

# The Origin of SARS-CoV-2

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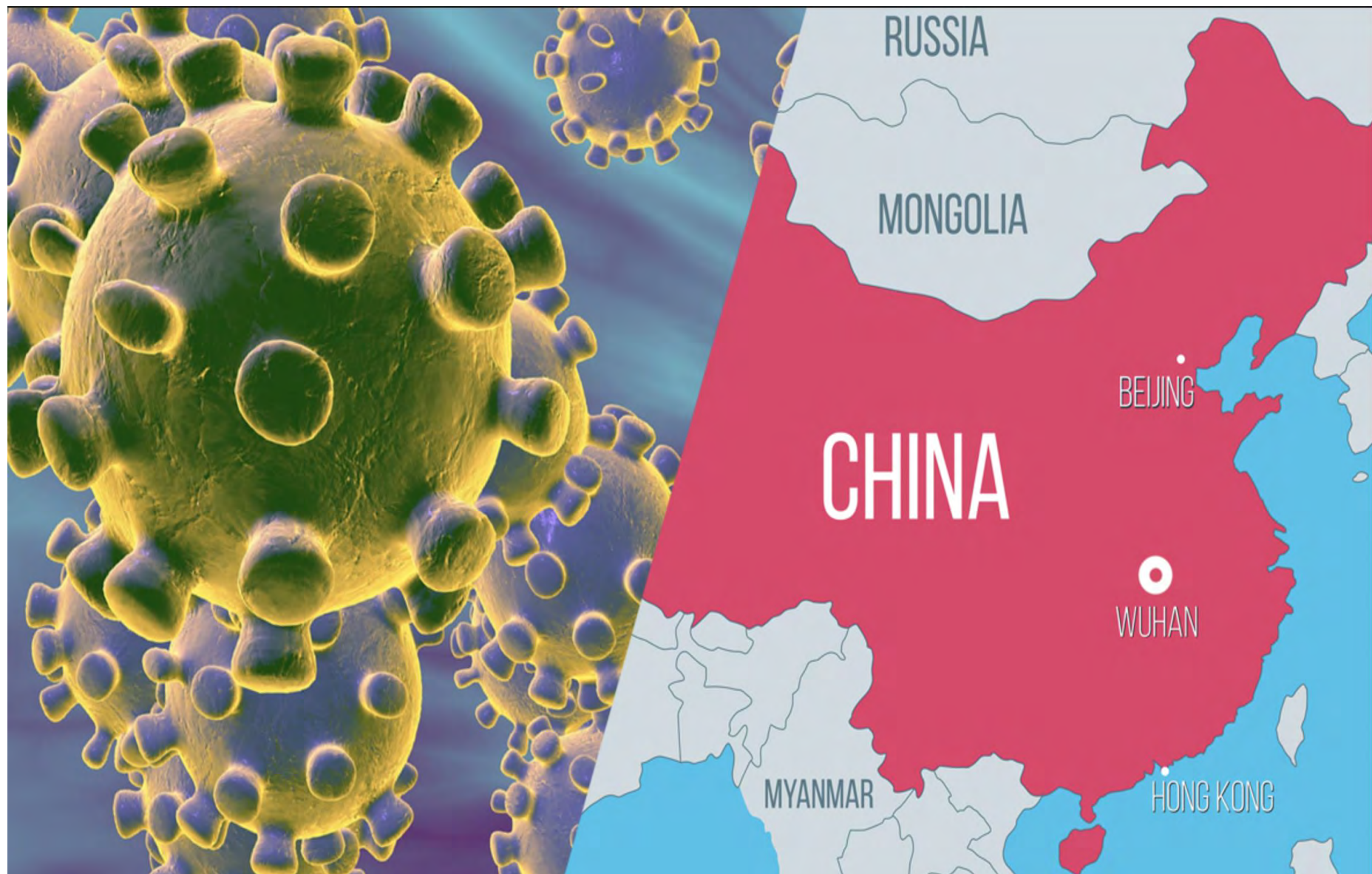
Perelman School of Medicine

The University of Pennsylvania

December 4, 2024

# Why is this issue important?

- In 2002, the SARS-1 pandemic caused 8,000 cases and 774 deaths.
- In 2012, the MERS pandemic caused 2,600 cases and 941 deaths.
- Beginning in 2019, the SARS-CoV-2 pandemic has caused more than 700 million cases and 7 million deaths.
- There will be another pandemic coronavirus. It is important to understand the exact origin of this virus to prevent or, at least, immediately respond, to the next one.



October-November 2019

# The Washington Times

*America's Newspaper*

## Coronavirus link to China biowarfare program possible, analyst says



By [Bill Gertz](#) - *The Washington Times* - Sunday, January 26, 2020





Wuhan Institute of Virology



Shi Zhengli, Wuhan Institute of Virology





Rand Paul grills Anthony Fauci, July 21, 2021

# Rand Paul

- “Dr. Fauci, we don’t know whether the pandemic started in a lab in Wuhan, but we should want to know. Instead, government authorities...say there is nothing to see here...To arrive at the truth, the U.S. government should admit that the Wuhan Virology Institute was experimenting to enhance coronaviruses ability to infect humans...The gain-of-function research has been funded by the NIH. Dr Fauci, do you still support funding the lab in Wuhan?”



## Dr. Tony Fauci

- “Senator Paul, with all due respect, you are entirely and completely incorrect that the NIH has ever done and does not now fund gain-of-function research at the Wuhan Institute.”

Did the NIH support coronavirus  
research at the Wuhan Institute of  
Virology?



# EcoHealth Alliance



中国科学院武汉病毒研究所  
WUHAN INSTITUTE OF VIROLOGY, CAS





Did the Wuhan Institute of  
Virology perform gain-of-function  
experiments?

# What is gain-of-function research?

- EcoHealth Alliance responded: “The phrase ‘gain-of-function’ has a very specific definition when applied to virological research. [Specifically], research that would genetically modify viruses, and might, in some cases, enable viruses that already are known to infect people to have ‘enhanced transmissibility or virulence’ in humans.
- The Wuhan Institute of Virology was studying bat coronaviruses that were never shown to be capable of infecting humans. Therefore, [it] was not conducting gain-of-function research.

## Dr. Shi Zheng-Li's "controversial" study

- In 2016, Dr. Shi Zheng-Li was studying a coronavirus strain called WIV-1 (Wuhan Institute of Virology-1): a bat coronavirus that could grow in monkey cells in the laboratory but didn't cause disease in people. The WIV-1 strain bore no resemblance to SARS-CoV-2. Zhengli combined WIV-1 with each of eight different bat coronaviruses that had been found in caves in and around Wuhan. None of the combination viruses that she created were more dangerous than WIV-1.



