Bret and Heather 10th DarkHorse Podcast Livestream\_ SARS-CoV...

Sat, 10/9 12:51PM • 1:01:16

**SUMMARY KEYWORDS**

virus, people, point, bat, china, lab, question, paper, study, emerged, research, engineered, human, sugars, wuhan, human subjects, strains, live stream, result, flaw

**SPEAKERS**

Bret, Heather

**Bret** 00:01

Hey folks, welcome to the Dark Horse podcast live stream. This is our 10th live stream. We're here, we're phoning it in just like you are, get used to it. I'm sitting with Dr. Heather Hyang. As has become our way here on the Dark Horse podcast. And we are ready to talk about developments over the last several days relative to the COVID-19 situation and much else. Let's see, we had a couple of announcements up front I'm not going to say housekeeping because for me that always brings up an image of Sam Harris and a French maid's outfit. For anyone so

**Heather** 00:35

and thank you for that. Yeah, for everyone listening. Thank you. So

**Bret** 00:39

we'll just say maintenance or something. Maintenance maintenance. All

**Heather** 00:41

right.

**Bret** 00:42

All right. You had announcements?

**Heather** 00:44

Well, yeah, I guess we wanted to start by saying as we did the end of the last q&a, and we will try to do this at the end of every of our live streams, please, if you're enjoying this, subscribe to the channel, like the video, try notifications share. And and we are going to continue to do what we've tried the last couple of times the guard to the Super Chat questions, which is spend a little about an hour doing this right now. And the Super Chat questions coming in will be logged, we will then take about a 15 minute break between live streams. And we'll go through and just rank order those questions mostly in terms of monetary value. But if anything jumps out at us, if we have time to see it. That's lower on the list. We'll try to get to that spent about a half an hour on the next live stream the q&a on that. And then we'll go in order received answering questions in the next live stream from Super Chat that comes in during that live stream. So that's the plan. And anything else.

**Bret** 01:41

Yeah, we had another announcement, which is that you and I are doing a it would be called a lecture coupled with an interrogation by Professor Robbie George at Princeton. That's right, I'm gonna try to pull this up while you're talking. All right, and this will be this coming week on Wednesday, Thursday,

**Heather** 02:01

it's going to be boy, I'm going to try to call this up as I'm talking to you. It's Wednesday, April 29, at 4:30pm. Eastern time. So that's 1:30pm. Pacific.

**Bret** 02:16

It's going to be done live. And the I think there's room for 1000 registrants. So I don't know if we'll hit 1000 registrants. But if you want to,

**Heather** 02:27

if you want to show the screen now, oops, almost. In order to watch it live, you do have to register. But there's no fee, you don't have to be associated with Princeton in any way. Here it is. And when it will be available later online, we'll be putting it up online.

**Bret** 02:45

So if you miss it, don't fret, you'll be able to find it. And we will provide links on our Twitter pages. The talk will involve a model of culture and consciousness that we can promise you you've never heard before. And anyway, it should be very interesting. So if that is your style of thing, please tune in. Okay, Zack,

**Heather** 03:06

you can drop it back to us. Thank you. All right, I'll just one other thing is that we are going to save explicit corrections that really don't feed into the conversation today until the end, we're going to try that this time. And so we're just gonna launch right into a conversation here. And then I've got a couple corrections that don't necessarily relate to the rest of what we're planning to talk about today. That will save for the end.

**Bret** 03:30

All right. So I wanted to start with to point to a stunning success of yours from I believe the last live stream. Well, I like the sound of this yes, no, it's good. You will no doubt have noticed that the Santa Clara paper that gets to live streams, live streams got a paper that you critiqued. And if I recall your position, your position was I don't necessarily this is I Heather do not necessarily disagree with the conclusion that this paper has reached. I think it's likely to be accurate, but the methodology is atrocious. And here's why. And then you went on to point out that the way they had solicited participants in the study was obviously flawed and suggested several ways in which there might be systematic bias.

**Heather** 04:16

So let me interrupt before you you go on the conclusion of the study, which I agree with, although I don't trust that this paper I didn't trust that this paper had actually gotten to these results, honestly, was that background rates of infection of SARS cov. Two are likely to be much higher than we currently know. And if that's true, that would lower the the mortality case fatality rate for source code,

**Bret** 04:42

which would be good news. And we both think that this is right based on the fact that Several studies have now suggested that pattern, however it emerged we learned from Kiko in Boston, a longtime Twitter friend of ours, that the study in question was was revealed to have a deep methodological flaw exactly where you had suspected it would be. And that flaw was that the wife of the PI on the study

**Heather** 05:10

of PII being the principal investigator, the main guy that made money getting guy yeah,

**Bret** 05:13

I had solicited participants by emailing I think it was an email list of parents of her kids classmates or something like this at some private school. But more importantly, I mean, that is not in and of itself a bad thing. But what she had done was she had said that they would get the participants would get tested for free with an FDA approved test that would tell them whether or not they were safe to return to work. And so a the test is not FDA approved. And B, this will tend to bring in people who think they may well have had it and may then get good news, which is your immune, and you can go back to work. And this is clearly going to result in a bias in favor of people who have had the disease or something that might be that might look like it. And what's more, it's suggest that we know something about immunity that we really don't know, which is, what is the fate of people who have had this, does their immunity last? Or does it decay? And are they again vulnerable down the road?

