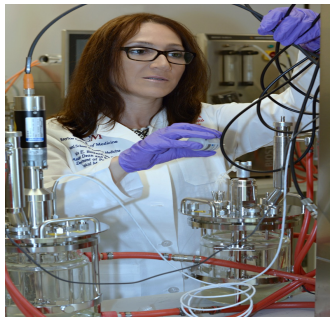
Behind the Scenes of a COVID-19 Vaccine for the World

The Intersection of Open Science and Diplomacy



Maria Elena Bottazzi PhD
Associate Dean and Professor
Division Chief, Pediatric Tropical Medicine
Co-Director, Texas Children's Center for Vaccine Development

A Decade at the Texas Medical Center

Two decades achieving Excellence trough Justice, Equity, Diversity and Inclusion

Baylor College of Medicine

NATIONAL SCHOOL OF TROPICAL MEDICINE

Texas Children's Hospital
Center for Vaccine Development

Pediatric Tropical Medicine

The **Division of Pediatric Tropical Medicine** is dedicated largely to the research of neglected **tropical diseases**, emerging **infectious diseases**, and diseases ...

The Diseases of Poverty an End-to End Strategy

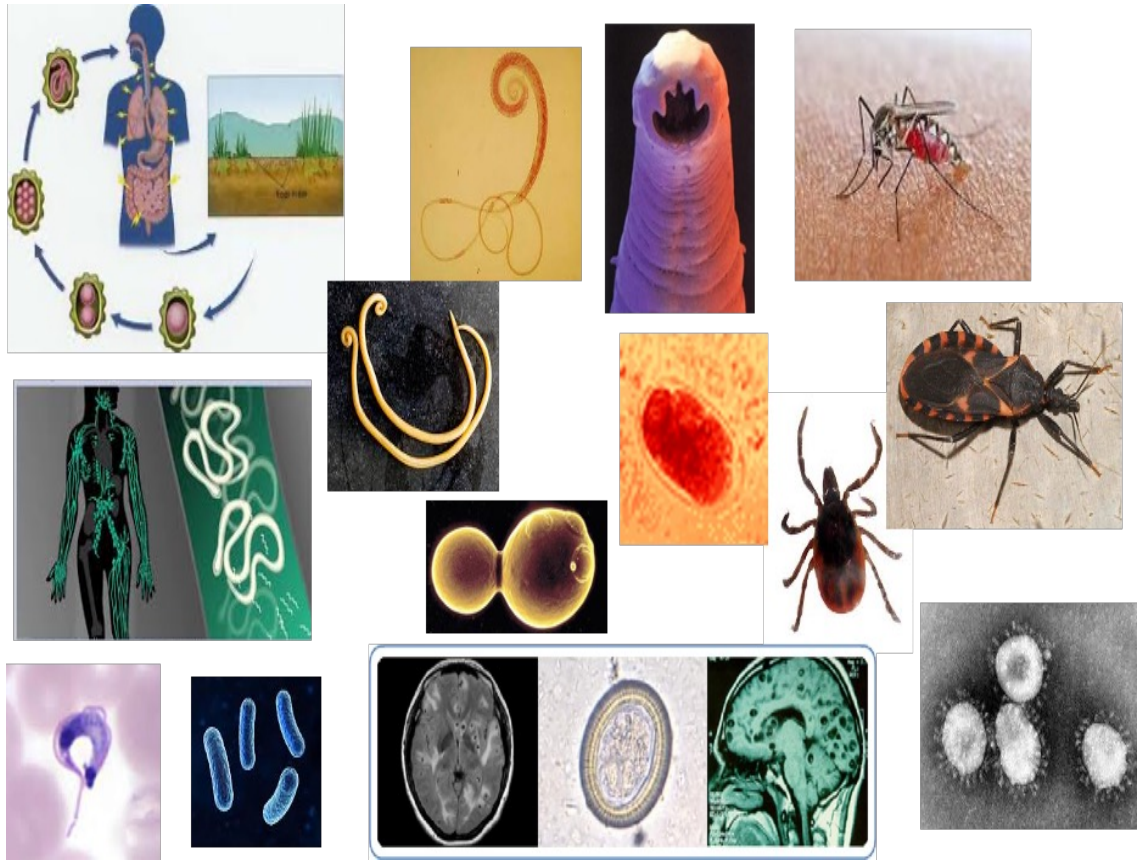
- 17 tropical and 20 emerging infections
- Highly prevalent - poverty promoting
- Leading cause of morbidity > 30 M DALYs
- Leading productivity losses > US $8 B