In 2022, Michael Worobey and  
coworkers found the epicenter of  
the outbreak

## CORONAVIRUS

# The Huanan Seafood Wholesale Market in Wuhan was the early epicenter of the COVID-19 pandemic

Michael Worobey<sup>1\*</sup>, Joshua I. Levy<sup>2</sup>, Lorena Malpica Serrano<sup>1</sup>, Alexander Crits-Christoph<sup>3</sup>, Jonathan E. Pekar<sup>4,5</sup>, Stephen A. Goldstein<sup>6</sup>, Angela L. Rasmussen<sup>7,8</sup>, Moritz U. G. Kraemer<sup>9</sup>, Chris Newman<sup>10</sup>, Marion P. G. Koopmans<sup>11,12</sup>, Marc A. Suchard<sup>13,14,15</sup>, Joel O. Wertheim<sup>16</sup>, Philippe Lemey<sup>17,18</sup>, David L. Robertson<sup>19</sup>, Robert F. Garry<sup>18,20,21</sup>, Edward C. Holmes<sup>22</sup>, Andrew Rambaut<sup>23</sup>, Kristian G. Andersen<sup>2,24\*</sup>

*Science* (2022) 377: 951-959





Huanan Seafood Market, December 2019



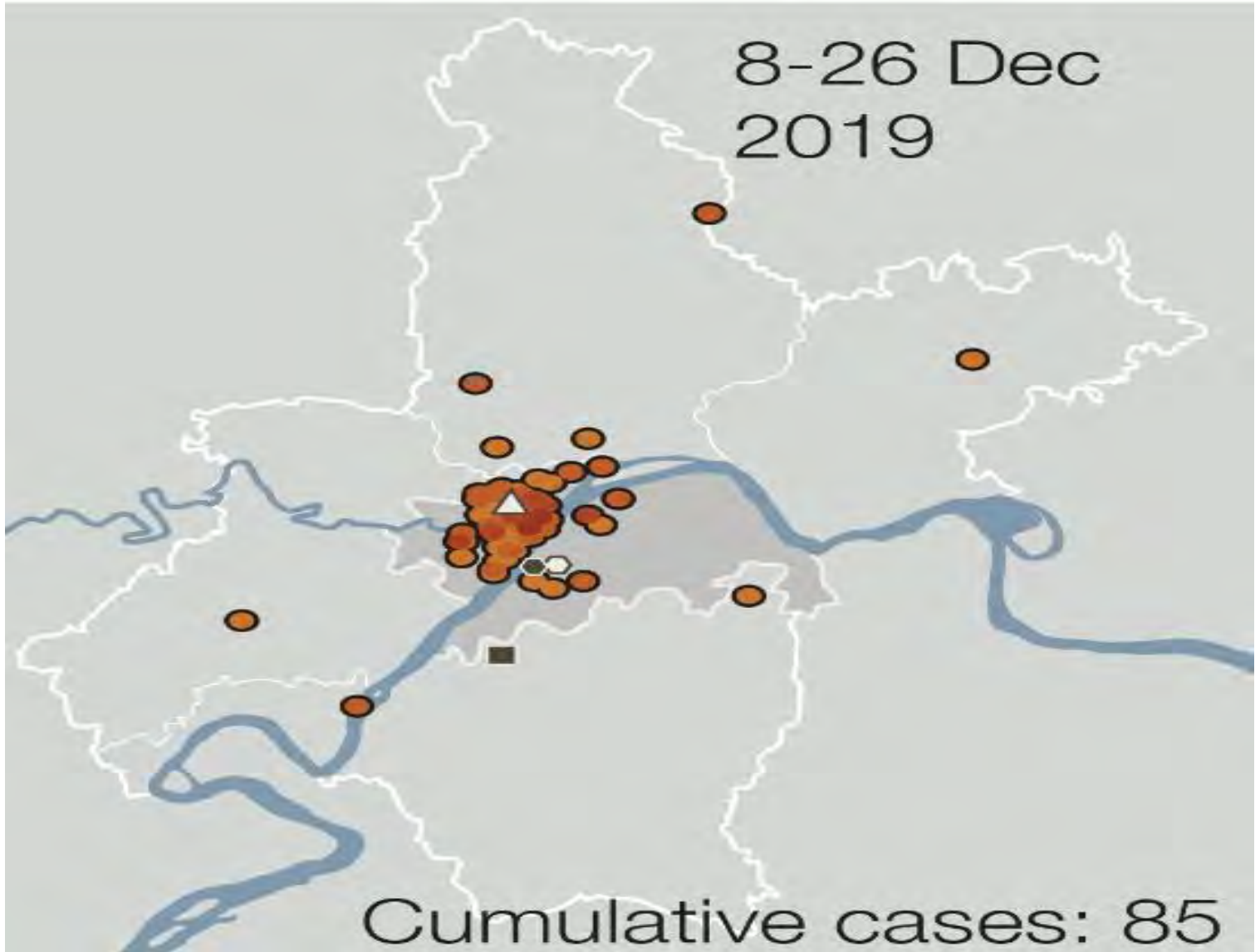
# 2 cases



# 39 Cases

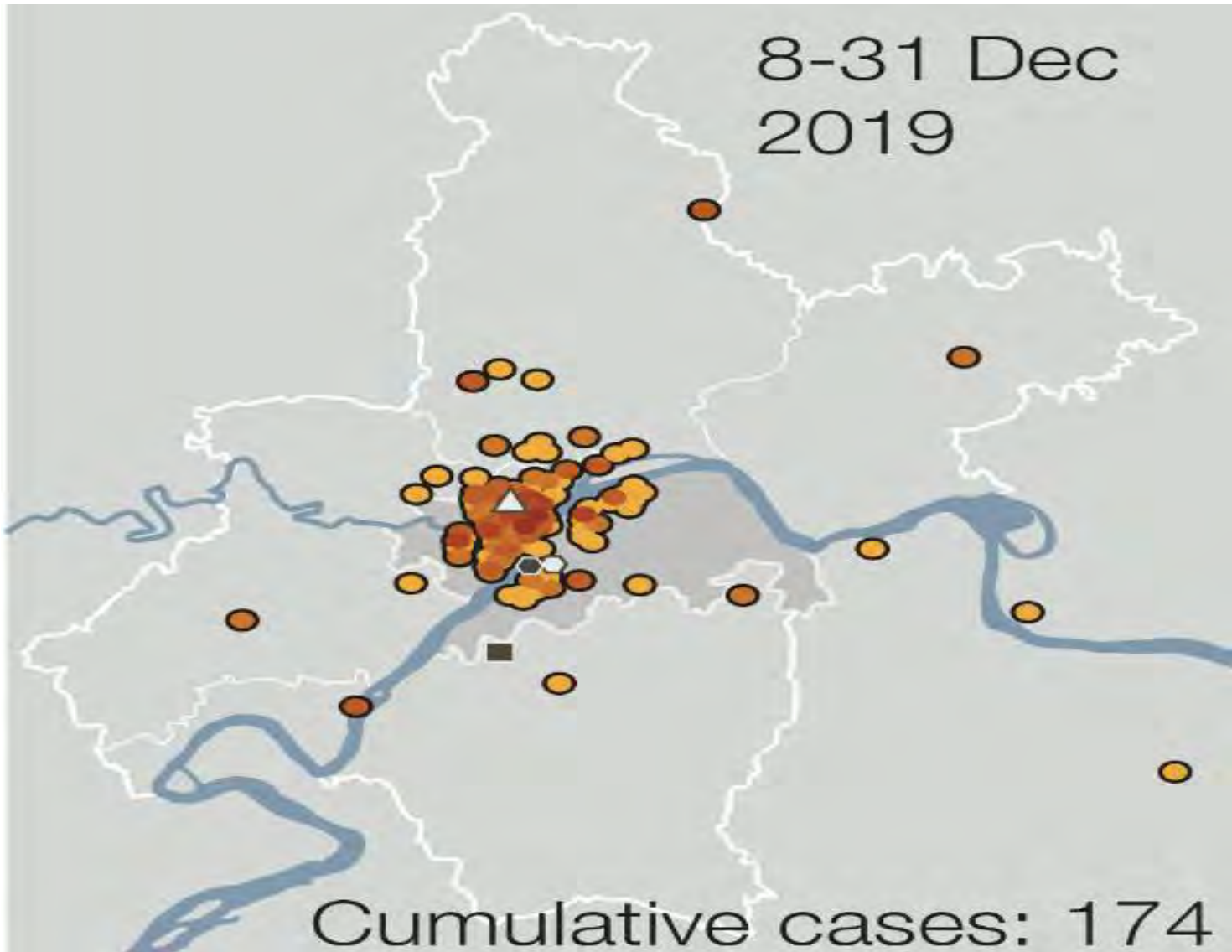


# 85 Cases





# 174 Cases





Huanan Seafood Market, December 2019



March 1, 2023

## Hopkins' Makary Tells Lawmakers COVID Lab Leak a 'No-Brainer'

— Other expert witnesses open to other origin theories



Marty Makary, MD, MPH, is a professor of transplant surgery at Johns Hopkins University

# FBI chief Christopher Wray says China lab leak most likely

1 March 2023

[Share](#)

**By Max Matza & Nicholas Yong**  
in Washington and Singapore



**FBI Director Christopher Wray has said that the bureau believes Covid-19 most likely originated in a Chinese government-controlled lab.**

# Covid-19 origin debate 'squashed', ex-CDC chief Dr Robert Redfield claims

8 March 2023

Share  Save 

**Nomia Iqbal at the hearing & Sam Cabral**

BBC News, Washington DC





# The New York Times

OPINION  
GUEST ESSAY

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## Why the Pandemic Probably Started in a Lab, in 5 Key Points

Alina Chan, June 3, 2024

This Week in Virology:

“SARS-CoV-2 virus still didn’t come  
