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SARS-CoV-2

Ian Lipkin was a prominent expert in the early stages of the Covid pandemic.[1][2][3][4] On January 29, 2020, to investigate the outbreak, he flew to China where he “assembled a formal written report” for the Chinese central government and helped develop a diagnostic test with scientists from China’s Central Disease Control.[5] He led the condemnation of "conspiracy theorists" that suggested a lab accident should be investigated.[6] He was a proponent of lockdowns as the best tool to control the spread of the disease,[7][8] saying "we should take a page from what the Chinese did".[9] Lipkin was also an advocate of plasma therapy as a treatment,[10] and more funding for GIDeoN, a public health organization he heads that aims to centralize world health data to aid “early detection and containment” of future pandemics.[11][12][13]Lipkin contracted Covid-19 in mid-March whilst doing media but was not hospitalized and recovered.[14]

Fact-finding mission to China

Ian Lipkin was one of the first western scientists to learn of the emergence of SARS-nCoV-2 Wuhan, saying "I first heard about this outbreak on the 15th Dec from Lu Jia-hai, a professor at Sun Yat-sen university, who runs a large one-health program (that's) been funded for about 6 months by the Chinese government. On January 29, 2020, Lipkin flew into Guangzhou China to “see for myself what the issues were” regarding the spread of SARS-nCoV-2.[15] Due to Lipkin’s long standing relationship with Chinese government officials and scientists[16] he said: “I would get more accurate information than the agencies (NIH and CDC) had about the number of cases, and what was known and not known, and who was doing what.”[17]

In Guangzhou he met with Chinese pulmonologist Zhong Nanshan, who updated him on the progress of the epidemic.[18] Lipkin then traveled to Beijing, where he met with Foreign Minister for Health Chen Zhu (□□), the Minister of Science and Technology, and the Premier, Li Keqiang,[19] who, according to the The China Straits Times, presented Lipkin with an award for his services to the PRC.[20] At these meetings Lipkin gained an understanding of the seriousness of the virus, whilst also providing input on measures to contain it.[21] In an interview with NPR, Lipkin said: “I work very closely with the people who are running these isolation areas within China. This is very, very difficult. It's stressful. I also don't like the idea of screening people with CT scans because there's a lot of radiation, which is potentially problematic as well.”[22] According to Columbia's website, Lipkin was an architect of China's bio-security system, who "helped develop the institutional infrastructure to ensure China would have the resources to detect and more rapidly respond to emerging infectious threats.”[16] Lipkin also claimed to be involved in formulating Australia's response to the virus.[23]

Media circuit upon return to US

Lipkin returned to the US around Feb 4, whereupon "I started going onto the news media and sharing as much as I could." [24] As an expert in virology who had recently been to China, his opinion was highly valued. He noted: "You can push with CNN and NBC - but that's not really where you need to push - you need to go onto Oz and talk to people who reach the entire country." [25] To this end, he said, "I never turn down Fox - it's an opportunity to preach in the wilderness."[26]

On the day of his return from China, the Columbia University website quoted Lipkin as saying: "So far, there is no evidence that the Wuhan virus will spread to the same extent as SARS."[27] Though he cautioned that this was not the time to be complacent.

Making an appearance on the Doctor Oz show on March 12 before a studio audience, Lipkin, to allay people's concerns about the need for masks, said: "One of the things I try to emphasize whenever I talk about this virus is ... we will almost certainly have additional fatalities ... but it is not as dangerous as some people may suggest - so if for example we look at this like seasonal flu - it's gonna be much less than say 1% of people - that's not to say that we won't lose lives and it's not important."[28]

Chinese government transparency

With regard to China's handling of the crisis, Lipkin said in an interview with TWIV: "They were transparent in sharing that this was a serious threat globally."[29] Lipkin added, "There's going to be some stuff that's going to come out that's going to show more insight into the origins of the outbreak. Some people are going to say this is evidence that they (Chinese Communist Party officials) withheld information - I'm gonna push back and say 'No, that's not the case.'[30] During his visit to China in late January, 2020, Lipkin "offered my services to President Xi Jin-ping, who I found very impressive."[31]