Identify appropriate access and delivery models – demand forecasting and community engagement

Identify effective business models to enable research to transition towards real solutions

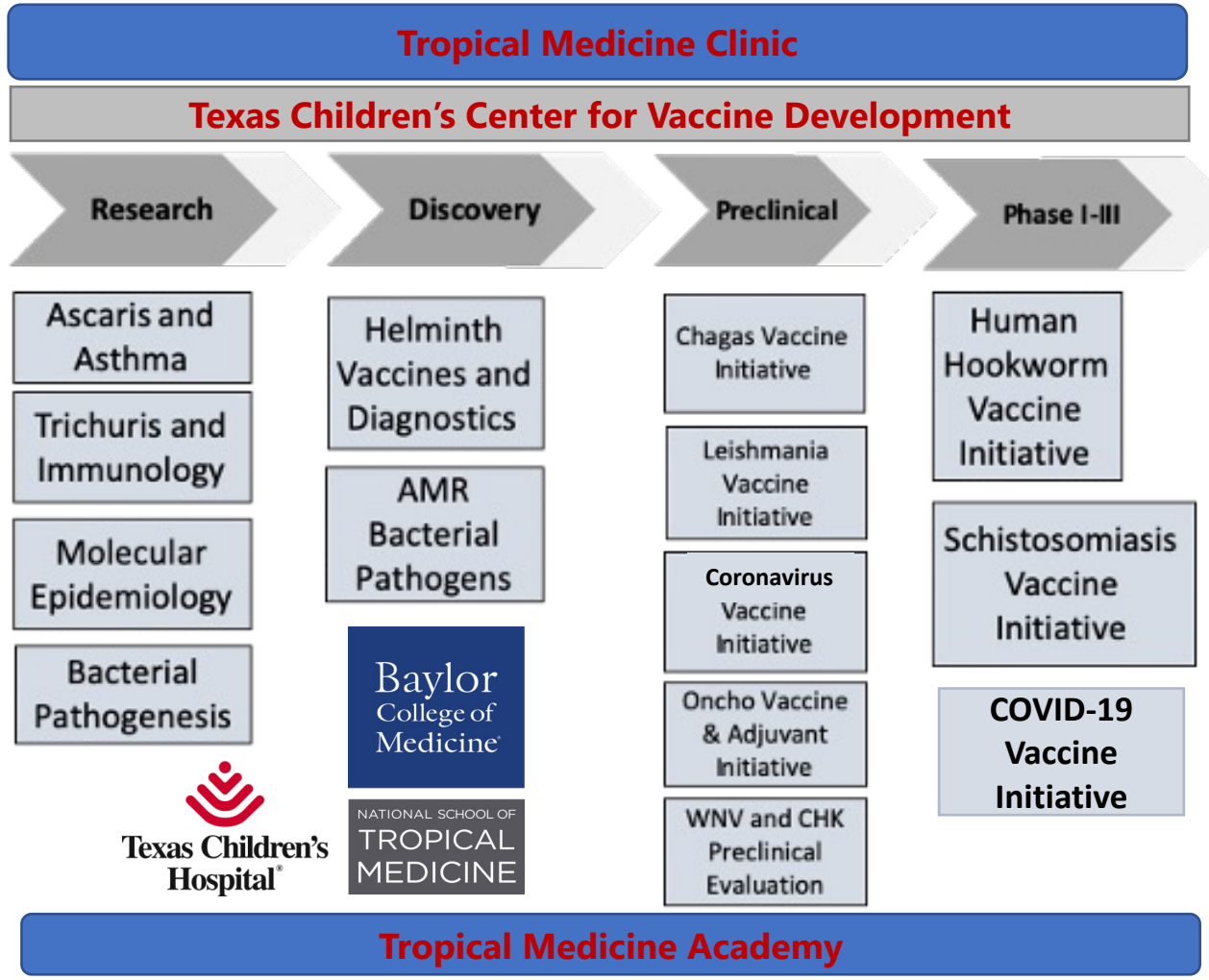
Essential to highlight the value proposition (rationale and significance of your work)

