

Covid-19: Uncovering the mystery

Abstract

Scientists believe that Covid-19, the disease caused by SARS-CoV-2, originated from bats because of the stark similarities to bat coronaviruses and several previous viruses that bats have strongly believed to have been the origins of. Scientists are still struggling to place the whereabouts of when and where humans were infected, however both a laboratory and a natural origin do seem feasible. The believed origin, a wet market in Wuhan, might not be the initial place humans were first infected, in fact it could be in a mine 1000km from Wuhan or in mainland Europe. However, the virus could have originated from a laboratory instead, due to dangerous research work being conducted in Wuhan, at two of the world leading facilities in bat coronaviruses. Equally important to note is that the World Health Organisation have sent a team of international scientists to Wuhan, which could help to answer questions surrounding this mystery.

Introduction

Scientists presume that the animal SARS-CoV-2 (the virus that causes Covid-19) originated from bats. Also, several possible locations of when and where humans were first infected have been identified by comparing genetic information from samples in these different locations with the genetic information of SARS-CoV-2 first identified in Wuhan. It is important to clarify that SARS-CoV-2 and SARS-CoV-1 are not the same virus, they are two different ones with the SARS-CoV-1 causing an outbreak in 2002-2004. Furthermore, Covid-19 is the name of the disease caused by SARS-CoV-2.

Why do scientists think that Covid-19 came from bats?

Since the outbreak in the Wuhan market, one of the questions that has arisen is which animal(s) did Covid-19 (disease caused by the virus SARS-CoV-2) originate from. Scientists comparing the genomes of SARS-CoV-2 and other similar viruses have found that SARS-CoV-2 is most closely related to bat coronaviruses.

This would not be the first time that a virus has originated from bats. Linfa Wang, a virologist with a decade researching bat immunology was the first to pinpoint that SARS-CoV-1 could have originated from horseshoe bats.

Apart from the genome of SARS-CoV-2 being most similar to bat coronaviruses, Wang believes that other reasons why SARS-CoV-2 originated from bats is because bats are the only mammals able to fly long distances, hence because of this they use around 20 times more energy than other mammals of a similar size. This additional energy usage causes chemicals called free radicals (molecules that contain at least one unpaired electron, also known as reactive oxygen species) to be produced. These molecules build up inside the bat cells and damage the DNA by removing the hydrogen atoms. This process releases fragments of DNA into the cell. But, during a viral infection, when the viruses hijack the cell's DNA replication system, parts of the DNA or RNA of the virus are also in the cell. For other mammals that don't perform demanding exercises like flying, their DNA scarcely leaks into their cells. So therefore, their immune system will attack any free DNA in the cell, classifying it as a threat and will attack the free DNA or RNA with antiviral substances, interferons. On the other hand, for bats, because their DNA leaks out quite often, if their immune systems followed the same principles, then the immune system would attack it's own DNA. So, scientists have assumed that bats have evolved to have weakened immune systems in response to their flying, allowing bats to tolerate viruses that pose a threat to other mammals.

But other virologists suggest that it could be because bats live in wide territories in large groups which would allow more viruses to spread. Whatever the reason, they agree that SARS-CoV-2 did most likely originate from bats and most possibly from Chinese rufous horseshoe bats.

Pangolins were also considered as the origin species since having also been origins of other deadly viruses, however, new research conducted suggests that pangolins weren't since SARS-CoV-2 is most similar to bat coronaviruses but could instead be an intermediate host (species that transmitted the virus to humans from bats) because of the similarities between a part of the virus and pangolin's receptor binder domain in pangolin coronaviruses (further information about this below).

Other viruses that bats were the sources of:

