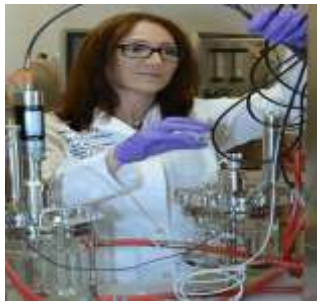

AAAS
IGNITING PROGRESS FOR THE NEXT 175
Center for Science Diplomacy

Academia de Ciencias de Cuba

Future of the U.S. – Cuba Scientific Cooperation Delegation Workshop in Cuba
March 19-23, 2023

Cooperation on Science: Addressing Shared Challenges on Communicable and Non-Communicable Diseases

Innovative Technology Transfer Models to Decolonize the Vaccine Sciences

Baylor College of Medicine

Texas Children's Hospital

NATIONAL SCHOOL OF TROPICAL MEDICINE

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ACADEMIA NACIONAL DE CIENCIAS DE HONDURAS

Disclosure: ***Co-inventor and patent holder of several vaccine technologies against NTDs. Co-inventor of a COVID-19 recombinant protein vaccine technology owned by Baylor College of Medicine (BCM) licensed non-exclusively and without patent restrictions to various manufacturing companies***

Texas Children's Hospital Center for Vaccine Development at Baylor College of Medicine

A **Product Development Partnership Model**
Established in Washington DC in 2000
Moved to **Texas Medical Center** in 2011
+ 50 scientific and technical staff
> 40 Global Partnerships

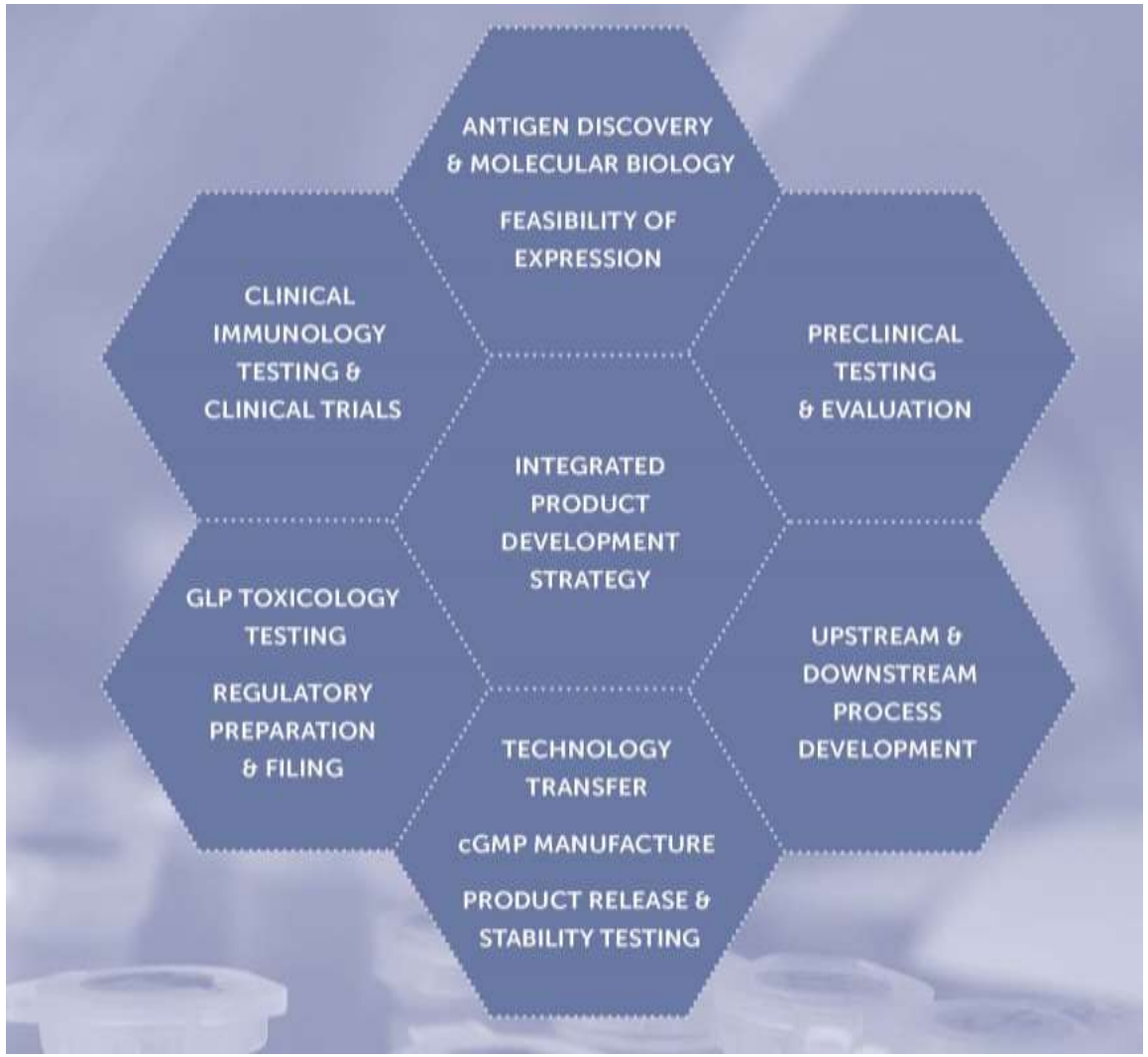
To develop and test new low-cost and effective vaccines against emerging and neglected tropical diseases

