

# Origin of SARS-CoV-2: Two Schools of Thought

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## ABSTRACT

Undisputedly, the horseshoe bats are the nearest known genetic relatives of the Sars-CoV-2 virus. However, most intriguing question is to explain how did a bat RNA virus evolve into a human pathogen and became so virulent and deadly unlike its predecessors of the likes Sars-Co V (November 2002- February 2003 started in Asia; 774 deaths) and MERS-CoV (September 2012 started in Saudi Arabia; 886 deaths) were also the bat coronaviruses but had infected very fewer humans (Ge et al., 2013). The scientists believe that either the Sars-CoV-2 virus had infected humans directly or via an intermediate temporary host such as pangolin, a palm civet or even a snake, i. e., the one that has an ACE2 cellular receptor (the molecule which allows cellular entry of the virus) intermediate in protein sequence (or at least structure) between the bat and the human one. They believe that the 6 miners who cleaned the facets of the bats from the abandoned mine (2012) situated in Mojiang after continuously working in the mine for long 15117 days fell severely ill and were treated in WIV, Wuhan.

They had got infected with the bat virus RaTG13 having a genome resembling the extent of 98.7% to that of the Sars-CoV-2 virus. Their samples having RaTG13 virus continued to remain covered in the WIV, Wuhan for long 6-7 years got evolved (fully blown) to the extent of 100% Sars-CoV-2 virus. While working on these samples in 2019, some researcher/s unwittingly got infected with this virus and became the first unsuspected victim/s i.e., directly got infected with the now fully evolved Sars-CoV-2 virus. Some others believe that the infected researcher/s reached the Wet- market; situated at a distance of barely 300m from WIV and came in touch with the bulk pangolins, palms civet or even the snakes which received bat virus from the unsuspected patient/s and the chain of infection of Sars-CoV-2 virus started. Either way, this School of Scientists believes the Sars-CoV-2 virus has a Natural or Zoonotic Origin; irrespectively whether it reached human beings directly from the bat or via pangolins, palms civet or even the snakes.

The 'Second School of Thought' of scientists suspects that the Coronavirus is man-made as indicated in the 2015 document where the Chinese scientists discuss using Coronavirus as a Bioweapon. But it remains to be an enigma for the scientists belonging to both the 'Schools of Thought' that the virus enters human cells using a viral spike protein that is a tremendous fit for its human receptor (a protein called ACE2). This close fit allows the virus to spread very efficiently between people, but such precision cannot plausibly have arisen by chance. Thus, the virus appears to have evolved in the presence of that human receptor. The present study discusses the arguments put forward by both Schools of Thought.

## Introduction

The causative pathogen, Severe Acute Respiratory Syndrome Coronavirus 2(SARS-CoV-2) also referred to as SC2 or H CoV-19 is the seventh coronavirus known to infect humans; SARS-CoV, MERS-

CoV and SARS-CoV-2 can cause severe disease, whereas HKU1, NL63, OC43 and 229E are associated with mild symptoms. In the COVID-19 pandemic, SARS-CoV-2 is the agent. The infectiousness

(ability to infect), pathogenicity (ability to cause disease) and the number of virus particles needed to get infected determine the disease pattern. SARS-CoV-2 is a respiratory virus, which spreads mainly through droplets that enter the nose and mouth. It can bind itself to a receptor, typically in our lungs. Some new strains of the virus have also emerged over the last few months. Every individual is a host for SARS-CoV-2. Health condition, risk of exposure and medical history determine an individual's response to the agent.

The behaviour of the host, such as hygiene practices, occupation, nutritional and immunologic status, age, gender and many other factors, determines the probability of getting infected as well as the disease outcome. While recent reports suggest more evidence towards an airborne transmission, it also does not negate other means of transmission. Physical distancing and the use of a well-ventilated mask will remain more relevant even if an airborne transmission is the only means of transmission. There are many theories around the origin of the virus, from being leaked of the Wuhan virus Lab to many of them linking it to the wet market in Wuhan. The reason remains unknown, though local health authorities initially thought the patients had fallen ill through exposure to the common infection source in the market and ruled out the pathogen as contagious until January 20.

In the press and the scientific literature, scenarios by which this natural zoonotic transfer might have occurred have been endlessly mulled were fueled by early findings that many of the earliest COVID-19 cases seem to have occurred in and around Wuhan's Huanan live animal market. Another point which could well be cited that there is a precedent that the two previous coronavirus near-pandemics of SARS (2002-3) and MERS (2012) both probably came from bats and both are thought (but not proven) to have transitioned to humans via intermediate animals (civets and dromedaries respectively), a natural zoonotic pathway is a reasonable first assumption [1]. On the contrary, the latest data are that 14 of the 41 earliest cases, including the first, had no connection to the animal market [2]. They destroyed evidence of it in laboratories and also refused to provide live samples to international scientists who were working on a vaccine. Many reports in the past have appeared that China deliberately suppressed or destroyed evidence related to the coronavirus outbreak and silenced doctors and whistle-blowers who spoke about the virus.

Reuters adds that a whistle-blower, who worked in the Chinese health care system, provided 117 pages of internal documents from the Hubei Provincial Centre for Disease Control and Prevention (CDC) to CNN. The files, which CNN had verified by six experts, showed how the region struggled to manage the coronavirus between October 2019 and April 2020. According to a report published in CNN, a document marked as "internal document, please keep confidential,". Irrespective of this observation of the expert committee of WHO, the scientists throughout the world

remain divided into two schools of thought on the origin of COVID-19, but it was the former US President Donald Trump who had commented that implied that SARS-CoV-2, the coronavirus that causes COVID-19, was made in a laboratory. Dr. Michael Ryan, an Irish, Executive Director of the World Health Organization's Health Emergencies Program responded to these claims by repeating that the novel coronavirus is believed to be natural in origin. Of course, the two laboratories, located close to the Wuhan wet market where China said the outbreak began, study bat-origin coronaviruses; laxity about safety requirements is quite common.

## Discussion

The author would try to argue supporting WHO at times while differing with its observations pending the complete report of WHO is made public.

### Two Schools of Thought Regarding Origin of SARS-CoV-2 Virus

There are many theories around the origin of the virus, from being leaked of the Wuhan virus Lab to many of them linking it to the wet market in Wuhan. In all fairness, we shall discuss the arguments forwarded by the researchers belonging to two diagonally opposed schools of thoughts, i.e. the one that believes that SARS-CoV-2 has originated naturally the one that believes that is lab-made.

### Did SARS-CoV-2 Originate Naturally or had Zoonotic Origin?

We offer a perspective on the notable features of the SARS-CoV-2 genome and discuss scenarios by which they could have arisen. Our analyses clearly show that SARS-CoV-2 is not a laboratory construct or a purposefully manipulated virus. The following arguments may prove it to have originated naturally.

### M M P (Mojiang Miners Passaging) Theory

The story dates back to April 2012 when 6 workers working in Mojiang mine, an abandoned situated) in Mojiang Hani, Yunnan Province, China) fell ill from a mystery illness while removing bat faeces. Three of the six subsequently died. For investigation swab samples of 20 bats (*Rhinolophus ferrumiquinum*) 9 rats (*R. Flavipectus*) and 5 musk shrews (*Crucidura dracula*) were collected by researchers from the lab of Zheng-li Shi, named as bat-woman, at the Wuhan Institute of Virology (henceforth WIV). The specifics of this mystery disease have been virtually forgotten. However, they are described in a Master's thesis written in the Chinese language in 2013 (later translated in English) by a doctor who supervised the treatment of the six ill miners who were admitted to the No. 1 School of Clinical Medicine, Kunming Medical University, Kunming, Yunnan province - 250 Km from Mojiang in late April and early May 2012. These miners were treated for infections. At the time of admission, all 6 miners had symptoms like- dry cough, sputum, high fevers, especially shortly before death, difficulty breathing and

myalgia (sore limbs). Some patients had hiccoughs and headaches. They were given treatment like ventilation (3 patients), steroids (all patients), antivirals (all except one), and blood thinners (two patients). They were also given antibiotics and antifungal medicines to counter secondary but significant co-infections.

