[redacted]

From: [redacted]
Sent: Tuesday, June 8, 2021 12:35 PM
To: [redacted]
Subject: New Daszak video going around

Classification: [redacted]

Classified By: [redacted]
Derived From: [redacted]
Declassify On: [redacted]
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Hey guys,

Just saw this video online. It's from a 2016 NY Academy of Medicine meeting where Daszak talks about his colleagues in China manipulating the spike protein on coronavirus to make them more virulent.

Sorry I can't glide the video over. I have a contact in OSE but we don't have access to a common shared drive location to drop the video. You'll have to retype the link into your browser on the low side.

https://rumble.com/vi8qwj-fauci-funded-daszak-describes-colleagues-in-china-manipulating-viruses-into.html

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Classification: [redacted]

[redacted]

From: [redacted]
Sent: Thursday, May 27, 2021 5:37 AM
To: [redacted]
Subject: Office of the Director of National Intelligence News Summary for Thursday, May 27, 2021 - [Link to Attachment(s)]

Classification: UNCLASSIFIED
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OFFICE OF THE DIRECTOR OF NATIONAL INTELLIGENCE NEWS SUMMARY

TO: THE DIRECTOR AND SENIOR ODNI STAFF

DATE: THURSDAY, MAY 27, 2021 5:30 AM EDT

TODAY'S TABLE OF CONTENTS

Contractors By End Of 2023. <>
+ US Lawmakers Seek Funding For Defense Industrial Facilities. <>

JUSTICE DEPARTMENT:
+ DOJ Reportedly Mulling Further Charges Over 2016 Election Misinformation. <>
+ Sources: DOJ Prepared To Sue Developer If He Does Not Register As Lobbyist Under FARA. <>

U.S. NEWS:
+ New Research Indicates COVID Immunity Could Last Over A Year. <>
+ GOP Expected To Filibuster January 6 Panel Thursday. <>
+ Biden Calls For Congressional Action In Wake Of San Jose Mass Shooting. <>
+ Amid Rising Crime, Cities Restore Police Funding. <>
+ Biden Expected To Tap Burns As Ambassador To China, Garcetti As Ambassador To India. <>
+ ATF Nominee Faces Pushback From GOP, But Likely To Be Confirmed. <>
+ Jean-Pierre Presides Over Historic First Televised White House Briefing. <>
+ Biden Under Pressure To Confront Anti-Semitism After Attacks. <>
+ Sen. Tim Scott: “June Or Bust” For Reaching Deal On Police Reform. <>
+ ExxonMobil Dealt “Major Blow” In Board Shake Up. <>
+ Diplomats Ask State Department To Provide More Support For “Havana Syndrome” Victims. <>
+ Execs Say Biden Plan To Import Metals For EVs Could Keep Us From Meeting Climate Goals. <>
+ Mayorkas Defends Title 42. <>
+ Democrats Unable To Move Forward With Plan To Lower Prescription Drug Prices. <>
+ Columnist Highlights GAO Report About Making Government More Efficient, With Savings Of $1B Or More. <>
+ Michigan Secretary Of State “Deeply Concerned About The Future Of Our Democracy.” <>

INTERNATIONAL NEWS:

Africa:
+ After Military Takeover, Interim President, PM Of Mali Resign. <>
+ Suspected Islamist Attack Kills 22 In The Democratic Republic Of Congo. <>
+ UN Official Warns That Ethiopia’s Tigray Region Is On The Brink Of Famine. <>
+ NBC: US “Quietly Returning” To Libya. <>
+ Report On Italian Ambassador’s Death In Congo Indicates “Poorly Planned, Clumsily Executed Act.” <>

Near East:
+ Blinken Departs Middle East With Cease-Fire Intact, Pledges To Aid With Rebuilding. <>
+ Assad Votes In Former Rebel Stronghold, Touts Election As Evidence Of Syrian Unity. <>

+ Iraqi Forces Arrest Militia Commander Over Alleged Involvement In Attacks On Air Base Used By US. <>
+ Hamas Leader Says 80 Fighters Killed. <>

Iran:
+ IAEA Head: Iran Enriching Uranium At Weapons-Grade Level. <>

Europe:
+ WHO COVAX Program Falls Short Despite Intentions Of Developed Nations, Vaccine Manufacturers. <>
+ EU Tells Brussels Court AstraZeneca Failed To Fulfill Its Vaccine Commitments. <>
+ Slovakia Authorizes Use Of Russia's Sputnik V Vaccine. <>
+ France Praises YouTube Users Who Resisted Vaccine Misinformation Campaign. <>

Russia & Eurasia:
+ Lukashenko Accuses West Of Engaging In "Hybrid War" Against Belarus. <>
+ Sasse Among Those Critical Of Biden's Decision To Meet With Putin. <>

China:
+ NSC's Kurt Campbell: Broad Engagement With China "Has Come To An End." <>
+ CRS: China Supplying Nuclear, Missile Technology To North Korea, Iran. <>
+ Senate GOP Could Block Bipartisan Plan To Confront China. <>
+ Senate Legislation Would Add National Security Reviews Of Chinese Donations To US Universities. <>
+ Tesla To Establish Data Center In China For Local Data Storage. <>
+ Closed Chinese Consulate In Houston Was "Major Hub" For Espionage, Study Indicates. <>

East Asia:
+ Japan Facing New COVID Surge Ahead Of Summer Olympics. <>
+ Espionage Trial Of Australian Blogger To Open In China On Thursday. <>
+ Campbell: US Hoping For Fall Quad Meeting On Infrastructure. <>
+ Kim Vows "Uncompromising Struggle" To Build Socialism In North Korea. <>
+ McConnell Praised Administration For Burma Coup Response. <>
+ US Envoy Confident Taiwan Can Deal With Spike On Covid Cases. <>

South Asia:
+ Taliban Warns Afghanistan's Neighbors Against Hosting US Troops. <>
+ Pakistani Journalist Alleges Intelligence Agents Attacked Him In His Apartment. <>
+ WhatsApp Sues Indian Government Over Message Traceability Rules. <>
+ NYTimes: Official Figures "Grossly Understate" Pandemic Impact In India. <>

Western Hemisphere:
+ AMLO's Party Expected To Maintain Control Of Lower House. <>
+ Mayoral Candidate Killed In Mexico, 34th Of This Election Cycle. <>

+ Former Bolivian Interior Minister Arrested In US For Money Laundering. <>

CYBERSECURITY:
+ Colonial Pipeline Rebuffed TSA Security Review Before Hack. <>
+ Biden Budget Request To Grow Cyber Command. <>
+ Russia's FSB Reports "Unprecedented" Hacking Campaign. <>
+ Facebook: Russia Top Producer Of Disinformation. <>
+ Hackers Release New Zealand Patient Data. <>
+ Canada Post Notifies Business Customers Of "Data Breach Affecting 950K Customers." <>
+ Bipartisan Encryption Bill Introduced In House. <>

EDITORIAL ROUNDUP:
+ Washington Post. <>
+ Wall Street Journal. <>

THE BIG PICTURE:
+ Headlines From Today's Front Pages. <>

Leading The News:

BIDEN DIRECTS INTELLIGENCE COMMUNITY TO INVESTIGATE ORIGINS OF CORONAVIRUS. <>
CNN

(5/26,Judd, 89.21M) reports on its website that on Wednesday, President Biden "said...he has directed the US intelligence community to redouble their efforts in investigating the origins of the Covid-19 pandemic and report back to him in 90 days." According to CNN, "The announcement comes after a US intelligence report found several researchers at China's Wuhan Institute of Virology fell ill in November 2019 and had to be hospitalized – a new detail that fueled further debate about the origins of the coronavirus pandemic."

USA Today

(5/26,Groppe, 12.7M) reports that Biden "also said he wants to know what further areas of inquiry are needed, including specific questions for China." But USA Today says "it's not clear how the administration will get cooperation from China, which has accused the United States of hyping 'the lab leak theory.'" On Wednesday, White House Principal Deputy Press Secretary Karine Jean-Pierre said, "We're just going to continue to work with (the World Health Organization) and WHO is going to continue to work with China on this." USA Today reports that Jean-Pierre "declined to say whether the 90-day report's conclusions will be made public."

Reuters

(5/26) reports that Biden "said that U.S. intelligence are looking into two different scenarios, that they do not have high confidence in their current

conclusions and that they are divided on which is most likely."Politico

(5/26, Leonard, 6.73M) says that in his statement, Biden "notably did not detail the two theories between which the intelligence community is split," but "did note that he had ordered a review of the pandemic's origins, 'including whether it emerged from human contact with an infected animal or from a laboratory accident.'" According to Politico, Biden "said two elements of the intelligence community lean toward one scenario while another element of the community leans toward another, 'each with low or moderate confidence.'" However, "the remainder of the intelligence community, which Biden said constituted its majority, 'do not believe there is sufficient information to assess one to be more likely than the other.'"

The New York Times

(5/26, Gamio, Glanz, 20.6M) reports that "in the past several days, the White House had downplayed the need for an investigation led by the United States and insisted that the World Health Organization was the proper place for an international inquiry." According to the Times, "Biden's statement was an abrupt shift, though officials declined to be specific about the shift."

The Washington Post

(5/26, 10.52M) reports that on Tuesday, Health and Human Services Secretary Becerra "told an annual ministerial meeting of the World Health Organization that international experts should be given 'the independence to fully assess the source of the virus and the early days of the outbreak.'" According to the Post, "Becerra's remarks...signaled that the Biden administration would continue to press the WHO to expand its investigation to determine the virus's origins." TheWall Street Journal

(5/26, A1, Leary,Gordon, Subscription Publication, 8.41M) reports that China responded to Secretary Becerra, arguing that the WHO completed its investigation earlier this year. The Chinese representative added that the WHO should begin investigating other nations instead.

The Washington Post

(5/26, 10.52M) says, "The new message from the White House reflects the rapidly changing views about the origins of the virus." According to the Post, "In recent weeks, a theory has gained more support that the source of the coronavirus...may have emerged from the Wuhan Institute of Virology in China, though that is far from proved." The Post adds, "Some Republicans had pushed the idea early on, including former president Donald Trump, who at times used inflammatory language to describe the virus and its origins in China. But the idea was dismissed by many influential scientists and Democrats, who viewed the GOP focus on the lab as part of a larger attack on China that fueled an increase in hate crimes against Asian Americans."

CNN

(5/26,Judd, 89.21M) notes that it “reported on Tuesday

that Biden’s team shut down a closely held State Department effort launched late in the Trump administration to prove that Covid-19 originated in a Chinese lab over concerns about the quality of its work.” However,The Hill

(5/26, Schnell, 5.69M) reports that “individuals in the Trump administration who worked on the project...rebuffed criticisms of their work...contending that their intention was to analyze scientific research and information from the U.S. intelligence community that bolstered the Wuhan lab leak theory, and reveal more information on how the virus could have leaked from a lab.”

Politico

(5/26,Desiderio, Banco, 6.73M) reports that at the same time, “support is growing in Congress for a probe of the origins of the Covid-19 pandemic, an effort that could pit Democratic lawmakers against the Biden administration as China hawks draw new attention to the theory that the virus leaked from a Wuhan lab.” According to Politico, “The ongoing discussions on Capitol Hill represent a remarkable bipartisan agreement” after Democrats “previously dismissed the lab leak theory as a GOP talking point. ... ‘As we analyze what went wrong and what we can do in the future, we have to have answers to these questions, too,’ said Sen. Tim Kaine (D-Va.), a member of the Senate’s health committee.”

Lauren Frias writes for Insider

(5/26, 2.74M) that “Rep. Adam Schiff said Wednesday it is ‘critical’ for the US to finish its investigation into the origins of COVID-19 to ‘avoid any premature or politically-motivated conclusions.’”

CNBC

(5/26,Wilkie, Mendez, 7.34M) reports on its website that “the hypothesis that the virus may have escaped from a Chinese laboratory, while initially dismissed by some as a conspiracy theory, has in recent months gained more mainstream traction.” CNBC points out that Centers for Disease Control and Prevention Director Rochelle Walensky “recently said in Senate testimony that a lab-leak origin ‘certainly’ was ‘one possibility.’” CNBC adds that “the scrutiny on that lab ramped up this week when The Wall Street Journal reported that three researchers there had been sick with Covid-like symptoms in November 2019, shortly before the first cases of the virus were reported.”

Primetime media coverage of Biden’s announcement includes NBC Nightly News

(5/26, story 2, 1:50, Holt, 4.76M),CBS Evening News

(5/26, story 2, 2:20,O'Donnell, 3.75M), and ABC World News Tonight

(5/26, story 2, 3:20,Muir, 6.02M).

Fox News

(5/26,Singman, 23.99M), Bloomberg

(5/26,Wingrove, 3.57M), and The Hill

(5/26,Chalfant, Weixel, 5.69M) provide additional coverage of Biden's announcement.

Senate Unanimously Passes Bill Ordering ODNI To Declassify Documents On COVID-19's Origin. Newsweek

(5/26,Villarreal, 2.67M) reports The Senate has unanimously passed "a bill declassifying federal information on the origins of COVID-19 as President Joe Biden ordered a deep investigation into the cause of the global pandemic." The Senate bill "orders the Director of National Intelligence (DNI) to declassify documents detailing any of the WIV's connections to COVID-19."

Fox News

(5/26, Ruiz, 23.99M) also reports.

Chinese Embassy In US Warns About Politicizing Origins Of COVID-19. Reuters

(5/27,Stanway) reports politicizing the origins of COVID-19 "would hamper further investigations and undermine global efforts to curb the pandemic, China's U.S. embassy said after President Joe Biden ordered a review of intelligence about where the virus emerged." In a statement on its website Wednesday evening, the embassy in Washington said "some political forces have been fixated on political manipulation and (the) blame game." The Chinese embassy said it supports "a comprehensive study of all early cases of COVID-19 found worldwide and a thorough investigation into some secretive bases and biological laboratories all over the world."

Fauci Defends US Funding To Chinese Research Organizations. Fox News

(5/26,McFall, 23.99M) reports that during an appearance at the Senate on Wednesday, NIAID Director Dr. Fauci "told lawmakers that he trusted Chinese scientists at the Wuhan Institute of Virology, saying he did not believe they attempted to modify viruses to make them more contagious." Sen. John Kennedy (R-LA) asked Fauci, "How do you know they didn't lie to you and use the money for gain of function research anyway?" Fauci, in his response, "explained that the National Institutes of Health (NIH) had seen the results of the experiments

conducted using U.S. government funds, adding that the viruses studied could also be found in public databases." Fauci said, "In our experience with grantees, including Chinese grantees…they're very competent, trustworthy scientists."

Facebook Reverses Policy, Allowing Posts Claiming COVID-19 Man-Made. Politico

(5/26,Lima, 6.73M) reports Facebook will no longer "take down posts claiming that Covid-19 was man-made or manufactured, a company spokesperson told POLITICO on Wednesday, a move that acknowledges the renewed debate about the virus' origins." Facebook's "policy tweak" arrives as support "surges in Washington for a fuller investigation into the origins of Covid-19 after the Wall Street Journal reported that three scientists at the Wuhan Institute of Virology were hospitalized in late 2019 with symptoms consistent with the virus." A Facebook spokesperson said Wednesday, "In light of ongoing investigations into the origin of COVID-19 and in consultation with public health experts, we will no longer remove the claim that COVID-19 is man-made from our apps."

The Hill

(5/26, Polus, 5.69M),Axios

(5/26,Falconer, 1.26M), and ABC News

(5/26,Pezenik, Gallagher, 2.44M) also report.

WPost: China Must Increase Transparency To Support International COVID Research. The Washington Post

(5/26, 10.52M) argues that the ongoing international investigation into COVID's origins is critical, and China "should help solve this mystery, but it so far has thrown a cloak over it." While China "steadfastly denies there was an inadvertent leak from the Wuhan Institute of Virology," the only way to resolve the question of China's potential culpability is to support the WHO's ongoing investigation.

WSJournal: The Lab-Leak Theory Deserves True Scrutiny. The Wall Street Journal

(5/26, Subscription Publication, 8.41M) examines the efforts made by scientists, media personalities, and government officials to disregard the lab-leak COVID origin theory last year, and it criticizes the slow reversal of opinion over the past few months. The Journal calls on scientists and other experts to conduct a thorough investigation in order to better protect the US from future pandemic threats.

Office of the Director of National Intelligence:

NCSC ACTING DIRECTOR TAKES PART IN "CNBC EVOLVE." <> CNBC

(5/26,Javers, 7.34M) reports its "CNBC Evolve: Cybersecurity" livestream event on May 26 explored "efforts to protect our nation's cyber infrastructure and identify threats, with actionable advice on ways the government and private enterprise can work together to anticipate threats before they happen." Eamon Javers led the "conversation with John Demers, Department of Justice's National Security Division Assistant Attorney General and Michael Orlando, National Counterintelligence and Security Center Acting Director."

CNBC

(5/26,Rosenbaum, 7.34M) reports separately that Orlando said, "We do know that countries like Russia and China, Iran and others certainly create safe havens for criminal hackers as long as they don't conduct attacks against them. But that's a challenge for us that we're going to have to work through as we figure out how to counter ransomware attacks." Orlando also "said it would be a mistake to focus only on ransomware, but it is true that the nation state actors are most interested in inserting malware into those systems."

THREE GOP SENATORS OPPOSE FONZONE'S NOMINATION OVER HUAWEI WORK. <> CNBC

(5/27,Ng, 7.34M) reports three Republican senators have "jointly voiced opposition to a Biden administration nominee for legal counsel at the Office of the Director of National Intelligence because of his past work for Chinese tech giant Huawei." Of the members of the "Senate Select Committee on Intelligence, four voted against Christopher Fonzone's nomination, including senators Ben Sasse of Nebraska, Marco Rubio of Florida and Tom Cotton of Arkansas."

Intelligence Community:

CIA:

TRUMP SENT CIA TO OBTAIN PPE AHEAD OF OTHER COUNTRIES DURING COVID-19 PANDEMIC, FORMER TOP UK AIDE SAYS. <> Newsweek

(5/26,Cole, 2.67M) reports Dominic Cummings "said that ex-President Donald Trump sent the CIA in order to obtain Protective Personal Equipment ahead of other countries during the coronavirus pandemic." The article adds that "Cummings, who left Downing Street in November 2020 after a bitter split with Johnson, said the U.K. had been lagging in its efforts to get essential equipment and that the British Department of Health's PPE procurement process was 'completely hopeless.'" Cummings added, "At this point we had Trump sending the CIA round trying to gazump everybody on PPE."

NSA:

NSA SHIFTS FOCUS TO "NEW PHYSICAL, VIRTUAL HUBS" FOR UNCLASSIFIED WORK. <>

FedScoop

(5/26,Mitchell) reports the NSA has developed "new physical and virtual workspaces to support collaboration around its unclassified work." The coronavirus forced the NSA "to accelerate the launch of the hubs where NSA personnel and contractors can securely work together in-person and online on unclassified workloads, said Rebecca Guzman, who leads the rollout of the Unclassified Work Environment program." Speaking to Riverbed's Network Transformation Summit, Guzman cited an effort to "establish a more agile, more efficient way to sustain our workforce, regardless of where they were coming from. And so as a result, we've created new unclassified options, both virtually and physically." Guzman also "said it forced NSA to bring greater focus to using non-customized commercial technologies both for the speed of delivery and the collaborative utility inherent in off-the-shelf software." In its physical collaboration spaces, NSA provides "modernized technology and smart devices to allow folks to have a space to be able to do some of that collaboration with partnership outside the agency," Guzman said.

Army:

SENATE REVERSES WORMUTH'S CONFIRMATION AS FIRST WOMAN ARMY SECRETARY. <> Army Times

(5/26, Winkie, 395K) reports Christine Wormuth nearly became "the first woman in US history to ascend to the Army's top civilian post when the Senate confirmed her Wednesday evening – until the body reversed her confirmation just hours later in an unusual development." CSPAN footage of the proceedings "shows Majority Leader Sen. Chuck Schumer, D-NY, announcing the reversal," and Schumer's staff did not "immediately respond to a request for clarification from Army Times, and the senator deleted a previous tweet hailing Wormuth's confirmation." In a tweet Wednesday, Roll Call reporter Andrew Clevenger called the move as "more like a procedural hiccup than a threat to her historic confirmation."

US ARL LAUNCHES $68M AI, ROBOTICS PARTNERSHIP WITH MARYLAND UNIVERSITIES. <> TheBaltimore Business Journal

(5/26,Eichensehr, Subscription Publication, 858K) reports the US Army Research Laboratory is "partnering with the University of Maryland, College Park and University of Maryland, Baltimore County to develop new artificial intelligence, robotics and autonomous technologies that can help soldiers and first responders operate more safely and efficiently in dangerous situations."

Air Force:

AIR FORCE SECRETARY SAYS NO FURTHER MQ-9 REAPER PROCUREMENT NEEDED. <> Defense News

(5/26,Insinna, 73K) reports a "battle is brewing" over the fate of "the MQ-9 Reaper, with a letter from the U.S. Air Force's top civilian signaling that the service will again seek to curtail procurement of the General Atomics-made drone in the upcoming fiscal 2022 budget."

AIR FORCE DEVELOPS STRATEGIES FOR DATA SHARING. <> ExecutiveGov

(5/26, Martin) reports the Department of the Air Force has developed "four options to guide the data-sharing activities of both the U.S. Air Force and U.S. Space Force, Breaking Defense reported Tuesday." The department developed "these options based on the results of the Data and Infrastructure Architecture Summit, which commenced in March and ran for two weeks." Air Force leaders will "assess the options and decide in June 2021 on which to execute. The department's Chief Architect Integration Office will then develop a minimum viable product based on what Air Force leadership decides on."

Department of Defense:

GEN. MILLEY CITES "FRAYING" RELATIONS WITH CHINA, RUSSIA. <> Fox News

(5/26,McFall, 23.99M) reports in a commencement address to "Air Force Academy graduates, General Mark Milley, Chairman of the Joint Chiefs of Staff, said the US is toeing a dangerous line in maintaining an appropriate level of competition with China and Russia." Milley told the graduates "We are now in the 76th year of the great power peace following WWII. And it is under stress, we can see it fraying at the edge," adding, "Right now we are in a great power competition with China and Russia. And we need to keep it at competition and avoid great power conflict."

DCSA'S TRUSTED WORKFORCE 2.0 INITIATIVE TO INCLUDE ALL AGENCIES, CONTRACTORS BY END OF 2023. <> Defense News

(5/26,Bur, 73K) reports the DCSA's new program for "continuously monitoring individuals with security clearances, Trusted Workforce 2.0, should have all agencies and contractors onboarded by the end of 2023, the agency's director, William Lietzau, said at a May 26 roundtable with the House Oversight and Reform Committee." Trusted Workforce 2.0 aims to "have clearance-holders undergo continuous vetting, meaning that investigation systems are continuously collecting data about individuals to evaluate their security risk."

DOD Making Progress On Security Clearance Progress, "But Reciprocity, IT Issues Remain." NextGov

(5/26,Jasper) reports as the DCSA makes progress "on an issue the National Security Commission on Artificial Intelligence pinpointed as in need of 'substantial reform,' problems around the status of both the legacy and new IT systems that deal with background investigations as well as with reciprocity, or the ability of one agency to accept an individual's security clearance

granted by another agency, remain." DCSA Director William Lietzau reported Wednesday to a House Committee on Oversight and Reform "government operations subcommittee roundtable hosted by Rep. Gerry Connolly, D-Va., chairman of the subcommittee." Within the last year, "the agency established a building block for its Trusted Workforce 2.0 continuous vetting program called Trusted Workforce 1.25, which has allowed for continuous vetting of some 3 million security clearances." Lietzau "acknowledged that there's still work left to be done."

US LAWMAKERS SEEK FUNDING FOR DEFENSE INDUSTRIAL FACILITIES. <> Politico

(5/26,Bender, 6.73M) reports bipartisan advocates of "military depots and arsenals are now pressing House leaders to incorporate funding for a host of defense industrial facilities into a potential multitrillion-dollar package." Reps. Cheri Bustos of Illinois "and Blake Moore of Utah, who co-chair the House Military Depot, Arsenal, Ammunition Plant and Industrial Facilities Caucus, are gathering support for a planned letter to Speaker Nancy Pelosi urging money for long-deferred upgrades for military industrial facilities as well as defense labs and test facilities and ranges be incorporated into an infrastructure proposal." However, Rep. John Garamendi, "who chairs the HASC panel that oversees shipyards, depots and arsenals, said he'll "seriously oppose" funding defense projects through the infrastructure plan instead of the normal defense budgeting process."

Justice Department:

DOJ REPORTEDLY MULLING FURTHER CHARGES OVER 2016 ELECTION MISINFORMATION. <> According toReuters

(5/26,Menn), "The indictment of a far-right internet activist on charges of interfering with the 2016 U.S. election reflects a strategic shift by the Department of Justice and sets the stage for new cases against more prominent right-wing actors." Reuters says "federal prosecutors debated for years whether and how to pursue criminal cases against Americans suspected of disseminating false voting instructions," but "after former...Attorney General William Barr resigned in December, a compromise emerged: One charge to start, against a demonstrably influential person," Douglass Mackey, "where evidence pointed to a real impact." The DOJ is expected to follow up with charges against others.

SOURCES: DOJ PREPARED TO SUE DEVELOPER IF HE DOES NOT REGISTER AS LOBBYIST UNDER FARA. <> Citing a Wall Street Journal

(5/26,Viswanatha, Subscription Publication, 8.41M) article, The Hill

(5/26,Castronuovo, 5.69M) reports unidentified individuals who are familiar with the matter said US Department of Justice (DOJ) prosecutors are prepared to sue Steve Wynn if the Las Vegas casino developer does not register as a lobbyist under the Foreign Agents Registration Act (FARA). The Hill specifies

that this matter is related to Wynn's alleged 2017 effort to have Guo Wengui, "who fled China in 2014 to seek asylum in" the US, sent back to China.

U.S. News:

NEW RESEARCH INDICATES COVID IMMUNITY COULD LAST OVER A YEAR. <> The New York Times

(5/26, Mandavilli, 20.6M) reports that, according to two new studies, COVID immunity "lasts at least a year, possibly a lifetime, improving over time especially after vaccination." The studies also "suggest that most people who have recovered from Covid-19 and who were later immunized will not need boosters," but vaccinated individuals "likely will need the shots." University of Pennsylvania Immunologist Dr. Scott Hensley said of the research, "The papers are consistent with the growing body of literature that suggests that immunity elicited by infection and vaccination for SARS-CoV-2 appears to be long-lived."

Vir Biotechnology Inc, GlaxoSmithKline PLC Announce FDA Approval Of COVID Antibody Drug. The Wall Street Journal

(5/26, Walker, Subscription Publication, 8.41M) reports Vir Biotechnology Inc and GlaxoSmithKline PLC announced that the FDA authorized their monoclonal antibody COVID drug, which is called sotrovimab. Sotrovimab is the third antibody medicine approved to treat patients at risk of severe infections, and a study of the drug found it reduced hospitalizatios or death by 85 percent.

CDC Warns Immunocompromised Americans To Continue Wearing Masks Following Vaccinations. The CBS Evening News

(5/26, story 7, 1:55,O'Donnell, 3.75M) reported that the CDC "is warning that 10 million Americans are compromised immune systems that they will need to continue wearing face masks, even after being vaccinated against COVID." Johns Hopkins transplant surgeon Dr. Dorry Segev said of the risks, "I'm hearing of transplant and other immunosuppressed people who got vaccinated and relaxed their safety behaviors, and are now being admitted to hospitals, and some are dying because they get COVID-19."

Health Officials Call For Continued Vigilance Ahead Of Holiday Weekend. NBC Nightly News

(5/26, story 3, 2:25, Holt, 4.76M) reported that while a growing share of Americans "have received at least one COVID vaccine dose," health officials continue to "warn, despite positive trends, [that] we have to remain on alert going into the holiday weekend." Domestic travel is "expected to be up 60% from last year with tens of millions planning to hit the roads, rails, and skies this weekend."

ABC World News Tonight

(5/26, story 3, 3:15,Muir, 6.02M) reported CDC Director Dr. Rochelle Walensky said of the holiday weekend, “If you are vaccinated, you are protected, and you can enjoy your Memorial Day. If you are not vaccinated, our guidance has not changed for you. You remain at risk of infection. You still need to mask and make other precautions.”

Law Firm Supporting Growing Movement To Challenge COVID Vaccine Mandates. The Washington Post

(5/26, A1,Stanley-Becker, 10.52M) reports that Siri & Glimstad, which “has done millions of dollars of legal work for one of the nation’s foremost anti-vaccination groups,” are supporting a new set of legal campaigns challenging state COVID vaccine mandates across the country. The lawsuits “show that a groundswell against compulsory immunization is being coordinated, at least in part, from a law office on Park Avenue in midtown Manhattan,” and the filings “offer a window into a wide-ranging and well-resourced effort to contest vaccine requirements in workplaces and other settings critical to the country’s reopening — a dispute with sweeping implications for public health, state authority and individual rights.”

Ohio To Announce First Vaccine Lottery Winners. The AP

(5/26,Welsh-Huggins) reports that two Ohioans will “be announced Wednesday night as the first winners of the state’s Vax-a-Million incentive prizes which include $1 million for those 18 and older and a full-ride college scholarship for teens.” Ohio Gov. Mike DeWine (R) “announced the program May 12 to boost lagging vaccination rates,” and it led to an additional 2.7 million adult vaccinations as well as 100,000 children between the ages of 12 and 17. TheNew York Times

(5/26,Mervosh, 20.6M) reports Athens County Health Department Administrator Jack Pepper said of the program’s impact, “I think we did close to 400 people in four hours.” He added, “Anywhere I go, people are joking with me, ‘Hey, when am I going to win my million dollars?’”

The CBS Evening News

(5/26, story 4, 1:50,O'Donnell, 3.75M) reported that other states “are rolling out incentives to get residents to roll up their sleeves,” and five states, including Colorado, are “offering $1 million to five vaccinated state residents.” The segment adds that Maryland “had its first $40,000 vaccine lottery winner” on Tuesday.

In an op-ed for the New York Times

(5/26, 20.6M), Ohio Gov. Mike DeWine (R) defends his decision to create a

lottery to encourage Ohioans to get the COVD vaccine. DeWine writes, “The decision to create Vax-a-Million...came about like those other pandemic decisions: out of necessity.” DeWine argues while some “have called it ‘a gimmick,’ an ‘insane $5 million bribe,’ a ‘misuse of money’ and ‘a waste of taxpayer dollars,’” the “real waste – when the vaccine is readily available to anyone who wants it – is not doing enough to save people’s lives.”

GOP EXPECTED TO FILIBUSTER JANUARY 6 PANEL THURSDAY. <> The AP

(5/27, Jalonick,Mascaro) reports that Senate Republicans are “ready to deploy” the filibuster to block legislation to create a commission to investigate the Jan. 6 insurrection, “shattering hopes for a bipartisan probe of the deadly assault on the U.S. Capitol and reviving pressure on Democrats to do away with the procedural tactic that critics say has lost its purpose.” The “vote expected Thursday would be the first successful use of a filibuster this year to halt Senate legislative action.”

Romney Warns Republicans Opposing Jan. 6 Commission Will Be Blamed For Hiding The Truth. CNN

(5/26,Raju, Barrett, 89.21M) reports on its website that Sen. Mitt Romney (R-UT) “warned Republicans they would be blamed for hiding the truth if they block a bill to investigate the January 6 Capitol attack.” Romney told CNN on Wednesday, “I think the perception is on the part of the public that the January 6 Commission just trying to get to the truth of what happened, and that Republicans would be seen as not wanting to let the truth come out. ... I don’t believe that’s what’s the motivation but I think that’s the perception.”

Collins Will Vote For Bill To Create Commission. Romney’s comments came the same day Sen. Susan Collins (R-ME) announced she “will vote for a House-passed bill to create a commission to probe the Jan. 6 Capitol attack during a key test vote that will take place as soon as Thursday,”The Hill

(5/26,Carney, 5.69M) reports. Collins “will support the bill during an initial hurdle so that she can offer an amendment making changes to the legislation, an aide confirmed to The Hill.” Collins told reporters, “I want to see a commission. ... There are a lot of unanswered questions, and I’m working very hard to secure Republican votes for a commission.” Collins is “the third GOP senator to say they will support the bill during an initial vote, where it will need 60 votes to move forward.”

A New York Times

(5/26,Hulse, 20.6M) analysis that with the vote on creating the commission, Democrats “are finally bumping up against the limits of what they can accomplish in the evenly divided Senate without changes to the filibuster rules.” Republicans “are poised to employ the procedural weapon to block the formation of the inquiry as early as Thursday, potentially dooming it while

underscoring the power of a determined Senate minority to kill legislation even if it is popular and has bipartisan support."

Sicknick's Mother, Partner Request Meetings With All GOP Senators. The Washington Post

(5/26, 10.52M) reports Gladys Sicknick and Sandra Garza, the "mother and partner of the late Capitol Police officer Brian D. Sicknick are requesting meetings with all Republican senators to urge them to establish an independent commission to investigate the Jan. 6 attack on the Capitol by a pro-Trump mob."

Milbank Condemns McConnell's Handling Of Issue. Dana Milbank writes in the Washington Post

(5/26, 10.52M) Senate Minority Leader McConnell this week "actually admitted" he puts "party before country" when he "told Republican colleagues that they should oppose the creation of a Jan. 6 commission, no matter how it is structured, because" it "could hurt the party's midterm election message." Earlier this month, Milbank writes, McConnell said, "One hundred percent of my focus is on stopping this new Administration," and, "true to his word, McConnell has blocked everything – even if it means undercutting Republican negotiators."

