Did Ralph Baric of UNC Design Omicron?

"COVID Bioweapon Against Mice" Patent 11225508

Igor Chudov
6 hr ago

This article will show that **Omicron is likely an outgrowth of experiments to develop a Covid-19 variant causing serious disease in wild-type mice**, and point at the person and the lab who was documented doing just that — **Ralph Baric of UNC**.

To give you a preview:

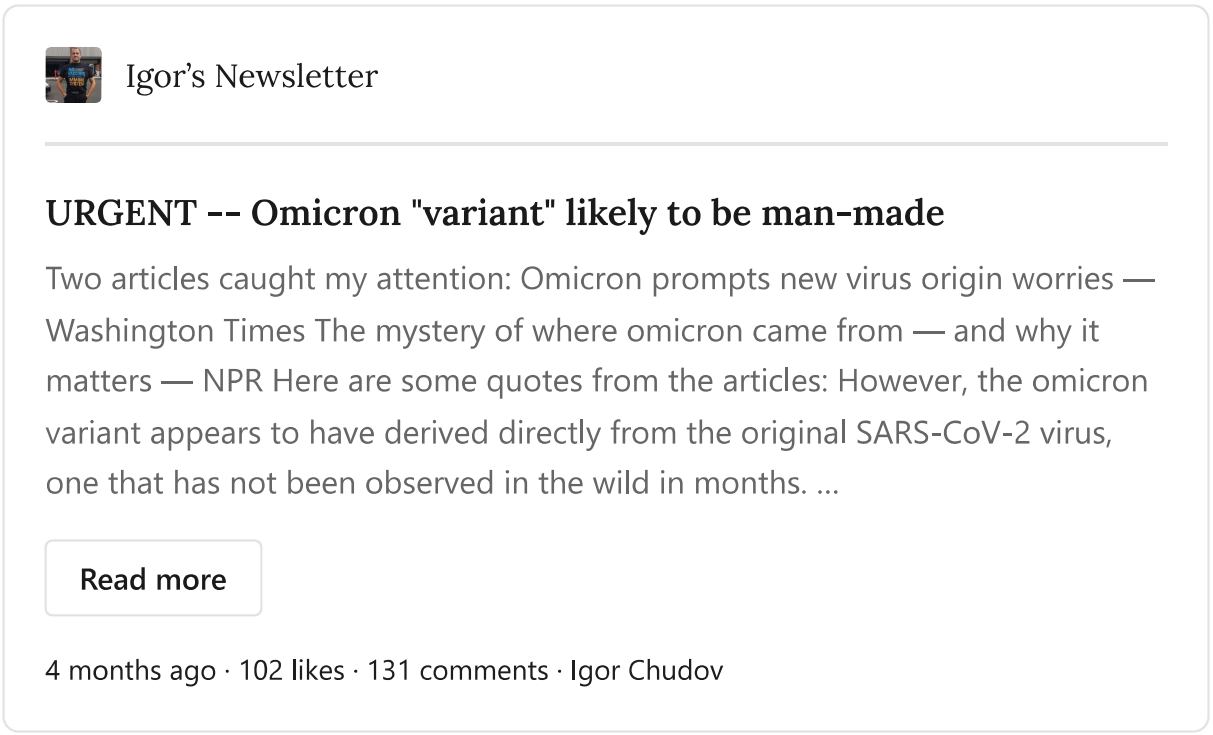
- **Omicron is very unlikely to be a product of natural evolution** of SARS-Cov-2 in infected people.
- While the original Sars-Cov-2 could NOT infect wild-type mice, **Omicron readily does infect wild mice**.
- It would take a very long time to naturally evolve Sars-Cov-2 to infect wild, non-humanized mice, without laboratory involvement.
- Baric's article in Nature describes steps to **genetically edit and develop a genome for such a mouse-infecting virus, derived from Wuhan Sars-Cov-2**.
- **Ralph Baric's UNC** owns **US patent 11,225,508**, which describes how he made a lab-made Covid-19 variant that infects mice and causes serious disease in mice (**making Baric's patented invention a bioweapon by definition**).
- This patent by Baric makes **UNC the only organization with a legal monopoly on his method of creating murine/human variants of Sars-Cov-2** due to patent protection
- Baric tested that his Mouse-Adapted (MA) virus is **still capable of infecting human cells**
- Baric also tested whether the **new mouse-adapted variant could evade existing spike protein vaccines.**

- **Any design of mouse-adapted version of Sars-Cov-2, like Omicron, could only be done with UNC's permission due to patent protection.**

Let's explore this if you are interested in details. If you are not, **the main conclusions are above and feel free to share of express your opinion in the comments section**.