To build capacity for vaccine development locally and with foreign nations

To guide and influence vaccine policy and advocacy

A diverse vaccine development portfolio against **neglected tropical and emerging** infections

- Hookworm, Schistosomiasis, Chagas, Leishmaniasis, Coronavirus, Tick-borne



Features and Impact of Global Morbidity Diseases

Neglected Tropical Diseases with vaccines under development

Disease	Stage of Vaccine Development	Prevalence in 2017[7]	Incidence in 2017[7]	Estimated DALYs in 2017[8]	Alternative disease burden estimates in DALYs
Hookworm Infection	**Phase 1-2**	**229 million**	**Not Determined**	**845,000**	**4.1 million[9]**
Schistosomiasis	**Phase 1-2**	**143 million**	**Not Determined**	**1.4 million**	**13-15 million[10]**
Dengue	Licensed (Dengvaxia)	6.3 million	105 million	2.9 million	0.3-5 million (+ arboviral diseases)[11]
Onchocerciasis	Preclinical	21 million	Not determined	1.3 million	128,000 additional[12]
Chagas disease	**Preclinical**	**6.2 million**	**162,500**	**232,000**	**806,170[13]**
Leishmaniasis	**Phase 1-2**	**4.1 million**	**669,100**	**774,000**	**>2 million just for cutaneous leishmaniasis[14]**
Leprosy	Phase 1	518,500	48,500	31,500	Local or regional estimates only
Yellow Fever	Licensed	2,600	97,400	314,000	0.3-5 million (+ arboviral diseases)[11]
Rabies	Licensed	500	13,400	634,000	3.7 million canine rabies[15]
Total NTDs	**-**	**~400 million**	**Not determined**	**8.5 million**	**> 30 million**

A Framework to Intersect Vaccine Science and Diplomacy

Open Science – technology transfer, share knowledge, data, reagents, open access publications and build capacity

Team-based approaches - Effective and holistic full spectrum of STE**A**M disciplines and beyond

Appropriate and diversified technologies - based on country/regional/global priorities. Early inclusion and understanding of community (local) needs and preferences

Reverse innovation with LMIC collaborations to **decolonize** the vaccine sciences with Transparency, Trust, Solidarity and Equity