Washington Man Arrested In Capitol Siege Probe. The AP

(5/26) reports from Battle Ground, Washington, "A southwest Washington man who federal investigators say was seen on video saying, 'Our house,' while inside the U.S. Capitol with his father on Jan. 6 made his first appearance in federal court in Portland, Oregon, on Wednesday." Jeremy Grace, of Battle Ground, "is accused of illegal entering, disorderly conduct and demonstrating inside the restricted building, The Oregonian/OregonLive reported. Grace, 37, was arrested in Molalla, Oregon, on Wednesday, according to federal officials. His father, Jeffrey Grace, 62, was arrested in February and charged with unauthorized entering or remaining in any restricted building or grounds. Although the senior Grace told FBI agents he didn't think his son had entered the Capitol, a search of the father's phone turned up video in a 'trash' folder that showed both men in the building, according to a federal complaint."

Florida Woman Charged In Capitol Siege Probe. The Palm Beach (FL) Post

(5/26,Musgrave, 223K) reports, "Using Facebook photos and video captured during the Jan. 6 riot at the U.S. Capitol, the FBI this week accused a one-time Palm Beach County commission candidate and former GOP heavyweight of joining the deadly rampage." Jody Tagaris, 67, "who lives near Jupiter, is charged with four federal misdemeanors, accusing her of illegally entering a restricted building and being disruptive and disorderly once inside. She faces a maximum year-long prison sentence on each count. After a brief video hearing before a U.S. magistrate in West Palm Beach on Tuesday, she was released after

posting a $50,000 bond. She is to appear in federal court in Washington at an unspecified date to enter a plea to the charges, court records show." The Post adds, "In court papers, FBI agents say Tagaris' undoing began when they were alerted that she had posted a photo of herself on Facebook, sitting in a broken window of the Capitol."

Texas Man Arrested In Capitol Siege Probe. HuffPost

(5/26,Reilly, 363K) reports, "Adam Weibling, a 38-year-old Texas man, made no secret in recent months of his contempt for the FBI, likening its agents to Nazis and 'terrorists' in a series of conspiracy-laden tweets. His dislike for them surely grew on Tuesday when they arrested him for storming the U.S. Capitol on Jan. 6." HuffPost adds, "FBI agents arrested Weibling in Katy, Texas, on charges of unlawfully entering restricted grounds and engaging in disorderly conduct inside the Capitol, according to court records. His first virtual appearance in D.C. court is scheduled for June 3. According to an affidavit filed May 19 in the U.S. District Court for the District of Columbia and signed by an FBI task force officer, Weibling can be seen in video recorded by a reporter pushing his way past police in riot gear to get inside the Capitol around 2:30 p.m. on Jan. 6."

Man Arrested In Connection With US Capitol Breach Allegedly Claimed To Be DEA Agent. The Houston Chronicle

(5/26, 982K) reports Dallas resident Troy Smocks has been arrested in connection with a US Capitol breach incident that occurred early this year. The Chronicle adds, "Smocks previously falsely presented himself as a DEA agent during the execution of a search warrant, a Secret Service agent, an FBI agent, an Army colonel and more," according to charging documents.

Oath Keepers Seek Dismissal Of Capitol Siege Lawsuit. The Washington Post

(5/26, Hsu, 10.52M) reports, "Lawyers for the Oath Keepers urged a federal judge Wednesday to toss out a lawsuit accusing the group, former president Donald Trump, lawyer Rudolph W. Giuliani and another far-right organization of inciting the Jan. 6 storming of the Capitol, calling its actions a form of peaceful political protest protected by the First Amendment." The Post adds, "The Oath Keepers said it was 'conclusory and speculative' to assert that its members planned anything other than to attend a speech of the president at the Ellipse near the White House that day, march to the Capitol and make known to Congress their views opposing the presidential election certification. The group added that 11 House lawmakers led by Homeland Security Committee Chairman Bennie Thompson (D-Miss.) had no right to file suit in their personal capacities or as individuals under the Ku Klux Klan Act...as opposed to a case brought by the whole House."

Alabama Man In Capitol Siege Probe Had Militia Ties, Reached Out To Cruz. The Decatur (AL) Daily

(5/26,
Fleischauer, 53K) reports that a Falkville, Alabama man "tied to the Jan. 6 Capitol riot had Molotov cocktails not only in D.C. but at his Alabama home, has ties to Texas militia dating back to 2014 and tried to speak with U.S. Sen. Ted Cruz about 'election fraud' weeks before the Capitol attack, according to court records." Lonnie Leroy Coffman, 71, "on Monday was denied his second request to be released from a Washington, D.C., jail in a 24-page opinion by" US District Judge Colleen Kollar-Kotelly. The Daily adds, "While much of the evidence relied upon by U.S. District Judge Colleen Kollar-Kotelly in denying pretrial release is under seal, her opinion adds new information about evidence collected during the FBI investigation surrounding a 17-count indictment that includes possession of unregistered destructive devices and numerous gun violations."

The Montgomery (AL) Advertiser

(5/24,Brown, 72K) reports that Judge Kollar-Kotelly "denied Lonnie Coffman's bid for pre-trial release, writing the evidence against Coffman demonstrates he could present 'a concrete and prospective threat to the community.' New evidence against Coffman was revealed in Kollar-Kotelly's order, including Coffman's 2014 militia ties and that Coffman made a trip to Washington D.C. just weeks before his arrest. His truck, where police would find gasoline-filled mason jars and weapons on Jan. 6, was tracked circling the U.S. Capitol and attempting to drive to Sen. Ted Cruz' home on Dec. 11." Coffman, 71, "was not charged with illegally entering a federal building or civil disorder, though prosecutors allege they have evidence that places him at the Capitol, but faces a slate of weapons charges."

BIDEN CALLS FOR CONGRESSIONAL ACTION IN WAKE OF SAN JOSE MASS SHOOTING. <> The Washington Post

(5/26,Wagner, 10.52M) reports that on Wednesday, President Biden "released a statement on the latest mass shooting, in which at least eight people were killed in a San Jose, Calif., rail yard, and urged Congress 'to help end this epidemic of gun violence in America.'" TheSan Jose Mercury News

(5/26, 432K) carries the President's full statement on the shooting, which reads, "There are at least eight families who will never be whole again. There are children, parents, and spouses who are waiting to hear whether someone they love is ever going to come home. There are union brothers and sisters – good, honest, hardworking people – who are mourning their own. ... Once again, I urge Congress to take immediate action" against gun violence

Asked on MSNBC

(5/26, 799K) about gun control legislation in the wake of a mass shooting in San Jose, California, White House Office of Public Engagement Director Cedric Richmond said, "There are bills right now...that the Senate could take up and

pass to protect people, protect families. There are eight families that have lost a loved one today. ... We should not only offer our prayers and condolences and our thoughts, but we ought to offer some action and do things to prevent this."

Gunman Kills Eight, Himself. The New York Times
(5/26, Fuller,
Hauser, 20.6M) reports that "a transit worker opened fire at a rail yard in San Jose, Calif., early Wednesday, killing eight people, many of them fellow employees, according to the Santa Clara County Sheriff's Office, which reported that the gunman was also dead." TheWashington Post
(5/26,
10.52M) reports that "the suspect is also dead, Santa Clara County Sheriff's Office spokesman Russell Davis said during a news conference." TheAP

(5/26,Gecker, Chea) reports that the employee launched his assault during a union meeting "in two buildings that are part of a light rail facility for the Valley Transportation Authority, which provides bus, light rail and other transit services throughout Santa Clara County, the most populated county in the San Francisco Bay Area."NBC Nightly News

(5/26, lead story, 3:15, Holt, 4.76M) reported the "massacre" is "the 61st mass shooting in the US in the month of May alone."

The CBS Evening News

(5/26, lead story, 3:35,O'Donnell, 3.75M) reported investigators "are still pouring over the scene" of the rampage and are "worried about possible explosives." CBS added that it was necessary to suspend "rail service for thousands of commuters" to allow investigators, including a bomb-sniffing dog, to "search for explosives they believe may have been left by" the shooter.

ABC World News Tonight

(5/26, lead story, 4:10,Muir, 6.02M) reported the "suspect" in the shooting is 57-year-old Samuel Cassidy. ABC added that "bomb squads" were "moving in on" Cassidy's home, which "authorities say he set fire to it just before driving to the rail yard."Reuters

(5/26) reports that Cassidy, "the eight victims shot dead, and a survivor who was hospitalized in critical condition were all employees of the transit agency." Reuters says Cassidy "had worked for the transit authority since at least 2012, when he was listed as an 'electro-mechanic,' and was promoted to 'substation maintainer' in 2015, according to records posted by the nonprofit website Transportation California."

The San Jose Mercury News

(5/26, 432K) reports that “the Santa Clara County Medical Examiner-Coroner’s Office identified the eight victims as 42-year-old Paul Delacruz Megia, 36-year-old Taptejdeep Singh, 29-year-old Adrian Balleza, 35-year-old Jose Dejesus Hernandez III, 49-year-old Timothy Michael Romo, 40-year-old Michael Joseph Rudometkin, 63-year-old Abdolvahab Alaghmandan and 63-year-old Lars Kepler Lane.”

USA Today

(5/26,Groppe, 12.7M) highlights President Biden’s “plea” for Congress to act on gun control legislation and notes the Administration’s prior efforts to address the issue in April through “half a dozen executive actions aimed at curbing the proliferation of so-called ghost guns, or untraceable weapons that can be constructed from parts purchased online, as well as tightening regulations on...stabilizing braces for pistols.”The Hill

(5/26,Rahman, 5.69M) reports that “while speaking to reporters at an event on broadband infrastructure,” Vice President Harris “called the shooting ‘absolutely tragic.’”

In another article, USA Today

(5/26,Bacon, Ortiz, Hauck, 12.7M) reports on California Gov. Newsom’s reaction to the shooting, writing that at a press conference on Wednesday afternoon, Newsom was “visibly emotional” and “expressed frustration.” Newsom “said he felt a ‘sameness’ and ‘numbness’ in the wake of yet another mass shooting.” USA Today also quotes the governor as saying, “‘It begs the damn question: What the hell is going on in the United States of America?’ ... ‘We rinse and repeat someplace else in this country.’”Politico

(5/26,Marinucci, 6.73M) adds, “the Democratic governor has long railed against gun violence and has criticized Republicans and the National Rifle Association in the past for opposing restrictions on weapons.”

The Wall Street Journal

(5/26,Carlton, Lazo, Mai-Duc, Subscription Publication, 8.41M) also reports on the shooting, among many others.

AMID RISING CRIME, CITIES RESTORE POLICE FUNDING. <> The Wall Street Journal

(5/26,Elinson, Frosch, Jamerson, Subscription Publication, 8.41M) reports that amid rising crime rates, some cities which pursued policies to defund the police in the wake of the George Floyd protests are reversing course and reinstating funds for police departments. The Journal cites actions by officials in New York City, Oakland, Baltimore, and Los Angeles as examples.

BIDEN EXPECTED TO TAP BURNS AS AMBASSADOR TO CHINA, GARCETTI AS AMBASSADOR TO

INDIA. <> The AP

(5/27,Balsamo, Blood) reports that President Biden "is expected to announce he is nominating former senior State Department official Nicholas Burns to serve as his ambassador to China and Los Angeles Mayor Eric Garcetti to be his ambassador to India, according to a person familiar with the matter." With the picks, the AP says, Biden "is turning to a seasoned diplomat and a longtime political ally to serve in two of the country's highest-profile diplomatic postings." It is not clear when the announcement will come.

Biden Expected To Nominate Wall Street Executive To Be His Ambassador To Israel. Reuters

(5/26) reports that President Biden is "expected to nominate Thomas Nides, an experienced diplomat and Wall Street executive, to serve as U.S. ambassador to Israel." Reuters adds, "It was not immediately known when Biden planned to announce Nides' nomination but a person familiar with the matter said it would happen soon."

ATF NOMINEE FACES PUSHBACK FROM GOP, BUT LIKELY TO BE CONFIRMED. <> The New York Times

(5/26,Thrush, 20.6M) reports that during a confirmation hearing on Wednesday, David Chipman, President Biden's nominee to head the Bureau of Alcohol, Tobacco, Firearms and Explosives, "faced withering criticism...from Republican senators over his history of scathing comments about gun ownership." The Times says Chipman, "a two-decade veteran of the A.T.F. who has served as an adviser to gun control groups, was chosen in part because of his willingness to bluntly confront" the gun industry.Roll Call

(5/26,Ruger, 130K) reports that Chipman "told senators that he took one position as an advocate on potential gun control laws, but would only enforce the current laws as director."

The Washington Post

(5/26,Kane, 10.52M) reports that in "an emotional moment to which gun critics point to illustrate ATF's importance, Sen. Dianne Feinstein (D-Calif.) informed Chipman that while he was testifying, an employee at a San Jose light-rail facility had opened fire, killing at least eight."

The Wall Street Journal

(5/26, Levy, Subscription Publication, 8.41M) reports that while Senate Judiciary Chair Dick Durbin said Chipman's "knowledge of the agency and its purview is unparalleled," Sen. Chuck Grassley, the panel's minority leader, likened Chapman's nomination to "putting a tobacco executive in charge of the Department of Health and Human Services."

The Hill

(5/26,Gangitano, 5.69M) reports that Chipman "said... he supports banning the AR-15." Chipman said, "I support a ban as has been presented in a Senate bill and supported by the president. The AR-15 is a gun I was issued on ATF's swat team and it's a particularly lethal weapon and regulating it as other particularly lethal weapons, I have advocated for." Chipman "was also questioned by Republicans on his support for Congress to ban assault weapons and for universal background checks during the hearing, two actions Biden also supports."

In a second piece, the New York Times
(5/26,
Russonello, 20.6M) reports that while the ATF has been without a director for 13 of the last 15 years, President Biden "is trying to become the second president since 2006 to fill the position." Chipman "stands a good chance: The Democrats' two most consistently centrist senators, Kyrsten Sinema and Joe Manchin, have signaled they're likely to support his nomination — and that may well be enough to get him confirmed," even if the GOP is united in its opposition.

JEAN-PIERRE PRESIDES OVER HISTORIC FIRST TELEVISED WHITE HOUSE BRIEFING. <> The New York Times

(5/26,Rogers, 20.6M) that on Wednesday, White House Principal Deputy Press Secretary Karine Jean-Pierre "held a televised briefing for the first time...a baptism-by-fire moment" following as it did a mass shooting in California and the President's request for an intelligence community investigation into the origins of the coronavirus. The Times adds that Jean-Pierre "showed little interest in getting ahead of the president or the Administration, a tactic that is frustrating to reporters, but one that drew praise from members of the Administration, including Ron Klain."

Politico

(5/26, Niedzwiadek, 6.73M) reports that Wednesday's briefing was "widely viewed as an audition to take over for White House press secretary Jen Psaki when she eventually steps down." According to Politico, "In addition to Jean-Pierre, some observers have pegged White House communications director Kate Bedingfield, Vice President Kamala Harris spokesperson Symone Sanders, and State Department spokesperson Ned Price as potential successors."

USA Today

(5/26,Gilbert, 12.7M) notes the historic nature of the appearance, reporting that Jean-Pierre "became the first Black woman in decades to lead a press briefing at the White House on Wednesday." She also "made history" by "being

the first openly gay spokeswoman as she stood behind the podium and answered journalists' questions."

The Hill

(5/26,Samuels, 5.69M) reports that when "asked about the rarity of a Black woman standing behind the podium," Jean-Pierre said, "I appreciate the historic nature. I really do. But I believe that being behind this podium, being in this room, being in this building isn't about one person. It's about what we do on behalf of the American people. Clearly the president believes representation matters, and I appreciate him giving me this opportunity."

BIDEN UNDER PRESSURE TO CONFRONT ANTI-SEMITISM AFTER ATTACKS. <> The New York Times

(5/26,Graham, Stack, 20.6M) (5/26, Graham, Stack, 20.6M) reports that "the past several weeks have seen an outbreak of anti-Semitic threats and violence across the United States, stoking fear among Jews in small towns and major cities. During the two weeks of clashes in Israel and Gaza this month, the Anti-Defamation League collected 222 reports of anti-Semitic harassment, vandalism and violence in the United States, compared with 127 over the previous two weeks."

The Hill

(5/26,Gangitano, 5.69M) says that "Democratic lawmakers and outside groups are pushing" President Biden to take additional action "to stop antisemitism" amid the rise "in violent attacks targeting the U.S. Jewish community." The Hills says "five prominent Jewish advocacy groups – the Anti-Defamation League...the American Jewish Committee, the Orthodox Union, the Jewish Federations of North America, and Hadassah, The Women's Zionist Organization of America, Inc. – in a Friday letter to Biden expressed concern about a surge in attacks." Additionally, Reps. Josh Gottheimer (D-N.J.), Elaine Luria (D-Va.) and Kathy Manning (D-N.C.) wrote to Biden on Tuesday and asked him to "nominate a United States ambassador-at-large to monitor and combat antisemitism."

Americans Believe Anti-Asian Discrimination Has Worsened. The AP

(5/26,Fingerhut) reports that a poll by the AP-NORC Center for Public Affairs Research shows "a majority of Americans across racial and ethnic groups believe discrimination has worsened in the last year against Asian Americans, who became the target of attacks after being unfairly blamed for the coronavirus pandemic." The poll "also finds about 6 in 10 Americans say racism in the US in general is a 'very' or 'extremely' serious problem. And a majority of Asian Americans say they feel unsafe in public because of their race."

Eighth Noose Found At Amazon Work Site In Connecticut. ABC World News Tonight

(5/26, story 7, 0:15,Muir, 6.02M) reported, “Tonight yet another disturbing discovery at the same construction site of a new Amazon facility in Windsor, Connecticut. The NAACP says an eighth noose was found at the work site. Construction shut down yet again days after restarting. The investigation under way.”

SEN. TIM SCOTT: “JUNE OR BUST” FOR REACHING DEAL ON POLICE REFORM. <> The Hill

(5/26,Carney, 5.69M) reports that the lead Republican negotiator Sen. Tim Scott (R-SC) told reporters on Wednesday that a deal on police reform is expected in June. Referring to the timeline, Tim Scott said, “I think it’s June or bust. ... I think we have three weeks in June to get this done.”

Richmond: Everybody Negotiating In “Good Faith.” Asked on MSNBC

(5/26, 799K) about the status of police reform proposals in Congress, White House Office of Public Engagement Director Cedric Richmond said, “I think everybody is negotiating in good faith trying to get to a substantive bill that one would honor the memory of George Floyd but more importantly would stop the carnage that we see on the streets in terms of the interactions between police and the communities they police.”

DOJ Official Says Civil Rights Probes Of Local Police Help Fight Crime. The Wall Street Journal

(5/26,Gurman, Subscription Publication, 8.41M) reports that Associate Attorney General Vanita Gupta said federal civil rights probes of local police departments help fight violent crime. The Journal says Gupta’s comments rebut criticism that the DOJ’s civil rights investigations are hurting officer morale at a time when violent crime is increasing.

EXXONMOBIL DEALT “MAJOR BLOW” IN BOARD SHAKE UP. <> Reuters

(5/26,Hiller, Herbst-Bayliss) reports that ExxonMobil suffered a “major blow” on Wednesday during a shareholder vote as at least two board members were unseated by a small hedge fund, Engine No. 1, in a move to “force the company’s leadership to reckon with the risk of failing to adjust its business strategy to match global efforts to combat climate change.” Reuters says the counting “is not finished, so Engine No. 1 could potentially see three of its four nominees join the Exxon board.” The group’s successful nominations so far are Gregory Goff, a former executive from Marathon Petroleum and Andeavor, and Kaisa Hietala, a former Neste Oyj executive.

The New York Times

(5/26,Krauss, 20.6M) reports the two Engine No. 1 candidates were “nominated by activist investors who pledged to steer the company toward cleaner energy and away from oil and gas.” The Times calls the result a “sharp rebuke” ExxonMobil

CEO Darren Woods, who opposed the board challenge. TheWall Street Journal

(5/26,Matthews, McFarlane, Subscription Publication, 8.41M) reports that the setback for ExxonMobil highlights the dramatic shift in landscape for oil and gas companies as pressure from environmental groups continues to mount.

The Wall Street Journal
(5/26,
Subscription Publication, 8.41M) editorializes that the upset to ExxonMobil is due to political pressure on its shareholders to appeal to progressives in power. The Journal warns that Exxon will not do well if it abandons fossil fuels to focus on renewables.

Dutch Court Orders Shell To Reduce Emissions By 45%. The AP

(5/26,Bussewitz) reports that Royal Dutch Shell was ordered by a district court in The Hague on Wednesday to reduce its net carbon emissions by 45% by 2030 compared to 2019 levels, following a case brought by climate change activists. The AP says the court "ruled that the energy giant had a duty to reduce emissions and that its current reduction plans were insufficient."

Protections For Lesser Prairie Chicken May Curb New Oil And Gas Development. The Hill

(5/26,Guzman, 5.69M) reports that on Wednesday the US Fish and Wildlife Service proposed categorizing the lesser prairie chicken as "endangered" in parts of New Mexico and Texas and "threatened" in more northern parts where the species is found. The Hill says that the "move by the Biden Administration could have big consequences for the fossil fuel industry as the range of the species that could be federally protected overlaps with the oil and gas-rich Permian Basin," adding that such "federal protections would likely impose restrictions on new oil and gas developments in the region where the birds roam."

Senators Introduce Bill Extending Tax Credits To Nuclear Power Plants. Reuters

(5/26,Gardner) reports three Democratic senators "introduced a measure on Wednesday to boost existing nuclear plants to a wide energy tax reform bill, after the Biden administration pushed for such a change to help curb carbon emissions."

DIPLOMATS ASK STATE DEPARTMENT TO PROVIDE MORE SUPPORT FOR "HAVANA SYNDROME" VICTIMS. <> The Hill

(5/26,Castronuovo, 5.69M) reports American diplomats and other "government officials who say they are victims of 'Havana Syndrome' attacks are calling on the State Department to do more to provide proper medical care and support." In a letter dated Tuesday and "obtained byNBC News

, a group of 21 government workers and their spouses demanded Deputy Secretary of State Brian McKeon adopt a series of recommendations to 'ensure injured employees and families' are 'fully supported' and that the US government is 'fully prepared to respond to future incidents.'" The 11 recommendations include "benefits assistance for victims of the attacks, care plans and responses for newly injured employees and their families, long-term monitoring of affected individuals and the establishment of an accountability review board for China and other countries that have had suspected Havana Syndrome cases." The signatories also argued that "counterparts in the defense and intelligence community have had a different level and frequency of engagement."

Pentagon Drafting "Havana Syndrome" Reporting Memo. CNN

(5/26,Starr, Williams, Herb, 89.21M) reports the Pentagon is drafting a "memo to the entire military and civilian workforce asking personnel to report any so-called anomalous health symptoms that might indicate they have been victims of a mysterious illness that has struck US diplomats, spies and military personnel around the world, according to two defense officials." No final decision has "been made on whether to issue the memo, but the fact it's being considered underscores the growing concern at the Pentagon's senior levels that they need to gather more information on what" has become known as "Havana Syndrome."

EXECS SAY BIDEN PLAN TO IMPORT METALS FOR EVS COULD KEEP US FROM MEETING CLIMATE GOALS. <> Reuters

(5/26, Scheyder) reports "industry executives" say the Biden Administration's "plan to rely on ally nations for most of the metals needed to build electric vehicles ignores the complexity of modern mining and could keep the United States from meeting aggressive climate goals." James Calaway, chairman of ioneer Ltd, said, "The approach is deeply naive and very dangerous to the United States supply chain for electric vehicles," and Jon Evans, chief executive of Lithium Americas Corp, said, "Given the administration's timeline, they have no choice but to allow more domestic mines." Although the Administration "may want to rely on mineral deposits in ally nations, it will have competition from China, which is willing to pay top dollar, industry leaders said."

MAYORKAS DEFENDS TITLE 42. <> The Hill

(5/26,Beitsch, 5.69M) reports that before a House Appropriations subcommittee on Wednesday, DHS Secretary Mayorkas "defended the Administration's retention of" Title 42, "a Trump-era policy that allows the swift removal of migrants due to COVID-19 as well as a narrowing in those sought for deportations by law enforcement officials." While there is "increasing pressure" to scrap Title 42, Mayorkas "reiterated [the] Administration's position that the policy is necessary as a public health measure." He added, "We will not restrict travel

one day more than the public health imperative requires. That is the assurance I can give."

DEMOCRATS UNABLE TO MOVE FORWARD WITH PLAN TO LOWER PRESCRIPTION DRUG PRICES. <> The Los Angeles Times

(5/26,Haberkorn, Stokols, 3.37M) reports, "Despite widespread support among Democrats, the idea" of implementing a plan to lower prescription drug prices "has sputtered." President Biden did not include such a plan in his infrastructure proposal and his budget is not expected to include one. Democrats in Congress, meanwhile, "remain noncommittal about how they might enact" a plan to lower prescription drug prices.

COLUMNIST HIGHLIGHTS GAO REPORT ABOUT MAKING GOVERNMENT MORE EFFICIENT, WITH SAVINGS OF $1B OR MORE. <> In an opinion piece for the Washington Post

(5/25, 10.52M), columnist Joe Davidson says that "as President Biden pushes big spending plans to spur the country's economic recovery, he might welcome suggestions for saving a few bucks – or much more." A new GAO "report about how to make the government more efficient includes 14 areas to target, each with possible savings of $1 billion or more." The "report said" another "potential efficiency" action is "improving coordination of infectious-disease work by the Department of Health and Human Services to better identify duplication and overlap among agencies." These include "extending cost-reduction and efficiency programs at two of the Energy Department's National Nuclear Security Administration sites to other locations" for a savings of $515 million over five years.

MICHIGAN SECRETARY OF STATE "DEEPLY CONCERNED ABOUT THE FUTURE OF OUR DEMOCRACY." <> In an interview with the AP

(5/26, Cassidy,Eggert), Michigan Secretary of State Jocelyn Benson (D) was asked about "GOP-controlled legislatures seeking to exert more control over election officials." Benson said, "I'm deeply concerned about the future of our democracy and about all of the things that we're seeing and have seen on a near weekly basis emerge throughout our country, but particularly in states that were high profile in 2020 – Michigan, Georgia, Arizona, Nevada – to consistently propagate the 'big lie,' propagate this idea, this falsehood that the election was anything but safe and secure, to codify legislation in furtherance of that and really undo a lot of the policies that led to such enormous turnout and security in 2020."

International News:

Africa:

AFTER MILITARY TAKEOVER, INTERIM PRESIDENT, PM OF MALI RESIGN. <> Reuters

(5/26) reports that the interim president and prime minister of Mail resigned on Wednesday, “two days after they were arrested by the military, an aide to the vice president said.” Miliary forces “led by interim Vice President Assimi Goita, arrested President Bah Ndaw and Prime Minister Moctar Ouane and took them to a military base on Monday after a cabinet reshuffle in which two officers lost their posts.” The actions by the military have jeopardized the nation’s return to democracy after a coup last year.

SUSPECTED ISLAMIST ATTACK KILLS 22 IN THE DEMOCRATIC REPUBLIC OF CONGO. <> Reuters

(5/26) reports that at least 22 civilians were killed with knives and machetes in a night-time raid by suspected Islamist militants in the eastern part of the Democratic Republic Of Congo. The attack “comes more than three weeks after the government declared martial law in North Kivu and Ituri, two provinces bordering Uganda, in an attempt to stem worsening bloodshed.”

UN OFFICIAL WARNS THAT ETHIOPIA’S TIGRAY REGION IS ON THE BRINK OF FAMINE. <> TheNew York Times

(5/26,Gladstone, 20.6M) reports that Mark Lowcock, the UN’s under secretary general for humanitarian affairs, is warning that “famine is now knocking on the door of Ethiopia’s Tigray region, where a civil war that erupted last year has drastically cut the food supply and prevented relief workers from helping the hungry.” The Times says that “in a confidential note to the United Nations Security Council,” Lowcock “said sections of Tigray, a region of more than 5 million people, are now one step from famine – in part because the government has obstructed aid shipments.”

NBC: US “QUIETLY RETURNING” TO LIBYA. <> NBC News

(5/27, 4.91M) reports the US is “wading back into Libya, with the Biden administration launching a fresh diplomatic bid to pull the country out of a violent spiral and making plans to reopen the U.S. Embassy in Tripoli seven years after it was closed.” Last week, the highest-ranking “US diplomat to visit the country since 2014 arrived in Tripoli, and the administration has deployed a team there to work out the daunting logistics of reopening the embassy, two sources familiar with the matter said.” A State Department spokesperson said, “Our intent is to begin to resume operations in Libya as soon as the security situation permits and we have the necessary security measures in place. The process for that to occur, however, entails careful logistical and security planning, plus interagency coordination to meet security and legal requirements. “

REPORT ON ITALIAN AMBASSADOR’S DEATH IN CONGO INDICATES “POORLY PLANNED, CLUMSILY EXECUTED ACT.” <> Reuters

(5/26, Holland, Katanty) reports from Goma, Democratic Republic of Congo that

a new incident report from the Virunga National Park Rangers regarding the "botched kidnapping" of Italian Ambassador Luca Attanasio "paints a picture of a poorly planned, clumsily executed act, and runs counter to the assumption among some officials and media at the time that Attanasio was the target of a carefully orchestrated operation." The report was "corroborated by three UN officials and an Italian judicial source – all with knowledge of probes into the attack." The attackers "never displayed awareness of ambassador Attanasio's identity or diplomatic status, two of the UN sources close to the investigations said."

Near East:

BLINKEN DEPARTS MIDDLE EAST WITH CEASE-FIRE INTACT, PLEDGES TO AID WITH REBUILDING. <> The New York Times

(5/26,Jakes, 20.6M) reports that as Secretary of State Antony Blinken left the Middle East on Wednesday, he "said he was returning to Washington from the brief but urgent visit with new promises to help fund a massive humanitarian and reconstruction effort in the Gaza Strip." Speaking to reporters in Amman after meeting with King Abdullah, Blinken said, "We see the cease-fire not as an end, but as a beginning – something to build on." Blinken "said Egypt had offered to contribute $500 million to rebuild Gaza, and noted Jordan's 'vital role' in working with the Palestinian Authority" in the West Bank.

Reuters

(5/26) reports that on Wednesday in Amman, Jordan, Blinken "said...he had a lengthy discussion with Egyptian President Abdel Fattah al-Sisi about Cairo's human rights record." Reuters adds that Blinken "also said he raised with Sisi the issue of Americans who have been detained in Egypt."

According to the AP

(5/26, Magdy,Federman), Blinken's "mission made little headway in resolving the deeper issues at the heart of the Israeli-Palestinian conflict." The AP adds, "After two days of talks with Israeli, Palestinian and Arab allies, Blinken acknowledged that any resumption of peace talks remained far off. In the meantime, he said he had made progress toward the more modest goals of cementing the cease-fire and rebuilding hard-hit Gaza."

Eviction Issue Continues To Test Cease-Fire. NBC Nightly News

(5/26, story 5, 1:40, Holt, 4.76M) reported, "That fragile cease-fire between Israel and Hamas is facing new pressure tonight over an Israeli plan to evict some Palestinians from their homes." NBC (Mitchell) added, "Protests today in East Jerusalem, where 700 more Palestinians are fighting evictions to make room for Jewish settlers. The first question I was asked when I got here is, 'What did Blinken say?'" about the situation. NBC (Mitchell) adds, "Today, they have

new hope after Blinken said Israel should stop demolishing their homes, trying to avoid a spark that could ignite another round of violence."

Boot: Preserving Status Quo With Iran Doesn't Boost Hamas. Max Boot writes in theWashington Post

(5/26, 10.52M) that "the right wing in Israel and the United States" believe "the recent 11-day Gaza war makes a compelling case against concluding a nuclear deal with Iran." However, Boot argues, the "negotiations to revive the nuclear deal are continuing. The Biden administration has not actually lifted sanctions on Iran." But that has not "hampered Hamas's ability to rocket Israel. ... It's hard to see how the U.S. exit from the JCPOA has hurt Hamas in any way. ... So I am struggling to figure out how preserving the status quo is enhancing Israel's security. Spoiler alert: It's not."

ASSAD VOTES IN FORMER REBEL STRONGHOLD, TOUTS ELECTION AS EVIDENCE OF SYRIAN UNITY. <> Reuters

(5/26) reports that on Wednesday, Syrian President Bashar al-Assad "voted...in an election certain to extend his rule...casting his ballot in the former rebel stronghold of Douma where a suspected chemical weapons attack in 2018 prompted Western air strikes." Assad said after voting, "Syria is not what they were trying to market, one city against the other and sect against the other or civil war. Today we are proving from Douma that the Syrian people are one."

According to the AP

(5/26,Aji), "The vote is the second presidential election since the country's conflict began 10 years ago and has been dismissed as a sham by the opposition and Western countries, including the United States. ... 'The Assad regime's so-called presidential election is neither free nor fair,' U.S. Secretary of State Anthony Blinken said in a Twitter post Wednesday." The AP says Assad "blasted countries that have dismissed the vote as illegitimate, saying most of those nations 'have colonial history' and 'we as a state are not concerned about such statements.'"

The Washington Post

(5/26, 10.52M) says the election "delivers a rebuke to a decade of Syria diplomacy by the United States and its allies aimed at securing a transition to democracy. By the time Assad's new term ends in 2028, he will have been in power for 28 years, topping the 27 years his father, Hafez, served as president."

CNN

(5/26, Karadsheh, 89.21M) reports on its website that in 2014, Assad "received 88.7% of the vote in an election that took place in government-controlled parts

of the country. At the time, opposition groups ran large swathes of Syria – Assad's forces have since wrested control over most of that territory." On its website,CBS News

(5/26, 5.39M) says, "Thanks to support from Russia that helped turn the tide in the war, Assad's rule is no longer seriously threatened by ISIS or the rebels who've enjoyed varying degrees of support from the West."