These Samples, which were later sent to the WIV in Wuhan and Zhong Nanshan, further confirmed that viral disease was strongly suspected. Some miners did test positive for coronavirus, though their number not given in the thesis. It was also concluded that *Rhinolophus sinicus*, a horseshoe bat was the source of this viral disease and the “the unknown virus lead to severe pneumonia could be: The SARS-like-CoV from the Chinese rufous horseshoe bat.” In short, the miners had a coronavirus, but it was not SARS itself. The new virus was called MojV after Mojiang, the locality of the mine [3]. All these symptoms and even the line of treatment, which caused the recovery of three of the six patients, point towards a very strong probability that they were the CORONA-19 patients [4,5]. The sampling by the Shi lab found that bat coronaviruses were unusually abundant in the mine [6]. They also found two beta-coronaviruses, the most-deadly of all coronaviruses both in SARS and MERS. One of which RaTG13, then known as BtCoV/4991, are the most closely related sequences to SARS-CoV-2 (98.7% and 96.2% identical respectively) has a special pandemic potential as was already reported by the Shi lab [7].

**\*Shi Zhengli, Head of bat Coronavirus Research at WIV is Renowned as the Bat-Woman of China:** Yet, there is an equal number of points to argue that considering the conditions inside the lungs of the miners were far from ordinary and the Ra TG13 might have evolved to the level of the genome sequence of SARS-CoV-2 in 7-8 years (2012-2020). They put forward the following arguments in their support.

1) The rapid evolution in new hosts is well known among corona- and other viruses because the selection pressure on the invading pathogen is high [8-11]. According to the Master's thesis, the miners' immune systems were compromised and remained so even for those discharged. This weakness on the part of the miners may also have encouraged the evolution of the virus. The CT scans of all the miners showed severe infections in their lungs because the miners were exerting themselves and therefore inhaling the disturbed bat guano deeply. One miner had suspected pneumoconiosis and/or a particulate matter was present that irritated the tissues and may have facilitated viral entry initially. In contrast, standard coronavirus infections are confined to the throat and upper respiratory tract. They do not normally reach the lungs [12]. Lungs are far larger tissues by weight (kg vs gm) than the upper respiratory tract. The human aero-digestive tract is approximately 20cm in length and 5cm in circumference, i.e. approximately 100 cm<sup>2</sup> in the surface area while the surface

area of a human lung ranges from 260,000-680,000 cm<sup>2</sup>. The amount of potentially infected tissue in an average lung is, therefore, approximately 4500fold (Appx average of 260000 and 68000) greater than that available to normal coronavirus infection [13]. There was, therefore, likely hood of a much larger quantity of virus inside the miners than would be the case in an ordinary coronavirus infection.

- 2) The length of infection experienced by the miners far exceeded that of an ordinary coronavirus infection- 57-117 days excluding the 14 days of incubation period when they continued to work in the mine while the ordinary surviving coronavirus period takes 10-14 days to cure [14].
- 3) Normally, Coronaviruses recombine at about 10% of all progenies in a cell [15-17].

But in the case of a coronavirus adapting to a new host where many mutations distributed all over the genome are required to fully adapt to the new host, the recombination rate is likely to be highly influential in determining the overall speed of adaptation by the virus population [8,18]. To recombine, viruses must be present in the same cell. In such a situation the particularities of lung tissues become potentially important because the existence of airways (bronchial tubes, etc.) allows partially adapted viruses from independent viral populations to travel to distal parts of the lung (or even the other lung) and encounter other such partially-adapted viruses and populations. This movement around the lungs would likely have resulted in what amounted to a passaging\* effect without the need for a researcher to infect new tissues. The M.S. thesis also mentions that the observation was made many a time that areas of the lungs of a specific patient would appear to heal even while other parts of the lungs would become infected. \*Passaging is a standard biological technique for adapting viruses to new species, tissues, or cell types. It is normally done by deliberately infecting a new host species or a new host cell type with a high dose of virus. This initial viral infection would ordinarily die out because the host's immune system vanquishes the ill-adapted virus. But, in passaging, before it does die out a sample is extracted and transferred to a new identical tissue, where viral infection restarts. Done iteratively, this technique (called “serial passaging” or just “passaging”) intensively selects for viruses adapted to the new host or cell type.

- 4) Not only bat coronaviruses were abnormally abundant but also there were many different kinds, often causing co-infections of the bats [19]. It is an accepted fact the Viral co-infections are often more infectious or more pathogenic [20].
- 5) Also, note carefully the observation that WIV researchers remarked about the bats in the mine:

“We observed a high rate of co-infection with two coronavirus species and interspecies infection with the same coronavirus species within or across bat families. These phenomena may

be owing to the diversity and high density of bat populations in the same cave, facilitating coronavirus intra- and interspecies transmissions, which may result in recombination and acceleration of coronavirus evolution" [21]. Combining these observations, it could be possible that the miners' lungs offered an unprecedented opportunity for accelerated evolution of a highly bat-adapted coronavirus into a highly human-adapted coronavirus and that the decades of ordinary coronavirus evolution could easily have been condensed into months [22].

### Notable Features of the SARS-CoV-2 Genome

- i. By comparing the genetic material of SARS-CoV-2 and other coronaviruses which have been sampled from different species, it has been shown that SARS-CoV-2 shares high sequence similarity with those coronaviruses found in bats. But strangely, the Receptor-Binding Domain (RBD) of SARS-CoV-2 is unlike those found in bats but shares high homology with those found in pangolins.
- ii. Based on computational structural studies [23-25] and biochemical experiments [25-27] SARS-CoV-2 is (appears to be) optimized for binding to the human receptor ACE2 (Angiotensin-converting enzyme 2). The following three points will lend support to the above argument that it is the selected human ACE2 receptor that can easily bound with the RaTG13 virus as follows:
  - a) The receptor-binding domain (RBD) is the region of the spike protein which is the most variable part of SARS-CoV-2, [25] in the region of the spike that physically contacts the human ACE2 receptor has recently been crystallized. Shang, et al [28] found close structural similarities between the spikes of SARS-CoV-2 and RaTG13 in how they bound the human ACE2 receptor. Six RBD amino acids are shown to be critical for binding to ACE2\* receptors and for determining the host range of SARS-CoV like viruses [23]. With the coordinates based on SARS-CoV, they are Y442, L472, N479, D480, T487 and Y4911, which correspond to L455, F486, Q493, S494, N501 and N505 in SARS-CoV-2 [23]. Five of these six residues differ between SARS-CoV-2 and SARS-CoV. The results based on the structural studies [23-25] and biochemical experiments [25-27] indicate that SARS-CoV-2 RBD binds with high affinity to ACE2 from humans, ferrets, cats and other species with high receptor homology [25] but not mice and rats. We found that, compared to human ACE2, rat ACE2 very less efficiently bound to the S1 domain of SARS-CoV-2 and supported less-efficient S protein-mediated infection [29].

\*ACE2 or Angiotensin-converting Enzyme 2 exists in various oral mucosal tissues, so, the oral cavity is considered a potential route for the entry of the COVID-19 virus. ACE2 is a protein that provides the entry point for the coronavirus to hook into and infect

a wide range of human cells." "Research has shown that other than the common organs like dry mouth, another symptom of the dry tongue now also known as COVID Tongue is a manifestation when the body fails to produce saliva that protects your mouth from bad bacteria. COVID tongue is often accompanied by a change to the tongue's sensation, as well as muscle pain while chewing due to persistent ulcers.

Three points to note are:

- i. Mutations do take place in the receptor-binding domain (RBD) of SARS-CoV-2.
- ii. Acquisition of polybasic cleavage site and O-linked glycans.

Both the polybasic cleavage site and the three adjacent predicted O-linked glycans are unique to SARS-CoV-2 and were not previously seen in lineage B beta coronaviruses. Sequences shown are from NCBI GenBank, accession codes MN908947, MN996532, AY278741, KY417146 and MK211376. The pangolin coronavirus sequences are a consensus generated from SRR10168377 and SRR10168378 (NCBI BioProject PRJNA573298). While the analyses above suggest that SARS-CoV-2 may bind human ACE2 with high affinity, computational analyses predict that the interaction is not ideal [23] and that the RBD sequence is different from those shown in SARS-CoV to be optimal for receptor binding [23,30]. Thus, the high-affinity binding of the SARS-CoV-2 spike protein to human ACE2 is most likely the result of natural selection on a human or human-like ACE2 that permits another optimal binding solution to arise [28] suggesting that there is strong evidence that SARS-CoV-2 is not the product of purposeful manipulation.