Artificiality and Mouse Origin of Omicron

I personally posted on this substack, on Dec 2, saying that **Omicron is likely to be lab made.**



By the standards of today, my article, while presenting a hypothesis that turned out to be correct, is missing many important details that only became known long after Dec 2, the date it was written. I am not editing to preserve it as a historical artifact.

Let me also point out to an excellent (as usual) contemporary article by Sharyl Atkisson about Omicron's artificial origin and affinity to mice. Please read it.

A typical natural evolution of a virus (due to host-to-host transmission) includes so called "synonymous" mutations, that alter unimportant genes that would not change any protein expression. Think of that as a innocent typo, that does not change the **mAEning** of a sentence. These innocent and **mAEningless** synonymous changes are carried along as the virus is passed on from replication to replication.

However, **almost all mutations in Omicron were non-synonymous**. The non-synonymous mutations actually change the proteins that the genes produce. Usually, genetic evolution includes a balanced mix of synonymous and non-synonymous mutations.

The so called dN/dS ratio (how many non-synonymous to how many synonymous mutations were encountered) is very much unlike the typical ratios encountered in human viral evolution. This means that these mutations were very unlikely to have been randomly selected in Covid patients, and thus **Omicron is a result of direct gene editing or serial passage in mice.**

This article explains it:

93 **RESULTS**

94 **Over-representation of nonsynonymous mutations in Omicron ORF *S* suggests**
95 **strong positive selection**

Another article explains why Omicron is a product of a lab, using all available evidence. Where was the lab work done? How did it happen? Read below.

Ralph Baric of UNC created a Mouse-Adapted version of Sars-Cov2 that Could Still Infect People

Ralph Baric, whose name is familiar to our readers, is a brilliant scientist at UNC who is the top name in research related to coronavirus modifications.

He is the researcher who

- experimented with adding HIV genes to SARS-1 spikes
- found ways to mutate nsp-14 protein to make SARS-1 to spawn 21 times more variants. Sars-Cov-2 inherited a 5% mutated nsp-14 from SARS-1, and is now producting endless variants, oddly enough
- Found ways to enhance function of SARS-1 in 2007, to cause much more severe disease in mice, killing most older mice

- Created chimeric coronaviruses engineered to effectively infect humans
- Was given a “Moderna Vaccine Candidate” on Dec 12, before Sars-Cov-2 was officially known.

Here in this story, Baric brilliantly created a “Mouse-Adapted Sars-Cov-2”, that successfully **infects mice as well as people**. He modified the original Wuhan virus taken from a person in Washington State in January 2020, so that it could infect regular wild type mice.

Article | Published: 27 August 2020

A mouse-adapted model of SARS-CoV-2 to test COVID-19 countermeasures

Kenneth H. Dinnon III, Sarah R. Leist, Alexandra Schäfer, Caitlin E. Edwards, David R. Martinez, Stephanie A. Montgomery, Ande West, Boyd L. Yount Jr, Yixuan J. Hou, Lily E. Adams, Kendra L. Gully, Ariane J. Brown, Emily Huang, Matthew D. Bryant, Ingrid C. Choong, Jeffrey S. Glenn, Lisa E. Gralinski, Timothy P. Sheahan & Ralph S. Baric ✉

Nature **586**, 560–566 (2020) | Cite this article

Abstract

Coronaviruses are prone to transmission to new host species, as recently demonstrated by the spread to humans of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of the coronavirus disease 2019 (COVID-19) pandemic[1]. Small animal models that recapitulate SARS-CoV-2 disease are needed urgently for rapid evaluation of medical countermeasures[2,3]. SARS-CoV-2 cannot infect wild-type laboratory mice owing to inefficient interactions between the viral spike protein and the mouse orthologue of the human receptor, angiotensin-converting enzyme 2 (ACE2)[4]. Here we used reverse genetics[5] to remodel the interaction between SARS-CoV-2 spike protein and mouse ACE2 and designed mouse-adapted SARS-CoV-2 (SARS-CoV-2 MA), a recombinant virus that can use mouse ACE2 for entry into cells. SARS-CoV-2 MA was able to replicate in the upper and lower airways of