Chinese media reported that Lipkin "lauded China's transparent and professional approach". His visit was promoted by the tabloid Global Times as evidence that China was willing to cooperate with foreign scientists,[32] despite accusations by Wuhan doctors and Professor Xu Zhangrun (□□□) of a cover up.[33][34] Following his return from China, Lipkin was interviewed by two "members of U.S. intelligence."[35]

Lipkin infected with SARS-CoV-2

Starting around March 13–14, Lipkin said he had "a mild upper respiratory tract infection for about a week".[36] On Mar 20, his symptoms worsened, specifically, "a very painful headache that literally woke me from sleep... I had it for two, three days thereafter and some night sweats. That's when ...I went in and had myself tested by one of our (Columbia) faculty members."[15]

This time-frame indicates that Lipkin was potentially contagious around the time of his media appearances in a high community-contact environment. Lipkin noted from his investigative tour of China: "Anybody who has any sort of suspicious respiratory tract infection, they're gonna be all over it with diagnostic tests ... and the ability to isolate and contain - which we don't do."[37] Instead, Lipkin continued travelling across New York conducting interviews to spread his messaging. On March 18 he made his last pre-quarantined appearance on Dr. Oz, where he warned: "(This virus) will percolate below the surface - then suddenly it hits a community or an individual who's very susceptible - and then it takes off like wildfire."[38]

Later whilst recovering, he remarked: "The irony is I went to China and everybody wears masks ... no problems. I come back ... I come out of confinement - I'm doing media - I'm travelling around the city - most of the time I'm very cautious - but when you start doing media it's very difficult ... there's a lot of community contact."[39]

Treatment

Initially, Lipkin was "very eager"[40] to try plasma therapy. "My close friend, the Foreign Minister of Health of China ... Chen Zhu, was going to send me (his own) plasma ...so i could get infused."[41] Plasma therapy involves transfusing the liquid portion of the blood from a recovered patient into an infected one.[42] But finally, "I was unable to get anybody to agree to allow me to be infused with this unknown plasma from China."[40]

The "Columbia IV people" also counseled Lipkin against it, saying, "we'll just do the hydroxychloroquine".[43] A few days later Lipkin began to rally and "hiked about a mile and a half". However coming back home on a slight uphill gradient, Lipkin experienced "shortness of breath".[44] It's unclear if this excursion was on Lipkin's property or outside his quarantine zone.

As to whether hydroxychloroquine had aided his recovery, Lipkin said he had "no idea", but reported "800 mg certainly makes you feel light-headed."[45]

Advice on face masks

In response to a question about masks on the Dr. Oz show, Lipkin said: "Well...ah..the...the really ...ah ... the messaging that you're getting from WHO, CDC, and others suggests that... masks are not useful."[46] As Director of the Northeast Biodefense Center and the WHO Collaborating Center, Lipkin headed a key WHO advisory body.[47] Lipkin added that masks should be left for healthcare professionals and "emphasized" that the virus was less dangerous than the flu.[48] He was not wearing a mask or practicing social distancing whilst on the show. At the time, Lipkin was aware of what he calls a “compelling” 2003 WHO study “that showed that face masks... had a dramatic impact on community transmission”.[49] Lipkin said “I thought a long time about trying to publish this (but) I didn’t proceed - so that’s something that unfortunately is going to go in the memoirs rather than the written record.”[50]

Lipkin also related a conversation with a colleague in early-mid Feb 2020 who was conducting modelling that showed a spike in infections was likely to hit New York. “One of these people doing the modelling said ‘But you know, all we need to do is put people into facemasks and everybody can go back to work tomorrow.' I said ‘Absolutely not! That’s crazy!' First of all most people don’t know how to use facemasks... and secondly - uhm - we don’t really have any data to support that.” [51] However, there was ample data that showed masks do provide cheap, effective protection against the virus,[52][53][54][55][56][57][58] including a hospital-based study during the 2003 SARS outbreak which found, "Wearing a mask can give a person dealing with SARS patients up to 13 times more protection compared with not wearing one."[52] Furthermore, George Gao, director-general of the Chinese Center for Disease Control and Prevention, who Lipkin met with on his China trip and described as a “trusted”,[59] friend, contradicted Lipkin’s advice. In an interview with *Science*, Gao said *not* advising the public to wear masks in the U.S at the beginning of the outbreak was a “big mistake”.[60]

