

# Developing a COVID-19 Vaccine at Pandemic Speed

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# An Unprecedented Pandemic

World Map

U.S. Map

Critical Trends

COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU)

Total Confirmed

12,813,864

Confirmed Cases by  
Country/Region/Sovereignty

3,286,025 US

1,839,850 Brazil

849,553 India

726,036 Russia

322,710 Peru

315,041 Chile

295,268 Mexico

291,154 United Kingdom

276,242 South Africa

Admin0

Last Updated at (M/D/YYYY)

7/12/2020, 3:34:39 PM

188

countries/regions

Lancet Inf Dis Article: [Here](#), Mobile Version: [Here](#).

Lead by JHU CSSE. Technical Support: [Esri Living Atlas team](#) and [JHU APL](#). Financial Support: [JHU](#) and [NSF](#). Resource support: [Slack](#), [Github](#) and [AWS](#). [Click here to donate to the CSSE dashboard](#).



Global Deaths

566,790

135,089 deaths  
US

71,469 deaths  
Brazil

44,904 deaths  
United Kingdom

34,954 deaths  
Italy

34,730 deaths

Global Deaths

US State Level

Deaths, Recovered

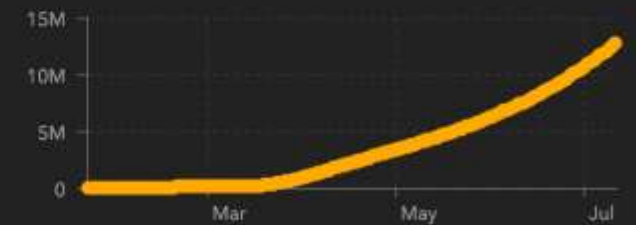
32,348 deaths, 71,477  
recovered  
New York US

15,525 deaths, 31,092  
recovered  
New Jersey US

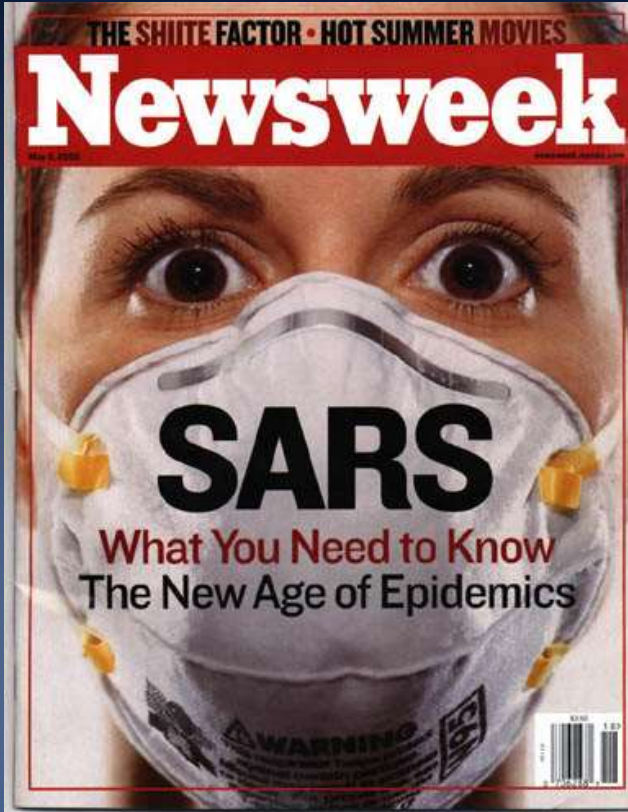
8,310 deaths, 94,347  
recovered  
Massachusetts US

7,207 deaths, 10,000  
recovered

US Deaths, Rec...



