



The History of Corona Virus, from Neanderthals to the Present Time: A Brief Review

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Abstract

Contrary to popular belief, 2019 was not the first time humans were infected by the Coronavirus. Coronavirus is one of the oldest viruses on the earth. This article discusses the history of this virus from Neanderthal time so far. We have collected a variety of articles related to coronaviruses and the extent of their interaction with humans from the first time probably appeared on earth, given that this virus is one of the ancient viruses. By examining and following the footsteps of coronaviruses in different works of literature, we found that the first homo that was infected with the coronavirus was Neanderthal. Moreover, we realized that in addition to risk factors such as age and background diseases, genetic evolution also plays an essential role in the protection of the body against coronavirus. On the other hand, this virus has evolved throughout history gradually, the same as humans. The presence of disease in humans, in any period of history, causes changes in human quality of life. Therefore, paying attention to the background of ancient diseases reveals principal information about the complexity of pathogens.

Keywords: COVID-19; Ancient viruses; Neanderthal

Introduction

In December 2019, a novel human coronavirus started a pandemic of severe pneumonia COVID-19 in Wuhan, Hubei, China (1).

The International Committee on Taxonomy of Viruses (ICTV) has suggested naming this virus as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) based on its phylogenetic relationship with SARS-CoV. However, the name SARS-CoV-2 implies this virus as a pathogen of SARS, but actually, COVID-19 is a disease dif-

ferent from SARS, and the name SARS-CoV-2 may mislead the treatment as well as prevention. Therefore, human coronavirus 2019 (HCoV-19) has been suggested as a new name (3).

Coronaviruses belong to the genus Betacoronavirus of the Orthocoronavirinae subfamily in the coronaviridae family, and they are enveloped non-segmented positive-sense RNA viruses. Regarding the phylogenetic tree, 2019-nCoV is clustered into the sarbecovirus subgenus with



other severe acute respiratory syndrome-related coronaviruses (SARSr-CoVs), such as SARS-CV and SARS r-CoV (4).

Secondary to phylogenetic analyses of 15 HCoV whole genomes, the highest nucleotide sequence identity exists between 2019-nCoV/SARS-CoV-2 and SARS-CoV (79.7%). Distinctively, the envelope and nucleocapsid proteins regions of 2019-nCoV/SARS-CoV-2 are well conserved throughout evolution (Fig. 1), which are the sequence identities of 96% and 89.6 %, respectively (5).

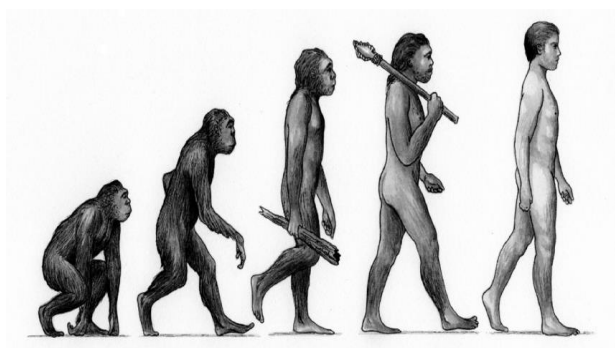


Fig. 1: Evolution stages of man (2)

Coronavirus in the 21st century

The world is currently experiencing its third outbreak with a highly virulent coronavirus causing severe pneumonia in humans, all three taking place in the 21st century. The first epidemic had origins in Guangdong Province, China, during late 2002 and lasted until 2004 (6). The outbreak was caused by severe acute respiratory syndrome coronavirus (SARS-CoV), killed at least 700 people, and infected over 8000 individuals in all six inhabited continents consisting of 27 countries (7).

SARS-CoV has not been reported in the human population before, except a few numbers of laboratory-related infections (8). The second epidemic designated as MERS-CoV (Middle East respiratory syndrome coronavirus) was first characterized in a man with pneumonia in Saudi Arabia in 2012, in which sporadic cases, small clusters, and large outbreaks of the same type were

reported over subsequent years in 24 affected countries (9, 10).