**Heather** 06:14

Yeah, it wasn't just a blanket Facebook ad, which I had plenty of critique for anyway. But it was a as it turns out, a targeted send out at least in part of that Facebook ad to people with the message that if you think you might be positive, this could do us some good. So it biased, the subjects participating in exactly the way that we were concerned that I was concerned, it would it might buy, it might have been biased,

**Bret** 06:39

those are the kind of thing that in my experience emerges over the course of years, typically in here, it's a matter of days. But in any case, very well done. This again, not the paper, right, the paper is not very well done spotting the flaw. It was very well done on your part. And this again points to and man behind the curtain issue where the peer reviewed literature has some backstory that you don't know can't see. And because it's gated, we often don't find out what the dirt is where the bodies are buried as it were underneath studies like this. So later on in today's podcast, we will talk more about comparisons between the peer reviewed literature, the archive the the archive literature, which is not peer reviewed, but is still official in some sense. And a paper that doesn't appear in either of those formats, which is well worth considering.

**Heather** 07:35

Yeah, I guess let me say one thing. This particular problem with this paper is that you know, the wife of the principal investigator of the paper went and basically solicited subjects participants in the study in a way that rendered the results not what they would appear does actually remind us of the value of human subjects review and human subjects review boards, which are comp which are prevalent or exists on every single campus and every single I imagine research organization in which human subjects are used, which is akin also to vertebrate animal committees, where if you're ever doing anything with vertebrates, you have to get permission you have to walk through all of what you're doing and basically get a board of usually well bored people who don't really want to be doing the work but who know that it's important that before you say engage in research on monkeys or engage in research on humans, that it passes the extent protocols for for engaging and I imagine that if this had had to go through human subjects review which this work couldn't it's you know, it's it's too fast. But one of one of the benefits of the brakes on the system is that human subjects were you would have made it really really clear that such such things wouldn't have been appropriate it might not have stopped it but it might it might at least have revealed in say the dinnertime conversations between the dude and his wife that you know this this actually is not something you're allowed to do.

**Bret** 09:09

Yeah, I hesitate to sign on to an embrace of human subjects review because although I believe there needs to be something that does this job in practice it's so absurd the way some things are granted, I mean, if you want if you wanted to run a study on a college campus where you stopped people, you know, in a public space and asked them whether they remembered their dreams from the prior night, for example, you would need to go through this process. So it and it has a there's a just a bureaucratic element to it. That's insane. But

**Heather** 09:43

so this is a complete aside. But another point against these kinds of reviews, vertebrate animal review, which you and I never worked on people as graduate students, but we both worked on vertebrate so we had to go through some of the vertebrate Animal Care committees at University of Michigan, where we did graduate work. And, you know, these, this, these forums are like 3040 pages long, they go on and on and on and on. And I was at that point working on the sex lives of poison frogs as one does. And I wanted to bring back tadpoles from I was working in the near tropics at that point, Costa Rica, Panama, I don't remember which, as I wanted to bring back some adult frogs, and also do some work on tadpoles to see if they would cannibalize each other at different rates, depending on their degree of relatedness. And so I had all these justifications, I'd gotten some grant money to do the work, but I needed or maybe I hadn't gotten the grant money yet I had, I had to get the vertebrate animal protocols in place. And when I got the review back from the vertebrate animal committee, everything involving tadpoles was struck out. And I thought, No, no, and I got on the phone with them. I was like, I was ready to defend the work that I was going to be doing. And they talked me through I thought, you know, they thought very patiently, and they figured they were dealing with someone a little bit dim on the other end of the phone. And they explained to me quite patiently that well, frogs are vertebrates, tadpoles are not in fact, vertebrates, and therefore I did not need any permission to do research on tadpoles. Now,

**Bret** 11:08

I should point out to any of our listeners who are tadpoles, you are vertebrates, don't worry about this. It was a mistake on their part.

**Heather** 11:14

Yeah. So I was able, you know, unfortunately, for people who might want to be doing an unacceptable work, the lesson was you can do whatever you want, as long as they're young enough that the vertebrate animal committee doesn't care. So anyway, these committees are bureaucratic, and they're often flawed, but but they they are set up to do good work, doesn't mean that they're doing good work.

**Bret** 11:37

Alright. Let's move on to a follow up not a correction. But a follow up to a prior discussion. Someone a listener to this podcast, alerted me in response to my suggesting that military bases would be good study populations to determine questions like, what is the damage to people who've had asymptomatic cases of COVID-19? Somebody said, actually, a recent study was done on the cruise ship that docked early in the pandemic in Japan, and in fact, they were testing for exactly that result. So can you put that up, Zack? So it's a study in radio and radiology and cardiothoracic imaging, and its chest CT findings in cases from a cruise ship diamond princess with Coronavirus, disease 2019. Okay, so you can see it now on your screen. And can you scroll a little bit?

**Heather** 12:37

I'm doing the scrolling. So where do you want me to start

**Bret** 12:41

stopped? Actually, the abstracts good enough? Okay, so they tested 104 cases, not a huge number, but a number enough to get the result. And what they found was something above half of the asymptomatic cases that they looked at had these ground glass like opacities in the lung. Now, I find this frightening and fascinating. How can it be that something that is doing significant damage to the lungs enough that it shows up on a CT scan is asymptomatic from the point of view of the person suffering the condition, maybe this is more common than I know. But that strikes me as very odd. In general, even if you have difficulty breathing as a result of a bad cold or something. If you don't have pneumonia, you go to the doctor, they look at your lungs, and they don't see very much. So maybe the CT scan is a bit different than a standard X ray.