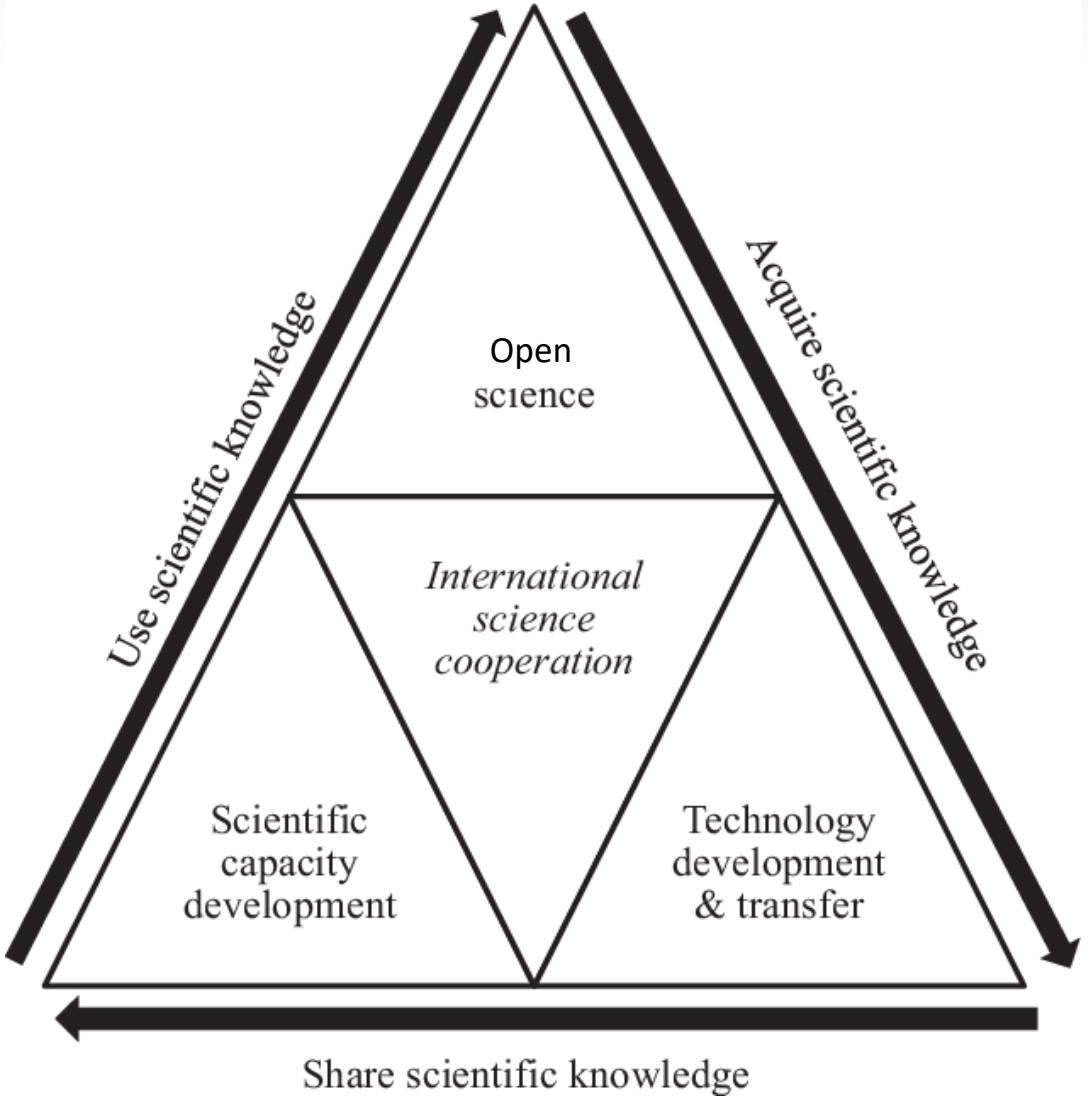
Incentivize disease-endemic **country ownership**

Achieve **improved health outcomes** in the most safe and cost-effective manner

Value science engagement connected to policymaking, education, governance, and dialogue with society

Remove **Barriers** (limited or no IP/Patents)

Out of the box **funding** - Traditional and alternative



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Adopted Coronaviruses (SARS/MERS) as Neglected Infections

Developed the first vaccine for human hookworm infection now entering phase 2 clinical trials

Developed the first vaccine for intestinal schistosomiasis now entering phase 2 clinical trials

Developed the first vaccine for Chagas disease now entering phase 1 clinical trials