As an alternative to masks, Lipkin promoted a video he’d provided advice for,[61] involving the lead actors from *Contagion*, which urged people to “shelter in place”, "wash your hands", and “listen to the experts”.[62]

Proximal Origin paper

On March 17, 2020, a paper Lipkin co-authored, titled *The proximal origins of SARS-CoV-2*, was published in *Nature Medicine*.[63] The premise of the paper was that SARS-CoV-2 arose through a process of natural evolution and therefore had not leaked from a laboratory. It was widely cited by media outlets throughout the world.[64][65][66][67][68][69][70]

Wet market/pangolin theory

The paper proposed that horseshoe bats, possibly from Yunan, infected Malayan pangolin, which were smuggled into Guangdong, then transported to the Huanan Seafood Wholesale Market in Wuhan, where they were slaughtered for sale. Before their death, the bat virus is theorized to have mutated in the pangolin until it became infectious to humans. Countering the notion that the virus may have leaked from a research facility, the authors write: "...pangolins...provide a much stronger and more parsimonious explanation" of how the virus originated through natural selection.[71]

This Wuhan wet market narrative, concurred with the initial explanation of Chinese authorities,[72] [73] although a paper published on Jan 26 by Chinese researchers reported that 13 of the first 41 cases had no epidemiological link with the market, including the first known case.[74]

Regarding the mutations in pangolin, the Proximal Origin authors remarked: "For a precursor virus to acquire both the polybasic cleavage site and mutations in the spike protein suitable for binding to human ACE2, an animal host would probably have to have a high population density (to allow natural selection to proceed efficiently)."[75] (authors' brackets) Although Wikipedia describes pangolin as "solitary animals, meeting only to mate", *Proximal Origins* inferred that the 'high-population density' threshold may have been met during transportation or at the market. A *Nature* article noted, "pangolins were not listed on an inventory of items sold at the market", but didn't dismiss the idea that they may have been sold there illegally.[76] As of January 2021, no evidence had emerged that pangolin were sold at the market.

On May 26, Chinese media reported that Gao Fu (George F. Gao), director of the Chinese Center for Disease Control and Prevention, had announced that, "no viruses were detected in the animal samples" collected from the Wuhan market in early January.[77] Lipkin referred to Gao Fu as a "close friend" who he consulted with on his investigative trip to China from Jan 29-Feb 4.

On May 26, Chinese media reported that Gao Fu (George F. Gao), director of the Chinese Center for Disease Control and Prevention, had announced that, "no viruses were detected in the animal samples" collected from the Wuhan market in early January. Lipkin referred to Gao Fu as a "close friend" who he consulted with on his investigative trip to China from Jan 29-Feb 4.

On June 3, 2021, Freedom of Information obtained emails, dated Feb 1, 2020, from lead author Kristian Andersen to Anthony Fauci, stated:

"I should mention that after discussions earlier today, Eddie (Holmes), Bob, Mike, and myself all find the genome inconsistent with expectations from evolutionary theory. But we have to look at this much more closely and there are still further analyses to be done, so those opinions could still change.

"The unusual features of the virus make up a really small part of the genome (<0.1%), so one has to look really closely at all the sequences to see that some of the features (potentially) look engineered."[78]

Andersen responded that upon further analysis and discussion, it was decided the virus wasn't engineered, hence the Proximal Origin paper. The authors stand by the paper's conclusion that the virus did not originate from an Wuhan lab.[79]

Natural origins

The *Proximal Origins* paper stated: "Our analyses clearly show that SARS-CoV-2 is not a laboratory construct or a purposefully manipulated virus" and presents "strong evidence" that SARS-nCoV-2 was the result of natural selection.[63] In an interview with India Today, Lipkin re-emphasized this point: "There is no evidence whatsoever that there was an effort to create anything of this sort. There is no evidence that there are animals in which it was passaged to create this problem."[80]