# Déjà vu?



**SARS-CoV**  
2003-2004



**MERS-CoV**  
2012-Present



**CoV X**  
Next 5 – 10 years?



# The Wake of Ebola – Preparing for Pathogen X



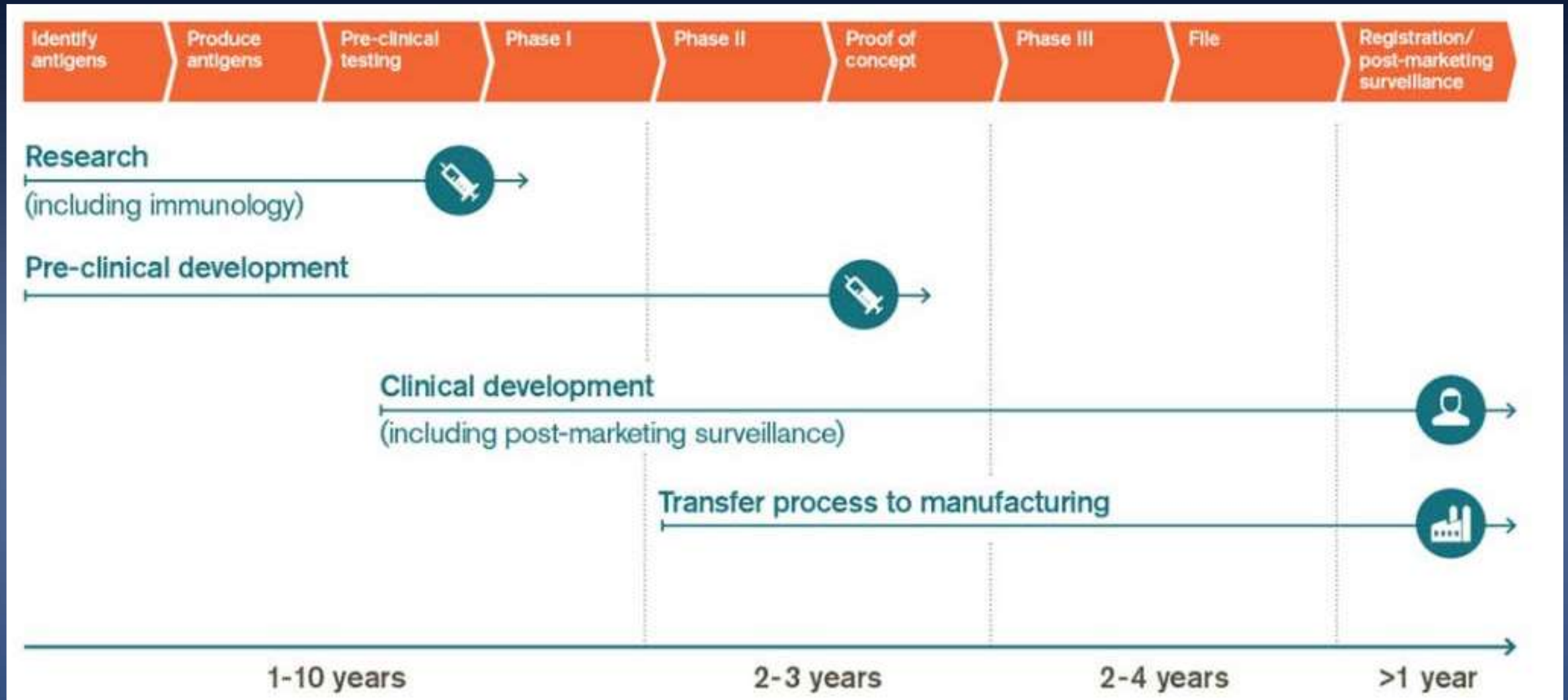
## A Global Plan to Defend Against the Future's Deadliest Diseases

\$460 million will go toward developing vaccines that prevent outbreaks like Ebola from taking the world by surprise.