- b) So much so, as with SARS-CoV-2, bat RaTG13 RBM [a region of the RBD] contains a similar four-residue motif in the ACE2 binding ridge, supporting the notion that SARS-CoV-2 may have evolved from RaTG13 or a RaTG13-related bat coronavirus.
- c) The L486F, Y493Q and D501N residue changes from RaTG13 to SARS-CoV-2 enhance ACE2 recognition and may have facilitated the bat-to-human transmission of SARS-CoV-2. The fact that SARS-CoV-2 having any natural zoonotic origin (Zoonotic diseases, also known as zoonoses, are caused by germs that spread between animals and people) can be proved by MMP as follows: The screen was performed on a line of green monkey cells. The researchers simultaneously tracked the interactions of virus and cells. The screens reconfirmed that the ACE2 receptor protein promotes infection by SARS-CoV-2, i.e., the SARS-CoV-2 spike protein has very high (10-20 times) affinity than that of the original SARS virus for the human ACE2 receptor and that it shows no such affinity in other species which can only be explained that the virus to have been strongly selected in the presence of a human ACE2 receptor [31-37]. The same is the case of the spike of RaTG13



that binds the human ACE2 receptor [38].

So, it looks highly probable that the RaTG13 virus, unlike most bat coronaviruses, in the mine was directly infected with the human lung cells. The main determinant of cell infection and species specificity of coronaviruses is initial receptor binding [39]. All this makes RaTG13 a highly likely direct ancestor of Sars-CoV-2 [40,41]. All this makes RaTG13 a highly likely direct ancestor of Sars-CoV-2. From the thesis we also know that blood and other samples were extracted from the miners and some of these were sent to the Wuhan Institute of Virology (WIV). We suggest that these samples contained highly human-adapted viruses and were used at the WIV for research. During this research the virus escaped, initiating the 2019 COVID-19 pandemic. As we show, the theory solves the currently mysterious evolutionary and biological features of SARS-CoV-2 as well as explaining its eventual appearance in Wuhan.

It also explains subsequent attempts to obscure the deaths of the miners and the Mojiang mine origin of RaTG13. It looks improbable that SARS-CoV-2 that is closely related to SARS-CoV-like coronavirus could have been manipulated in the laboratory. As noted above, the RBD of SARS-CoV-2 is optimized for binding to human ACE2 with an efficient solution different from those previously predicted. [23,29]. Furthermore, if genetic manipulation had been performed, one of the several reverse-genetic systems available for beta coronaviruses would probably have been used [42]. However, the genetic data irrefutably show that SARS-CoV-2 is not derived from any previously used virus backbone [43]. Instead, we propose two scenarios that can plausibly explain the origin of SARS-CoV-2:

- (i) Natural selection in an animal host before zoonotic transfer; and
- (ii) Natural selection in humans following zoonotic transfer.

Mutations, insertions and deletions can occur near the S1-S2 junction of coronaviruses [44]. The finding of SARS-CoV-like coronaviruses from pangolins with nearly identical RBDs, however, provides a much stronger and more parsimonious explanation of how SARS-CoV-2 acquired these via recombination or mutation [42].

### How did the Virus Reach Human Beings?

The Scientists are divided into two groups to put forwards two different arguments as follows

**Lab-Leak Theory:** It is possible that when frozen samples derived from the miners were opened in late 2019 at the Wuhan lab, they were already highly adapted to humans to an extent possibly not anticipated by the researchers. One small mistake or mechanical breakdown could have led directly to the first human infection in late 2019. This looks quite probable because of the

following two arguments:

- a) On June 27th, 2012, the doctors performed an unexplained thymectomy (the surgical removal of the thymus gland, which is located just under the breast bone which is an immune organ that on one patient and it could have -19 can potentially be removed without greatly harming the patient) contained large quantities of virus. This patient is most likely is patient zero of the COVID epidemic.
- b) The sheer proximity of the Wuhan Institute of Virology (WIV), China's first and only Biosafety Level 4 (BSL-4 - the highest pathogen security level) facility) and WDCPC (Wuhan Center for Disease Control & Prevention) a BSL-2 lab, situated at a distance of 8 miles and 250 meters respectively from the Huanan live-food market, the outbreak and the nature of their work represent evidence that can hardly be ignored. Moreover, there is a long international history of lab escapes and biosafety concerns from the labs in many countries like Russia, Britain and South America. The WIV, since 2018, has been collecting large numbers of coronaviruses from bat samples ever since the original SARS outbreak of 2002-2003; including collecting more in 2016 [7].

Led by researcher Zheng-Li Shi, WIV scientists have also published experiments in which live bat coronaviruses were introduced into human cells. Moreover, US Embassy staff after visiting the WIV in 2018 had expressed grave safety concerns about biosecurity there. Bat coronaviruses have been kept in the WDCPC lab in the past. Thus, the lab escape theory is that researchers from one or both of these labs may have picked up a Sars-CoV-2-like bat coronavirus on one of their many collecting (aka "virus surveillance") trips. Alternatively, a virus they were studying, passaging, engineering, or otherwise manipulating, escaped.

**Virus Reached the Wuhan Seafood Market:** Since there is usually very limited close contact between humans and bats, it is more likely that transmission of SARS-CoV-2 to humans happened through an intermediate host that is another animal species more likely to be handled by humans. The Wuhan Center for Disease Control and Protective Prevention, where researchers engaged in bat research without using appropriate protective equipment, was "right around the corner" from the Wuhan Seafood Market, the location tied to multiple initial carriers of the virus—apparently, less than 300 meters away. If argument (a) holds good, it would look highly probable that the RaTG13 virus, unlike most bat coronaviruses, in the mine has directly infected human lung cells. The main determinant of cell infection and species specificity of coronaviruses is initial receptor binding. On the contrary, if we go for (b) argument then SARS-CoV-2 jumped the species barrier and infected humans from another animal host.

It will be of interest to know that the RBD of SARS-CoV-2 is unlike those found in bats but shares high homology with those found in pangolins especially Malayan pangolins (*Manis javanica*) illegally imported into Guangdong province contain coronaviruses similar to SARS-CoV-2 have been present at the Huanan market in Wuhan. That is why many scientists have proposed pangolins as an intermediate host due to the similarity of the receptor-binding domain (RBD) for pangolin coronavirus to SARS-CoV-2 RBD. (c). There can be another way whereby humans can get infected with this virus as follows: Coronaviruses are also known to undergo genetic recombination, in which they swap genetic material. This happens when two different coronaviruses find themselves infecting the same host. It's therefore highly likely that SARS-CoV-2 arose from a recombination event between two coronaviruses, possibly from bats and pangolins, which was then able to jump into humans.

### Scientists Put Forward Two Hypotheses

- a) The virus arose in animals and, through natural selection, acquired the necessary genetic changes needed to infect humans, whereupon it jumped the species barrier and infected people.
- b) The virus jumped from an animal species into humans, whereupon it spread through the human population and, through natural selection, acquired the genetic changes needed to successfully cause a pandemic. Of the two possibilities, the first looks more probable. It is explained as follows: In argument (a), only bat animal is involved that possessed RaTG13 to ultimately evolved itself to SARS-CoV-2 Argument (b) proposes that RaTG13 from bat reached another animal say pangolins being sold in the Wuhan Seafood Market and evolved itself to SARS-CoV-2. It is like SARS (2002-03) pandemic which is assumed to spread as follows. It is believed that in SARS, the original bat virus infected a civet and evolved in this animal for a short time but not enough to cause a civet pandemic. Before it died out in these infected civets, it was picked up by a human who became the first human i.e., patient zero.

