

**CROI**

Conference on Retroviruses  
and Opportunistic Infections

# **The Research Response to COVID-19: A View from NIAID**

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**Director**

**National Institute of Allergy and  
Infectious Diseases**

**National Institutes of Health**

**March 10, 2020**



National Institute of  
Allergy and  
Infectious Diseases

**CROI** 2020

For live Q & A at the end of the session, please email Questions to: [CROIroom312@gmail.com](mailto:CROIroom312@gmail.com)

#virtualCROIQandASS01



January 11, 2020

# Science

## NEWS

# **Chinese Researchers Reveal Draft Genome of Virus Implicated in Wuhan Pneumonia Outbreak**

Jon Cohen

# **NIH Research on SARS-CoV-2/COVID-19**

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- **Basic Research/Animal Model  
Development/Resources for Researchers**
- **Diagnostics**
- **Therapeutics**
- **Vaccines**



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# Exploring Small and Large Animal Models

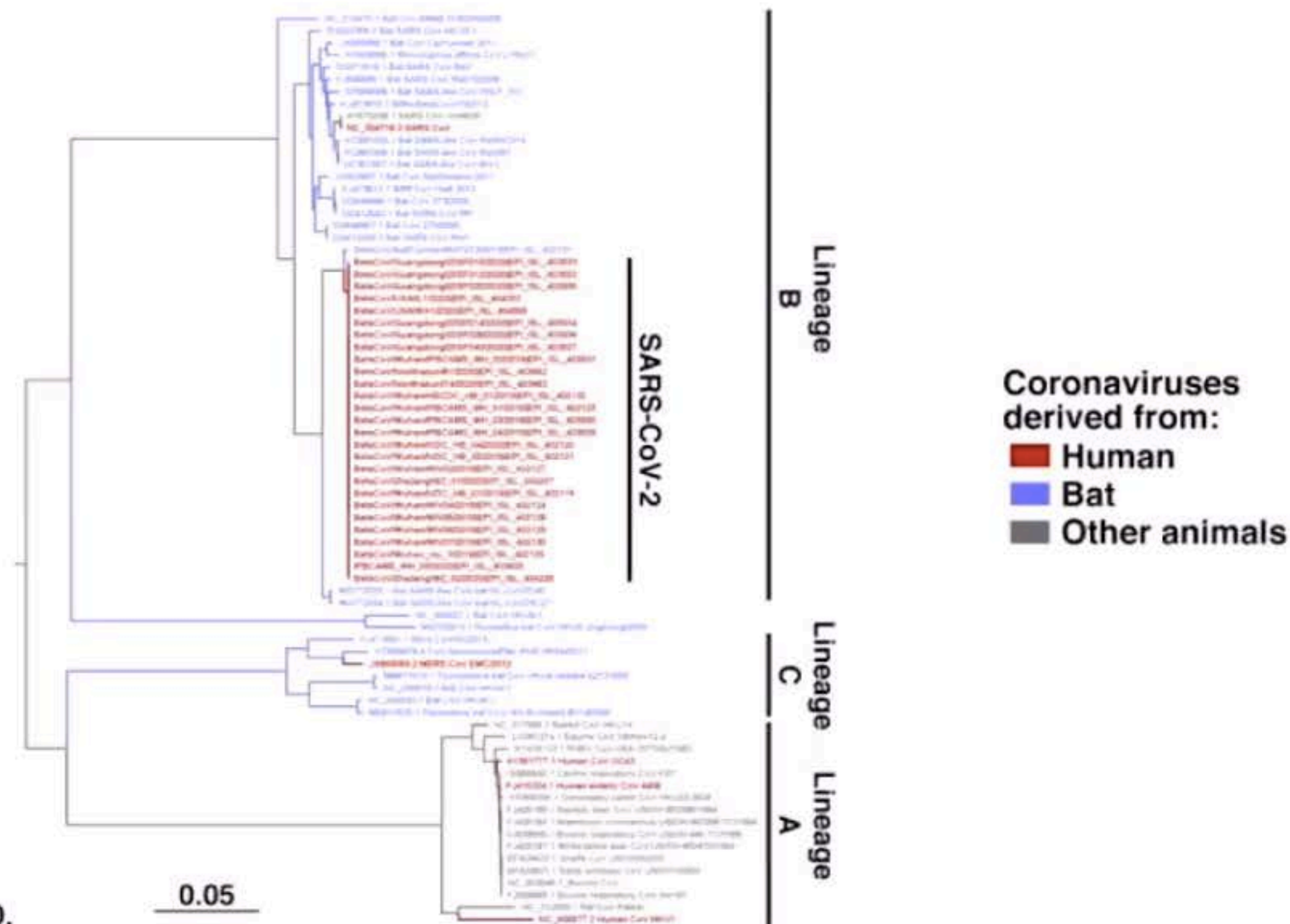
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- **Supplements to coronavirus and/or animal model experts to spur model development**
- **Support to intramural researchers including biocontainment labs**
- **Task orders for contract work for countermeasure developers**