from a lab”

# The TWiV Team



From top left, clockwise: Vincent Racaniello (virologist), Jolene Ramsey (microbiologist), Brianne Barker (immunologist), Rich Condit (viral geneticist), Alan Dove (microbiologist)

## Alina Chan, *New York Times*, June 3, 2024

- “Although how the pandemic started has been hotly debated, a growing body of evidence—gleaned from public records released under the Freedom of Information Act, digital sleuthing from online databases, scientific papers analyzing the virus and its spread, and leaks from within the U.S. government—suggests that the pandemic most likely occurred because a virus escaped from a research lab in Wuhan, China. If so, it would be the most costly accident in the history of science.

# Chan's Key Points

- “Even at hot spots where these viruses exist naturally in bats in southwestern China and Southeast Asia...**bat coronavirus spillover into humans is rare.**”






LETTER



## Serological Evidence of Bat SARS-Related Coronavirus Infection in Humans, China

Ning Wang<sup>1,2</sup> · Shi-Yue Li<sup>3</sup> · Xing-Lou Yang<sup>1</sup> · Hui-Min Huang<sup>3</sup> · Yu-Ji Zhang<sup>1</sup> · Hua Guo<sup>1,2</sup> · Chu-Ming Luo<sup>1,2</sup> · Maureen Miller<sup>4</sup> · Guangjian Zhu<sup>4</sup> · Aleksei A. Chmura<sup>4</sup> · Emily Hagan<sup>4</sup> · Ji-Hua Zhou<sup>5</sup> · Yun-Zhi Zhang<sup>5,6</sup> · Lin-Fa Wang<sup>7</sup> · Peter Daszak<sup>4</sup> · Zheng-Li Shi<sup>1</sup> 

Received: 21 November 2017 / Accepted: 8 January 2018 / Published online: 2 March 2018  
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Dear Editor,

Severe acute respiratory syndrome coronavirus (SARS-CoV) is the causative agent of the 2002–2003 SARS pandemic, which resulted in more than 8000 human infections worldwide and an approximately 10% fatality rate (Ksiazek et al. 2003; Peiris et al. 2004). The virus infects both upper airway and alveolar epithelial cells, resulting in mild to severe lung injury in humans (Peiris et al. 2003).