Coronavirus partnerships launched first in 2011 and expanded in 2020:

- Focused on low-cost technology using microbial fermentation in yeast
- Targeted the Receptor Binding Domain as vaccine target
- Ensured scalability, ease of production, efficacy, safety, regulatory enabled path and affordability
  - NIH/NIAID and other seed funding instrumental
- Leveraged SARS/MERS lessons to advance Coronavirus (and COVID-19) vaccine R&D

SARS RBD Vaccine:

- Pre-clinical data (regulatory enabling) package complete
- MCB, PCB and Drug Substance produced at WRAIR
- Preclinical efficacy and safety

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New York Blood Center

utmb Health

Working together to work wonders.

WRAIR Walter Reed Army Institute of Research

NIH National Institute of Allergy and Infectious Diseases

Grant: R01AI098775, AI14087201

PATH

IDRI Transforming Science into Global Health Solutions

AAHI

MilliporeSigma

Merck

bioFarma

BE Biological E. Limited

ImmunityBio

Incepta Pharmaceuticals Ltd

Scientific and Technical Strategy

- Engineer yeast-produced recombinant RBD vaccine antigens – **THE STARTER KITS**
  - Production of seeds and research cell banks fully characterized
- Process development, formulation and preclinical testing:
  - Scale-up to 10L fermentation and purification design of experiments – **THE RECIPES**
- Develop and qualify analytical (biochemical/biophysical) and functional release and stability indicating assays – **THE ASSAYS FOR QUALITY, STABILITY and EFFICACY**
- Technology transfer to pilot and/or industrial manufacturers
  - Co-develop and support manufacturing maturity and the transition to GLP toxicology and Clinical Trials – **SHARE (Publish) WIDELY – Intentional IP, non-exclusive licensing and NO PATENT**