IRAQI FORCES ARREST MILITIA COMMANDER OVER ALLEGED INVOLVEMENT IN ATTACKS ON AIR BASE USED BY US. <> Reuters

(5/26) reports that the Iraqi military said that security forces on Wednesday arrested militia commander Qasim Muslih in a "move security sources said was linked to attacks on a base that hosts U.S. forces." A pair of security sources told the news outlet that Muslih "was arrested in Baghdad for involvement in several attacks including recent assaults on Ain al-Asad air base, where U.S. and other international forces are housed."

The AP

(5/26) reports "tensions mounted in Iraq's capital" on Wednesday after the arrest. Shortly after, forces "affiliated with the PMF, which maintains offices inside the heavily fortified Green Zone, were deployed surrounding Prime Minister Mustafa al-Kadhimi's headquarters." Tensions reached a "fever pitch when Iraqi security forces and the elite Counter-Terrorism Service were deployed to protect the government and diplomatic missions, sparking fears of violence. Some armed PMF factions gathered around the Green Zone's entrance gates."

HAMAS LEADER SAYS 80 FIGHTERS KILLED. <> The AP

(5/26,Akram, Akram) reports Hamas' leader in the Gaza Strip "on Wednesday said 80 militants were killed during the 11-day war with Israel that ended last week, providing the group's first official tally for losses sustained in the fighting." Gaza's Hamas-run Health Ministry has "put the number of Palestinians killed in the Israeli offensive this month at 254, including 66 children, 39 women, and 17 people above the age of 60" but did not provide "a breakdown between civilians and combatants." Speaking to The Associated Press, "Hamas leader Yehiyeh Sinwar said those killed last week included 57 members of his group's armed wing, 22 members of the smaller Islamic Jihad group and one member of a small group called the Popular Resistance Committees."

Iran:

IAEA HEAD: IRAN ENRICHING URANIUM AT WEAPONS-GRADE LEVEL. <> Insider

(5/26,Haltiwanger, 2.74M) reports Iran is enriching uranium "up to purity levels that 'only countries making bombs are reaching,' the head of the UN's

nuclear watchdog warned in an interview with the Financial Times." Rafael Grossi, director-general of the International Atomic Energy Agency (IAEA), told the Times, "A country enriching at 60% is a very serious thing – only countries making bombs are reaching this level." Grossi added, "You cannot put the genie back into the bottle – once you know how to do stuff, you know, and the only way to check this is through verification. The Iranian programme has grown, become more sophisticated so the linear return to 2015 is no longer possible. What you can do is keep their activities below the parameters of 2015."

Europe:

WHO COVAX PROGRAM FALLS SHORT DESPITE INTENTIONS OF DEVELOPED NATIONS, VACCINE MANUFACTURERS. <> The Wall Street Journal

(5/26, A1,Steinhauser, Hinshaw, McKay, Subscription Publication, 8.41M) reports about why the WHO's COVAX program has struggled to provide shots to developing countries despite its good intentions. By December 2020, "Moderna, Pfizer, AstraZeneca, Sinopharm and Sputnik V had all announced promising efficacy results from clinical trials." However, concerns about coronavirus variants and material shortages caused agreements between the WHO, developed nations, and vaccine manufacturers to follow through.

WHO Needs More Information To Authorize Sinovac's COVID-19 Vaccine. The Wall Street Journal

(5/26, Deng,Hinshaw, Subscription Publication, 8.41M) reports the WHO is requesting more data from Sinovac as it considers approving the Chinese company's COVID-19 vaccine, Coronavac. While it is not clear what information is missing, the agency cleared another Chinese vaccine from rival Sinopharm around the same time it met to discuss Coronavac.

EU TELLS BRUSSELS COURT ASTRAZENECA FAILED TO FULFILL ITS VACCINE COMMITMENTS. <> The AP

(5/26,Petrequin) reports that on Wednesday, the European Union "took on vaccine producer AstraZeneca in a Brussels court...and accused the drugmaker of acting in bad faith by providing shots to other nations when it had promised them for urgent delivery to the EU's 27 member countries." According to the AP, "During an emergency hearing, the EU asked for the delivery of missing doses and accused AstraZeneca of postponing deliveries so the Anglo-Swedish company could service Britain, among others." The AP adds that AstraZeneca "denies any wrongdoing and said it has always done its best to fulfill delivery commitments."

The New York Times

(5/26, Pronczuk,Stevis-Gridneff, 20.6M) reports that "lawyers representing the bloc told the judges in a Brussels courtroom that they would seek €10 (about

$12) a dose for each day that delivery is delayed, along with €10 million a day for each of four alleged breaches of contract." According to the Times, "The bloc is demanding 90 million doses from the company by the end of June, and another 180 million by the end of September. The proposed penalties, if accepted by the judge, would begin on July 1 and could quickly balloon into billions of euros."

SLOVAKIA AUTHORIZES USE OF RUSSIA'S SPUTNIK V VACCINE. <> The AP

(5/26) reports that on Wednesday, Slovakia "became the second European Union country to authorize use of the Russian-made Sputnik V vaccine, which has not yet been approved by the bloc's drug regulator." According to the AP, "The Slovak government asked Health Minister Vladimir Lengvarsky – who has expressed reservations about the Russian COVID-19 vaccine – to make it available by June 7." The AP says Slovakia "has 200,000 doses of Sputnik V in stock but had not allowed its use until now."

FRANCE PRAISES YOUTUBE USERS WHO RESISTED VACCINE MISINFORMATION CAMPAIGN. <> TheAP

(5/26,Leicester) reports France's government offered "strong praise Wednesday to YouTubers and other social media influencers who resisted a mysterious effort to recruit them for a smear campaign to spread disinformation to their millions of young followers about the Pfizer COVID-19 vaccine." Multiple France-based influencers "with sizable audiences on Twitter, Instagram and other platforms said they were contacted with offers of hush-hush payments to make bogus claims about supposed deadly Pfizer vaccine risks."

Russia & Eurasia:

LUKASHENKO ACCUSES WEST OF ENGAGING IN "HYBRID WAR" AGAINST BELARUS. <> Axios

(5/26,Allassan, 1.26M) reports that on Wednesday, Belarus President Aleksandr Lukashenko, "who diverted a passenger airplane carrying a journalist and government dissident on board this week, defended his actions Wednesday as necessary to quell a bomb threat." Axios adds, "EU nations have banned Belarusian airlines, told European airlines not to fly over the country, and promised more economic sanctions. Lukashenko described the retaliation as a 'hybrid war' to 'strangle' Belarus."

Reuters

(5/26) reports that Lukashenko also alleged that Raman Pratasevich, the journalist "pulled off a plane that was forced to land in Minsk, had been plotting a rebellion." According to Reuters, "In his speech to parliament, Lukashenko gave no details of the 'bloody rebellion' he accused...Protasevich of planning." TheAP

(5/26, Karmanau) reports that Lukashenko "also warned his other foes abroad that the authorities will go after them," saying, "We know your faces, and it's just a matter of time for you to be brought to account before the Belarusian people."

The Washington Post

(5/26, 10.52M) reports that Lukashenko, who is "known for often outlandish remarks, suggested that by diverting the plane, he also prevented a potential nuclear catastrophe, as the airliner could have triggered the defense systems on the country's Astravec power plant." The Post reports that Lukashenko "said the decision to intercept the plane filled with Lithuanian tourists coming back from Greece was prompted by a bomb threat, which he now claims originated from Switzerland." The Post says Belarusian officials "previously said the threat came via email from Hamas."

Politico Europe

(5/26, 15K) reports that Lukashenko "also downplayed reports that the plane was forced to turn for Minsk by a fighter jet, putting the blame for the decision to land in the Belarusian capital on the crew, and saying that the fighter had been scrambled 'according to all the rules.'" Politico adds, "Those justifications are unlikely to lessen the outrage over the Ryanair incident, and its impact on European aviation."

The New York Times

(5/26,Troianovski, 20.6M) says that with his decision to divert the flight, Lukashenko has "ushered in a new and even more brittle phase in one of the post-Soviet region's most convoluted and consequential relationships: the one between" Lukashenko and Russian President Vladimir Putin. According to the Times, "The two are increasingly leaning on each other in the face of conflict with the West, but they have sharply diverging interests."

SASSE AMONG THOSE CRITICAL OF BIDEN'S DECISION TO MEET WITH PUTIN. <> CNBC

(5/26,Ellyatt, 7.34M) reports on its website that ahead of President Biden and Russian President Vladimir Putin's summit in Geneva next month, "there are doubts whether the summit can achieve much, given the poor state of relations." And CNBC adds that "not everyone is happy about the summit even going ahead." Sen. Ben Sasse (R-NE), a member of the Senate Select Committee on Intelligence, "was among those voicing disapproval of the Biden-Putin summit." Sasse released a statement reading: "We're rewarding Putin with a summit? ... Instead of treating Putin like a gangster who fears his own people, we're giving him his treasured Nord Stream 2 pipeline and legitimizing his actions with a summit. This is weak." Andrius Tursa, Central and Eastern Europe advisor at Teneo Intelligence, is quoted a saying, "The Russian state-owned media will spin the Putin-Biden summit in a way that emphasizes Russia's great power status and its

indispensable role in addressing various global challenges."

Rubin: Putin Summit "Doesn't Make The US Look 'Weak.'" The Washington Post

's (5/26, 10.52M) Jennifer Rubin writes that good behavior "has never been the precondition for US presidents meeting with adversarial powers," and that a "meeting in which Biden signals the free pass from the United States has expired may prompt Putin to more carefully assess the costs and benefits of future conduct. If that is the outcome, it will have been worth the trip."

China:

NSC'S KURT CAMPBELL: BROAD ENGAGEMENT WITH CHINA "HAS COME TO AN END." <> Bloomberg

(5/26, 3.57M) reports the US is entering a "period of intense competition with China as the government running the world's second-biggest economy becomes ever more tightly controlled by President Xi Jinping, the White House's top official for Asia said Wednesday." Speaking at a Stanford University event, Kurt Campbell, the US coordinator for Indo-Pacific affairs on the National Security Council, said, "The period that was broadly described as engagement has come to an end." Campbell predicts US policy toward China will now operate under a "new set of strategic parameters," adding that "the dominant paradigm is going to be competition." Chinese policies under Xi "are in large part responsible for the shift in U.S. policy, Campbell said, citing military clashes on China's border with India, an 'economic campaign' against Australia and the rise of China's 'wolf warrior' diplomacy." Beijing's behavior was "emblematic of a shift toward 'harsh power, or hard power' which 'signals that China is determined to play a more assertive role,' he said."

CRS: CHINA SUPPLYING NUCLEAR, MISSILE TECHNOLOGY TO NORTH KOREA, IRAN. <> The Washington Times

(5/26,Gertz, 626K) reports China is continuing to "sell dangerous nuclear technology and missiles around the world, mainly to North Korea and Iran, according to the Congressional Research Service." A CRS report published "earlier this month reveals that the Chinese government seems to have ceased direct involvement in nuclear arms proliferation and sales of complete missile systems in favor of hiding behind cutout entities." In specific, the report states the Chinese government "has apparently ended its direct involvement in the transfer of nuclear- and missile-related items, but Chinese-based companies and individuals continue to export goods relevant to those items, particularly to Iran and North Korea."

SENATE GOP COULD BLOCK BIPARTISAN PLAN TO CONFRONT CHINA. <> Politico

(5/26,
Desiderio, Bade, 6.73M) reports Senate Republicans "are indicating that they may derail debate on" a bipartisan measure "confronting China's growing

economic and geopolitical influence before the Senate leaves town for a recess later this week. Some in the GOP are pressing for more votes on their amendments to the China legislation, a top priority of Majority Leader Chuck Schumer." Sen. Mike Crapo (R-ID) "said he was particularly frustrated by what he described as Democratic leadership's refusal to consider a trade amendment" he has offered with Sen. Ron Wyden (D-OR). Politico says the "latest Republican resistance imperils Schumer's plans for a final vote on the bill, which allocates billions in new funding for scientific research and technology to counter China's economic rise."

The Hill

(5/26,Bolton, 5.69M) reports, "Some Republicans now say Schumer won't get the 60 votes he needs to advance the bill unless he relents and allows a vote on" the Crapo-Wyden measure. After Wednesday's lunch, a GOP senator said "'it would be hard to imagine' the China bill getting 10 Republican votes to advance until Schumer backs down and allows a vote on the Wyden-Crapo deal to update and reauthorize expired trade programs."

SENATE LEGISLATION WOULD ADD NATIONAL SECURITY REVIEWS OF CHINESE DONATIONS TO US UNIVERSITIES. <> Reuters

(5/26,Zengerle) reports US senators introduced legislation "on Wednesday that would require national security reviews of major Chinese gifts and contracts to US universities." They hope that limiting "such reviews to China alone would ease concerns in academia that reviews of foreign funding could threaten research." The measure, an "amendment to a broad bill seeking to boost U.S. competitiveness with China, would require the federal government's Committee on Foreign Investment in the United States (CFIUS) to review grants and contracts from China whose value exceeds $1 million." TheWashington Times

(5/26,Taylor, 626K) also reports.

TESLA TO ESTABLISH DATA CENTER IN CHINA FOR LOCAL DATA STORAGE. <> TechCrunch

(5/26, Liao, 502K) reports, Tesla "said it has established a data center in China to carry out the 'localization of data storage,' with plans to add more data facilities in the future, the company announced through its account on microblogging platform Weibo." All data generated "by Tesla vehicles sold in mainland China will be kept domestically." Tesla is acting in "response to new requirements drafted by the Chinese government to regulate how cameras- and sensors-enabled carmakers collect and utilize data."

CLOSED CHINESE CONSULATE IN HOUSTON WAS "MAJOR HUB" FOR ESPIONAGE, STUDY INDICATES. <> The Washington Times

(5/26,Lovelace, 626K) reports, "The Chinese consulate in Houston, ordered closed by the Trump administration last year, was a 'major hub' for Beijing's

global science and technology collection efforts, according to a newstudy

." Georgetown University's Center for Security and Emerging Technology "examined 642 'international technological cooperation opportunities' between 2015 and 2020 identified by Chinese diplomats and found the Houston post was the key hub for science and technology (S&T) collection globally." US critics "say intellectual property theft and piracy have been key to China's drive to close the technology gap with the U.S. and the West."

East Asia:

JAPAN FACING NEW COVID SURGE AHEAD OF SUMMER OLYMPICS. <> NBC Nightly News

(5/26, story 6, 1:30, Holt, 4.76M) reported that the Summer Olympics will open in eight weeks, but Japan is "reporting roughly 5,000 new COVID cases a day" and Tokyo OIC organizers "say they're not considering cancelling the Olympics." Japanese apprehension to cancel the Olympics is leading to new pressure both domestic and international, and US scientist "say 'calling off the games may be the safest option.'"

Henry Olsen writes in the Washington Post

(5/26, 10.52M) while there is growing pressure on Japanese Prime Minister Yoshihide Suga "to again postpone this summer's Olympic Games in Tokyo," the games "should go on as scheduled, and the world should chip in to help ensure the Japanese people stay safe as they do." Olsen argues the world "needs an example that life can be normal again."

ESPIONAGE TRIAL OF AUSTRALIAN BLOGGER TO OPEN IN CHINA ON THURSDAY. <> Reuters

(5/26) reports that a Chinese court "will hear an espionage case on Thursday against Australian blogger Yang Hengjun, detained by Chinese authorities two years ago as he arrived from New York, against a backdrop of worsening ties between the two nations." Details of the case "have been shrouded in secrecy," and Australia has "complained that Chinese authorities have not provided 'any explanation or evidence for the charges.'"

CAMPBELL: US HOPING FOR FALL QUAD MEETING ON INFRASTRUCTURE. <> Reuters

(5/26,Brunnstrom, Martina) reports that the US is "looking to convene an in-person meeting of its partners the Quad group of countries – Australia, India and Japan – in the fall with a focus on infrastructure in the face of the challenge from China," Kurt Campbell, President Biden's policy coordinator for the Indo-Pacific, said Wednesday. Speaking during an online event, Campbell said, "We want to look this fall to convene an in-person Quad and the hope will be to make a similar kind of engagement on infrastructure more generally," adding that if "there are other countries that believe that they'd like to engage and work with us, the door will be open as we go forward."

KIM VOWS “UNCOMPROMISING STRUGGLE” TO BUILD SOCIALISM IN NORTH KOREA. <> The AP

(5/27,Kim) reports North Korean leader Kim Jong Un has “vowed an ‘uncompromising struggle’ against anti-socialist elements at home, state media reported Thursday, as he tries to fortify his power amid pandemic-related difficulties and US-led economic sanctions.” Kim’s comments come “as doubts increase about both North Korea’s economy and whether it will engage in serious disarmament talks with Washington.”

MCCONNELL PRAISED ADMINISTRATION FOR BURMA COUP RESPONSE. <> The Hill

(5/26,Axelrod, 5.69M) reports that Senate Minority Leader McConnell “offered rare praise Wednesday for the Biden Administration over its response to the military coup in Myanmar.” McConnell said, “I have been in close touch with the Biden Administration on Burma, discussing how to best support opposition to the junta while standing up new targeted sanctions and export licensing bans to hit the leaders of the military coup where it hurts: in the wallet. And I’ve been encouraged by the Administration’s swift response.”

US ENVOY CONFIDENT TAIWAN CAN DEAL WITH SPIKE ON COVID CASES. <> Reuters

(5/26) reports that on Wednesday, Brent Christensen, “the outgoing de facto U.S. ambassador in Taipei,” maintained that he is “confident Taiwan could control a spike in COVID-19 cases, noting its infection numbers remained quite low, and that they were in talks on vaccines though did not say shots were on the way.” According to Reuters, “After months of relative safety, Taiwan is battling a surge in domestic COVID-19 cases, but has only vaccinated around 1% of its more than 23 million people.” Last week, Taiwan’s health minister “spoke to his U.S. counterpart to ask for help after President Joe Biden said he would send at least 20 million more COVID-19 vaccine doses abroad by the end of June.”

South Asia:

TALIBAN WARNS AFGHANISTAN’S NEIGHBORS AGAINST HOSTING US TROOPS. <> Reuters

(5/26) reports that on Wednesday, the Taliban “warned nearby nations against allowing the United States to use their territory for operations in the country after they withdraw from Afghanistan.” According to Reuters, “Experts and diplomats have speculated that Washington’s future role in the region could include bases in nearby countries, especially Pakistan.” Reuters adds that “in recent days, there has been a spate of talks between senior Pakistani and U.S. officials, including a meeting between Biden’s National Security Adviser Jake Sullivan and his Pakistani counterpart.”

US Carrier To Move To Support Afghan Withdrawal. In an “exclusive,” the Wall Street Journal

(5/26,Youssef, Lubold, Subscription Publication, 8.41M) reports that the Pentagon is expected to move the USS Ronald Reagan, the only carrier in the Asia-Pacific region, toward the Middle East to support the withdrawal of US forces. The warship is expected to depart its home port of Yokosuka, Japan and head for the region this summer, and operate there for three to four months.CNN

(5/27, 89.21M) reports analysts "say the move could leave a gap in US carrier coverage in East Asia at a time when Beijing is turning up the heat over the South China Sea and Taiwan."

In an editorial, the Wall Street Journal
(5/26,
Subscription Publication, 8.41M) says that the move will leave the US without a carrier in the Western Pacific, which sends a clear message that the US needs to boost its naval assets and adjust its strategies to current realities.

PAKISTANI JOURNALIST ALLEGES INTELLIGENCE AGENTS ATTACKED HIM IN HIS APARTMENT. <> The AP

(5/26) reports a journalist critical of "Pakistan's powerful military and intelligence agencies was severely beaten by three unidentified men in an attack at his apartment in Islamabad, the journalist and colleagues said Wednesday." Asad Ali Toor, who works "for the Aaj News Pakistani TV channel, told police in a statement the attackers claimed they were intelligence agents."

WHATSAPP SUES INDIAN GOVERNMENT OVER MESSAGE TRACEABILITY RULES. <> The AP

(5/26, Saaliq,Soo) reports new regulations for technology companies that operate in India prompted WhatsApp to file a lawsuit "in the Delhi High Court." The suit, which was filed against India's government, alleges that "rules regarding the traceability of messages are unconstitutional and undermine the fundamental right to privacy." WhatsApp "uses end-to-end encryption for its messaging service, which encrypts messages in such a way that no one apart from the sender and receiver are able to read the messages sent between them."Reuters

(5/26,Menn) reports that when it was asked to comment on its suit, WhatsApp stated, "Requiring messaging apps to 'trace' chats is the equivalent of asking us to keep a fingerprint of every single message sent on WhatsApp, which would break end-to-end encryption."

NYTIMES: OFFICIAL FIGURES "GROSSLY UNDERSTATE" PANDEMIC IMPACT IN INDIA. <> The New York Times

(5/25, Gamio, Glanz, 20.6M) examines the ongoing COVID surge in India, and, while India "recorded the largest daily death toll for any country during the pandemic," the official figures "grossly understate the true scale of the

pandemic." The Times interviewed a variety of public health experts to better understand the scope of the tragedy facing India, and their assessment found that estimated infections and death "far exceed official figures." The "most pessimistic" conclusions "show a toll on the order of millions of deaths — the most catastrophic loss anywhere in the world."

Western Hemisphere:

AMLO'S PARTY EXPECTED TO MAINTAIN CONTROL OF LOWER HOUSE. <> Reuters

(5/26) reports Mexican President Andres Manuel Lopez Obrador's "National Regeneration Movement (MORENA) and its allies are expected to maintain control of the lower house of Congress in elections on June 6, but with fewer seats, an opinion poll showed Wednesday." The May 15-18 survey "of 1,500 registered voters by polling firm GEA-ISA showed the leftist MORENA winning 209 seats in the 500-seat lower house, compared to the 253 it currently holds." MORENA's allies the "Green Party and the Labor Party were seen picking up 50 seats between them to ensure a majority, giving their alliance 259 in total, the poll said."

MAYORAL CANDIDATE KILLED IN MEXICO, 34TH OF THIS ELECTION CYCLE. <> The AP

(5/26,Arredondo) reports Mexican mayoral candidate Alma Barragán was killed Tuesday "while campaigning for the mayorship of the city of Moroleón in violence-plagued Guanajuato state." Barragán's death brings "to 34 the number of candidates murdered nationwide ahead of the June 6 elections." President Andrés Manuel López Obrador "said Wednesday the killing was 'without doubt' the work of organized crime gangs."

FORMER BOLIVIAN INTERIOR MINISTER ARRESTED IN US FOR MONEY LAUNDERING. <> The AP

(5/26,Goodman) reports Bolivia's former interior minister "has been arrested in the US for allegedly taking part of $602,000 in kickbacks from Florida-based businessmen accused of selling tear gas at inflated prices to the conservative government of former interim President Jeanine Áñez." Arturo Murillo was charged "with a single count of conspiring to commit money laundering, according to a Department of Justice statement on Wednesday."

Cybersecurity:

COLONIAL PIPELINE REBUFFED TSA SECURITY REVIEW BEFORE HACK. <> The Wall Street Journal

(5/26,Uberti, Subscription Publication, 8.41M) reports that Colonial Pipeline Co. last year did not submit to a requested federal security review of its facilities and was in the process of arranging a separate audit of its computer networks when it was hacked earlier this month. The Journal adds that it is

unclear if the TSA security assessment would have uncovered network vulnerabilities that were exploited by the hacking group DarkSide, authorities said.

TSA, CISA Working With Private Companies On Cybersecurity. The AP

(5/25) reports TSA and CISA "are working with private companies to address cyber threats," according to statements by DHS.. "The Biden Administration is taking further action to better secure our nation's critical infrastructure," it said. The American Petroleum Institute "said in a statement that its members are working with the administration to develop reporting policies and that any new regulations" should include "reciprocal information sharing and liability protections."

The Washington Post

(5/26,Schaffer, 10.52M) reports DHS plans to go "even further in coming weeks, releasing mandatory cybersecurity protections that pipeline companies must implement and steps they must take if they're hacked." The companies would face "financial penalties if they fall short on those cyber protections." Federal agencies are themselves "still far behind in protecting against cyberattacks that tunnel in through their web of IT contractors, a government auditor yesterday told lawmakers on the House Committee on Science Space and Technology."

NPR

(5/26,Schneider, 3.69M) also reports.

GAO: Federal Agencies "Struggling" With Supply Chain Security. Gov Info Security

(5/26,McGee) reports more than five months "after the SolarWinds supply chain attack came to light, federal agencies continue to struggle with supply chain security, according to a Government Accountability Office official who testified at a congressional hearing Tuesday." Since the attack, "only a handful of executive branch departments have made updates to their security protocols, and none are fully protected against these types of intrusions, Vijay D'Souza, GAO's director of information technology and cybersecurity, testified." The GAO released an "audit in December 2020 that found 14 of 23 large federal agencies had not implemented any of seven supply chain risk management practices that the agency had previously recommended." Since that report was "released, only six of the 23 agencies have provided the GAO with updates about plans to implement more of the supply chain risk management protections, D'Souza told members of Congress."

BIDEN BUDGET REQUEST TO GROW CYBER COMMAND. <> Politico

(5/26,Matishak, Seligman, 6.73M) reports President Biden's upcoming "budget request will propose growing US Cyber Command's main digital warfighting force over the next two years, according to two people familiar with the request, as the new administration reels from a series of cyberattacks." Biden wants to "increase the size of the Cyber Mission Force – a cadre of roughly 6,200 personnel culled from the military branches and divided into 133 teams – by about 600 people, or 10 percent." The exact "composition of the proposed teams remains unclear, one of the people said." Such a move "would mark the first expansion of the Cyber Mission Force since its structure was set in 2012."

RUSSIA'S FSB REPORTS "UNPRECEDENTED" HACKING CAMPAIGN. <> Reuters

(5/26) reports foreign hackers compromised "Russian federal agencies in a digital espionage campaign that Russian officials described as unprecedented in scope and sophistication." The "little-noticed report" published this month by the FSB and Rostelecom-Solar provides an "unusually detailed look at a purportedly state-backed cyber spying operation aimed at the Russian state." Citing the hackers' "'thorough preparation' and their intimate knowledge of Russian antivirus firm Kaspersky Lab's software," the report said, "Assessing the attackers' level of preparedness and qualification...we are inclined to refer to this group as cyber mercenaries, pursuing the interests of a foreign state." Kaspersky told Reuters it "was aware of the report, but had no information to suggest that the hackers had exploited any vulnerabilities in its products."

FACEBOOK: RUSSIA TOP PRODUCER OF DISINFORMATION. <> The Washington Post

(5/26, 10.52M) says "a Facebook report released Wednesday says that Russia is still the largest producer of disinformation." According to the Post, Facebook "says it has uncovered disinformation campaigns in more than 50 countries since 2017," and the report "highlights how such coordinated efforts have become more sophisticated and costly to run in recent years – even as these operators struggle to influence large numbers of people as they once did."

CNN

(5/26,Fung, 89.21M) reports that in addition to Russia, Iran was also tagged as a major producer of disinformation. However, during the 2020 elections, "it was US domestic actors, not foreign operatives, who were increasingly responsible for sowing disinformation."

The AP

(5/26,Lardieri) reports that according to the "report, of the 150 networks Facebook has dismantled since 2017, 45% were targeting domestic audiences, with 38% targeting countries abroad. Of the countries most frequently targeted by foreign disinformation networks, the US was the top target, followed by Ukraine and the United Kingdom."

NBC News

(5/26, 4.91M) reports Facebook "says it shut down 150 networks of fake accounts between 2017 and the end of 2020." Facebook doesn't attribute "the campaigns to governments, but many of the Russian and Iranian campaigns had all the hallmarks of intelligence influence operations, private researchers said." The report does not cover "the post-election misinformation campaign that paved the way for the Jan. 6 capital riots, which did not involve fake accounts."

Sex Trafficking Survivor Asks Facebook To Delay End-To-End Encryption Messaging Plan. The Daily Dot

(5/26, Goforth, 353K) reports "sex trafficking survivor Sarah Cooper" asked Facebook to study sex trafficking on its site "before it adds additional end-to-end encryption to its messaging services." Cooper made that request on Wednesday, during "Facebook's annual shareholders meeting." Copper's request comes after a US Department of Justice push to gain access to encrypted messages prompted some, including a Tufts University computer security professor named Susan Landau, to express concern. In 2019, Landau stated, "It is very easy to listen in on communications. Securing data is a clear national security interest." But on Wednesday, Cooper said a failure to delay implementing Facebook's end-to-end encryption messaging plan would make Facebook "one of the world's most dangerous platforms for children." Cooper said Facebook "should absolutely delay expanding encryption on its platform until it can protect children."

HACKERS RELEASE NEW ZEALAND PATIENT DATA. <> The Hill

(5/26,Miller, 5.69M) reports hackers sent patient data "stolen during an attack on New Zealand's Waikato District health system to local media outlets on Wednesday, with the outlets declining to publish the sensitive information." The Waikato District Health Board (DHB) "confirmed the attack" in a statement Wednesday, saying that it is "aware that the media have received what appears to be personal and patient information from Waikato DHB information systems."

CANADA POST NOTIFIES BUSINESS CUSTOMERS OF "DATA BREACH AFFECTING 950K CUSTOMERS." <> CTV News (CAN)

(5/26, 278K) reports the Canada Post has informed "44 of its large business customers that information relating to more than 950,000 customers was compromised after one of its suppliers fell victim to a malware attack late last week." On Wednesday, the postal agency "announced that Commport Communications, an electronic data interchange solution supplier, had notified them that manifest data held in their systems, which are associated with Canada Post customers, had been 'compromised' in an attack on May 19."

BIPARTISAN ENCRYPTION BILL INTRODUCED IN HOUSE. <> MeriTalk

(5/26, Polit) reports Reps. Ted Lieu (D-CA) and Nancy Mace (R-SC) led a "bipartisan group of legislators in reintroducing the Ensuring National Constitutional Rights for Your Private Telecommunications (ENCRYPT) Act." The legislation, which was "first introduced in 2016, would supersede state and local government encryption laws to ensure a uniform, national policy for the interstate issue of encryption technology."

Editorial Roundup:

WASHINGTON POST. <> "Who Were The First Coronavirus Cases? China Should Help Solve The Mystery." The Washington Post

(5/26, 10.52M) argues that the ongoing international investigation into COVID's origins is critical, and China "should help solve this mystery, but it so far has thrown a cloak over it." While China "steadfastly denies there was an inadvertent leak from the Wuhan Institute of Virology," the only way to resolve the question of China's potential culpability is to support the WHO's ongoing investigation.

"John Warner Was The Kind Of Republican The Country Needs Now." The Washington Post

(5/26, 10.52M) said that while former Sen. John W. Warner (R-VA) was a "rock-ribbed Republican," his "brand of Republicanism — suspicious of populism, repelled by extremists, prizing principle over partisanship — is all but unrecognizable today." The Post notes that he endorsed by Hillary Clinton in 2016 and Joe Biden in 2020. Today, the Post concludes, "in an era of lockstep party loyalty, Mr. Warner may look like a throwback. In fact, he was the embodiment of patriotic public service."

WALL STREET JOURNAL. <> "The Virus Lab Theory's New Credibility." The Wall Street Journal

(5/26, Subscription Publication, 8.41M) examines the efforts made by scientists, media personalities, and government officials to disregard the lab-leak COVID origin theory last year, and it criticizes the slow reversal of opinion over the past few months. The Journal calls on scientists and other experts to conduct a thorough investigation in order to better protect the US from future pandemic threats.

"The Proxy Coup At Exxon."

"Illinois's Big Labor Bill Of Rights."

"The Missing Aircraft Carrier." The Wall Street Journal
(5/26,
Subscription Publication, 8.41M) says in an editorial that on Wednesday, the

Pentagon will dispatch the USS Ronald Reagan to the Middle East to cover the U.S. and NATO withdrawal from Afghanistan, thus leaving the U.S. without a carrier in the Western Pacific for several months. The Journal refers to this move by President Biden as a misuse of naval resources, commenting that it would have made more sense for the U.S. to remain in Afghanistan with reduced forces.

The Big Picture:

HEADLINES FROM TODAY'S FRONT PAGES. <>

Wall Street Journal:
Oil Giants Are Dealt Major Defeats On Climate-Change As Pressures Intensify

Biden Calls For Intelligence Report On Origins Of Covid-19

Why A Grand Plan To Vaccinate The World Against Covid Unraveled

Cities Reverse Defunding The Police Amid Rising Crime

Google Strikes Deal With Hospital Chain To Develop Healthcare Algorithms

Americans Are On The Move. Their Stuff Doesn't Always Follow.

Washington Post:
Biden Asks For Report On Virus's Origins

Group's Legal Blitz Deters Vaccine Mandates

Worker Fatally Shoots 8 At Calif. Rail Yard

Stockholders, Court Deliver Reckoning To Big Oil

5-Term Senator From Va. Often Went His Own Way

Amazon Expands Its Hollywood Ambitions

Financial Times:
Cummings Launches Stinging Attack On Johnson And Handling Of Covid Crisis

Climate Activists Hail Breakthrough Victories Over Exxon And Shell

Labour Shortages Hit Advanced Economies Despite Many Out Of Work

Amazon Agrees Deal To Buy MGM For $8.45BN

Story Lineup From Last Night's Network News:
ABC: San Jose Shooting; COVID Origins; COVID Update; Severe Weather; California-BB Gun Shootings; Idaho-Daybell Case; Amazon-Noose At Work Site; Sen. John Warner Death; Chadwick Boseman Tribute; Man With Down Syndrome Hired Full Time At UPS.
CBS: San Jose Shooting; COVID Origins; Memorial Day Travel; COVID Update; Severe Weather; Idaho-Daybell Case; COVID-Immunocompromised Folks; Sen. John Warner Death; Amazon-MGM; Boston-Apartment Fire; Lunar Eclipse; Remembering Samuel E. Wright.
NBC: San Jose Shooting; COVID Origins; COVID Update; Marjorie Taylor Greene Comments; Israel/Gaza; Tokyo Olympics; Sen. John Warner Death; Amazon-MGM; Los Angeles-Criminal Justice System; 10-Year-Old Chess Master.