Crucial to advance appropriate Research & Development



Crosscutting & Interdisciplinary Tropical Medicine Research

- ✓ **Decolonize science** by establishing global partnerships to build and strengthen capacity locally and in LMICs
- ✓ Use **adaptation strategies** to meet cultural needs
- ✓ **Integrate disciplines** - technology, population health, regulatory, policy, finance and access strategies
  - ✓ *Vaccines-linked to chemotherapy approaches*
  - ✓ *Greener strategies for vector control*
  - ✓ *Transmission dynamics and model ecological niches based on climate and spatial epidemiology*
  - ✓ *Epidemiological mapping and outbreak/disaster investigations*
- ✓ **Community training, inclusion and awareness**



A Framework to Intersect Science and Diplomacy

Open Science - share knowledge, data, reagents

Effective and holistic team-based approaches - full spectrum of STEAM disciplines

Appropriate technologies - based on country/regional/global priorities

Remove Barriers (limited or no IP/Patents)

Cooperate to Decolonize the vaccine sciences with Transparency - leads to Trust Solidarity and Equity

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

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

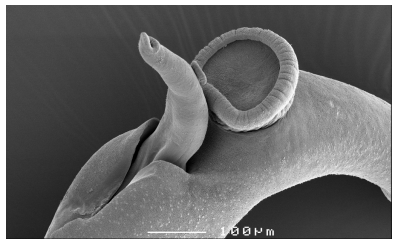
To build capacity for vaccine development locally and with foreign nations

To guide and influence vaccine policy and advocacy

A diverse vaccine development portfolio against neglected tropical and emerging infections

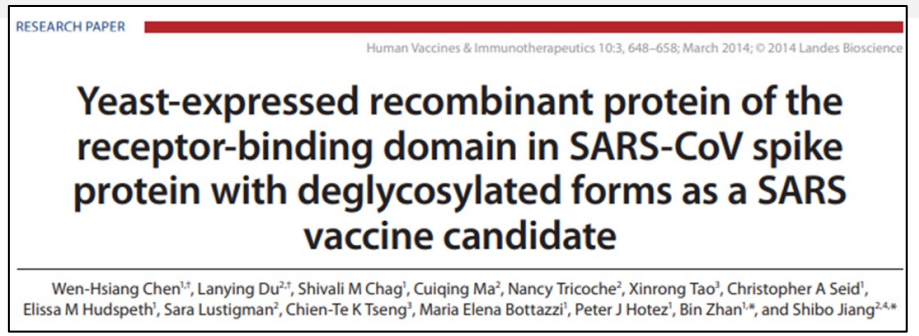
Portfolio and Major Accomplishments

- 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
- Developed innovative vaccines for emerging coronavirus infections: COVID-19, SARS and MERS
- Signed and implemented historic capacity building agreements with Brazil, Mexico, Malaysia and the Kingdom of Saudi Arabia



Adopting the Coronaviruses as Neglected Infections

- Coronavirus partnerships launched in 2011 when interest in coronavirus research was declining
- NIH/NIAID and seed funding to fashion a SARS vaccine product - SARS/MERS (2011-16)
- Focused on low-cost using microbial fermentation in yeast
- Ensured scalability, ease of production, regulatory enabled path and affordability
- Leveraged SARS/MERS lessons towards COVID-19 (2020)