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Engineering Strategy: Selection of SARS CoV-2 RBD 219-N1C1 Construct (residues 331–549) and RBD 203-N1 Construct (residues 332-533)

```
RBD219-WT     NITNLCPFGEVFNATRFASVYAWNRKRISNCVADYSVLYNSASFSTFKCYGVSPTKLNDL 60
RBD219-N1     -ITNLCPFGEVFNATRFASVYAWNRKRISNCVADYSVLYNSASFSTFKCYGVSPTKLNDL 59
RBD219-N1C1   -ITNLCPFGEVFNATRFASVYAWNRKRISNCVADYSVLYNSASFSTFKCYGVSPTKLNDL 59
                ************************************************************

RBD219-WT     CFTNVYADSFVIRGDEVRQIAPGQTGKIADYNYKLPDDFTGCVIAWNSNNLDSKVGGNYN 120
RBD219-N1     CFTNVYADSFVIRGDEVRQIAPGQTGKIADYNYKLPDDFTGCVIAWNSNNLDSKVGGNYN 119
RBD219-N1C1   CFTNVYADSFVIRGDEVRQIAPGQTGKIADYNYKLPDDFTGCVIAWNSNNLDSKVGGNYN 119
              ************************************************************

RBD219-WT     YLYRLFRKSNLKPFERDISTEIYQAGSTPCNGVEGFNCYFPLQSYGFQPTNGVGYQPYRV 180
RBD219-N1     YLYRLFRKSNLKPFERDISTEIYQAGSTPCNGVEGFNCYFPLQSYGFQPTNGVGYQPYRV 179
RBD219-N1C1   YLYRLFRKSNLKPFERDISTEIYQAGSTPCNGVEGFNCYFPLQSYGFQPTNGVGYQPYRV 179
              ************************************************************

RBD219-WT     VVLSFELLHAPATVCGPKKSTNLVKNKCVNFNFNGLTGT 219
RBD219-N1     VVLSFELLHAPATVCGPKKSTNLVKNKCVNFNFNGLTGT 218
RBD219-N1C1   VVLSFELLHAPATVCGPKKSTNLVKNKAVNFNFNGLTGT 218
              *************************** ***********
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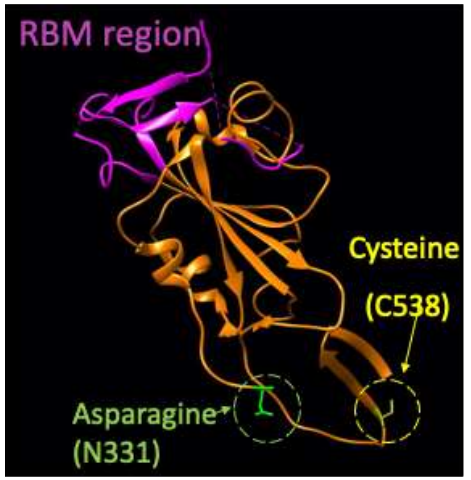
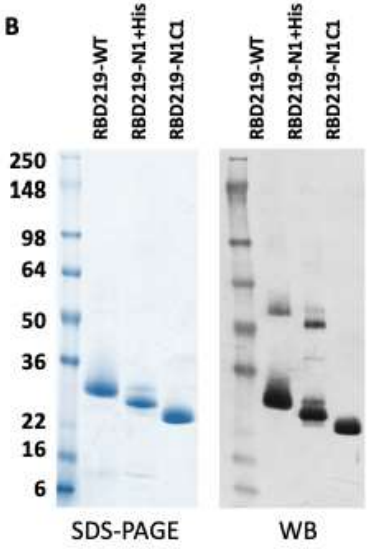




https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7955913/

Technology Transfer and Commercial Strategy

Core invention. Well known recombinant protein technology

- IP centered around genetic engineering of the viral RBD antigen
- Less room for broad patent fence covering related novel technologies
- Less interest from multinationals looking for broad IP protection

Protein technology initially perceived as slow during a pandemic response

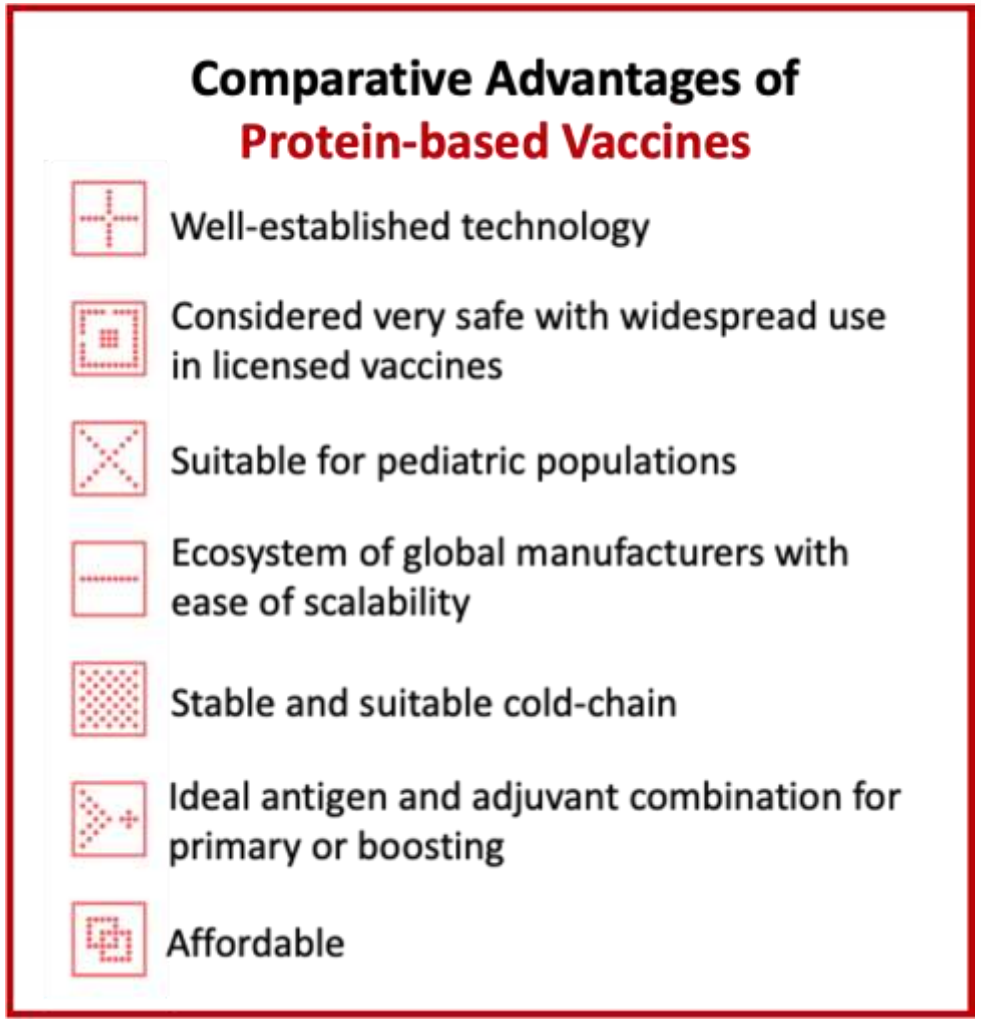
- Albeit 10-yr prior SARS/MERS vaccine experience
- Technology would not have first mover advantage
- Regulatory fast-track uncertain

Previous experience prosecuting a SARS patent application

- Anticipated Office Action response/rejection
- Previous SARS application would likely serve as prior art for COVID-19

Additional considerations

- Rapid evolution of new variants - WT RBD as core IP = narrow claims
- IP protection would become obsolete prior to realization of value
