Houston Methodist Update

Marc L. Boom, MD
September 29, 2022

HOUSTON Methodist
LEADING MEDICINE

THE VISION FOR THE SECOND CENTURY

Houston Methodist will set a new standard for leading academic medical centers through ***unparalleled safety, quality, service and innovation***.

HOUSTON Methodist®
LEADING MEDICINE

WHEN YOU FOCUS ON THE FUNDAMENTALS…

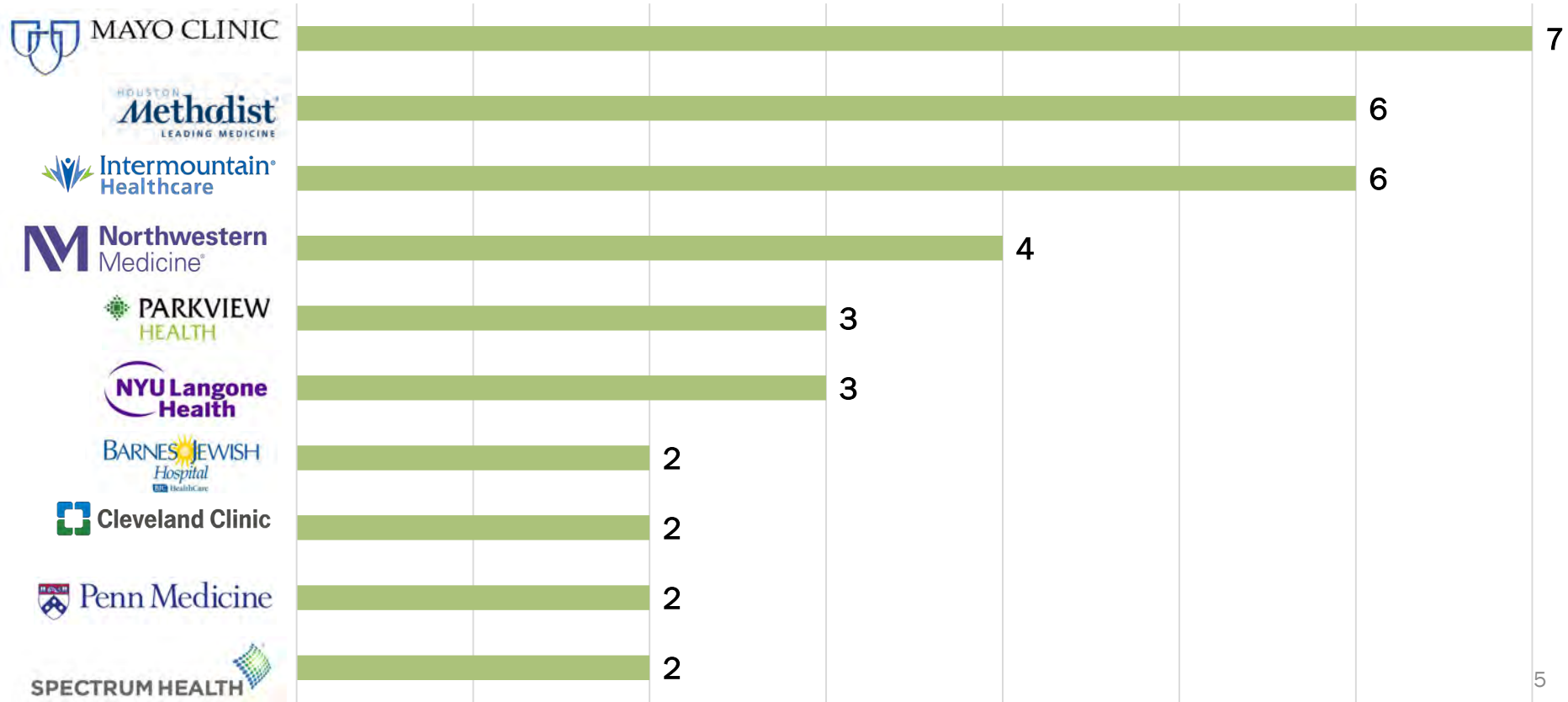
THE AWARDS WILL FOLLOW.

Vizient Q&A Ranking Trend by Hospital

HOUSTON Methodist LEADING MEDICINE

	2016	2017	2018	2019	2020	2021	2022
HMH	9 / 102 ★★★★★	15 / 107	8 / 99 ★★★★★	11 / 93 ★★★★★	6 / 100 ★★★★★	6 / 101 ★★★★★	6 / 107 ★★★★★
HMSL	25 / 124	59 / 161	11 / 100	2 / 79 ★★★★★	2 / 97 ★★★★★	4 / 117 ★★★★★	2 / 124 ★★★★★
HMB	80 / 124	104/161	28 / 100	34 / 82	17 / 100	8 / 121 ★★★★★	2 / 145 ★★★★★
HMW	12 / 124 ★★★★★	20 / 161	5 / 100 ★★★★★	10 / 82	7 / 100 ★★★★★	4 /121 ★★★★★	3 / 145 ★★★★★
HMWB	38/124	63 / 161	16 / 100	5 / 82 ★★★★★	8 / 100 ★★★★★	9 / 121 ★★★★★	6 / 145 ★★★★★
HMTW	–	–	–	3 / 82 ★★★★★	5 / 100 ★★★★★	1 / 121 ★★★★★	1 / 145 ★★★★★
HMCL	30 / 124	27 / 161	50 / 93	52 / 95	53 / 135	22 / 226	34 / 267

Vizient Q&A: Number of Ranked Hospitals by System



Newsweek's Best Smart Hospitals

HOUSTON Methodist
LEADING MEDICINE

Houston Methodist Hospitals ranked
#10 Best Smart Hospitals by Newsweek

Awards and Accolades

HOUSTON Methodist LEADING MEDICINE

Houston Methodist named
One of America's Best-in-State Employers 2022
by Forbes

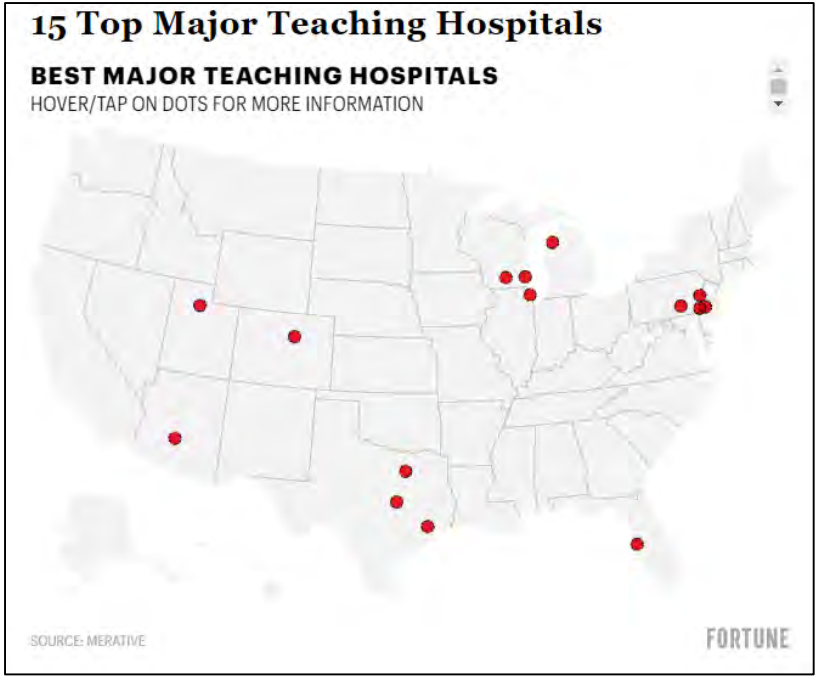
Awards and Accolades

HOUSTON Methodist LEADING MEDICINE

100 TOP HOSPITALS

FORTUNE | merative

Houston Methodist Hospital
Named #13
Best Major Teaching Hospital 2022
by Fortune and Merative



Awards and Accolades

HOUSTON Methodist LEADING MEDICINE

HOUSTON Methodist LEADING MEDICINE

Center for
Performing Arts Medicine

Houston Methodist's Center for Performing Arts Medicine
Honored with Texas Medal of Arts Award
by the Texas Cultural Trust

National Visibility

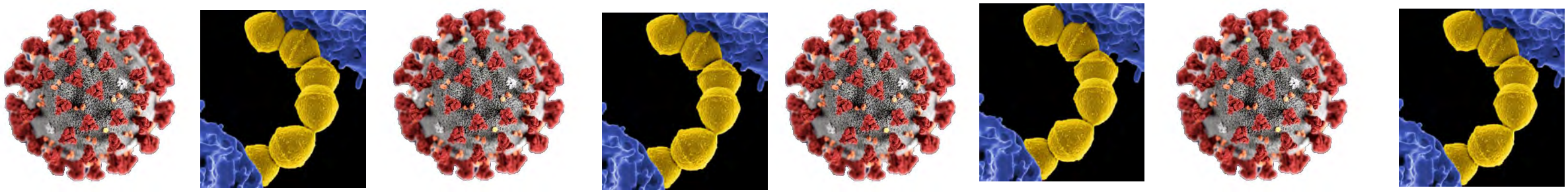
HOUSTON Methodist LEADING MEDICINE

National Visibility

HOUSTON Methodist LEADING MEDICINE

SARS-CoV-2 Response Overview and Center for Infectious Diseases Development

HOUSTON Methodist RESEARCH INSTITUTE



Jim Musser, MD, PhD

Fondren Presidential Distinguished Endowed Chair
Chair, Department of Pathology and Genomic Medicine
Director, Center for Infectious Diseases
Houston Methodist Hospital System and Research Institute
Houston, Texas

September 29, 2022

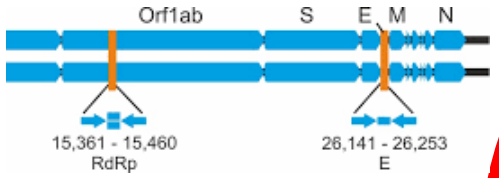
Key take-home message

HOUSTON Methodist RESEARCH INSTITUTE

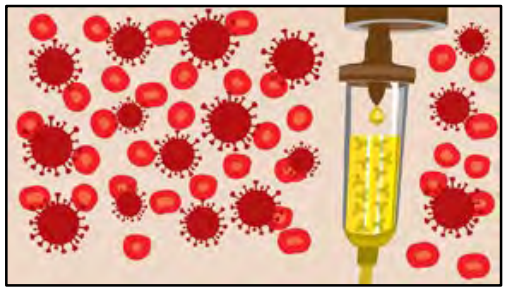
In the Department of Pathology and Genomic Medicine we have used the devastating SARS-CoV-2/COVID-19 pandemic to hone our strategies for subsequent pandemics, regardless of what they are or when they occur: the “Disease X” scenario.

Dept. of Pathology & Genomic Medicine: Very Early – an Integrated Strategy to Fight SARS-CoV-2/COVID-19

Molecular diagnostics (RT-PCR, TMA)

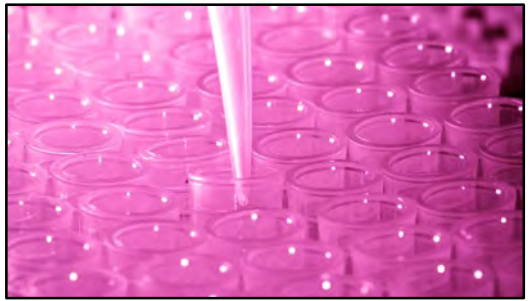


Antibody therapy in HMH patients



Virus genome sequencing

Antibody tests: healthcare workers + patients + Houston residents



SARS-CoV-2 Integrated Effort

HOUSTON Methodist RESEARCH INSTITUTE

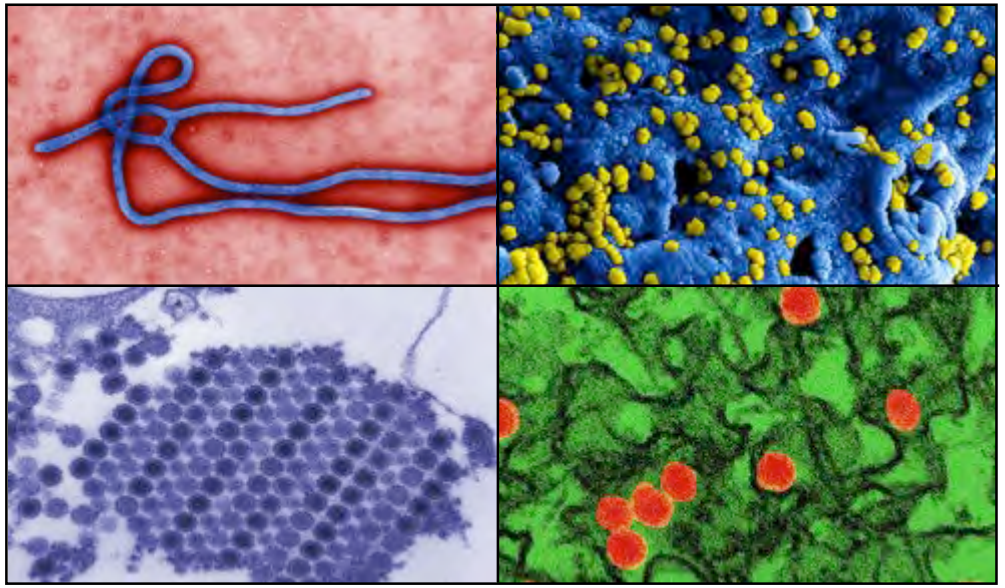
- **Randy Olsen, MD, PhD**
  Molecular diagnostics and genomics
- **Wesley Long, MD, PhD**
  Whole genome sequencing and analysis
- **Eric Salazar, MD, PhD**
  Convalescent plasma therapy
- **Paul Christensen, MD**
  Clinical and research informatics; data integration

