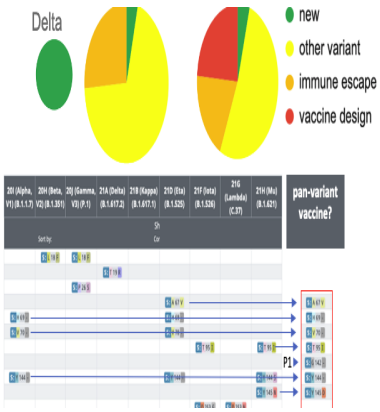

Molecular evidence indicates a synthetic origin of SARS-CoV2 Omicron

Description

Molecular evidence indicates a synthetic origin of SARS-CoV2 Omicron

brief introduction: a synthetic virus, again???

(skip to get directly to the science)
You may think "*Didn't these guys always say SARS2 already escaped from a lab? What is this, the next crazy idea? Can't they just shut up, we have plenty of real problems to worry about!*"
To this I can only say *I wish I could*. I also have plenty of other things I'd rather do in my few free evenings. Like drinking a glass of wine with my love. But I can't, both because she has 3 long night shifts at COVID ICU this weekend, and because this matters. We must take a critical look at a very small field of natural sciences. Guess we can call it synthetic virology. More and more scientists apparently love making artificial viruses or virus parts. They may initially believe they are helping mankind. They may not be ill-intendet. But they are VERY dangerous. Everybody makes mistakes. But a tiny mistake in the hand of a synthetic virologist may cost millions of lifes. Synthetic virologists are taking such bets to follow their personal scientific interests. Technological advancements have enabled them to build viruses within weeks, at the cost of only a few hundred dollars.

SARS2 never before evolved that fast or in complete isolation

Normal SARS2 variants emerge when a few mutations (~2-6 of those in the spike protein) accumulate in currently circulating virus.
Omicron (red line) emerged from a most recent common ancestor (MRCA) virus that was last seen ~April 2020, and accumulated more than 25 new spike mutations in complete isolation.
That means omicron was evolving at a never before seen speed (3.3x faster) and without infecting others. Yes, there are regions in the world where viruses are hardly ever sequenced. But keep in mind

that people travel, and that omicron is much more transmissible than even delta. We should have seen many “a bit more transmissible” variants going around the world almost as fast as omicron much earlier. A lab escape would both explain the high number of mutations as well as the isolated evolution.

SARS2 never before evolved 25 sequential nonsynonymous mutations.

There are two type of mutations in any nucleic acid (DNA or RNA), so called synonymous (or silent, dS) and nonsynonymous (dN) mutations. As 64 nucleotide codons (a combination of 3 of the nucleotide or “letters” A, U, C or G in the case of RNA) code for only 20 amino acids, some changes in the RNA sequence do not change the resulting amino acid sequence and are thus mostly irrelevant. In natural evolution, RNA mutations occur completely randomly. They are then often just carried along if they are synonymous. In the case of nonsynonymous mutations, many of those make a virus less fit and are thus selected against and rarer. Several dN mutations can only accumulate under conditions that allow very high viral loads and in regions under very high selective pressure. Here, beneficial dN can outpace others. Thus, we have seen up to 8 dN spike mutations accumulating in immunocompromised patients. However, many omicron dN mutations reduce viral fitness. And in the pre-outbrake omicron spike, there are 26 dN mutations in a row (-> source picture), without a single dS mutation in between. That many non-synonymous mutations in a row have never before seen in natural, but a few times in synthetic sarbecoviruses.

SARS2 never before copied 25 mutations from publications

As mentioned before, SARS2 variants usually inherit a few mutations from the parental strain and then evolve a few new ones themselves (CoVariants provides a nice overview here). Scientists then try to figure out what the new mutations do.
Instead of inheriting only parental mutations, omicron “copied” almost all of it’s spike mutations from other variants (with often younger MRCAs!) or publication! That’s a bit like directly inheriting genes not only from your father, but also from 6 younger cousins and 5 classmates you first met when you were 7.
Almost all of omicron dN mutations were already known about half a year BEFORE omicron emerged! Those not from variants were mostly known to confer resistance towards vaccines, or from vaccine-associated publications.
Keep in mind that this virus has ~10,000 amino acids, and each one could mutate into 19 other amino acids. The chance that only a known mutation evolves by chance is 1 in 190,000/500 (=# known mutations), so 1 in 400. For 20 it’s 1 in 400^20, basically impossible, that’s 1 in a 60+ digit number.

Mehr lesen

Scientists made SARS2 spikes with 20 “greatest hits” mutations

Another weird fact on omicron is that it is resistant to virtually all human antibodies. This pretty much excludes that omicron evolved in a single immunocompromised patient or some animals, which initiatially do not have SARS2-specific antibodies at all. So let’s have a look at origin options virologists seem to forget about. We know that publicly known lab leaks happen about twice a year. We also know

that scientists selectively made vaccine-resistant SARS2 viruses in labs by culturing them with diluted sera from vaccinated donors. Others made "greatest hits" synthetic polymutant SARS2 spikes that contain 20 nonsynonymous mutations known to enable vaccine escape or from other variants. The latter experiment was done in a pseudovirus, but those can also escape and their spike can then be copied into SARS2 by a process called template switching. We also know that their partner lab in Durban collected, froze and later cultured exactly the SARS2 variant which is not circulating anymore out there and from which omicron evolved. And they did patient sera virus culturing experiments. Such a lab leak would explain the extinct MRCA, isolated "evolution" and precise inclusion of only published nonsynonymous spike mutations.

Scientists designed mRNA vaccine spikes with many mutations

In 2020, some variants emerged that were more resistant towards Wuhan SARS2 spike based vaccines. Thus, companies such as Moderna, Pfizer, Gavi?, Gritstone and likely many others started to develop next generation, pan-variant effective vaccines. The idea was to include many key mutations from circulating variants into one vaccine spike. Such a universal booster would induce antibodies that help against many different variants, possibly also against immune escape variants. Sounds like an omicron spike, right?
If such a vaccine is NOT based on DNA or RNA, and NOT given to SARS2 infected patients, it's a good strategy. But variant-adapted mRNA vaccines were tested in HIV patients which are known to often have persistant SARS2 infections (an otherwise extinct MRCA could have survived here) with high viral loads. Here, the SARS2 RNA copying enzyme (RdRp) could have easily replaced variable parts of its own spike RNA with this new, highly similar spike mRNA (template switching).This may even have happened in several patients, giving rise to Omicron BA.1, BA.2. and BA.3.

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