- Opportunities to build future commercialization in the global south



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Vaccine Development Business Models

Scenario 1 – Evaluative MTAs, Tech Transfer and Non-Exclusive Licensing

The India, Indonesia and Bangladesh Case

- Established industrial manufacturers with prior Hepatitis B Vaccine, WHO PQ & international experience
- Aligned global health mission/vision

Scenario 2 – Capacity Building

The Botswana Case

- Limited workforce capability
- No vaccine development infrastructure

Botswana launches COVID-19 vaccine manufacturing plant

NantBotswana
ImmunityBio
Biological E. Limited
Celebrating Life Every Day

Scenario 3 – Open Science

The Cuban Case

- Similar engineering and process development strategy – monomeric RBD on Alum
- Prior yeast *(Pichia)* Experience with Hepatitis B Vaccine

The Abdala vaccine reportedly consists of **a monomeric receptor binding domain subunit, residues 331-530 of the Spike protein of SARS-CoV-2 strain 156 Wuhan-Hu-1**, expressed in the yeast Pichia pastoris at 30–40 mg/L fermentation yield.

First-rate Innovation (first in class) versus Follow-on Product Development

An alternative to the Multinational Model of Vaccine Development

Paradigm Shift

Technology Transfer

dcvmn

Developing Countries Vaccine Manufacturers Network

Biological E. Limited

Celebrating Life Every Day

India

Indonesia

incepta

Incepta Pharmaceuticals Ltd

Bangladesh

ImmunityBio

Botswana

Baylor College of Medicine

Texas Children's Hospital

One Hundred (100) Million Vaccinations

(Covid-19 vaccine: rRBD + Alum + Dynavax CpG1018)

https://www.biologicale.com/corbevax.html

CORBEVAX™ had 50% fewer adverse events than COVISHIELD™ no serious adverse events

Continuous monitoring show high persistence of immune response = durability

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India

Halal-certified COVID-19 Vaccine

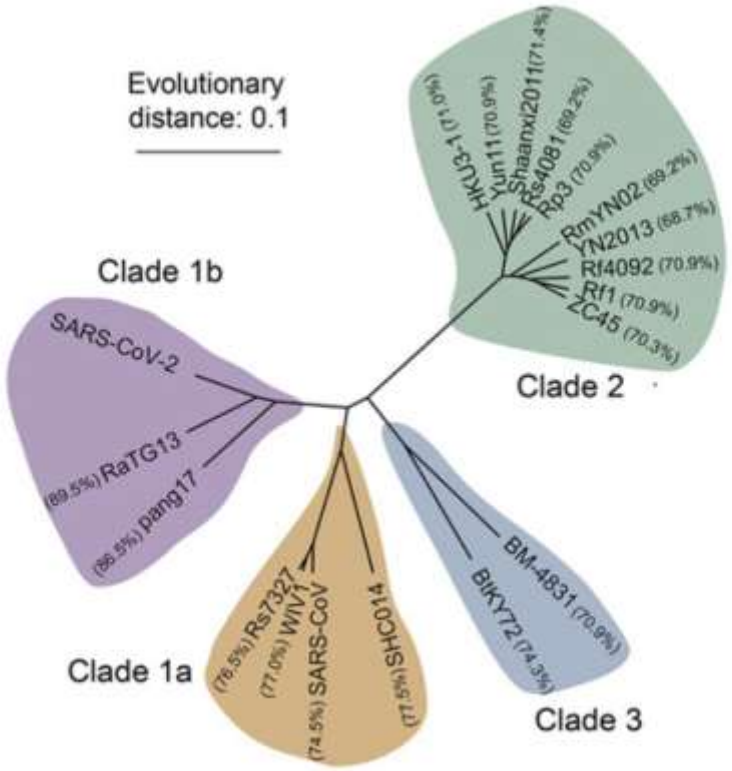
Indonesia

https://www.mohfw.gov.in/pdf/CummulativeCovidVaccinationReport18Mar2023.pdf

What's Brewing?

Development of next-generation, more broadly effective coronavirus vaccines

- Bivalent COVID-19 vaccine with BA4/5 protein construct
- Combination (co-formulation and co-administration) vaccines (with SARS-1, SARS-2 (including VoCs) and Clade 2 candidates) to induce epitope broadening
- New consensus coronavirus vaccine antigen (Clade 1a, 1b and 2) to induce epitope broadening:
