

Origins of SARS-CoV-2: Focusing on Science

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The COVID-19 pandemic, caused by the severe acute respiratory syndrome virus 2 (SARS-CoV-2), has resulted in over 110 million confirmed cases and more than 2.4 million deaths globally as of February 23, 2021.^[1] China succeeded in containing the nationwide spread of COVID-19 by implementing a lockdown in the city of Wuhan, where the first outbreak occurred. Following the containment of the first outbreak, China experienced more than a dozen small clusters of cases in other cities due to virus transmission by travelers and cold-chain transmission. However, widespread transmission of the virus was prevented by implementing strict quarantine policies and social distancing measures. Although great progress has been made in understanding the epidemiology, virology, immune response, and clinical outcomes of this disease 1 year after the start of the pandemic, the origin of the virus remains unresolved.

Speculations on SARS-CoV-2 origin

At the beginning of the outbreak, most of the early COVID-19 cases were linked to the Huanan seafood market, and it was believed that the market is the earliest source of SARS-CoV-2.^[2,3] However, later studies by different teams in China questioned this speculation. First, some of the early cases had no epidemiological link to the market.^[3,4] Second, massive sampling and testing for the detection of SARS-CoV-2 in frozen meats and domestic animals around Wuhan city yielded negative results.^[5] Furthermore, coronaviruses that were phylogenetically related to SARS-CoV-2 were found in rhinolophus bats in South Asian countries including China, Japan, Cambodia, and Thailand^[2,6–8] and in pangolins smuggled to China from South Asian countries.^[9,10] In addition, several small clusters of COVID-19 cases in China were confirmed to be caused by food contamination of cold-chain transmission from other countries.^[11–13] All these data suggest that the origins of the virus are far more complicated than expected.

During the global fight against the pandemic, enormous speculations on the SARS-CoV-2 origins went viral and misled the public and policymakers alike. Some of the speculations include that the virus is a man-made bioweapon generated by gene modifications, an accidental laboratory leak led to the

outbreak, and the virus was unintentionally introduced by scientists during field work. The scientific community strongly dismisses these unproven and misleading speculations and generally accepts that the SARS-CoV-2 has a natural origin and was selected either in an animal host before zoonotic transfer, or in humans following zoonotic transfer.^[14,15]

Wuhan Institute of Virology (WIV), Chinese Academy of Sciences, has engaged in a long-term study on natural reservoirs of SARS-CoV^[16–18] and is among the first institutions that identified the SARS-CoV-2 after the COVID-19 outbreak.^[2,19] In addition, WIV discovered a virus sequence (RaTG13) that shows a 96.2% genomic sequence identity match with the SARS-CoV-2 genome, in its archived bat samples collected in 2013.^[2] These results lay a foundation for understanding the origin of SARS-CoV-2, development of diagnostic methods, antiviral drug screening, and vaccine development; the findings also provide an important clue pertaining to the natural origin of SARS-CoV-2. Sadly, WIV was at the center of the misleading speculations regarding the origin of the virus, which were not fully clarified until a recent joint study was performed by an international expert team led by the World Health Organization (WHO) and Chinese experts.

Global study of SARS-CoV-2 origin: China

The joint expert team has been working in three groups, the epidemiology, molecular research, and animal and environment groups.^[20] The experts have been working together through video conferences, onsite interviews and visits, and extensive discussions. Over the course of 4 weeks, the joint team studied massive volumes of epidemic-related data and visited some facilities, including the Wuhan Jinyintan Hospital, the Wuhan Center for Disease Prevention and Control, and the Wuhan National Biosafety Laboratory (Wuhan P4 laboratory) run by WIV; in addition, they also visited the Huanan seafood market. The team interviewed local medical workers, laboratory researchers, scientists, market managers, residents, and recovered COVID-19 patients.

The joint team visited the Wuhan P4 laboratory, a facility which is the most widely speculated place of origin of the SARS-CoV-2. The Wuhan P4 laboratory is the first of such facilities to be constructed in China and runs high-level biosafety checks. The laboratory is a state-of-the-art design by French experts, jointly constructed by French and Chinese engineers and accredited by the China National Accreditation Service for Conformity Assessment (CNAS). It was designed to be a laboratory studying highly classified pathogens and an international collaboration research center on emerging infectious diseases. All activities in this laboratory on specific viruses were qualified by the China National Health Commission (CNHC). All administration and management have been strictly regulated and regularly examined

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and reviewed by these two Chinese authorities. It has been examined by CNAS and CNHC four and three times, respectively, since its opening at the end of 2017. Currently, this laboratory is approved to study the Nipah virus, Ebola virus, Xinjiang hemorrhagic fever virus, and SARS-CoV-2. This laboratory has played a pivotal role in fighting the COVID-19 pandemic by way of animal model studies and inactivated vaccine development, drug screenings and tests, and basic research for understanding SARS-CoV-2.

The WHO joint team has had extensive exchanges with the laboratory manager, scientists, and staff and has highly appraised the cooperation, transparency, and openness of the WIV leadership and staff. The team concluded, “They upheld a very stringent and high-quality management system. Also proceeding from the current evidence, we regard the lab leak hypothesis as extremely unlikely” in a statement released to the media on February 9, 2021, Wuhan.^[5]

The joint team also released some other information regarding the source of SARS-COV-2 to the public. The sources include direct zoonotic spillover, cold-chain foodborne transmission, and intermediary host species. The team suggested that the introduction of the virus through an intermediary host species is “the most likely” passway; direct transmission or introduction through cold-chain foodborne transmission is “also likely.” The team recommends further studies through the large-scale testing of animal and human samples not only from China but also from all over the world to better understand the origin of SARS-CoV-2.

In the past several decades, more than 70% of emerging or reemerging infectious diseases are zoonoses and were transmitted to humans from their animal reservoirs through intermediate hosts. A huge number of unknown viruses exist in their natural reservoirs and continue to evolve, which results in the generation of new strains. Many of these viruses may have intrinsic characteristics that enable them to cross species barriers and infect humans. The rapid global economic development, including urbanization, land usage, animal domestication, and intensive agriculture, increases the chances of contact between humans and wildlife, thereby increases the risk of interspecies transmission of viruses carried by wild animals. To prevent future zoonosis, the best strategy is long-term and extensive surveillance based on science. We need to learn about unknown viruses, assess the potential risks of interspecies transmission, pinpoint the hotspots of animal-human interfaces, and eventually prepare diagnosis methods and use them for monitoring high-risk animal and human populations. With this prophylactic strategy, we can rapidly identify and limit the rapid spread of emerging pathogens at the very early stage and prevent the next epidemic. To this end, it is necessary to unify experts from different disciplines, including microbiologists, epidemiologists, veterinarians, clinical specialists, ecologists, sociologists, and policymakers, to work together on the basis of science.

Conflicts of Interest

None.

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