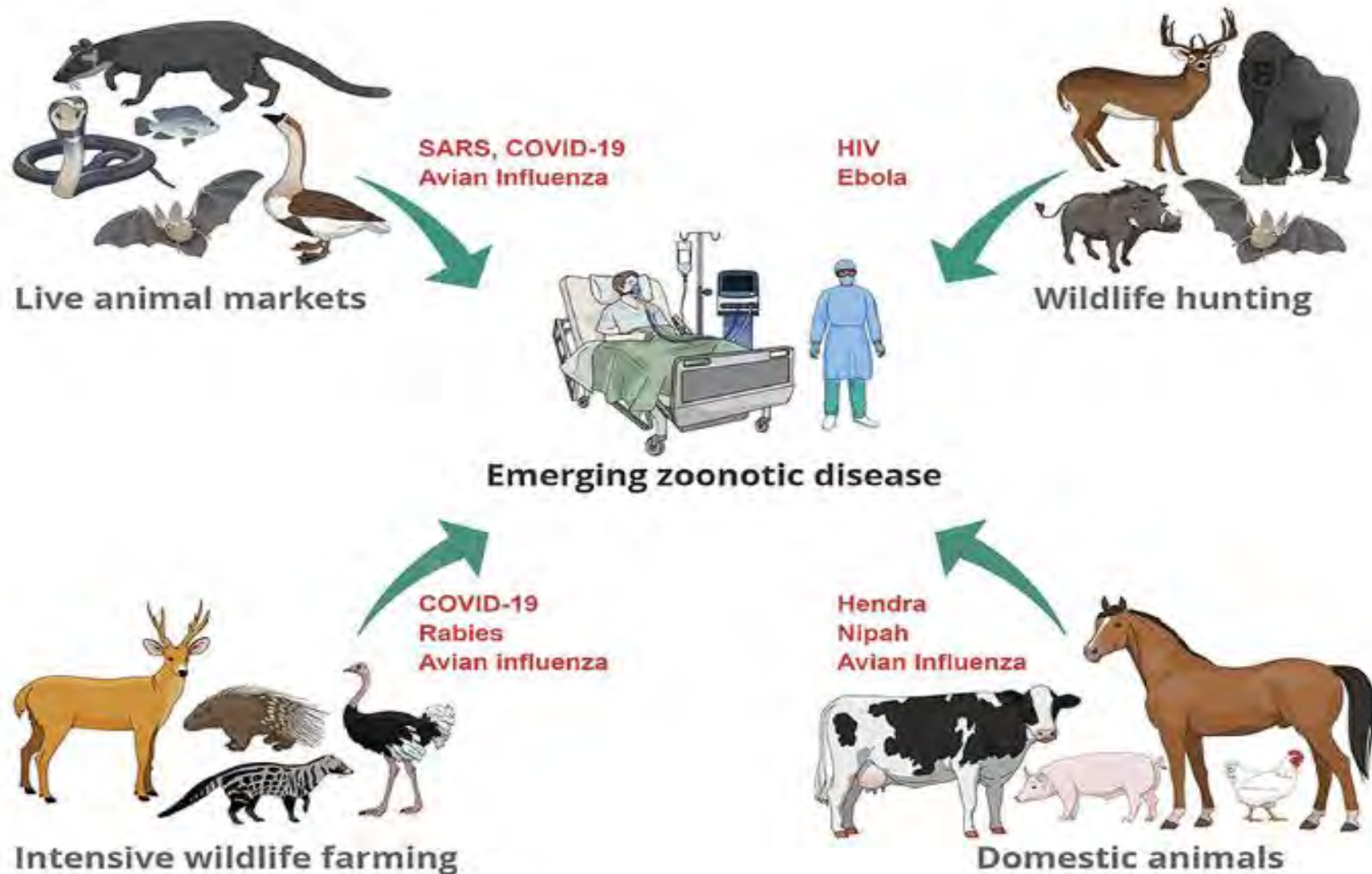
(Guan et al. 2003). Subsequent work identified genetically diverse SARSr-CoVs in Chinese horseshoe bats (*Rhinolophus sinicus*) in a county of Yunnan Province, China and provided strong evidence that bats are the natural reservoir of SARS-CoV (Ge et al. 2013; Li et al. 2005; Yang et al. 2016). Since then, diverse SARS-related coronaviruses (SARSr-CoVs) have been detected and reported in bats in different regions globally (Hu et al. 2015). Importantly, SARSr-CoVs that use the SARS-CoV receptor, angiotensin converting enzyme 2 (ACE2) have been isolated (Ge et al.

# Bat-to-human spillover events aren't rare

- Serum samples were obtained from 218 residents in four rural villages in Yunnan Province near two caves with horseshoe bats known to harbor SARS-like viruses. This region was not affected by SARS-1 pandemic. Most residents had contact with bats. 6 of 218 samples (2.7%) had antibodies to SARS-like viruses.
- Control group included 240 random blood samples from inhabitants that didn't live near caves or have contact with wild animals, including bats. 0 of 240 samples positive.

# Bat-to-human spillover events aren't rare

- Palm civets were the intermediate host in the wet market that was the origin of the SARS-1 pandemic.
- An infected civet sold in a wet market in Wuhan would average 7 human contacts per hour. This would allow the civet to infect more than 50 people per day.
- Animal-to-human spillover events are responsible for about 70 percent of human pathogens: influenza (birds), HIV (chimps), Ebola virus (bats), mpox (rodents), SARS-1 (bats), MERS (bats).



**Animal-to-human spillover events are common**



# Chan's Key Points

- “It **remains unclear** whether researchers in the Wuhan Institute of Virology possessed the precursor of the pandemic virus.”

# SARS-CoV-2 precursor

- WIV-1 is similar to SARS-1 but distant from SARS-CoV-2.
- The only remote evidence of a precursor to SARS-CoV-2 at the Wuhan Institute of Virology was RTG13, which is 1,200 base pairs different from SARS-CoV-2, far from a precursor.
- Two U.S. intelligence reports in 2020 and 2023, now declassified, showed that the Wuhan laboratory was unaware of the existence of SARS-CoV-2 until the start of the outbreak.

# Chan's Key Points

- “Scientists on the [Wuhan] team **fell ill with COVID** in the fall of 2019.”

# Respiratory illnesses in the lab

- Some scientists at the Wuhan Institute of Virology had a respiratory illness in the fall of 2019.
- None of them tested positive for SARS-CoV-2. It was, after all, influenza, RSV, and parainfluenza season.
- A U.S. intelligence assessment in 2023 confirmed that no researchers in the lab were sick with COVID prior to the outbreak.



# Chan's Key Points

- “The Wuhan lab pursued this work under **low biosafety conditions** that could not have contained an airborne virus as infectious as SARS-CoV-2.”

# Biocontainment

- Coronavirus research in the Wuhan lab was carried out under Biosafety Laboratory-2 (BSL-2) conditions.
- Biocontainment conditions, which range from BSL-1 to BSL-4, differ in requirements for personal protective equipment and various engineering measures.
- BSL-2 containment is considered adequate for laboratories currently working with SARS-CoV-2.
- BSL-2 is also considered adequate for researchers working with measles, which is far more contagious than SARS-CoV-2.