Network TV At A Glance:
San Jose Shooting – 11 minutes, 0 seconds
COVID Origins – 7 minutes, 30 seconds
COVID Update – 7 minutes, 30 seconds
Sen. John Warner Death – 0 minutes, 55 seconds

[redacted]
Watch Officer – Team 1| DNI Watch
Office of the Director of National Intelligence
[redacted]

==========
Classification: UNCLASSIFIED

From: [redacted]
To: [redacted]
Cc: [redacted]
Subject: FW: [AIN] FW: Today"s Call/meeting info - [Link to Attachment(s)]
Date: Wednesday, July 21, 2021 2:36:44 PM
Attachments: image001_converted.pdf
Agenda- 2019-nCoV_converted.pdf
SOW_converted.pdf
Agenda- 2019-nCoV_converted.docx
SOW_converted.docx

Classification: UNCLASSIFIED[redacted]
==========[redacted]==========

[redacted]

[redacted] and I discussed who else might serve as a reviewer for the IC 90-Day COVID Origins effort; [redacted] who is a member of the National Academies and supporting the initial NAS engagement on COVID back in February 2020. As far as we know, he has not taken any public position. Let us know if we can support an outreach once the DNI has approved your proposed list.

Vr,
[redacted]

From: [redacted]
Sent: Wednesday, July 21, 2021 1:58 PM
To: ALANSM[redacted]
Subject: [AIN] FW: Today's Call/meeting info - [Link to Attachment(s)]

CLASSIFICATION: **UNCLASSIFIED**

AIN EMAIL

[redacted]

[redacted]

[redacted]

Profile of [redacted]

[redacted]h Baric

[redacted]

Call/meeting info

Thank you for participating in today?s meeting of experts at the National Academies to discuss and identify what data, information and samples are needed
to understand the evolutionary origins of 2019-nCoV and more effectively respond to the outbreak and resulting misinformation.

Attached for your information are:

Agenda

Scope of Work

A list of participants will be sent along shortly

Please let me know if you have any questions of problems with connecting.

?Zoom? Call-in info is as follows (and is included at top of agenda):

Zoom Dial-in Info:

Time: Feb 3, 2020 02:00 PM Eastern Time (US and Canada)

Join from PC, Mac, Linux, iOS or Android: [redacted]

Telephone: [redacted]

Meeting ID: [redacted]

International numbers available: [redacted]

[redacted]

[redacted]

&* ORIGINAL EMAIL ATTACHMENTS HAVE BEEN QUARANTINED ***

The following original attachment(s) are awaiting your approval:

- image001.png
- Agenda- 2019-nCoV.docx
- SOW.docx

If you trust the sender, click the following to have your message and original attachments resent to you:

Quarantine link ---> https://glide.cia/glide/Quarantine/Quarantine.html?id=1240695673

These attachment(s) will be available for retrieval for 14 days (Wed Aug 04 13:59:04 EDT 2021). For additional information regarding the attachment removal (quarantine) function, please visit the following site: https://confluence.devops.cia.ic.gov/display/ECDSSUP/ANTE+Up+Overview .

========== ==========

Classification: UNCLASSIFIED[redacted]

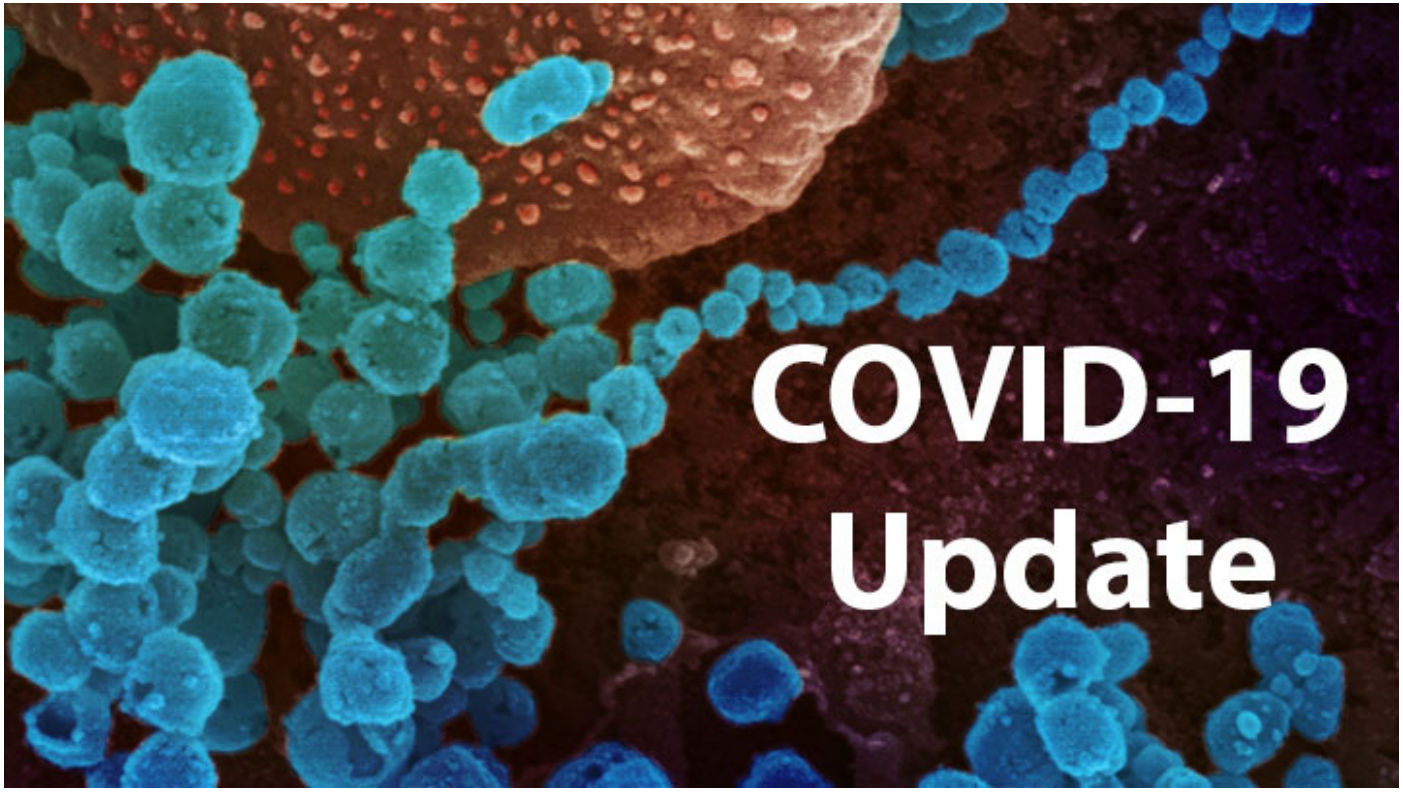
NIH Director's Blog

Search The Blog

Genomic Study Points to Natural Origin of COVID-19

Posted on March 26th, 2020 by Dr. Francis Collins

Recent Items



Blog Archives

Select Month

No matter where you go online these days, there's bound to be discussion of coronavirus disease 2019 (COVID-19). Some folks are even making outrageous claims that the new coronavirus causing the pandemic was engineered in a lab and deliberately released to make people sick. A new study debunks such claims by providing scientific evidence that this novel coronavirus arose naturally.

The reassuring findings are the result of genomic analyses conducted by an international research team, partly supported by NIH. In their study in the journal *Nature Medicine*, Kristian Andersen, Scripps Research Institute, La Jolla, CA; Robert Garry, Tulane University School of Medicine, New Orleans; and their colleagues used sophisticated bioinformatic tools to compare publicly available genomic data from several coronaviruses, including the new one that causes COVID-19.

The researchers began by homing in on the parts of the coronavirus genomes that encode the spike proteins that give this family of viruses their distinctive crown-like appearance. (By the way, "corona" is Latin for "crown.") All coronaviruses rely on spike proteins to infect other cells.

But, over time, each coronavirus has fashioned these proteins a little differently, and the evolutionary clues about these modifications are spelled out in their genomes.

The genomic data of the new coronavirus responsible for COVID-19 show that its spike protein contains some unique adaptations. One of these adaptations provides special ability of this coronavirus to bind to a specific protein on human cells called angiotensin converting enzyme (ACE2). A related coronavirus that causes severe acute respiratory syndrome (SARS) in humans also seeks out ACE2.

Existing computer models predicted that the new coronavirus would not bind to ACE2 as well as the SARS virus. However, to their surprise, the researchers found that the spike protein of the new coronavirus actually bound far better than computer predictions, likely because of natural selection on ACE2 that enabled the virus to take advantage of a previously unidentified alternate binding site. Researchers said this provides strong evidence that that new virus was not the product of purposeful manipulation in a lab. In fact, any bioengineer trying to design a coronavirus that threatened human health probably would never have chosen this particular conformation for a spike protein.

The researchers went on to analyze genomic data related to the overall molecular structure, or backbone, of the new coronavirus. Their analysis showed that the backbone of the new coronavirus's genome most closely resembles that of a bat coronavirus discovered after the COVID-19 pandemic began. However, the region that binds ACE2 resembles a novel virus found in pangolins, a strange-looking animal sometimes called a scaly anteater. This provides additional evidence that the coronavirus that causes COVID-19 almost certainly originated in nature. If the new coronavirus had been manufactured in a lab, scientists most likely would have used the backbones of coronaviruses already known to cause serious diseases in humans.

So, what is the natural origin of the novel coronavirus responsible for the COVID-19 pandemic? The researchers don't yet have a precise answer. But they do offer two possible scenarios.

In the first scenario, as the new coronavirus evolved in its natural hosts, possibly bats or pangolins, its spike proteins mutated to bind to molecules similar in structure to the human ACE2 protein, thereby enabling it to infect human cells. This scenario seems to fit other recent outbreaks of coronavirus-caused disease in humans, such as SARS, which arose from cat-like civets; and Middle East respiratory syndrome (MERS), which arose from camels.

The second scenario is that the new coronavirus crossed from animals into humans before it became capable of causing human disease. Then, as a result of gradual evolutionary changes

over years or perhaps decades, the virus eventually gained the ability to spread from human-to-human and cause serious, often life-threatening disease.

Either way, this study leaves little room to refute a natural origin for COVID-19. And that's a good thing because it helps us keep focused on what really matters: observing good hygiene, practicing social distancing, and supporting the efforts of all the dedicated health-care professionals and researchers who are working so hard to address this major public health challenge.

Finally, next time you come across something about COVID-19 online that disturbs or puzzles you, I suggest going to FEMA's new Coronavirus Rumor Control web site. It may not have all the answers to your questions, but it's definitely a step in the right direction in helping to distinguish rumors from facts.

Reference:

[1] The proximal origin of SARS-CoV-2. Andersen KG, Rambaut A, Lipkin WI, Holmes EC, Garry RF. Nat Med, 17 March 2020. [Epub ahead of publication]

Links:

Coronavirus (COVID-19) (NIH)

COVID-19, MERS & SARS (National Institute of Allergy and Infectious Diseases/NIH)

Andersen Lab (Scripps Research Institute, La Jolla, CA)

Robert Garry (Tulane University School of Medicine, New Orleans)

Coronavirus Rumor Control (FEMA)

NIH Support: National Institute of Allergy and Infectious Diseases; National Human Genome Research Institute

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Posted In: News

Tags: ACE2, bats, bioengineering, camels, civets, coronavirus, Coronavirus Rumor Control, COVID-19, evolutionary biology, FEMA, genomics, man-made, MERS, natural, natural origin, new coronavirus, pandemic, pangolin, SARS, SARS-CoV-2, social distancing, spike protein, viral pandemics, virology

26 Comments

***Wagner* says:**
March 27, 2020 at 2:19 am
In their paper under #1 – "Mutations in the receptor-binding domain of SARS-CoV-2" – last paragraph, last 2 sentences. Thus, the high-affinity binding of the SARS-CoV-2 spike protein to human ACE2 is MOST LIKELY THE RESULT OF natural selection on a human or human-like ACE2 that permits another optimal binding solution to arise. This is STRONG EVIDENCE that SARS-CoV-2 is not the product of purposeful manipulation.

Huh? How can you use "most likely the result of" and then "strong evidence" in the same paragraph? If you have to say – most likely the result of – then its not proven yet.

I felt this paper did anything but "prove" it wasn't genetically engineered. More like a paper to refer to when trying to prove a point. Like on Facebook. Refer to this published article as my reference of stated fact.

And as matter of fact, this paper has been used as such in several articles so far…

Reply

***Bill Hutchins* says:**
March 27, 2020 at 3:12 am

So you are 100% sure that it was not designed in a lab because it resembles something else? I can imagine that virus design involves genetic engineering. But there are also other methods to steer natural selection, aren't there?
The state of the art in virus design is at least not such that a massive financial market move could be designed, with changes for the travel industry, oil prices, pension funds, culture even, what else. That is the work of wind makers. Cut out the news on animated "markets" and the verb "surge" at all and not 1/10th of USD 2 trillion would flow through Wall Street. 50% of investment had become "passive" so active traders could only benefit from turmoil.
It's interesting that you are dipping your toe into the "media."
A research director for RKI in Germany said in an interview that he expects the national statistical death rate to be in the same range as a normal year. So, what the media and all the comment bots on internet make of it, should be taken as sales/advertising /engagement messages anyway.

Which doesn't take away: Social distancing is currently advised! Not a vaccine but effective!! Stay home if you are sick or have a cold, fever or cough. Once people start infecting less than one other individual the epidemic slows.

Reply

Richard **says:**
March 27, 2020 at 4:24 am
Thank you for this info.
Might I suggest that we use the more accurate term adaptation instead of evolution. The virus remains a Corona Virus; It is not busy changing into a Spirochete.

Reply

« Previous 1 2

Leave a Comment

Enter your comment here...

About the NIH Director

Francis S. Collins, M.D., Ph.D.

Appointed the 16th Director of NIH by President Barack Obama and confirmed by the Senate. He was sworn in on August 17, 2009. On June 6, 2017. President Donald Trump announced his selection of Dr. Collins to continue to serve as the NIH Director.

More about Dr. Collins

@NIHDirector on Twitter

Who would have thought 2020 would bring an #NIH social media collab w/3-time NBA champ @StephenCurry30? He's hostin… https://t.co/7Qu4Awur6r **20 hours ago**

New genomic study debunks claims that the novel #coronavirus causing #COVID-19 was created in a lab. Learn more.… https://t.co/EXRhxEsGUI **23 hours ago**

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Blog Info

Editor

Kendall Morgan, Ph.D.

Comments and Questions

If you have comments or questions not related to the current discussions, please direct them to **Ask NIH**.

You are encouraged to share your thoughts and ideas. Please review the **NIH Comments Policy**

National Institutes of Health
Turning Discovery Into Health

[redacted]

Dear Chairman Warner, Vice Chairman Rubio, Chairman Schiff, and Ranking Member Nunes,

(U) I am committed to ensuring that the congressional intelligence committees have the information they need to perform their important oversight functions on behalf of the American people.

[redacted] To that end, I am writing to inform you that I have asked the Acting Inspector General of the Intelligence Community ("IC IG") to transmit to you a whistleblower complaint she received relating to the origins of COVID-19. Specifically, the complaint alleges that congressional testimony from a government official suggesting "that no gain-of-function research occurred (or at least wasn't 'paid for' by [the National Institutes of Health]) at the Wuhan Institute of Virology" was incorrect.

[redacted] Although the whistleblower complaint does not specify the date of the congressional testimony in question, it may be referring to testimony Dr. Anthony Fauci, the Director of the National Institute of Allergy and Infectious Diseases, provided to the Senate Health, Education, Labor and Pension (HELP) Committee on May 11, 2021, when he stated that "the NIH has not ever and does not now fund gain of function research in the Wuhan Institute." (Dr. Fauci made a similar point during a July 20, 2021 hearing before the HELP Committee.)

[redacted] As detailed in her August 10, 2021 letter to me, the Acting IC IG determined that this complaint did not constitute a matter of urgent concern that must be provided to the congressional intelligence committees. Nevertheless, consistent with my commitment to effective and appropriate congressional oversight, I have asked the Acting IC IG to transmit the whistleblower complaint to you.

(U) It is of fundamental importance that Congress and the American public have confidence that their government officials provide accurate statements and testimony. After consulting with the Secretary of Health and Human Services ("Secretary"), I have thus requested that the Acting IC IG also transmit this complaint to the Secretary, and I have committed to ensuring that the Secretary has access to the information necessary to undertake a complete review of the concerns raised in this complaint.

Sincerely,

Classified By: [redacted]
Derived From: [redacted]
Declassify On: [redacted]

[redacted]

[redacted]

From: Christopher C. Fonzone-DNI-
Sent: Monday, August 16, 2021 9:08 PM
To: Avril D. Haines-DNI-
Cc: [redacted] Matthew C. Rhoades-DNI-; [redacted]
Subject: Talking Points and Letter on Whistleblower Issue
Attachments: [redacted] Letter to DNI re COVID origin urgent concern with enclosures Signed.pdf; HPSCI SSCI WB Transmittal Letter v.3.docx

Follow Up Flag: Follow up
Flag Status: Flagged

Classification: [redacted]

Classified By: [redacted]
Derived From: [redacted]
Declassify On: [redacted]
==========

Avril –

Given everything that's going on, I'm sure this is the last thing that you want to deal with. But, as we discussed late last week, we've pulled together: (1) some draft points that you could use to call S/HHS or DS/HHS (or I could use, with slight adaptations, to call GC/HHS) concerning the whistleblower complaint; and (2) a letter that you (or potentially you and S/HHS) could send to accompany the transmission of the complaint to Congress. (I've also attached the relevant letter so you have it all in one place.)

I know your schedule is probably a mess tomorrow (and in coming days), but, if you have a minute after tomorrow morning's stand-up, perhaps we can touch base quickly on next steps. Of course, if that doesn't work or isn't a good time, I am happy to try to make work any time that is good for you.

Many thanks,

Chris

DRAFT TALKING POINTS

- I wanted to call to tell you about a whistleblower complaint the Acting Inspector General of the Intelligence Community ("IC IG") recently brought to my attention.
- The complaint alleges that there is intelligence reporting contradicting Dr. Fauci's testimony to the Congress that no "gain-of-function research" occurred (or at least wasn't "paid for" by NIH) at the Wuhan Institute of Virology.

- The Acting IC IG could not conclude that the intelligence reporting cited by the complaint contradicted the relevant testimony, and my understanding, based on a conversation my team had with our expert on the topic, is that there is substantial disagreement within the scientific community as to what even constitutes "gain-of-function research."
- Nonetheless, given the nature of the complaint – which is classified – I believe we should provide it to the congressional intelligence committees.
- Before we did so, however, I wanted to reach out to you to make sure you were aware of the situation and to discuss what steps it would be appropriate to take – and inform Congress we were taking – in light of the complaint.
- To that end, one idea would be for the Acting IC IG to transmit the complaint to HHS's Inspector General, so that official can also take a look. If we go that route, I would commit to ensuring that the HHS IG has access to the intelligence necessary to review the complaint.
- We could also then simultaneously inform Congress of the complaint and our plans for addressing it.

==========

Classification: [redacted]

[redacted]

From: Christopher C. Fonzone-DNI-
Sent: Thursday, August 19, 2021 9:13 PM
To: Avril D. Haines-DNI-
Cc: Stacey A. Dixon-DNI-; Morgan Muir-DNI-; [redacted]; Matthew C. Rhoades-DNI-; [redacted]
Subject: Whistleblower Issue -- Revised Letter after Discussion and Transcript Review
Attachments: HPSCI SSCI WB Transmittal Letter v.4 -- clean.docx; HPSCI SSCI WB Transmittal Letter v.4.docx; [redacted] Letter to DNI re COVID origin urgent concern with enclosures Signed.pdf

Follow Up Flag: Follow up
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Classified By: [redacted]
Derived From: [redacted]
Declassify On: [redacted]
==========

Avril –

Following up on our conversation this morning, we have reviewed transcripts from some of Dr. Fauci's appearances on the Hill.

Based on that review, it seems likely that the whistleblower complaint was referring to exchanges Dr. Fauci had with Senator Paul on May 11 and July 20. During the May 11 hearing, Dr. Fauci stated that "the NIH has not ever and does not now fund gain of function research in the Wuhan Institute." During the July 20 hearing, Senator Paul confronted Dr. Fauci on the prior statement, asking him if he wanted to retract it; Dr. Fauci of course stood behind it.

Thus, while it is possible that Dr. Fauci has spoken to Congress about gain-of-function research at some other point (he's testified a number of times!), I think the key thing is that what we've seen is consistent with the point that Secretary Becerra made to you – that this is something they've considered and that Dr. Fauci has point he's repeated about the NIH not funding gain-of-function at the WIV.

We've thus updated the draft letter to note this point and to refer the complaint to Secretary Becerra, rather than the HHS IG; tracked changes and clean versions are attached. We've also attached the original letter from the IC IG, so you have everything in one place.

Many thanks, and happy to discuss, if it would be helpful to do so,

Chris

==========
Classification: [redacted]

http://2013.igem.org/Team:WHU-China/noteProtocal
http://2013.igem.org/Team:WHU-China/teammember#our_team
Hello world, we are 2013 iGEM WHU-China.
We are the third team of Wuhan University attending iGEM jamboree. Of course, it is great to have a good tradition here, the senior team member lead us to this amazing field of synthetic biology and give us tremendous help either in experiment or other parts of this match.
What is more important is that we combine those with our novel ideas, passion and efforts. Every time when we carry out a brain storm, when we debate for a better solution or when we do experiment throughout the whole night, fire are burning in our heart, because we know the world will be a little different, a little better by what we are doing.
From December 2012, we have passed 8 months. And steps never stop, even in the Spring Festival, meeting online kept our minds together. Although we have experienced the pains of member changing, everyone who loves this team devotes what he or she can.
Now it is the time for WHU-China to give you all a surprise.
And it is time for us to give a answer to ourselves!
Here we come.

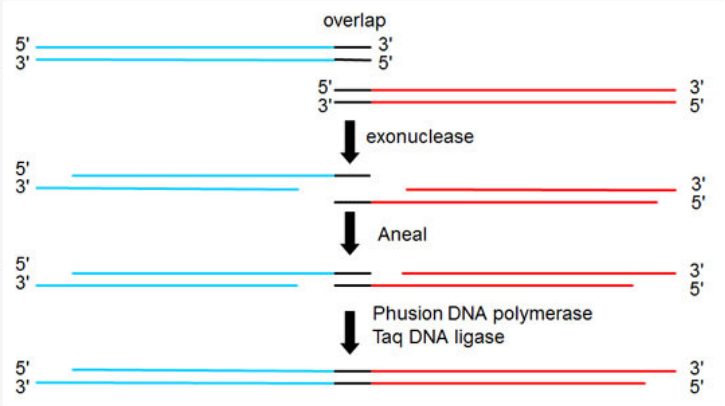
Yang LIU | Senior in Biological Sciences
Yang is our funny and optimistic buddy, the “laughs producer”. He has participated in a molecular virology lab for more than two years. His skill in experiment is indispensable. He is also the lab manager and diplomatist, who tackles with issues with our funder and keeps the experiment run. He never let us down.

Yu CHEN
Our instructor, Dr. Chen joined the virology department of college of life science in Wuhan University as associate professor in July, 2009, having moved from biotechnology research institute, the University of Helsinki, where he held the project of the mechanism of RNA virus’ RNA capping. His degree is BA in Biotechnology in Wuhan University (2003), followed by PhD in modern molecular virology in Wuhan University (2008). Doctor Chen’s research interests extends from SARS Coronavirus Nonstructural Protein nsp16, siRNA to the mechanism of RNA virus replication and transcription.
Doctor Chen is a responsible and approachable teacher and he offered us a lot of constructive suggestions based on his rich experience in molecule cloning.

http://2013.igem.org/Team:WHU-China/noteProtocal

Gibson assembly

In order to accomplish an efficient and economical DNA fragments assembly, we adopted an enzymatic assembly method named “Gibson assembly”[1]. Gibson assembly is wildly used because of its’ high efficiency in yielding deserted DNA fragments that may from several to hundreds kilobases. In our project, we adopt the original Gibson assembly protocol.



This figure indicates the basic principle of Gibson assembly. In this figure, two DNA fragments which share the same overlapping pieces, are joined together in a one-step isothermal reaction (or precisely called One-step isothermal in vitro recombination). Because the two adjacent DNA fragments share terminal sequence overlap, when T5 exonuclease remove nucleotides from 5’ ends of double-stranded DNA, the single-strand overlap region can pair with each other, just like two sticky ends. After two overlapping single-strand DNA annealed, Phusion DNA polymerase fill the gaps and Taq ligase, seals the nicks.

http://2013.igem.org/Team:WHU-China/introduction

Introduction

Blueprint of our project

If people want to drive a system to work for them, even if the system is a simple one, simply keep pushing the system toward the goal may not be the best shoot. For example, if a professor is too pushing, his students may, on the contrary, unable to perform their best; if a farmer adding too much fertilizer, the land may be damaged in the long run, etc.

Biological systems are extremely complex, and the components in the system are intensely interconnected. So in order to exploit the maximum potentiality of a biological system, we'll have to keep the protein or metabolic product production in a desired range. Not too high, as it may hurt the cell or inhibit its growth; either not too low, as it will be economically inefficient.

So how can we reach a desired range of expression? We need to properly combine the transcription and translation initiation elements, just as an recent published Nature article suggested[1]. But that paper just used the throughly studied E.coli expression elements in E.coli. What if we are doing engineering in a non-model organism that we just have data about a handful of expression elements, can we create the elements we need?

Our project proposed a way to employ a limited set of promoters to reach any desired expression level, or even switch between several expression level.

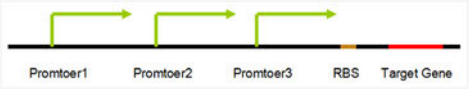


Fig.1 Tandem promoter

First, we combined the known promoter into tandem promoter system. We've done experiments and modeling to show how can we use a 0.1 promoter and a 0.3 promoter to reach expression level from 0.1 to the maximum. Please check experiment here and modeling here.

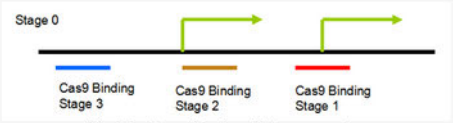


Fig.2 Cas9 regulated multistage promoter

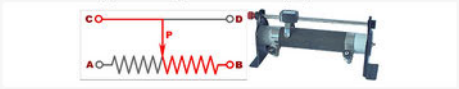


Fig 3. An analog to slide rheostat

Then, we made the tandem promoter a "slide rheostat" by using d/aCas9 to regulate it. This enable the tandem promoter to switch between several designable expression level, and become a multistage promoter. This is different from the normal regulated promoter that usually has only two stage: on and off (Fig.4). To see our experiment about this multistage promoter, please click here. It's also important to ensure the orthogonality of this multistage promoter. So the off-target tendency of Cas9 is modeled and analyzed by combining the data of six paper about Cas9 off-target. For the modeling result, please click here.

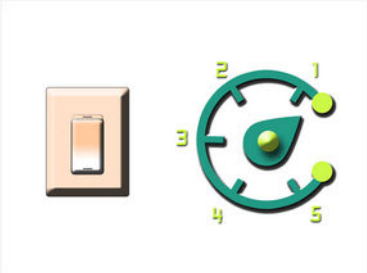


Fig 4. Bi-stage promoter and multistage promoter

Reference

[1]Mutalik, Vivek K., et al. "Precise and reliable gene expression via standard transcription and translation initiation elements." Nature methods 10.4 (2013): 354-360.

[redacted]

From: [redacted]
Sent: Thursday, March 5, 2026 9:18 AM
To: [redacted]
Subject: FW: (U) Interest in a discussion about COV SARS2 and gain of function research
Attachments: s41591-020-0820-9_converted.pdf; Genomic Study Points to Natural Origin of COVID-19 - NIH Director's Blog.pdf
Signed By: [redacted]

Classification: [redacted]

Classified By: [redacted]
Derived From: [redacted]
Declassify On: [redacted]
==========

The IC took direction straight from NIH .... the people that funded the Wuhan Lab ....

A complex web of money and politics influencing analysis.

From: [redacted]
Sent: Friday, March 27, 2020 9:58 AM
To: [redacted]
Cc: [redacted]
Subject: RE: (U) Interest in a discussion about COV SARS2 and gain of function research

Classification: [redacted]

Classified By: [redacted]
Derived From: [redacted]
Declassify On: [redacted]
==========

Sharing a recently published *Nature* commentary and a NIH directors blog entry referring to it (both attached). BLUF:

Our analyses clearly show that SARS-CoV-2 is not a laboratory construct or a purposefully manipulated virus.

- [redacted]

[redacted]

[redacted]

When in doubt, follow the science

From: [redacted]
Sent: Wednesday, March 25, 2020 6:09 PM
To: [redacted]
Cc: [redacted]
Subject: RE: (U) Interest in a discussion about COV SARS2 and gain of function research

Classification: [redacted]

Classified By: [redacted]
Derived From: [redacted]
Declassify On: [redacted]
==========

[redacted] called me today. [redacted] used to work for DOE and is now a MITRE fellow working for NIM-CI. Some colleagues in DOE who know [redacted] for [redacted] PhD in biodefense + the chief medical officer at MITRE have been reaching out to [redacted] to get [redacted] thoughts. [redacted] said [redacted] has not been volunteering these views with others, including the State Dept.

[redacted]

[redacted] briefly mentioned [redacted] as another report giving him concern, although I reassured him that the IC has been talking to a lot of experts about furin in the past two months. For your reference I have attached the enclosure associated with that report.

I flagged the attached March 17 article (thanks to NCPC) as an example of the scientific community walking through some of these "oddities," quoting the conclusion that "our analyses clearly show that SARS-CoV-2 is not a laboratory construct or a purposefully manipulated virus." [redacted] countered that the problem is that no one is working off the same facts/part of the code and I didn't have time to ask what [redacted] meant by that.

If I had to guess, people are flagging these flashy reports for [redacted] to get [redacted] thoughts but aren't flagging the other reports from technical experts that support the opposite claims. Largely, it seemed like [redacted] just wanted to confirm that the IC

was aware of these technical oddities and was taking the open-source research into account in our analysis. I explained that IC analysts with technical backgrounds have discussed this topic at length with experts and shared the following links as evidence.

[redacted]

[redacted] phone number at DOE is [redacted] and email is [redacted] if anyone would like to reach out to [redacted]/get into the technical details. I'm sure [redacted] would appreciate it, but I didn't want to volunteer anyone's name as a POC given the fact that we have a large workload and reduced staff. For your reference, our phone call was about 35 minutes long.

Have a good evening,

[redacted]

In the event I am out of the office (esp weeks of 3/30 and 4/13), please contact the following alternate POCs at the NIC:
- [redacted] PDNIO – WMD & Proliferation ([redacted])
- NIC COVID alias: [redacted]
- NIO WMD & Proliferation: [redacted]

-----Original Message-----
From: [redacted]
Sent: Monday, March 23, 2020 3:42 PM
To: [redacted]
Subject: RE: (U) Interest in a discussion about COV SARS2 and gain of function research --- UNCLASSIFIED[redacted]

Classification: UNCLASSIFIED[redacted]
==========

Nope - nothing from me either. I got a group of cleared virologists together a few weeks ago to look at the open source stuff (please see attached readout). We were planning a more detailed follow-on but things got delayed due to the travel restrictions. I'd be happy to rally the troops though if we want to reconvene the discussion - and it might be a good idea if there are other thoughts floating around out there.

I've been detailed down to OSD to manage the science portfolio for DoD's COVID-19 TF. I've been focused mostly on modeling coordination so far (since Thursday...) but this definitely fits with my current mission also.

[redacted]

[redacted]

Chief Intelligence Officer

Joint Program Executive Office for CBRN Defense

Department of Defense

[redacted]

[redacted]

From: [redacted]
Sent: Monday, March 23, 2020 3:02 PM
To: [redacted]
Cc: [redacted]
Subject: RE: (U) Interest in a discussion about COV SARS2 and gain of function research

Classification: UNCLASSIFIED[redacted]
==========

Nothing further from me. I have not responded to any of [redacted] emails yet because I haven't had time today and have higher priorities.

From: [redacted]
Sent: Monday, March 23, 2020 2:54 PM
To: [redacted]
Cc: [redacted]
Subject: RE: (U) Interest in a discussion about COV SARS2 and gain of function research --- UNCLASSIFIED[redacted]

Classification: UNCLASSIFIED[redacted]
==========

Does anyone have more info on the "colleague who has put together an analysis that may be wise to discuss at some point."?? Some of our policymakers have heard from a specific person at MITRE claiming the virus is genetically engineered - but we haven't seen any specific analysis supporting the claim. Would love to learn more if someone has seen this sort of analysis.

[redacted]

[redacted]

Bureau of Intelligence and Research

U.S. Department of State

[redacted]

[redacted]

[redacted]

From: [redacted]
Sent: Monday, March 23, 2020 11:32 AM
To: [redacted]
Subject: RE: (U) Interest in a discussion about COV SARS2 and gain of function research

Classification: UNCLASSIFIED[redacted]
==========

Nothing to add; just letting everyone know [redacted] is out this week, so you're stuck with me in NIO S&T. My molecular biology and genetics are pretty thin, but my BS meter is strong. Please keep me in the loop and let me know if there's anything I can do to assist.

- [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

From: [redacted]
Sent: Friday, March 20, 2020 6:54 PM
To: [redacted]
Cc: [redacted]
Subject: RE: (U) Interest in a discussion about COV SARS2 and gain of function research

Classification: UNCLASSIFIED[redacted]
==========

Hi [redacted]

When I saw in the cc line- "COV SAR2 and gain of function research", it got my attention.