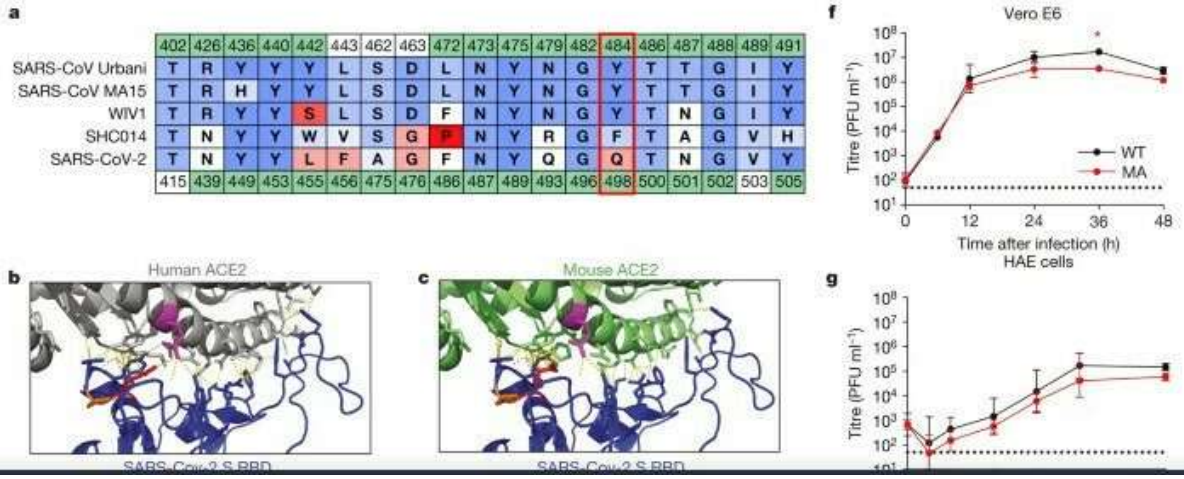
This is a big deal. Unlike SARS-1, the new SARS-Cov-2 (Covid-19) virus was not capable of infecting wild mice, except for "humanized" mice, genetically modified to have human ACE2 protein in the lungs. Normally, people do not interact with mice the way they closely interact with cats or dogs. So, if human Sars-Cov-2 does not infect mice, it could take a very long time before enough mutations happen, by purely random accident of nature, to create a virus that could infect **both** mice and people.

Ralph Baric short circuited this natural process. He used "reverse genetic engineering" to computer guess correct mutations that need to happen, in order to create a version of spike protein receptor that interacts with human ACE2 as well as murine (mouse) ACE2 called mACE2.

diminish binding efficiency. Thus, substitution of residue Q498 and the adjacent P499 with Y and T, respectively, from WIV1 and SARS-CoV might restore the interaction with Q42 of mouse ACE2 while preserving the interaction with human ACE2 (Fig. 1d, e). Using reverse genetics[22], we engineered Q498Y/P499T into the SARS-CoV-2 *S* gene and recovered the recombinant virus (SARS-CoV-2 MA). Notably, SARS-CoV-2 MA replicated with slightly lower titres compared with parental wild-type virus in Vero E6 cells (Fig. 1f) and primary differentiated bronchiolar human airway epithelial (HAE) cells (Fig. 1g). In contrast to wild-type SARS-CoV-2, SARS-CoV-2 MA RNA could be detected in cells expressing mouse ACE2 by 24 h after infection (Fig. 1h).

Omicron is known to infect bronchi preferentially!

Fig. 1: Generation of SARS-CoV-2 MA.