ED YONG | JAN 18, 2017 | SCIENCE

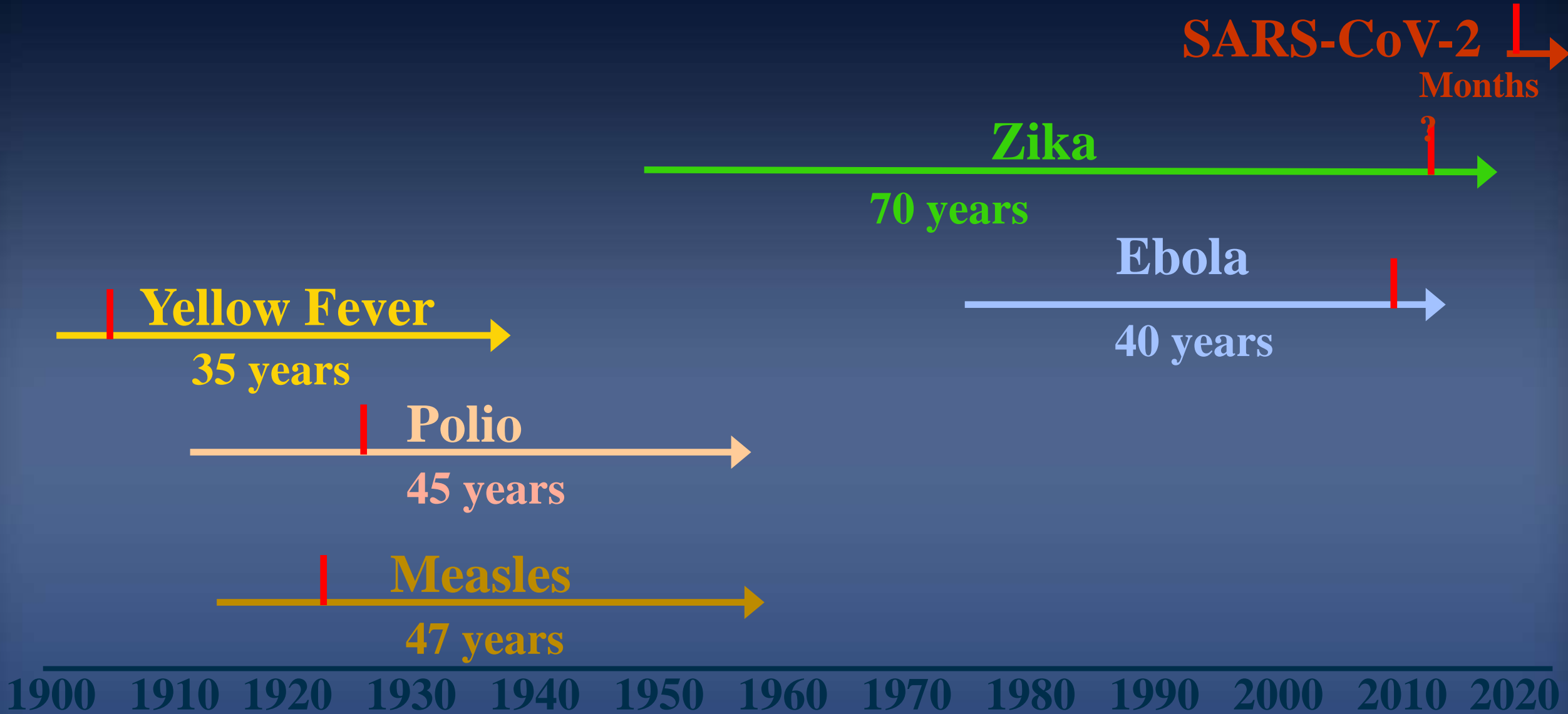
The image is a screenshot of the CEPI (Coalition for Epidemic Preparedness Innovations) website. The header includes the CEPI logo and navigation links: "About us", "Get involved", and "Research &amp; development". Below the header, there are three main sections: "Our portfolio", "Platform Technology", and "Priority diseases". The "Priority diseases" section is highlighted with a red border and contains a list of diseases: MERS-CoV, Lassa, Nipah, Disease X, Rift Valley fever, and Chikungunya. A white text box on the left side of the screenshot contains a quote from Jeremy Farrar: "[CEPI] will fund the development of more Ebola vaccines, since rVSV only works against one of several dangerous strains. 'The vaccine was a turning point for global health, but we haven't finished the job,' says Jeremy Farrar." The "MERS-CoV" item in the list is also highlighted with a red box.