# Phylogenetic Analysis of SARS-CoV-2 Within Betacoronaviruses

Phylogenetic tree reconstructed with data from the GISAID and NCBI databases



Analysis by Seifert & Munster, NIH/NIAID, Virus Ecology Section, 27-Jan-2020



# **Viral Isolates and Reagents Made Available to the Research Community**

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b | e | i RESOURCES

SUPPORTING INFECTIOUS DISEASE RESEARCH

**World Reference Center for Emerging  
Viruses and Arboviruses**

The University of Texas Medical Branch

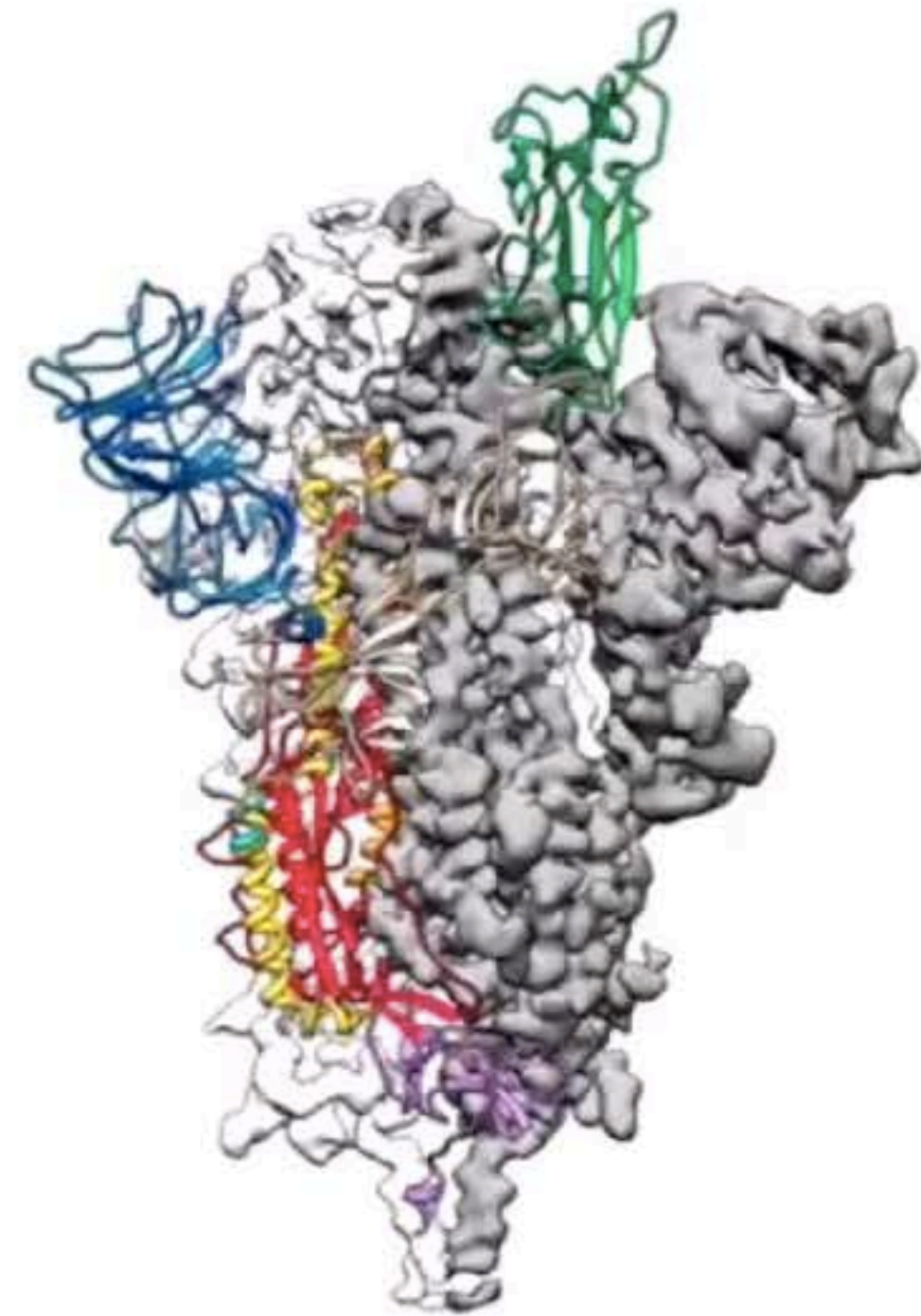


Published online February 19, 2020

# Science

## **Cryo-EM Structure of the 2019-nCoV Spike in the Prefusion Conformation**

D Wrapp, N Wang, KS Corbett, JA Goldsmith,  
C-L Hsieh, O Abiona, BS Graham, JS McLellan



Viral membrane

**Atomic-level structure of SARS-CoV-2 spike protein. Receptor binding domain is colored green.**



# **NIH Research on SARS-CoV-2/COVID-19**

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# **Critical Importance of Diagnostics:**

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- **Wide availability of diagnostic tests for state and local health departments and hospital centers**
- **Serologic assays for sero-surveillance**



# **Diagnostics for SARS-CoV-2 (COVID-19)**

- CDC has developed an rRT-PCR test that can diagnose COVID-19 in respiratory and serum samples from clinical specimens
- NIH developing additional diagnostic tests
  - PCR-based assays