# Chan's Key Points

- “If the virus had escaped from the lab in 2019, it most likely have **gone undetected** until it was too late.”

# Lab Leak

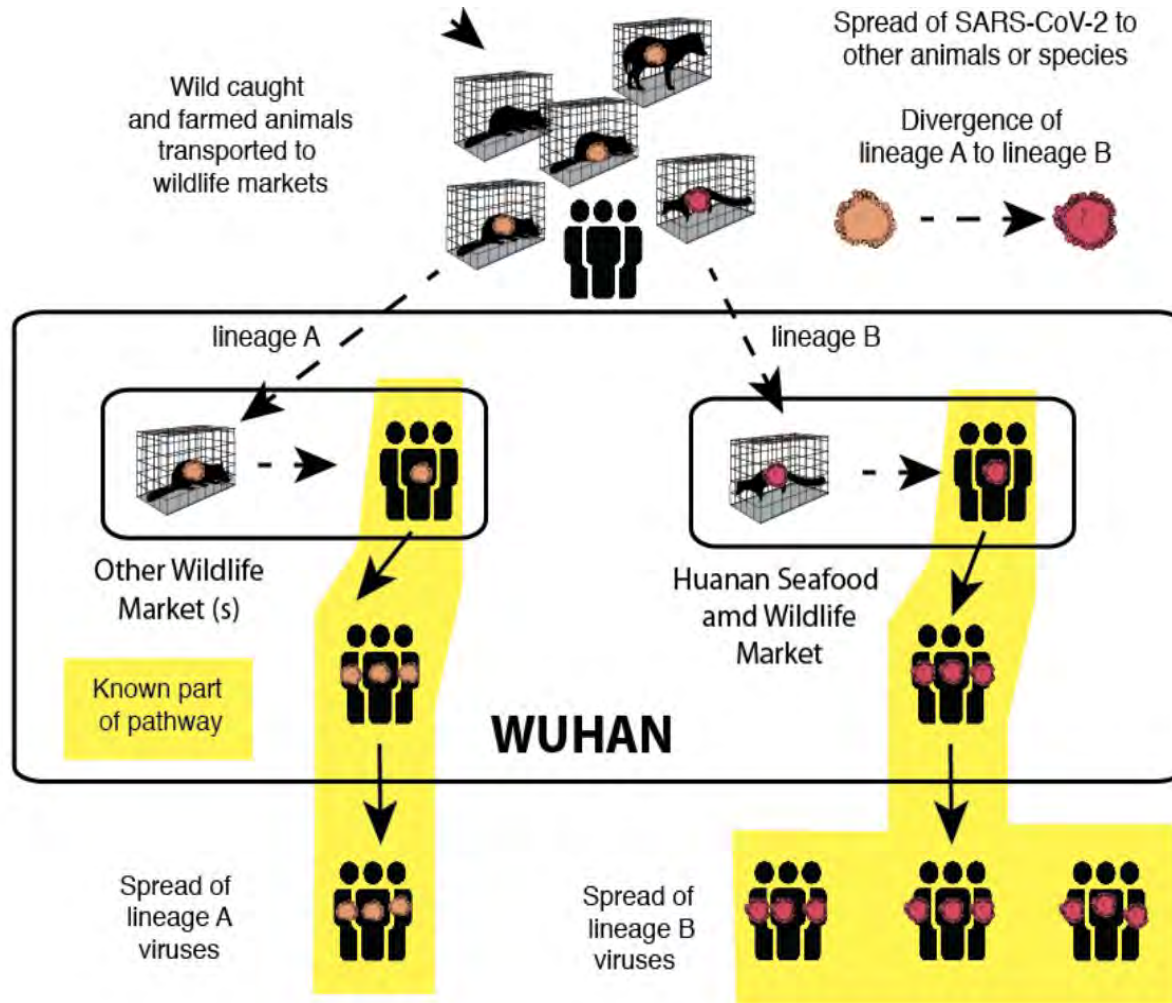
- If the virus leaked from the Wuhan Institute of Virology, then all the early cases—which were identified at the beginning of the pandemic—should have been clustered around the Institute, not 9 miles away on the other side of the Yangtze River at a site where an animal-to-human spillover event would have most likely occurred.

# Chan's Key Points

- “The hypothesis that COVID-19 came from an animal at the Huanan Wholesale Seafood Market is not supported by strong evidence. We can't distinguish between the market and a **human superspreader**.”



# Two Separate Lineages of SARS-CoV-2



# Human Superspreaders

- The presence of two separate lineages of SARS-CoV-2 further supports the natural origin of this virus.
- If we are to believe Chan, two human superspreaders who were infected with two different lineages in the Wuhan lab, both traveled to the southwestern section of the Huanan Wholesale Seafood Market and introduced the virus.
- Why didn't either of those superspreaders go to any of the other 10,000 places in Wuhan where a pandemic would have reasonably started?

# Chan's Key Points

- “**Not a single infected animal** has ever been shown to be infected with SARS-CoV-2.”

|  | <b>SARS</b><br>2002 | <b>MERS</b><br>2012 | <b>COVID-19</b><br>2019 |
|--|---------------------|---------------------|-------------------------|
| Infected animals found   | Yes                 | Yes                 | No                      |
| Earliest known cases exposed to live animals   | Yes                 | Yes                 | No                      |
| Antibody evidence of animals and animal traders having been infected   | Yes                 | Yes                 | No                      |
| Ancestral variants of the virus found in animals   | Yes                 | Yes                 | No                      |
| Documented trade of host animals between the area where bats carry closely related viruses and the outbreak site | Yes                 | Yes                 | No                      |





Huanan Wholesale Seafood Market, January 2020



# Chan's Key Points

- “Chinese authorities have **not done an intense search** for animals infected with SARS-CoV-2.”

# The New York Times

## *New Data Links Pandemic's Origins to Raccoon Dogs at Wuhan Market*

Genetic samples from the market were recently uploaded to an international database and then removed after scientists asked China about them.

March 16, 2023

## *New York Times*

- “An international team of virus experts...found genetic data from a market in Wuhan, China, linking the coronavirus with raccoon dogs...adding evidence to the case that the worst pandemic in a century could have been ignited by an infected animal.
- The genetic data was drawn from swabs taken from in and around the Huanan Seafood Wholesale Market starting in January 2020, shortly after the Chinese authorities had shut down the market...By then, the animals had been cleared out, but researchers swabbed walls, floors, metal cages and carts often used for transporting animal cages.”