The virus survived in this patient, perhaps only barely, but was passed on to another human marking the first case of human-to-human transmission. This way, the human-to-human chain started making a few human hosts where the virus rapidly evolved, adapting itself to better infect the new hosts. After a few such tentative transmissions, the proper pandemic began; though the saving grace with it was that it did not prove to be that fatal. The argument (c) also talks of two animals -the bats and pangolins undergo recombination and then would enter into humans of the three, the argument (c) would not stand the test as to how RaTG13 from the bat would swap cent per cent with that of the

virus of pangolins to evolve into the pure one virus- SARS-CoV-2, the moment the two meet in the Wuhan Seafood Market. The Master's thesis is silent on the specifics of what sampling was done, for what purpose, and where each particular sample went.

### Summary

Virologist Jonathan Latham and molecular biologist Allison Wilson believe as follows: In our search for the origins of the pandemic, we focused on the nearest genetic relative of SARS-CoV-2, a bat coronavirus called RaTG13. This virus was obtained during 2012 and 2013 virus collecting trips to a mine where, shortly before, six miners had developed a mystery illness while shovelling bat faces. To learn more, we arranged the translation of a neglected Chinese Master's thesis that documented the symptoms and hospital treatment of these miners. This thesis contains many surprises. Foremost, the miners were diagnosed as having coronavirus infections, and second, their symptoms are now recognizable as those of classic COVID-19. This and other information in the thesis caused us to rethink everything we thought we knew about the origins of the pandemic.

In A Proposed Origin for SARS-CoV-2 and the COVID-19 Pandemic, we set out what we call the Mojiang Miners Passaging hypothesis. The theory proposes (1) that the miners acquired a coronavirus from the bats in the mine and (2) that this bat virus evolved extensively inside their bodies to become a highly human-adapted virus. This evolution occurred during a hospitalization period that, for some of them, lasted many months. From the thesis, we also know that blood and other samples were extracted from the miners and some of these were sent to the Wuhan Institute of Virology (WIV). We suggest that these samples contained highly human-adapted viruses and were used at the WIV for research. During this research the virus escaped, initiating the 2019 COVID-19 pandemic. As we show, the theory solves the currently mysterious evolutionary and biological features of SARS-CoV-2 as well as explaining its eventual appearance in Wuhan.

It also explains subsequent attempts to obscure the deaths of the miners and the Mojiang mine origin of RaTG13. Thus all evidence so far points to the fact the COVID-19 virus is naturally derived and not manmade," as explained by immunologist Nigel McMillan (Menzies Health Institute Queensland) as follows: "If you were going to design it in a lab the sequence changes make no sense as all previous evidence would tell you it would make the virus worse. No system exists in the lab to make some of the changes found." "Two features of the virus, the mutations in the RBD portion of the spike protein and its distinct backbone, rule out laboratory manipulation as a potential origin for SARS-CoV-2." But even this school of thought admits that it may have 'escaped' a research facility, with most of the speculation - most probably from

the Wuhan Institute of Virology (WIV). However, it remains just speculation.

## Second School of Thought: SARS-Cov-2 is Cultured in a Laboratory

Other than assuming that the virus escaped accidentally or has been intentionally leaked by those who had been working in WIV on the covered samples of the 6 miners, another group of scientists suspect that the lab was genetically engineering or manipulating a Sars-CoV-2-like virus which then escaped or was leaked. Before we take up the possibility of SARS-Cov-2 being a man-made virus and has been cultured in some laboratory in China (WIV and WDCP), we have categorized their doubts under six different categories 5.1 to 5.6.; some of which are further subdivided.

### Five Intriguing Points Left Unanswered

The following are listed 5 happenings that look like the most intriguing.

**China 'Refused to Give Data' to WHO Team:** China refused to hand over key data to the World Health Organization (WHO) team investigating the origins of Covid-19. Microbiologist Dominic Dwyer told Reuters, the Wall St Journal and the New York Times that the team requested raw patient data from early cases, what he called "standard practice". He said they only received a summary. China has not responded to the allegation but has previously insisted it was transparent with the WHO [45].

**Samples Destroyed:** When asked about the availability of the samples of the 6 miners, then the standard answer was that samples have been destroyed". It is standard practice; rather than a rule, with every researcher to keep everything intact till their theses are evaluated and the degrees are recommended to be awarded by their peers.

**No data, No Notes of Researches and No Comparative data Available:** Of course, Shi Zhengli, head of bat coronavirus research at WIV, was emphatic that when she first received samples from early COVID-19 patients, she immediately did a thorough investigation at her department, finding no match between the viruses her lab had been working on, and COVID-19 patients. At least these comparison results prepared under her as the head of WIC should have been made available to the medical/ science faculty of the world. So much so, there is the non-availability of researchers' book notes in most of the cases and wherever some written work is available, their reproducibility, which is a must for any research work, was not available.

**Serology of Ms. Shi and Her Colleagues was not Performed:** The serology of Ms. Shi and her colleagues should have been performed there and then. If they passed the virus, they must have the IgG (for details, just Google).

### Death of 3 of 6 Miners not Discussed in 2 Original Papers:

Still another point: Six miners who cleared the debris (mainly bat faces) from the same mineshafts suffered from typical pneumonia and 3 of them died. This reference also has not been mentioned in Zhou et al 2020. But a recently unveiled U.S. intelligence report [46] found that three researchers from China's WIV got so sick that they went to the hospital in November 2019 before the first confirmed outbreak of the novel coronavirus [46].

### Over 14 of Scientific Doubts That Remain Unanswered

There are quite a few points that remain unanswered in the Mojiang mine origin of RATG13 as follows:

**Propagation through Pangolin Looks Unlikely:** Although two pangolin coronaviruses [7] exhibited strong binding to human ACE2 (hACE2), binding to pangolin ACE2 was approximately tenfold weaker and binding to bat *Rhinolophus ferreus* ACE2 was very weak, with similar relative binding relationships exhibited by SARS-CoV-2 [47]. This indicates that neither pangolin coronavirus had adapted well to pangolins and that more research is required to validate the viability of coronaviruses to spread naturally between pangolins.

**Bt Co V/4991 not Explained:** Also, why Bt Co V /4991 and the paper about the isolation of coronaviruses from abandoned mine shafts have not been mentioned at all in Zhou et al 2020 [7] when the same corresponding author had published the findings in 2016 This would have helped the readers understand the exact isolation source of RaTG13. All this has caused credibility- crisis in her arguments, i.e. may have been hiding some vital link If BatCoV RaTG131 and BtCoV/4991 refer to the same virus, why was this fact not mentioned in the first place? More so, if RaBtCoV4991 and RaTG13 are the SL-coronaviruses from the same sample, why the sequencing of RaTG13 was performed after the discovery of SARS-CoV-2 [7].

**Infects only Human ACE2 Receptor-Crafting Virus a Possibility:** The most compelling information was the finding that the COVID-19 virus binds 10-fold better to human ACE2 receptor than to the original SARS virus and that it shows no such affinity in other species.

**SARS-CoV-2 Possesses Furin Site but its Originator RaTG13 Does Not:** SARS-CoV-2 possesses a furin site whereas RaTG13 does not have one under normal conditions. (Furin is an enzyme that in humans is encoded by the *FURIN* gene. Some proteins are inactive when they are first synthesized and must have sections removed to become active. Furin cleaves these sections and activates the proteins. The gene was known as *FUR* and, therefore, the protein was named furin. Furin is also known as PACE (Paired basic Amino acid Cleaving Enzyme). A member of family S8, furin is a subtilisin-like peptidase site). Furin is a ubiquitously expressed 794-amino-acid type-i transmembrane protein that is found in all vertebrates

and many invertebrates. The presence of Furin site in the SARS-CoV-2 which has a region on its spike protein and makes it a powerful pathogen (a bacterium, virus, or another microorganism that can cause disease) by allowing the virus to access multiple cell types and thus making it able to infect and spread through lungs and other tissue types are always found to be missing in its other closest known virus relatives closely related coronaviruses SARS-CoV, MERS-CoV, HKU1, NL63, OC43 and 229E) possess this site. Its presence still needs to be explained thoroughly [48,49].