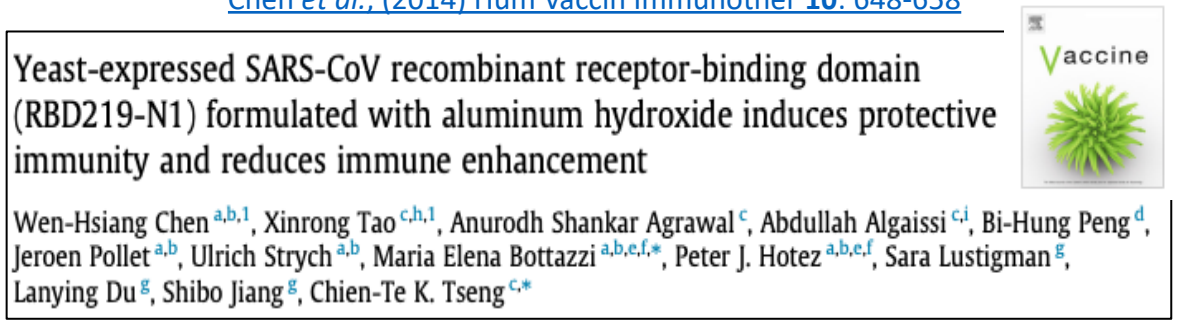

RESEARCH PAPER

Human Vaccines & Immunotherapeutics 10:3, 648–658; March 2014; © 2014 Landes Bioscience

Yeast-expressed recombinant protein of the receptor-binding domain in SARS-CoV spike protein with deglycosylated forms as a SARS vaccine candidate

Wen-Hsiang Chen[1,†], Lanying Du[2,†], Shivali M Chag[1], Cuiqing Ma[2], Nancy Tricoche[2], Xinrong Tao[3], Christopher A Seid[1], Elissa M Hudspeth[1], Sara Lustigman[2], Chien-Te K Tseng[3], Maria Elena Bottazzi[1], Peter J Hotez[1], Bin Zhan[1,*], and Shibo Jiang[2,4,*]

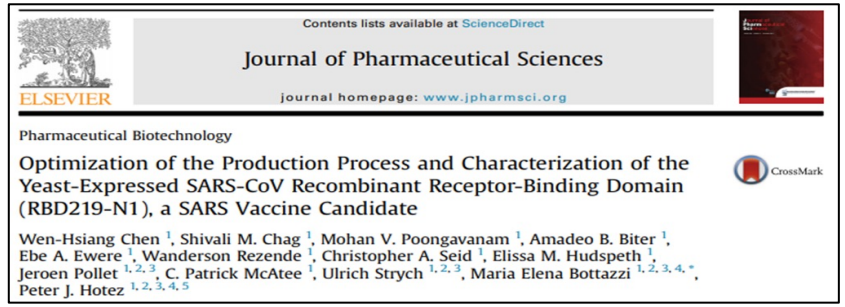
Chen *et al.*, (2014) Hum Vaccin Immunother **10**: 648-658


Yeast-expressed SARS-CoV recombinant receptor-binding domain (RBD219-N1) formulated with aluminum hydroxide induces protective immunity and reduces immune enhancement

Wen-Hsiang Chen [a,b,1], Xinrong Tao [c,h,1], Anurodh Shankar Agrawal [c], Abdullah Algaissi [c,i], Bi-Hung Peng [d], Jeroen Pollet [a,b], Ulrich Strych [a,b], Maria Elena Bottazzi [a,b,e,f,*], Peter J. Hotez [a,b,e,f], Sara Lustigman [g], Lanying Du [g], Shibo Jiang [g], Chien-Te K. Tseng [c,*]

Vaccine

https://europepmc.org/backend/ptpmcrender.fcgi?accid=PMC7508514&blobtype=pdf


Contents lists available at ScienceDirect

Journal of Pharmaceutical Sciences

journal homepage: www.jpharmsci.org

ELSEVIER

Pharmaceutical Biotechnology

Optimization of the Production Process and Characterization of the Yeast-Expressed SARS-CoV Recombinant Receptor-Binding Domain (RBD219-N1), a SARS Vaccine Candidate

Wen-Hsiang Chen [1], Shivali M. Chag [1], Mohan V. Poongavanam [1], Amadeo B. Biter [1], Ebe A. Ewere [1], Wanderson Rezende [1], Christopher A. Seid [1], Elissa M. Hudspeth [1], Jeroen Pollet [1,2,3], C. Patrick McAtee [1], Ulrich Strych [1,2,3], Maria Elena Bottazzi [1,2,3,4,*], Peter J. Hotez [1,2,3,4,5]