# The Smoking Gun

- In the southwestern section of the Huanan Market, SARS-CoV-2 virus genome was detected in carts, drains, a feather-and-hair remover, a metal cage, and machines that process animals after they've been slaughtered.
- In the same specimens, researchers found mammalian DNA consistent with raccoon dogs, bamboo rats, and palm civets, all of which could have been intermediate hosts for bat coronaviruses to enter the human population.

## Article

# Genetic tracing of market wildlife and viruses at the epicenter of the COVID-19 pandemic

Alexander Crits-Christoph,<sup>20</sup> Joshua I. Levy,<sup>3</sup> Jonathan E. Pekar,<sup>21</sup> Stephen A. Goldstein,<sup>22</sup> Reema Singh,<sup>4</sup> Zach Hensel,<sup>12</sup> Karthik Gangavarapu,<sup>7</sup> Matthew B. Rogers,<sup>4</sup> Niema Moshiri,<sup>23</sup> Robert F. Garry,<sup>9,10,11</sup> Edward C. Holmes,<sup>6</sup> Marion P.G. Koopmans,<sup>8</sup> Philippe Lemey,<sup>19</sup> Thomas P. Peacock,<sup>13,14</sup> Saskia Popescu,<sup>15</sup> Andrew Rambaut,<sup>5</sup> David L. Robertson,<sup>16</sup> Marc A. Suchard,<sup>17</sup> Joel O. Wertheim,<sup>18</sup> Angela L. Rasmussen,<sup>4</sup> Kristian G. Andersen,<sup>3,\*</sup> Michael Worobey,<sup>2,\*</sup> and Florence Débarre<sup>1,24,\*</sup>

<sup>1</sup>Institut d'Écologie et des Sciences de l'Environnement (IEES-Paris, UMR 7618), CNRS, Sorbonne Université, UPEC, IRD, INRAE, Paris, France

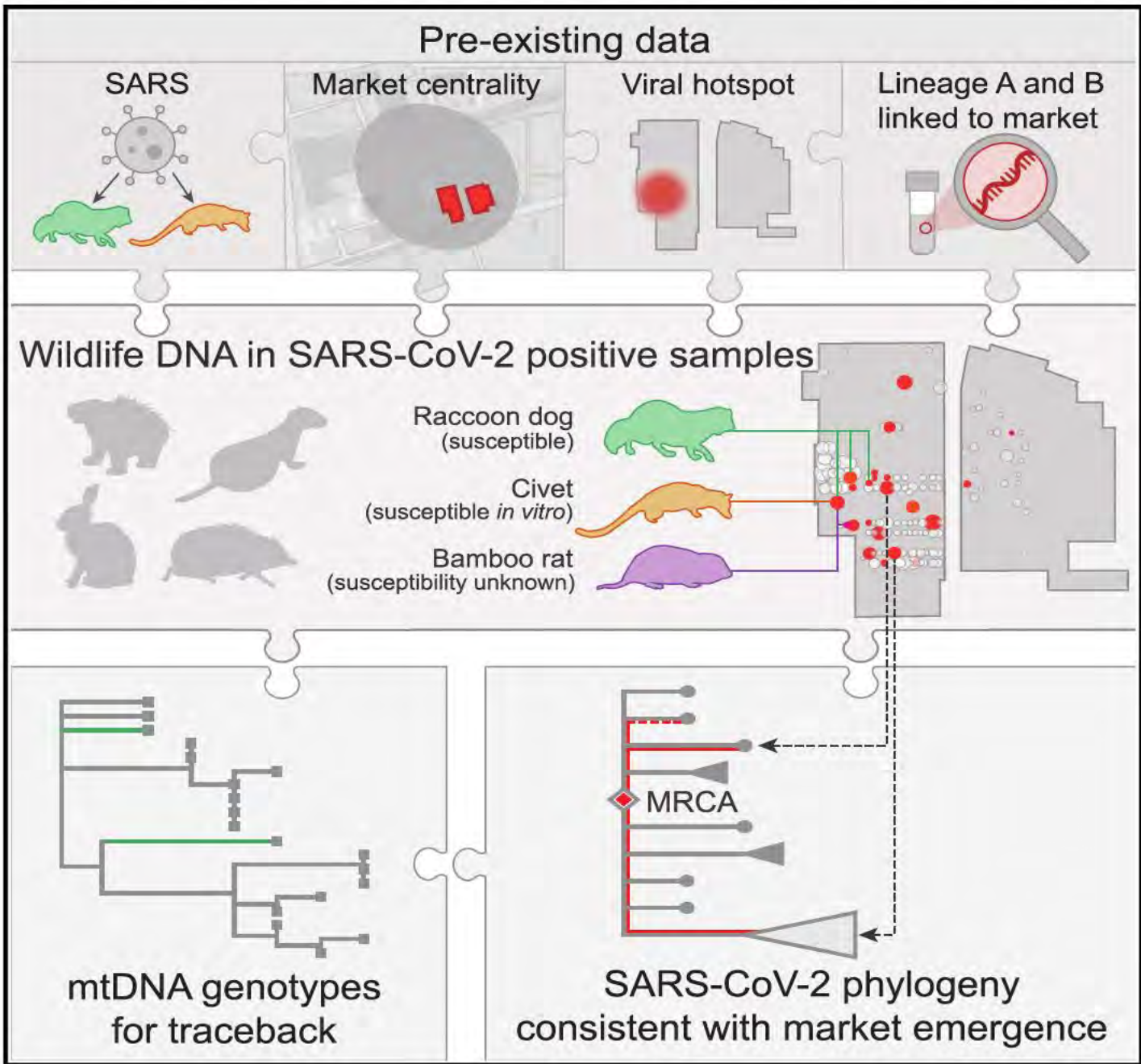
<sup>2</sup>Department of Ecology and Evolutionary Biology, University of Arizona, Tucson, AZ, USA