The furin cleave site is a site near the spike protein of SARS-CoV-2 that cleaves the virus into two subunits when it comes in contact with some enzymes present in the human body. It is possible to introduce such a site into a virus of zoonotic origin in the laboratory to make it infectious for humans. The functional consequence of the polybasic cleavage site of furin\* and O-linked glycans in SARS-CoV-2 is unknown, and it will be important to determine its impact on transmissibility and pathogenesis in animal models. Experiments with SARS-CoV have shown that insertion of a furin cleavage site at the S1-S2 junction enhances cell-cell fusion without affecting viral entry [50]. Besides, efficient cleavage of the MERS-CoV spike enables MERS-like coronaviruses from bats to infect human cells [51]. In avian influenza viruses, rapid replication and transmission in highly dense chicken populations select for the acquisition of polybasic cleavage sites in the hemagglutinin (HA) protein [52] which serves a function similar to that of the coronavirus spike protein. Acquisition of polybasic cleavage sites in HA, by insertion or recombination, converts low-pathogenicity avian influenza viruses into highly pathogenic forms [52]. The acquisition of polybasic cleavage sites by HA has also been observed after repeated passage in cell culture or through animals [53].

**RaTG13 Needs Decades to Evolve to the Level of SARS-CoV-2:** Although RaTG13 is the closest known relative of SARS-CoV-2 is a bat virus that was kept at the W I V, yet Prof. Holmes [47,48] believes that it should take 20-50 years for RaTG13 to evolve to the level of the genome sequence of SARS-CoV-2.

**It could Infect Humane Directly- Not Necessarily Through Pangolins:** On pangolins are sold in the Wet market of Wuhan See Timothy Stout "A Rebuttal to "the Proximal Origin of SARS viz-aviz pangolin (10 July 2020)- [See (iv) under discussion of W.H.O. Report].

**No time to Adapt to Humans Similar to its Close Relatives- SARS and MERS:** SARS-CoV-2's structurally closest known viruses especially SARS and MERS that recently jumped from bats or to any other species to humans had undergone a period of rapid adaptation to its new host, yet till today SARS-CoV-2 mutations, no doubt, have happened but the virus has hardly evolved (in an adaptive sense) at all.

### **It is Structured to be a Close Fit to Human Receptor (ACE2)**

**Only:** SARS-CoV-2, the virus responsible for the current pandemic, is in many ways an enigma to virologists. First, the virus enters human cells using a viral spike protein that is a tremendous fit for its human receptor (a protein called ACE2). This close fit allows the virus to spread very efficiently between people but such precision cannot plausibly have arisen by chance. Thus, the virus appears to have evolved in the presence of that human receptor. Thus, Current zoonotic origin theories for SARS-CoV-2 have no satisfactory explanation for any of these evolutionary puzzles. Indeed, recent studies have made natural zoonotic origin hypotheses even less viable. For example, the Chinese CDC has ruled out Wuhan's live market as the epidemic's origin. [54,55].

**Why were the Early Warnings by Dr. Li Ignored?:** In the early days of the virus, it was traced to a so-called "wet market" in Wuhan, Hubei province, and it was suggested that this was where it made the leap from animals to humans. But experts now believe it may simply have been amplified there. Research suggests that coronaviruses capable of infecting humans may have been circulating undetected in bats for decades [56]. Last December, a Chinese doctor at Wuhan Central Hospital - Li Wenliang - tried to warn fellow medics about a possible outbreak of a new disease but was told by police to "stop making false comments" and was investigated for "spreading rumors". Dr. Li died in February after contracting the virus while treating patients in the city.

**Amateur Sleuths' Force the World to Consider Wuhan Lab Leak Theory about Covid-19:** A Group called DRASTIC (Decentralized Radical Autonomous Search Team) Investigating COVID-19 discovered that the WIV was actively working with the viruses uncovered in the bat cave, "using inadequate safety protocols, in ways that could have triggered the pandemic, and that the lab and Chinese authorities have gone to great lengths to conceal these activities". The first cases of Covid-19, it turns out, had appeared "weeks before the outbreak at the Huanan wet market that was once thought to be ground zero" Their suspicion is based on three very solid reasons as stated below [57].

**Retrieved Screenshots of the Deleted Database of Viruses:** "The Indians who made the world take Chinese lab leak theory seriously' [58] are part of a group called DRASTIC-a global alliance of internet strangers who came together to discover some compelling evidence that the virus originated, not in a seafood market as China would have us believe, but from a lab in Wuhan. Their theory, once dismissed as a conspiracy, has now grabbed global attention, with US President Joe Biden even ordering a probe. They somehow retrieved screenshots of the now-deleted database of viruses collected by the WIV and shared them with the world to reveal how it was taken down just on 12 September 2019,



weeks before the first cases of Covid-19 were reported in that city to prove the association of China's "Bat woman" Dr. Shi Zhengli, the administrator of the database.

**Bat woman Shi Denies:** "In Dec 2020, Shi Zhengli explained in a BBC interview that access to the DB [database] was stopped to prevent cybersecurity attacks."

"On the 26<sup>th</sup> January 2021, Shi Zhengli confirmed again that the database has been taken offline 'during Covid-19 pandemic' in an email answer to Tommy Cleary."

"On the 10<sup>th</sup> March 2021, during a Chatham House interview, Peter Daszak repeated the exact reason given by Shi Zhengli in her email to Tommy Cleary above."

**Denial Causes more Suspicion:** "These three statements do not make any sense since the main database was taken offline on the 12 Sep 2019, 3 months at least before the official start of the pandemic. So either the reason given for taking the database off is not correct (which raises more questions), or the statement points at an outbreak in Sep 2019."

**"Journal Environmental Chemistry Letters" Accepts a Paper of the DRASTIC Group:** An editorial [59] that appeared in the "Journal Environmental Chemistry Letters" points to quite a few scientific objections to the original theory about the natural origin of the virus, including the furin cleavage site. The contention is that it was not linked to any pre-existing, known virus backbone, and the fact that the virus that is hypothesized to have originated in bats is a worse fit for bat receptors than it is for human ones. Their objections may be summarized as follows:

- i. How is it that there is "The low binding affinity of SARS-CoV-2 to bat ACE2"? The study to date does not support Chiroptera as a direct zoonotic agent.
- ii. Furthermore, the reliance on pangolin coronavirus receptor-binding domain (RBD) similarity to SARS-CoV-2 as evidence for natural zoonotic spillover is flawed, as pangolins are unlikely to play a role in SARS-CoV-2's origin and recombination is not supported by recent analysis.
- iii. Genomic analyses pointed out that SARS-CoV-2 exhibits multiple peculiar characteristics not found in other Sarbecoviruses.
- iv. A novel multi-basic Furin Cleavage Site (FCS) confers numerous pathogenetically advantageous capabilities, the existence of which is difficult to explain through natural evolution; SARS-CoV-2 to human ACE2 binding is far stronger than SARS-CoV, yet there is no indication of the amount of evolutionary adaptation that SARS-CoV or MERS-CoV underwent.
- v. Why the incidents such as the 2012 pneumonia outbreak in miners in China's Mojiang was not reported to the WHO?

Strangely, this fact was not known at all before 2020. It also asks whether a similar outbreak in miners in Yunnan was reported to W.H.O.

**Another Paper Replicates Mojiang, Yunnan: Something to hide or an innocent mistake?:** Another paper published [60] by Monali Rahalkar and Rahul Bahulikar of the MACS Agharkar Research Institute and BAIF Development Research Foundation, respectively, wrote: "It was found that RaTG13/BtCoV4991 was collected from Tongguan mineshaft in Mojiang, Yunnan, China, in 2013. Surprisingly, the same mineshaft was also associated with a severe pneumonialike illness in miners in 2012 killing three of the six miners. (See I. I) The cases were remotely monitored by a prominent pulmonologist in China. Retrospective analysis of the pneumonia cases shows striking similarities with COVID-19."

### Confusion Compounded

There is a clear pattern of obfuscation and lack of transparency concerning the provenance of RaTG13, as well as its sequence data as follows: "How is it possible that the pandemic prevention workflow for discovering a novel SARS virus in a cave where miners got ill with SARS-like pneumonia was to throw the virus in a freezer until a pandemic from a closely related virus breaks out? Why has the exact, detailed list of all WIV samples, isolates, etc. as well as the Wuhan University and the Hubei CDC samples and isolates not been shared with the WHO or other countries?" asks the DRASTIC paper.