We Have Always Developed Molecular Tests for Problematic Pathogens

HOUSTON Methodist RESEARCH INSTITUTE

Over the years, we have rapidly developed, validated, and implemented diagnostic tests for viral pathogens causing global health concerns and with potential for Houston epidemics, examples include:

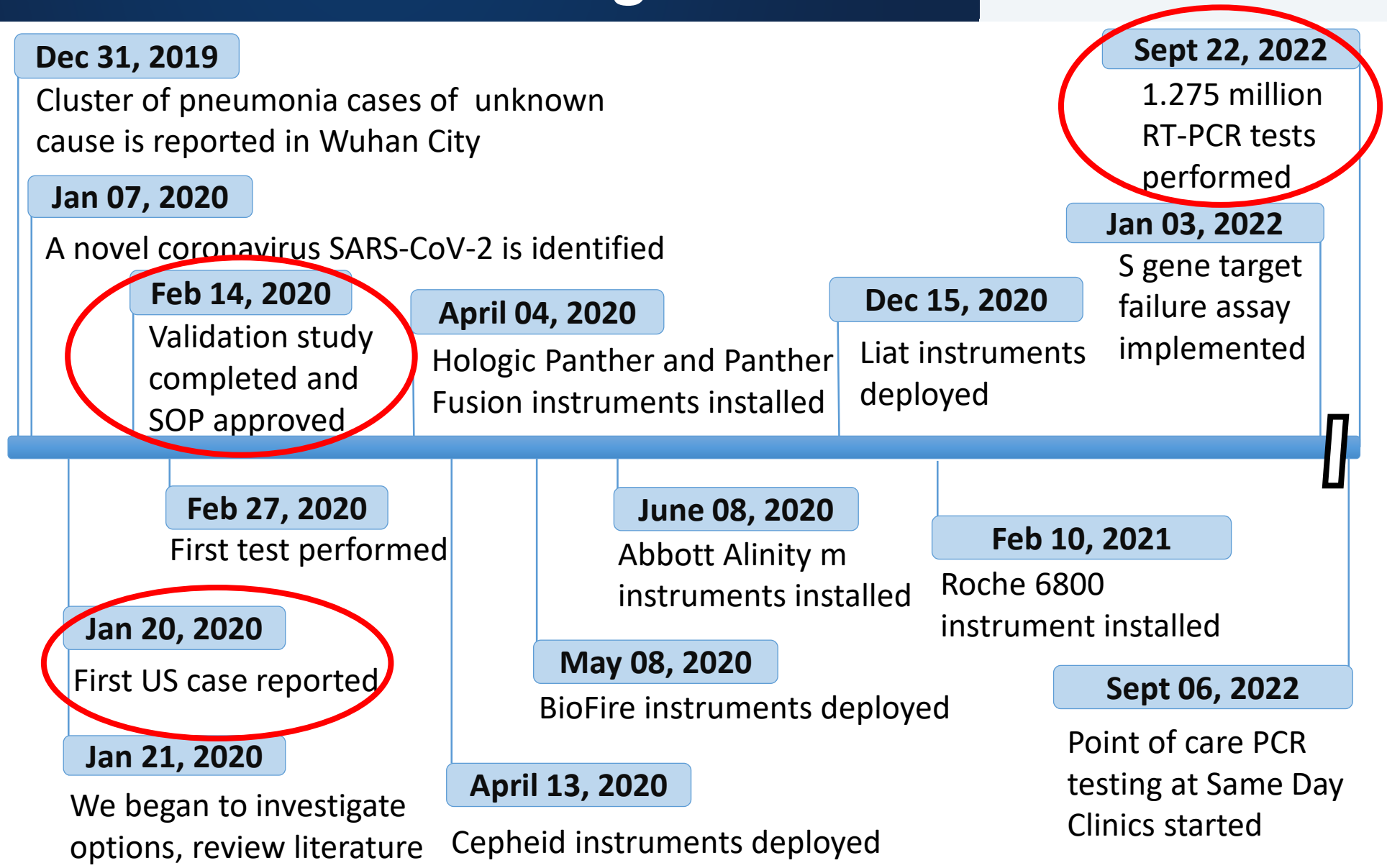
- H1N1 (2009)
- MERS (2012)
- Chikungunya (2013)
- Ebola (2014)
- Zika (2016)
- SARS-CoV-2 (2020)
- Monkeypox (2022)



Rapid development and deployment of molecular diagnostic tests taught us how to rapidly formulate SARS-CoV-2 diagnostics early on

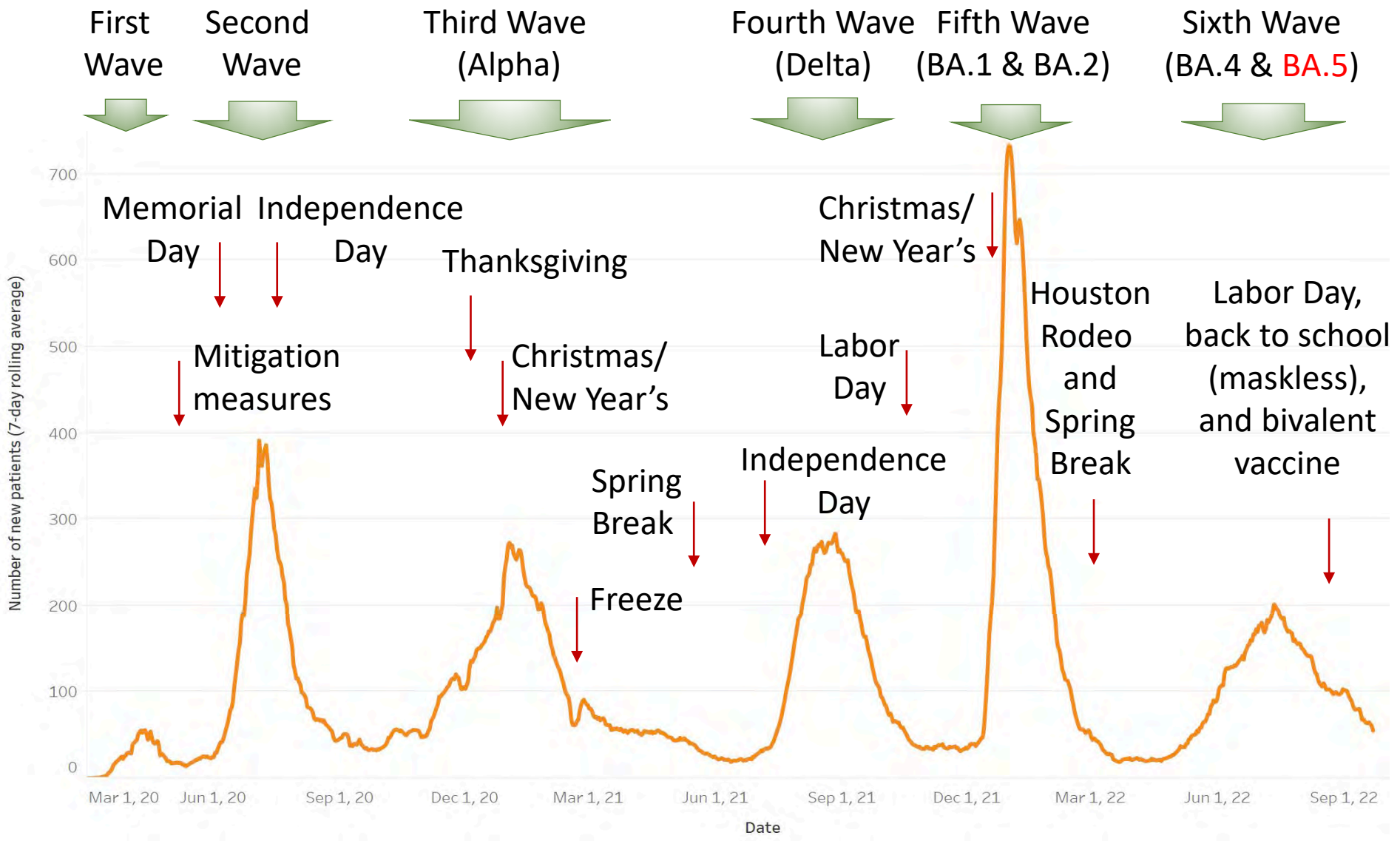
SARS-CoV-2 timeline for Methodist Molecular Diagnostics

HOUSTON Methodist RESEARCH INSTITUTE



Six waves of SARS-CoV-2 Infections in Houston

HOUSTON Methodist RESEARCH INSTITUTE



The Houston Methodist Experience (as of 9/22/2022)

HOUSTON Methodist RESEARCH INSTITUTE

1,274,725 SARS-CoV-2 PCR tests performed

556,704 unique patients tested

103,598 (18.6%) patients had a positive test

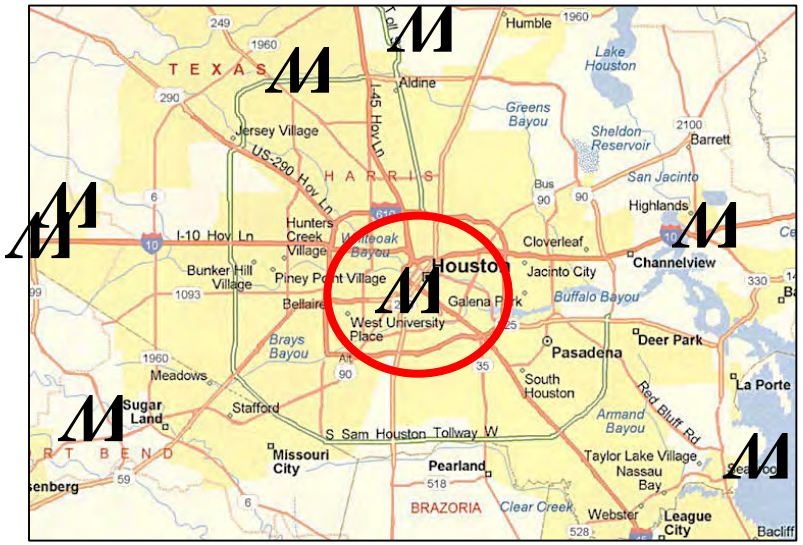
37,854 total hospitalizations (cumulative)

>115,000 SARS-CoV-2 genomes sequenced

Methodist covers metropolitan Houston: ~7.2M population

HOUSTON Methodist RESEARCH INSTITUTE

- Our eight hospitals serve Houston and metro region, ~2,500 beds and growing
- Ethnically and socioeconomically highly diverse patients; each hospital distinct
- Single friction-free, extremely integrated diagnostic, sequencing, informatics, and therapeutic infrastructure
- State-of-the-art Research Institute with outstanding infrastructure, **directly linked to main hospital – logistically seamless – this is crucial**



Methodist hospitals in metro Houston
Red circle = our main hospital

- **These and other facts create an outstanding opportunity for unique infectious disease preparedness, response, and research in a very large metropolitan area**

SARS-CoV-2 Genomics, Convalescent Plasma Treatment, and Integrated Metadata Analyses

HOUSTON Methodist RESEARCH INSTITUTE

Our integrated activities and analyses have led the nation in many areas, and garnered extensive national and international attention:

Three examples.

SARS-CoV-2 Genomics and Integrated Analyses: Houston, Texas

HOUSTON Methodist RESEARCH INSTITUTE

Analysis of 5,085 Houston-area SARS-CoV-2 strains.

AMERICAN SOCIETY FOR MICROBIOLOGY | mBio AN OPEN ACCESS JOURNAL PUBLISHED BY THE AMERICAN SOCIETY FOR MICROBIOLOGY

Molecular Architecture of Early Dissemination and Massive Second Wave of the SARS-CoV-2 Virus in a Major Metropolitan Area

S. Wesley Long, Randall J. Olsen, Paul A. Christensen, David W. Bernard, James J. Davis, Maulik Shukla, Marcus Nguyen, Matthew Ojeda Saavedra, Prasanti Yerramilli, Layne Pruitt, Sishir Subedi, Hung-Che Kuo, Heather Hendrickson, Ghazaleh Eskandari, Hoang A. T. Nguyen, J. Hunter Long, Muthiah Kumaraswami, Jule Goike, Daniel Boutz, Jimmy Gollihar, Jason S. McLellan, Chia-Wei Chou, Kamyab Javanmardi, Ilya J. Finkelstein, and James M. Musser

Long et al. 2020. mBio.

Multiple genetic lineages entered Houston and spread rapidly

HOUSTON Methodist RESEARCH INSTITUTE

The Washington Post

Massive genetic study shows coronavirus mutating and potentially evolving amid rapid U.S. spread

The largest U.S. genetic study of the virus, conducted in Houston, shows one viral strain outdistancing all of its competitors, and many potentially important mutations.

September 23, 2020

Convalescent Plasma Treatment: We Were First
Final Analysis of 351 Transfused Patients

HOUSTON Methodist RESEARCH INSTITUTE

The American Journal of PATHOLOGY
Discoveries in Basic and Translational Pathobiology

Significantly decreased mortality in a large cohort of COVID-19 patients transfused early with convalescent plasma containing high titer anti-SARS-CoV-2 spike protein IgG

Eric Salazar .... and James M. Musser

Salazar et al. 2020. Amer. J. Path.