**Heather** 13:40

It raises questions about how homogenous how homogeneous. sensory neurons are across humans and lungs alveolar function, you know, all sorts of things. How could you have a lung CT, that looks far different? And by all measures that we tend to use far worse than it did two months earlier? And you feel no effect?

**Bret** 14:02

Actually, can you scroll up? We can see some of the No no. Up the other way. Sorry. You and I scroll in different directions. And one of the places we don't get along all that well keep going to the fingers. Yes, no, no. The images There we go. So here you can see the arrows in this image point to one of these ground glass opacities. It's not the least bit subtle, and this one is from a 70 year old asymptomatic woman. Right so 70 year old woman had severe damage to her lungs during an infection in which she showed no symptoms. That is a fascinating and frightening result.

**Heather** 14:45

Yeah.

**Bret** 14:47

All right. I think that's enough. There. You have someplace you want it to go next.

**Heather** 14:55

I thought I think you're going to start us off right? Okay.

**Bret** 14:58

So I want To call our attention to something that another Twitter friend of ours alerted me to just yesterday and I must say, this one caught me off guard. I fell into this. Here.

**Heather** 15:16

You're looking for the medium piece. Yes, right. The piece not yet sack I don't know

**Bret** 15:21

is on medium. And it was written by somebody who is there. Okay, yep. Okay, it was written by, I apologize if I get your name wrong Yuri Deegan, and Yuri Deegan is not a biologist, at least not by training. He is a life extension person focused on epigenetic alterations of cells. So in general, I don't get along very well with the life extension people because I think they're largely barking up the wrong tree. Although, if I had to pick an area that was promising epigenetic reset, is probably highest on the list or close to it. In any case, URI has written an analysis of the SARS Cove to research and what it says about the possibility that this pandemic was triggered by a virus that is not in effect natural. Now we should talk about what that means. But let me say upfront that he starts this piece by saying that he was a skeptic. And then he began to dive into this research in the hopes of arming himself so that he could properly challenge and defeat claims that this was a synthetic virus when he encountered them. And at some point, he says he was infected by the virus of doubt. Now, I read this, hoping that I would spot on this remain up, not at the moment, we can come back to it. I read it in the hopes of finding flaws in what he said not that the entire analysis would necessarily be flawed. But it would be interesting if there was this analysis in which he had come to believe that there was a strong possibility of a synthetic virus. And it would be great to have a counterpoint to that. And I must say, I was a bit shocked by how thorough he had been, how careful he had been, and how compelling the overall analysis was, is very careful. Even in the conclusion, he says this doesn't nail anything down. But what it does is mean that the possibility is life. So let me say a bit about what it would mean for this to be a synthetic virus, it does not mean that somebody invented it, it would mean that it is a kind of era of pieces from different viruses that had been created by natural selection. And that kind Mehra would have an increased capacity to infect people on the basis of having, you know, the molecular machinery from this virus over here that facilitates binding to the surface of a human cell and molecular machinery from over here that facilitates cleaving a particular protein that would make it more likely to invade the cell. So in any case, I want to point out that this is the CounterPoint here on medium, a not very widely read post at this point, is challenging a paper that was published in Nature that we covered in an earlier live stream and the paper in nature said there's almost no chance that this is a synthetic virus and made several arguments.

**Heather** 18:42

Although a lot of their argument which I objected to at the time was that it didn't look to them like it was engineered because it wasn't the people engineering would have made choices that didn't seem like the right choices, not that it wasn't possible to have made those choices. But there was inference about the the choices made by the would be engineers, rather than an argument that it wasn't possibly engineering.

**Bret** 19:09

So this raises a number of questions. One is what would it be engineered for. And I want to make very clear that the idea that this virus was engineered in the lab is not synonymous with the idea that this is a bio weapon. It could be one of the reasons you might engineer a virus in the lab would be to use it in an offensive way. But there are plenty of other reasons to engineer a virus in the lab. And in fact, one of the things that this paper does so beautifully, is it reveals what this very small network of laboratories that are studying bat coronaviruses is actually doing and one thing that I think is quite clear from This analysis is that there is an incredibly dangerous subfield, building viruses routinely in the lab with gain of function cameras, and that is to say where they borrow function from one virus, put it in another, and then infect cells of one type or another type. So these gain of function research protocols create novel viruses that do not exist in nature. And there is always the chance that one of these things will escape. Now, did that happen in this case? We don't know. But the fact of one of the two primary labs involved in this research, it's not that these labs are all over the place, there are really two primary labs studying bat Corona viruses. And their potential threat to human health. One of these labs is in Wuhan, China. So the coincidence of this virus having emerged there, and the story that it is connected to a so called wet market, when in fact, the indications that it came from the wet market are quite insecure. There were early cases, numerous early cases, more cases than were connected to the wet market that had no connection to it than anyone could find at all. And so there is a small number of scientists engaged in finding novel viruses by collecting bats from other parts of China, abstracting their viruses and then tinkering by playing around with their molecular machinery and the level of danger there would be hard to overstate. Yeah.