# Standard Vaccine Development Timeline



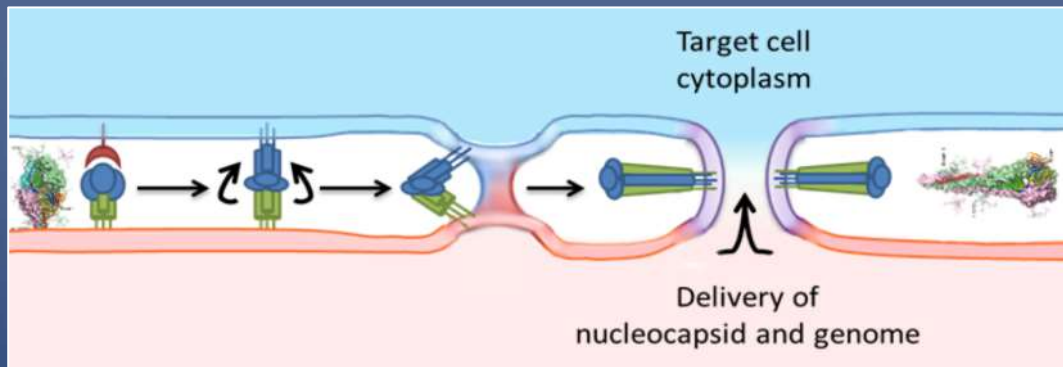
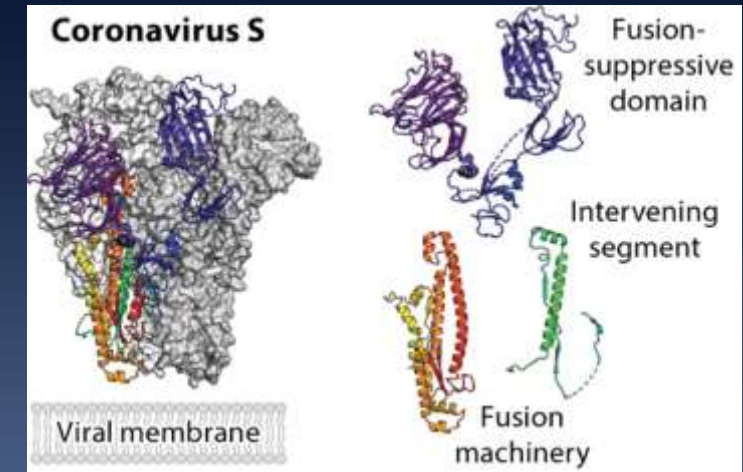
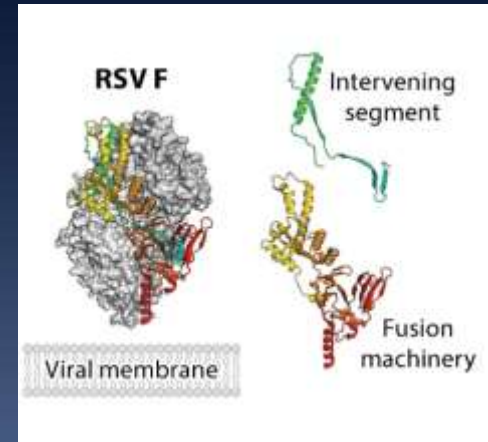
Source: GSK <https://www.gsk.com/en-gb/research/our-approach/how-we-discover-new-vaccines/>

# The Incredible Shrinking Vaccine Timeline

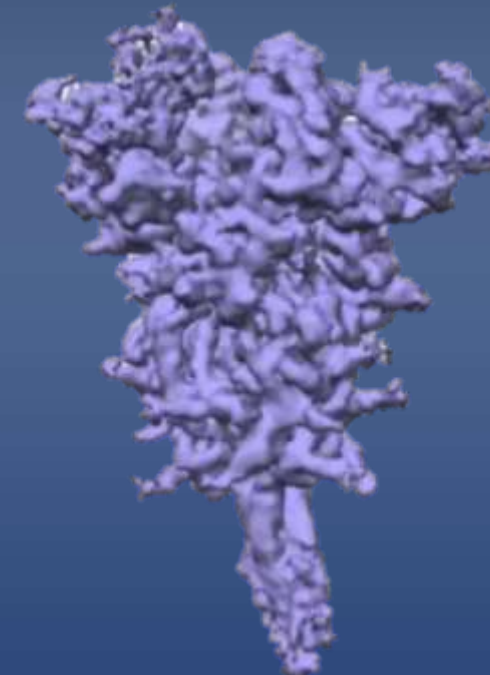


# How to Compress the Timeline

- Priority Pathogen
- Prototype Pathogen
- Platform (“Plug & Play”)