Omicron Arrived

HOUSTON Methodist RESEARCH INSTITUTE

The American Journal of PATHOLOGY
Discoveries in Basic and Translational Pathobiology

Signals of Significantly Increased Vaccine Breakthrough, Decreased Hospitalization Rates, and Less Severe Disease in Patients with Coronavirus Disease 2019 Caused by the Omicron Variant of Severe Acute Respiratory Syndrome Coronavirus 2 in Houston, Texas

Christensen PA, Olsen RJ, Long SW, Snehal R, Davis JJ, Saavedra MO, Reppond K, Shyer MN, Cambric J, Gadd R, Thakur RM, Batajoo A, Mangham R, Pena S, Trinh T, Kinskey JC, Williams G, Olson R, Gollihar J, Musser JM. 2022 Apr 1;192(4):642-52. Epub ahead of print.

Why Did Things Work Very Well for Us? Two Critical Reasons

HOUSTON Methodist RESEARCH INSTITUTE

1. Rapid, clear, unambiguous, and unwavering support from Dr. Boom and all Methodist leadership.

2. Extraordinarily generous community support from day 1.

Without 1 & 2 above, little would have been accomplished.

Why Did Things Work Very Well for Us? A Few Lessons Learned (Short List)

HOUSTON Methodist RESEARCH INSTITUTE

1. We have always had a pandemic mentality in the Department.

2. Great majority of pieces to the puzzle were under one roof (one culture) and were seamlessly integrated.

3. Department of Pathology and Genomic Medicine faculty built over years had extensive expertise in many of the key areas that were needed to confront the pandemic rapidly.

4. The extremely flat administrative structure at Methodist and our culture permitted us to move unusually fast, decisively, and keep moving with minimal impediments. Decisions were made rapidly.

5. Our hospital and philanthropic community quickly (days!) provided very substantial resources that permitted us to rapidly attack the pandemic.

Birth of the Center of Excellence in Infectious Diseases

HOUSTON Methodist RESEARCH INSTITUTE

We recognized very early on in the pandemic that

we had several limitations, deficiencies

to address, and gaps to fill.

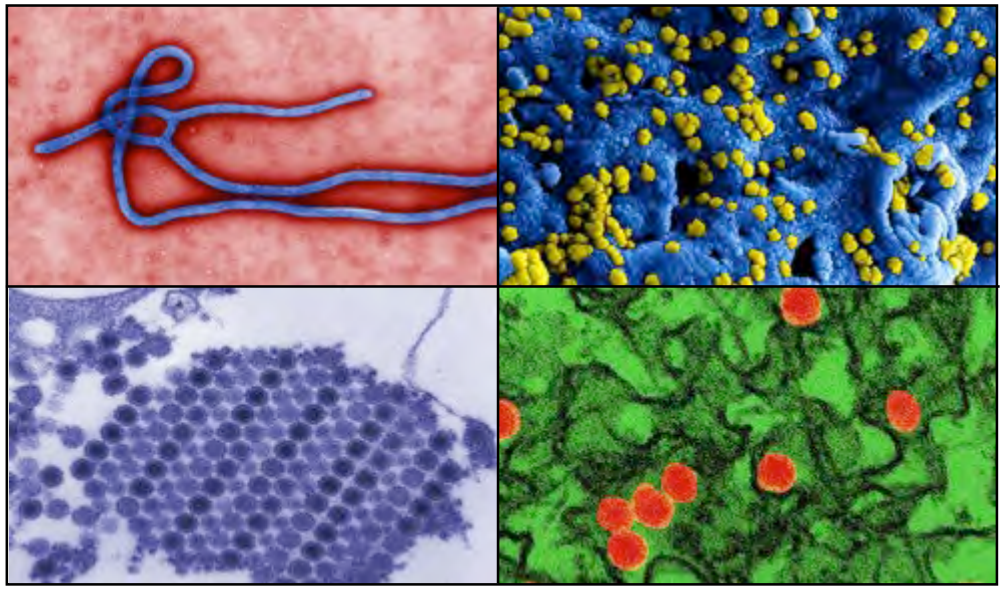
Center of Excellence in Infectious Diseases

HOUSTON Methodist RESEARCH INSTITUTE

The Challenges to Our City, Society and World Are Immense and Urgent

COVID-19 pandemic has exposed many serious local, national and global vulnerabilities to infectious agents. A next global infectious disease crisis is inevitable ("Disease X" scenario) because of (a short list):

- Globalization
- Urbanization
- Bioterrorism
- Rogue nation-states
- Susceptibility to infection
- Ease of genetic manipulation of pathogens



Center of Excellence in Infectious Diseases

HOUSTON Methodist RESEARCH INSTITUTE

Creation of the **Center of Excellence ("COE") in Infectious Diseases** — Methodist's 7th COE

- Comprehensive diagnostic, treatment, research and education center that can be activated, supercharged, and turned on a dime when necessary.
- Tremendous benefit to our patients, the Houston community, and beyond.
- **Key goal is to be exceptionally well prepared and equipped, and have the ability to address the new threat extremely rapidly.** We are bringing together multiple diverse disciplines: infection treatment, ID immunology, vaccinology, artificial intelligence, synthetic biology, and analytics, to name a few. **We have excellent ID-oriented investigators.**
- **However, many gaps to be filled, all the while continuing to focus on common pathogen problems such as MRSA, other drug-resistant bacteria, sepsis, etc.**

Center of Excellence in Infectious Diseases: Development Strategy

HOUSTON Methodist RESEARCH INSTITUTE

First, we recruited a world-class Co-Director who is a visionary infectious diseases physician-scientist and outstanding clinician

- Extensive national and international search performed.
- Extraordinarily strong pool of candidates identified and interviewed
- Candidates included individuals with expertise in all areas of infectious diseases: virology, parasitology, and bacteriology.
- One individual was head and shoulders above all others…

Cesar Arias, MD, PhD
Co-Director, Center for Infectious Diseases

HOUSTON Methodist RESEARCH INSTITUTE

- Chief, Division of Infectious Diseases, Department of Medicine
- John F. III and Ann H. Bookout Distinguished Chair
- Internationally known for his research on antimicrobial resistance
- Infectious diseases physician par excellence
- Extremely well-funded by NIH
- Editor-in-Chief, *Antimicrobial Agents and Chemotherapy*

Center of Excellence in Infectious Diseases: Development Strategy

HOUSTON Methodist RESEARCH INSTITUTE

Then, to fill a critical research portfolio gap: (2022)

Antibody discovery and therapy development platform: agile, flexible, and very high throughput platform for rapid therapeutic human monoclonal antibody discovery using synthetic biology, artificial intelligence, and protein engineering

Jimmy D. Gollihar, PhD

Head, Laboratory of Antibody Discovery & Accelerated Protein Therapeutics (ADAPT)

HOUSTON Methodist RESEARCH INSTITUTE

- PhD, University of Texas at Austin. Centers for Systems and Synthetic Biology. Protein engineering and synthetic biology expertise. Background as Special Ops – USAF.
- Previously: Chief Technology Officer, BioMADE – Office of the Undersecretary of Defense for Research & Engineering
- Previously: Chief Technology Officer, Synthetic Biology Essential Research Program, Army Research Laboratory
- Extensive collaborations over the past 32 months
- Extremely interested in commercialization of unique therapeutic proteins. Holds multiple patents on biomedically relevant proteins

Center of Excellence in Infectious Diseases: Development Strategy

HOUSTON Methodist RESEARCH INSTITUTE

Research portfolio gaps to be filled: (ongoing recruitments)

- Human virologist
- Immunologist – focus on human infection immunology
- RNA vaccinology – leverage our outstanding expertise in RNA biology; various ongoing collaborations with Dr. John Cooke's mRNA group

HOUSTON Methodist RESEARCH INSTITUTE

Thank you!

COVID-19, Monkeypox, Polio and Other Infectious Diseases Threats

Cesar A. Arias MD PhD
Chief, Division of Infectious Diseases
John F. III and Ann H. Bookout Distinguished Chair
@SuperBugDoc

Weill Cornell Medicine

HOUSTON Methodist LEADING MEDICINE

Disclosures

- **Grant Recipient**: MeMed diagnostics, Merck and Entasis Pharmaceuticals

Objectives

- Discuss the status of the COVID-19 pandemic with updates in vaccination
- Present some data on the Monkeypox outbreak
- Comment on the emergence of polio in the United States
- Delineate other infectious diseases threats like antimicrobial resistance and new zoonotic viruses

COVID-19 Numbers, United States

HOUSTON Methodist LEADING MEDICINE

COVID Data Tracker

Maps, charts, and data provided by CDC, updates Mon-Fri by 8 pm ET

COVID-19 Ho

CDC recommends use of COVID-19 Community Levels to determine the impact of COVID-19 on communities and to take action. CDC also provides Transmission Levels (also known as Community Transmission) to describe the amount of COVID-19 spread within each county. Healthcare facilities use Transmission Levels to determine infection control interventions.

Daily Update for the United States

Cases
New Cases (Daily Avg)
53,376
Case Trends

Aug 2022 Sep 2022

Deaths
New Deaths (Daily Avg)
356
Death Trends

Aug 2022 Sep 2022

Hospitalizations
New Admissions (Daily Avg)
3,933
Admission Trends

Aug 2022 Sep 2022

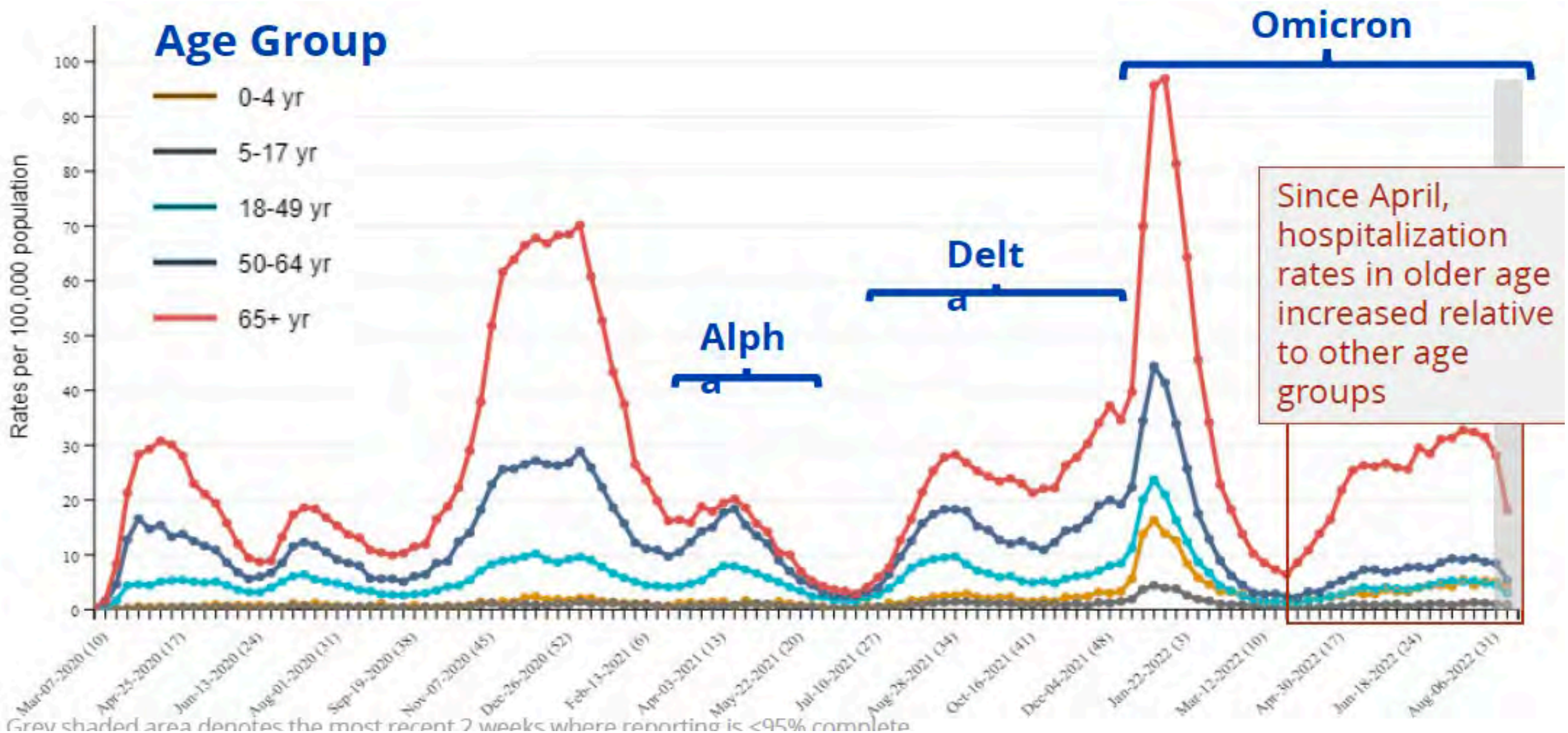
Vaccinations
% First Booster Dose
35.1%
People Age 5+