I've been tracking this pretty closely in the literature, and would advise to set a very high threshold for any GOF interpretation as an origin of SAR COV-2.

Not saying it is impossible, but I think Occam's razor is the best guidance here.

While clearly the S protein furin cleavage site appears consistent with a GOF modification, there is precedent for co-circulating COV strains recombining.

Different coronaviruses do co-circulate in hosts, and this amino acid sequence is present in COVs circulating in other bat hosts that are regionally co-located with the host from which RaTG13 was isolated.

Also, phylogenic analysis identifies this site as undergoing a high degree of homoplasy - so it's an adaptation hot spot.

So- lots of room for a natural explanations-many that I've captured and highlighted in my attached notes.

[redacted]

[redacted]

To be honest - I cannot imagine the Chinese NOT doing this type of research, but an escaped P3+/P4 LAI would be extraordinary.

[redacted] is on the fence with this, and maybe leaning toward the GOF explanation, but as an actual trained coronavirus virologist, he would be the first person I'd ask (and I have).

If he goes all in on the GOF assessment, I'd bring [redacted] ii.

I think the IC needs to be very thorough with this analysis.

Hopefully you will find my notes helpful, but feel free to ignore them... they are really just for my own use as you will see.

I'm out next week, unless [redacted] or [redacted] are unable to come in.

Good luck, and stay healthy!

[redacted]

[redacted]

National Intelligence Council / Office of the Director of National Intelligence

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

From: [redacted]
Sent: Friday, March 20, 2020 2:03 PM
To: [redacted]
Cc: [redacted]
Subject: RE: (U) Interest in a discussion about COV SARS2 and gain of function research

Classification: UNCLASSIFIED[redacted]
==========

From: [redacted]
Sent: Friday, March 20, 2020 2:02 PM
To: [redacted]
Cc: [redacted]
Subject: (U) Interest in a discussion about COV SARS2 and gain of function research

Classification: UNCLASSIFIED[redacted]
==========

(U[redacted]) Hi [redacted] - [redacted] provided me your name when I called him a few minutes ago. We are colleagues from DOE-IN. I recently took a three year appointment as a [redacted] at [redacted] hence the different email.

(U[redacted]) I was hoping we could discuss the various information and analysis that is churning around regarding S protein manipulation in the virology community and how the NIC is interpreting the information. I have a colleague who has put together an analysis that may be wise to discuss at some point.

(U[redacted]) If there is a good time and number to reach you on Monday, please let me know.

Sincerely,

[redacted]

[redacted]

[redacted]

[redacted]

Support to ODNI

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The proximal origin of SARS-CoV-2

To the Editor — Since the first reports of novel pneumonia (COVID-19) in Wuhan, Hubei province, China[1,2], there has been considerable discussion on the origin of the causative virus, SARS-CoV-2[3] (also referred to as HCoV-19)[4]. Infections with SARS-CoV-2 are now widespread, and as of 11 March 2020, 121,564 cases have been confirmed in more than 110 countries, with 4,373 deaths[5].

SARS-CoV-2 is the seventh coronavirus known to infect humans; SARS-CoV, MERS-CoV and SARS-CoV-2 can cause severe disease, whereas HKU1, NL63, OC43 and 229E are associated with mild symptoms[6]. Here we review what can be deduced about the origin of SARS-CoV-2 from comparative analysis of genomic data. We offer a perspective on the notable features of the SARS-CoV-2 genome and discuss scenarios by which they could have arisen. Our analyses clearly show that SARS-CoV-2 is not a laboratory construct or a purposefully manipulated virus.

Notable features of the SARS-CoV-2 genome

Our comparison of alpha- and betacoronaviruses identifies two notable genomic features of SARS-CoV-2: (i) on the basis of structural studies[7–9] and biochemical experiments[1,9,10], SARS-CoV-2 appears to be optimized for binding to the human receptor ACE2; and (ii) the spike protein of SARS-CoV-2 has a functional polybasic (furin) cleavage site at the S1–S2 boundary through the insertion of 12 nucleotides[8], which additionally led to the predicted acquisition of three O-linked glycans around the site.

1. Mutations in the receptor-binding domain of SARS-CoV-2. The receptor-binding domain (RBD) in the spike protein is the most variable part of the coronavirus genome[1,2]. Six RBD amino acids have been shown to be critical for binding to ACE2 receptors and for determining the host range of SARS-CoV-like viruses[7]. With coordinates based on SARS-CoV, they are Y442, L472, N479, D480, T487 and Y4911, which correspond to L455, F486, Q493, S494, N501 and Y505 in SARS-CoV-2[7]. Five of these six residues differ between SARS-CoV-2 and SARS-CoV (Fig. 1a). On the basis of structural studies[7–9] and biochemical experiments[1,9,10], SARS-CoV-2 seems to have an RBD that binds with high affinity to ACE2 from humans, ferrets, cats and other species with high receptor homology[7].

While the analyses above suggest that SARS-CoV-2 may bind human ACE2 with high affinity, computational analyses predict that the interaction is not ideal[7] and that the RBD sequence is different from those shown in SARS-CoV to be optimal for receptor binding[7,11]. Thus, the high-affinity binding of the SARS-CoV-2 spike protein to human ACE2 is most likely the result of natural selection on a human or human-like ACE2 that permits another optimal binding solution to arise. This is strong evidence that SARS-CoV-2 is not the product of purposeful manipulation.

2. Polybasic furin cleavage site and O-linked glycans. The second notable feature of SARS-CoV-2 is a polybasic cleavage site (RRAR) at the junction of S1 and S2, the two subunits of the spike[8] (Fig. 1b). This allows effective cleavage by furin and other proteases and has a role in determining viral infectivity and host range[12]. In addition, a leading proline is also inserted at this site in SARS-CoV-2; thus, the inserted sequence is PRRA (Fig. 1b). The turn created by the proline is predicted to result in the addition of O-linked glycans to S673, T678 and S686, which flank the cleavage site and are unique to SARS-CoV-2 (Fig. 1b). Polybasic cleavage sites have not been observed in related 'lineage B' betacoronaviruses, although other human betacoronaviruses, including HKU1 (lineage A), have those sites and predicted O-linked glycans[13]. Given the level of genetic variation in the spike, it is likely that SARS-CoV-2-like viruses with partial or full polybasic cleavage sites will be discovered in other species.

The functional consequence of the polybasic cleavage site in SARS-CoV-2 is unknown, and it will be important to determine its impact on transmissibility and pathogenesis in animal models. Experiments with SARS-CoV have shown that insertion of a furin cleavage site at the S1–S2 junction enhances cell–cell fusion without affecting viral entry[14]. In addition, efficient cleavage of the MERS-CoV spike enables MERS-like coronaviruses from bats to infect human cells[15]. In avian influenza viruses, rapid replication and transmission in highly dense chicken populations selects for the acquisition of polybasic cleavage sites in the hemagglutinin (HA) protein[16], which serves a function similar to that of the coronavirus spike protein. Acquisition of polybasic cleavage sites in HA, by insertion or recombination, converts low-pathogenicity avian influenza viruses into highly pathogenic forms[16]. The acquisition of polybasic cleavage sites by HA has also been observed after repeated passage in cell culture or through animals[17].

The function of the predicted O-linked glycans is unclear, but they could create a 'mucin-like domain' that shields epitopes or key residues on the SARS-CoV-2 spike protein[18]. Several viruses utilize mucin-like domains as glycan shields involved immunoevasion[18]. Although prediction of O-linked glycosylation is robust, experimental studies are needed to determine if these sites are used in SARS-CoV-2.

Theories of SARS-CoV-2 origins

It is improbable that SARS-CoV-2 emerged through laboratory manipulation of a related SARS-CoV-like coronavirus. As noted above, the RBD of SARS-CoV-2 is optimized for binding to human ACE2 with an efficient solution different from those previously predicted[7,11]. Furthermore, if genetic manipulation had been performed, one of the several reverse-genetic systems available for betacoronaviruses would probably have been used[19]. However, the genetic data irrefutably show that SARS-CoV-2 is not derived from any previously used virus backbone[20]. Instead, we propose two scenarios that can plausibly explain the origin of SARS-CoV-2: (i) natural selection in an animal host before zoonotic transfer; and (ii) natural selection in humans following zoonotic transfer. We also discuss whether selection during passage could have given rise to SARS-CoV-2.

1. Natural selection in an animal host before zoonotic transfer. As many early cases of COVID-19 were linked to the Huanan market in Wuhan[1,2], it is possible that an animal source was present at this location. Given the similarity of SARS-CoV-2 to bat SARS-CoV-like coronaviruses[2], it is likely that bats serve as reservoir hosts for its progenitor. Although RaTG13, sampled from a *Rhinolophus affinis* bat[1], is ~96% identical overall to SARS-CoV-2, its spike diverges in the RBD, which suggests that it may not bind efficiently to human ACE2[7] (Fig. 1a).

Malayan pangolins (*Manis javanica*) illegally imported into Guangdong province contain coronaviruses similar to SARS-CoV-2[21]. Although the RaTG13 bat virus remains the closest to SARS-CoV-2 across the

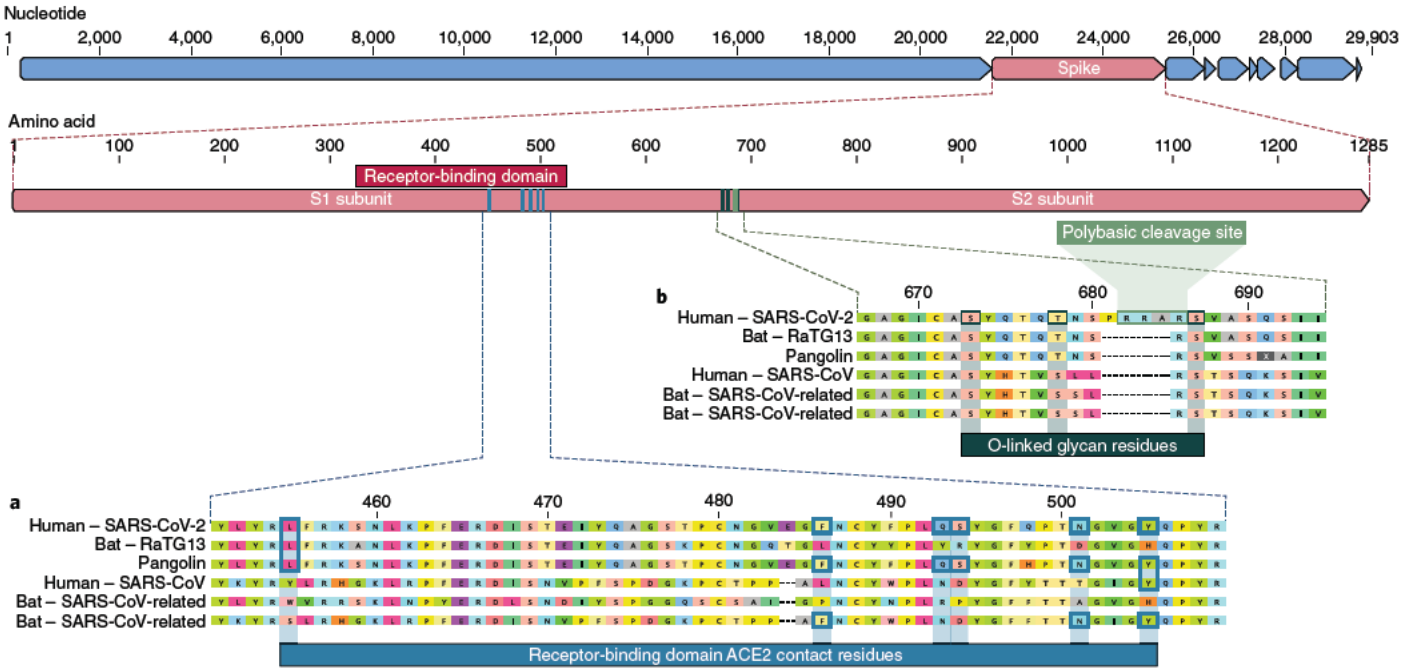

Fig. 1 | Features of the spike protein in human SARS-CoV-2 and related coronaviruses. a, Mutations in contact residues of the SARS-CoV-2 spike protein. The spike protein of SARS-CoV-2 (red bar at top) was aligned against the most closely related SARS-CoV-like coronaviruses and SARS-CoV itself. Key residues in the spike protein that make contact to the ACE2 receptor are marked with blue boxes in both SARS-CoV-2 and related viruses, including SARS-CoV (Urbani strain). **b**, Acquisition of polybasic cleavage site and O-linked glycans. Both the polybasic cleavage site and the three adjacent predicted O-linked glycans are unique to SARS-CoV-2 and were not previously seen in lineage B betacoronaviruses. Sequences shown are from NCBI GenBank, accession codes MN908947, MN996532, AY278741, KY417146 and MK211376. The pangolin coronavirus sequences are a consensus generated from SRR10168377 and SRR10168378 (NCBI BioProject PRJNA573298)[29,30].

genome[1], some pangolin coronaviruses exhibit strong similarity to SARS-CoV-2 in the RBD, including all six key RBD residues[21] (Fig. 1). This clearly shows that the SARS-CoV-2 spike protein optimized for binding to human-like ACE2 is the result of natural selection.

Neither the bat betacoronaviruses nor the pangolin betacoronaviruses sampled thus far have polybasic cleavage sites. Although no animal coronavirus has been identified that is sufficiently similar to have served as the direct progenitor of SARS-CoV-2, the diversity of coronaviruses in bats and other species is massively undersampled. Mutations, insertions and deletions can occur near the S1–S2 junction of coronaviruses[22], which shows that the polybasic cleavage site can arise by a natural evolutionary process. 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) and an ACE2-encoding gene that is similar to the human ortholog.

2. Natural selection in humans following zoonotic transfer. It is possible that a progenitor of SARS-CoV-2 jumped into humans, acquiring the genomic features described above through adaptation during undetected human-to-human transmission. Once acquired, these adaptations would enable the pandemic to take off and produce a sufficiently large cluster of cases to trigger the surveillance system that detected it[1,2].

All SARS-CoV-2 genomes sequenced so far have the genomic features described above and are thus derived from a common ancestor that had them too. The presence in pangolins of an RBD very similar to that of SARS-CoV-2 means that we can infer this was also probably in the virus that jumped to humans. This leaves the insertion of polybasic cleavage site to occur during human-to-human transmission.

Estimates of the timing of the most recent common ancestor of SARS-CoV-2 made with current sequence data point to emergence of the virus in late November 2019 to early December 2019[23], compatible with the earliest retrospectively confirmed cases[24]. Hence, this scenario presumes a period of unrecognized transmission in humans between the initial zoonotic event and the acquisition of the polybasic cleavage site. Sufficient opportunity could have arisen if there had been many prior zoonotic events that produced short chains of human-to-human transmission over an extended period. This is essentially the situation for MERS-CoV, for which all human cases are the result of repeated jumps of the virus from dromedary camels, producing single infections or short transmission chains that eventually resolve, with no adaptation to sustained transmission[25].

Studies of banked human samples could provide information on whether such cryptic spread has occurred. Retrospective serological studies could also be informative, and a few such studies have been conducted showing low-level exposures to SARS-CoV-like coronaviruses in certain areas of China[26]. Critically, however, these studies could not have distinguished whether exposures were due to prior infections with SARS-CoV, SARS-CoV-2 or other SARS-CoV-like coronaviruses. Further serological studies should be conducted to determine the extent of prior human exposure to SARS-CoV-2.

3. Selection during passage. Basic research involving passage of bat SARS-CoV-like coronaviruses in cell culture and/or animal models has been ongoing for many years in biosafety level 2 laboratories across the world[27], and there are documented instances

of laboratory escapes of SARS-CoV[28]. We must therefore examine the possibility of an inadvertent laboratory release of SARS-CoV-2.

In theory, it is possible that SARS-CoV-2 acquired RBD mutations (Fig. 1a) during adaptation to passage in cell culture, as has been observed in studies of SARS-CoV[11]. The finding of SARS-CoV-like coronaviruses from pangolins with nearly identical RBDs, however, provides a much stronger and more parsimonious explanation of how SARS-CoV-2 acquired these via recombination or mutation[19].

The acquisition of both the polybasic cleavage site and predicted O-linked glycans also argues against culture-based scenarios. New polybasic cleavage sites have been observed only after prolonged passage of low-pathogenicity avian influenza virus in vitro or in vivo[17]. Furthermore, a hypothetical generation of SARS-CoV-2 by cell culture or animal passage would have required prior isolation of a progenitor virus with very high genetic similarity, which has not been described. Subsequent generation of a polybasic cleavage site would have then required repeated passage in cell culture or animals with ACE2 receptors similar to those of humans, but such work has also not previously been described. Finally, the generation of the predicted O-linked glycans is also unlikely to have occurred due to cell-culture passage, as such features suggest the involvement of an immune system[18].

Conclusions

In the midst of the global COVID-19 public-health emergency, it is reasonable to wonder why the origins of the pandemic matter. Detailed understanding of how an animal virus jumped species boundaries to infect humans so productively will help in the prevention of future zoonotic events. For example, if SARS-CoV-2 pre-adapted in another animal species, then there is the risk of future re-emergence events. In contrast, if the adaptive process occurred in humans, then even if repeated zoonotic transfers occur, they are unlikely to take off without the same series of mutations. In addition, identifying the closest viral relatives of SARS-CoV-2 circulating in animals will greatly assist studies of viral function. Indeed, the availability of the RaTG13 bat sequence helped reveal key RBD mutations and the polybasic cleavage site.

The genomic features described here may explain in part the infectiousness and transmissibility of SARS-CoV-2 in humans. Although the evidence shows that SARS-CoV-2 is not a purposefully manipulated virus, it is currently impossible to prove or disprove the other theories of its origin described here. However, since we observed all notable SARS-CoV-2 features, including the optimized RBD and polybasic cleavage site, in related coronaviruses in nature, we do not believe that any type of laboratory-based scenario is plausible.

More scientific data could swing the balance of evidence to favor one hypothesis over another. Obtaining related viral sequences from animal sources would be the most definitive way of revealing viral origins. For example, a future observation of an intermediate or fully formed polybasic cleavage site in a SARS-CoV-2-like virus from animals would lend even further support to the natural-selection hypotheses. It would also be helpful to obtain more genetic and functional data about SARS-CoV-2, including animal studies. The identification of a potential intermediate host of SARS-CoV-2, as well as sequencing of the virus from very early cases, would similarly be highly informative. Irrespective of the exact mechanisms by which SARS-CoV-2 originated via natural selection, the ongoing surveillance of pneumonia in humans and other animals is clearly of utmost importance. ❐

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References

1. Zhou, P. et al. *Nature* https://doi.org/10.1038/s41586-020-2012-7 (2020).
2. Wu, F. et al. *Nature* https://doi.org/10.1038/s41586-020-2008-3 (2020).
3. Gorbalenya, A. E. et al. *bioRxiv* https://doi.org/10.1101/2020.02.07.937862 (2020).
4. Jiang, S. et al. *Lancet* https://doi.org/10.1016/S0140-6736(20)30419-0 (2020).
5. Dong, E., Du, H. & Gardner, L. *Lancet Infect. Dis.* https://doi.org/10.1016/S1473-3099(20)30120-1 (2020).
6. Corman, V. M., Muth, D., Niemeyer, D. & Drosten, C. *Adv. Virus Res.* **100**, 163–188 (2018).
7. Wan, Y., Shang, J., Graham, R., Baric, R. S. & Li, F. *J. Virol.* https://doi.org/10.1128/JVI.00127-20 (2020).
8. Walls, A. C. et al. *bioRxiv* https://doi.org/10.1101/2020.02.19.956581 (2020).
9. Wrapp, D. et al. *Science* https://doi.org/10.1126/science.abb2507 (2020).
10. Letko, M., Marzi, A. & Munster, V. *Nat. Microbiol.* https://doi.org/10.1038/s41564-020-0688-y (2020).
11. Sheahan, T. et al. *J. Virol.* **82**, 2274–2285 (2008).
12. Nao, N. et al. *MBio* **8**, e02298-16 (2017).
13. Chan, C.-M. et al. *Exp. Biol. Med.* **233**, 1527–1536 (2008).
14. Follis, K. E., York, J. & Nunberg, J. H. *Virology* **350**, 358–369 (2006).
15. Menachery, V. D. et al. *J. Virol.* https://doi.org/10.1128/JVI.01774-19 (2019).
16. Alexander, D. J. & Brown, I. H. *Rev. Sci. Tech.* **28**, 19–38 (2009).
17. Ito, T. et al. *J. Virol.* **75**, 4439–4443 (2001).
18. Bagdonaite, I. & Wandall, H. H. *Glycobiology* **28**, 443–467 (2018).
19. Cui, J., Li, F. & Shi, Z.-L. *Nat. Rev. Microbiol.* **17**, 181–192 (2019).
20. Almazán, F. et al. *Virus Res.* **189**, 262–270 (2014).
21. Zhang, T., Wu, Q. & Zhang, Z. *bioRxiv* https://doi.org/10.1101/2020.02.19.950253 (2020).
22. Yamada, Y. & Liu, D. X. *J. Virol.* **83**, 8744–8758 (2009).
23. Rambaut, A. *Virological.org* http://virological.org/t/356 (2020).
24. Huang, C. et al. *Lancet* https://doi.org/10.1016/S0140-6736(20)30183-5 (2020).
25. Dudas, G., Carvalho, L. M., Rambaut, A. & Bedford, T. *eLife* **7**, e31257 (2018).
26. Wang, N. et al. *Virol. Sin.* **33**, 104–107 (2018).
27. Ge, X.-Y. et al. *Nature* **503**, 535–538 (2013).
28. Lim, P. L. et al. *N. Engl. J. Med.* **350**, 1740–1745 (2004).
29. Wong, M. C., Javornik Cregeen, S. J., Ajami, N. J. & Petrosino, J. F. *bioRxiv* https://doi.org/10.1101/2020.02.07.939207 (2020).
30. Liu, P., Chen, W. & Chen, J.-P. *Viruses* **11**, 979 (2019).

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Competing interests

R.F.G. is co-founder of Zalgen Labs, a biotechnology company that develops countermeasures to emerging viruses.

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Statement of Work

Rapid Response for Assessment of Data Needs for 2019-nCoV

February 3, 2020

Statement of Task:

In response to a request from OSTP, the NASEM will examine information and identify data requirements that would help determine the origins of 2019-nCoV, specifically from an evolutionary/structural biology standpoint. NASEM will also consider whether this should include more temporally and geographically diverse clinical isolates, sequences, etc. Although a widely-disputed paper posted on a pre-print server last week has since been withdrawn, the response to that paper highlights the need to determine these information needs as quickly as possible. As part of a broader deliberative process, this review will help prepare for future events by establishing a process for quickly assembling subject matter experts for evaluation of other potentially threatening organisms.

Workplan:

NASEM will hold a meeting of experts to assess what data, information and samples are needed to address the unknowns, in order to understand the evolutionary origins of NCoV and more effectively respond to both the outbreak and any resulting misinformation. A statement from the National Academies will be prepared and published on the Web as a "Based on Science" article that summarizes the status and needs for more and what types of data. A more in-depth examination of the issues will be established as a follow up as needed.

(U) Total Chemical Synthesis,Assembly of Human Torque Teno Virus Genome

(U) Entity Type : Publication

(U [redacted]) Discipline : China RDA

(U) Keywords : Torque teno virus(TTV)

(U) Type : Journal article

(U) Journal : 中国病毒学 ISTIC

(U) Journal : VIROLOGICA SINICA

(U) Journal : 2011, 26(3)

(U) Date of Publication : 2011

(U) Author/Co Authors : [redacted]

(U) Affiliation : State Key Laboratory of Virology,Wuhan Institute of Virology,Chinese Academy of Sciences,Wuhan 430071,China

(U) Abstract : Torque teno virus(TTV)is a nonenveloped virus containing a single-stranded,circular DNA genome of approximately 3.8kb.We completely synthesized the 3808 nucleotides of the TTV(SANBAN isolate)genome,which contains a hairpin structure and a GC-rich region.More than 100 overlapping oligonucleotides were chemically synthesized and assembled by polymerise chain assembly reaction(PCA),and the synthesis was completed with splicing by overlap extension(SOEing).This study establishes the methodological basis of the chemical synthesis of a viral genome for use as a live attenuated vaccine or gene therapy vector.

(U) Funding Details : The Knowledge Innovation Program of the Chinese Academy of Sciences

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MELON PATCH

DATE OF INFORMATION

Initial Record Date: **01/01/2013**
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SOURCES

Data collected via the following sources:

- (U) [redacted]

(U [redacted]) [redacted]

View Entity in SpyGLAS

No Relationships

Synthetic recombinant bat SARS-like coronavirus is infectious in cultured cells and in mice

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Edited by Peter Palese, Mount Sinai School of Medicine, New York, NY, and approved October 14, 2008 (received for review August 18, 2008)

Defining prospective pathways by which zoonoses evolve and emerge as human pathogens is critical for anticipating and controlling both natural and deliberate pandemics. However, predicting tenable pathways of animal-to-human movement has been hindered by challenges in identifying reservoir species, cultivating zoonotic organisms in culture, and isolating full-length genomes for cloning and genetic studies. The ability to design and recover pathogens reconstituted from synthesized cDNAs has the potential to overcome these obstacles by allowing studies of replication and pathogenesis without identification of reservoir species or cultivation of primary isolates. Here, we report the design, synthesis, and recovery of the largest synthetic replicating life form, a 29.7-kb bat severe acute respiratory syndrome (SARS)-like coronavirus (Bat-SCoV), a likely progenitor to the SARS-CoV epidemic. To test a possible route of emergence from the noncultivable Bat-SCoV to human SARS-CoV, we designed a consensus Bat-SCoV genome and replaced the Bat-SCoV Spike receptor-binding domain (RBD) with the SARS-CoV RBD (Bat-SRBD). Bat-SRBD was infectious in cell culture and in mice and was efficiently neutralized by antibodies specific for both bat and human CoV Spike proteins. Rational design, synthesis, and recovery of hypothetical recombinant viruses can be used to investigate mechanisms of transspecies movement of zoonoses and has great potential to aid in rapid public health responses to known or predicted emerging microbial threats.

emerging pathogens | synthetic biology | vaccine development | zoonoses

Emergence of zoonotic-human pathogens is increasingly recognized as a threat to public health (1). Human population growth and environmental changes have created new opportunities for contact between humans and zoonotic organisms that may result in cross-species transmission and human disease (1, 2). Recent examples include RNA viruses such as severe acute respiratory syndrome coronavirus (SARS-CoV), Ebola, Hanta, Nipah, and Chikungunya viruses (2). However, the determinants regulating successful transspecies movement remain poorly understood due to challenges in identifying viral precursors and animal reservoirs, thereby complicating vaccine and therapeutic design (3). SARS-CoV, which exemplifies the challenges inherent in studying emerging pathogens, was the first 21st century emerging virus to exhibit efficient human-to-human transmission and rapid global spread (4–6). Although zoonotic SARS-CoV strains were isolated from civets and raccoon dogs (7–9), the epidemic likely originated from strains circulating in bats (Bat-SCoVs) (10–12). Bat CoVs cluster in both major mammalian CoV taxonomic groups, raising the possibility that Bat CoVs may be progenitors to all 4 known pathogenic human CoVs (11, 13). Bats are also predicted to function as reservoirs for other important emerging human and animal viruses (14, 15). Although several complete Bat CoV genome sequences are available, no Bat CoV has been successfully cultivated in cell culture or in animals (11, 13), severely limiting the identification of determinants of zoonotic CoV transspecies movement.

The SARS-CoV Spike is a 180-kDa type I membrane glycoprotein that contains a well-defined receptor-binding domain (RBD). The SARS-CoV genome is likely a mosaic of sequences derived from multiple recombination events, although this hypothesis is somewhat controversial (16). However, recombination within Spike has been described often (17), suggesting that the RBDs may be interchangeable between strains (18–20). During the SARS-CoV outbreak, evolution in the Spike RBD allowed for more efficient use of human angiotensin-converting enzyme 2 (hACE2) as a receptor for entry (21, 22). Because future zoonoses are likely, it is critical to identify strategies used by viruses to adapt in human populations. In this study, we have combined phylogenetic and bioinformatics analyses, large-scale cDNA synthesis, chimeric gene design, and reverse genetics to generate a consensus Bat-SCoV. Successful recovery of the infectious chimeric virus, Bat-SRBD, which includes the RBD within Spike from human SARS-CoV, demonstrates the plasticity of the CoV type I glycoprotein. The synthetic reconstruction and recovery of this novel chimeric virus identifies a necessary genetic element for CoV cross-species transmission, establishes a model system for testing experimental evolution of zoonotic CoVs, and allows for testing of vaccine and therapeutics against possible future zoonotic strains.

Results

Consensus Bat-SCoV Sequence Design and Construction. When this study was initiated, 4 Bat-SCoVs had been identified (HKU3–1, HKU3–2, HKU3–3, and RP3) as the virus reservoir populations from which SARS-CoV emerged (10–12). Because none had been recovered in culture, the infectivity of the reported viral genomic RNA sequences was hypothetical, having been derived from RT-PCR sequencing of bat fecal or rectal swab samples. Sequence databases have error frequencies from 1/500 to 1/10,000, making viable genome reconstruction problematic with increasing size (23). Therefore, we used the 4 reported Bat-SCoV sequences to establish a putative consensus Bat-SCoV sequence (GenBank accession no. FJ211859) and designed cDNA fragments with junctions precisely aligned to the existing SARS-CoV reverse genetics system [Fig. 1*A*; supporting information (SI) Fig. S1] (24). The defined and functional SARS-CoV 5′ UTR and transcriptional regulatory sequences

Author contributions: M.M.B., R.L.G., E.F.D., R.S.B., and M.R.D. designed research; M.M.B., R.L.G., E.F.D., B.R., and A.C.S. performed research; R.L.G., E.F.D., T.S., R.J.P., D.C., and R.E.J. contributed new reagents/analytic tools; M.M.B., R.L.G., E.F.D., B.R., A.C.S., R.J.P., and R.S.B. analyzed data; and M.M.B., R.L.G., R.S.B., and M.R.D. wrote the paper.

Conflict of interest statement: R.E.J. is a coinventor of the Venezuelan Equine Encephalitis (VEE) expression vector technology and holds an equity interest in AlphaVax, Inc., the company that has licensed this technology from the University of North Carolina.

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Data deposition: The sequences reported in this paper have been deposited in the GenBank database (accession nos. FJ211859 and FJ211860).

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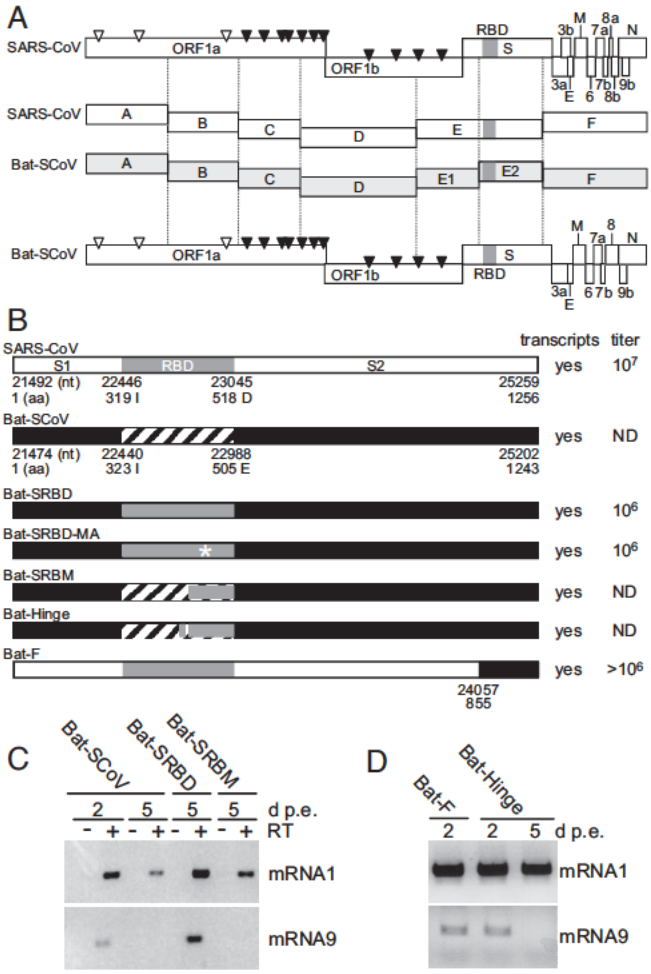

Fig. 1. Schematic representation of SARS-CoV and Bat-SCoV variants. (*A*) Schematic representation of SARS-CoV and Bat-SCoV (GenBank accession no. FJ211859) genomes and reverse genetics system. (*Top*) Arrowheads indicate nsp processing sites within the ORF1ab polyprotein (open arrowheads, papain-like proteinase mediated; filled arrowheads, nsp5 [3C-like proteinase] mediated). Immediately below are the fragments used in the reverse genetics system, labeled A through F. The fragments synthesized to generate Bat-SCoV exactly recapitulate the fragment junctions of SARS-CoV with the exception that the Bat-SCoV has 2 fragments, Bat-E1 and Bat-E2, which correspond to the SARS-E fragment. (*B*) Schematic representation showing organization of the SARS-CoV and Bat-SCoV Spike proteins. The engineered Spike proteins are pictured below with the virus name to the left. Bat-SRBD includes all of the Bat-SCoV Spike sequence except that the Bat-SCoV RBD (Bat-SCoV amino acid 323–505) is replaced with the SARS-CoV RBD (amino acid 319–518) (GenBank accession no. FJ211860). Bat-SRBD-MA includes the MA15 Spike RBD change at SARS-CoV aa Y436H. Bat-SRBM includes the minimal 13 SARS-CoV residues critical for ACE2 contact, resulting in a chimeric RBD of Bat-SCoV amino acid 323I-429T and SARS-CoV amino acid 426R-518D. Bat-Hinge is Bat-SRBM sequence, with Bat-SCoV amino acid 392L-397E replaced with SARS-CoV amino acid 388V-393D. Bat-F includes nt 1–24057 of SARS-CoV (to Spike amino acid 855), with the remaining 3′ sequence from Bat-SCoV. To the right of the schematic representations, observation of transcript activity and approximate stock titers at passage 1 (P1) are indicated. ND indicates no infectious virus detected by plaque assay. (*C* and *D*) Presence of genomic and subgenomic transcripts after electroporation of in vitro transcribed viral RNA. Band corresponding to mRNA1 indicates the presence of genomic RNA, either electroporated genomic RNA or progeny genomic RNA, and the presence of a band corresponding to mRNA9 indicates the presence of leader-containing subgenomic RNA, consistent with mRNA transcription.

were used because the 5′ UTRs of the Bat-SCoVs were incomplete. The genomic cDNA fragments were commercially synthesized, inserted into vectors, assembled into a full-length cDNA, and transcribed in vitro to yield genomic RNA. Initial attempts to recover and passage infectious Bat-SCoV failed. Electroporated cells contained high levels of genome and leader-containing subgenomic transcripts on day 2, but not day 5 postelectroporation (p.e.) (Fig. 1*C*), indicating that the synthetic consensus Bat-SCoV genome expressed a functional replicase. We did recover infectious virus consisting of SARS-CoV genome fragments A–E and Bat fragment F (Fig. 1 *B* and *D*). The resulting virus, Bat-F, encoded a chimeric Spike. Thus, the amino-terminal two-thirds of SARS-CoV Spike, including the RBD, and the fusion core contained within the carboxyl-terminal third of Bat-SCoV Spike can successfully drive productive infection. Also, because Bat-F contained Bat-SCoV accessory and structural genes 3′ to the Spike gene, these downstream ORFs are clearly interchangeable.