  - Enzyme-linked immunosorbent assay (ELISA)
- NIH-supported researchers from Hong Kong University have developed a molecular diagnostic, published their protocol on the WHO site, and distributed reagents to 12 countries to enable diagnosis





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# **Therapeutics for SARS-CoV-2 (COVID-19)**

- Antivirals, monoclonal antibodies and other agents are being tested
  - **Remdesivir (nucleotide analogue)**, has shown promise against coronaviruses in animal models
  - **Kaletra (lopinavir/ritonavir) (protease inhibitors)** and **interferon-beta** have been used investigationally for other coronaviruses
  - Other **broad-spectrum antivirals**
  - **Chloroquine**
  - **Drug screening and targeted drug design**
  - **Monoclonal antibodies being isolated and tested**





# Preclinical Evidence of Remdesivir's Potential for Treating Human Coronavirus Infections



## **Broad-Spectrum Antiviral GS-5734 Inhibits Both Epidemic and Zoonotic Coronaviruses**

TP Sheahan, RS Baric et al.



## **Comparative Therapeutic Efficacy of Remdesivir and Combination Lopinavir, Ritonavir, and Interferon Beta Against MERS-CoV**

TP Sheahan, RS Baric et al.



Published online  
February 13, 2020

PNAS

Proceedings of the National Academy of Sciences of the United States of America

# **Prophylactic and Therapeutic Remdesivir (GS-5734) Treatment in the Rhesus Macaque Model of MERS-CoV Infection**

E de Wit, H Feldmann et al.