Total Cases	Total Deaths	Current Hospitalizations	Total First Booster Dose
95,795,378	1,050,631	24,035	109,578,270

https://covid.cdc.gov/covid-data-tracker/#datatracker-home

Weekly Trends in COVID-19-Associated Hospitalization

HOUSTON Methodist LEADING MEDICINE

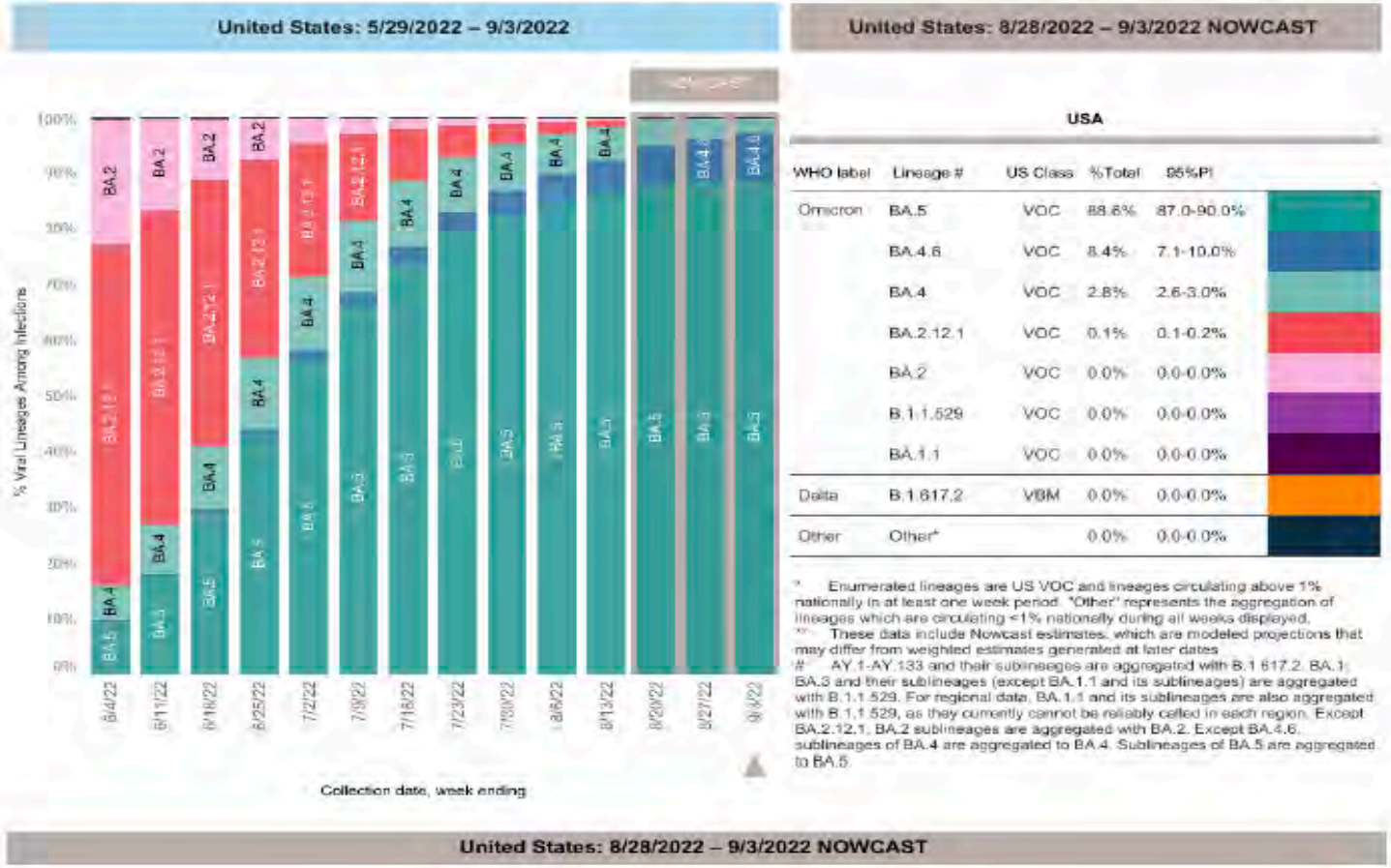


Evolution of SARS-Cov-2, USA

HOUSTON Methodist LEADING MEDICINE

FDA

Recent Evolution of SARS-CoV-2



USA

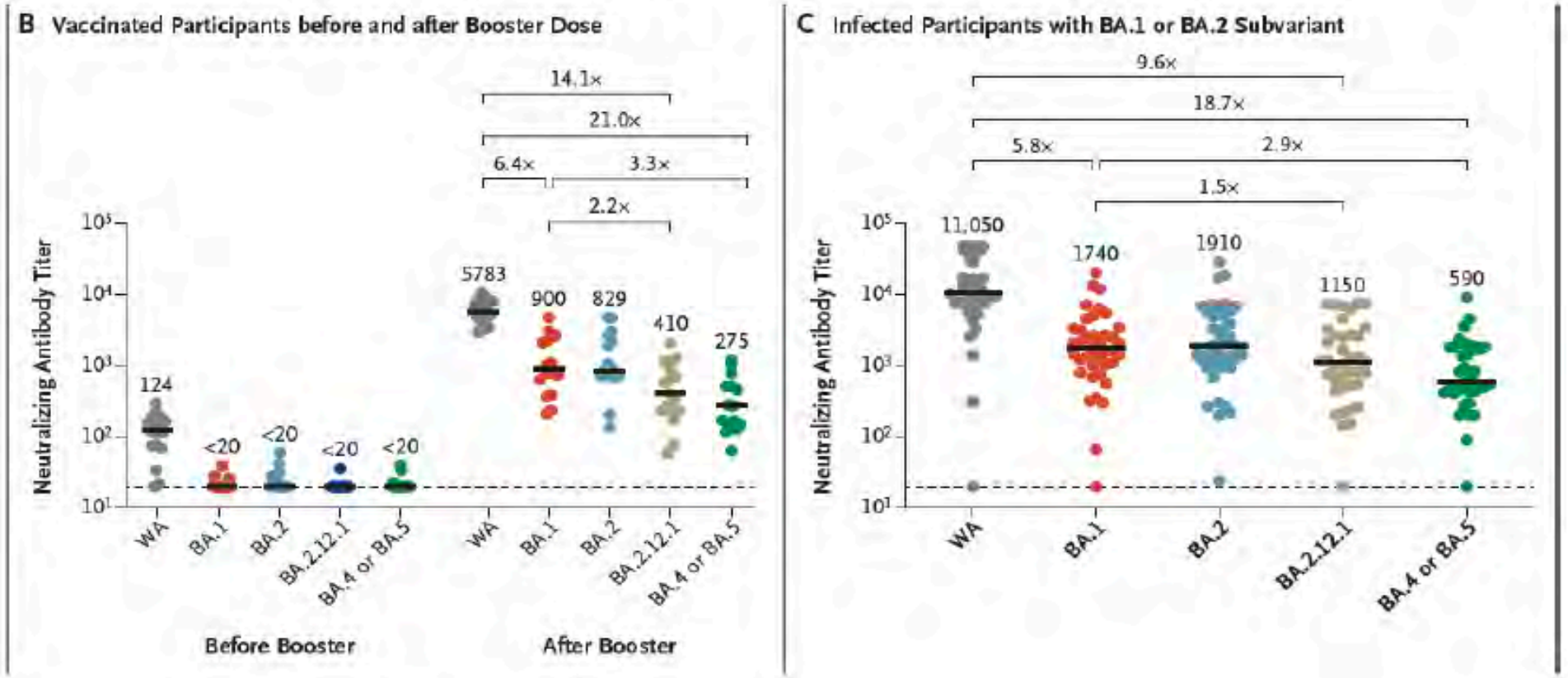
WHO label	Lineage #	US Class	%Total	95%PI
Omicron	BA.5	VOC	88.6%	87.0-90.0%
	BA.4.6	VOC	8.4%	7.1-10.0%
	BA.4	VOC	2.8%	2.6-3.0%
	BA.2.12.1	VOC	0.1%	0.1-0.2%
	BA.2	VOC	0.0%	0.0-0.0%
	B.1.1.529	VOC	0.0%	0.0-0.0%
	BA.1.1	VOC	0.0%	0.0-0.0%
Delta	B.1.617.2	VBM	0.0%	0.0-0.0%
Other	Other*		0.0%	0.0-0.0%

* Enumerated lineages are US VOC and lineages circulating above 1% nationally in at least one week period. "Other" represents the aggregation of lineages which are circulating <1% nationally during all weeks displayed.
** These data include Nowcast estimates, which are modeled projections that may differ from weighted estimates generated at later dates.
# AY.1-AY.133 and their sublineages are aggregated with B.1.617.2. BA.1, BA.3 and their sublineages (except BA.1.1 and its sublineages) are aggregated with B.1.1.529. For regional data, BA.1.1 and its sublineages are also aggregated with B.1.1.529, as they currently cannot be reliably called in each region. Except BA.2.12.1, BA.2 sublineages are aggregated with BA.2. Except BA.4.6, sublineages of BA.4 are aggregated to BA.4. Sublineages of BA.5 are aggregated to BA.5.

https://covid.cdc.gov/covid-data-tracker/#variant-proportions

Neutralizing Antibody Titers Against Omicron Variants

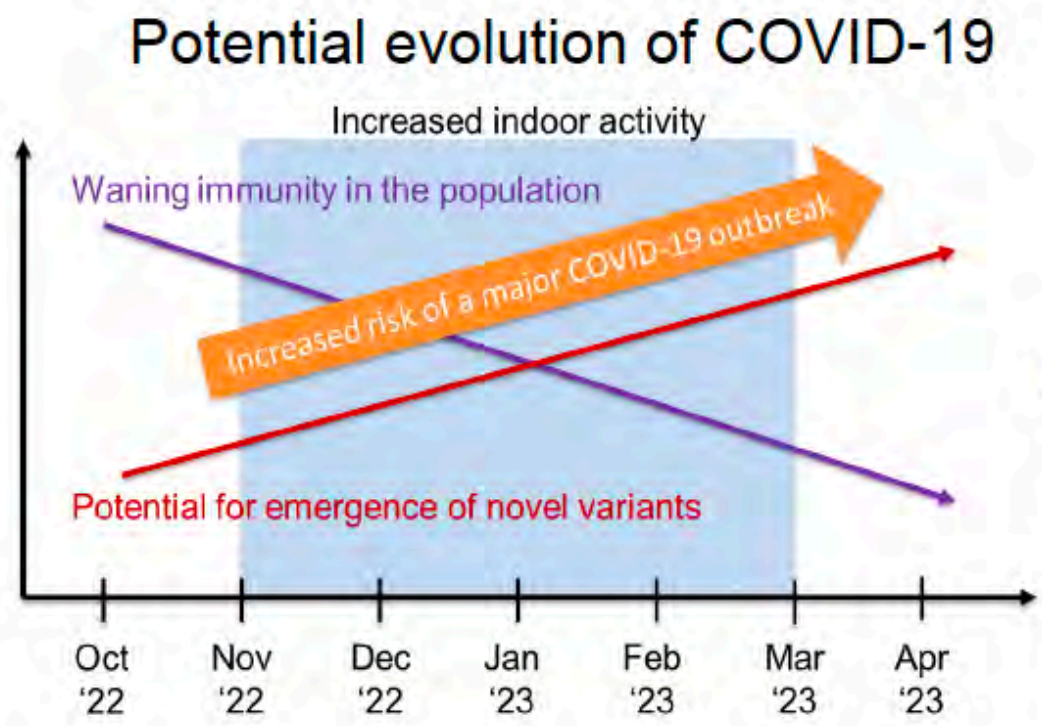
- BA.1 or BA.2 infection after vaccination increases antibody titers against Omicron variants
- Titers against BA.2.12.1 and BA.4/BA.5 lower than titers against BA.1 or BA.2



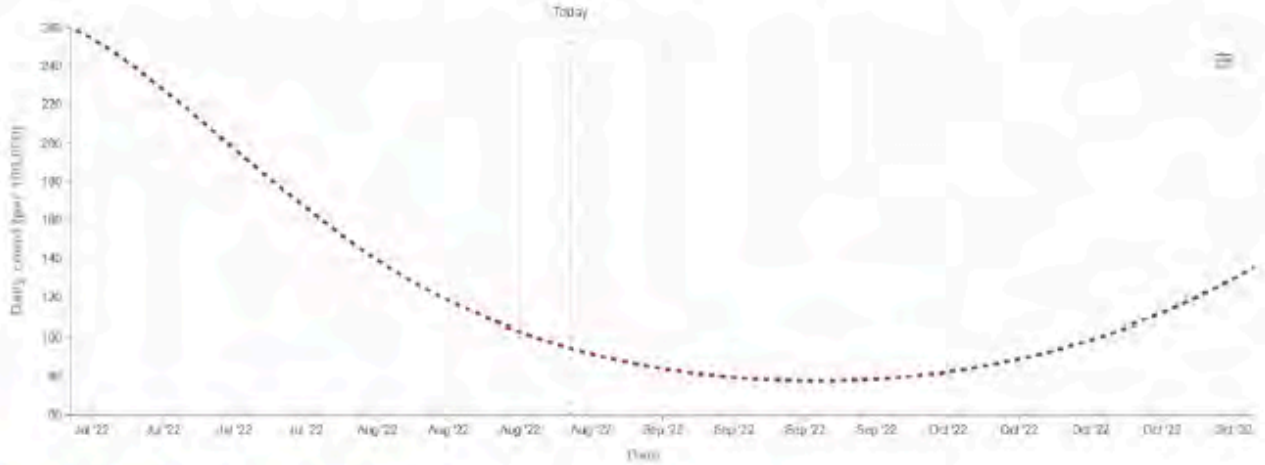
HachmannNP et al 2022 N EnglJ Med DOI: 10.1056/NEJMc2206576