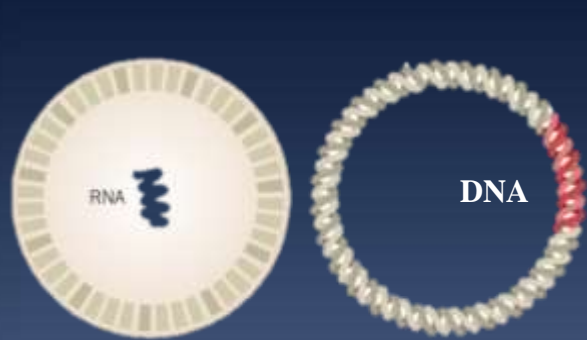


Graham et al. *Annual Review of Medicine* 2019





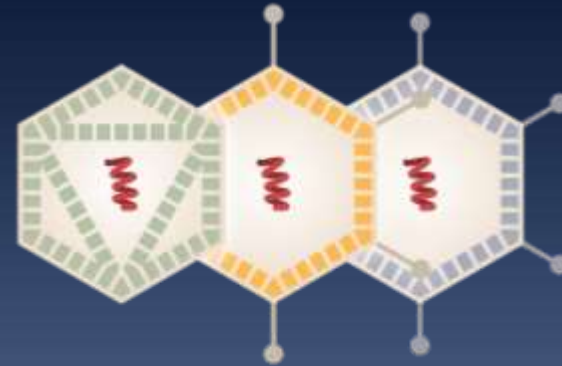
# Platform Approaches for Rapid Vaccine Development



## Nucleic Acid



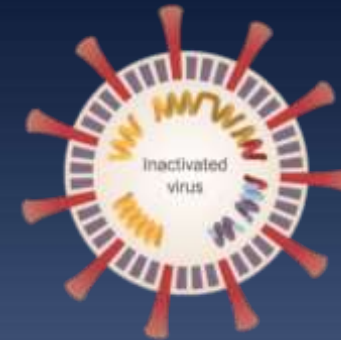
- Ability to scale
- Speed of production
- Unlicensed platform
- Expense & > 1 dose



## Viral Vector



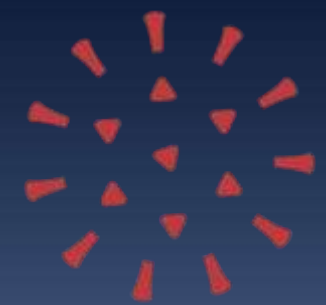
- Single dose for replicating
- Medium speed
- Safety concern for replicating
- Concern for Ab to vector



## Inactivated



- Ability to scale
- Successful licensure
- Concern for VAED
- Adjuvant/ >1 dose



## Protein



- Focused response
- Licensed platform
- Longer to manufacture
- Adjuvant / > 1 dose