1 2 3 4 5 6						
Recruitment status	Prospective Registration	Main ID	Public Title	Date of Registration	Results available	
Not Recruiting	Yes	CNCTR2000030164	A cross-sectional study of novel coronavirus pneumonia (COVID-19) patients in ICU	2020-02-24		
Not Recruiting	Yes	CNCTR2000030163	A Medical Based Retrospective Real World Study for Assessment of Effectiveness of Comprehensive Traditional Chinese Medicine in the treatment of Novel Coronavirus Pneumonia (COVID-19)	2020-02-24		
Not Recruiting	Yes	CNCTR2000030135	A randomized controlled trial for high-dose Vitamin C in the treatment of severe and critical novel coronavirus pneumonia (COVID-19) patients	2020-02-24		
Not Recruiting	Yes	CNCTR2000030168	A real world study for Compound Houtuyiniae Mixture for prevention of novel coronavirus pneumonia (COVID-19)	2020-02-24		
Not Recruiting	Yes	CNCTR2000030187	Clinical study for Lopinavir and Ritonavir in the treatment of novel coronavirus pneumonia (COVID-19)	2020-02-24		
Recruiting	Yes	CNCTR2000030188	Clinical study for Lopinavir and Ritonavir in the treatment of novel coronavirus pneumonia (COVID-19)	2020-02-24		
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Not Recruiting	Yes	CNCTR2000030115	A clinical research for the changes of blood cortisol/ACTH level and adrenal morphology in blood cortisol to guide the application of individualized hormone in severe novel coronavirus pneumonia (COVID-19) patients	2020-02-23		
Not Recruiting	Yes	CNCTR2000030118	A clinical study for "Huo-Shen" particles in the treatment of novel coronavirus pneumonia (COVID-19)	2020-02-23		
Recruiting	Yes	CNCTR2000030099	A medical records based study for optimization and evaluation of the comprehensive diagnosis and treatment of novel coronavirus pneumonia (COVID-19) and the assessment of risk factors for severe pneumonia	2020-02-23		
Recruiting	Yes	CNCTR2000030102	A multicenter randomized controlled trial for scone autophagy therapy in the treatment of novel coronavirus pneumonia (COVID-19)	2020-02-23		
Recruiting	No	CNCTR2000030117	A multicenter randomized open parallel controlled trial for the evaluation of the effectiveness and safety of Xiyangqing injection in the treatment of common type novel coronavirus pneumonia (COVID-19)	2020-02-23		
Not Recruiting	No	CNCTR2000030091	A prospective randomized controlled trial for the home exercise intervention in nursing students during epidemic of novel coronavirus pneumonia (COVID-19)	2020-02-23		
Recruiting	No	CNCTR2000030092	Assessment of cardiac function in patients with Novel Coronavirus Pneumonia (COVID-19) by echocardiography and its new techniques	2020-02-23		
Not Recruiting	Yes	CNCTR2000030094	Effects of novel coronavirus pneumonia (COVID-19) on menstruation, TCM body constitution and psychological state for female at different ages	2020-02-23		
Not Recruiting	Yes	CNCTR2000030114	Lung ultrasound in the diagnosis, treatment and prognosis of pulmonary lesions of novel coronavirus pneumonia (COVID-19)	2020-02-23		
Recruiting	No	CNCTR2000030113	Randomized controlled trial for safety and efficacy of Favipiravir in the treatment of novel coronavirus pneumonia (COVID-19) with severely respiratory distress syndrome	2020-02-23		