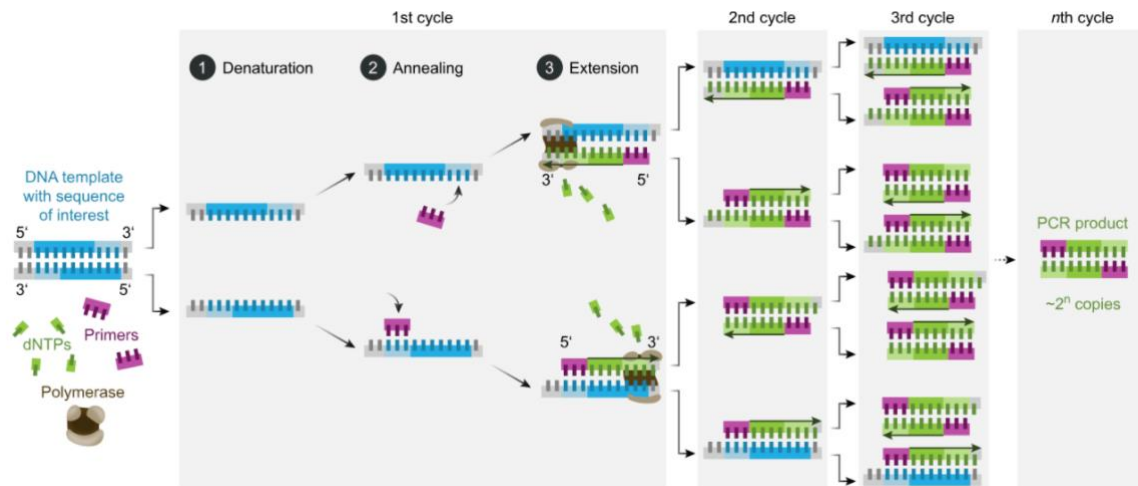
- Ebola
- Rabies
- Nipah and Hendra virus infections
- Marburg virus disease
- Strains of influenza A virus
- SARS-CoV-1 (virologists believe originated from horseshoe bats).

When and where do scientists think that humans were infected?

The mysterious miner's illness:

In 2012 6 miners in the Yunnan province (1000km away from Wuhan) in China were tasked with cleaning out bat faeces in the mine. After working for 14 days, four of the miners fell ill from a mysterious virus, symptoms comparable with other respiratory illnesses. For the other two miners, it only took 4-5 days for them to become ill, with similar symptoms to the other miners. 3 out of the 6 miners died from the illness. Bat faeces were collected from the mine and taken to the Wuhan Institute of Virology. One sample was discovered to have RaTG13 (96.2%) and BtCoV/4991(98.7%). These two viruses are the most closely related to SARS-CoV-2. However, these two coronaviruses share a common ancestor with SARS-CoV-2 but are not an ancestor of SARS-CoV-2 meaning that SARS-CoV-2 did not originate from these coronaviruses.

Scientists have also found remnants of SARS-CoV-2 in untreated sewage in European countries which has led to questioning the official origins of SARS-CoV-2. They have identified these using a method called polymerised chain reaction which allows scientists to make millions of copies of a very small DNA sample. This is done by thermal cycling, which involves heating the sample at a mixture of temperatures, allowing the DNA to denature and split into separate strands where primers are added. Annealing is the process of recombining DNA into the double helix shape.



Process of polymerised chain reaction

https://upload.wikimedia.org/wikipedia/commons/thumb/a/ab/Polymerase_chain_reaction-en.svg/1920px-Polymerase_chain_reaction-en.svg.png

For example, in Barcelona, frozen raw sewage was analysed from two large wastewater plants. These samples were from 2018, 2019 and 2020. The first presence of the virus was January 15th, 2020, 41 days before Barcelona's first reported case. Of course, this could be explained by several reasons such as testing had not begun for Covid-19 (the disease caused by SARS-CoV-2) or that people had not isolated on return from Wuhan or surrounding areas before repatriation flights began. However, fragments of IP2 and IP4 (parts of SARS-CoV-2) were discovered in a sample from March 12th, 2019, before initial reports of infections in Wuhan, China. A criticism of this research is that this has not been peer reviewed by other scientists. This is a cause of concern as scientists will criticise other scientist's work questioning the legitimacy, accuracy and results confirming that the source can be trusted. Without the peer review it is crucial to not fully trust these results although there is a correlation with the miners' experience and this research: they both locate potential origins of SARS-CoV-2 outside of Wuhan.

Natural vs laboratory origin:

The answer to this question will indicate where humans were first infected and when.

When referring to these two different options: natural is when the disease spreads to humans with no interference from humans whereas with a lab origin the disease spreads to humans accidentally or non-accidentally from a laboratory that was doing research on this disease.

Initially, scientists agreed with a review paper in Nature Medicine (it received 700 citations), that dismissed any possibility of a laboratory origin. However, when explaining their reasoning, the authors did not fully explain the reasoning behind a natural origin. Important gaps were noted by other scientific articles, such as one by Independent Science News, including the lack of explanation for why this virus was so well adapted in humans, yet had only started infecting humans recently? But, when approaching the question of a laboratory origin, the authors only provided reasons against a laboratory origin, completely disregarding the other side of the argument. Furthermore, the authors in the Nature Medicine article had higher standards for explanations of a laboratory origin than a natural origin. All of this points to the conclusion that the authors have not compared

both options equally and hence their conclusion cannot be relied on. But the authors did do extensive research comparing genomes of the SARS-CoV-2 hence their research is still a valuable tool in answering when and where humans were first infected with Covid-19 (the disease caused by SARS-CoV-2).