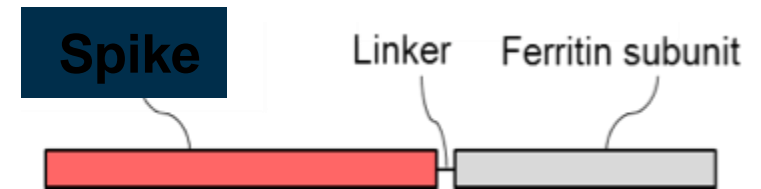
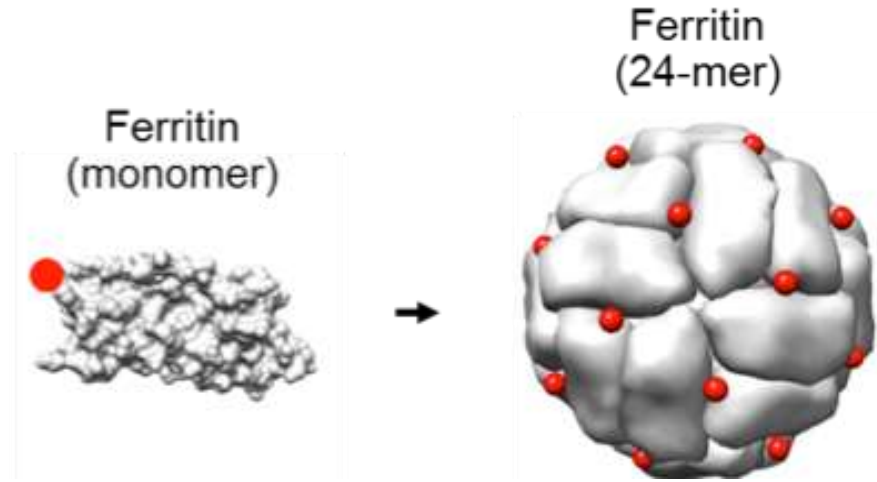
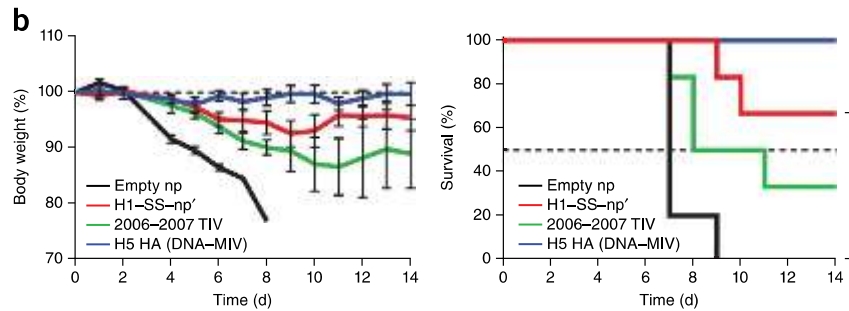
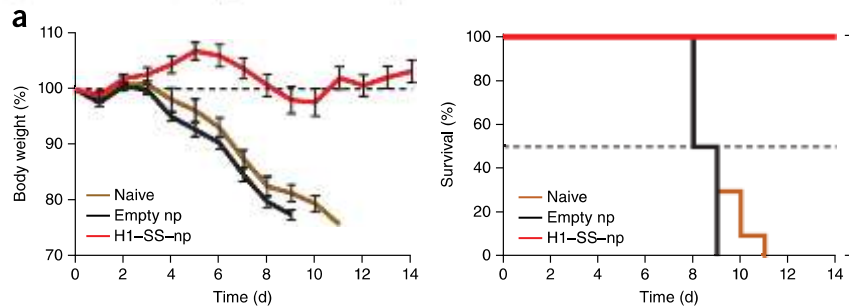
# The longer, broader approach