However, a 2008 paper published in *Journal of Virology*, titled *Difference in Receptor Usage between SARS and SARS-Like Coronavirus of Bat Origin,* did detail a purposeful manipulation of a bat virus (SL-CoV S). A 'gain-of-function' experiment was performed to make the virus more infectious to humans. They wrote: "A series of S chimeras was constructed by inserting different sequences of the SARS-CoV S into the SL-CoV S backbone." In terms of Ace2-binding, or enhancing the ability of the virus to infect human cells, the experiment was successful: "ACE2-binding activity of SL-CoVs was easily acquired by the replacement of a relatively small sequence segment of the S protein from the SARS-CoV S sequence." The paper concluded: "It remains to be seen whether a recombinant SL-CoV containing a CS protein (e.g., CS14-608) will be capable of infecting experimental animals and causing disease."[81] An additional paper from WIV scientists and Peter Daszak in 2016 detailed "the construction of WIV1 (a bat virus) mutants."[82] According to a co-author of *Proximal origins,* Edward C. Holmes, the closest known virus was RaTG13 (96.2% identical) which was held at WIV.[83]

Lipkin maintained that the types of changes observed in SARS-CoV-2 that differentiate it from RaTG13 "would not have occurred... unless it was being passed somehow either in animals or in people" and that "if it had been modified in the Wuhan Institute of Virology, they would have used a different sequence for that purpose because this was not obvious." Lipkin lamented that “rumors have their own life - there doesn’t seem to be any good way to choke them."[84]

Reaction

Lipkin's paper was widely cited by media outlets as evidence debunking growing "conspiracy theories" that the virus may have accidentally escaped from an Wuhan lab.[85][86][87][88] In China, the tabloid CCP controlled *Global Times* said, "US scientists, such as the world's leading "virus hunter" W. Ian Lipkin, have been sticking to the facts and insisting on scientific integrity when it comes to research and cooperation with China."[89] The China Daily praised Lipkin as an "intellectual giant" who had "shared profound insights and lessons".[90] A spokesperson for the Chinese Consulate General in Sydney referenced *Proximal Origins* and WHO experts, saying "the novel coronavirus originated through natural processes and was not manipulated or produced in a laboratory." It noted: "The scientific community has ...reported that the virus is possibly related to bats and pangolins."[91]

Other international experts also agreed with Lipkin's analysis. Maureen Miller, an epidemiologist who had cooperated with WIV researchers, said the idea the virus may have escaped from a lab was an "absolute conspiracy theory",[92] while disease ecologist Peter Daszak, who had also collaborated with WIV, branded any accidental escape scenario as "pure baloney".[93] WHO emergencies chief Michael J. Ryan said WHO had "listened again and again to numerous scientists" and "(w)e are assured that this virus is natural in origin."[94] Researchers from Duke University, which operates a joint research institute with Wuhan University,[95] also agreed with the Proximal Origins' pangolin premise, stating that "SARS-CoV-2 appears to be a hybrid between bat and pangolin viruses."[96]

In addition, a Lancet petition written by Peter Daszak[97], president of EcoHealth Alliance, with links to *Proximal Origins,* was circulated through the scientific community. It stated: "The rapid, open, and transparent sharing of data (by China) on this outbreak is now being threatened by rumours and misinformation around its origins. We stand together to strongly condemn conspiracy theories suggesting that COVID-19 does not have a natural origin. We support the call from the Director-General of WHO to promote scientific evidence and unity over misinformation and conjecture."[98]

There was some dissent, however. Professor Richard Ebright of Rutgers University's Waksman Institute of Microbiology, said the paper provided "no basis to rule out a lab accident" and was itself just conjecture. Ebright pointed out that bat viruses collected by WIV researchers were also studied at the less secure Wuhan Center for Disease Control, a BSL-2 facility, "which provides only minimal protections against infection of lab workers". He cautioned that "Virus collection, culture, isolation, or animal infection at BSL-2 with a virus having the transmission characteristics of the outbreak virus, would pose substantial risk of infection of a lab worker, and from the lab worker, the public."[99] With regard to the authors' claim that the virus's 'signature' showed no signs of human intervention, thereby proving its non-lab origin, Ebright noted that WIV and US scientists had previously "constructed a series of novel chimeric viruses ...using 'seamless ligation' procedures that leave no signatures of human manipulation."[100]

Similarly, in Nov 2020, Rossana Segreto and Yuri Deigin suggested that, "genetic manipulations (may) have been performed in order to evaluate pangolins as possible intermediate hosts for

bat-derived CoVs that were originally unable to bind to human receptors." They noted that "Both cleavage site and specific RBD could result from site-directed mutagenesis, a procedure that does not leave a trace."[101]