**Heather** 21:56

So I guess a number of things just to add into the mix here, Zach, if you want to put up the screen here we have another preprint server paper that is to say not on not yet peer reviewed, but written as if the goal is for it to be peer reviewed. This is actually from over a month ago now, March 19 2020. Evidence of the recombinant origin and ongoing mutations in severe acute Respiratory Syndrome coronavirus to SARS cov two and these these authors argue that there is it's the spike protein on the surface of the virus that appears to be pangalan in origin and it is the rest of the virus that appears to be batten in origin and so they're using this this word recombinant not to presume that it was human recombination not in the way of say a recombinant tomato which has a fishy fishy inserted into it to make it more freeze resistant as an as in the style of various GMOs but that this this would have happened naturally right and you know, we have to be careful with this word natural of course but when we're using it here we mean is we mean not in a lab not by human directed research. What it what it leaves open, though, is well how did and we've talked about this a little bit in previous live streams, how exactly did this particular bat where this virus is understood to be transmitted virus to a pangolin in the first place? And then how did the pangolin transmit that to humans? And you know, we have explored Okay, yes, people do eat pangolin sometimes, but it's actually the pet the bat pangalan connection, which is one of the most difficult ones to understand and ecological level whereas and maybe because I take it down for a minute while I find here we have Yeah, you can put this up now Zach, so this is the site for the National Center for biodiversity information. NCBI. And it's a clearinghouse for taxonomy. It's not just viruses, we'll show you in a little bit. Really good site that is was created by some bioinformatics people to specifically track emerging pathogens, but this is a site that is used across the taxonomic world across all organisms on Earth as a as a place to go to find to find genomes and such. So here you have the the lineage that is not very exciting page as the way with both government and taxonomic sites generally, but this lineage basically reads left to right where the left most thing viruses is the most inclusive and everything to the right of that, you know, if if, if Rob avaria are viruses then so are Coronavirus A and so is everything to the right of us right. So we have here this particular species, severe acute Respiratory Syndrome related coronaviruses but even that is a category right so if I click on that, look at all of the SARS related coronaviruses It goes on and on and on and on. There are a tremendous number of them. And so you know, how many of these were, in fact, created in a lab versus were created organically out there in the world when organisms came into contact with one another? Some of them are creations, almost certainly. And some of them, some of them are not. And, you know, for, for legitimately lab created viruses, presumably, much of the information is out there. Now, somewhere on here we have, I can't find is just too much here. We have, you know, civet, viruses and pangolin, viruses and lots and lots and lots of bat viruses. So take it back off sack. Well, I find one more.

**Bret** 25:47

So can we can we talk a little bit about the ecological question. This is one of the things that I think is most important, we have two lines of inquiry developing one has to do with how this virus functions and how we're going to defeat it. And then there's another question about where it came from. And what that implies. In other words, if somebody released a bio weapon that obviously calls for one kind of response, if it was an accidental release from a lab, it's another kind of response, we actually need to know the answer to this question. And if you think about the fact that there are a couple of primary labs that are doing this work of creating novel viruses, whether they were involved or not, we need what they know. We need that expertise. And at the moment, we use Vang Lee, who is the head of the lab in Wuhan that does this work is experiencing a situation in which there's wild speculation on the internet about what her involvement was. Can you put up the the Scientific American paper that is coming out I believe in their June if you Oh, you don't have I don't know. All right. Scientific American is going to can search but I mean, this No, sorry for this. It's all right. Sure, exactly. It is a paper that they put out basically a a profile of the family which describes her laboratories work and concludes that we know that her laboratory was not involved in having created this thing. So what the function of that article is, is a little hard to say, but again, the coincidence here is spectacular. Let me I think I found it. Yeah, that's the one. Alright, Zack is gonna put this up and we will put links to this in the description. Okay, so we can Yeah. Okay, good. So how China's bat woman hunted down viruses from SARS to the new Coronavirus, and the virus that bears the most resemblance to the currently circulating human Coronavirus is from Hunan Province in, I believe southwestern China. And there is interesting discussion in the paper on medium about the fact that that sample that is closest to the human circulating virus was apparently collected in 2013, by the Zhang Li. And again, I apologize if I'm getting your name wrong. There's jangly lab. Though they did not publish on it at the time, they revealed in the present that this was the closest sequence and it is anomalously close in almost all regards, except the spike protein, where it has this pangolin sequence. And so you raise the right point, which is, is there an ecological

**Heather** 29:04

my computer so I can find something to show you guys, is there an ecological path

**Bret** 29:07

for a recombination event to have taken the pangolin spike protein and put it into this this virus from Rhino Lofa bat or not, now, I can't say one way or the other. What I can say from the years of work I did as a bat researcher is that I bet the number of people who have expertise on relevant bats is very, very small. We need to know who they are. And we need to talk to them about what the ecology of these animals is, there's not very much available but some graduate students somewhere may have studied these animals and we can know something about whether or not pangolins and these bats ever encountered encountered each other because would have to take place for that recombination event. I believe somebody should correct me if I've got it wrong, but the only mechanism I can see for a recombination event Is that an individual animal, either bad or pangolin. Presumably bad since that would be the more likely route for it to get back out to humans would have to be infected with two Corona viruses. And those two viruses would have to invade the same cell in order for there to be genetic exchange, that's a very unlikely y tilde in order to get so you've got the spike protein from one from the pangolin, and you've got the rest of the genome from the bat, some animal has to have both in order for nature to have recombined these things. So in so what we're learning is I guess