Generation and Recovery of Chimeric Bat-SRBD. The ectodomain of Spike can be exchanged among CoVs, altering host-range specificity (25, 26). To test whether the RBDs of Bat-SCoV and SARS-CoV were interchangeable, we replaced the Bat-SCoV RBD (amino acid 323–505) with the SARS-CoV RBD (amino acid 319–518) (27, 28) (GenBank accession no. FJ211860), simulating a theoretical recombination event that might occur during mixed infection in vivo (Fig. 1*B*). After electroporation, Bat-SRBD genome RNA and leader-containing subgenomic mRNA transcripts were detected (Fig. 1*C*), and progeny virions were detected by plaque assay. After 2 additional passages, the population genome sequence was identical to the Bat-SRBD molecular clone. However, 4 nucleotides exhibited dual peaks on the sequencing electropherograms, suggesting quasispecies variation at these positions (Table S1). Recovery and passage of Bat-SRBD demonstrated the functional interchangeability of human and animal SARS-CoV-like RBDs.

The crystal structure of SARS-CoV RBD complexed with its receptor, hACE2 (29), implicated 13 residues within the carboxyl terminus of the RBD (amino acid 426R-518D) in ACE2 engagement. Homology modeling indicated that this receptor-binding motif (RBM) may be sufficient to allow ACE2 engagement, and further predicts that inclusion of 6 residues amino-terminal to the RBM (amino acid 388V-393D) may enhance ACE2 engagement by functioning as a distal "hinge." To test this possibility, chimeric Bat-SCoV genomes were constructed containing either the SARS-CoV RBM (Bat-SRBM) or the RBM plus the distal hinge residues (Bat-Hinge) (Fig. 1*B*). Electroporation yielded genome and subgenomic leader-containing transcripts at day 2, but not 5, p.e. (Fig. 1 *C* and *D*), and progeny virions could not be successfully passaged in culture.

Virus Replication in Primate and Murine Cells. We next infected Vero cells, murine delayed brain tumor (DBT) cells, and DBT cells expressing hACE2 or civet (c)ACE2 (DBT-hACE2 and DBT-cACE2) (22) with Bat-SRBD or SARS-CoV at a multiplicity of infection (MOI) of 0.01 or 1 plaque forming unit (PFU) per cell (Fig. 2). Bat-SRBD and SARS-CoV exhibited productive growth in Vero, DBT-hACE2, and DBT-cACE2 cells that was remarkably similar in kinetics and peak titers (Fig. 2). In contrast, DBT cells lacking ACE2 expression did not support growth of either SARS-CoV or Bat-SRBD (data not shown). These data indicate that Bat-SCoV expressing the SARS-CoV RBD is capable of entering cells by using ACE2 from humans, nonhuman primates, or civets as receptor, and replicating efficiently.

Detection of Bat-SRBD Replicase Proteins by SARS-CoV Antibodies. Comparison of SARS-CoV and Bat-SRBD predicted high, but not complete, identity of amino acid sequences across replicase proteins (Table S2). Because antibody cross-reactivity is a potential tool for detection and analysis of Bat-SCoVs, we tested whether antibodies specific for SARS-CoV proteins (30) could also detect Bat-SRBD homologues. Immunoblots were performed by using rabbit polyclonal antibodies (pAbs) specific for SARS-CoV nsp1, nsp8, nsp9,

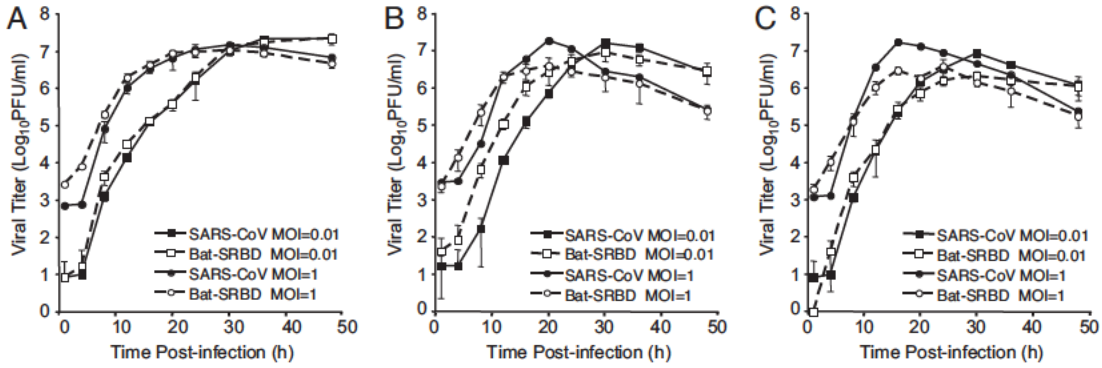

Fig. 2. Growth of SARS-CoV and Bat-SRBD in 3 different cell types. (*A–C*) Vero cells (*A*), DBT-hACE2 cells (*B*), or DBT-cACE2 cells (*C*) were infected with SARS-CoV at a MOI = 1 (■) or MOI = 0.01 (●), or Bat-SRBD at a MOI = 1 (□) or a MOI = 0.01 (○). Infected cultures were sampled, in triplicate, at the times indicated and viral titer was quantified by plaque assay on Vero cells. Error bars indicate SD.

and nsp10 (Fig. S2 and *SI Materials and Methods*). Proteins of the predicted size were detected in cells infected with SARS-CoV or Bat-SRBD demonstrating cross-reactivity of the antibodies and confirming expression of the cognate replicase proteins in Bat-SRBD.

Neutralization of Bat-SRBD. To examine antigenic relatedness, the Bat-SCoV Spike was cloned into Venezuelan Equine Encephalitis viral replicon particle (VRP) vectors, and pools of mouse (m)pAbs were tested for neutralization of Bat-SRBD infectivity. All Bat-SCoV Spike-specific sera efficiently neutralized Bat-SRBD, with 50% neutralization titers ranging from 1/100 to 1/400 dilutions (Fig. 3*A*). In parallel, these sera did not neutralize SARS-CoV infectivity, suggesting that the antibodies recognize epitopes in Spike outside the RBD in Bat-SRBD. Because the RBD appears to be the minimal motif required to alter host range of the Bat-SCoV precursor, we also tested whether Bat-SRBD could be neutralized with human monoclonal antibodies (hmAbs S109.8, S227.14, and S230.15), which recognize unique epitopes within the SARS-CoV RBD and cross-neutralize human and zoonotic SARS-CoV isolates in vitro and in vivo (31). The hmAbs neutralized Bat-SRBD, demonstrating the accessibility of the neutralizing epitopes of SRBD in the background of the Bat-SCoV Spike (Fig. 3*B*). Neutralization also functions as an important safety feature in design and study of Bat-SRBD viruses.

Bat-SRBD Replicates in Human Airway Epithelial (HAE) Cell Cultures. Because Bat-SRBD grew equivalently to SARS-CoV in culture, we tested whether Bat-SRBD could replicate in primary HAEs, which recapitulate the epithelium of the human conducting airway. We have previously identified zoonotic SARS-CoV variants that replicated efficiently in Vero cells, but not in HAE cultures (22, 32). Therefore, HAE cultures provide a more relevant and stringent measure of the replicative potential of chimeric recombinant zoonotic SARS-CoV viruses in the human host. HAE cultures were inoculated by means of the apical surface and the media sampled at different times postinfection (p.i.). Peak titers of SARS-CoV and Bat-SRBD were similar, although Bat-SRBD growth was delayed, compared with SARS-CoV (Fig. 4*A*). Because hACE2 is detected primarily on the apical surface of ciliated cells in HAEs (33), we looked for differences in targeting of Bat-SRBD and SARS-CoV infection in HAEs. Histological sections from HAE at 144-h p.i. were probed with Spike-specific antisera, and localization assessed by indirect immunofluorescence. For both viruses, Spike was detected predominantly on the apical surface of ciliated cells (Fig. 4 *B* and *C*), but was not detected in nonciliated cells.

SARS-CoV Mouse-Adapted Spike Mutation Enhances Bat-SRBD Replication in Mice. SARS-CoV replicates in mouse lungs, but causes only slight morbidity (34, 35). Replication and pathogenesis are enhanced in infections of BALB/c mice with MA15, a mouse-adapted SARS-CoV containing 6 amino acid changes, including a Y436H substitution in the Spike RBD (36). Although modeling predicts that Y436H enhances RBD-mACE2 receptor engagement (Fig. S3), both SARS-CoV and MA15 replicate efficiently in mouse lungs, complicating assignment of Y436H contributions. To test the

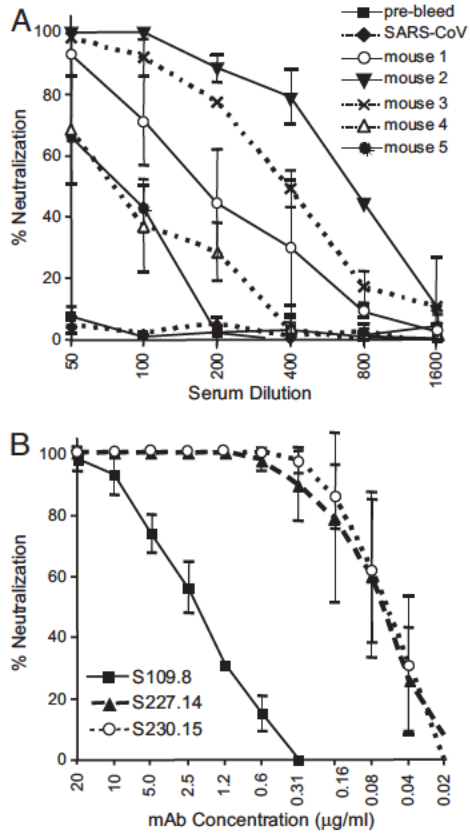

Fig. 3. Neutralization of the Bat-SRBD by mouse serum and human mAbs. (*A*) Immune sera from 5 mice (1, ○; 2, ▼; 3, ×; 4, △; and 5, ⋆) vaccinated with Bat-SCoV Spike were used to neutralize Bat-SRBD. Controls include prebleed serum (■) and Mouse 1 serum used to neutralize SARS-CoV (♦). (*B*) Human mAbs S109.8 (■), S227.14 (▲), and S230.15 (○) were used to neutralize Bat-SRBD. Results are expressed as the percentage of neutralization. Error bars indicate SD.

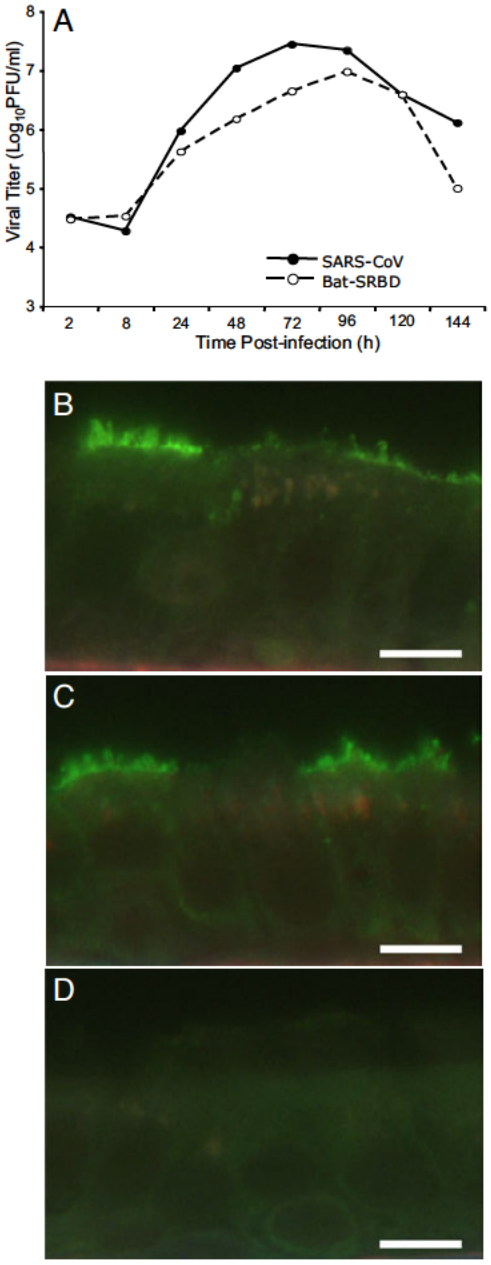

Fig. 4. Efficient replication of Bat-SRBD in human ciliated airway epithelial cells. (*A*) Growth curves for SARS-CoV and Bat-SRBD were obtained from apical washes of human ciliated airway epithelial cell cultures inoculated with either virus. Samples were serially diluted and titers determined by plaque assay on Vero cells. Titers are expressed as PFU per mL. Both SARS-CoV and Bat-SRBD replicated to titers of $\approx 10^7$, although Bat-SRBD growth was delayed compared with SARS-CoV. All inoculations were performed in duplicate. SARS-CoV, ●; Bat-SRBD, ○. (*B–D*) Representative histological sections of HAE 144 h p.i. with SARS-CoV (*B*), Bat-SRBD (*C*), or vehicle alone (*D*) and probed with mouse polyclonal sera directed against the Bat-CoV Spike and visualized with mouse-specific secondary antibodies conjugated to AlexaFluor 488 (green). Detection of Spike immunoreactivity was localized specifically to the apical surface of ciliated cells indicating that SARS-CoV and Bat-SRBD both infect ciliated cells after apical inoculation. Note that at 144 h p.i. cilial morphology shows considerable cytotoxicity. Spike immunoreactivity was not observed in nonciliated cell-types. (Scale bar, 5 μm.)

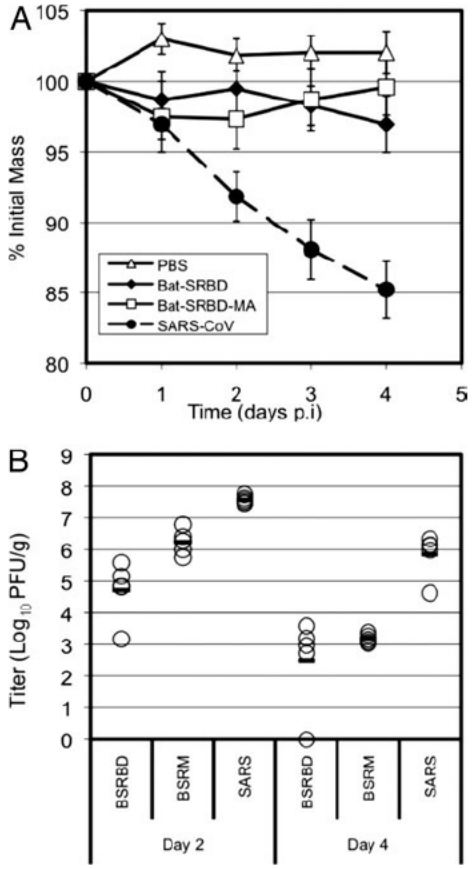

Fig. 5. Weight loss and viral replication of Bat-SRBD, Bat-SRBD-MA, and SARS-CoV in aged BALB/c mice. Ten 14-month-old female BALB/c mice were infected intranasally with 10^5 PFU of the indicated virus or an equivalent volume (50 μL) of PBS. (*A*) Weights of all surviving mice per infection group were recorded each day, averaged, and plotted as a percentage of starting weight. Error bars indicate SD. (*B*) On days 2 and 4 p.i., 5 mice per group were killed and lungs were harvested. Lung homogenates were titered on Vero cells. Circles represent titers of individual mouse lungs. Bars represent the average titer of each infection group. BSRBD, Bat-SRBD; BSRM, Bat-SRBD-MA; SARS, SARS-CoV.

hypothesis that Y436H enhances interaction with mACE2, Bat-SRBD was constructed with this substitution (Bat-SRBD-MA). Electroporation with Bat-SRBD-MA genome RNA resulted in production of infectious virus with titers similar to Bat-SRBD (Fig. 1*B*). Next, 14-month-old BALB/c mice were infected with Bat-SRBD, Bat-SRBD-MA, or SARS-CoV. Mice were weighed and monitored daily for morbidity, and on days 2 and 4 p.i., mice were euthanized and lungs harvested (Fig. 5). Mice infected with chimeric viruses did not exhibit significant weight loss or morbidity after infection (Fig. 5*A*). However, although Bat-SRBD replicated in infected lungs, Bat-SRBD-MA replicated $\approx$1.5 logs more efficiently at day 2 (Fig. 5*B*), providing support for the hypothesis that the Y436H substitution in Bat-SRBD-MA may improve mACE2 receptor engagement.

Discussion

Reverse genetic systems have revolutionized our understanding of the molecular basis of viral replication, pathogenesis, and vaccine design for many virus families. However, application of these technologies to emerging pathogens has been limited by factors involved in constructing and manipulating molecular clones and characterizing recombinant viruses, particularly those with large genomes. Also, standard approaches for development of infectious clones have required availability of viral RNA or DNA, and consequently have been mostly limited to viruses that replicate in culture. Last, classical approaches to combat emerging or deliberately introduced human pathogens may not allow responses in a timeframe adequate to significantly reduce mortality or morbidity.

Thus, new methodologies to rapidly recover and test emerging zoonotic pathogens are critical. Recent studies have provided crucial steps toward the goal of synthetic reconstruction of large microbial genomes. The 7.5- and 5.6-kb genomes of poliovirus and ϕX174, respectively, were reconstructed from known sequences by using commercially synthesized cDNA fragments and PCR assembly (37, 38). Similarly, the segmented genome of the 1918 strain of influenza was reconstructed, in part, by using synthetic design (39). Human endogenous retroviruses were assembled by PCR-directed assembly of synthetic oligonucleotides into a consensus provirus (40), and recombinant SARS-CoVs bearing synthetic zoonotic Spike sequences were derived by our group (22, 32). Last, the cloning of the 580-kb microbial genome of *Mycoplasma genitalium* was reported, although this work has not yet yielded a replicating organism (41). To our knowledge, no studies to date have used a synthetic approach to assess potential mechanisms of zoonotic emergence of a noncultivable virus.

Because it is possible that even minor events of recombination and mutation-driven evolution can alter CoV population structure and promote emergence (22, 32, 42), CoVs may select for alterations in discrete regions of Spike to achieve host-range expansion. The CoV Spike, a type I fusion protein, contains 2 discrete regions, a carboxyl-terminal S2 region that encodes fusion and heptad repeat domains in an arrangement shared by other viral attachment proteins possessing type I architecture (43), whereas the S1 region encodes the RBD. Studies in our and other laboratories have identified mutations in both S1 and S2 regions associated with CoV host-range expansion (42, 44). These 2 regions may also independently or cooperatively mediate transspecies expansion and neutralization escape, in that some mAbs that target the SARS-CoV S1 RBD select for escape mutants in the RBD, but also in the S2 region (45). These data suggest that coordinated interactions between the S1 RBD and select S2 domains may be important in epitope presentation and Spike function.

We have identified several hmAbs that bind distinct, conserved locations in the SARS-CoV RBD and neutralize strains that originate from animal and human hosts (31). These hmAbs did efficiently neutralize Bat-SRBD, an important finding as it was not previously clear that mAbs targeting the SARS-CoV RBD would neutralize virus in the context of a different Spike backbone. It is also informative that antibodies specific for the Bat-SCoV Spike protein neutralize Bat-SBRD, which expresses a chimeric Spike protein, but not SARS-CoV, indicating the existence of neutralizing antibodies that target portions of Spike outside the RBD. Importantly, these results suggest that hmAbs specific for SARS-CoV, and by inference the current panel of SARS-CoV vaccines, may provide significant protection against other SARS-like CoVs that emerge from zoonotic pools by natural recombination or are deliberately designed to cross species. Second, both SARS-CoV RBD-specific hmAbs and Bat-SCoV mpAbs specific for Spike epitopes outside of the RBD are able to recognize and neutralize virus even in the setting of a chimeric Spike, providing important safety features for studies of emerging zoonotic CoVs.

It has been shown that the 5′ UTRs of CoVs can influence the capacity of the virus to replicate in cells (46). Although the 5′ UTR in the synthetic Bat-SCoV originated from SARS-CoV, the sole difference between Bat-SCoV, which was not capable of amplification in cell culture, and Bat-SRBD, which could be recovered, was the RBD derived from SARS-CoV. Our results also confirm and extend a previous report predicting that deletions and mutations within the Bat-SCoV RBM ablate interaction with hACE2 and cACE2 molecules (47). Thus, in this report, we show that the CoV Spike RBD is interchangeable, is sufficient to confer efficient growth and infectivity in cells from multiple species, and likely represents a critical determinant of transspecies movement of zoonotic CoVs.

To protect against future emerging zoonotic pathogens, it is crucial to develop cell culture and animal models to test vaccines and therapeutics, ideally against entire families of organisms, such as CoVs. Both SARS-CoV and Bat-SRBD replicated efficiently in HAE cultures, providing a direct human airway model for comparison of existing and new antivirals. However, Bat-SRBD replicated poorly in vivo, calling for additional modifications to facilitate studies in mouse models. Robust structural information exists on the RBD-ACE2 interaction (29), mutations affecting this interaction have been identified (22, 31), and Rosetta-modeling of short range RBD-mACE2 receptor interfaces can identify key residues essential for retargeting the host specificity of Bat-SRBD (Fig. S3) (48). Previous studies had identified a mutation in the RBD of the MA15 strain, Y436H, but its exact role in vivo was not clear (36). By using structural modeling algorithms, we predicted that the Y436H substitution would enhance the interaction of Bat-SRBD with mACE2. Bat-SRBD-MA did exhibit increased growth efficiency in aged mice. However, this did not result in clinical disease, suggesting the requirement for additional adaptive changes. For example, SARS-CoV encodes at least 5 IFN antagonists, predicted to function in virulence (49–52). Our model system will allow mapping of the domains in the Bat-SCoV and SARS-CoV genetic backgrounds involved in regulation of virulence in aged animals.

In this report, sequence and structural information was integrated with synthetic genomics, reverse genetics, and protein design to recover a zoonotic precursor virus from a hypothetical infectious sequence. The resulting chimera exhibited cross-reactivity with previously identified therapeutics and highlighted possible previously undescribed mechanisms for host-range expansion. Here, we articulate a model to predict and directly test tenable emergence pathways. Paired with a greater availability of reagents and therapeutics, our studies represent an approach for rapid recovery and testing of newly identified pathogens, and which may improve public health preparedness and intervention strategies against natural or intentional zoonotic-human epidemics.

Materials and Methods

Cells and Viruses. VeroE6 cells (Vero) were maintained in MEM (Invitrogen), and delayed brain tumor (DBT, murine astrocytoma) cells were maintained in Dulbecco's MEM (Invitrogen) containing 10% FBS. DBT-hACE2 and DBT-cACE2 cells were cultured as described (22). HAE cells were plated and differentiated as described (33). SARS-CoV Urbani strain (hereafter, SARS-CoV) and Bat-SCoV wild type and chimeric viruses were propagated and assessed by plaque assay on Vero cells. All studies with viable SARS-CoV and SARS-CoV-like viruses were performed in certified BSL3 laboratories in biological safety cabinets, by using safety protocols that were reviewed and approved by the Institutional Biosafety Committees of Vanderbilt University and the University of North Carolina at Chapel Hill.

Determining the Consensus Sequence for Synthetic Bat-SCoV and Conceptual Design of the Bat-SCoV Clone. HKU3–1 (DQ022305), HKU3–2 (DQ084200), HKU3–3 (DQ084199), and RP3 (DQ071615) genomes were aligned by using ClustalXv1.83 to determine a consensus sequence (Fig. S1 and Figs. S4–S6) (GenBank accession no. FJ211859). The consensus Bat-SCoV sequence was designed to ligate interchangeably with the SARS-CoV infectious clone (24). Notably, there was no consensus at the 5′end of the Bat-SCoV genomes, so we used the 5′ most region of SARS-CoV to append the T7 promoter site to the 5′ end of the Bat-A fragment.

Construction of Chimeric Spike Variants. Insertions of SARS-CoV sequence in place of Bat-SCoV sequence were engineered by using PCR and the primers shown in Table S3. PCR amplicons for Bat-SRBD (GenBank accession no. FJ211860) and Bat-SRBM were generated by using fragments Bat-E2, and SARS-E. PCR amplicons for Bat-Hinge (Bat-SRBM plus 6 additional residues from SARS-CoV Spike) were generated by using Bat-SRBM as template. PCR-generated products were cloned into the Bat-E2 plasmid by using unique 5′-BstBI and 3′-MscI sites. Successful insertions of SARS-CoV sequence were confirmed by restriction digestion and nucleotide sequencing across the region of PCR amplification.

Generation of SARS-CoV and Bat-SCoV Mutant Viruses. Viruses containing PCR-generated insertions within the viral coding sequence were produced by using the SARS-CoV assembly strategy (24, 33, 53) with the following modifications. Briefly, for Bat-F virus, full-length cDNA was constructed by ligating restriction products from SARS-CoV fragments A–E and Bat-SCoV fragment F, which required a BglI-NotI digestion. For Bat-SCoV and Bat-SRBD, Bat-SRBM, and Bat-

Hinge, plasmids containing the 7 cDNA fragments of the Bat-SCoV genome were digested by using BglI for Bat-A, Bat-B, Bat-C, and Bat-D, BglI and AflII for Bat-E1 and Bat-E2, and BglI and NotI for Bat-F. Digested, gel-purified fragments were simultaneously ligated together. Transcription was driven by using a T7 mMessage mMachine kit (Ambion), and RNA was electroporated into Vero cells (24, 53). Virus viability was determined by cytopathic effect and progeny viruses were passaged at low MOI. RNA was recovered from infected cell monolayers by using TRIzol (Invitrogen) according to the manufacturer's instructions, and genome origins were verified by RT-PCR and nucleotide sequencing.

Assay for Bat-SCoV Leader-Containing Transcripts in Electroporated Cells and Mouse Lungs. At days 2 and 5 p.e., generation of leader-containing N (ORF9) and genome (ORF1) transcripts was determined by RT-PCR. Briefly, RT-PCR was performed by using random hexamers (ABI) and SuperScript III (Invitrogen) to generate first-strand cDNA at an extension temperature of 55 °C for 1 h. Leader-containing cDNAs were amplified by PCR by using Taq with Thermopol buffer (NEB) and the following primers: 5′-CAGGAAAAGCCAACCAACCTTG (leader) and 5′-CGCTACGACCGAACTGAATGCC to detect Bat-SCoV genomic RNA; and leader and 5′-GTGAGAGCTGTGAACCAAGACG to detect mRNA 9 transcripts. Presence or absence of PCR products was assessed by electrophoresis on 1.5% agarose gels.

Viral Growth and Plaque Assays. Vero, DBT, DBT-hACE2, or DBT-cACE2 cells were infected at a MOI of 1 or 0.01 PFU/cell. After 1 h at 37 °C, the inocula were removed, cells were washed and samples were taken at different times p.i. To determine viral titer, samples were diluted, inoculated onto Vero cell monolayers in 6-well plates for 1 h, and overlaid with complete media plus 1% agar. Plaques were visualized between 48 and 52 h p.i. by neutral red staining (Sigma).

Generation of Polyclonal Bat-SCoV Spike-Specific Sera and Neutralization Assay. Murine pAbs specific for the Bat-SCoV Spike were generated as previously described (33). Neutralizing titers for mpAbs and hmAbs S109.8, S227.14, and S230.15 were determined by plaque reduction neutralization titer assay (PRNT50%) (31). The percentage of neutralization was calculated as follows: 1-(number of plaques in the presence of antibody/number of plaques in the absence of antibody) x 100%.

Infection of Aged BALB/c Mice. Ten each of aged (14 months) female BALB/c mice (National Institute of Aging) were lightly anesthetized and infected intranasally with 10^5 PFU of Bat-SRBD, Bat-SRBD-MA, or SARS-CoV; 5 additional mice were inoculated with an equivalent volume (50 μL) of PBS. Mice were weighed daily through 4 days p.i., and on days 2 and 4 p.i., 5 mice of each group were killed and lungs harvested for determination of viral titer. Lungs were weighed and homogenized in 500 μL of PBS at 6,000 rpm for 60 s in a MagnaLyser (Roche). Clarified homogenates were then diluted serially, and titers were determined by plaque assay on Vero cells.

