

Mojiang mine, RaTG13, miners' disease and related samples remain essential clues in the origin SARS-CoV-2

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We had published an article about the link between the Mojiang mineshaft, RaTG13, and the miners' disease (2012), Yunnan, China which has gained a lot of attention in the question on the origin of the COVID-19. The miners' pneumonia resembled COVID-19 in many aspects on retrospective analysis. Recently, Frutos et al. reported that the miners did not have SARS-CoV-2 infection, and hence they tried to debunk the laboratory origin of the coronavirus. In the present article, we indicate the flaws in the interpretation and analysis of Frutos et al. We also discuss how Wuhan Institute of Virology (WIV), China, shared the information about the mine, miners and RaTG13 in an incomplete and delayed manner. None of the samples have been shared with the international community so far. Many of the journalists' attempts to visit the mineshaft were in vain, as they were not allowed to reach the site. We also discuss why all the information related to the Mojiang mine samples, details of experiments done on these and sequences of all the SARS-like viruses would be crucial for the investigation on the origins of SARS-COV-2.

Keywords: Clues, COVID-19, miners' disease, origin, SARS-CoV-2.

It is still a mystery how SARS-COV-2, the virus responsible for the COVID-19 pandemic killing millions and devastating the whole world, appeared in the city of Wuhan, China. As demanded by scientists worldwide, there has to be an in-depth study regarding this to prevent subsequent pandemics^{1,2}. A research-related origin of COVID-19 is plausible³. It may have occurred at sampling sites, during transportation or in the laboratory and might have involved natural, selected or engineered viruses. For an unbiased study, all evidence related to SARS-CoV-2 and similar viruses must be examined until there is a clear answer. The natural reservoir and hotspot of SARS-CoV-2 and other SARS-like coronaviruses are horseshoe bats living a thousand miles away from Wuhan in Yunnan, Province, and Guangdong, China⁴.

Initially, in a pre-print⁵ and then published as a perspective article in October 2020 (ref. 6), we had documented a vital clue in the mystery of the origins of SARS-CoV-2. That is, the closest relative of SARS-CoV-2, RaTG13, was collected in 2013 from an abandoned mineshaft in Mojiang, Yunnan Province by scientists from the Wuhan

Institute of Virology (WIV). Our paper also provides links to the fact that from the same mine six persons who went to collect bat faeces had contracted fatal pneumonia, and three of them had died; the disease was similar to COVID-19.

The present article provides a discussion about the interpretations by Frutos *et al.*⁷ (who try to disassociate the Mojiang mine from the COVID-19 origin mystery). We also discuss about the late disclosure of facts related to Mojiang mine by WIV and questions about the mine being inaccessible to reporters and researchers. In the end, we summarize and provide important suggestions regarding the samples and the genomic information which could be obtained from them, and how this would be necessary in solving the mystery of the SARS-CoV-2 origin.

Discussion about the interpretations by Frutos *et al.*⁷

In a recent study, Frutos *et al.*⁷ have attempted to disprove that the miners who worked in a mineshaft in 2012 in Tongguan, Mojiang, Yunnan Province, had SARS-CoV2 infection. They further mentioned that the laboratory leak theory based on the Mojiang mine incident was false. They talk about a narrative that it was proposed that the six miners were infected with COVID-19 and SARS-CoV-2 was collected from the mine. Neither our paper⁶ nor the

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commentary to our paper⁸ proposed that the miners were infected with SARS-CoV-2 and hence had COVID-19. What we have presented in our paper is the resemblance between COVID-19 and the miners' pneumonia. Except no human to human transmission was reported after these cases happened in 2012.

Major symptoms and radiological features of the miners' pneumonia consistent with COVID-19