Fall 2022, Predictive Modeling

HOUSTON Methodist LEADING MEDICINE



Modelers predicting next peak in late November



https://covid19.healthdata.org/united-states-of-america?view=infections-testing&tab=trend&test=infections

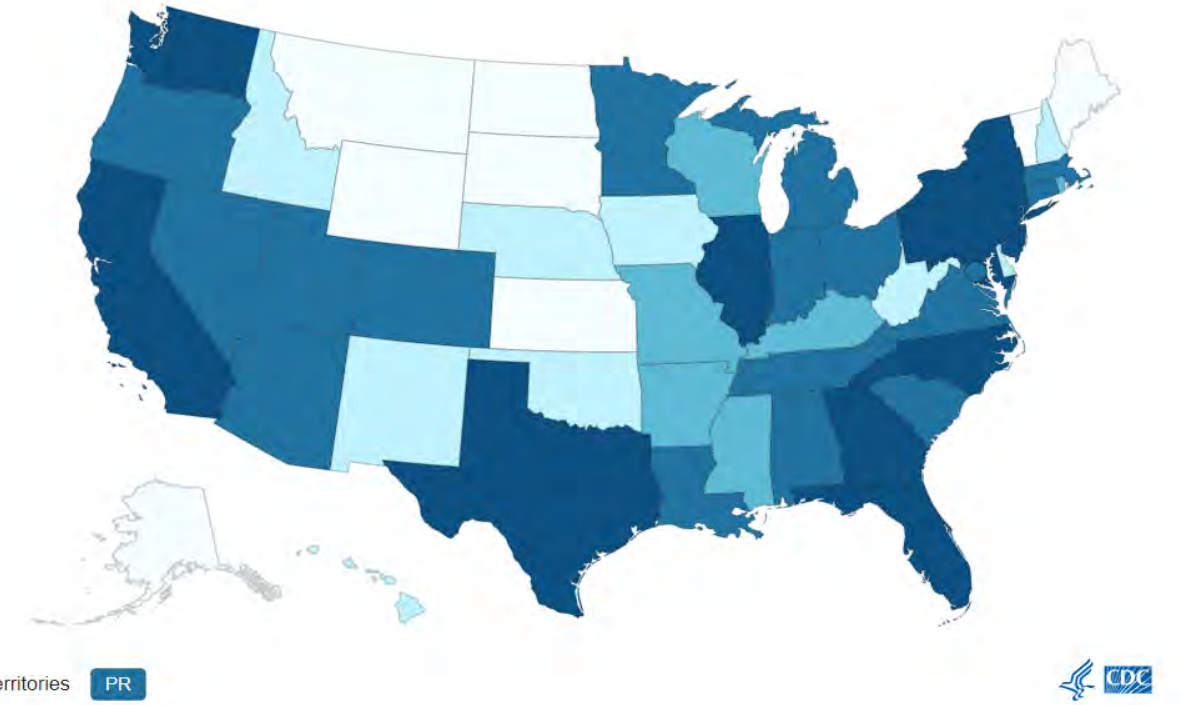
Current FDA Vaccine Recommendations

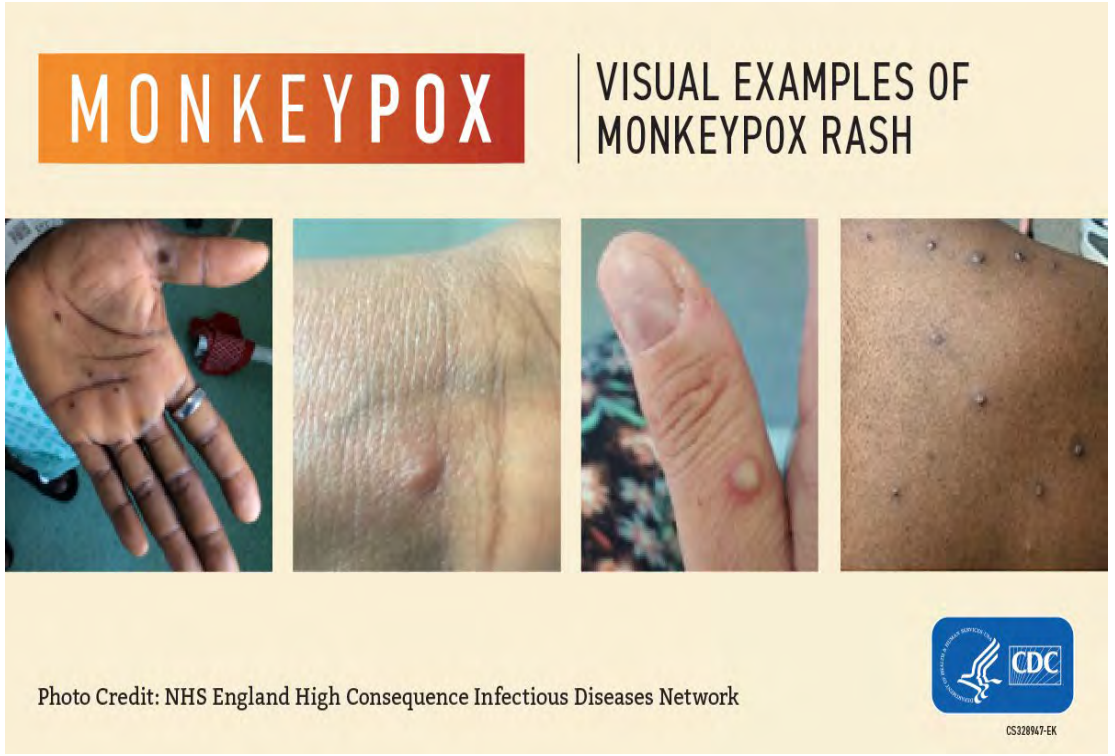
- Moderna Bivalent COVID-19 Vaccine (Original + BA.4/BA.5) authorized for individuals ages 18 and older
- Pfizer BioNTech Bivalent COVID-19 Vaccine (Original + BA.4/BA.5) authorized for individuals ages 12 and older
- Primary series doses continue with monovalent Moderna and Pfizer BioNTech COVID-19 vaccine
- Authorizations for monovalent Moderna and Pfizer BioNTech COVID-19 vaccine boosters revoked

Monkeypox Update – Cases USA

24,846 Total confirmed monkeypox/orthopoxvirus cases

*One Florida case is listed here but included in the United Kingdom case counts because the individual was tested while in the UK.





Texas: 2,225 cases

Monkeypox – Global Case Counts

HOUSTON Methodist LEADING MEDICINE

65,415
Total Cases

64,835
in locations that have not historically reported monkeypox

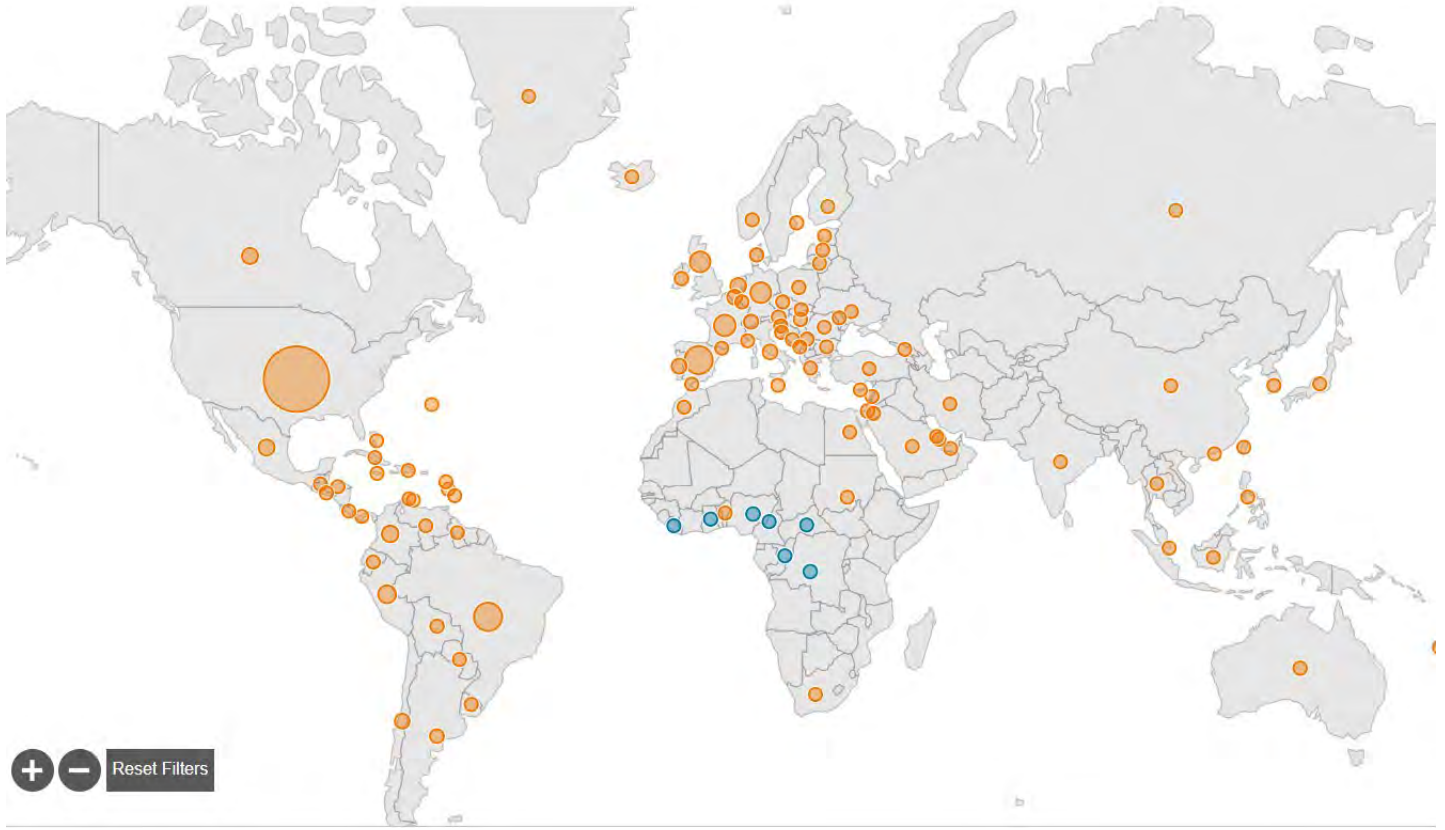
580
in locations that have historically reported monkeypox

Locations with cases

106
Total

99
Has not historically reported monkeypox

7
Has historically reported monkeypox



Monkeypox Transmission

HOUSTON Methodist LEADING MEDICINE

Transmission

- **Spread person-to-person through:**
  - **Direct contact** with the infectious rash, scabs, or body fluids
  - **Respiratory secretions** during prolonged, face-to-face contact, or during intimate physical contact, such as kissing, cuddling, or sex
  - **Touching items (such as clothing or linens)** that previously touched the infectious rash or body fluids
  - **Through placenta** in an infected pregnant person to their fetus
- **Patients are infectious once symptoms begin (whether prodromal or rash symptoms) and remain infectious until lesions form scabs, scabs fall off, and a fresh layer of skin forms**

Vaccination against Monkeypox

HOUSTON Methodist LEADING MEDICINE

MONKEYPOX

JYNNEOS Vaccine

Total number of vaccine doses shipped (9/7/22) **775,033**

https://aspr.hhs.gov/SNS/Pages/JYNNEOS-Distribution.aspx

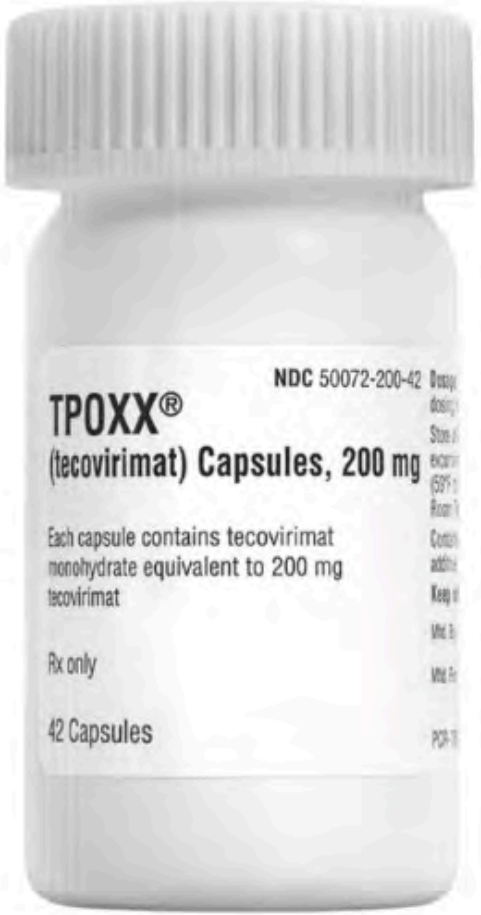
Total number of vaccine doses administered (9/7/22) **461,049**

https://www.cdc.gov/poxvirus/monkeypox/response/2022/vaccines_data.html

- **Primary prevention -- PreP**
- **Post-exposure prophylaxis with vaccine**
  - Available for people with known or presumed exposure to monkeypox
- **JYNNEOS vaccine considered safe for people with HIV**
  - Live but **non-replicating** virus vaccine (modified vaccinia Ankara, or MVA)