nature  
medicine

## Hemagglutinin-stem nanoparticles generate heterosubtypic influenza protection

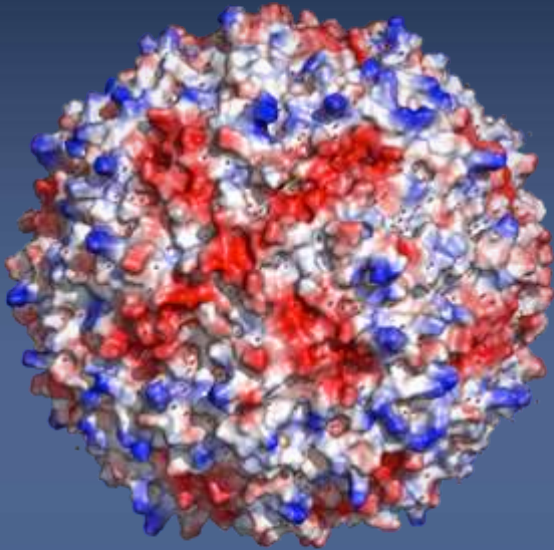
Text

Hadi M Yassine<sup>1,6</sup>, Jeffrey C Boyington<sup>1,6</sup>, Patrick M McTamney<sup>1,5,6</sup>, Chih-Jen Wei<sup>1,5,6</sup>, Masaru Kanekiyo<sup>1</sup>, Wing-Pui Kong<sup>1</sup>, John R Gallagher<sup>2</sup>, Lingshu Wang<sup>1</sup>, Yi Zhang<sup>1</sup>, M Gordon Joyce<sup>1</sup>, Daniel Lingwood<sup>1,5</sup>, Syed M Moin<sup>1</sup>, Hanne Andersen<sup>3</sup>, Yoshinobu Okuno<sup>4</sup>, Srinivas S Rao<sup>1,5</sup>, Audray K Harris<sup>2</sup>, Peter D Kwong<sup>1</sup>, John R Mascola<sup>1</sup>, Gary J Nabel<sup>1,5</sup> & Barney S Graham<sup>1</sup>

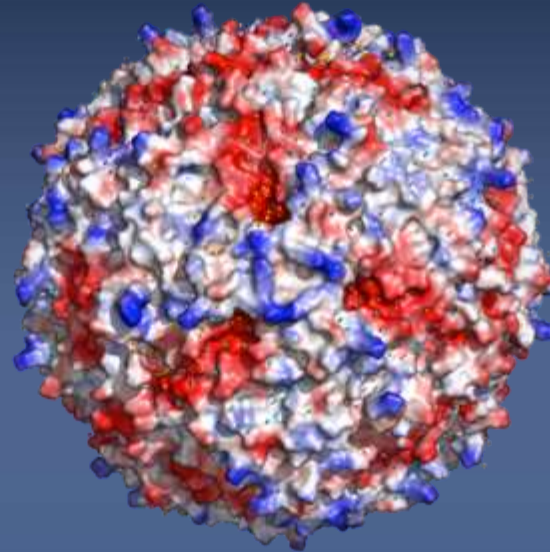


# Ferritin Nanoparticle Design

4-fold axis



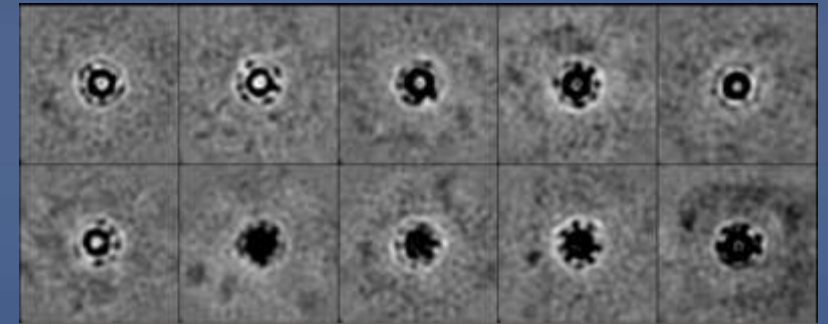
3-fold axis



*Helicobacter pylori* Ferritin  
electrostatic representation



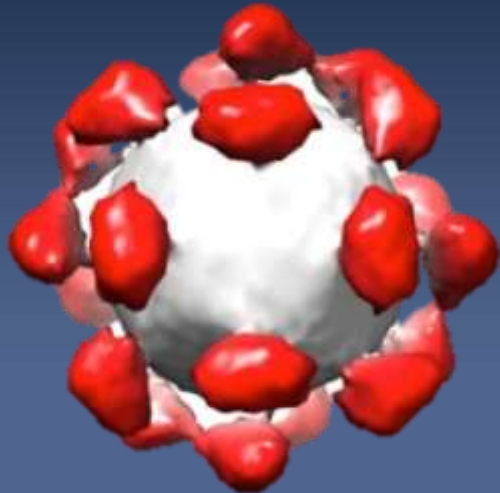
X=linker length variation



SARS-Cov-2 RBD-Ferritin Negative-stain EM  
2D class averages

# Heterologous nanoparticle

Homogeneous assembly  
(single building block)



Heterogeneous assembly  
(multiple building blocks)