# 261 Records for COVID-19 in WHO's International Clinical Trials Registry Platform as of March 3, 2020





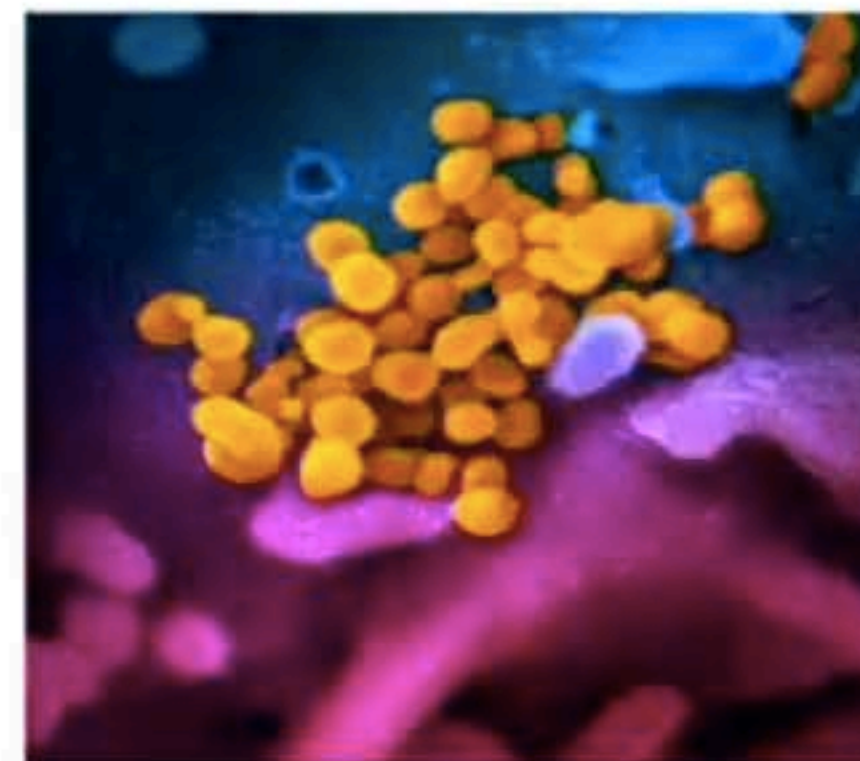
National Institute of  
Allergy and  
Infectious Diseases

February 25, 2020

## News Release

# NIH Clinical Trial of Remdesivir to Treat COVID-19 Begins

- First clinical trial in US to evaluate experimental treatment for COVID-19
- Initial trial participants are Americans repatriated after being quarantined on the Diamond Princess cruise ship
- Study can be adapted to evaluate additional investigative treatments and to enroll participants at other sites





# Lopinavir/Ritonavir: Clinical Benefit for SARS Patients

March 2004 Volume 49 Issue 3

**Thorax**  
AN INTERNATIONAL JOURNAL OF RESPIRATORY MEDICINE

RESPIRATORY INFECTION

## **Role of Lopinavir/Ritonavir in the Treatment of SARS: Initial Virological and Clinical Findings**

CM Chu, KY Yuen et al. on behalf of the HKU/UCH SARS Study Group

thorax.bmj.com

BMJ



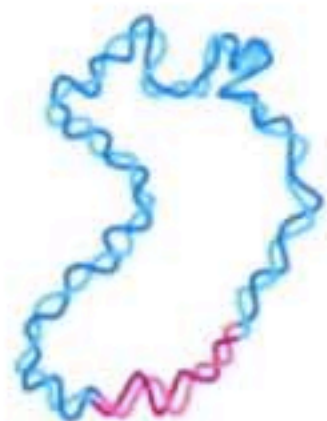
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# Vaccine Platform Technologies in Development for COVID-19