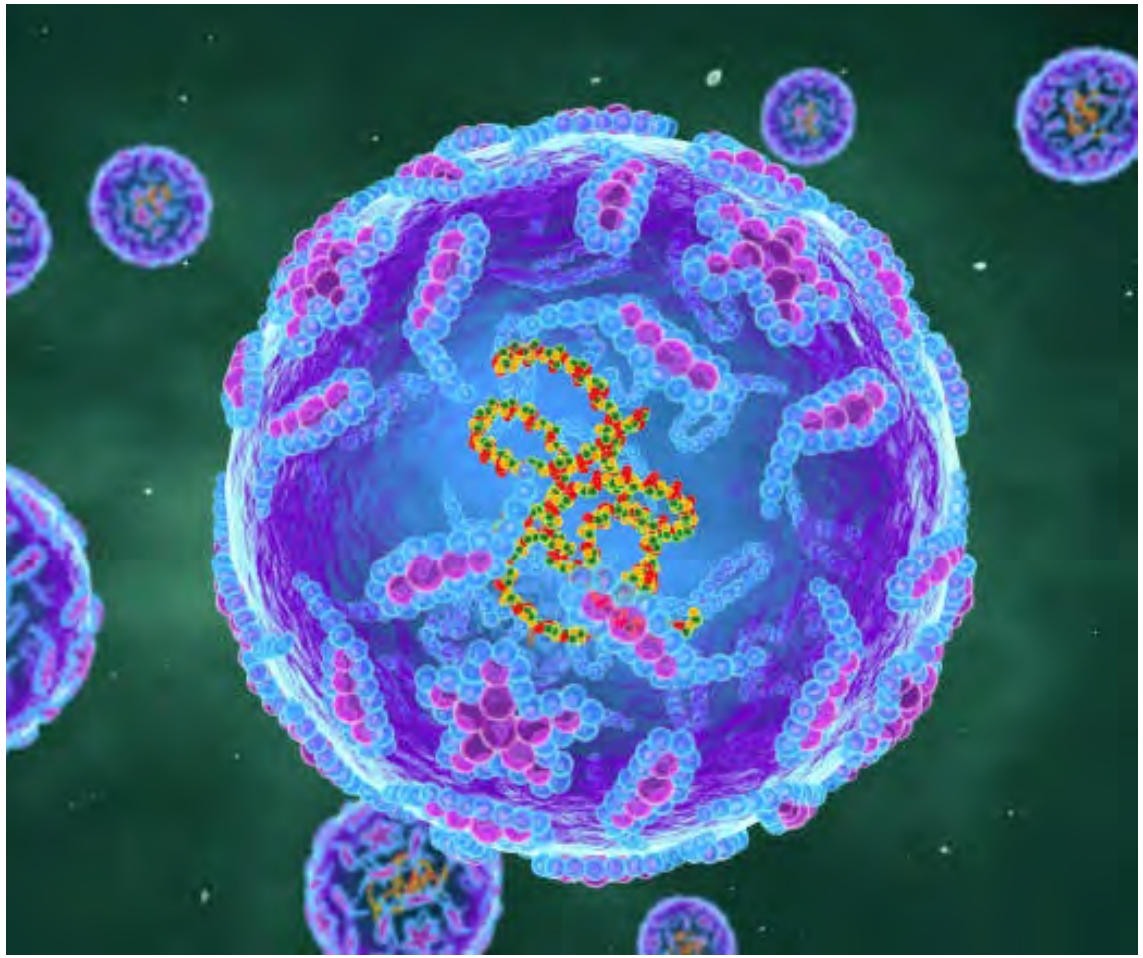
Source: JYNNEOS Vaccine | Monkeypox | Poxvirus | CDC

Tecovirimat (TPOXX) for Monkeypox



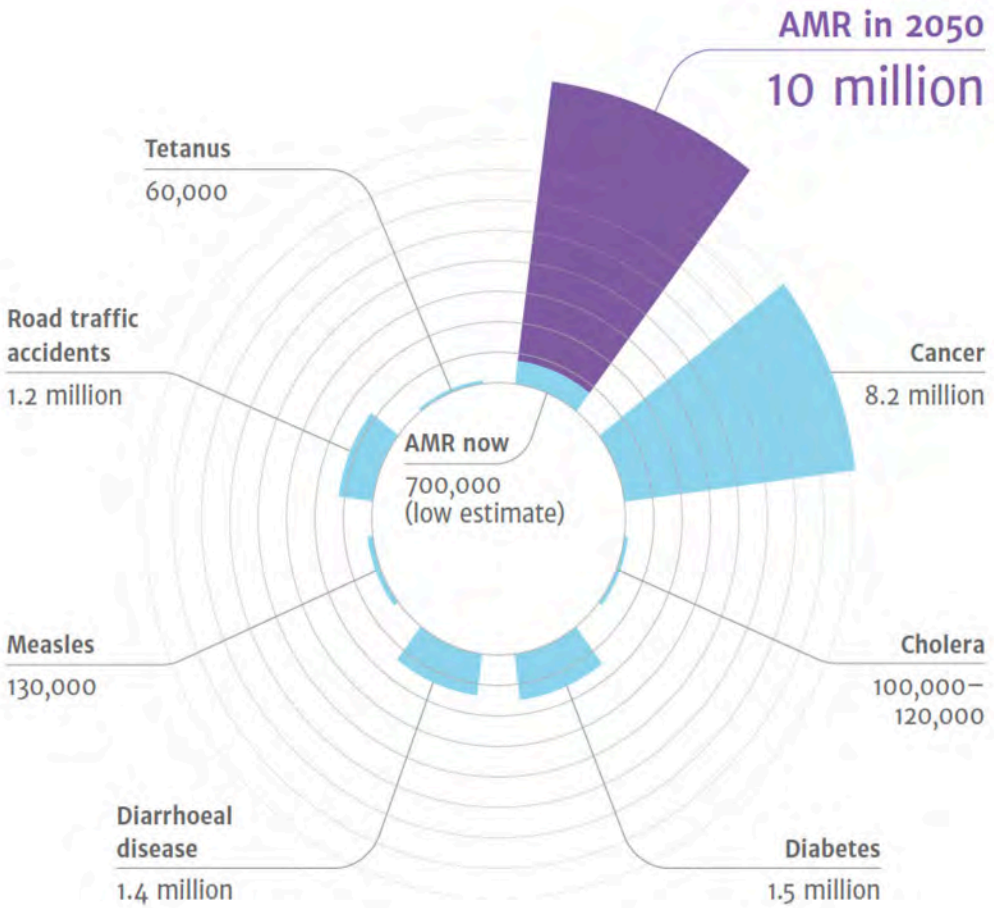
- Oral and IV formulations
- 14 days of treatment
- Clinical data on effectiveness more anecdotal
- Clinical trial in progress

Polio Virus in NY, 2022



CDC today announced that polioviruses found in New York, both from the case of paralytic polio in an unvaccinated adult in Rockland County and in several wastewater samples from communities near the patient's residence, meet the World Health Organization (WHO)'s criteria for circulating vaccine-derived poliovirus (cVDPV) – meaning that poliovirus continues to be transmitted in Rockland County, NY, and surrounding areas

AMR Continues to Be a Major Public Health Burden



Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis

*Antimicrobial Resistance Collaborators**

Findings On the basis of our predictive statistical models, there were an estimated 4·95 million (3·62–6·57) deaths associated with bacterial AMR in 2019, including 1·27 million (95% UI 0·911–1·71) deaths attributable to bacterial AMR. At the regional level, we estimated the all-age death rate attributable to resistance to be highest in western sub-Saharan Africa, at 27·3 deaths per 100 000 (20·9–35·3), and lowest in Australasia, at 6·5 deaths (4·3–9·4) per 100 000.

Lancet, 2022

New Emergent Diseases

HOUSTON Methodist LEADING MEDICINE

Shrews

A Zoonotic Henipavirus in Febrile Patients in China

TO THE EDITOR: The Hendra virus and the Nipah virus, which belong to the genus henipavirus in the family Paramyxoviridae, are known to infect humans and cause fatal disease; however, other related henipaviruses have been detected in bats, rodents, and shrews.[1-4] During sentinel surveillance of febrile patients with a recent history of animal exposure in eastern China, a phylogenetically distinct henipavirus, named Langya henipavirus (LayV), was identified in a throat swab sample from one patient by means of metagenomic analysis and subsequent virus isolation. The genome of LayV is composed of 18,402 nucleotides with a genome organization that is identical to that of other henipaviruses (Fig. 1A).[1] LayV is most phylogenetically related to Mojiang henipavirus, which was discovered in southern China (Fig. 1B).[3]

Subsequent investigation identified 35 patients with acute LayV infection in the Shandong and Henan provinces of China, among whom 26 were infected with LayV only (no other pathogens were present). These 26 patients presented with fever (100% of the patients), fatigue (54%), cough (50%), anorexia (50%), myalgia (46%), nausea (38%), headache (35%), and vomiting

*A*ntibody *D*iscovery & *A*ccelerated *P*rotein *T*herapeutics (*ADAPT*)

Platform technologies

Jimmy D Gollihar, PhD
Head of ADAPT

HOUSTON Methodist
LEADING MEDICINE

We are changing the face of therapeutics development from discovery to ultra high-throughput protein engineering and driving a new era of precision treatments for targets across the disease spectrum, using the best of modern synthetic biology for better outcomes for patients worldwide.

HOUSTON Methodist
LEADING MEDICINE

Our purpose is to rapidly discover and engineer therapeutics using the tools of synthetic biology

HOUSTON Methodist LEADING MEDICINE

ADAPT lives at the intersection of **systems immunology, synthetic biology, and machine learning**.

ADAPT discovers and engineers **monoclonal antibodies, vaccine candidates, enzymes, and so forth**.

ADAPT core technology areas:

1. *Development of Artificial Intelligence/Machine Learning models*
2. *Computational protein design*
3. *High-throughput screening and selection*
4. *Turnkey automation pipelines*

Antibody Discovery & Accelerated Protein Therapeutics

HOUSTON Methodist LEADING MEDICINE

Jimmy Gollihar, PhD

Head of ADAPT
- Protein engineering & synthetic biology
- Fmr CTO BioMADE

Raghav Shroff, PhD

Artificial Intelligence
- Neural networks
- Protein engineering

Daniel Boutz, PhD

Protein biochemistry
- Antibody methods
- Structure & proteomics

Andrew Horton, PhD

Systems biology & informatics
- Antibody methods
- Pipeline automation

Thomas Segall-Shapiro, PhD

Synthetic biology
- Genetic circuit design
- Lab automation

Jule Goike, PhD

Antibody discovery
- Humanization of yeast
- Yeast/PLCs

Michell Byrom

Laboratory Supervisor
- Molecular biology
- Protein expression

Shaunak Kar, PhD

Synthetic biology
- Enzyme engineering
- Genetic circuit design

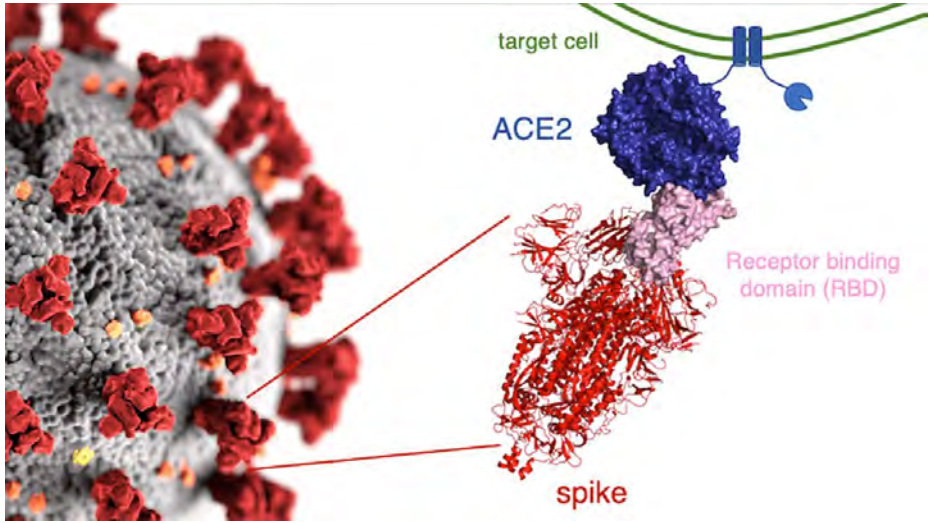
1. Prototyping virus proteins at the speed of discovery & immune escape

NextGen Antigen Testing & Engineering

HOUSTON Methodist
LEADING MEDICINE

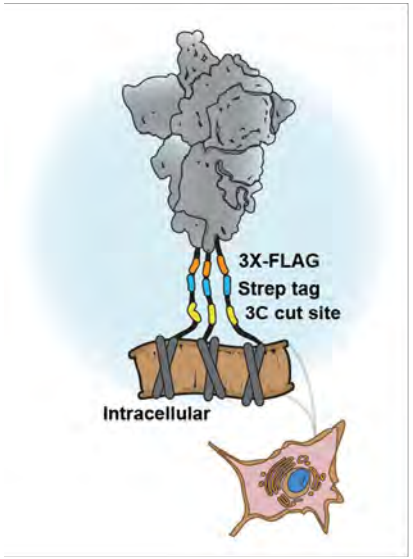
SARS-CoV-2 Spike Protein is the target

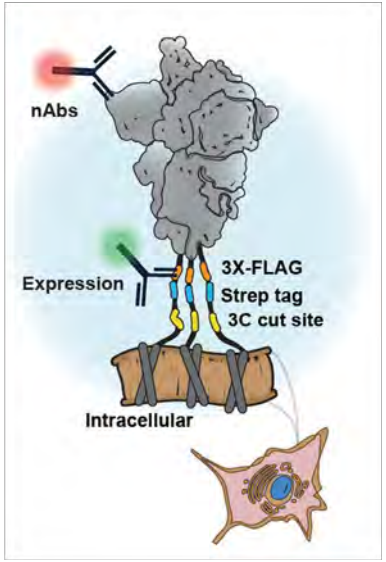
- SARS-CoV-2 is the causative agent of COVID-19
- Virus coated with Spikes (S-Ectodomains)
- Spike protein is key determinant of host and tissue tropism
- **Primary vaccine and therapeutic target**

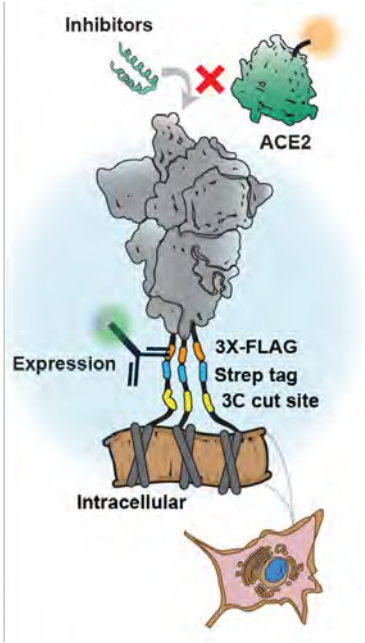


How do we safely build and test spike proteins to determine if our countermeasures are effective against new variants?