In July 2020, researchers from the Broad Institute of MIT and the University of British Columbia cast further doubt on the hypothesis that the virus evolved naturally in pangolin. In a review of the literature related to different pangolin CoV genomes, they discovered that researchers had all relied on the same 2019 dataset sourced from a single pangolin by Liu et al.[102]

In August 2020, a collective of scientists writing on the ResearchGate platform questioned the conclusions of Proximal Origins, saying "Although based on phylogenetic analysis SARS-CoV-2 seems to be related to BatCoVs RaTG13 or RmYN02 ...(t)he host tropism pattern has major discrepancies compared to other CoVs, raising questions concerning the proximal origin of SARS-CoV-2. "[103]

Gain-of-function research

Gain-of-function (GoF) experiments aim to increase the virulence and/or transmissibility of pathogens, in order to better understand them and inform public health preparedness efforts.[104] This includes targeted genetic modification (to create hybrid viruses), the serial passaging of a virus through a host animal (to generate adaptive mutations), and targeted mutagenesis (to introduce mutations).[105] Lipkin is a listed “supporter” of GoF advocate group, *Scientists for Science*,[106] which was co-founded by Columbia colleague Vincent Racaniello.[107] The US National Institutes of Health placed a moratorium on GoF research in October 2014, and lifted the moratorium in December 2017, after the implementation of stricter controls.[108][109]

Lipkin's views

Lipkin, while not endorsing every GoF experiment, has said that "[t]here clearly are going to be instances where gain-of-function research is necessary and appropriate." In the example of Ebola, which is incapable of airborne transfer, Lipkin believes that "researchers could make a case for the need to determine how the virus could evolve in nature by engineering a more dangerous version in the lab." Lipkin believes that there should be guidelines in place to govern GoF experiments.[110]

Regarding the security level of labs in which work on dangerous pathogens can be performed, Lipkin noted, "(w)ork is more expensive and less efficient when pursued at biosafety level 4 (BSL-4) than at BSL-3 or... BSL-3-Ag (agriculture).” Whereas BSL-4 requires facilities to be inspected daily, personnel to be monitored for symptoms of disease, and virus samples, equipment, and personnel to be logged in and out, Lipkin noted: "These measures are not required at BSL-3".[111] He said BSL-3 labs (such as the ones at Columbia and Sun Yat-sen University,[112] with which Lipkin and Columbia collaborate[113]), should be allowed to conduct GoP work on globally active viruses in order to expedite research for a vaccine, though he added "there should be some sort of guidelines”.[114]

To illustrate his stance, Lipkin referenced *Contagion,* where the maverick scientist (played by Elliot Gould), conflicts with health authorities, a story which was “loosely based on my experiences during the West Nile Virus outbreak in 1999.” In the movie, the researcher is told to “cook his samples” and that all research is to be moved to the BSL-4 lab due to security concerns, but he “ultimately find(s) a way to grow the virus and make a vaccine” and save the world. In real life, Lipkin recounted: “Although our team identified the causative agent (WNV), political wrangling delayed permitting and shipment of the virus to our laboratory. To expedite diagnostics and drug development, I decided to recover the virus by transfecting genomic viral RNA.”[114] Unlike the movie, no effective vaccine for humans was found for West Nile Virus,[115] as a result of GoF research.[116]

Criticism of GoF

Ian Mackay (University of Queensland, Australia), said: “One cannot legislate for every accident or human error; all manner of things can go wrong, and if an outbreak spreads to the community the consequences could be horrendous.”[109] Marc Lipsitch (Harvard University, MA, USA) argued that GoF research is dangerous and unnecessary, saying that deliberate mutations of viruses have not produced novel insights.“There is nothing for the purposes of surveillance that we did not already know. Enhancing potential pandemic pathogens in this manner is simply not worth the risk.”[109] According to a Lancet article, the moratorium on GoP was prompted by a slew of accidents in the US at BSL facilities in 2014: "The news that dozens of workers at the Centers for Disease Control and Prevention (CDC) might have been exposed to anthrax, that vials of smallpox virus had been left lying around in an NIH storeroom, and that the CDC had unwittingly sent out samples of ordinary influenza virus contaminated with H5N1, shook faith in the country's biosafety procedures."[109] Funding for GoP research in the US resumed in 2017.[117]

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