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The genetic jump that turned the new coronavirus into a specialist in infecting

A well-succeeded adaptation of SARS-CoV-2 is responsible for the current pandemics. The virus found in the ACE2 protein a gateway to easily infect the host cell

Maria Cátira Bortolini, UFRGS' faculty member and researcher, who holds a PhD in Genetics and Molecular Biology, is the coordinator of the study that analyzed 70 mammals' genomes aiming to identify the variations on the codifier gene of the protein that the new coronavirus (SARS-CoV-2) uses to infect the host cells and, thus, helping to find its role on the infection of human beings and the disease's development related to it (Covid-19).

The first scientific publication in the world about the matter was released in January 2020, immediately followed by the publication of scientific articles about the ACE2, the host's protein. This protein, whose function is related to the cardiac system metabolism, is opportunistically used by SARS-CoV-2 to infect the cell. From then on, the research group led by Bortolini has dived right into ACE2. "We selected 70 genomes – available in public data bases – from other mammals and analyzed the gene that codifies this protein, compared it to the existing genetic modifications and performed evolutionary tests to check if there were any signs of natural selection in this gene history," explains Bortolini, elucidating the research's phases.



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Two relevant contributions are the results of this study: the first one shows that SARS-CoV-2 uses important amounts of ACE2 protein to log into the cell and, as the human populations have the same amino acids in strategic spots of contact between SARS-CoV-2 and ACE, every human being is potentially susceptible to get the virus; the second one shows that there are important genetic differences between species, which would explain why some are affected and others are not. "Humans, as the virus' hosts, turned out to be perfect to the virus; in other words, SARS-CoV-2 dominated a human protein that made its introduction into the cells easier and, because of its ability, shaped by natural selection, showed a successful evolutionary infection outcome. That would not happen so easily to other species because of the differences in ACE2," says Bortolini. That is why pets would not be so easily infected by the virus as humans, for example.

This scientific contribution draws particular attention to the organism evolution by analyzing the ACE2 protein, particularly to 30 contact positions with the virus that are diverse between the species but do not show differences between human beings. However, the predisposition to the disease and the recovery from it, despite being connected to environmental conditions (social isolation, access to treatment, etc) are also related to other conditions, such as unknown genetic factors, the way the individual's immunological system responds, and also the different virus' lineages that have already been circulating. Another important observation made by the researcher is that the variations in other parts of ACE2 (that are not present in the molecule that has the 30 positions analyzed) cannot be discarded as elements that influence the infection and its outcomes.

Genetic Adaptation

A successful adaptation from the SARS-CoV-2 virus is responsible for the current covid-19 pandemics. The virus found in the human membrane's protein (ACE2) a gateway for the host cell infection. A perfect scenery and natural selection turned this new coronavirus into a specialist in infecting humans.

The evolutionary history shows a jump between species, something that had happened before, at least twice in the last 20 years. This is the third coronavirus that migrates from animals to humans. The earlier epidemics had their origins in a coronavirus that, due to mutations/re-combinations, was able to "jump" from a wild animal to human beings. However, in these two earlier events, we had experienced a curve much different from the tragic one that we have been experiencing so far. "The mutations are fortuitous and occur all the time in viral genomes, so "jumps" between species like these may happen in a recurring way," says Cátira.

The coronavirus is a virus whose RNA genetic material (ribonucleic acid: a molecule whose main function is to contain the information for the production of proteins) has high mutation rate. Thus, every molecule that self-replicates may have errors. At a given moment, the mutated virus may "jump" and find another host that has an appropriate organism to host it. "It is at this moment that the new coronavirus uses the ACE2 protein from humans and finds anchorage in the host. Since it is a protein present in the alveoli and blood vessels surface, the cardiovascular function is compromised," explains the researcher, who possesses broad knowledge in Human Genetics and Biological Evolution.

By finding a favorable host, the SARS-CoV-2 accesses the cell through ACE2, gets installed and replicates itself. From this point on, natural selection takes its course: as long as the virus multiplies itself, it increases the frequency of contagion, infecting other humans. "This virus has high tropism in humans. Our study shows that it can infect, perhaps with the same efficiency, big apes (chimpanzees, gorillas) that have a genetic identity similar with that of humans," elucidates Bortolini, revealing that, like mutations are random, nothing prevents this virus from mutating again and finding other organisms more favorable to derived forms of the SARS-CoV-2.

According to the researcher, from the moment the species start interacting and coexisting, these "jumps" become inevitable. "In the evolutionary history of the species, this has always happened, so much that defense mechanisms against virus invasions may be observed in any live form". The difference now, in the case of humans, is that the population is huge, concentrated in urban centers, served with mobility solutions, what favors the dispersion of a virus.

We belong to a primate species with more than 7.5 billion individuals in this world, linked to one another in a way never seen before. The big difference between the epidemics of earlier times and the current one is that, today, a person travels from China to the US, for example, in less than 24 hours. "This is the big difference: pathogens have always existed in the history of any species, it would not be different with ours: how many times coronaviruses must have infected human populations? Probably since the Homo sapiens emerged.

Maria Cátira says that the coronavirus infection – in the global proportions and impact that we have currently been witnessing – is caused by these factors: increased populational size and urban concentration, as well as facilitated mobility.

The complete study is available at the "Revista da Sociedade Brasileira de Genética" (Journal of the Brazilian Society of Genetics) - Genetics and Molecular Biology (GMB): <https://www.gmb.org.br/>

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