**'Gain of Function Research'-US and China Collaborate: Points a Needle toward the USA?:** Before Wuhan row, the University of North Carolina (US) and WIV had been working together in a research program named 'Gain of Function Research' (2015) whose name was to create the SARS-like virus which may show its pandemic potential. The study was published in the journal 'Nature' is an example of a 'gain of function' research because they involve manipulating pathogens in a way that they gain an advantage in or through a function, such as increased transmissibility\* [61]. This study was primarily conducted in the US lab where the team had taken the spike protein of SHC014-CoV, a virus that was circulating in the Chinese horseshoe bat populations and attached it to a SARS-like virus that could infect mice. The results of the study showed that viruses with the SHC014 spike protein can effectively use the human angiotensin-converting enzyme II (ACE2) to replicate efficiently in the human lung cells and potentially cause an epidemic.

They concluded that the replication of the artificial virus in mouse lung could not be treated with available SARS-based immune-therapeutics and preventive drugs as the antibody therapies and vaccine approaches failed to neutralize and protect from infection with CoVs using the novel spike protein. Strangely, the spike protein in this study had been supplied to the US lab by Zhengli-Li Shi, the noted Chinese virologist who researches SARS-

like coronaviruses of bat origin at the Wuhan Institute of Virology. When the SARS-CoV-2 pandemic broke out last year, this 2015 study came under scanner not only because the pathogenesis and characteristics of the artificially generated virus were similar to what was observed with the Covid-19 pandemic, but also because of the involvement of the W I V, which is located in the same city where the virus broke out. There may be the probability that some features of the virus might have been engineered at WIV and thus a thorough investigation is the need of the hour. China has now retaliated, suggesting that the US is peddling “conspiracy theories”. \*Of course the Obama administration temporarily paused funding of such research studies.

**241 Missing Genetic Sequences:** The US National Institutes of Health (NIH) said (24 June 2021) that the data that was initially submitted to ‘the US-based Sequence Read Archive in March 2020’ was requested to be withdrawn by the same researchers three months later in June last year due to “version control issues”. No doubt “submitting investigators hold the rights to their data and can request withdrawal of the data,” but Jesse Bloom, a virologist at the Fred Hutchinson Cancer Research Center in Seattle, released a report that he had recovered deleted files from Google Cloud that reveal 13 early coronavirus sequences, for some of the earliest Covid-19 cases in Wuhan genetic sequences. Bloom apprehends that “It seems likely that the sequences were deleted to obscure their existence,” (the report is yet to be peer-reviewed or published in a scientific journal). The virologist Bloom claimed to have stumbled upon the missing data in the online database while reviewing genetic data published by different groups on a March 2020 spreadsheet that included information on 241 genetic sequences collected at Wuhan University and indicated that they were uploaded to the US managed database ‘Sequence Read Archive’ [62]. But when he looked for the Wuhan sequences, the search result returned a message that read: “no items found”.

### **Chinese Scientists Discussed using Coronavirus as a Bioweapon in 2015**

A document has been found in which Chinese scientists and health officials can be found discussing a “new era of genetic weapons” that could be “artificially manipulated into an emerging human disease virus, then weaponized and unleashed”. The document was written in 2015, five years before goes as follows: The report published in the paper suggested that the discussions between the Chinese officials suggested that the third world war would be fought with biological weapons. The paper also revealed that Chinese scientists were discussing the weaponization of coronaviruses five years before the COVID-19 pandemic hit across the world. The executive director of the Australian Strategic Policy Institute (ASPI), Peter Jennings, said the document is as close to a “smoking gun as we’ve got”. “I think this is significant because it clearly shows that Chinese scientists were thinking about military

application for different strains of the coronavirus and thinking about how it could be deployed,” Jennings was quoted as saying by news.com.au.

“It begins to firm up the possibility that what we have here is the accidental release of a pathogen for military use,” he said, adding this could one of the reasons why China did not want outside investigations into the origins of COVID-19. “If this was a case of transmission from a wet market it would be in China’s interest to co-operate... We’ve had the opposite of that,” he noted. According to news.com.au, a cybersecurity specialist has analyzed leaked Chinese government documents and found them to be genuine. “We reached a high confidence conclusion that it was genuine. It’s not fake but it’s up to someone else to interpret how serious it is,” Robert Potter, the analyst, said. “It emerged in the last few years, but they (China) will almost certainly try to remove it now it’s been covered” [63].

### **World Leaders Smell Fishy in the ‘Natural Evolution’ of SARS-CoV-2**

Agreeing that the lab leak theory is not fool-proof, nor is it proven, yet many world leaders are coming around the argument that ‘only a proper investigation can lead us closer to the truth of how we got here. and how not to get here again’.

#### **They Suspect that China Using Coronavirus as a Bioweapon:**

China, an iron-walled country, would neither allow free access to the outside world nor would permit the free press to reports the events as and when they happen. So most of the world leaders allege that China has intentionally let –lose the Coronavirus to use it as a Bioweapon that had caused a huge loss of human lives and wrecked the economy of almost all the countries of the world. Following findings have given credence to this suspicion.

#### **Brazilian President Suspects China on COVID-19 Origin:**

Brazilian President Jair Bolsonaro (5 May 2021), a strategic partner of China, suggested that China could have developed the pathogen in a laboratory and disseminated it as “biological warfare” for economic gain. He remarked: “Are we not facing a new war?” He went on to add: “It’s a new virus. Nobody knows whether it was born in a laboratory or because a human ate some animal they shouldn’t have”. “But the military knows all about chemical, biological and radiological warfare. Could we be fighting a new war?” In an indirect reference to an abnormal increase in China GDP by 2.3% in 2020 (rising roughly \$14.7 trillion whereas the 2017-19 years were dismal for China: courtesy Wind Information data) and has the potential to surpass the United States as the world’s top economy in 2026 which is two years before what was anticipated while most of the world witnessed a steep decline in their economy owing to unprecedented and prolonged shutdowns of businesses, he sarcastically added: I wonder. “Which country’s GDP has grown the most?” [64].

**Dr. Anthony Fauci not Convinced about 'Natural Origin' of Covid-19:** America's top expert on infectious diseases, Dr Anthony Fauci said (21 May 2021) that he is "not convinced" the novel coronavirus developed naturally and has called for an open investigation into the origins of the Covid-19 virus. He added, "We should continue to investigate deeper [65] as to what went on in China's Wuhan lab". "Certainly, the people who investigated it say it likely was the emergence from an animal reservoir that then infected individuals, but it could have been something else, and we need to find that out. So, you know, that's the reason why I said I'm perfectly in favour of any investigation that looks into the origin of the virus," [66] Dr. Fauci asked Beijing to release the medical records of nine people whose ailments might provide vital clues in COVID-19's origin. Dr Fauci and his colleagues noticed earlier that COVID-19 may have leaked from Wuhan's laboratory.

The theory was released in more than 3000 pages of emails obtained through Freedom of Information Act (FOIA) requests by few media organisations, from January to June 2020. US intelligence agencies still examining reports that the researchers at the Chinese virology laboratory in Wuhan were seriously ill in November 2019 which is a month before the first COVID-19 case was reported [67]. But Chinese have flatly refused as follows: "WIV has clarified that they had not contacted the novel coronavirus before December 30, 2019. US should invite WHO experts to the US to study virus origins and explain their more than 200 bio labs all over the world including the Fort Detrick lab," Wenbin said as quoted by the leading portal [67,68].

**G7 Leaders Demand Probe into 'Lab-Leak Theory': WHO Director-General Consents:** World leaders gathered at the G7 Summit in Cornwall (U.K) on 11 June 2021 discussed the possibility that a laboratory- leak in central China's Wuhan city may have a connection with the start of the COVID-19 pandemic, with the WHO chief saying all hypotheses behind the origins of the deadly disease remain in play [69]. UK Foreign Secretary Dominic Raab said that officials "compared notes" over the theory that the pandemic may have originated from a leak from a lab in Wuhan, calling for further investigations. However, he asserted that the UK's "best information" remained that it "jumped" from animals to humans but admitted they did not have "all the answers". "That's why internationally we wanted the review to be able to go into China to get all the answers so that we have the full picture rather than these possible, potential, plausible options," Mr Raab told 'Sky News'. "But, on balance, we do not believe that it came from a laboratory. We think it is much more likely to have jumped from animal species," he said.