Mammalian display offers a near native assay modality





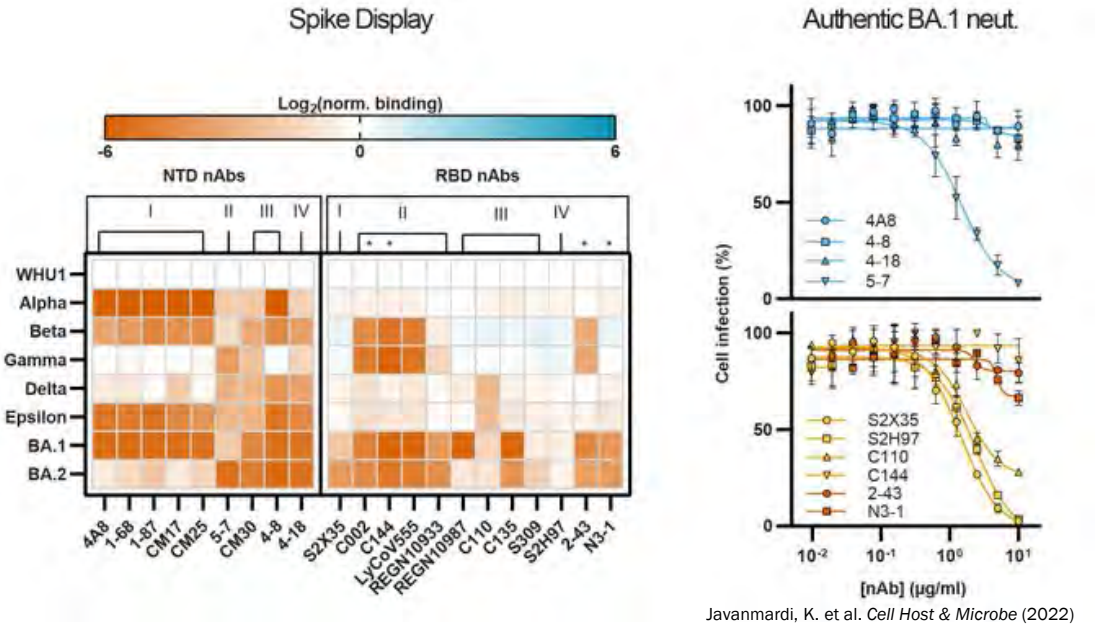


Javanmardi, K. et al. *Mol. Cell* (2021)

Omicron mutations are distributed across all domains of the spike protein

HOUSTON Methodist LEADING MEDICINE

- Different VOCs demonstrate escape from different classes of NTD- and RBD-targeting nAbs.
- Omicron shows the most comprehensive level of escape compared to the other VOCs, for these given sets of antibodies—validated with authentic live virus neutralization.

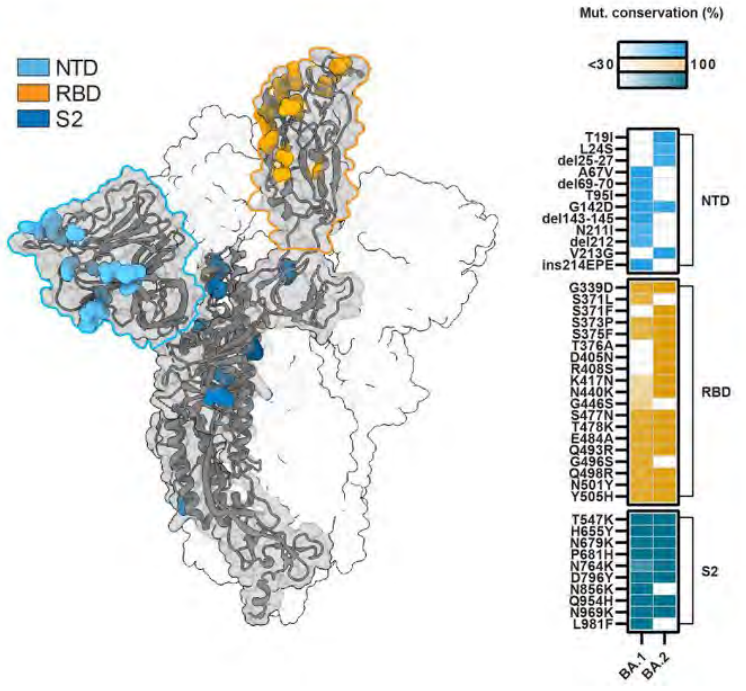


Javanmardi, K. et al. *Cell Host & Microbe* (2022)

Omicron escapes major classes of neutralizing antibodies

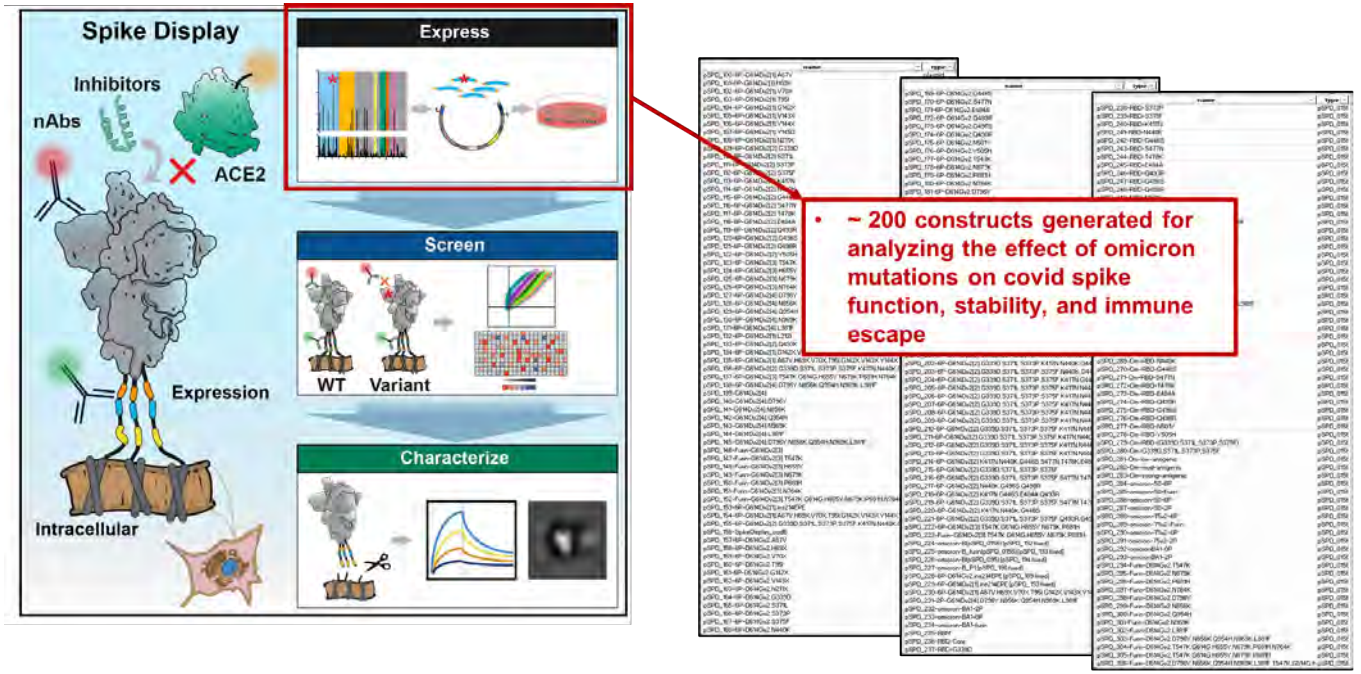
HOUSTON Methodist LEADING MEDICINE

- Omicron BA.1 and BA.2 spike proteins have an unprecedented 33 and 29 mutations.
- Mutations are distributed throughout the spike NTD, RBD, and S2—contributions to escape are largely unknown.



Javanmardi, K. et al. *Cell Host & Microbe* (2022)

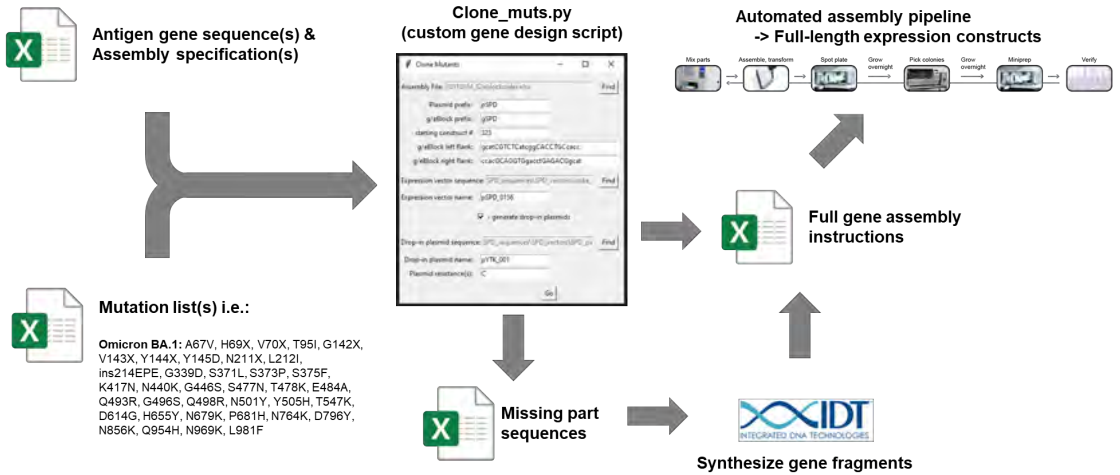
Proving the platform by rapidly generating all Omicron spike protein mutations



High-throughput design and assembly platform

We also develop computer software to automate synthesis and design of spike variants

- Designing DNA by hand becomes the bottleneck at med-high throughput!
- Mutations are mapped, DNA is designed, and assembly instructions generated for our liquid handling robots.