**Genetic immunization  
(DNA and RNA vaccines)**

**NIAID/Moderna, CureVac/NIAID,  
Inovio/Beijing Advaccine**



**Recombinant protein**

**Baylor and collaborators**



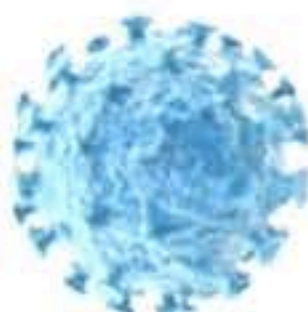
**Viral vector  
(ex: adenovirus)**

**Johnson & Johnson,  
Jenner/NIAID**



**Nanoparticle  
(viral protein on particle)**

**Novavax**



**Live attenuated**

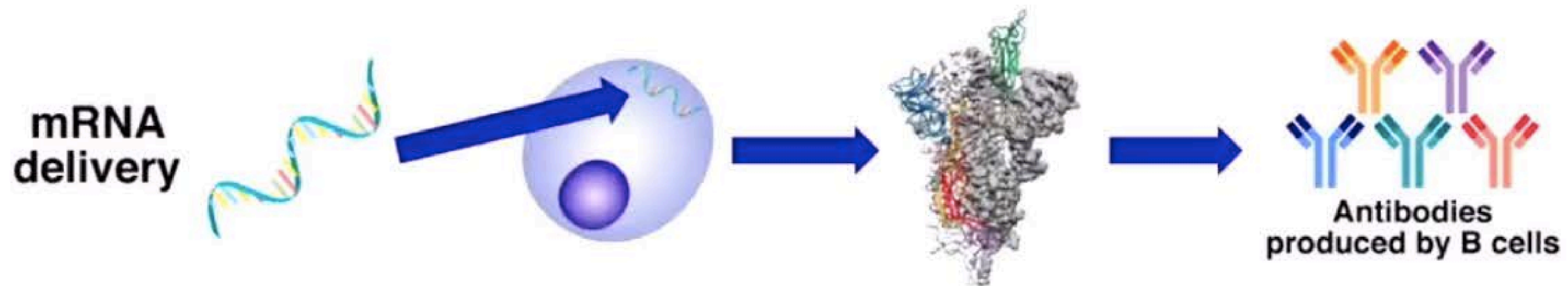
**Codagenix**

**Selected development programs**



# COVID-19 mRNA Vaccine Development

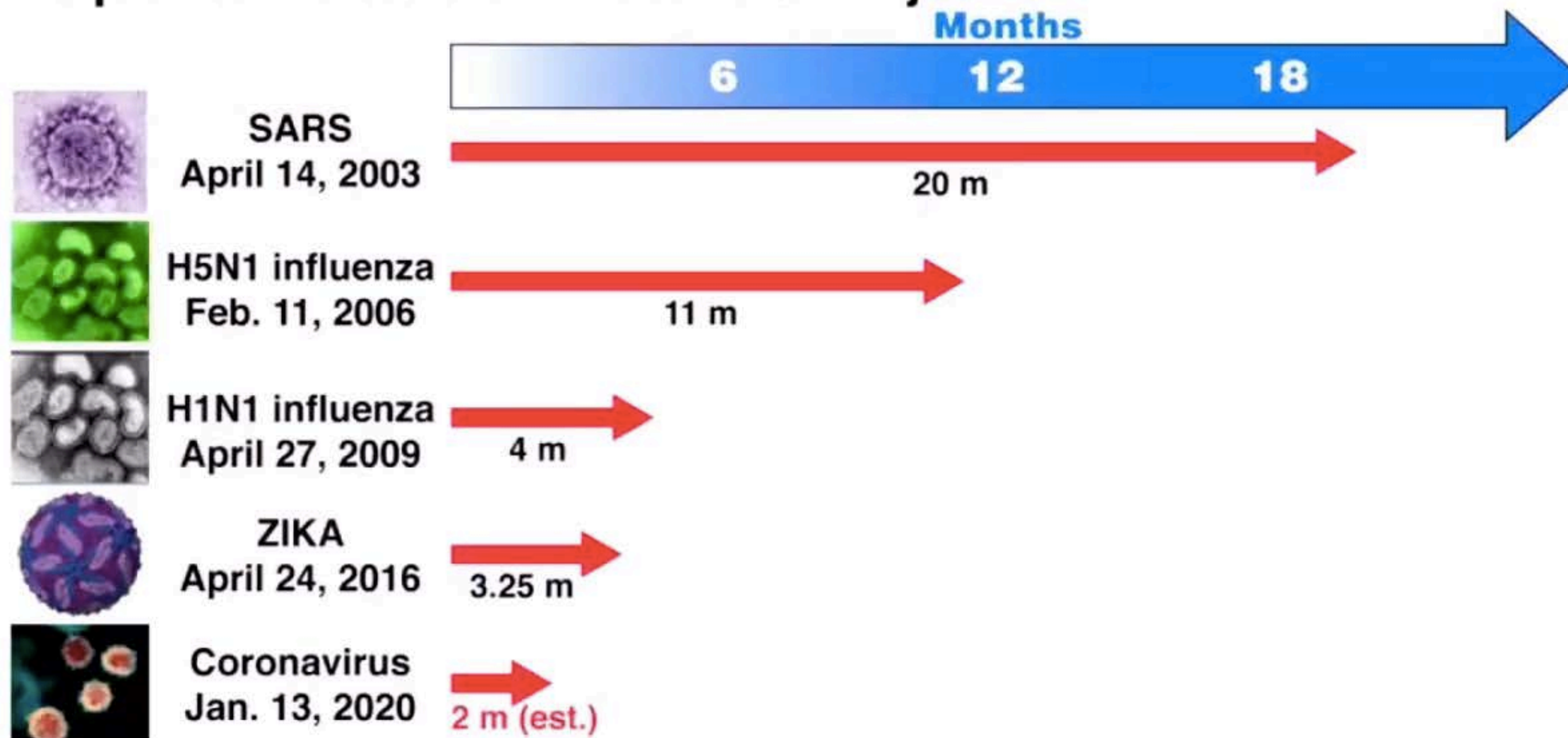
- **NIAID Vaccine Research Center (VRC)** is collaborating with Moderna and the **Coalition for Epidemic Preparedness Innovations (CEPI)** on an mRNA vaccine candidate expressing the viral spike protein of COVID-19
- Production fast-tracked and GMP product for clinical trial shipped to trial site February 2020