According to the World Health Organization, the most common symptoms listed for COVID-19 are fever, cough and tiredness, similar to those reported in the six miners (who had worked in the Mojiang mine in 2012 and cleaned the bat faeces) https://www.who.int/health-topics/coronavirus#tab=tab_3. Fever (80.4%), fatigue (46%), cough (63.1%) and expectoration (41.8%) were the most common clinical manifestations in a meta analysis of 3062 patients⁹. Frutos *et al.*⁷ noted that the less common symptoms in COVID-19 such as diarrhoea, headache, etc.⁹ were absent in the miners, but these are not the most typical signs present in all COVID-19 patients¹⁰. Secondly, the cough in COVID-19 is dry and also productive as expectoration has been commonly observed (41.8% cases)⁹. The third point is on radiological features compared in the miner patients and COVID-19 patients. The most common findings in the CT scans in COVID-19 patients are ground-glass opacities, consolidation and bilateral involvement of the lungs^{10,11}. All of these main features were seen in the CT scans of the miners, especially in patients 2, 3 and 4 – the most serious cases – who had worked in the mine for a longer time. The differences highlighted by Frutos *et al.*⁷ were mainly the mediastinal lymphadenopathies present in majority of the miners. Though mediastinal lymphadenopathies or lymph node enlargement was not initially considered a typical feature as mentioned by Frutos *et al.*⁷, a French study published in April 2020, documents that 66% of the critically ill cases had this condition, and it may be associated with serious COVID-19 patients¹². Similarly, pleural effusion has been observed in critically ill COVID-19 cases¹³. The radiological features of the miners' pneumonia had also been inspected by an expert radiologist in Pune, India, who was already examining several COVID-19 X-rays and CT scans daily (June 2020). According to him, 'Most of the cases (patients 2, 3 and 4) have the following findings. (1) Diffuse ground-glass opacities; (2) Peripheral subpleural ground-glass opacities; (3) Some areas of peripheral consolidation. These are consistent with what we see nowadays in COVID-19. Consolidation can be due to superadded infection in these patients, bacterial fungal, etc. The miners' pneumonia resembled COVID-19 to a considerable extent but did not show human to human transmission. Also, exposure to a high viral load might have led to the infection as people visiting the mine never got infected before¹⁴.

IgG antibodies to SARS-like coronaviruses

One of the essential contradictions in the miners' incident is the positive IgG antibodies to SARS-like viruses, documented in the Ph.D. thesis of Huang¹⁴ (<https://www.documentcloud.org/documents/20694207-canping-huang-phd-novel-virus-discovery-in-bat-isn-translation>). According to the thesis¹⁴, WIV tested four of the six miners serum samples and all of them had IgG antibodies to SARS-like viruses. Frutos *et al.*⁷ have not taken into consideration these positive IgG antibody tests in their analysis. Huang was a student of George Gao, the present director of China Centre for Disease Control and Prevention. On the contrary, WIV reported in the addendum that 13 samples did not show any positive antibodies for SARS-like or SARS-CoV-2 infection. It is also surprising that they have preserved the samples for eight years. In an interview, Gao mentioned that the four miners showed positive IgG for SARS-like coronavirus infection, but he could not pinpoint if the infection was from the mine or earlier, or by a new virus (https://www.francetvinfo.fr/sante/maladie/coronavirus/video-coronavirus-le-mystere-des-origines_4328629.html) (ref. 15). The positive tests were documented in Huang's Ph.D. thesis in 2016, long before the pandemic and hence should be unbiased in contrast to the addendum, which was presented 11 months after the pandemic. Also, the confirmation of the positive antibodies test in the four miners by Gao is significant.

Opinion about the serious miners: primary viral pneumonia

Frutos *et al.*⁷ did not take into consideration the diagnosis by Zhong Nanshan, one of the prominent pulmonologists in China. Nanshan was consulted by the doctors from Kunming Hospital, by video-conferencing on 19 June 2012; he had examined all the reports and suggested that the two miners admitted (patients 3 and 4) had interstitial pneumonia, a high possibility of virus infection and secondary infection in the form of invasive pulmonary aspergillosis. He had asked the doctors to send a throat swab for detection of SARS-like viruses and also do a SARS-antibodies test in WIV. He suggested using antifungals for secondary fungal infections and a bronchoscope to clear out the mucus¹⁶. As Nanshan was the most prominent doctor during the SARS outbreak in 2002–03, his opinion about investigating which types of horseshoe bats were present in the Mojiang mine suggests that he suspected the illness due to SARS-like coronaviruses. Also, the testing of throat swabs and antibodies against SARS or SARS-like coronaviruses is suggestive that he considered that the patients had an infection due to a SARS-like coronavirus arising from horseshoe bats, which also happens to be the conclusion of the Master's thesis by Xu.

Discussion about the late disclosure of facts related to the Mojiang mine by WIV

Addendum to Zhou et al. confirmed Mojiang mine incident (November 2020)

After one month of the publication of our article⁶, an Addendum¹⁷ was published. The authors declared for the first time that WIV had been sampling the Mojiang mine-shaft for three years, from 2012 to 2015. Shi Zhengli and her colleagues had suspected that the miners had been infected by an unknown virus, and hence they sampled bats, rats and musk shrews in and around the cave¹⁷. Out of a total of 1322 samples collected, they detected 293 diverse coronaviruses, which comprised a total of nine SARS-like coronaviruses, including RaTG13 (ref. 17). The eight SARS-like coronaviruses were not reported in their pre-pandemic and post-pandemic papers^{18,19}. Shi Zhengli and co-workers also admitted that they had analysed 13 serum samples collected between July and October 2012 from four of the patients (miners), of which the patient who had died showed severe respiratory disease. However, neither did they publish the remaining partial or complete sequences of these eight SARS-like coronaviruses nor disclose their sequence Ids¹⁷. Also, the addendum did not reveal any detailed information of the 2012 miners' pneumonia.

