Understanding the Path to a COVID-19 Vaccine

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Leading the development and testing of low-cost and effective vaccines against emerging and neglected tropical diseases
Branding of “Other Diseases” Viral, parasitic, and bacterial diseases highly prevalent and emerging that mainly affect the world's poorest people.

Adopted by WHO and Global Agencies “Neglected and Emerging Infectious Diseases”

Gates Foundation launched the Product Development Partnership Model - PDPs To advance Global Health Technologies spanning all modalities: vaccines, drugs and diagnostics

Launched our PDP “TCH and BCM Center for NTD Vaccine Development”

New Centers of Excellence for Biodefense Research & Development
Texas Children’s Hospital Center for Vaccine Development
Closing the Global Health Gaps for Neglected and Emerging Infectious Diseases

Established in 2001

Build and strengthen capacity and increase knowledge sharing for the prevention, diagnosis and treatment of tropical and emerging diseases

- **Research & Development** to develop/test "innovative" technologies for global use
- **Translate vaccines** from the R&D to the clinic
- Establish robust **value propositions** (or rationale)
- Apply effective **business models** to ensure licensure for global use
- Identify appropriate access and delivery models — demand forecasting and community engagement

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(12)61127-1/fulltext
Our Approach
Towards Global Health Vaccines

In Scope With and a PATH Towards

- Complex Funding Portfolio
- Product Development
- Bench Clinic Policy
- Trusted Collaborations
- Strict Compliance
Coronavirus Vaccine Initiative

Product Development Partnership
Led by Texas Children’s Hospital Center for Vaccine Development, Baylor College of Medicine
Partnership launched in 2011 with New York Blood Center (Jiang, S. & Du, L.), University of Texas Medical Branch (Tseng, C-T) & WRAIR

Fact Sheet: Basic Information about SARS

SARS
Severe acute respiratory syndrome (SARS) is a viral respiratory illness caused by a coronavirus, called SARS-associated coronavirus (SARS-CoV). SARS was first reported in Asia in February 2003. Over the next few months, the illness spread to more than two dozen countries in North America, South America, Europe, and Asia before the SARS global outbreak of 2003 was contained. This fact sheet gives basic information about the illness and what CDC has done to control SARS in the United States. To find out more about SARS, go to www.cdc.gov/sars/ and www.who.int/csr/sars/en/.

The SARS outbreak of 2003
According to the World Health Organization (WHO), a total of 8,098 people worldwide became sick with SARS during the 2003 outbreak. Of these, 774 died. In the United States, only eight people had laboratory evidence of SARS-CoV infection. All of these people had traveled to other parts of the world with SARS. SARS did not spread more widely in the community in the United States. For an update on SARS cases in the United States and worldwide as of December 2003, see www.cdc.gov/mmwr/preview/mmwrhtml/mm5249a2.htm.

Middle East Respiratory Syndrome (MERS)

Middle East Respiratory Syndrome (MERS) is viral respiratory illness that is new to humans. It was first reported in Saudi Arabia in 2012 and has since spread to several other countries, including the United States. Most people infected with MERS-CoV developed severe respiratory illness, including fever, cough, and shortness of breath. Many of them have died.
Running the Gauntlet towards the Development of a Coronavirus Vaccine

*SARS CoV RBD 219-N1 Vaccine Candidate* – A Protein-based Vaccine using a Proven Technology

2011 Funded to develop an anti-SARS-CoV vaccine

**Mechanism of Action**

Block (neutralize) the binding (and entry) of the virus into lung cells to:

- Reduce infection, disease and transmission

**Target** Minimally-required immunogenic domain

SARS-CoV Receptor Binding Domain

2016 Vaccine candidate manufactured for clinical evaluation

2016 - 2020 PARTIAL PAUSE

2020 Could our SARS-CoV Vaccine protect against SARS-CoV-2?
SARS-CoV and COVID-19 spike proteins are structurally very similar