  - Chimeric poly-valent
  - Mono-cistronic fusions bi- and tri-clade



Alternative delivery and formulation science (IN and oral)

Structure-function interactions studies

Variant- and clade-specific monoclonal antibodies

Variant and clade specific pseudovirus

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https://www.sciencedirect.com/science/article/pii/S2211124722007938

Lessons from COVID-19 & poverty-associated infectious disease vaccines for future epidemic & pandemic preparedness

Vaccine Insights 2022; 1(1), 115 –120

Table 1 Lessons learned from COVID-19 and poverty-associated infectious disease (PAID) vaccine development to enable future efficient and equitable epidemic or pandemic responses.

Lesson	Category	What we learned
1	Funding	Early, continuous, and sustainable funding for de-risking of the vaccine development pathway is needed
2	Regulatory	Concurrent and expedited regulatory review procedures instituted globally are essential. This should include close coordination between regulatory agencies and other actors such as governmental agencies, industry, non-profits, and academics.
3	Manufacturing capacity	Large multinationals and small and medium biotechnology companies, as well as the Developing Country Vaccine Manufacturing Network (DCVMN), need an equal share of the funding for production accountability
4	Equity and access	The pace and cost of introduction for vaccines developed for PAIDs need to be revisited to enable better equity and access in LMICs
5	Absorption capacity	An adaptable framework for setting efficient supply chains, staffing, equipment, and data collection, with strategic communications and community engagement are key for successful vaccination
6	Leadership	Coordinated and clear accountability is needed to plan and execute end-to-end, without incoordination delay

VACCINE INSIGHTS

Jerome H. Kim,

Maria Elena Bottazzi

https://www.insights.bio/vaccine-insights/journal/article/2494/Lessons-from-COVID-19-poverty-associated-infectious-disease-vaccines-for-future-epidemic-pandemic-preparedness

Cuba, June 2022

http://mediccreview.org/wp-content/uploads/2022/10/MEDICC-Cuba-COVID-19-Vaccine-Executive-Summary_2022.pdf

Sponsors: Robert J. Kleberg Jr. and Helen C. Kleberg Foundation, Fifth Generation, Inc. (Tito's Handmade Vodka), JPB Foundation, NIH-NIAID (AI14087201), Texas Children's Hospital Center for Vaccine Development Intramural Funds and many philanthropic donations via BCM and TCH.