Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Origin of COVID-19: Dismissing the Mojiang mine theory and the laboratory accident narrative

Roger Frutos a, *, Emilie Javelle b, c, d, Celine Barberot b, Laurent Gavotte e, Herve Tissot-Dupont c, Christian A. Devaux c, f

a Cirad, UMR 17, Interryp, Montpellier, France
b Laveran Military Teaching Hospital, Marseille, France
c IHU Mediterranee Infection, Marseille, France
d Aix Marseille Univ, IRD, AP-HM, SSA, Vitrome, Marseille, France
e Espace-Dev, Université de Montpellier, Montpellier, France
f CNRS, Marseille, France

ARTICLE INFO
Keywords:
COVID-19
Origin of SARS-CoV-2
Mojiang mine
Clinical diagnosis

ABSTRACT
The origin of SARS-CoV-2 is still the subject of a controversial debate. The natural origin theory is confronted to the laboratory leak theory. The latter is composite and comprises contradictory theories, one being the leak of a naturally occurring virus and the other the leak of a genetically engineered virus. The laboratory leak theory is essentially based on a publication by Rahalkar and Bahulikar in 2020 linking SARS-CoV-2 to the Mojiang mine incident in 2012 during which six miners fell sick and three died. We analyzed the clinical reports. The diagnosis is not that of COVID-19 or SARS. SARS-CoV-2 was not present in the Mojiang mine. We also bring arguments against the laboratory leak narrative.

1. Main

The origin of SARS-CoV-2 is the subject of a strongly debated controversy between the natural origin and the laboratory accidental leak hypotheses. The latter covers two excluding hypotheses: the accidental release of a natural virus or that of an engineered virus. The laboratory accident theory was dismissed by the report of the WHO inspectors who deemed it “very unlikely” (WHO, 2020) but was recently reactivated following President Biden’s call for a report from the US intelligence services on the virus origin. Nevertheless, these US intelligence reports could not bring either any evidence of a laboratory escape. Bloom and colleagues published in Science a call for another WHO-led investigation taking into account the laboratory accident theory (Bloom et al., 2021) arguing that not enough space was given to this hypothesis in the initial WHO report. The laboratory leak narrative is mostly based on arguments initially developed by Rahalkar and Bahulikar (2020) and relayed by others, very often by so-called “independent scientists” or journalists (Latham and Wilson, 2020; Speciale, 2021; Segreto and Deigin, 2021; Segreto et al., 2021; Sirotkin and Sirotkin, 2020; Relman, 2020). One specific narrative states that the Wuhan Institute of Virology (WIV) team headed by Dr. Shi Zheng Li visited the Mojiang mine in 2012 following an accident involving six miners and that they collected SARS-CoV-2 from this mine. Rahalkar and Bahulikar, and followers, make a clear link between the Mojiang mine incident, WIV and SARS-CoV-2. Here, we show, based on the clinical reports, that the Mojiang miners did not develop COVID-19 or even SARS and were not infected by SARS-CoV-2. We thus dismiss the Mojiang mine as the origin of SARS-CoV-2. Dismissing the Mojiang mine theory leaves the laboratory leak narrative without any scientific support thus making it simply an opinion-based narrative.

The Mojiang mine incident. Six cases of severe pneumonia with 50% lethality which occurred in 2012 were described in a Master thesis from Kunming Medical University (Yunnan, China). In a retrospective analysis of the clinical and radiological data of this report, Rahalkar and Bahulikar found clues to the laboratory origin of SARS-CoV-2 in this event (Rahalkar and Bahulikar, 2020). We propose a more balanced interpretation of this case series and highlight major discrepancies with COVID-19 (Table 1). Clinically, the SARS-CoV-2 pneumonia typically associates dry cough with dry crackles, whereas productive cough, colored mucus and moist crackles or normal auscultation were mainly reported in the six cases. Hemoptysis occurred in three cases, whereas it is unusual in COVID-19 patients, including critical ones (Wei et al.,...
Table 1
Features reported in the analysis by Li Xu of six miners with severe pneumonia cases who presented at the first affiliated Hospital of Kunming in China in April–May 2012.