**Heather** 30:37

the proposal in the paper, though, is that a bat infected a pangolins, the pangolin has the virus that it has and the bat infects the pangolin. with whatever the vibrate bat has, so there's there's has to be for several has to be simultaneously be a reservoir for two foreign viruses. In order if you're that pangolin, which, you know, we're sort of raising questions about whether or not that really makes sense as an ecological sort of transfer. But you just have to be a bat that's infected, that somehow transfers your virus into the pangolin. And you know, and then the recombination happens by right now that's a, that's a big black box right there, just

**Bret** 31:12

being sick with the two viruses is not likely to do it, they have to end up in the same cell, which may be very likely depending upon how widespread it is in the body. But my point is, somehow, it will not necessarily be very valuable with respect to figuring out what to do about this virus circulating in the human population. But in terms of figuring out what it is and how this happened, and how it can never happen again, and is somebody responsible in a way that needs to be addressed. We have to gather people with various different kinds of expertise. So I find I'm now struggling. I have two kinds of expertise relevant to the story just by accident. One of them is phylogenetic systematics, and one of them is bats.

**Heather** 31:53

So phylogenetic systematics for those people who don't know what that means, which is to say all but probably two of the people watching right now just refers to the science of figuring out who is related to whom it is not the science of naming organisms, which is taxonomy. But it is figuring out once you have a bunch of organisms, what the history of relationships was, and

**Bret** 32:13

so in some sense, phylogenetic systematics almost never comes up in the news. But at the moment, it's news. Why? Because when you try to draw a phylogeny of these viruses, you don't get a clear signal. Why? Because part of it is coming from pangolin. And part of it is coming from bat. So that could be the result of a natural fact. Or it could be the result of an artificial fact. And before you go to that, let me just say, so I can say something about bats. I can say something about phylogenetic systematics. I'm not a virologist. I'm not an epidemiologist. And I'm not a molecular biologist. Right? I would say at least you want those five kinds of expertise in order to navigate a question about could this have come from nature.

**Heather** 32:58

So the three things again, are bat biology, which you have and I have a little bit but mostly through you. phylogenetic systematics, which we both have and which we know to be pretty rare even among biologists. It's considered kind of niche, and you have to have ended up in the right place with the right people to end up with with deep understanding of it. You have said virology epidemiology and what was your fifth that we are not expert in biology, epidemiology and molecular biology.

**Bret** 33:25

Okay, especially molecular techniques. So what I think you want is a roomful of people. You know, it doesn't have to be a lot of people, but there has to be some expertise on all of these things. And you know, for me to say I'm a bat biologist, I have almost no experience with Rhino love and bats. I have captured them on a couple of occasions when I've done some work in the old world. But my bad expertise doesn't bind me very much, except that I know that these animals are likely to be found in caves that those caves might have multiple species in them, not necessarily from the same family. So there's a pipistrelle bat that also shows up to have a tiny sequence homology to the circulating human virus. That's an entirely different family. Could they be roosting together? They very definitely could be. But in any case, the pangolin experts, we need to talk to them. The bad experts, especially the rhino ofit experts, we need to talk to them, we need to put them in contact with the virus ologists and the molecular biologists in order to have a conversation about what could possibly explain what we are seeing.

**Heather** 34:30

Yeah, especially given this sack would you put this up coming out of nature? A week little more than a week ago, China is tightening its grip on Coronavirus research. And some scientists are saying no, this is good. We need the research coming out of China to be to be accurate, but it looks of too many of us like an attempt to control information right? So if papers that were up even on these preprint servers are being pulled and basically here's the first paragraph Just it's a news article in nature, it's not a research article. Over the past few months, China's government appears to have quietly introduced policies that require scientists to get approval to publish or publicize their results. According to documents seen by nature and some researchers, this means as we have alluded to, in the past, that regardless of which of the three main hypotheses for the origin of this virus is true, it is completely organic and emerged out of a wet market. It was engineered and was being engineered in pursuit of better understanding these viruses so that public human public health globally could be improved. Or it was engineered, and it was being engineered for the purpose of bioweapons, regardless of which of those three hypotheses is actually true. And we are both you and I are both leaning strongly towards that middle one. But there was some engineering going on, but it wasn't for nefarious purposes. Regardless of why. If China is obscuring research and keeping people from talking, then we cannot simply trust what China is telling us. And we need smart people in a room with the relevant background and ability to troubleshoot and problem solve and say, Oh, I hadn't thought of that. And I was wrong about this. And oh, holy hell, what if, and you'll be allowed to hypothesize in ways that might seem extraordinary without those hypotheses coming back to haunt them? Because they were wrong?