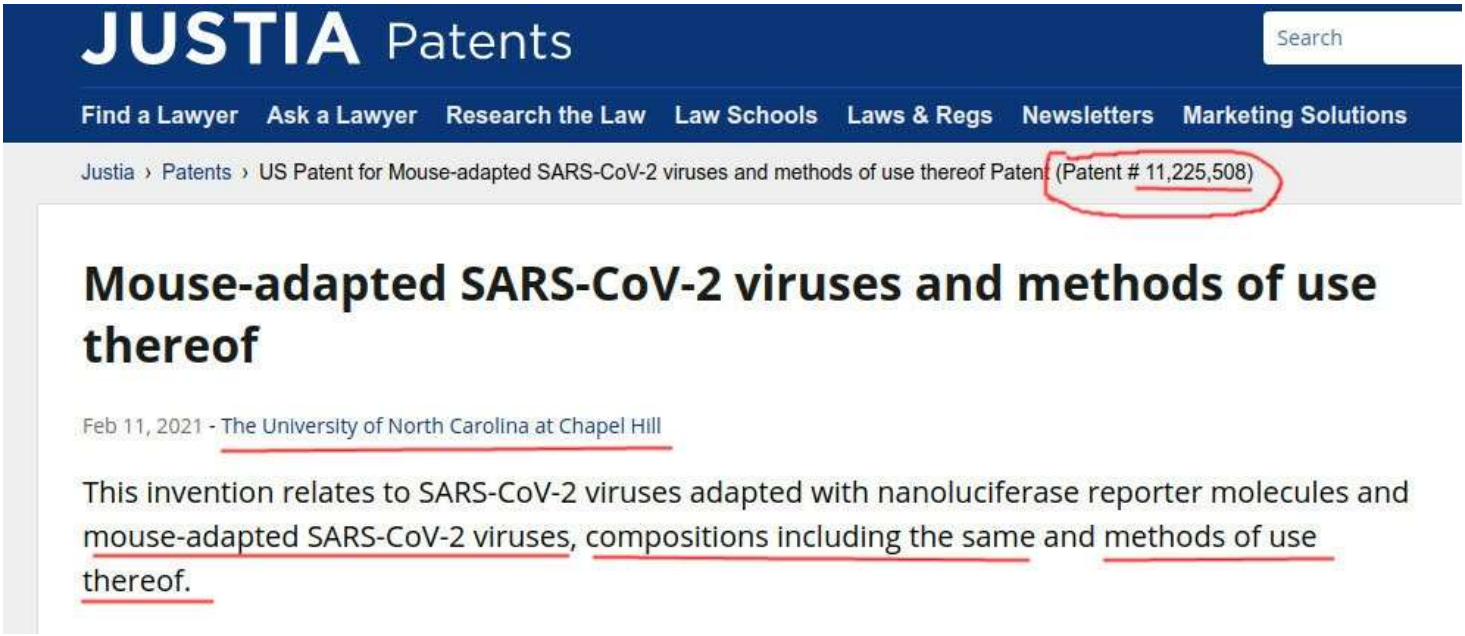


He brilliantly succeeded and created a **mouse-adapted SARS-COV-2 MA**, that can infect both mouse (murine) cells, as well as human cells.

Why did he do this? **To give UNC a legal monopoly on above described human-to-mouse research.**

Patent 11225508

Ralph Baric patented his approach to design such a human/mouse Frankenstein virus in a patent for an obvious reason. He wanted his employer to have a patent, a legal monopoly, on their specific method of creating such species-jumping viruses so that only UNC could do any future work on this.



In plain language, this patent protects UNC's rights to create mouse versions of SARS-Cov-2 using Baric's methods. Thus, **any such murine SARS-Cov-2 work done legally, would need to have UNC's permission** due to patent protection, usually involving a payment of money, which is the whole point of patent protection.

So: **if a mouse-infecting Omicron was created in a lab under a legal framework, it was done with UNC's permission as the patent holder**. Omicron is lab made, and it does infect mice, so then **Omicron was created with UNC's permission, right**? We are not sure if the answer is yes, of course, but we can ask this question.

Baric Designed "Sars-Cov-2MA" to be Pathogenic and Tested if it Evades Vaccine Immunity

This is, perhaps, the strangest part of the Nature article. In addition to designing human and mouse-capable version of Sars-Cov-2, **researchers made sure that SARS-Cov-2MA is highly pathogenic to old mice**, as well as checked if it **evades spike vaccine-created immunity in vaccinated mice**.

populations throughout the COVID-19 pandemic[27]. Additionally, wild-type and mouse-adapted SARS-CoV show highly age-dependent disease phenotypes in humans and mice, respectively[28,29]. To determine whether the infection of aged mice with SARS-CoV-2 MA would recapitulate the age-dependent increase in disease severity observed in humans with COVID-19, we infected one-year-old BALB/c mice with SARS-CoV-2 MA. In contrast to young adult mice, aged BALB/c mice exhibited a transient but significant decrease in body weight at 3–4 dpi compared with mock-infected mice (Fig. 3a) (old versus young, $P < 0.0001$ (3 dpi) and $P < 0.0040$ (4 dpi)). Similar to young adult mice, aged mice had high viral titre in the lung at 2 dpi, but in contrast to young adult mice, viral clearance in the aged mice was delayed, as indicated by detectable virus at 4 dpi (Fig. 3b). Similarly, replication in the upper airway persisted in half of the aged mice at 4 dpi (Fig. 3c). The loss of pulmonary function was more pronounced in aged animals, as shown by significant differences in PenH and Rpef among mock-infected and SARS-CoV-2 MA-infected mice (Fig. 3d, e). PenH was significantly higher in aged mice infected with SARS-CoV-2 MA at 2 dpi compared with young mice infected with SARS-CoV-2 MA ($P = 0.0457$). Rpef was significantly lower in aged infected mice at 2 dpi ($P = 0.0264$) and 4 dpi ($P = 0.0280$). Compared to young mice, aged mice infected with SARS-CoV-2 MA displayed increased epithelial damage, peribronchiolar lymphocytic inflammation, haemorrhage and oedema in the lung at 2 dpi and 4 dpi, and viral antigen was found in conducting airway epithelium, interstitium and nasal epithelium, with minimal antigen staining at 4 dpi, concordant with detection of viral titre (Fig. 3b, f–h). Additionally, levels of several proinflammatory cytokines were increased in the lung but not in the serum at 2 dpi, indicative of a localized cytokine and chemokine response (Extended Data Fig. 3).