| Cases | Underlying diseases | Work in mine | Symptom onset | Hospital admission | Clinical presentation | Thoracic CT-scan | Biological results | Outcome | Treatments |
|-------|---------------------|--------------|---------------|-------------------|-----------------------|------------------|-------------------|----------|------------|
| Case 1, male, 63 y | Suspicion of cancer but no confirmation | 02.16/04 | 16/04 | 26/04 (D10) | Dry cough, high grade fever, headache, dizziness, ear congestion, insomnia and loss of appetite, dry crackles | 25/04 Extensive and patchy consolidated exudate bilaterally, elevated bronchovascular shadows and lung markings, no pleural effusion, some nodules in different sizes, parts calcified, mediastinal lymph node enlargement, partially calcified, 30/04 Pleural thickening and pleural effusion in both lungs | 06/05 Severe ascites | 07/05 (D21) | Methylprednisolone, Meropenem, Vancomycin, Voriconazole, Acyclovir, Pleural draining |
| Case 2, male, 42 y | Chronic hepatitis B, colleagues | 02 to 16/04 | 11/04 | 25/04 (D14) | Fever, dyspnea, rusty-colored mucus with blood clots, hypotension 90/55, moist crackles | 26/04 CRP 117 mg/L and decreasing CRP with time despite worsening (23/05 CRP 23.5 mg/L) | | 26/08 Invasive ventilation | 13/08 (D120) | Methylprednisolone, Amikacin, Gentamicin, Vancomycin, Meropenem, Voriconazole, Sulfamethoxazole |
| Case 3, male, 45 y | Bowel obstruction surgery 1985 | 02 to 16/04 | 13/04 | 27/04 (D14) | Productive cough with yellow and greenish mucus, blood, fever, shortness of breath, headache, soreness in limbs, cyanosis, slightly moist crackles in lower right lung, no dry crackles from either lung | 25/04 Septal thickening, multiples nodules and floccular exudate, multiple inflamed lymph nodes in mediastinum | | | |
| Case 4, male, 46 y | None, colleagues | 02.16/04 | 16/04 | 26/04 (D10) | Productive cough and hemoptysis, photophobia, rough sound from lungs, moist crackles, cyanosis, Babinski on both sides | 29/04 multiple patchy opacity and exudative consolidation, pleural effusion in both lungs | | | |

(continued on next page)
## Table 1 (continued)

| Cases | Underlying diseases | Work in mine | Symptom's onset | Hospital admission | Clinical presentation | Thoracic CT-scan | Biological results | Outcome | Treatments |
|-------|---------------------|--------------|-----------------|--------------------|-----------------------|------------------|-------------------|----------|------------|
| 29/05 | Sub-pleural aerial cavity 12/06 Right pleurisy to be evacuated (28/06 3.1 cm) 06/07 Multiple big inflamed lymph nodes in mediastinum 18/08 Air bronchogram in the large consolidation exudation in the right lung, multiple lymph nodes in mediastinum | 29/05 | with giant cells (86%) and adenosine deaminase 16.8 U/L 29/06 and 02/07 CSF: neutrophils and then mixed cell reaction 18/05 Acinetobacter baumanii in mucus 28/05 Acinetobacter baumanii + E coli in mucus 02/07 Klebsiella pneumoniae in blood 12/08 CRP 90 mg/L | 28/08 (D35) | Recovery | Moxifloxacin | Meropenem | Linezolid | Cefoperazone | sulbactam | Piperacillin | tazobactam | Levofloxacin | Heparin | Warfarin | Haloperidol | Thymosin |
| Case 5, male, 30 y | None | 22-26/04 04 | 27/04 (D5) | Cough with white slimy mucus, fever, chest tightness, shortness of breath, headache, soreness in limbs, sweating, dizziness, loss of strength, paroxysmal dyspnea at night and edema, little moist crackles sound | 28/04 Bilateral multiple chestnut shaped nodules, multiple inflamed big lymph nodes in mediastinum 13/05 Decrease in nodules and lymph nodes | 02/05 CRP 21.3 mg/L 07/05 PCT 0.75 mg/L 09/05 SAA 44.10 ng/L | 28/05 (D30) | Recovery | Sulbencillin | Fluconazole | Methylprednisolone | Prednisolone | Thymosin |
| Case 6, male, 32 y | Inhalation of much irritating gas | 22-26/04 04 | 22/04 26/04 | Cough with white and slimy mucus, fever, difficulty in breathing, rough sound without crackle in lungs | 26/04 Bilateral multiple chestnut shaped nodules, increase in lung marking with thickening, multiple inflamed big lymph nodes in mediastinum 29/04 Thickening on the left back side of the pulmonary pleurae 07/05 Local emphysema and bullae | 27/04 CRP 34.2 mg/L, SAA 79 ng/L 18/05 D Dimer 3.9 μg/mL, PCT 0.04 ng/mL, SAA 230 ng/L | 28/05 (D35) | Recovery | Ganciclovir | Piperacillin | tazobactam | Methylprednisolone |

Data inconsistent with COVID-19 are shown in italic bold. Dates are DD/MM in 2020. Abbreviations: D = delay in days after onset of symptoms; y = age in years; CMV = cytomegalovirus; CRP = C-reactive protein, CSF = cerebrospinal fluid; CT = computed tomography; EBV = Epstein-Barr virus; PCT = procalcitonin; SAA = serum amyloid A.
Environmental Research 204 (2022) 112141

Ge et al., 2016) and that WIV staff members have been tested for SARS-CoV-2 and were reported negative (Cohen, 2020). One must also consider that SARS-CoV-2 was never found in this mine (Wu et al., 2014; Ge et al., 2016) and that WIV staff members have been tested for SARS-CoV-2 and were reported negative (Cohen, 2020). One must also wonder why a virus which killed more than 4 million and infected more than 200 million in 18 months did not cause any illness in 7 years from 2012 to 2019. The WIV team was not the only one to have visited the Mojiang mine and considering the high transmissibility of SARS-CoV-2 it is highly surprising that no cases were recorded at that time.