**Bret** 36:30

Absolutely. I would also say I'm very dismayed, as you point out about the way China has behaved, controlling information false and this is extremely destructive, dangerous behavior, that's certainly costing lives. On the other hand, one of the things that this, this medium post alerted me to was just how international this effort to study these dangerous coronaviruses is. And so yes, the laboratory in question is in Wuhan, China. The NIH gave a grant to study this. So

**Heather** 37:07

the National Institutes of Health, which is the main funder, American United States funder of medical research,

**Bret** 37:13

right, and the main competitor laboratories in the US. Ralph Barak, I think is the name of the pie in that lab, and they sort of trade back and forth, one upping each other in terms of their sophistication at modifying coronaviruses. And so anyway, this is something you could be pretty well unaware of. And then suddenly, virus emerges in Wuhan, and we're all grappling with Oh, there happens to be a lab there. What does that mean? Oh, they were studying bat coronaviruses. And the one with the greatest analogy to the circulating virus happens to have been one they collected in 2013 and didn't publish about. So all of these things are potentially connected. Also the case that it turns out that the reason that we know that there is an analogy of the spike protein to the pangolin virus is that a number of pangolins were confiscated. They were being smuggled in China. They died in captivity at a rehab center from Coronavirus symptoms, swabs were taken sent to labs, where do we think they went, they may very well have ended up in these labs who may very well have spotted a spike protein whose function they wanted to investigate. And if you look at the Publication history of these labs, swapping these components out and seeing what the result and virus can do is just standard practice. So could this virus have been created as a result of just basic research it could have and

**Heather** 38:49

which we don't know if that's what happened. But it points to the potential not the guarantee. But the potential danger of doing recombinant engineering on organisms, which is what GMOs are. Right, it points to the potential for great danger far greater than what we are hoping no one intended in this case, and certainly no one intends when they're trying to make safe crops less susceptible to pests in such.

**Bret** 39:13

Yep, I would also point out that the danger of skullduggery here is also spectacular, I still believe that this virus is an odd one to have created if your intent was to release it into the world to cause havoc. On the other hand, let's say that somebody and again, one of the points from the medium article is that the technology to swap components of the virus is now within reach of a graduate student at the level, you know who's studying these viruses, and so that's a that's a pretty large number of people who might have the laboratory capacity to do this sort of work. Let's say that somebody decided to wreak havoc well If they were going to release the thing for the purpose, and you know, I would just come up with a placeholder for a purpose. If somebody, let's say somebody's sociopathic enough not to care that they were going to cause a lot of death, but interested in making some money, wanted to short a bunch of markets, knowing that havoc on Earth would lead to markets collapsing, where would they release it so as not to have their fingerprints on it? Well, probably, they would release it somewhere where it would be traced back to some laboratory that might not have been involved. So we have to be really careful, just because the connection between this virology lab in Wuhan and the viruses they studied, and this virus that is now traversing the globe seems to paint a very clear picture. Of course, the problem is that very clear picture could be real, or it could be what somebody wants us to see for their own purposes. And we, because we don't know their purpose, can't infer it from what has been released.

**Heather** 41:02

Yep. Okay, should we talk a little bit about the diversity in the virus, which is to say, we have Well actually, excuse me, Zack, he will put up this screen. And this is from a different site, not NCBI. The last site we were talking about was the National Center for biodiversity information, which is a federal site, this is an organization. Actually, I'm going to just flip the screen for a moment. This is an organization that was written about in a peer reviewed paper in 2018, which is private, and it aims to do real time tracking of pathogen evolution. And so these are bioinformatics people, not necessarily phylogenetic systemic tests. And so you know, it's really hard to, to know, and also assess the various methodologies here. And probably this is not the place to go into the various methodological problems with a number of the approaches and systematics. But take a look at this at this on the left here. This is your unlike a classic cladogram. On the horizontal oops, on the horizontal axis here, we actually have time, because each time a genome was collected from an infected person, a viral genome was collected from an infected person, we know exactly when that happened. And so time is on the I want to say x axis, but it's not the x axis. And, and you have beginning in December, early December, going all the way to this is sort of mid April. And what these authors The site has done is basically color coded, change the color of the viral genomes, every time there is sufficient change for it to feel like it's a different strain to them. Now, this is obviously a judgment call, we got a question last livestream with a link to an article that said, oh, there's 30 strains now. And that article turned out to be very frustrating, because none of the links were to actual research. They were always two more articles within that same not particularly valuable newspaper. And there was no way to figure out from the article what research it was referencing, actually. But are there 30 strains? Are there eight strains? Are there 800 strains? Are there as many strains as there are people who are infected? It's something something in there, right. So as I think you said last time, Brett, I mean, I think I think you said just this, that they are by some by some counts, as many strains is there are as there are infection moments, right?

**Bret** 43:41

Well, the problem is, that's not even the upper bound, you could have multiple strains in an individual depending upon mutation rate, I think the mutation rate here is not high enough that we're liable to have a number as large as the number of infected people are greater. But my complaint the last time was that 30 strains might be the number of strains that have gotten a toehold in the world and moved forward. So because the world is editing down these strains to the very rare, more successful ones, that's what we see. It doesn't mean that there aren't innumerable, many strains circulating somewhere at this point, right.