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1. Weiss RA, McMichael AJ (2004) Social and environmental risk factors in the emergence of infectious diseases. *Nat Med* 10:S70–76.
2. Woolhouse ME, Gowtage-Sequeria S (2005) Host range and emerging and reemerging pathogens. *Emerg Infect Dis* 11:1842–1847.
3. Webby R, Hoffmann E, Webster R (2004) Molecular constraints to interspecies transmission of viral pathogens. *Nat Med* 10:S77–81.
4. Drosten C, *et al.* (2003) Identification of a novel coronavirus in patients with severe acute respiratory syndrome. *N Engl J Med* 348:1967–1976.
5. Ksiazek TG, *et al.* (2003) A novel coronavirus associated with severe acute respiratory syndrome. *N Engl J Med* 348:1953–1966.
6. Peiris JS, *et al.* (2003) Coronavirus as a possible cause of severe acute respiratory syndrome. *Lancet* 361:1319–1325.
7. Tu C, *et al.* (2004) Antibodies to SARS coronavirus in civets. *Emerg Infect Dis* 10:2244–2248.
8. Kan B, *et al.* (2005) Molecular evolution analysis and geographic investigation of severe acute respiratory syndrome coronavirus-like virus in palm civets at an animal market and on farms. *J Virol* 79:11892–11900.
9. Guan Y, *et al.* (2003) Isolation and characterization of viruses related to the SARS coronavirus from animals in southern China. *Science* 302:276–278.
10. Li W, *et al.* (2005) Bats are natural reservoirs of SARS-like coronaviruses. *Science* 310:676–679.
11. Shi Z, Hu Z (2008) A review of studies on animal reservoirs of the SARS coronavirus. *Virus Res* 133:74–87.
12. Lau SK, *et al.* (2005) Severe acute respiratory syndrome coronavirus-like virus in Chinese horseshoe bats. *Proc Natl Acad Sci USA* 102:14040–14045.
13. Dominguez SR, O'Shea TJ, Oko LM, Holmes KV (2007) Detection of group 1 coronaviruses in bats in North America. *Emerg Infect Dis* 13:1295–1300.
14. Halpin K, *et al.* (2007) Emerging viruses: Coming in on a wrinkled wing and a prayer. *Clin Infect Dis* 44:711–717.
15. Calisher CH, *et al.* (2006) Bats: Important reservoir hosts of emerging viruses. *Clin Microbiol Rev* 19:531–545.
16. Holmes EC, Rambaut A (2004) Viral evolution and the emergence of SARS coronavirus. *Philos Trans R Soc Lond B Biol Sci* 359:1059–1065.
17. Lai MM, Cavanagh D (1997) The molecular biology of coronaviruses. *Adv Virus Res* 48:1–100.
18. Stavrinides J, Guttman DS (2004) Mosaic evolution of the severe acute respiratory syndrome coronavirus. *J Virol* 78:76–82.
19. Li W, *et al.* (2006) Animal origins of the severe acute respiratory syndrome coronavirus: Insight from ACE2-S-protein interactions. *J Virol* 80:4211–4219.
20. Li W, *et al.* (2007) The S proteins of human coronavirus NL63 and severe acute respiratory syndrome coronavirus bind overlapping regions of ACE2. *Virology* 367:367–374.
21. Li W, *et al.* (2005) Receptor and viral determinants of SARS-coronavirus adaptation to human ACE2. *EMBO J* 24:1634–1643.
22. Sheahan T, *et al.* (2008) Mechanisms of zoonotic severe acute respiratory syndrome coronavirus host range expansion in human airway epithelium. *J Virol* 82:2274–2285.
23. Pruitt KD, Tatusova T, Maglott DR (2003) NCBI Reference Sequence project: Update and current status. *Nucleic Acids Res* 31:34–37.
24. Yount B, *et al.* (2003) Reverse genetics with a full-length infectious cDNA of severe acute respiratory syndrome coronavirus. *Proc Natl Acad Sci USA* 100:12995–13000.
25. Kuo L, *et al.* (2000) Retargeting of coronavirus by substitution of the spike glycoprotein ectodomain: Crossing the host cell species barrier. *J Virol* 74:1393–1406.
26. Haijema BJ, Volders H, Rottier PJ (2003) Switching species tropism: An effective way to manipulate the feline coronavirus genome. *J Virol* 77:4528–4538.
27. Chakraborti S, Prabakaran P, Xiao X, Dimitrov DS (2005) The SARS coronavirus S glycoprotein receptor binding domain: Fine mapping and functional characterization. *Virol J* 2:73.
28. Wong SK, *et al.* (2004) A 193-amino acid fragment of the SARS coronavirus S protein efficiently binds angiotensin-converting enzyme 2. *J Biol Chem* 279:3197–3201.
29. Li F, Li W, Farzan M, Harrison SC (2005) Structure of SARS coronavirus spike receptor-binding domain complexed with receptor. *Science* 309:1864–1868.
30. Prentice E, *et al.* (2004) Identification and characterization of severe acute respiratory syndrome coronavirus replicase proteins. *J Virol* 78:9977–9986.
31. Rockx B, *et al.* (2008) Structural basis for potent cross-neutralizing human monoclonal antibody protection against lethal human and zoonotic severe acute respiratory syndrome coronavirus challenge. *J Virol* 82:3220–3235.
32. Rockx B, *et al.* (2007) Synthetic reconstruction of zoonotic and early human severe acute respiratory syndrome coronavirus isolates that produce fatal disease in aged mice. *J Virol* 81:7410–7423.
33. Sims AC, *et al.* (2005) Severe acute respiratory syndrome coronavirus infection of human ciliated airway epithelia: Role of ciliated cells in viral spread in the conducting airways of the lungs. *J Virol* 79:15511–15524.
34. Subbarao K, Roberts A (2006) Is there an ideal animal model for SARS? *Trends Microbiol* 14:299–303.
35. Roberts A, *et al.* (2008) Animal models and vaccines for SARS-CoV infection. *Virus Res* 133:20–32.
36. Roberts A, *et al.* (2007) A mouse-adapted SARS-coronavirus causes disease and mortality in BALB/c mice. *PLoS Pathog* 3:e5.
37. Smith HO, Hutchison CA, III, Pfannkoch C, Venter JC (2003) Generating a synthetic genome by whole genome assembly: PhiX174 bacteriophage from synthetic oligonucleotides. *Proc Natl Acad Sci USA* 100:15440–15445.
38. Cello J, Paul AV, Wimmer E (2002) Chemical synthesis of poliovirus cDNA: Generation of infectious virus in the absence of natural template. *Science* 297:1016–1018.
39. Tumpey TM, *et al.* (2005) Characterization of the reconstructed 1918 Spanish influenza pandemic virus. *Science* 310:77–80.
40. Lee YN, Bieniasz PD (2007) Reconstitution of an infectious human endogenous retrovirus. *PLoS Pathog* 3:e10.
41. Gibson DG, *et al.* (2008) Complete chemical synthesis, assembly, and cloning of a Mycoplasma genitalium genome. *Science* 319:1215–1220.
42. McRoy WC, Baric RS (2008) Amino acid substitutions in the S2 subunit of mouse hepatitis virus variant V51 encode determinants of host range expansion. *J Virol* 82:1414–1424.
43. Lamb RA, Jardetzky TS (2007) Structural basis of viral invasion: Lessons from paramyxovirus F. *Curr Opin Struct Biol* 17:427–436.
44. Schickli JH, Thackray LB, Sawicki SG, Holmes KV (2004) The N-terminal region of the murine coronavirus spike glycoprotein is associated with the extended host range of viruses from persistently infected murine cells. *J Virol* 78:9073–9083.
45. Mitsuki YY, *et al.* (2008) A single amino acid substitution in the S1 and S2 Spike protein domains determines the neutralization escape phenotype of SARS-CoV. *Microbes Infect* 10:908–915.
46. Hofmann MA, Senanayake SD, Brian DA (1993) A translation-attenuating intraleader open reading frame is selected on coronavirus mRNAs during persistent infection. *Proc Natl Acad Sci USA* 90:11733–11737.
47. Ren W, *et al.* (2008) Difference in receptor usage between severe acute respiratory syndrome (SARS) coronavirus and SARS-like coronavirus of bat origin. *J Virol* 82:1899–1907.
48. Li W, *et al.* (2004) Efficient replication of severe acute respiratory syndrome coronavirus in mouse cells is limited by murine angiotensin-converting enzyme 2. *J Virol* 78:11429–11433.
49. Kopecky-Bromberg SA, *et al.* (2007) Severe acute respiratory syndrome coronavirus open reading frame (ORF) 3b, ORF 6, and nucleocapsid proteins function as interferon antagonists. *J Virol* 81:548–557.
50. Kopecky-Bromberg SA, Martinez-Sobrido L, Palese P (2006) 7a protein of severe acute respiratory syndrome coronavirus inhibits cellular protein synthesis and activates p38 mitogen-activated protein kinase. *J Virol* 80:785–793.
51. Frieman M, *et al.* (2007) Severe acute respiratory syndrome coronavirus ORF6 antagonizes STAT1 function by sequestering nuclear import factors on the rough endoplasmic reticulum/Golgi membrane. *J Virol* 81:9812–9824.
52. Wathelet MG, Orr M, Frieman MB, Baric RS (2007) Severe acute respiratory syndrome coronavirus evades antiviral signaling: Role of nsp1 and rational design of an attenuated strain. *J Virol* 81:11620–11633.
53. Graham RL, *et al.* (2005) The nsp2 replicase proteins of murine hepatitis virus and severe acute respiratory syndrome coronavirus are dispensable for viral replication. *J Virol* 79:13399–13411.

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Position paper about the possible origin of the SARS-CoV-2 coronavirus

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The COVID-2019 coronavirus pandemic, which originated in Wuhan city, Peoples' Republic of China (PRC) in December 2019, is rapidly expanding around the world, including to the Russian Federation. The virus was named SARS-CoV-2 because of the proximity of the symptoms of disease to Severe Acute Respiratory Syndrome (SARS), an epidemic which occurred in 2002 in China. The SARS-CoV-2 genome is most similar to the genome of the bat coronavirus, Bat-CoV-RaTG13. Coincidence of the causative agent genomes is 96.2%. However, the difference in the neutral sections of the genome constitutes 17%, which makes it possible to postulate a more significant degree of divergence between these two viruses [1]. Coincidence of the SARS-CoV-2 genome with the genome of the SARS-CoV coronavirus – the causative agent of SARS, comprised about 79%, and homology with the causative agent of MERS-CoV (Middle Eastern Respiratory Syndrome - about 50% [2.3].

The SARS-CoV-2 genetic information is presented in the form of (+) - a chain of linear single-chain RNA, presenting as mRNA. The transcription process in coronaviruses occurs via synthesis with the aid of the RNA-dependent negative chain polymerase RNA, which serves subsequently as a matrix for (+) – RNA chain accumulation. The size of the SARS-CoV-2 genome is 29903 nucleotides. The GC-composition of genomic RNA - about 40%.

The SARS-CoV-2 genome can be recorded simply as follows - 5 ' - UTR-ORF1a/b (rep) - S-E-M-N-UTR-3'-polyA (figure 1).

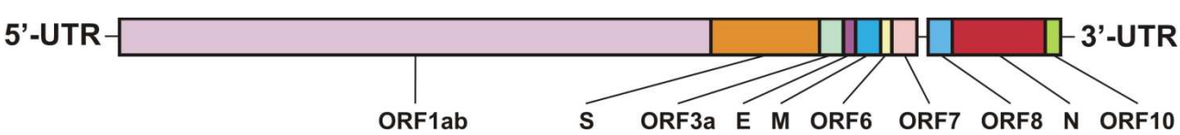

Figure 1 - Simplified diagram of the genomic organization of SARS-CoV-2

The coronavirus RNA has on the 5'-end a methylated cap and untransmitted region with an extent of 200 to 400 nucleotides. On the 3' - molecule ends RNA also is an untransmitted region of 200- 400 nucleotides and then the poly (a) - sequence. In SARS-CoV-2, the first open reading frame (ORF1a/b) occupies about an entire two thirds of the whole genome and codes 16 nonstructured proteins (nsp), initially organized into two polypeptides - 1a and 1b, designated as replicase/transcriptase 1A and 1B. Further there follows four ORFs, which code four structural proteins – spike protein S, the small protein of the shell E (envelope), the membrane glycoprotein M, and the nucleocapsid protein N. Additionally, in this region of the genome are present nucleotide sequences which encode a series of auxiliary peptides with unknown functions. The determination of the biological functions of these proteins is a purpose of further studies. Possibly just one or several of them have an observable effect in the course of the pandemic, selectivity of the course of the disease, and size of the lethality among the population of the different countries, determining genetic predisposition toward the end of the disease.

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A comparison of 95 full genomic sequences of SARS-CoV-2 isolates from the different countries of the entire world showed their very high homology (from 99.91% to 100%) [4]. In addition, a comparison was conducted of full genomes of the SARS-CoV-2 isolate sequenced in Thailand with 23 other SARS-CoV-2 isolates from different countries showed that there exists from 0 to 9 single nucleotide distinctions in their genomes, which is extremely small taking into account the length of the molecular RNA of almost 30,000 nucleotides [5]. As can be seen from given data, the RNA sequence of SARS-CoV-2 practically does not change (figure 2). This proves the low frequency of the appearance of mutations during the multiplication of the corona virus of SARS-CoV-2 due to the presence of exoribonuclease (ExoN), which edits the replication of coronavirus RNA in the eukaryotic cell. Mutations, which were discovered in the S-gene spike, lead to the amino-acid replacements of nos. 49 and 860, occurring external to the preserved sector, responsible for binding with the receptor of the S-protein sector (figure 2).

TABLE 2 The major locus of nucleotide or amino acid variation in SARS-CoV-2 isolate strains (≥3/95)

Regions (ORF)	Nucleotide mutations			Amino acid mutations		
	site	No.	Type	Site	No.	Type
1a	2662	3	C→T	3606	6	L→F
	8782	28	C→T/Y			
	11083	6	G→T			
1b	17373	3	C→T			
	18060	3	C→T			
S	21707	4	C→T	49	4	H→Y
	24034	7	C→T/Y	860	3	V→Q
3a	26144	6	G→T	251	6	G→V
M	26729	5	T→C/Y			
8	28077	5	G→C/S	62	5	V→L
	28144	29	T→C/Y	84	29	L→S
N	28854	6	C→T/Y	194	6	S→L
	29095	11	C→T			

Abbreviations: M, Membrane; N, Nucleoprotein; ORF, open-reading frame; S, Spike; SARS-COV-2, severe acute respiratory syndrome coronavirus 2; 1a, open-reading frames 1a; 1b, open-reading frames 1b; 3a, open-reading frames 3a; 8, open-reading frames 8.

Figure 2. Table, summing up fundamental substitutions in RNA, found as a result of the full genome sequencing of the isolates of the SARS-CoV-2 coronavirus [4]

In the course of studies, it is confirmed that for the penetration into the cells of human alveolar tissue, the SARS-CoV-2 coronavirus uses a receptor angiotensin converting enzyme of II (ACE2) as with the SARS-CoV virus [6]. During the alignment of S-genes of SARS-CoV, Bat-CoV-RaTG13 (bat coronavirus), SARS-CoV-2 and Pangolin-CoVMT084071.1 (mammalian pangolin coronavirus) a unique insert of 12 nucleotides-TCCTCGGCGGGC (figure 3) in the genome of SARS-CoV-2 coronavirus was revealed.

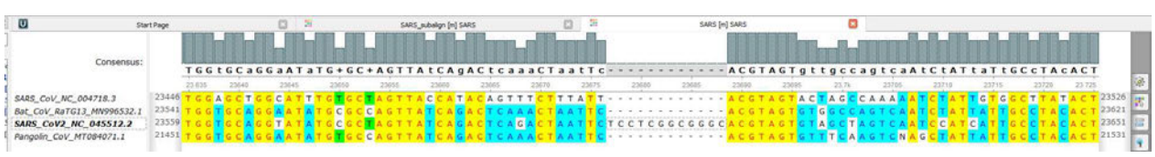


Figure 3. result of the realignment of the S-gene of SARS-CoV, Bat-CoV-RaTG13, SARS-CoV-2 and Pangolin-CoVMT084071.1

A search in the BLAST NCBI computer program produced a correlation of 91.7% with the nucleotide sequence of the detected insert and the six nucleotides of SARS-CoV-2 (TAATTCTCCTCGGCGGG) preceding it, the SARS-CoV-2 with the fragment of misc-RNA of the large brown bat (Eptesicus fuscus) (fig. 4). misc-RNA performs a majority of functions, including

enzyme-like catalysis and processing RNA. It is assumed that misc-RNA serves for switching - turning on or turning off, of genes.

Figure 4 – Result of the comparison of the nucleotide sequence of the 12 nucleotide insert of SARS-CoV-2 with fragments of large brown bat genome RNA.

It should be noted that for creating the specialized cellular lines intended for the cultivation of coronaviruses, eucaryotic cells obtained from the cells of the kidney of the large brown bat are used [7]. Therefore, it is completely probable that the inclusion of segments of genetic material from a eukaryotic cell into the genome of the virus SARS-CoV-2 occurred during cultivation. The probability percentages of this type of insertion into the genome of virus increase with repeated laboratory passages using the cultures of the designated cellular line.

It is known that the 6 amino-acid remainders appear (Y442/L455, L472/F486, N479/Q493, D480/S494, T487/N501, Y491/Y505), which lie at the region of the SARS-CoV/SARS-CoV-2 coronavirus S-protein, coded as the S-gene [8], are the most significant for binding with the receptor ACE2. Likely, this is associated with a change in the tertiary structure of S-the protein, which forms "spikes" on the surface of the SARS-CoV-2 coronavirus, and, consequently, an increase in its affinity with the receptors of the ACE2 transmembrane protein. (figure 5).

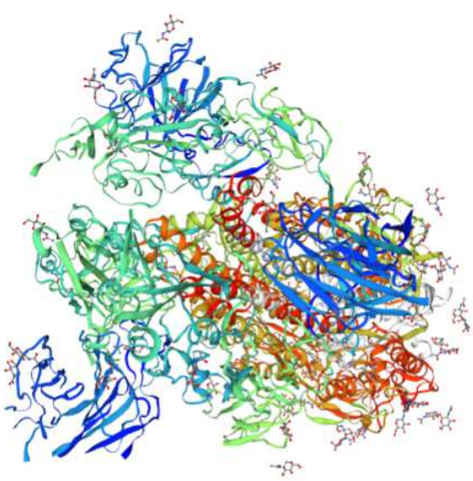


Figure 5 – Model of the S-protein of the SARS-CoV-2 coronavirus (this simulation was produced on the open resource https://swissmodel.expasy.org/). Green indicates the RBD region.

The bioinformation analysis of the amino-acid sequences of S - proteins of SARS-CoV, BatRaTG13 (MN996532) and SARS-CoV-2 showed a difference in five of six amino acids, which

characterize the effectiveness of the virus to penetrate the cells of the human lung alveoli - the high virulence of causative agent is due to this (table below). In this case, the SARS-CoV-2 coronavirus and RaTG13 bat coronavirus genomes possess a 96.2% match [1].

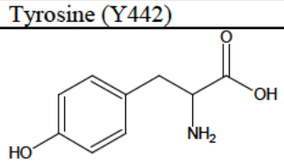
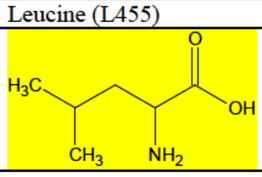
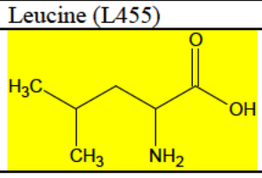
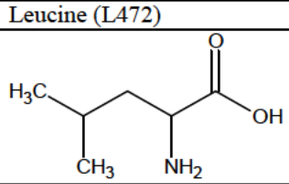
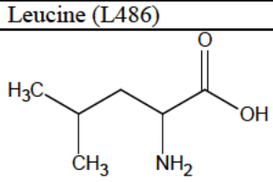
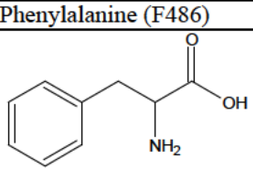
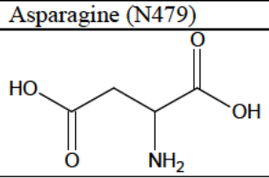
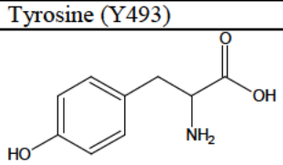
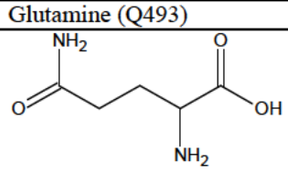
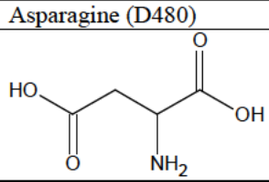
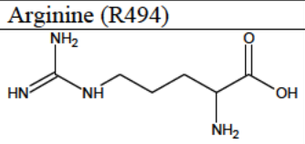
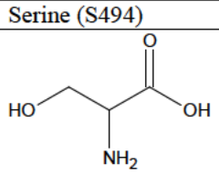
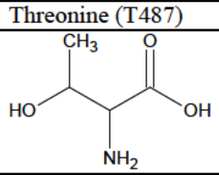
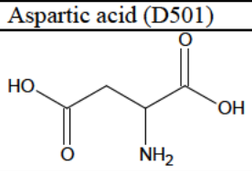
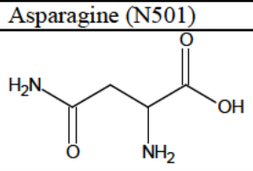
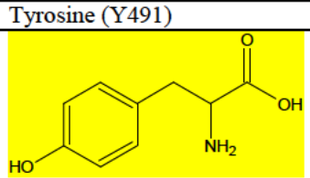
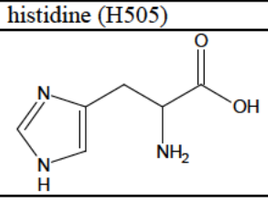
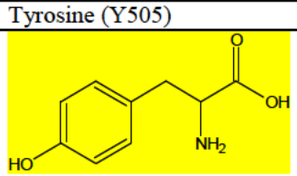
Causative agent	SARS-CoV	Bat RaTG13	SARS-CoV-2
Codon	UAU	CUC	UUG
amino acid	Tyrosine (Y442)	Leucine (L455)	Leucine (L455)
Structure			
Codon	CUU	CUA	UUU
amino acid	Leucine (L472)	Leucine (L486)	Phenylalanine (F486)
Structure			
Codon	AAU	UAU	CAA
amino acid	Asparagine (N479)	Tyrosine (Y493)	Glutamine (Q493)
Structure			
Codon	GAU	AGA	UCA
amino acid	Asparagine (D480)	Arginine (R494)	Serine (S494)
Structure			
Codon	ACU	GAU	AAU
amino acid	Threonine (T487)	Aspartic acid (D501)	Asparagine (N501)
Structure			
Codon	UAC	CAC	UAC
amino acid	Tyrosine (Y491)	histidine (H505)	Tyrosine (Y505)
Structure			

Table - comparison of six amino acids of the S-protein of the three causative agents SARS-CoV, BatRaTG13 and SARS-CoV-2 (coinciding amino acids are highlighted with yellow)

Furthermore, empirical Bayesian Analysis makes it possible to assume that 10 amino acids sites demonstrate the strong signals of the positive selection of the SARS-CoV-2 virus, and, which is interesting, three of these amino acids (N439, V483 and Q493) are located in the receptor-binding domain (RBD) of the S-protein of the spike, including one of them - in the active site (Q493, see table). Thus, although coronaviruses usually are under strong negative selection pressure, positive selection also occurs and answers for the evolution of protein sequences [1].

It is necessary to especially note that the three-dimensional structural analysis showed that the S-gene of the shaft of SARS-CoV-2 has 10-20 times higher affinity for binding with ACE2, than did SARS-CoV [9, 10].

At the same time, analysis of the amino-acid sequences of the SARS-CoV-2 and pangolin coronavirus MT084071.1 S-proteins showed complete congruence of all six amino acids, and the viruses S-gene sequences practically completely coincide [11]. In this case comparison of the genomes of the coronavirus of SARS-CoV-2 and pangolin coronavirus MT084071.1 showed sufficiently low homology of their nucleotide sequences -79%.

There has been discussion abroad of an alternative version about the origin of the SARS-CoV-2 coronavirus through the natural recombination of the S-genes of the bat and pangolin coronaviruses in the pangolin. However, Xiaolu Tang and co-authors in their studies showed that with the synonymous speed of substitution, which is 1.67 - 4.67 x 10^3 sites/year, this recombination had to occur 19.8-55.4 years ago, but not now. Thus, this hypothesis is improbable [1]. In the opinion of the authors, the general identity of the critical sections of SARS-CoV-2 and GT Pangolin-CoV S-genes can be caused by random mutations in combination with natural selection [1]. However, in the study, there is no calculation data about the period of the time which is required for the natural appearance of the pool of such mutations in one strain of virus.

With the comparison of many full genomic sequences of SARS-CoV-2 isolated by foreign authors, is reliably proven that the sequence RNA of corona virus is sufficiently conservative and practically did not change during the time of the pandemic. In their genomes, there are from 0 to 9 single nucleotide replacements, which is extremely small taking into account the length of the virus RNA molecule of approximately 30,000 nucleotides [5]. The low mutability in the coronaviruse genome of is explained by the exoribonuklease activity of the ExoN ferment, whose gene enters into the composition of the coronovirus genomes of this family, which edits the coronavirus replication RNA in the eukaryotic cell. Therefore, the concrete change of four of five key nucleotides in the Bat-CoV-RaTG13 coronavirus S-gene in the acquisition of virulence for humans, whose general genome has greatest homology with the SARS-CoV-2 genome, in the process of evolution and natural selection, it is extremely difficult to explain by random mutations.

One of the circumstantial confirmations of the artificial origin of SARS-CoV-2 is the presence in Wuhan city, where the epidemic began, the virological laboratories (Laboratory of Special Pathogens and Biosafety, Wuhan Institute of Virology, Chinese Academy of Sciences), which have for more than 5 years conducted molecular-biological studies of coronaviruses.

It is necessary to note that up to now, the "zero patient", the first person infected by COVID - 19, has not been reliably established - The information agency, [named U.S. media organization], on April 16, 2020, citing numerous sources, offered the theory of the artificial origin of the SARS-CoV-2 virus. The authors of the investigation assert that the coronavirus was created in the Laboratory of Special Pathogens and Biosafety (city of Wuhan) to demonstrate to the USA the outstanding results achieved by Chinese scientists in the study of viruses. Following the accidental infection of the indicated laboratory researcher, the infection spread, causing the epidemic. The [named UK media organization] previously advanced a similar version. However, the PRC officially refutes the indicated information. However, the authorities of China, upon the appearance of the first cases of COVID-19 infection, when still nothing it was officially known about the disease, took unprecidented measures for the non-admission of the propagation of infection (declaration of total

quarantine, the notification of the population regarding the danger of infection), and also the elimination of unnecessary witnesses and elimination via arson of the place of the assumed initial infection, a market for sea products, which also indirectly confirms assumption about the artificial origin of the virus of SARS-CoV-2.

Thus, in the course of the conducted primary theoretical and experimental investigations, on the basis of the analysis of the genomes of the enumerated corona viruses, and taking into account circumstantial confirmation, there is a high probability of a ***laboratory-produced genetically altered variant - SARS-CoV-2***, for example, from the corona virus of the bat of BatRaTG13, by replacing the nucleotide sequence of the S-protein of parental strain in the sequence of the S-protein of the MT084071.1 strain of the coronavirus of the mammalian pangolin, or by the difficultly demonstrated target localized single nucleotide replacements with the use of laboratory technology CRISPR-CAS9. In this case, in the stage of conducting repeated laboratory passages of the SARS-CoV-2 virus on the culture of the specific cellular line obtained from the eukaryotic cell of Eptesicus Fuscus (large brown bat), in the RNA-virus genome occurred random 12 nucleotide insertions of the misc - RNA fragment.

On the basis of details outlined above, the following conclusions are made:

1. The insertion of corresponding fragment misc-RNA of large brown bat (Eptesicus Fuscus) into the SARS-CoV-2 genome.
2. For compiling of the specialized cellular lines, intended for the cultivation of corona viruses, eukaryotic cells obtained from the cells of the kidney of the large brown bat, are used.
3. Five of six amino acids of the S-strain of SARS-CoV-2, which specify the effectiveness of the penetration of coronavirus into the cells of human lung alveoli due to this the high virulence of agent, differ from the same found in SARS-CoV and Bat-CoV-RaTG13.
4. One of the different amino acids of the S-protein of the spike of the SARS-CoV-2 coronavirus, Q493, enters into the active center of receptor-binding domains (RBD).
5. SARS-CoV-2 has 10-20 times higher affinity than SARS-CoV of binding with ACE2.
6. The natural recombination of the S-genes of the bat and pangolin coronaviruses in pangolins is improbable.
7. Based on conclusions 1-6, it is possible to assume the high probability of a **laboratory** producing the genetically changed version of the SARS-CoV-2 coronavirus.
8. During further investigations, it is advisable to define the function of unknown proteins transmitted from the sequences of the open reading frames of the genome SARS-CoV-2 with the goal of determination of the genetic predisposition different ethnic groups to outcome of illness
9. It is necessary to reliably define determinants of the causative agent’s immunogenicity.

Source listing

1. Xiaolu Tang, Changcheng Wu, Xiang Li, Yuhe Song, Xinmin Yao, Xinkai Wu, YuangeDuan, Hong Zhang, Yirong Wang, Zhaohui Qian, Jie Cui, Jian Lu, On the origin and continuing evolution of SARS-CoV-2, National Science Review, nwaa036, https://doi.org/10.1093/nsr/nwaa036.
2. Lu R. et al., Genomic characterization and epidemiology of 2019 novel coronavirus: implication for virus origins and receptor binding // Lancet. 2020 doi:10.1016/S0140-6736(20)30251-8.
3. Gralinski L.E. et al., Return of coronavirus:2019-nCoV // Viruses. 2020. 12. 2 doi:10.3390/v12020135.
4. Wang C, Liu Z, Chen Z, et al.The establishment of reference sequence for SARS-CoV-2and variation analysis// J Med Virol. 2020;1–8.

5. Okada P. et al., Early transmission patterns of coronavirus disease 2019(COVID-19) in travelers from Wuhan to Thailand, January 2020 // Euro Surveill. 2020;25(8):pii=2000097. https://doi.org/10.2807/1560-7917.ES.2020.25.8.2000097.

6. Zhou P et al., Discovery of a novel coronavirus associated with recent pneumonia outbreak in humans and its potential bat origin // bioRxiv. 2020.

7. Banerjee Aet al., Generation and Characterization of Eptesicusfuscus (Big brown bat) kidney cell lines immortalized using the Myotis poliomavirus large T-antigen // J.Virol Methods. 2016. Nov 237: 166-173.

8. Vinet D Menachery et al., A SARS-like cluster of circulating bat coronaviruses shows potential for human emergence // Nature Medicine. 2015. doi:10.1038/nm.3985.

9. Wrapp D, Wang N, Corbett KS, Goldsmith JA, Hsieh C-L, Abiona O, et al. Cryo-EM Structure of the2019-nCoV Spike in the Prefusion Conformation. bioRxiv. 2020:2020.02.11.944462. doi:10.1101/2020.02.11.944462.

10. Hoffmann, M.; Kleine-Weber, H.; Schroeder, S.; Kruger, N.;Herrler, T.; Erichsen, S.; Schiergens, T. S.; Herrler, G.; Wu, N.-H.; Nitsche, A.; Muller, M. A.; Drosten, C.; Pohlmann, S. SARS-CoV-2Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. Cell 2020, DOI: 10.1016// j.cell.2020.02.052. [Epub ahead of print]

11. Wong MC, Cregeen SJJ, Ajami NJ, Petrosino JF. Evidence of recombination in coronaviruses implicating pangolin origins of nCoV-2019. bioRxiv. 2020.

Expert Meeting
Rapid Response for Assessment of Data Needs for 2019-nCoV
Agenda
February 3, 2020
2:00 p.m.-3:0 (ET)

[redacted]droid: [redacted]
Telephone: [redacted]
Meeting ID: [redacted]
Internationa[redacted]vailable: [redacted]
Meeting Objective: Assess what da[redacted]eeded to understand the evolutionary origins of 2019-nCoV and more effectively respond to the outbreak and resulting misinformation.

Welcome and Introductions (5 mins)

[redacted]

2:05 p.m. Statement of Work (10 mins)

[redacted]

U.S. Department of Health and Human Services

2:15 p.m. Perspective from NIH/NIAID (10 mins)

Anthony ("Tony") S. Fauci
Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health

2:25 p.m. Discussion of Meeting Objective (30 mins)

2:55 p.m. Determine Next Steps (5 mins)

3:00 p.m. Adjourn

Statement of Work
Rapid Response for Assessment of Data Needs for 2019-nCoV
February 3, 2020

Statement of Task:
In response to a request from OSTP, the NASEM will examine information and identify data requirements that would help determine the origins of 2019-nCoV, specifically from an evolutionary/structural biology standpoint. NASEM will also consider whether this should include more temporally and geographically diverse clinical isolates, sequences, etc. Although a widely-disputed paper posted on a pre-print server last week has since been withdrawn, the response to that paper highlights the need to determine these information needs as quickly as possible. As part of a broader deliberative process, this review will help prepare for future events by establishing a process for quickly assembling subject matter experts for evaluation of other potentially threatening organisms.

Workplan:
NASEM will hold a meeting of experts to assess what data, information and samples are needed to address the unknowns, in order to understand the evolutionary origins of NCoV and more effectively respond to both the outbreak and any resulting misinformation. A statement from the National Academies will be prepared and published on the Web as a "Based on Science" article that summarizes the status and needs for more and what types of data. A more in-depth examination of the issues will be established as a follow up as needed.

BRAD R. WENSTRUP, D.P.M.
CHAIRMAN

ONE HUNDRED EIGHTEENTH CONGRESS

RAUL RUIZ, M.D.
RANKING MEMBER

Congress of the United States

House of Representatives

SELECT SUBCOMMITTEE ON THE CORONAVIRUS PANDEMIC

2157 RAYBURN HOUSE OFFICE BUILDING

WASHINGTON, DC 20515–6143

Majority (202) 225–5074
Minority (202) 225–5051

September 26, 2023

The Honorable Christi A. Grimm
Inspector General
U.S. Department of Health and Human Services
Office of Inspector General
330 Independence Avenue SW
Washington, D.C. 20201

Dear Inspector General Grimm:

The Select Subcommittee on the Coronavirus Pandemic (Select Subcommittee) has received concerning information regarding the Central Intelligence Agency's investigation into the origins of COVID-19.

According to information gathered by the Select Subcommittee, Dr. Anthony Fauci, then-director of National Institute of Allergy and Infectious Diseases, played a role in the Central Intelligence Agency's review of the origins of COVID-19. The information provided suggests that Dr. Fauci was escorted into Central Intelligence Agency (CIA) Headquarters—without a record of entry—and participated in the analysis to "influence" the Agency's review. Our goal is to ensure the scientific investigative process regarding the origins of COVID-19 was fair, impartial, and free of alternative influence.

The Select Subcommittee's goal is to ensure accountability and transparency. The American people deserve the truth—to know the origins of the virus and whether there was a concerted effort by public health authorities to suppress the lab leak theory for political or national security purposes. Accordingly, information regarding specific movements of Dr. Fauci throughout the pandemic is reasonable and hardly intrusive, especially considering he is no longer employed by the federal government, he is no longer a protectee of the Inspector General, and we are not requesting any information regarding his current movements.

To assist the Select Subcommittee with its investigation, we request the following documents and information as soon as possible but no later than October 10, 2023:

1. Documents sufficient to show any Department of Health and Human Services Office of Inspector General authorized, supported, or otherwise affiliated movements of Dr. Anthony Fauci from January 1, 2020 through December 31,

2022 into any CIA owned, operated, or occupied building, including but not limited to the George Bush Center of Intelligence.

2. All documents and communications between or among employees or contractors of the Department of Health and Human Services Office of Inspector General regarding the admittance or entry of Dr. Anthony Fauci into any CIA owned, operated, or occupied building, including but not limited to the George Bush Center of Intelligence.

3. All documents and communications between or among employees or contractors of the Department of Health and Human Services Office of Inspector General and employees or contractors of the CIA regarding the admittance or entry of Dr. Anthony Fauci into any CIA owned, operated, or occupied building, including but not limited to the George Bush Center of Intelligence.

4. All documents and communications between or among employees or contractors of the Department of Health and Human Services Office of Inspector General and employees or contractors of the U.S. Marshals Service regarding the admittance or entry of Dr. Anthony Fauci into any CIA owned, operated, or occupied building, including but not limited to the George Bush Center of Intelligence.

5. All documents and communications between or among employees or contractors of the Department of Health and Human Services Office of Inspector General and employees or contractors of the Department of Health and Human Services, including but not limited to the National Institutes of Health and National Institute of Allergy and Infectious Diseases, regarding the admittance or entry of Dr. Anthony Fauci into any CIA owned, operated, or occupied building, including but not limited to the George Bush Center of Intelligence.

