Twitter Thread by Philipp Markolin, PhD



Philipp Markolin, PhD
@PhilippMarkolin

@threadreaderapp Actually, I've taken the time now to look at all the arguments brought forward in the above twitter thread.

Although I applaud the creativity, I am not convinced.

But before going deeper, let me first acknowledge that I respected the paper you and Yuri published, and 1/n

@Rossana38510044 @threadreaderapp in general the scientific arguments being put forward here and elsewhere, instead of pure conjecture without any evidence basis.

Okay, so let's go into the thread.
I'll try to steelman your argument first and then poke holes into it.

If I summarize correctly, you are 2/

@Rossana38510044 @threadreaderapp offering a potential scenario where WIV researchers tried to create a pan-CoV vaccine, be it in the form of a LAV or related strategies. Both Ratg13 and SARS-CoV-2 (and potentially other CoVs from undisclosed backbones) were part of that research effort. Some features have 3/

@Rossana38510044 @threadreaderapp been engineered first as to:
I) increase the spectrum of immunicity the vaccine provokes (like introducing an 'inactive' FCS that will allow the immune system to develop defenses against FCS-containing 'wild' CoVs)
II) as a strategy to attenuate the virus (less dangerous)
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@Rossana38510044 @threadreaderapp III) as a means to protect the LAV from re-activation via recombination with 'wild' CoVs.

To support these claims, you link to research that suggests attenuation strategies (like Baric's TRS) and the proline-induced 'glycoshild' in the FCS (although that did not work out).
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@Rossana38510044 @threadreaderapp Furthermore, you provide some evidence of research and grant ideas proposing very similar or at least related work that has been done or was planned to be done.

This is the main thrust of the argument, but we both keep in mind the background info of proximal origins and your
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@Rossana38510044 @threadreaderapp Bioassays paper with Yuri, because issues raised there still apply obviously and might strengthen certain aspects of the above mentioned 'thrust'.

Does that seem like a fair summary of your position? Maybe I can add that you do not claim a high certainty, rather possibility
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@Rossana38510044 @threadreaderapp Because we might agree that the hard data we have is insufficient to rule out both zoonosis or lab leak completely.
We are both trying to assess likelyhoods here.

And this brings me to my disagreement.
Let's start with the obvious:
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@Rossana38510044 @threadreaderapp A) There is no evidence of that kind of research being performed at WIV or elsewhere. Since there must be a long paper, experiment, money and animal trail by the simple nature of complexity of suggested LAV development, we have to assume either a secret program, or cover up.
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@Rossana38510044 @threadreaderapp A secret program carried out at a serious scientific facility like WIV, with Westerners coming in and out as they please, Western money and grants supporting it, is a bit curious to say the least. Also, why keep 'LAV research' secret in the first place? Doesn't seem likely.
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@Rossana38510044 @threadreaderapp Next, cover-up. I think we can both agree that there was no need for a cover-up until after the pandemic started.
So here, the lack of info on research performed at least a few years in advance assumes that the cover-up must have been great at eliminating earlier traces
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@Rossana38510044 @threadreaderapp reaching potentially as far forward as 2013 and the RatG13 sequencing (which apparently they missed to cover up... also, why were they the ones publishing it again?) Not claiming this is impossible, but opens more questions than it answers tbh.
Ok, let's move on.
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@Rossana38510044 @threadreaderapp B) The alleged knowledge supremacy and engineering prowess. This is always something that is astonishing to me. Your scenario would require WIV researchers being on the cutting edge not only in one area of expertise, but many. Computational modeling of ACE2, Heparin binding,

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@Rossana38510044 @threadreaderapp furin cleavage predictions, glycosylation predictions, structural biology, viral recombination, novel vaccine development strategies, genome engineering, seemless cloning, immunology ... all has to come together pretty neatly in order to make your scenario work.
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@Rossana38510044 @threadreaderapp Does this match with the group size, the people's expertise there, the financial, practical and lab-equippment restrains?
Also, you seem to suggest that although parts were engineered (like the FCS), there was still some GoF serial passage step in between, potentially
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@Rossana38510044 @threadreaderapp rendering part of the engineering useless or, as you seem to suggest, helping the pre-curser LA-virus escape attenuation and become super dangerous.
And even after all of that expertise and dangerous experiments, somehow a lab accident happened unnoticed until too late?
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@Rossana38510044 @threadreaderapp Again, nothing is impossible, but just being theoretically possible does not necessarily make it high odds.

Anyways, lets move on.

III) Cherry-picking. Taking bits and pieces of scientific facts from a huge body of evidence in support of a narrative is always problematic.
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@Rossana38510044 @threadreaderapp First, for almost any scenario, one can look at the hundreds of papers published around SARS-CoV-2 and find little nuggets of what parts support my scenario, while ignoring the rest, including the author's conclusions of what the context of that nugget might be.
Again, I am
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@Rossana38510044 @threadreaderapp not saying that facts cannot be taken from others and used to support ones claim, especially if presented appropriately, what I contend is that often, appropriate use requires context.
There is no need for maliciousness or deceit here either, we humans are great at finding
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@Rossana38510044 @threadreaderapp patterns, connections and associations when we already have a frame to connect it too. Unfortunatly, we also have a tendency to make facts fit or to find reasons to discard them when they do not.
Let's look at one of these examples you listed above: The TRS leader sequence
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@Rossana38510044 @threadreaderapp In Baric's 2018 paper, he aims to manipulate a viruses recombination potential by changing TRN sequences, with some successes.

He identifies certain sequence motifs that are TRS in SARS.
And low-and-behold, one of them is also found in SARS-CoV-2 and RATG13.
Suspicious?
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@Rossana38510044 @threadreaderapp Well, not really. First, finding ANY 7nt motif in a 30k bp genome is expected. 4 to the power of 7 = 16384 , so on average we will find 1-2 of these motifs. The motif in question is UGGUCGC, and it happens to be there exactly once. Just randomly looking at AGGACGC yields the
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@Rossana38510044 @threadreaderapp same result, found exactly once. So not really that unique or exciting.
Also, in Baric's paper, these sequences where at the start of the coding elements/viral genes/orfs, not in the middle. In SARS-CoV-2, it's just in the middle, not where we expect it to do anything.
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@Rossana38510044 @threadreaderapp All that is to say that a cherry picked element in itself does not really add much to the whole thing, other than seem to 'fit' to the narrative one wants to believe.
Many of your examples unfortunately have a cherry-picked character that does not hold up that well when
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@Rossana38510044 @threadreaderapp investigated deeper.
In any case, I am out of time since my daughter woke up from her nap, so I will leave it at that for now.

In the end, I wished we would coalize more about a common narrative how to prevent all future pandemic sources, rather than putting our stake and
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@Rossana38510044 @threadreaderapp energy in figuring out who is to blame for this one.

Even if this pandemic did not start from a lab leak, the next might, and we better learn from our mistakes, starting from wild markets, habitat invasion, lab transparency, GoF virology regulation and early detection.
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