**Heather** 44:22

So sorry, that keeps having hard time with this trackpad. We can look at the same information in a different view, a radial view, which I often find very confusing, but in this case, the middle of the circle is the beginning of time for this virus, which again, and this is December 3 2019. And it's also a spatial, it's its spatial representation. So again, you see in purple, the original virus coming out of coming out of China, and then pretty quickly mutating into a number of different strains, which again, these authors have have color coded, color coded. So let even play the show play this animation Brett, why not? I just have a very hard time making this work. Okay, unfortunately, I can't make that full screen. So the animation on the right is the map showing its spread out of China. And you have the comparable move in the radial file gram on the left of how it is moving in the in the tree that was created. So one of the changes

**Bret** 45:37

in color on the map on the right are what are being counted as new strains that are emerging, spreading the dots or the spread within a country. And then the lines are transmissions that are inferred between countries

**Heather** 45:53

exactly the size of the.is relative caseload according to you know, what's being reported, which of course, we've, as we've talked about many, many times that information is is very incomplete. And I want to say to that, you know that what are we going backwards now? Okay? The distinction between strains is somewhat arbitrary, and certainly is not going to be the judge the same way by every person looking at them, just like the distinction between species is not a hard and fast line. So complex systems, complex categories tend to have fuzzy boundaries between them. And the idea that we can count exactly eight are exactly 30, or exactly some number of strains, is asking a bit much for a rapidly evolving RNA virus.

**Bret** 46:47

Yeah, I don't think we need to know I think it is worth understanding that this thing, and we should expect this having just met the human population, it is liable to be a poor match in many ways. And rapid evolution is what you expect, because you have innumerable individual copies in each person who's infected, you have large numbers of infected people and any discovery, any mutation that results in greater transmission will obviously show up as an ancestor to some large nucleus of the stuff. So we should expect to see that here and, and we are seeing it.

**Heather** 47:28

I think you can take it down as act. Thanks.

**Bret** 47:31

So what is your takeaway about the discovery that there is apparently a very rapid, small, sociological cluster of people augmenting the function of coronaviruses found in nature, for the purpose ostensibly of figuring out how to prevent them from escaping and killing people?

**Heather** 47:58

So sociological cluster, meaning

**Bret** 48:01

Read, read all number of people who go to the same conferences and read each other's papers and one up each other? and that sort of thing? Yeah, it's

**Heather** 48:11

not surprising at all, is it? I mean, I, of course, and we can all act surprised that we didn't know about this particular thing before now. But this is the risk that has come to meet us. And there are presumably many others, with many other clusters of researchers working on dangerous things, that the work itself being risky, does not mean it shouldn't be done. But what kind of oversight if this was engineered an accidental release? What kind of oversight could have been in place to prevent the release? Is it in fact possible isn't in fact possible in a globalized world, where you have researchers from at least two of the world's major superpowers, and presumably more than that, actively involved in the research with their own not just political differences, because of the governments that live under, but also presumably personality differences, you know, just two, to two individual labs, within a university, you're going to have differences much less between universities, much less between universities and nations?

**Bret** 49:19

Well, I have to say, I am disturbed. It's not that this was unknown, obviously, it was in the literature and there was a certain amount of pushback in 2015 over a paper that was published in Nature which revealed some of what was going on and alarmed a number of people but it there's an obvious question about the value of this research in preventing future hazards and the danger that it will cause one of these hazards to emerge. Obviously, shutting down official research does not prevent people from doing this privately off label. So the danger may exist irrespective of what The official position is, but I'm shocked at the discovery that this gain of function research is absolutely commonplace working with viruses that are absolutely known to be potential emergent hazards. And you asked, what kind of safeguards Could you put in place? The only good one I can think of, is, maybe if this research needs to be done, it needs to be done on ships. And there needs to be some protocol where the work is done. At some point, the samples are destroyed, the ship doesn't dock for two weeks. You know, I don't know what the right protocol would be. But I don't like the sense. And in fact, this reminds me of something I have thought each time we've had one of these major emergent disasters of late right. We had Fukushima, we had the Deepwater Horizon, we had Aliso Canyon in Los Angeles, right, we're gonna

**Heather** 51:02

have to spell that one out. For most viewers, I think, Well, that

**Bret** 51:05

was a release of gases from a mine that had been used as a natural gas storage facility. So some large cavern underground had been that had had natural gas pumped into it. And it sprung a leak. That was poisoning people in the local neighborhood and was on pluggable in the same way that the Deepwater Horizon leak was on pluggable. So anyway, each time one of these things have to Oh, you should also put on the list the financial collapse of 2008, where we discovered the degree of leveraging and all this, each time one of these things happen. I have the sense of Okay, it took the disaster for me to find out what it was that somebody needed to tell me what's happening, right, I needed to know that mortgage backed securities were being played with in this particular way, in order to understand how much risk we were at, I needed to know about, you know, fuel pools and spent fuel in nuclear reactors. And the possibility of a, you know, prompt criticality causing one of these pools to bust before Fukushima I find out after

**Heather** 52:20

Well, this is part of what long form investigative journalism is for. And we've seen a decline in long form investigative journalism, with the change in the in basically the financial model for journalism, where it's about clicks, and very short term attention spans, and it's hard to get funding to send someone to do what might be a six or nine month research project, and result in you know, a 10 minute documentary or a 5000 word. Think piece.

**Bret** 52:47

This is true, but it is also, you know, as Eric has been repeatedly raising, there's a question about what could possibly explain the level of dysfunction in investigative journalism. It's hard to account for and so what I want to know, discovering that this, what looks to me like an extremely well researched reason and careful article on medium describing the scenario that might have unfolded explaining our current global pandemic, that that piece has cleared none of the hurdles, right. This is just something somebody decided to write and publish, for their own purposes. Now the question is, given that Head Start, is that going to get picked up by any major publication?