In addition to these documents, we request you make Special Agent Brett Rowland available for a voluntary transcribed interview at a date to be determined. Accordingly, the Committees will contact you to schedule the interview. The Committees reserve their right to conduct follow-up interviews or request testimony from other witnesses pertinent to our investigation.

The Select Subcommittee on the Coronavirus Pandemic is authorized to investigate "the origins of the Coronavirus pandemic, including but not limited to the Federal Government's funding of gain-of function research" and "executive branch policies, deliberations, decisions, activities, and internal and external communications related to the coronavirus pandemic" under H. Res. 5. To schedule the briefing or ask any follow-up or related questions, please contact Select Subcommittee staff at (202) 225-5074.

Thank you for your attention to this very important matter.

Sincerely,

Brad R. Wenstrup, D.P.M.
Chairman

cc: The Honorable Raul Ruiz, M.D., Ranking Member
Select Subcommittee on the Coronavirus Pandemic

(U) Table of Contents

Identifiers

Document Number: 18 WUHAN 38

[redacted]

(U//[redacted]) E.O. 13526: N/A
TAGS: SHLH, PGOV, CN, PREL, TBIO, KGHI, CDC, EAID, KHIV, IN, JP, TW, TSPL, PINS, SENV
SUBJECT: China Virus Institute Welcomes More U.S. Cooperation on Global Health Security

REF: 18 BEIJING 138
17 BEIJING 2458
11 MUMBAI 630
17 TOKYO 716
13 SEOUL 790

1. ([redacted]) Summary with Comment: China's Wuhan Institute of Virology, a global leader in virus research, is a key partner for the United States in protecting global health security. Its role as operator of the just-launched Biosafety Level 4 (or "P4") lab -- the first such lab in China -- opens up even more opportunities for expert exchange, especially in light of the lab's shortage of trained staff (Ref A). Given the legacy of SARS and the likelihood that the next global pandemic will originate in China, the United States should prioritize expanding our already significant cooperation with this institute. This should include partnering with the institute on basic science research and the Global Virome Project (Ref B), and possibly trilateral U.S.-China-EU projects, building on the institute's strong ties with France. End Summary with Comment.

2. (U) Wuhan Institute of Virology researchers and staff gave an overview of the lab and current cooperation with the United States to visiting Environment, Science, Technology and Health Counsellor Rick Switzer and Consulate Wuhan Consul General Jamie Fouss in late March. In the last year, the institute has also hosted visits from the National Institutes of Health (NIH), National Science Foundation, and experts from the University of Texas Medical Branch in Galveston. The institute reports to the Chinese Academy of Sciences in Beijing.

P4 Lab is Open and Transparent, Officials Emphasize

3. ([redacted]) The Wuhan P4 lab, referring to labs with the highest level of safety precautions, became fully operational and began working with live viruses early this year. Institute officials said they believed it is the only operational P4 lab in Asia aside from a U.S. Centers for Disease Control (CDC)-supported facility in Pune, India (Ref C). China plans to stand up a second P4 lab in Harbin. Institute officials said Japan's biosafety labs are "old" and lack cutting-edge equipment, so they consider Japan's labs to be "P3 Plus" (Note: the Japanese government says it has one P4-level lab in the Tokyo suburbs, though its activities are limited, and Japan is building a new P4 lab in Nagasaki, see Ref D. Taiwan operates at least HYPERLINK "https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5404250/"one P4 lab. South Korea was close to

HYPERLINK "http://www.koreaherald.com/view.php?ud=20170316000902"opening a P4 lab as of last year, see Ref E. End Note.) Wuhan's lab is located about 20 miles from the city center in Zhengdian district, and the institute plans to gradually consolidate its other training, classroom and lab facilities at that location.

4. (U) Officials described the lab as a "regional node" in the global biosafety system and said it would play an emergency response role in an epidemic or pandemic. The lab's English brochure highlighted a national security role, saying that it "is an effective measure to improve China's availability in safeguarding national bio-safety if [a] possible biological warfare or terrorist attack happens."

5. ([redacted]) Institute officials said there would be "limited availability" for international and domestic scientists who had gone through the necessary approval process to do research at the lab. They stressed that the lab aimed to be a "worldwide, open platform" for virology. They said they welcomed U.S. Centers for Disease Control (CDC) experts, noting that the Chinese Academy of Sciences was not strong on human disease expertise, having only focused on it in the last 15 years, after the SARS outbreak. A Wuhan-based French consulate official who works on science and technology cooperation with China also emphasized that the lab, which was initiated in 2004 as a France-China joint project, was meant to be "open and transparent" to the global scientific community. "The intent was to set up a lab to international standards, and open to international research," he said. French experts have provided guidance and biosafety training to the lab, which will continue, the French official said. Institute officials said that France provided the lab's design and much of its technology, but that it is entirely China-funded and has been completely China-run since a "handover" ceremony in 2016.

6. (U) In addition to French assistance, experts from the NIH-supported P4 lab at the University of Texas Medical Branch in Galveston have trained Wuhan lab technicians in lab management and maintenance, institute officials said. The Wuhan institute plans to invite scientists from the Galveston lab to do research in Wuhan's lab. One Wuhan Institute of Virology researcher trained for two years at the Galveston lab, and the institute also sent one scientist to U.S. CDC headquarters in Atlanta for six months' work on influenza.

NIH-Supported Research Revises SARS Origin Story

7. (U) NIH was a major funder, along with the Natural Science Foundation of China (NSFC), of SARS research by the Wuhan Institute of Virology's Shi Zhengli and Cui Jie. The researchers spent five years of investigation and genome sequencing to show that a population of bats in a cave in Yunnan Province harbored a virus with all the "building blocks" of SARS. This lends weight to the theory that SARS originated in bat populations before jumping first to civet cats (likely via bat feces) and then to humans, after people transported the civet cats from Yunnan to Guangdong Province animal markets. The results were published late last year in HYPERLINK "https://www.nature.com/articles/d41586-017-07766-9"Nature and other publications. Shi said that U.S. scientist Peter Daszak, a leading expert on emerging diseases and president of the New

York-based EcoHealth Alliance, was a "strong partner." Daszak's team has provided support in statistical modeling to assess the risk of more coronaviruses like SARS crossing over to human populations.

Ready to Help with the Global Virome Project

8. (U) Institute officials expressed strong interest in the Global Virome Project (GVP), and said Chinese funding for the project would likely come from Chinese Academy of Sciences funding already earmarked for One Belt, One Road-related initiatives. The HYPERLINK "http://science.sciencemag.org/content/359/6378/872.full"GVP aims to launch this year as an international collaborative effort to identify within ten years virtually all of the planet's viruses that have pandemic or epidemic potential and the ability to jump to humans. "We hope China will be one of the leading countries to initiate the Global Virome Project," one Wuhan Institute of Virology official said. China attended a GVP unveiling meeting in January in Thailand and is waiting for more details on the initiative. The officials said that the Chinese government funds projects similar to GVP to investigate the background of viruses and bacteria. This essentially constituted China's own Virome Project, officials said, but they noted the program currently has no official name.

9. ([redacted]) The Wuhan Institute of Virology's Shi Zhengli is the China Country Coordinator for the USAID-funded PREDICT project, which is designed to show "proof of concept" and be a forerunner to the Global Virome Project. Li Hongying, with the EcoHealth Alliance (a New York City-based NGO that is working with the University of California, Davis to manage the PREDICT project), recently planned to visit Wuhan to meet with Shi. Li noted that China has expressed interest in building the GVP database, which would put China in a leadership position. Other countries have confidence in Chinas ability to build such a database, but are skeptical on whether China could remain transparent as a "gatekeeper" for this information, she said. Li expressed frustration with the slow progress so far in launching GVP, noting that the effort lacked funding sources, needed to hire a CEO, and would have to boost its profile at G7, G20 and other high-level international meetings.

U.S.-China Workshop Explores Research Partnerships

10. (U) The Institute also has ongoing collaboration with the U.S. National Science Foundation, including a just-concluded workshop in Shenzhen, involving about 40 scientists from the United States and China, on the topic of the "Ecology and Evolution of Infectious Diseases." Co-sponsored by the Natural Science Foundation of China (NSFC), the Chinese lead for this workshop was the Wuhan Institute of Virology's Hu Zhihong, and the U.S. co-chair was the University of Oklahoma's Xiao Xiangming. The workshop explored opportunities for U.S.-China research cooperation in areas like using "big data" to predict emerging infectious diseases, climate changes effect on vector-borne diseases, and pathogen transmission between wildlife, domestic animals and humans.

11. ([redacted]) Some workshop participants also expressed skepticism about the Global Virome Project's (GVP) approach, saying that gaining a predictive understanding of viruses with pandemic potential would require going beyond the GVPs strategy of sample collection, to take an "ecological" approach that considers the virome beyond vertebrate systems to identify mechanisms driving pathogen evolution. A follow-on workshop will be held in June at the University of Berkeley. NSF and NSFC hope to jointly announce a funding call for collaborative projects later this year.

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- 18 BEIJING 138 17 BEIJING 2458 11 MUMBAI 630 17 TOKYO 716 13 SEOUL 790

(U) Table of Contents

(U[redacted]) China Opens First Bio Safety Level 4 Laboratory

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1. [redacted] Summary and Comment: The Chinese Academy of Sciences (CAS) has recently established what is reportedly Chinas first Biosafety Level 4 (BSL-4) laboratory in Wuhan. This state-of-the-art facility is designed for prevention and control research on diseases that require the highest level of biosafety and biosecurity containment. Ultimately, scientists hope the lab will contribute to the development of new antiviral drugs and vaccines, but its current productivity is limited by a shortage of the highly trained technicians and investigators required to safely operate a BSL-4 laboratory and a lack of clarity in related Chinese government policies and guidelines. China must invest in the development of the technical and scientific expertise needed to safely and efficiently operate this facility if it wishes to become a fully-engaged and collaborative global partner in infectious disease research and control. In addition, government BSL research decision-making processes need to be more transparent so that international partners and Chinese scientists are confident that the government is providing informed oversight that meets the highest global standards. To achieve full operation of this facility, China is likely to need additional technical assistance and advice from the international community. End Summary and Comment.

China Investing in Infectious Disease Control

2. (U) Between November 2002 and July 2003, China faced an outbreak of Severe Acute Respiratory Syndrome (SARS), which, according to the World Health Organization, resulting in 8,098 cases and leading to 774 deaths reported in 37 countries. A majority of cases occurred in China, where the fatality rate was 9.6%. This incident convinced China to prioritize international cooperation for infectious disease control. An aspect of this prioritization was Chinas work with the Jean Merieux BSL-4 Laboratory in Lyon, France, to build Chinas first high containment laboratory at Wuhans Institute of Virology (WIV), an institute under the auspices of the Chinese Academy of Sciences (CAS). Construction took 11 years and $44 million USD, and construction on the facility was completed on January 31, 2015. Following two years of effort, which is not unusual for such facilities, the WIV lab was accredited in February 2017 by the China National Accreditation Service for Conformity Assessment. It occupies four floors and consists of over 32,000 square feet. WIV leadership now considers the lab operational and ready for research on class-four pathogens (P4), among which are the most virulent viruses that pose a high risk of aerosolized person-to-person transmission.

Unclear Guidelines on Virus Access and a Lack of Trained Talent Impede Research

3. [redacted] In addition to accreditation, the lab must also receive permission from the National Health and Family Planning Commission (NHFPC) to initiate research on specific highly contagious pathogens. According to some WIV scientists, it is unclear how NHFPC determines what viruses can or cannot be studied in the new laboratory. To date, WIV has obtained permission for research on three viruses: Ebola virus, Nipah virus, and Xinjiang hemorrhagic fever virus (a strain of Crimean Congo hemorrhagic fever found in Chinas Xinjiang Province). Despite this permission, however, the Chinese government has not allowed the WIV to import Ebola viruses for study in the BSL-4 lab. Therefore, WIV scientists are frustrated and have pointed out that they wont be able to conduct research project with Ebola viruses at the new BSL-4 lab despite of the permission.

4. [redacted] Professor Zhengli Shi, one of the few Chinese scientists with BSL-4 lab training, commented that NHFPCs decision-making process regarding virus research permission is not transparent. Dr. Shi primarily studies coronaviruses including SARS and Middle East Respiratory Syndrome (MERS). As a result, WIV requested permission to work on SARS in the new lab. NHFCP denied this request without providing a clear reason, according to Professor Zheng. Thus, while the BSL-4 lab is ostensibly fully accredited, its utilization is limited by lack of access to specific organisms and by opaque government review and approval processes. As long as this situation continues, Beijings commitment to prioritizing infectious disease control - on the regional and international level, especially in relation to highly pathogenic viruses, remains in doubt.

5. [redacted] During interactions with scientists at the WIV laboratory, they noted that the new lab has a serious shortage of appropriately trained technicians and investigators needed to safely operate this high-containment laboratory. University of Texas Medical Branch in Galveston (UTMB), which has one of several well-established BSL-4 labs in the United States (supported by the National Institute of Allergy and Infectious Diseases (NIAID of NIH)), has scientific collaborations with WIV, which may help alleviate this talent gap over time. Reportedly, researchers from GTMB are helping train technicians who work in the WIV BSL-4 lab. Despite this, technicians at the WIV lab stated that they would welcome more help from U.S. and international organizations as they establish gold standard operating procedures and training courses for the first time in China. As China is building more BSL-4 labs, including one in Harbin Veterinary Research Institute subordinated to the Chinese Academy of Agricultural Sciences (CAAS) for veterinary research use (according to WIV scientists), the training for technicians and investigators working on dangerous pathogens will certainly be in demand.

Despite Limitations, WIV Researchers Produce SARS Discoveries

6. [redacted] The ability of WIV scientists to undertake productive research despite limitations on the use of the new BSL-4 facility is demonstrated by a recent publication on the origins of SARS. Over a five-year study, Drs. Shi and Cui Jie (and their research team) widely sampled bats in Yunnan province with funding support from NIAID/NIH, USAID, and several Chinese funding agencies. The study results were published in PLoS Pathogens online on Nov. 30, 2017 (1), and it demonstrated that a SARS-like coronaviruses isolated from horseshoe bats in a single cave contain all the building blocks of the pandemic SARS-coronavirus genome that caused the human outbreak. These results strongly suggest that the highly pathogenic SARS-coronavirus originated in this bat population. Most importantly, the researchers also showed that various SARS-like coronaviruses can interact with ACE2, the human receptor identified for SARS-coronavirus. This finding strongly suggests that SARS-like coronaviruses from bats can be transmitted to humans to cause SARS-like disease. From a public health perspective, this makes the continued surveillance of SARS-like coronaviruses in bats and study of the animal-human interface critical to future emerging coronavirus outbreak prediction and prevention. It is interesting that WIV scientists are allowed to study the SARS-like coronaviruses isolated from bats while they are precluded from studying human-disease causing SARS coronavirus in their new BSL-4 lab until permission for such work is granted by the NHFCP.

1. Hu B, Zeng L-P, Yang X-L, Ge X-Y, Zhang W, Li B, et al. (2017) Discovery of a rich gene pool of bat SARS-related coronaviruses provides new insights into the origin of SARS coronavirus. PLoS Pathog 13(11): e1006698. https://doi.org/10.1371/journal.ppat.1006698
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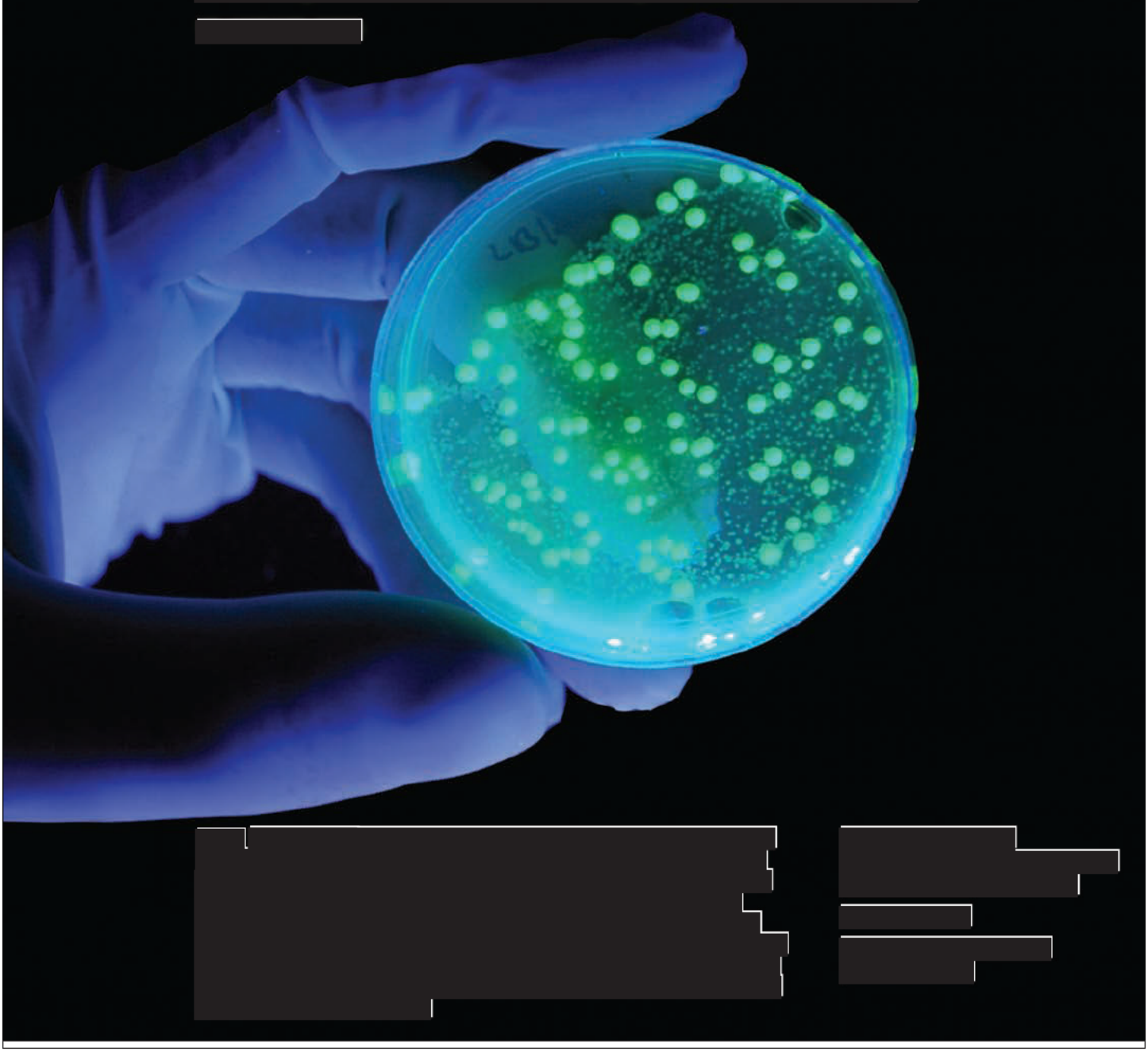

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(U) Produced under the auspices of the Chief of Analysis, Weapons and Counterproliferation Mission Center. Comments and queries are welcome and may be directed to the Chief of Analysis on (703) 874-5411 [redacted]

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(U) Key Findings

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[a] (U) See figure 1.
[b] (U) See figure 2.
[c] (U) See figure 3.

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(U) Scope Note

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- (U [redacted]) Two separate studies by a Dutch, UK, and US team and a Japanese and US team in 2011 using separate experimental strategies each modified naturally occurring H5N1 avian influenza viruses to become airborne-transmissible in ferrets. Naturally occurring avian influenza viruses have shown only limited, unsustained spread between people, but both groups were seeking to identify mutations to enhance disease surveillance that could lead to sustained aerosol transmission between humans.

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[d] (U) See figure 1.
[e] (U) See figure 2.
[f] (U) See figure 3.

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(U/[redacted]) Gain-of-Function (GOF) Research Provides Valuable Public Health Data

(U//FOUO) GOF experiments can generate strains of pathogens—including viruses, bacteria, fungi, and toxins—suitable for laboratory research that might help scientists predict or understand how pathogens could mutate in nature and whether those mutations will affect human health. GOF experiments can also inform biosurveillance and countermeasure development or selection.

- (U/[redacted]) In early 1999, Western scientists described adapting *Ebolavirus zaire* for guinea pigs, providing a safer and less expensive animal model than monkeys for studying the virus, how it affects its animal host, and how to develop treatment options, according to a scientific journal article. Such adaptation experiments are routinely performed to extend the host range of various pathogens for use in research and drug development, especially for high-risk pathogens or those with limited host range.
- (U/[redacted]) According to a presentation in December 2014 by a leading influenza researcher, GOF research on influenza viruses has provided data to inform policymaker decisions about which vaccines to stockpile based on viral pandemic potential and has enabled researchers to assess the risk of currently circulating virus strains. The utility of these experiments is most likely reduced, however, in cases where the molecular mechanisms of the disease are not well-understood, such as for coronaviruses—a family of viruses that includes those that cause Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS)—and other emerging pathogens.
- (U/[redacted]) In late 2014, researchers used data from influenza GOF experiments to inform the selection of specific viral groups and strains from which to produce seasonal and pandemic vaccines, according to commentary by scientists on the vaccine strain selection committee. Influenza is a unique case compared with other potential pandemic-causing pathogens, because seasonal spread of the virus drives vaccine and countermeasure development. Other viruses may not have a similarly high rate of mutation, according to scientific journal articles.

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(U/[redacted]) States Probably Weighing Costs Against Benefits

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(U) US Laboratory Biosafety and Biosecurity Definitions

(U) Laboratory biosafety is a set of preventative measures used in bioscience and biomedical research to reduce or eliminate exposure of laboratory workers, other persons, and the environment to potentially hazardous agents. Biosafety levels (BSLs) indicate the amount of protection—levels one through four—appropriate to limit the risk of working with agents. The levels build on one another, for example, BSL-3s encompass BSL-1 and BSL-2 requirements.

- (U) BSL-1 laboratories allow for open benchwork, provide basic protection from agents that do not consistently cause disease in healthy adults, and prevent minimal environmental hazard.
- (U) BSL-2 laboratories are used for work with agents that can cause human disease but often have effective countermeasures and limited potential for transmission. These laboratories typically require limited access and use biosafety cabinets (BSCs) and personal protective equipment (PPE) for pathogen work that may cause splashes or aerosols.
- (U) BSL-3 laboratories are designed to contain infectious agents that have effective countermeasures but may cause serious or potentially lethal diseases from contact or inhalation, or become a serious environmental threat if released. These laboratories typically require controlled access, negative airflow into laboratories, BSCs and PPE for all open pathogen work, and double-door access to laboratories through an anteroom.
- (U) BSL-4 laboratories are maximum-containment facilities used for work on highly infectious agents that pose serious or lethal human or animal disease risk, are readily transferred directly or indirectly to the researcher or environment, and have no effective vaccines or countermeasures. These laboratories require controlled access; clothing change upon entering; shower upon exit; BSCs and a full-body, air-supplied-positive pressure suit for pathogen work; and an isolated zone with supply and exhaust, vacuum, and decontamination systems.

(U) Laboratory biosecurity complements biosafety by providing guidelines for securing pathogens, toxins, and related equipment and research material to reduce the risk of loss, theft, misuse, exploitation, or diversion.

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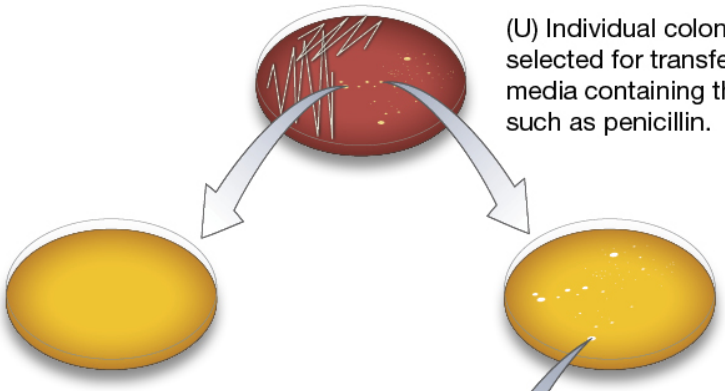
(U) Figure 1: Serial Passage of Bacteria *In Vitro* To Increase Antibiotic Resistance

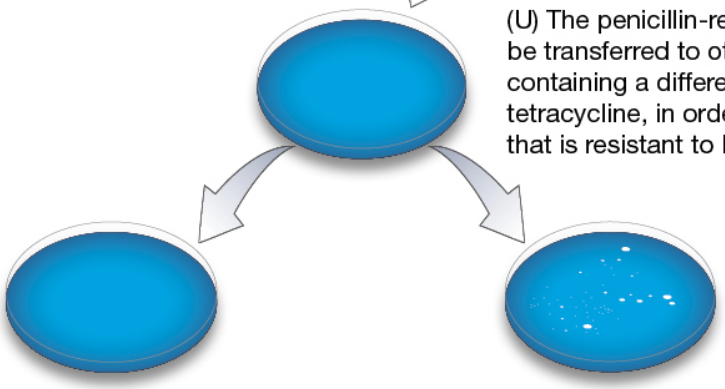
(U) Researchers have used serial passage techniques to increase antibiotic resistance in bacteria. This type of serial passage involves exposing bacteria multiple times to an antibiotic, usually in growth media, until a bacterial strain mutates to acquire resistance to and grow in the presence of the antibiotic. The process can be repeated with other antibiotics to create strains of bacteria that are resistant to multiple drugs. The bacteria may lose other capabilities such as pathogenicity, however, as a result of gaining functions like antibiotic resistance. A loss of other capabilities could potentially be overcome by serial passage in animals to regain features like pathogenicity or transmissability, but also could result in loss of antibiotic resistance.



(U) Individual colonies of bacteria are selected for transfer to new growth media containing the selected antibiotic, such as penicillin.

(U) The bacteria do not grow on the media with penicillin because they do not have the gene for penicillin resistance.

(U) The bacteria grow on the media with penicillin because they already possessed the gene for penicillin resistance or they mutated to become resistant to penicillin. Multiple iterations of this process probably would be required to isolate and grow bacteria resistant to a specific antibiotic.



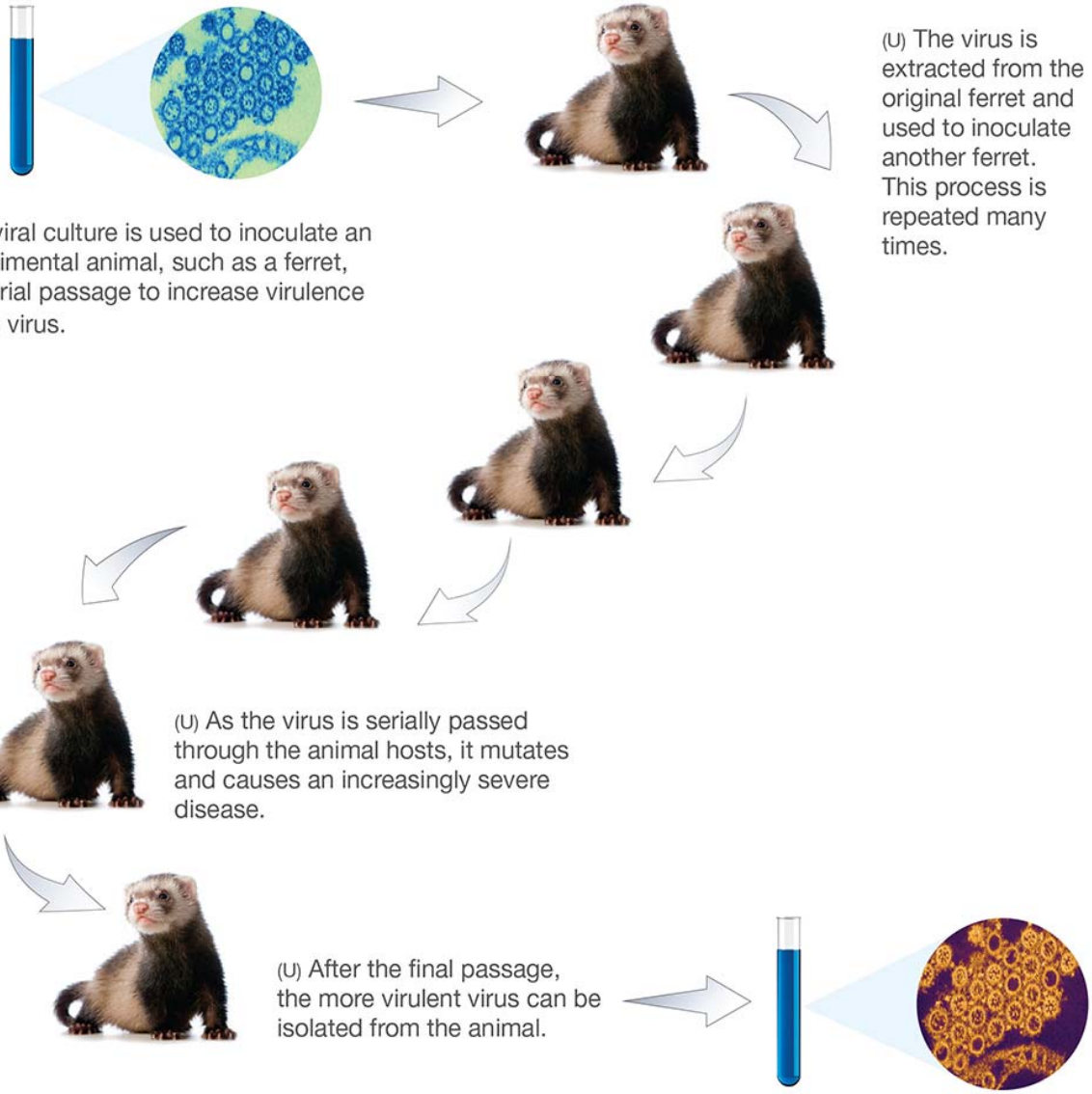
(U) The penicillin-resistant bacteria can be transferred to other growth media containing a different antibiotic, such as tetracycline, in order to create a strain that is resistant to both antibiotics.

(U) The penicillin-resistant bacteria do not grow on the media with tetracycline because they do not have the gene for tetracycline resistance.

(U) The penicillin-resistant bacteria grow on the media with tetracycline because they already possessed the gene for tetracycline resistance or they mutated to become resistant to tetracycline.

(U) Figure 2: Serial Passage of a Virus *In Vivo* To Increase Virulence

(U) Researchers could use serial passage techniques to increase viral virulence, the severity of disease caused by a virus. This type of serial passage involves infecting or inoculating an experimental animal with a virus, allowing the virus to reproduce, isolating the virus from the animal, then infecting another animal with the isolated virus. The process can be repeated multiple times in multiple animal hosts to create strains of the virus that have increased virulence. The virus mutates as it replicates and can adapt to cause more severe disease in the host by evading the host immune system. The virus may lose other capabilities such as transmissibility, however, as a result of gaining functions like increased virulence.



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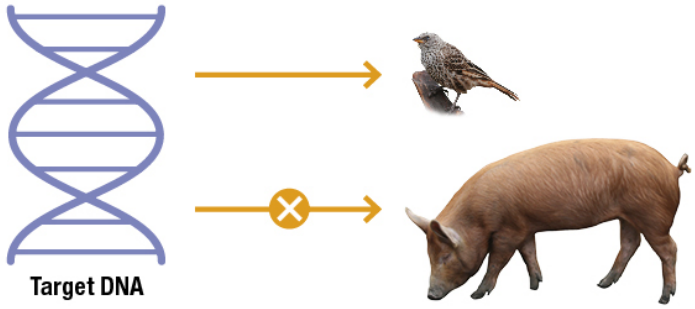
(U) Figure 3: Genetic Engineering of a Virus *In Vitro* To Expand Host Range

(U) Genetic engineering is the process of altering an organism's genetic information to change its characteristics. In gain-of-function (GOF) experiments, genetic engineering techniques can be used to provide pathogens with new or enhanced biological properties such as increased transmissibility, virulence, or expanded host range. This graphic shows how one genetic engineering technique, CRISPR-Cas9, could be used to alter the host range of a virus.

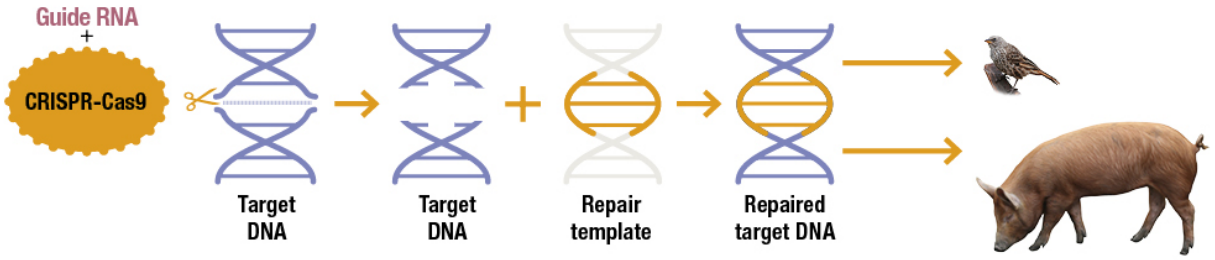
(U) Researchers would need to know which viral genes code for viral surface proteins that bind to host cell receptors in order to use genetic engineering techniques to expand host range. These surface proteins determine what kind of host, such as animals or humans, the virus can infect.

(U) The unaltered target deoxyribonucleic acid (DNA) coding for viral surface proteins allows the virus to infect some species of birds but not pigs.



CRISPR-Cas9 Process

(U) CRISPR-Cas9 could be used to alter genes that code for viral surface proteins by targeting and cleaving the viral DNA at a site specified by the guide ribonucleic acid (RNA). Cellular machinery then uses the repair template—which in this case contains a sequence for a different surface protein—to incorporate the new sequence into the viral genome. The altered target DNA now codes for viral surface proteins that allow the virus to infect some species of birds and pigs.



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