### **Likelihood of China having prepared Pre- Pandemic Vaccine**

Now that the Chinese scientists had started synthesizing coronavirus as a Bioweapon in 2015, they were in the know of the acute fatality power, SOPs of its prevention as well as its genomes. In

a way, the Chinese were well aware of its highly infectious nature and thus the use of mask and keeping the social distance was the only way to control it from being spreading by the infected person/s. So it looks highly probable that they would have also been working on some sort of vaccine/s to control it and, thus, would have been able to prepare some vaccine well before they let the world know about this highly infectious SARS-CoV-2 pathogen causing COVID-19 disease. The following sequence of events points toward some sort of fraud that had been played on the whole of the world. In the above-stated document written in 2015 [63], it is mentioned that the Chinese vaccine for the Coronavirus was already prepared by 5 January 2020.

China declared the first death in Wuhan City on 11 January 2020 but informed the world about this virus on 25 January 2020 without letting the world know its highly infectious and extremely fatal nature. China would put only the Wuhan city under lockdown; instructs its residents to use masks, keep social distance, remain indoors and keep on washing their hands repeatedly. And Lo! In a few days, the Corona is controlled in the whole length and breadth of China- a country having area 3.5 times (approx.) of India without putting any other city, what to talk of any one of its provinces under lockdown. It exports people in large numbers by its air-crafts and Lo! this dragon of Corona-19 engulfs every nook and corner of the whole world. It looks highly probable that China would have vaccinated a big chunk of its population well before January 2020 so that the population would have attained herd immunity. Sadly, the whole world undergoes turmoil causing a colossal loss of lives and shatters the economy of the whole world. But yes, China does two good things: intentionally or unintentionally.

One it lets the whole world know the method to control its spread (use masks, keep social distance, remain indoors and keep on washing hands) and secondly it tells its genomes to the whole world by February end 2020. But even these good-looking intentions would make China look suspicious in the eyes of the scientists of the whole world. One- how could China know SOPs of its prevention in a few days of the evolution of Coronavirus? Secondly, how could it control the virus without putting the whole country under lockdown? Thirdly, how could it declare the availability of quite a few vaccines on 22 July 2020; just 4 months after the first case of this virus was detected in India [67].

### **Multiple Mutations observed in SARS-CoV-2 in India Look Suspicious**

No doubt, all viruses including SARS-CoV-2, the virus that causes COVID-19, evolve with time. When a virus replicates or makes its copies, it sometimes changes a little bit, which is normal for a virus. These changes are called "mutations". A virus with one or more new mutations is referred to as a "variant" of the original virus. When a virus is widely circulating in a population and causing many infections, the likelihood of the virus mutating increases. The

more opportunities a virus has to spread, the more it replicates and the more opportunities it has to change. Most viral mutations have little to no impact on the virus's ability to cause infections and disease. But depending on where the structural changes are located in the virus's genetic material, they may affect a virus's properties, such as transmission (for example, it may spread more or less easily) or severity (for example, it may cause more or less severe disease). Different types of coronaviruses, i. e. 'Variants of Concerns' (VOCs) have been found in many countries (including India); including three important variants- South Africa's B.1.351, Brazil's P.1 and Britain's B.1.1.7. It looks suspicious that the last two mutations coming from two different countries get merged to form one 'Doubly Mutated B.1.617 Variant' which was first observed only in India.

There have been two changes in the same form of the virus that carries what's being called the E484Q and L452R mutation which generally act separately and are found in other coronavirus variants also. In a way, the B.1.617 lineage evolved when two mutated strains, E484Q and L452R, came together to form a third strain. The E484Q strain is from the U.K and South Africa and L452R is a Californian strain. This Doubly Mutated B.1.617 strain has now spread in 44 other countries, including the US and UK, The issue of greater concern is that when combined, these two mutations are far more infectious and dangerous because they have a higher potential of removing the antibodies from a human body and cannot escape from the immune system of the body. The virus mutates continuously; the genome sequences of the two samples would have some differences and needed a novel SOP of treating this doubly mutated variant. The evolution of this 'Double Mutation COVID Variant' primarily in India was like a 'Tsunami'. Its sudden spread in this vast country should be taken with a pinch of the salt on two accounts.

First, it appeared when there were only around 1.5 lacs active Covid-19 patients out of a total of over 1,75 crores of the infected cases and this minuscule number of active cases waning day by day, India could well have been out of the woods by the time. Some may put a counterargument that like England, Brazil and quite a few other European countries, India, being the second most populated country in the world with very high population density, are struggling with all the more furious second wave of COVID-19. But one doubt that is lurking in the minds of a large number of biotechnologists remains unanswered is-how come the two different strains coming from two different countries merge to form a single form of mutation. Again they need the answer as to how these two different strains are existing as one unit called 'Doubly Mutated B.1.617 Variant' and are inseparable while the reverse is reported in the case previously found naturally evolving viruses. Gordon Chang, an American writer, commentator and author of 'The Great U.S.-China Tech War' says [70]. 'Somebody should get to the bottom of this (India's second wave).

It is entirely possible China released another pathogen'. Moreover, how is it that no major mutation observed in SARS-CoV-2 till mid-March 2021? [71]. To make the things look all the more doubtful to already reported 'Double Strain Variant', is a new strain called 'Triple Mutation COVID Variant' which has never been heard before the naturally occurring viruses has also appeared in India as follows: Here both the E484Q mutation and L452R mutation of the B.1.617 variant have been associated with much greater binding and antibody escape capabilities of the B.1.617 variant. The third mutation evolved from the double mutation where three different COVID strains combined to form a new variant - B.1.618. Has the Dragon already made India a battlefield for testing its Bioweapon-the CORONA-19 a question that should not be laughed away.

### Yes, the two Schools of Thought do Overlap at Some Points as Follows

There are two ways to explain how RaTG13 could develop a furin site; though both need further investigation.

- a) It arose due to the high selection pressure which existed in the miner's lungs which, in general, worked to ensure that the virus became highly adapted to the lungs. It also means that the furin site was not acquired by recombination with another coronavirus and simply represents convergent evolution.
- b) another possibility is that SARS-CoV-2 acquired its furin site directly from the miner's lungs as follows: Humans possess an epithelial sodium channel protein called ENaC-a -whose furin cleavage site is identical over eight amino acids to SARS-CoV-2. ENaC-a protein is present in the same airway epithelial and lung tissues infected by SARS-CoV-2 [1].

But it looks hard to believe as the high selection pressure alone could so much change because of the following two reasons:

- i. First, it evolves to the level of the genome sequence of SARS-CoV-2 in 7-8 years instead of the normal requirement of 20-50 years
- ii. Second, it makes human epithelial sodium channel protein (ENaC-a) furin cleavage site adapt to over eight amino acids to SARS-CoV-2 and get infected with the SARS-Co V. It needs an above bold unambiguous explanation.

### How did this Genetic Change Occur in SARS-CoV-2?

Starting with an accepted conclusion that the mutation allows for increased pathogenicity, Genetic Change is possible to happen both ways whether we assume SARS-CoV-2 has Zoonotic Origin or it was Lab-made. It is explained as follows:

- a) It arose during repeated the human-to-human transmission, similar to what we saw in birds with flu implying that after making the jump from bats/pangolins/unknown species to



human, SARS-COV-2 spread through the human populace, acquiring this mutation, and then setting off the chain of events which led to the pandemic. Such a phenomenon has already occurred in SARS where the virus jumped from camels to humans and then spread from human to human for a short period. But here the saving grace was that SARS had not yet been able to sustain its human-human transmission while the present SARS-COV-2 has sustained to cause the pandemic.

- b)** It is also possible that this mutation arose in the progenitor(ancestor) to SARSCOV-2 in an animal host. This looks to be less probable because to have arisen this would require sustained transmission between hosts that are in high density and have human-like ACE2 receptors.

It appears that most of the early cases had a contact history with the original seafood market. Additionally, researchers are still investigating if the necessary mutations for causing the new disease occurred before or after SARS-CoV-2 made the jump to humans. As the global COVID-19 pandemic continues - viral variants have become the latest concern. But variants are complicated. Each one is made up of a collection of mutations, all of which have the potential to change the SARS-CoV-2 virus in unexpected ways.