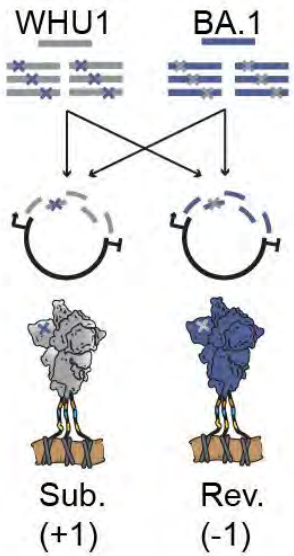


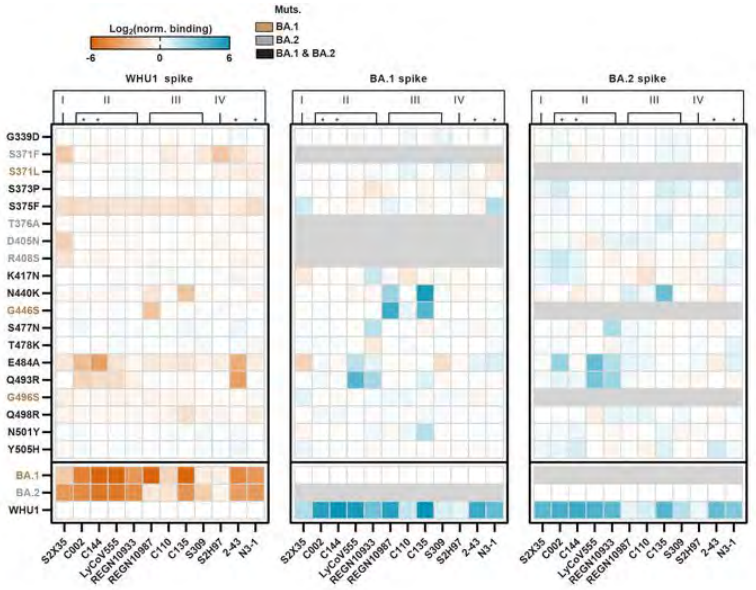
And remember, this strategy works for ANY pathogen!
****Now linked to in-house sequencing database****

Breakdown of Omicron spike protein reveals determinants of evasion

HOUSTON Methodist LEADING MEDICINE

- **Our platform is informative for understanding monoclonal antibody escape mechanisms.**
- **Contextual effects identified cryptic cross-domain stabilization, allowing for more virulent mutations in the receptor binding domain (RBD)**





Javanmardi, K. et al. *Cell Host & Microbe* (2022)

What we are doing next to combat “Disease X” of tomorrow…

1. Increase throughput of variants that can be tested in a single experiment

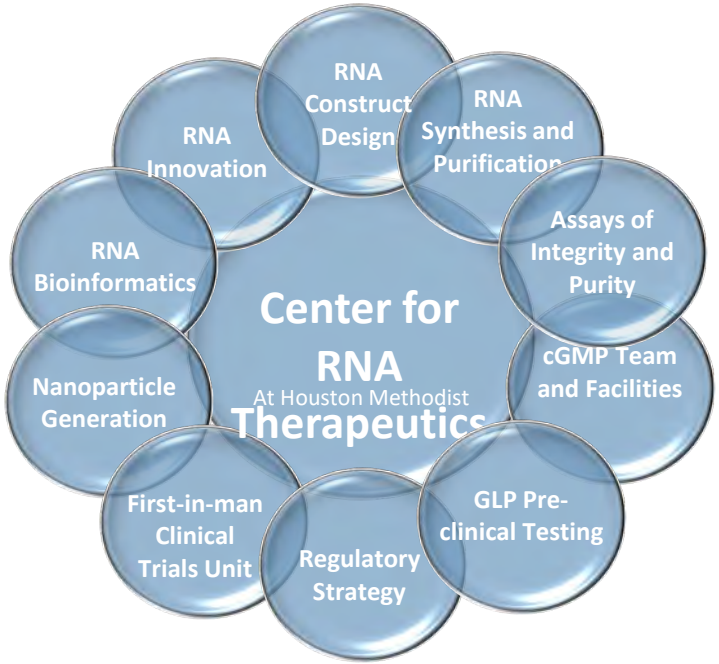
2. Expand this rapid-response technology for new and emerging viruses

3. Develop vaccine candidates for emerging viral threats

So that next time we’re pulling countermeasures out of the freezer!

Hospital-based RNA Therapeutics
We develop, manufacture, deliver, and test novel RNA Therapies AND PATHOGEN VACCINES

HOUSTON Methodist
LEADING MEDICINE



2. Rapid Response Biological Countermeasures

NextGen Antibody Discovery

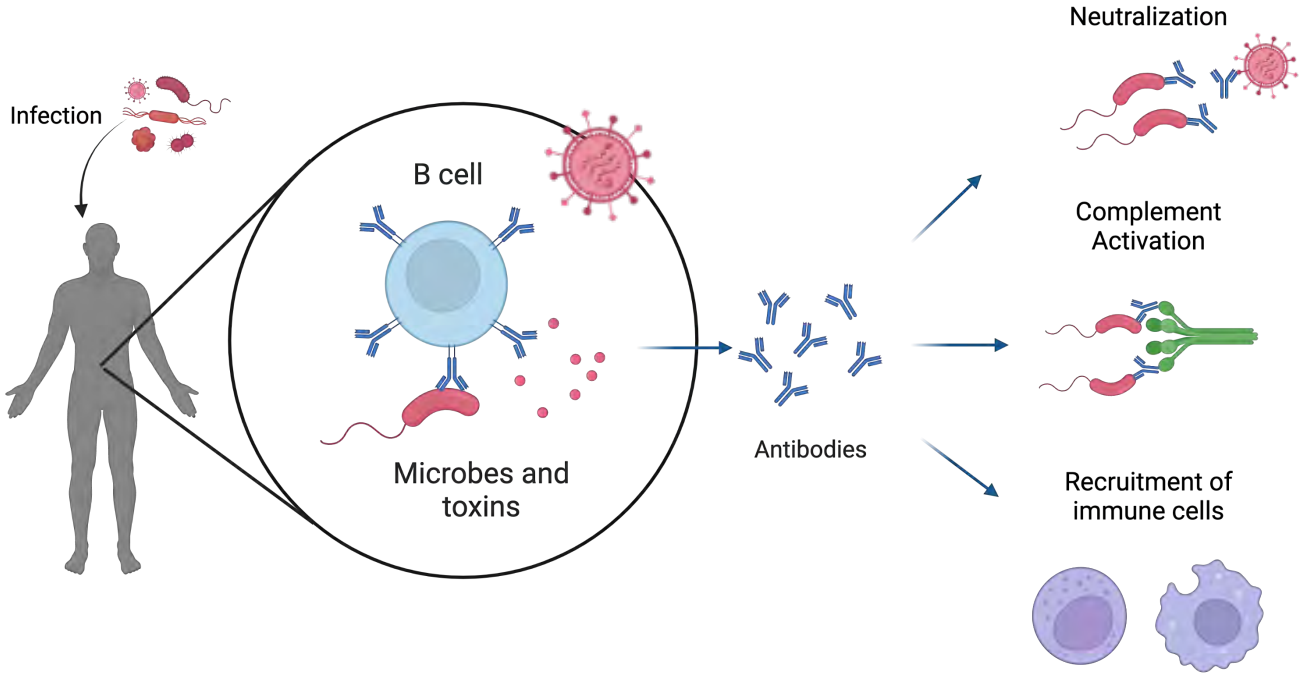
HOUSTON Methodist
LEADING MEDICINE

Antibody structure and function

HOUSTON Methodist LEADING MEDICINE

Antibodies protect us from pathogens

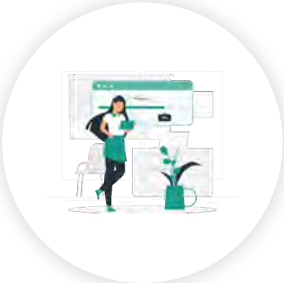
Protection modalities



Critical need for very rapid antibody discovery

HOUSTON Methodist LEADING MEDICINE

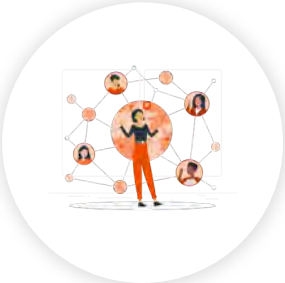
The COVID-19 pandemic showed the world that demand for rapid antibody development platforms is growing faster than ever



Traditional antibody development requires

Controlled Time points

Many patient samples



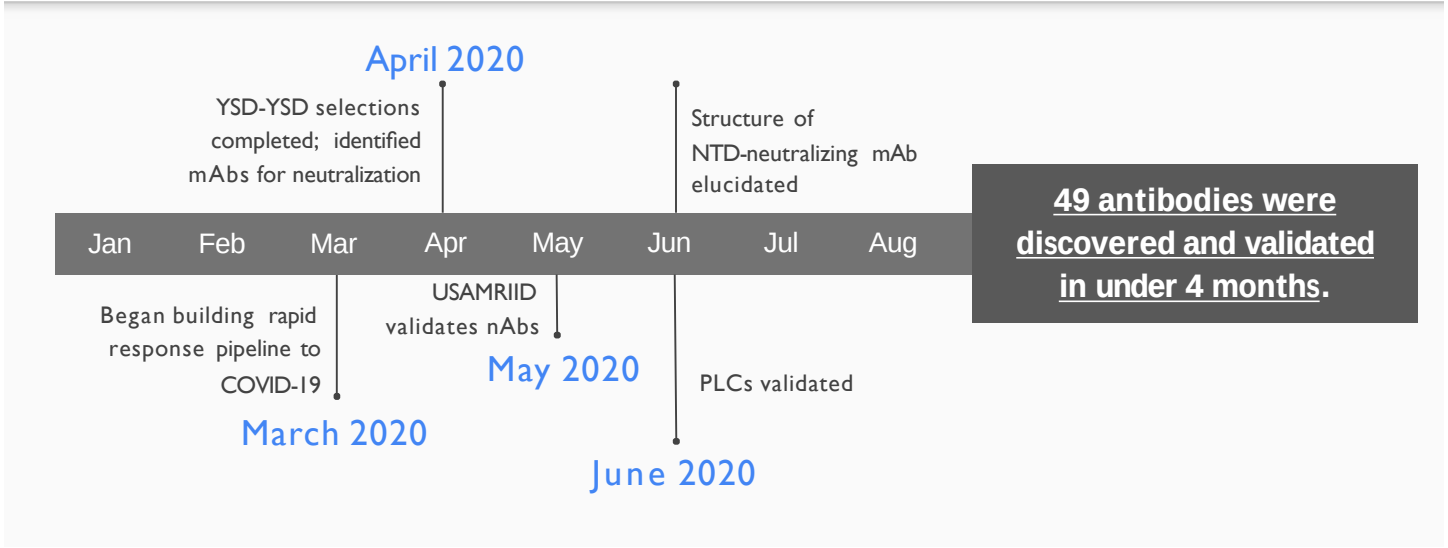
We select & engineer ***"the best"*** candidates from

Limited resources

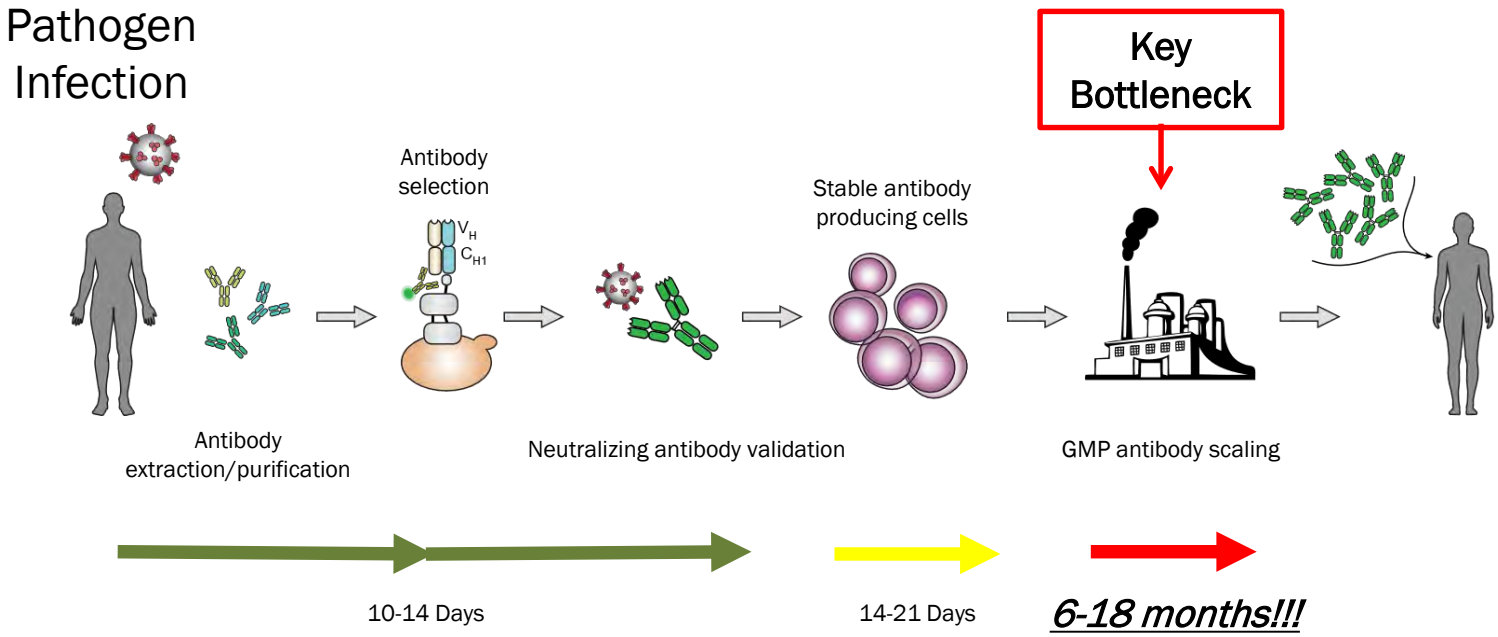
Under less-than-ideal conditions

The ADAPT discovery platform selects for the best antibodies from low quality starting samples by combining natural and engineered libraries

The ADAPT platform was built rapidly under immense time pressure



Antibody development process



We exploit artificial intelligence/machine learning to:

HOUSTON Methodist LEADING MEDICINE

1. Engineer enzymes for mRNA vaccine manufacturing
2. Identify scalable monoclonal antibody candidates during discovery
3. Enhance medically-relevant proteins of interest
4. Develop models to improve the speed of biological engineering

Platform technologies designed for—SPEED, SPEED, SPEED…

HOUSTON Methodist LEADING MEDICINE

Our Research Institute is connected to the Hospital, allowing us to go through Phase II trials under one roof!

The Houston Methodist Research Institute was built to do *very* rapid translational activities—such as those required during pandemics.

Contact: jgollihar2@houstonmethodist.org
https://gollihar.hmailabs.org/


HOUSTON
Methodist
LEADING MEDICINE