**Heather** 53:38

Well, so let me also point to long before that, well, I don't know long. But before that medium piece came out that medium pieces just the last day or two, I think, a few days before that, actually. Now we have this is Zack, you put this up. Now, this is on GitHub. This is version 7.6. This is an ongoing, I think it's basically a wiki document, between among many, many authors, and everything is public here. The title being evidence that stars code to emerge from a Biological Laboratory in Wuhan, China. And they just they do an incredibly careful job of spelling out absolutely everything that they assume everything they think they know, everything and you know, including, you know, here's the section on if we're right, what it means if we're wrong, either way, what doesn't change something or nomenclature. You know, why we call it or what we're calling these things. And then finally, sir, I'm going to go back up to the top, and they say, if you'd like to see a summarized version of every claim in this document, please see the conclusion. And my God, it's really, really careful. It's, it's remarkable. And you know, this, this right here is investigative journalism. That's not what these guys are calling themselves but that's what this is. So it's very similar in some ways to the medium piece that you began The show talking about, except this is effectively a group effort. And we're on version, I think it said z 7.6. So it's got a lot of iterations. If this

**Bret** 55:11

is GitHub, then it's an open source collaborative project. This is an entirely different mechanism for doing journalism. The medium piece is one person's incredible effort to summarize material, this is a different way of doing it. But think of the comparison here at the same point that this widely reported study in, in Santa Clara County, is having to be corrected because of an obvious methodological flaw that any pie should have understood was a no, it was a completely unacceptable method, right? What is it that fosters that kind of spectacular error being published in a highly regarded journal and being widely reported by the world's newspapers? Right, at the same time that we have authors collaborating on this high quality work on GitHub, and we have other people doing the work on medium? I mean, to me, this is really, the it's the vindication for those of us who have believed that peer review was the problem, not the solution.

**Heather** 56:25

And it actually provides a reason for optimism, believe it or not, you know, that, that this kind of this quality of work, both this GitHub piece and the medium piece are out there now, and are getting some attention? And are garnering careful critique, and being spread around is, is exactly as you say, some something of it's not even a consolation prize, it's you know, what? Isn't? Isn't there some evidence that peer review was, in fact, at least part of the problem?

**Bret** 56:59

And what's more, for anybody who would say, No, we need peer review to keep the junk out? Well,

**Bret** 57:04

there it is. On the internet, you can find it too. If you are a highly placed individual and you think this stuff is nonsense. Let's hear why. Let's expose that out in the open rather than behind closed doors where you usually shut work like this down. Alright.

**Heather** 57:23

How long are we at Tech? All right. All right. I just had one thing I wanted to say, as a as a correction from last time. Unless there's more that you want to say before, before we switch gears. Yeah. All right. So in the last q&a, we were talking about food, I think someone asked about the role of sugar in the diet, the clear implication of the question being we now well understood that sugar is a poison effectively. And I, I, as part of my answer said, Absolutely, and we tend to eat real sugars. And then I mentioned fructose, and that's, you know, not not a particularly healthy sugar molecule. In fact, although I'm going to pull up not yet, Zack, this is for those who are interested in seeing. Zack, if you want to now show the screen, so 2009 article, which specifically looked at the effects of fructose versus glucose sweetened beverages on people who are otherwise healthy, but somewhat overweight. They had these people increase their caloric intake every day by 500 more calories of pure fruit to support with your glucose is kind of appalling, actually, that they the human subjects review let these people do this research. But they found except for actual weight gain, all the other measures of health were much worse on a pure glucose, a pure fructose increase versus a pure glucose increased something you take that down as so that's true. That glucose is in fact, you know, if you're going to pick your sugars at the molecular level, it would be better to choose glucose over fructose. But it's also interesting to see that my brief ill advised foray into production ism, which I don't tend to engage in prompted a number of people to spell out exactly why particular molecules were better for you than others. And this is actually exactly antithetical to what the kind of answer I was trying to give and what you know what the message that I was trying to provide, which was many people have far too much faith in this modern mindset that sounds like science, but it's actually scientism that sounds like big emergent theory, but is actually reductionism. You know, it's data driven rather than hypothesis driven, and breaking things into their component parts. And then assuming that you found all the component parts and that you can accurately count them and that neither none of them are contingent on any of the others. Isn't Part of the problem. So if sugar is clearly pretty clearly a dietary toxin, but eating maple syrup eating honey eating sugars that are Merten eating fruit in moderation is far far better for you than eating those sugars that have been parsed out and turned into their constituent parts and then pieced back together for you and created you know, provided for you in an easy form so that you can bake them and you end up with a nice sheen on your cake or something and you know, I as I said before, like I do that I bake I enjoy doing it. But the the sugars that are more holistically emerging from the plants from which they came are going to be healthier alternatives.

**Bret** 1:00:44

All right. All right. So we will return in 15 minutes. Yep. So

**Heather** 1:00:50

subscribe. Yes,

**Bret** 1:00:53

we would like you to subscribe, hit like hit notify and spread the word that would be very useful to us. And we appreciate it. We will see you in about 15 minutes. There will be a link in the description to this video to the q&a section.

**Heather** 1:01:08

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