### W.H.O. Report: Discussed

Ever since the first report of novel pneumonia (COVID-19) in Wuhan, Hubei province, China, there has been considerable discussion on the origin of the causative virus-SARS-CoV-2. But ending the year-long speculations over the origins of COVID-19, the World Health Organisation (WHO) expert Peter Ben Embarek, who led the Wuhan mission, states that:

- a)** The WHO team was ultimately unable to determine which population of bats, or which intermediary species, carried the virus. According to the WHO report, researchers believed that the first animal to human transmission happened in the fall of 2019, in October of November, months before China shut down wildlife farms in February 2020.
- b)** No firm conclusion about the role of the Huanan market in the origin of the outbreak.
- c)** WHO Expert on Why Lab Leak Theory Is Untrue

An Australian doctor who was part of the World Health Organization (WHO) team that visited China's Wuhan, Dominic Dwyer wrote in a first-person account explaining why the origin of the novel coronavirus, SARS-CoV-2 is unlikely to be either the seafood market in the city or leaked from Wuhan lab. Defying major conspiracy theories claiming that the highly infectious virus was leaked from a lab researching pathogens, the Australian scientist explained why the leak from Wuhan lab is also "extremely unlikely"

in a lengthy article. He wrote that the team of international experts sent to Wuhan to investigate the origins of the novel coronavirus visited the lab in the center of all theories, Wuhan Institute of Virology. After speaking to scientists working there, the experts found no evidence of coronavirus antibodies. The WHO team, as Dwyer explained, looked at the closest virus to SARS-CoV-2 that the researchers were working on in the lab, which is the virus RaTG13. However, all scientists had a genetic sequence for the virus and they had not been able to grow in culture. Dwyer wrote: "We spoke to the scientists there. We heard that scientists' blood samples, which are routinely taken and stored, were tested for signs they had been infected. No evidence of antibodies to the coronavirus was found. We looked at their biosecurity audits. No evidence" [72].

- d)** The author agrees but with a rider, as follows: If this is the case then the Bat virus has directly adapted itself to human and no other animal/ bird was involved in infecting the humans.
- e)** The discovery of other cases before the Huanan market outbreak suggests it may have started elsewhere that went undetected and that could be a link between the market and earlier cases. The author would humbly differ as follows: Just look at another unexplained puzzle regarding the seropositive studies around the Yunnan Caves and Southern China (where Mojipang mines situated). They were looking for evidence of zoonotic transfers in the local "high risk" populous. What they found was evidence of low rates (2.7%) of seropositive for Bat like SARS- CoV in Yunnan, and non in southern China while the Wuhan city of the population over 836500(2020) and situated 600KM from Mojipang mines and over 1500KM from Yunnan Caves was found to be the most infected. This proves the pandemic started only and only from Wuhan; irrespectively it infected human directly from the bat or via pangolins.
- f)** The report is non-committal as to how the infection was introduced into the market".

In a way, the committee's views should be respected. If we assume that the bat virus infected some scholar directly who became the first patient of SARS- CoV-2, then a never-ending chain would start even without the involvement of any other livestock which may be present in the market.

- g)** It says that the infection transmitted to humans from bats via another animal like pangolins Maybe or may not be. Note the following three arguments.
- i.** As reported in 'Nature', pangolins were not listed on the inventory of items being sold in Wuhan, although this omission could be deliberate as it's illegal to sell them.
- ii.** "Whether the poor pangolin was the species at which it jumped, it's not clear," Turner says.

“It’s either mixed in something else, mixed in a poor pangolin, or it’s jumped into people and evolved in people.”

- iii. Another study ruled out pangolins as an intermediary altogether because samples of similar viruses taken from pangolins lacked a chain of amino acids seen in the virus now circulating in humans.
- iv. Analysis of the first 41 Covid-19 patients in the ‘Medical Journal the Lancet’ found that 27 of them had direct exposure to the Wuhan market. But the same analysis found that the first known case of the illness did not.

This might be another reason to doubt the established story.

- v. Finally, if a SARS-like coronavirus was the source of their illness, the implication is that it could directly infect human cells.
- vi. Also find a detailed view of the Human/ Pangolin virus Timothy Stout “A Rebuttal to “the Proxima1. Origin of SARS viz-a-viz pangolin (10 July 2020). I did a lengthy analysis using references from over 100 journal articles. It appears that the virus is man-made using Directed Evolution, the technology resulting in the 2018 Nobel Prize in chemistry. I published the analysis in a preprint article at <http://www.osf.io/usx58>. There are some issues. There are about half a dozen amino acids that differ in key locations between the 2002 SARS virus and this one. These are the ones that attach the virus to the ACE2 receptor. However, there is strong selection pressure against any of these changes individually. With all changing simultaneously, the backbone becomes more flexible, and the new shape makes it more effective than that of SARS. Simultaneously, disparately located amino acids are very difficult to change with simultaneous mutations. This is trivial for directed evolution. A pangolin virus is held up as having the same sequence as people. There is a problem here. Tests show that the static field of the backbone with these amino acid changes is different. This change prevents the normal cleavage site of the spike from being effective. However, the new virus has is what is called a polybasic cleavage site which does not appear in the earlier SARS virus. This addition overcomes the static interference of the new backbone. In other words, without the polybasic cleavage site, the new backbone can’t infect. The pangolin virus does not have one. This raises the question of whether the pangolin virus genome as published is even capable of causing an infection. For more details, the article might be considered.
- h) The committee dismissed the lab leak theory of COVID-19, calling it “extremely unlikely”

On the contrary, there is a very strong probability of the lab leak theory as has been explained. (See Lab-leak Theory), irrespectively

it has directly infected some person/s working in WIV or the virus reached the humans through another animal/ bird being sold in the Live-stock Market of Wuhan.

- i) Of course, the closest relative of the virus that causes COVID-19 has been found in bats.

The author agrees but with a rider, as follows:

How to reconcile that BatCoV RaTG131 and BtCoV/4991 are two different viruses obtained from the bat

- j) However, it states that “the evolutionary distance between these bat viruses and SARSCoV-2 is estimated to be several decades, suggesting a missing link”.

MMP (Mojiang Miners Passaging) Theory as given above could explain it as follows: There are several points to argue that considering the conditions inside the lungs of the miners were far from ordinary and the Ra TG13 might have evolved to the level of the genome sequence of SARS-CoV-2 in 7-8 years (2012-2020) which, otherwise, would have taken decades to evolve to the level of SARS-CoV-2.

- k) It further stated that highly similar viruses have been found in pangolins, but also noted that mink and cats are susceptible to the COVID virus, which suggests they could be carriers.

## A Word of Caution

There is a general reluctance on the part of Publishing Houses as given below. This is not because scientists fail to prove their points leading to its being man-made due to ‘other points of conflicts’. Anyone who doubts this pressure should read the interview with Birger Sørensen in Norway’s Minerva magazine in which Sørensen discusses the “reluctance” of journals to publish his assessment that the existence of a virus that is “exceptionally well adjusted to infect humans” is “suspicious” and “cannot have evolved naturally”. The source of this reluctance, says Sørensen, is not rationality or scientific evidence. Yesterday a prominent Chinese virologist from Hong Kong who fled China and did early work on the Coronavirus said the genome pattern indicates the origin was a laboratory and has promised more paper on the assertion. The Chinese Communist Party has tried to silence her and she is in hiding. But she has been recently interviewed on the Fox news channel. The entire rest of the news media so far in the last 48 hours have ignored the story. She promises more paper on the subject shortly. I highly suspect the WHO and most of the scientific world has been in complicit propaganda on this all along. People with unimpressive credentials in a chorus denied laboratory origin could be possible. Really? Remember the SARS virus escaping from a Chinese laboratory? Did they forget that? And the laboratory in Wuhan was criticized before this crisis for not having the properly trained staff for such a high containment facility. It’s amazing how much information

is censored. How much is hidden from us? Soon the entire world will be like China. All of our news will be filtered and controlled. (16 September 2020). Though the Xi Jinping government rejected accusations outrightly made by the United States and other Western governments that it deliberately concealed information relating to the outbreak of the virus. The WHO team, headed by an Australian who was looking into this matter, has made certain observations.

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