inserts can correspond to a random single-point mutation, which usually affects only one amino acid and not a series of specifically delimited amino acids, or can cause a shift in the reading frame, usually resulting in a non-functional protein. 2 of the inserts present a deletion, a break in their sequence, which not only both retains the functionality but specifically increases the density of the positive charges at the surface of the molecule. Usually a deletion is lethal and results in a non-functional protein. By what process did these new molecules, with new properties emerge?

2.3 A coronavirus biomimetic of HIV?

A North American research team confirmed the existence of these extra-sequences (Beal et al., 2020). Into the surface glycoprotein they determines the cell receptors that are potentially recognizable for the entry of the virus into a cell. Into the poly-protein which codes for the viral enzymes, which are activated by cuttings by viral or cellular proteases, they determine the proteases properties. As RNA viruses, coronaviruses have a very high mutation rate, 100,000 times that of host cells. This implies a random accumulation of errors in the genome, that is usually unfavorable for the virus survival. We know into every genome the existence of spots where mutations are most frequent. Reconstructing the history of emergence of these mutations allowed, in HIV clades, to trace the lineage and evaluate the evolution potential of a gene. For HIV, the envelope protein env is much more evolutionarily stable than the pol and Gag proteins. How can we explain that in the new virus the evolution trend is exactly the opposite (Bricage, March & May 2020). Why would it have led naturally to a new protein S, homologous to env, rather to have led to the modified proteins homologous to pol and Gag?

Are these changes at random? A team of Chinese researchers disqualified the role of these insertions by modeling the interaction between the protein S and its target receptor ACE2 (Zhang et al., 2020). The inserts being located outside the recognition site that binds to the receptor, they would not have a functional effect. Isn't ignoring the fact that the functional properties of a protein emerge from the remote interactions between its different peptide modules? The whole is always both more and less than the sum of its parts (Bricage, April & May 2020)! In addition, the cutting of the poly-proteins, according to the protease that cuts and the site where it cuts, can give birth to a family of homologous proteins. The viral proteases and envelope protein synthesized by the same cell are multiple in terms of functional structure. Haven't high-resolution 3-D models shown that the protein S in SARS-CoV-2 resembles both those of a coronavirus and HIV? HIV inhibitors have very specific structures in adequacy with the topology of the HIV protein. The topology of the coronavirus protease is strangely similar to that of HIV and the same inhibitors can be effectively used.

3 Why couldn't be the new coronavirus a HIV candidate vaccine?

Isn't it technologically possible to modify an ancestor of SARS-CoV-2 to produce a biomimetic coronavirus of HIV so as to develop a potential AIDS vaccine? The genetic engineering of coronaviruses has been the subject of numerous detailed laboratory protocols. The construction of genetic chimeras has been published (Tang et al., 2011; Ao et al., 2019) and patents registered (Baric et al., 2018). For over 20 years, North American researchers have been working on domestic animals coronaviruses. Isn't the genome structure of a coronavirus the same as that of a retro-virus such as HIV? Isn't it possible to construct a coronavirus biomimetic of HIV? Isn't it at least one laboratory able of that intellectual and technological feat (Bricage, March 2020)?

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3.1 Don't we get a technology to built a HIV biomimetic coronavirus?

Prof. Dr. Frank Plummer, an expert on AIDS, with over 300 publications and 16,000 citations, head of the Department of Medical Microbiology and Infectious Diseases of the University of Manitoba, chair at The National Microbiology Laboratory of Canada (NMLC), that acquired a strain of MERS in 2013, was the first to highlight the existence of individuals resistant to HIV infection (Fowke et al., 1996). Since 2004, with teams of Chinese researchers hosted within the NMLC he has been interested in both AIDS and SARS (Berry et al. 2004), and especially in the protein S. He was working with Ms Xiangguo Qiu, director of the antiviral vaccine therapy program of the NMLC, an exceptional researcher, with more than 4,000 citations. The teams in which they both worked developed skills in building vaccines (e.g. for the Lassa fever, Ebola fever and Marburg viruses), with as animal model the civet, the SARS-CoV-1 vector! Teams carried out works on the production of biomimetic HIV clones (Wong et al., 2018) and published results about the viral structural proteins and their genetic modifications in relation to the phenomena of virus entry and replication in its host cells. Skills in using artificial intelligence software tools were expressed in these teams. Under the leadership of Plummer and the guidance of Qiu, other teams have built biomimetic HIV viruses expressing modified proteases or modified surface proteins (Luo et al., 2011, 2012). What was needed more to build a candidate HIV vaccine? Only a humanized and supposed harmless coronavirus was necessary (Bricage, May 2020)! Couldn't we protect ourselves from AIDS only with the risk of a simple cold (Bricage, March 2020)? Everything was in place in 2012, before the acquisition of the MERS strain. Couldn't the manufacture of a HIV biomimetic coronavirus then be considered?