# NIH Vaccine Research Center: Vaccines for Emerging Diseases

## Sequence Selection to 1st Human Injection





# The Washington Post

January 30, 2020

## Coronavirus Vaccine Research is Moving at Record Speed

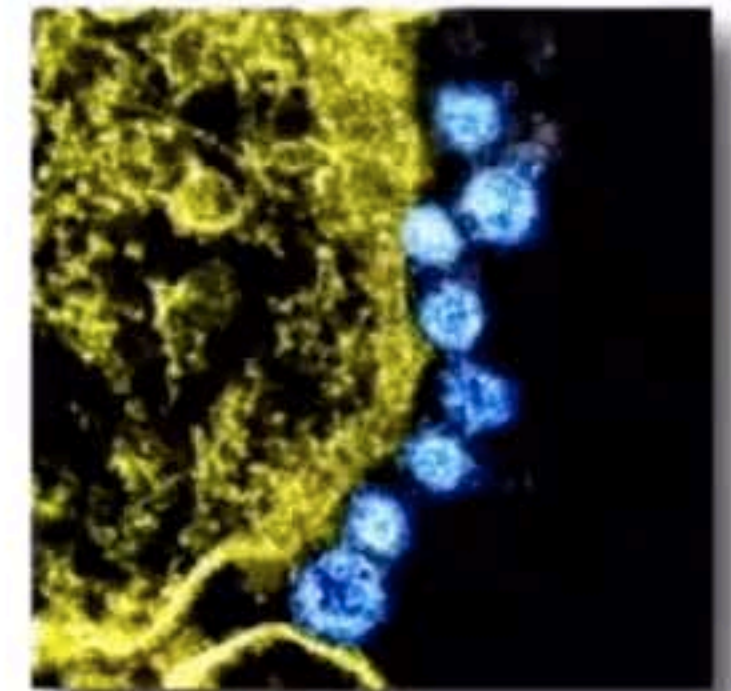
- Multiple COVID-19 vaccine candidates being pursued by >30 organizations globally