SARS-CoV-2, RaTG15, RaTG13 and seven other coronaviruses from the mine form Clade 4 (May and December 2021)

A manuscript co-written by Shi Zhengli and Peter Daszak⁴ and published in 2020 does not document that the eight SARS-like coronaviruses (Ids 7909, 7896, etc.) were from the Mojiang mineshaft, and only 'Yunnan' is mentioned. In May 2021, after 1.5 years of the pandemic, Shi Zhengli published a pre-print followed by a publication²⁰ reporting that eight more viruses are in the same clade as SARS-CoV-2 and RaTG13, all collected from the Mojiang mine.

The sample 7909 (ref. 4) was renamed RaTG15, in this paper²⁰, a publication after about two years after the pandemic. However, it is surprising that though WIV mentioned these viruses in 2021, they were working on some of these viruses before the pandemic. A Master's thesis under the guidance of Shi Zhengli in 2019 (ref. 21) (https://drive.google.com/file/d/14dLB8uDw5NEO-A3H_pPuCab_MO-UVsa21/view?usp=sharing) mentions the sequencing of a few (7909, 7896, etc.), making it clear that many samples from the Mojiang mine were being studied in WIV. The WHO report on COVID-19 origins (<https://www.who.int/publications/i/item/who-convoked-global-study-of-origins-of-sars-cov-2-china-part>) also lacks any comments on the miners incident, except that 'WIV researchers think that the miners died due to a fungus in the mine', a fact also

discussed by Alex⁸. In the WHO report annexe, Shi Zhengli has mentioned that Clade 4 (consisting of SARS-CoV-2, RaTG13, RaTG15, etc.) is specific for Yunnan. The question is why none of these sequences were published before or immediately after the pandemic. Many crucial facts regarding RaTG13, RaTG15 and the Mojiang mine were not disclosed by WIV in a timely manner, which would have been essential with respect to the question of how the virus originated. Hence, as recently mentioned by Vineis and Salmaso²¹, the case is still open.

Mojiang mine inaccessible and closed for reporters and researchers

Access to the Mojiang mine has been denied by China. Reporters from various new agencies could not enter the area because of roadblocks and secret police in late 2020 and 2021 (refs 15, 23–25). If there is nothing to hide, why is access to the mine denied? Also, Shi Zhengli had confirmed in an interview that the Mojiang mine was closed for outsiders after 2012 and probably accessed by WIV researchers at least till 2015 (ref. 17).

Summary and future suggestions

WIV collected coronavirus samples, including SARS-like coronaviruses from the Mojiang mine, an abandoned mine in Yunnan, South China, including RaTG13, one of the nearest neighbours of SARS-CoV-2 and eight more from the clade.

It was from the same mine that six people went to clean the bat faecal matter, fell ill with severe pneumonia and three of them died in 2012. The miners' pneumonia and complications were probably caused by SARS-like coronaviruses in horseshoe bats in the mine, as concluded in the Masters' thesis⁶ and as suggested by Nanshan. It resembled COVID-19 on retrospective analysis done by us, although we have never claimed earlier or here that it was COVID-19.

We have not proposed any 'Mojiang miners' theory', but just show the connections of the miners' pneumonia incident and RaTG13 to WIV, Wuhan. WIV scientists visited the mines and collected 1322 samples during their visits from 2012 to 2015. No third party has access to these samples and information about the samples as the databases from WIV has been offline since September 2019 (ref. 26). Also, they have at least 13 serum samples from the miners who fell seriously ill in 2012. These should be submitted to international researchers.

We suggest that all the samples from the miners (serum samples, throat swabs, etc.) should be given to a third-party international research laboratory. Metagenomic data from all these samples would clarify the situation, as suggested by Alex⁸. It would be important to know if any of the samples from the mines or miners had the progenitor

of SARS-CoV-2, which could have either infected the laboratory worker, or was being studied and got released by accident.

Also, all the information about the samples and sequencing done, especially on the Mojiang mine samples and the miners' samples, should be shared with the international community for scrutiny.

Further it would be crucial to understand what kind of experiments were performed on RaTG13 or other SARS-like coronaviruses collected from the mine. These would include culturing, sequencing, cloning or artificial synthesis and recovery of viruses. This is important as WIV was doing extensive genetic engineering work on SARS-like coronaviruses²⁷.

The Mojiang mine should be opened to international researchers for sampling with proper PPE kits and precautions taking into consideration that it has SARS-like coronaviruses. The sequences of the viruses can be compared with SARS-CoV-2.

Conflict of interest: None.

Translations: Xu, L., Master's thesis, 2013; <https://www.documentcloud.org/documents/6981198-Analysis-of-Six-Patients-With-Unknown-Viruses.html>

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