This **exceptional intellectual and technological feat** was unfortunately not achieved! Why was the vaccine candidate not produced? In early July 2019, an administrative investigation led to the sudden expulsion from the P4 Laboratory in Winnipeg of X. Qiu, with all her research teams escorted out of the NMLC. The University of Manitoba ended all their accreditations and reassigned the students to other structures, formally prohibiting students and staff from traveling to China. Why did the National Agency of Public Health of Canada launch an administrative investigation in May 2019, the subject of which was never specified? Weren't the facts reported by Canadian and Chinese daily newspapers and seen on Canadian TV before July 2019? Why were they taken over, and where and by whom were they distorted and reclassified as fake news after the outbreak in Wuhan? Does it seem enough to add the label of fake new to deliberately discredit a truth? Isn't it easy to take back a real information, to modify it, to give it the appearance of reality, to better disqualify it, and thus to be able to decline any information referring to it (Bricage, May 2020)?

3.2 The whole is always both more and less than the sum of its parts.

Wouldn't the acceptance of the fact that SARS-CoV-2 is related to a vaccine candidate initially designed to fight HIV allow to explain the particularities of COVID-19? How can we explain that the disease, an expression of the physiological interactions between the viral and infected cells genomes, seems to change its face continuously depending on the patient? Simply by thinking that SARS-CoV-2 is a HIV biomimetic virus (Bricage, May 2020), with variable properties depending on how it interacts with its host cells! It can either go unnoticed as a common cold coronavirus or it can trigger symptoms usually associated with AIDS such as lymphopenia or express HIV properties such as neurotropism. Couldn't it have emergent properties associated with new target cells and new symptoms? Doesn't the fact that it is potentially more or less an HIV, and more or less a coronavirus, and more or less something else…, account for the biodiversity of the symptoms and thus the diversity of the treatments involved (Bricage, May 2020), some of which have nothing to do with anti-viral medication? Does this banal scenario of the dependent interactions between the parts of a system have anything impossible? Analysis of the evolution of the viral populations showed the existence of at least 2 subpopulations of SARS-CoV-2. The most frequent type, which is the most recent, is the most aggressive. The oldest, the least frequent type is also the least aggressive. This is totally the opposite of the observed natural genetic evolution of wild viruses. Would several different types of coronavirus be freed from the beginning?

3.3 Isn't the societal story of the virus being rewritten?

Why did a group of 27 prominent scientists insist on discrediting the artificial origin of the new coronavirus? How **to set up a system of governance of science research**, and of ethical control of this research, which could be satisfactory both at the local and global level? Would transparency not prevent this kind of political and media imbroglio? How can we avoid the mix of economics and health that undermines the social and environmental responsibility of both companies and individuals? Models exist: - publishing in **open access** under the Creative Commons license, without paying copyrights but mentioning them, - contributing freely to archive information in an open access and **open discussion** way, in a structure accessible to everybody, as *wikipedia* for teaching and *Research Gate* for research, - encouraging original, individual or collective innovations, rather than repressing them by deterring them, refusing or drowning them under constraints or accumulation of other more consensual informations.

And especially, when the fake news label is attributed to a news, to be able to systematically *"check that it is not the fake news that is itself a fake news!"*

How to avoid resentment while maintaining emulation? It is not because a proposal is not proven that it is automatically false, many commit this error of logic. This does not mean that it is true either, but if the source has some legitimacy, as for a simple honest testimony, isn't it worth testing it? Why are the arguments in favor of the consensus track of a wild virus being expressed as quickly as possible, in the form of letters, reports and not scientific publications? Why are only the aspects validating this track accepted and published? Why are papers dealing with non-consensual versions always rejected? Isn't it an attempt to hide parts of the reality to re-write the story of the virus and pandemic? **Can we be a judge and a part** of such an important investigation for humanity? Does mathematical economics and profit justify the liberal management of health research and societal services?

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