The third pandemic was first reported in Hubei Province, China, in late 2019 and is still ongoing as of April 2020 caused by another novel coronavirus, known as the human coronavirus 2019 (11). It spread drastically and globally leading to over 5,550,000 deaths and 340,000,000 cases reported from over 200 countries, areas, or territories as in January 2022 according to WHO dashboard Coronavirus (COVID-19) Dashboard (12). Sequencing results have showed that there was over 75% genomic similarity of HCoV-19 to SARS-CoV to date (13). The impact of this pandemic on the human's life pattern, everyone's lifestyle, and also the appearance of ethical disturbances, and opportunistic groups are not refutable (14).

Following of these novel coronaviruses origins reveals important implications for the control and prevention of related infectious diseases in humans. Initially, some theories were suggesting that HCoV-19 is created in the laboratory artificially; but, respecting the information obtained from the SARS-like coronaviruses (Bat-CoV-RATG13) studies conducted on bats, there was a similarity of more than 95% to HCoV19. So, it can be concluded that the source of coronavirus is probably bats (15). In addition, there is a region in the cleavage site between S1 and S2 which is found in a coronavirus genome identified in bats (16).

The interaction between the receptor of different hosts is a critical and determinative exigence for inter-species transmission of a virus. Considering that, after the identification of human ACE2 as the cellular receptor for HCoV-19 elucidates the route of the virus transmission from animal to human (1, 17). Distinguish the reciprocal action between spike (S) protein and ACE2 of different species is a good signal to survey the origins, probable hosts, as well as the development of medicines and vaccine (17, 18).

Ancient Coronavirus

Among researches for a better understanding of Coronaviruses, it is noticed that the Coronavirus

has traces beyond this date related to thousands of years ago (19). Periodically, before our time, the coronavirus had infected prehistoric humans and was probably the cause of population extinction. The fact that evolutionary information from tens of thousands of years ago exists in the modern human genetic material is notable, and it can be utilized to point out viruses with the effect on human's ancestors, or to predict upcoming pandemics (19, 20).

According to paleogenetics studies, adaptation mechanisms in the host genome is an informative address to ancient viral epidemics. Paleovirology evaluations have provided affirmations that coronaviruses history goes that back to more than 20000 years ago, and originates in east part of Asia. Discovering the "footprint" of an ancient coronavirus epidemic in this region in 1000 genome project (perusal of over 2.500 individuals from 26 worldwide populations) is a good example of researches disclosing the background of ancient coronavirus epidemic in the east Asia (19, 20).

Regarding researches from Neanderthals, modern humans have interacted with them at least twice in the last twelve thousand years. Neanderthals are hominids living all over Europe and parts of Asia about 400,000 to 40,000 years ago and very close to present human. There are some evidences that Neanderthals interbred with modern humans (21). Based on evidences purifying selection has removed the main part of Neanderthal DNA transferred into modern human genome, and the information about the remained portions is not still available (21).

It is hypothesized that getting infected by new viruses, and obtaining the adaptive ability of resistance against them can be explained by the interbreeding between Neanderthals and *Homo sapiens* (17). Viral infections and the ancient alleles selection happening as its result have caused evolution in human genome due the cross action with Neanderthal about 60,000 to 40,000 years ago, and these haplotypes has entered human genome by this gene flow (22).

Recently, groups of researchers have discovered a region on chromosome 3 related to strong

COVID-19, which is also associated to Neanderthal genes (22). Moreover, another haplotype on chromosome 12 has been found related to milder type of COVID-19 (22% lesser risk) which is interestingly inherited from Neanderthals. As a result, the Neanderthal haplotype can be possible risk factor for COVID-19 in some people apart from other ones (14, 23).

Conclusion

The background of ancient diseases reveals principal information about the complexity of pathogens, so it might be considered as an important step in analyzing the pandemics.

Ethical considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

Conflict of interest

The authors declare that there is no conflict of interest.

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