I am not sure what is the point of making sure that his Sars-Cov-2MA is pathogenic to old mice, but the article seems to make a point that it is a valuable research finding. Strictly speaking, while mice are not people and researchers do not have the same ethical obligations towards them as they do towards people, **this work created a new biological weapon directed against aged wild mice**. Make of this what you want.

If they can make a virus particularly pathogenic to **aged mice**, that lab or someone else can make a virus particularly pathogenic to **aged people**. Was that actually done by anyone at some point? We do not know.

They also **tested Sars-Cov-2MA for vaccine evasion.**

Vectored vaccine and IFN-λ1a efficacy

As demonstrated with mouse-adapted strains of SARS-CoV[25], the replication-competent SARS-CoV-2 MA strain facilitates the identification of virus and host factors that guide pathogenesis and disease severity and enables rapid testing of intervention strategies in standard laboratory mice. Using a virus replicon particle (VRP) system, we vaccinated ten-week-old BALB/c mice against SARS-CoV-2 S and nucleocapsid (N), with GFP as a control, with a boost after three weeks, and challenged them four weeks after the boost with SARS-CoV-2 MA. Three weeks after the boost, serum from mice vaccinated with S—but not from mice vaccinated with GFP or N—potently neutralized SARS-CoV-2 reporter virus expressing nanoluciferase (nLUC) (Fig. 4a). Upon challenge with SARS-CoV-2 MA, only mice vaccinated with VRP expressing S exhibited significantly diminished viral titre in the lungs and nasal turbinate (Fig. 4b, c). So, the mouse spike protein vaccine worked

They found, luckily for the mice, that the "mouse Covid vaxx" was still effective against this new frankenvirus. What happened after this article was written? Did someone modify this virus further to engineer it for immune evasion, kind of like Omicron?

Was this virus later serially passed through immunized mice to evade vaccine immunity?

Sars-Cov-2MA is NOT Omicron

Sars-Cov-2MA has some similarities to Omicron. It infects mice and people. Both have a mutation in Q498 gene. But many other mutations are different. Omicron has many

more mutations (52) compared to Sars-Cov2MA, whose mutations are listed below. (ignore the luciferase one, it is for lab purposes)

SUMMARY OF THE INVENTION

A first aspect of the present invention provides a recombinant SARS-Cov-2 virus particle comprising: a spike protein comprising a Q493K, Q498Y and/or P499T substitution(s); a nsp4 protein comprising a T285I, G309C and/or H313Y substitution(s); a nsp7 protein comprising a K2R substitution; a nsp8 protein comprising a E23G and/or K196R substitution; a nsp9 protein comprising a T67A substitution; a ORF6 protein comprising a F7S substitution; and/or a nanoluciferase (nLUC) luminescence reporter sequence substituted in place of a wildtype ORF7, wherein the numbering is based on the reference amino acid sequence of SEQ ID NO:2 (spike protein), SEQ ID NO:3 (nsp4 protein), SEQ ID NO:4 (nsp7 protein), SEQ ID NO:5 (nsp8 protein), SEQ ID NO:6 (nsp9 protein) or SEQ ID NO:7 (ORF6 protein), respectively.