Figure 1. Comparison of the known structure SARS-CoV RBD (A), the deduced molecular model of 2019-nCoV, generated by performing molecular simulation (B), and the two structures superimposed.
Serum from a convalescent SARS patient cross-neutralizes SARS CoV-2 S-driven entry

Convalescent SARS patients exhibit a neutralizing antibody response directed against the viral S protein*

Serum from a convalescent SARS patient inhibited SARS-S- but not Vesicular Stomatitis Virus Glycoprotein (VSV-G)-driven entry in a concentration dependent manner

Serum reduced 2019-nCoV-S-driven entry, although with somewhat lower efficiency as compared to SARS-S

Evidence of **RBD Vaccine Cross Neutralization and Cross Protection**

![Graphs showing inhibition of viral entry](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7091888/)

Courtesy Dr. Lanying Du

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7091888/
Protein-based RBD vaccine strategy induces HIGH neutralizing antibodies

RBD Vaccine high levels of neutralizing antibodies
• Titer range: 640 to 1,280

Compared to:
• DNA: Median Titer 74
• Adenovirus: hAd5: 14.5 to 34
• Adenovirus: ChAdOx1: 5 to 40
• Convalescent Plasma (possibly RNA): 93 to 212
• Purified Inactivated: up to 4000

https://www.biorxiv.org/content/10.1101/2020.05.15.098079v1.full.pdf
https://www.biorxiv.org/content/10.1101/2020.05.13.093195v1.full.pdf
https://science.sciencemag.org/content/early/2020/05/06/science.abc1932.long
https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31208-3/fulltext
https://science.sciencemag.org/content/early/2020/05/19/science.abc6284
Ensuring low potential for mechanisms of immune-enhancement

$T_H^{17}$ responses may direct cellular responses observed by inactivated viruses and vaccines delivered in virus vectors.

Link between $T_H^{17}$ cell development and IL-6 in patients with COVID-19 who experience cytokine storm (together with IL-8 induction).

Role of IL-17 in promoting the activation, recruitment and extravasation of eosinophils into target organs.

Finding that immunopathology is least protein-based RBD and alum vaccines.

Editorial ● Full text access

The potential role of Th17 immune responses in coronavirus immunopathology and vaccine-induced immune enhancement

Peter J. Hotez, Maria Elena Bottazzi, David B. Corry
In Press, Corrected Proof, Available online 17 April 2020

https://www.nature.com/articles/s41577-020-0323-4

Comment | Published: 28 April 2020

COVID-19 vaccine design: the Janus face of immune enhancement

Peter J. Hotez, David B. Corry, Maria Elena Bottazzi

Nature Reviews Immunology (2020) | Cite this article

https://www.nature.com/articles/s41577-020-0323-4
Current Strategy: Aligning to Achieve Global Access

Partnership between PATH Center for Vaccine Innovation and Access (CVIA) for a 2-stage approach
- An accelerated US-based time schedule clinical testing
- Transition to a developing country vaccine manufacturer

A shovel-ready SARS COV candidate as a heterologous vaccine against COVID-19
- cGMP Formulation, Fill-and-Finish
- Parallel GLP (Rabbit) Toxicology Testing
- All-in Strategy: securing a SARS CoV-2 regulatory strategy with a SARS CoV vaccine candidate
- Proposed Phase 1 randomized, placebo-controlled, observer-blind trial to assess the safety and immunogenicity in healthy adults 18 through 45 years of age.

https://www.bcm.edu/news/infectious-diseases/partnership-research-covid-19-vaccine
Ensuring scalability, affordability and production
Providing additional value towards the COVID-19 vaccine development efforts

Global call to action by Dr. Seth Berkley, CEO of Gavi, the Vaccine Alliance: “...how do we produce vaccines specifically for the developing world if this is a truly global epidemic?”

.....”In the race to develop a coronavirus vaccine, everyone everywhere should be winners.”

THANK YOU

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The Traditional Pharmaceutical Development Continuum

Average 10-20 yrs