**Engineering of SARS-CoV-2 from RaTG13.** RaTG13 is not a virus but only a sequence generated by metagenomics (Ge et al., 2016; Zhou et al., 2020b). Therefore, there is no evidence that this sequence corresponds to any real and viable virus or even that all reads are coming from the same virus. The RaTG13 sequence might also be a chimera with fragments coming from different viruses. RaTG13 has never been isolated as a virus and replicated in cell cultures. It has no physical existence and thus cannot leak from a laboratory. Furthermore, considering the very high number of mutations separating RaTG13 from SARS-CoV-2 and their phylogenetic distance, RaTG13 can hardly be considered a progenitor of SARS-CoV-2 even if it corresponded to a real virus. The suggested engineering of SARS-CoV-2 for gain of function through in vitro synthesis from the RaTG13 sequence is a narrative making no sense from an operational standpoint. Engineering a complete virus is beyond current technical possibilities. There are too many subtle sequences, interactions and functions to master that we still do not understand. Building de novo a fully viable virus is far more complicated than expressing a single gene and is still not possible. It is possible to make a synthetic sequence from a well-known and validated sequence coming for an isolated and cultivated virus but this is not the case of RaTG13. There is no solid ground for trying to engineer a virus after the RaTG13 sequence and why should a laboratory invest all resources to engineer de novo a virus for which there is no evidence that it is viable and can be cultivated, a mandatory condition for gain of function experiments. The furin activation site in SARS-CoV-2 has also been mentioned as a proof of genetic engineering. However, furin activation sites are naturally occurring in different viruses, including coronaviruses, and thus cannot be a proof of genetic engineering (Frutos et al., 2021). WIV has conducted gain-of-function experiments but it was in the framework of an official and publicly available NIH grant (https://www.documentcloud.org/documents/21055989-understanding-risk-ba t-coronavirus-emergence-grant-notice). Results were published in peer-reviewed journals (Menachery et al., 2015). The experiments conducted within the framework of this NIH grant involved several bat SARS-CoV-like viruses, i.e. WV1, WV16, SHC014 and Ra4231. The objective was to assess potential changes in pathogenicity to ACE2-humanized mice when swapping the spike protein on a WV1 background. All spike proteins tested were genetically distant from those from SARS-CoV-2 and RaTG13 (Fig. 1). The swapping of spike proteins only led to slight variations. The maximum effect, a 20% weight loss, was observed with the spike protein of SHC014. Other recombina nts did not yield measurable effects. This work showed that the consequences of gain-of-function experiments on SARS-CoV-like viruses were extremely limited and certainly not to the magnitude of an epidemic as imagined by tenants of a laboratory accident. Furthermore, these experiments were conducted on viruses phylogenetically distant from SARS-CoV-2 and RaTG13 and no gain-of-function experiment was done on either SARS-CoV-2 or RaTG13 (Cohen, 2020). Not only the engineering of SARS-CoV-2 is merely a narrative but technical evidence indicate that no such engineering could generate a pandemic virus. There is today no evidence and no rationale to support this laboratory engineering narrative.

As a conclusion, there is no evidence to support the Mojiang mine origin of SARS-CoV-2 and any of the laboratory leak theories. These are narratives expressing differing and also contradictory opinions. If the virus is engineered, it cannot be the accidental leak of a natural virus and vice-versa. These narratives are not evidence-based scientific conclusions. They are also built on the weaknesses of the “Spillover” theory and the absence of reservoirs and intermediaries in the wild. In a time of geopolitical conflicts characterized by hidden agendas, false information and manipulations, it is essential to rely only on scientific and evidence-based conclusions and to avoid opinion-based narratives.
The phylogenetic tree was built using the maximum likelihood method with GTR-G-I evolutionary model and 500 bootstrap repeats. Rs4231. The spike protein gene of MERS-CoV was used as outgroup to root the tree. Sequences were aligned using MUSCLE in the SeaView package (Gouy et al., 2010). The phylogenetic tree was used for genetic engineering. The genes used for genetic engineering are those described in the NIH Grant 1RO1 Al 110,964.

**Ethics**

This is a retrospective analysis of previously published data. No primary clinical data were used.

**Conflicts of interest**

During the period 2005–2010, CD was the representative of the French Ministry of Research assisting the Chinese Ministry of Health for the building of the P4 laboratory facility in Wuhan.

The opinions expressed in this article are those of the authors and not those of the Ministry of Armies. The authors declare that there is no commercial conflict of interest.

**Authors contribution**

All authors participated to the design and writing of the article. EJ did the clinical diagnosis. CB did the radiographic analysis.

**Declaration of competing interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.