# Other NIH COVID-19 Vaccine Development Efforts

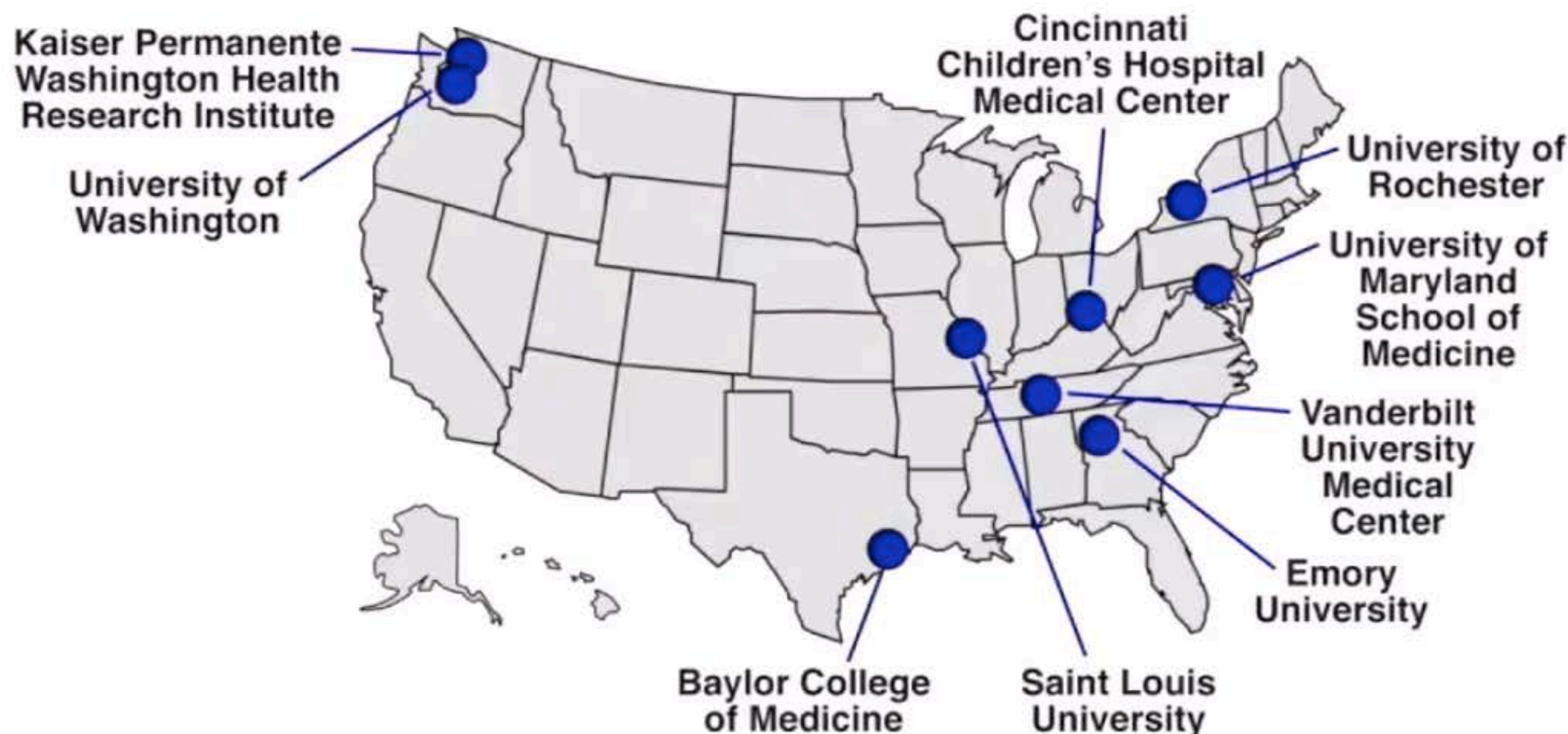
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- **Chimpanzee adenovirus-vectored vaccine** candidate (NIAID Rocky Mountain Laboratories/Oxford University)
- **SARS recombinant protein vaccine** candidate being evaluated for cross-neutralization (Baylor College of Medicine)
- **Additional concepts**, e.g. recombinant spike protein vaccines, other nucleic acid vaccine platforms





# NIAID's New Infectious Diseases Clinical Research Consortium (IDCRC)



■ The Vaccine and Treatment Evaluation Units (VTEUs), established in 1962, are part of the new NIAID IDCRC



# **Current Funding Opportunities**

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- **Notice of Special Interest Regarding the Availability of Urgent Competitive Revisions for Research on the 2019 Novel Coronavirus (2019-nCoV)\***
  - Improve understanding of 2019-nCoV
  - Development of medical countermeasures
  - Development of animal models
- **2020 NIAID Omnibus Broad Agency Announcement**
  - Solicits development of 2019-nCoV\* vaccines

\*SARS-CoV-2