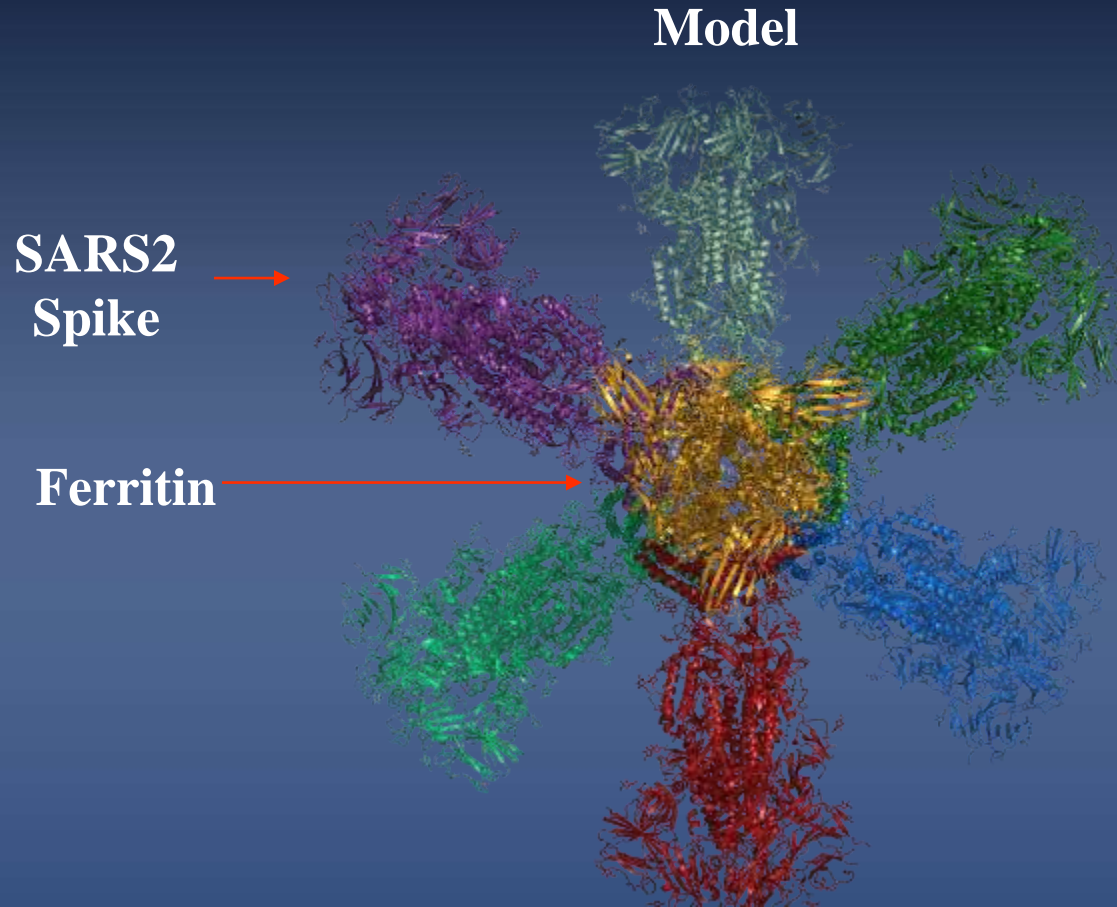
Single  
building block



Multiple  
building blocks



# WRAIR SpFN Vaccine



## Pre-fusion SARS2 Spike Trimer on Ferritin Nanoparticle

- Displays 8 Spike Trimers
- Has mutations in Spike to stabilize pre-fusion conformation
- Has mutations to enhance C-terminal coiled coil trimerization, followed by a flexible linker



# Summary

- The emergence of coronaviruses in human populations is accelerating.
- Tools exist now that allow the rapid scale-up of vaccines for emerging pathogens.
- Novel platforms, though unproven, will be tested in the current pandemic for their strengths and drawbacks.
- The platforms available for rapid vaccine development must be leveraged for anticipation & preparation for the future pandemics, not just response to the current one.

# Acknowledgements

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U.S. MILITARY HIV RESEARCH PROGRAM



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