Possibility of a laboratory origin:

Laboratory origins are not rare. In fact, laboratory outbreaks are accepted to have resulted in the Venezuelan Equine Encephalitis and swine flu (H1N1). Considering that two of the world leading research facilities on bat coronaviruses are in Wuhan (Wuhan Institute of Virology and Wuhan Centre for Disease Control), a laboratory outbreak could be highly likely. This is an especially likely outcome considering criticisms of the facilities' biosafety. In late 2015, a group of scientists published an article in the Nature Medicine, suggesting of a new group of bat coronaviruses engineered by the Wuhan Institute of Virology that had the potential to infect humans. The purpose of the research and summarised article is to warn others of bat coronaviruses transmitting to humans. The article describes how the virologists were able to create a new "hybrid virus" with a sequence from the same species of bats that Covid-19 is believed to have originated from-horseshoe bats. However, the Wuhan Institute of Virology has a biosafety level of 4- the highest available questioning the possibility of a laboratory outbreak but the Wuhan Centre for Disease control only has a biosafety level of 2.

Possibility of a natural origin:

One of the facts of SARS-CoV-2 is that it is quite adapted to humans. This means that the virus has evolved for some time meaning that the virus could have a natural origin. Proof of this, is in one research study detailed in the Science Direct magazine, where SARS-CoV-2 was found not to be able to replicate in bat kidney or lung cells, yet SARS-CoV-1 was able to. In the Nature Medicine review paper, the authors firstly compared the genomes for the spike proteins. These spike proteins in SARS-CoV-2 are able to bind to a protein in human cells, a similar feature to the SARS-CoV-1 virus. Furthermore, a computer model predicted that this coronavirus wouldn't bind as well as SARS-CoV-1 but the virus surprised scientists by binding better than expected. The scientists stated that this was not what a bioengineer would choose if intending to create a harmful virus. However, more proof lies in the structure where the area that causes the binding to the ACE2 receptor. It most closely resembles pangolin coronaviruses which would have come about as a product of natural selection. This receptor binding is part of the spike protein in viruses such as coronaviruses (giving it a crown like appearance hence corona, Latin for crown). This binding allows the virus to bind to ACE2 receptor and enables the virus to gain entry to the cells to reproduce, a vital requirement for viruses. When scientists develop organic substances in laboratories, they usually use known organic structures unlike this pangolin structure (it was barely known of beforehand). So therefore, natural selection has caused this unknown binding to become prominent, further evidence for a natural origin. The two possibilities offered by the review paper in Nature medicine are that either the virus evolved in its host, most likely bats, proposed by my review above, and mutated so it was able to damage human cells as well, or that the virus was transmitted from animals to humans and has been evolving ever since until it has now become capable of damaging human cells. Both are reasonable options which would explain when SARS-CoV-2 started to infect humans and will help to indicate where humans were first infected.

Conclusion

To conclude, the evidence strongly supports bats as being the origin of SARS-CoV-2. SARS-CoV-2's nearest relatives are bat coronaviruses and SARS-CoV-2's predecessor, SARS-CoV-1, was also believed to have originated from the same species of bats: the Chinese rufous horseshoe bats. Bats have been identified to have been the origin to other viruses as well. The whereabouts of where humans were first infected by the SARS-CoV-2 virus has still not been established. This is because evidence supporting different locations has arisen. In European cities, genetic fragments of SARS-CoV-2 have been discovered in frozen sewage before their first supposed cases, and in some cases before the acknowledgement of SARS-CoV-2 in Wuhan, China. The miners' case, 1000km from Wuhan, establishes another possible origin of when humans were first infected. Unfortunately, there is not sufficient evidence to either link or disprove these individual past cases. If there was a link, was it only because citizens and scientists did not have an awareness of Covid-19 (the disease caused by SARS-CoV-2) as its mild or even more extreme symptoms can be associated with other familiar diseases such as the common cold. Taking all this into account means that there is no clear conclusion as of this moment of time as to where and when the first humans were infected with Covid-19. But it is vital to note that as of this year, the World Health Organisation are sending a team of international scientists to Wuhan to determine if the virus did originate in Wuhan or elsewhere. This research will hopefully answer the mystery surrounding Covid-19.

Whether they are linked or individual cases, unfortunately these discoveries may not pinpoint the true origin of when and where humans were first infected. But scientists can use the newfound knowledge to help prevent or contain future similar outbreaks.

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