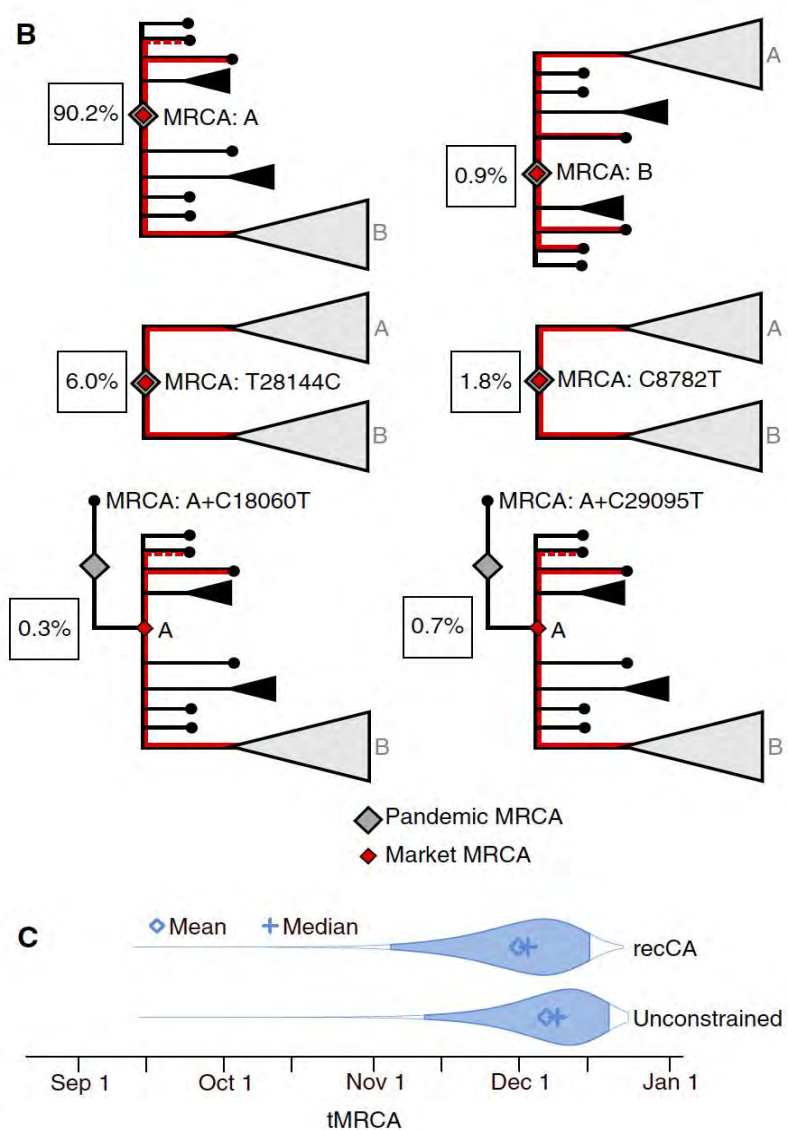
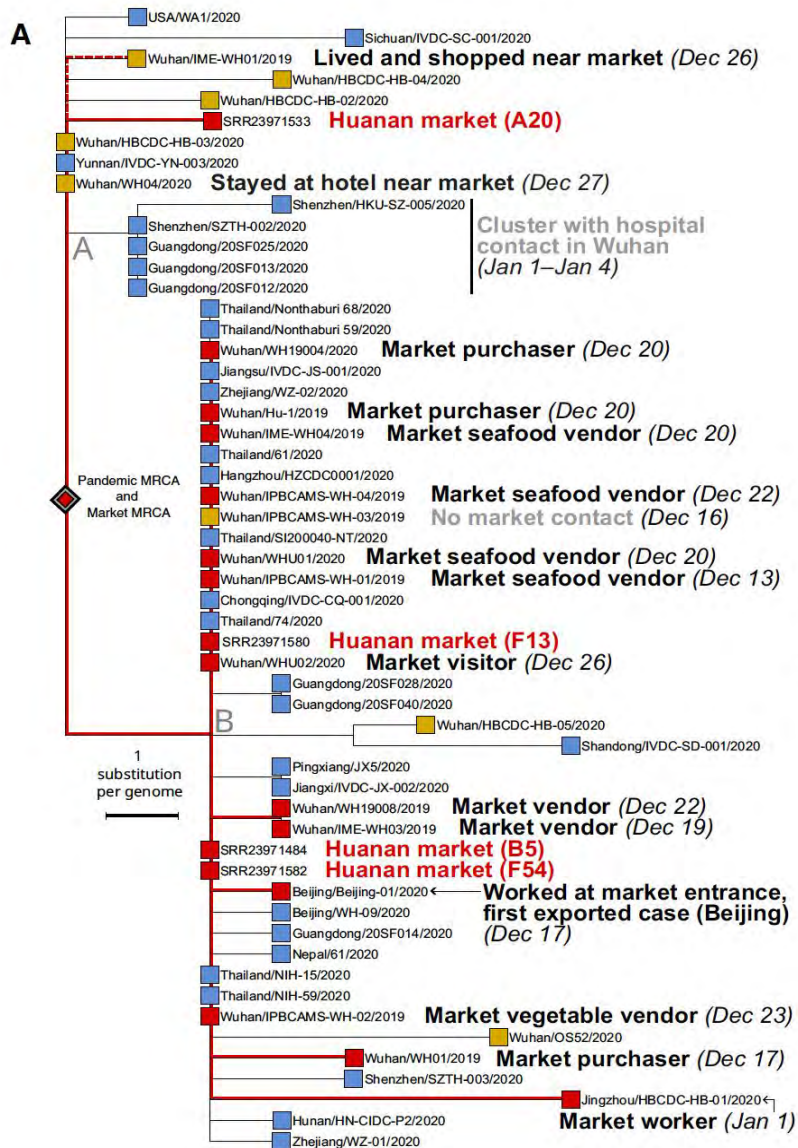
<sup>3</sup>Department of Immunology and Microbiology, The Scripps Research Institute, La Jolla, San Diego, CA 92037, USA

<sup>4</sup>Vaccine and Infectious Disease Organization, University of Saskatchewan, Saskatoon, SK, Canada

*Cell* (2024) 187: 5468-5482.







Phylogenetic analysis of SARS-CoV-2 from early Covid-19 cases compared with virus sequences obtained from the Huanan Market

The lab leak theory requires belief  
in the following series of events

# The Lab Leak Theory

- The Wuhan lab was working with viral strains that were precursors to SARS-CoV-2.
- According to Chan, the Wuhan lab took these SARS-CoV-2-like strains and forced them to adapt to bats, pigs, primates, civets, and humanized mice.
- Laboratory personnel were inadvertently infected with SARS-CoV-2.
- Two lab workers infected with different lineages of SARS-CoV-2 traveled to the southwestern section of the Huanan Wholesale Seafood Market and became superspreaders.