Most importantly, both are mouse-adapted and both are carrying mutations that are computer-designed and likely directly genetically edited:

Viruses, cells and transfections

All viruses used were derived from an infectious clone of SARS-CoV-2, which was designed using similar strategies for SARS-CoV and MERS-CoV[22,46,47]. The Q498Y/P499T substitutions were generated by site-directed mutagenesis using the following primers: forward: 5′-ATATGGTTTCTACACG ACTAATGGTGTTGGTTACCAACC-3′, reverse: 5′-TAGTCGTGTAGAAACCAT ATGATTGTAAAGGAAAGTAACAATT AAAACCTTC-3′. Viruses were

Direct genetic Editing

In addition, **the date of the progenitor variant for Sars-Cov-2-MA**, a virus strain MN985325.1, **roughly matches the date of Omicron progenitor** as well. MN985325.1 is dated January 2020 and was obtained from a patient in Washington State.

Product Description:

Virus Classification: *Coronaviridae*, *Betacoronavirus*

Species: Severe acute respiratory syndrome-related coronavirus 2 [Note: This virus was originally deposited to BEI Resources as 2019 Novel Coronavirus, but subsequently named SARS-CoV-2 by the International Committee on Taxonomy of Viruses (ICTV). Please note that the depositor's original nomenclature was used on the product label.]

Isolate: USA-WA1/2020

Original Source: Severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2), isolate USA-WA1/2020 was isolated from an oropharyngeal swab from a patient with a respiratory illness who had recently returned from travel to the affected region of China and developed clinical disease (COVID-19) in January 2020 in Washington, USA.[1]

Comments: Under the nomenclature system introduced by GISAID (Global Initiative on Sharing All Influenza Data), SARS-CoV-2, isolate USA-WA1/2020 is assigned lineage A and GISAID clade S using Phylogenetic Assignment of Named Global Outbreak LINeages (PANGOLIN) tool.[2,3,4] The complete genome of SARS-CoV-2, USA-WA1/2020 has been sequenced (the isolate - GenBank: MN985325 and GISAID: EPI_ISL_404895 and after one passage in Vero cells - GenBank: MT020880). The complete genome of SARS-CoV-2, USA-WA1/2020 has been sequenced after four passages in Vero cells in collaboration with Database for Reference Grade Microbial Sequences (FDA-ARGOS; GenBank: MT246667).

Trying to put a time stamp on the progenitor of Omicron puts it close:

Over-representation of nonsynonymous mutations in Omicron ORF *S* suggests strong positive selection

To first identify mutations that accumulated in the SARS-CoV-2 genome prior to the Omicron outbreak, we constructed a phylogenetic tree that included the genomic sequences of the reference SARS-CoV-2, two variants in the B.1.1 lineage which were genetically close to Omicron, and 48 Omicron variants sampled before November 15th, 2021 (**Fig. 1A**). These two B.1.1 variants were sampled during April 22nd–May 5th, 2020, which suggested that the progenitor of Omicron diverged from the B.1.1 lineage roughly in mid-2020. Intermediate versions have gone largely undetected, thus resulting in an exceptionally long branch leading to the most recent common ancestor (MRCA) of Omicron in the phylogenetic tree (**Fig. 1A**). We hereafter refer to this long branch as Branch O.

So... If Omicron was lab designed... And it was engineered to infect mice... And the process was patented... Was Omicron designed with UNC's knowledge?

We have a lot of questions, but now **we know who to ask.**

brucha613@gmail.com ✓

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Tatjana 6 hr ago ♥ Liked by Igor Chudov

Igor Thank you for all the effort, skill, knowledge, attention to detail you put into every single article you publish. Your thinking & consistency in adhering to the principles of critical thinking as well as clarity in which you present and approach the themes you cover is exemplary. Your work is perfect in so many ways and should be used to teach critical thinking & Big Data Analysis in schools and/or on the job learning. Public Service in Australia, every policy department is lacking adequate Data Analysis skills. Thank you for the outstanding articles that are well researched, analysed, presented, easy to understand and accessible.

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Brian Mowrey Writes Unglossed · 6 hr ago ♥ Liked by Igor Chudov

There were multiple mouse-adapted (gain of function) studies, not just MA10. All of them used either pre-B.1.1 isolates or in the UNC case, a house-grown clone of the Wuhan strain, and none of them "reproduced" the B.1 mutation signature (including D614G). That includes MA / MA10 (the latter is the subject of the patent, see the mutation list in Fig 1 of https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7510428/ - no D614G).

So if Omicron (BA.1 / BA.2) has the B.1 mutation signature, it didn't come from any published mouse study. This was extensively considered in my own review of the evidence. It had to be from a non-published lab "experiment" (i.e. intentional gain of function using a B.1 template) https://unglossed.substack.com/p/omicron-origins-part-2

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6 replies by Igor Chudov and others

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