# The Lab Leak Theory

- These two lab superspreaders could have traveled to any of the 10,000 other places in Wuhan to begin a pandemic, but instead they traveled to the same stall at the southwestern section of the Huanan Wholesale Seafood Market where civets, racoon dogs, red foxes, bamboo rats, and other animals known to be susceptible to SARS-like viruses were being sold illegally.

Extraordinary claims should be  
backed by extraordinary evidence

--Carl Sagan



# Animal-to-human spillover event

- The first cases of Covid-19 occurred in vendors who worked in the southwestern section of the Huanan market. Early cases were tied directly or indirectly to the Huanan market.
- No early cases of Covid-19 occurred in or around the Wuhan Institute of Virology.
- Genetic evidence of SARS-CoV-2 was detected in carts, drains, a feather-and-hair remover, a metal cage, and machines that process animals after they've been slaughtered.

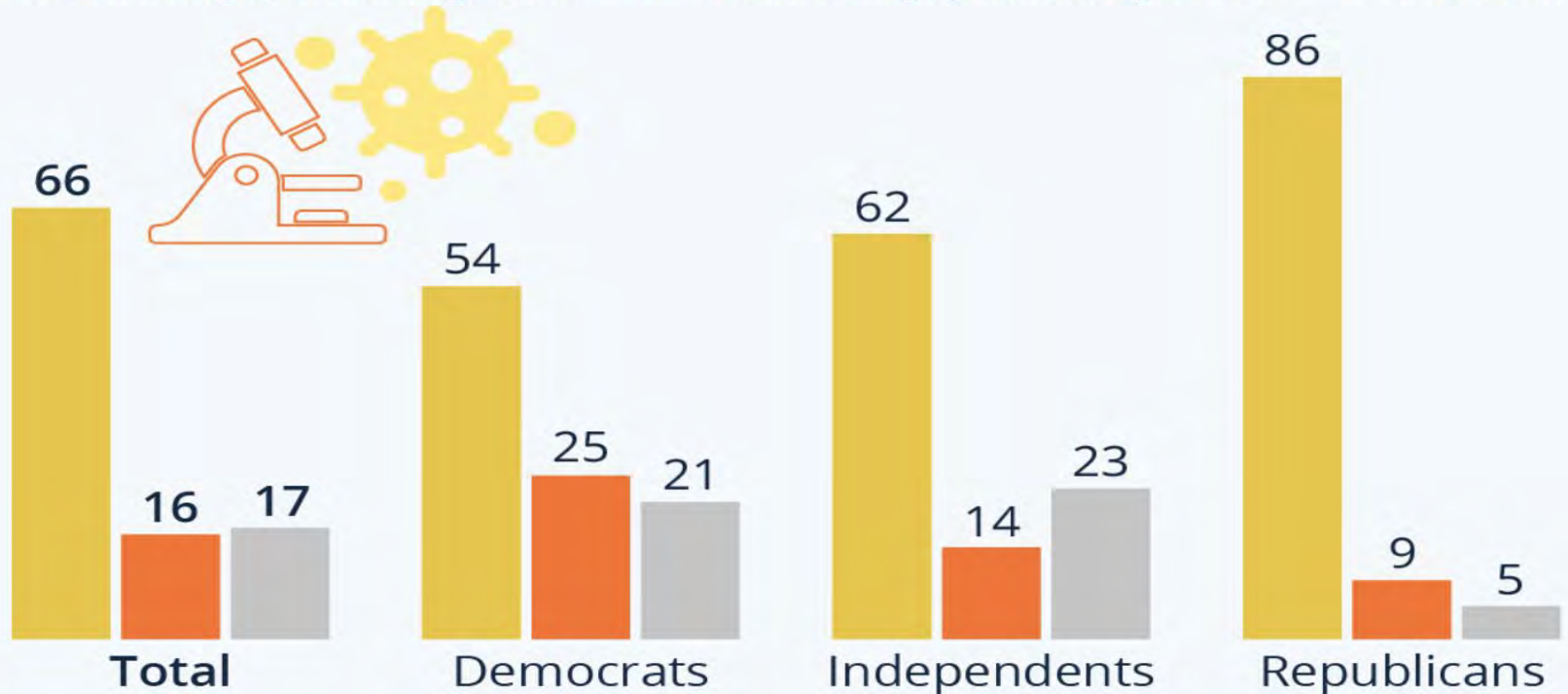
# Animal-to-human spillover event

- Mammalian DNA from palm civets, bamboo rats, and raccoon dogs were detected in specimens containing genetic evidence of SARS-CoV-2.
- These events mimic the SARS-1 animal-to-human spillover that occurred in Foshan, Guangdong Province in November 2002 that resulted in a pandemic. Palm civets served as the intermediate host in that outbreak.

# Two Thirds of U.S. Adults Think Covid Likely Started in a Lab

U.S. adults' opinion on the theory that Covid-19 originated from a laboratory in China (in percent)

■ Definitely/probably true ■ Definitely/probably false ■ Not sure



1,498 U.S. adults surveyed Mar. 4-7, 2023

Source: The Economist/YouGov

The lab leak theory has been a  
costly, unnecessary diversion



Dr. Fauci answers questions about the U.S. role in supporting the Wuhan lab before a congressional committee, June 3, 2024



But who is really to blame?



Mother Nature



Chinese government and Chinese health authorities bear much of the blame for the events in Wuhan

# Avoiding the next pandemic

- Chinese officials consistently claimed that no illegal mammals had been sold at their markets.
- Four markets in Wuhan sold illegal wildlife, including civets and raccoon dogs, known reservoirs for SARS-like viruses.
- Between May 2017 and November 2019, Chinese market vendors sold about 47,000 live animals across 38 species, 31 of which were protected under Chinese law and were therefore sold illegally.
- Chinese officials failed to learn from the SARS-1 pandemic.

# Avoiding the next pandemic

- Chinese officials immediately destroyed animals likely to have been the source of the virus, making it difficult for scientists to find the source of the outbreak.
- Chinese officials were reluctant to allow an international team of scientists to enter China and examine the Wuhan market or the Wuhan lab, only fueling conspiracy theories like a lab leak.
- Public health officials in other countries shouldn't have had to depend on a whistleblower in Wuhan to alert the world that a novel virus was spreading unchecked throughout the city.





Dr. Li Wen-liang, 34-year-old ophthalmologist



976 x 549

Dr. Li Wen-Liang, February 6, 2020

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