Chen *et al.*, (2017) J. Pharm. Sci. **106**: 8 1961-1970

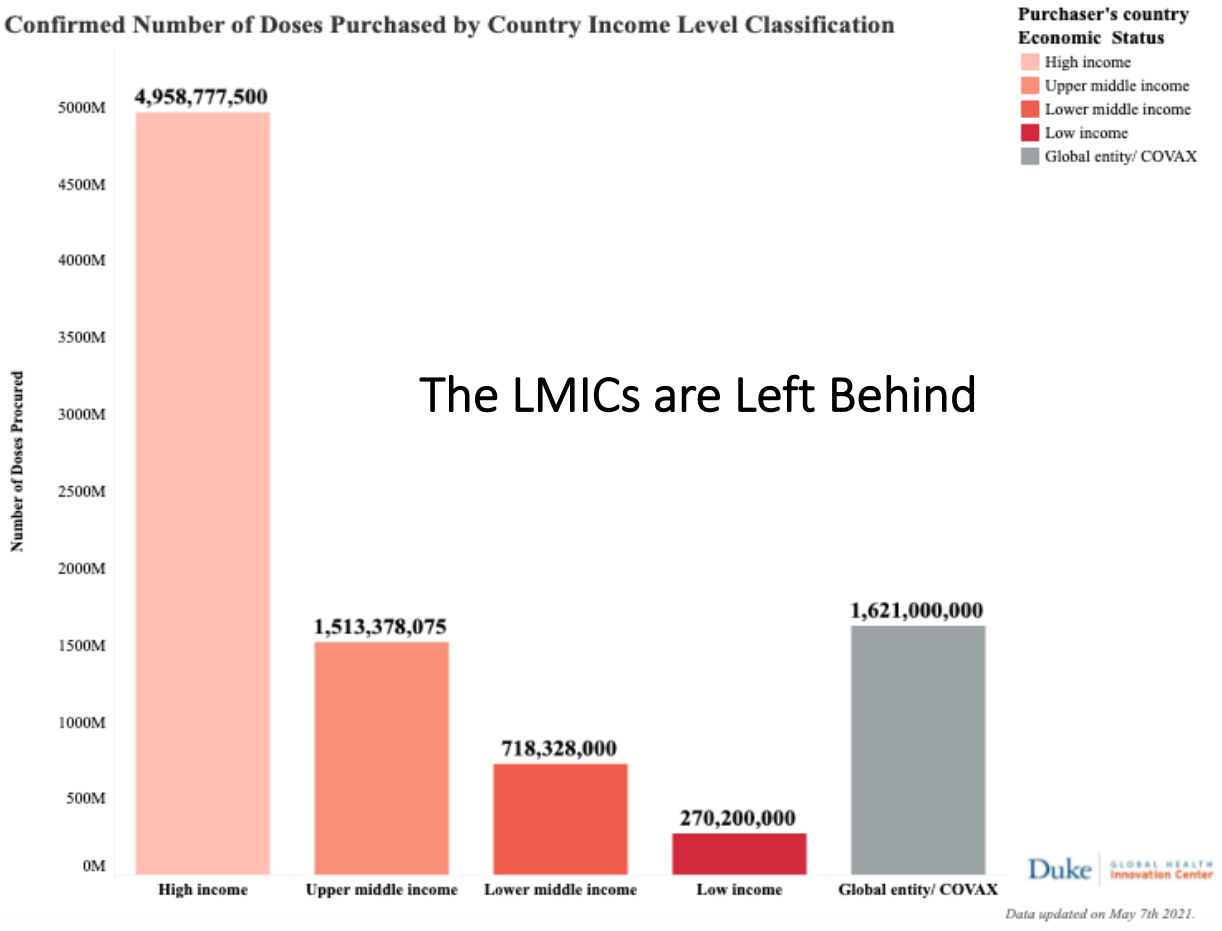
Grant: R01AI098775, AI14087201

PLoS NEGLECTED TROPICAL DISEASES
a peer-reviewed open-access journal published by the Public Library of Science

Will COVID-19 become the next neglected tropical disease?

Peter J. Hotez, Maria E. Bottazzi, Sunit K. Singh, Paul J. Brindley, Shaden Kamhawi

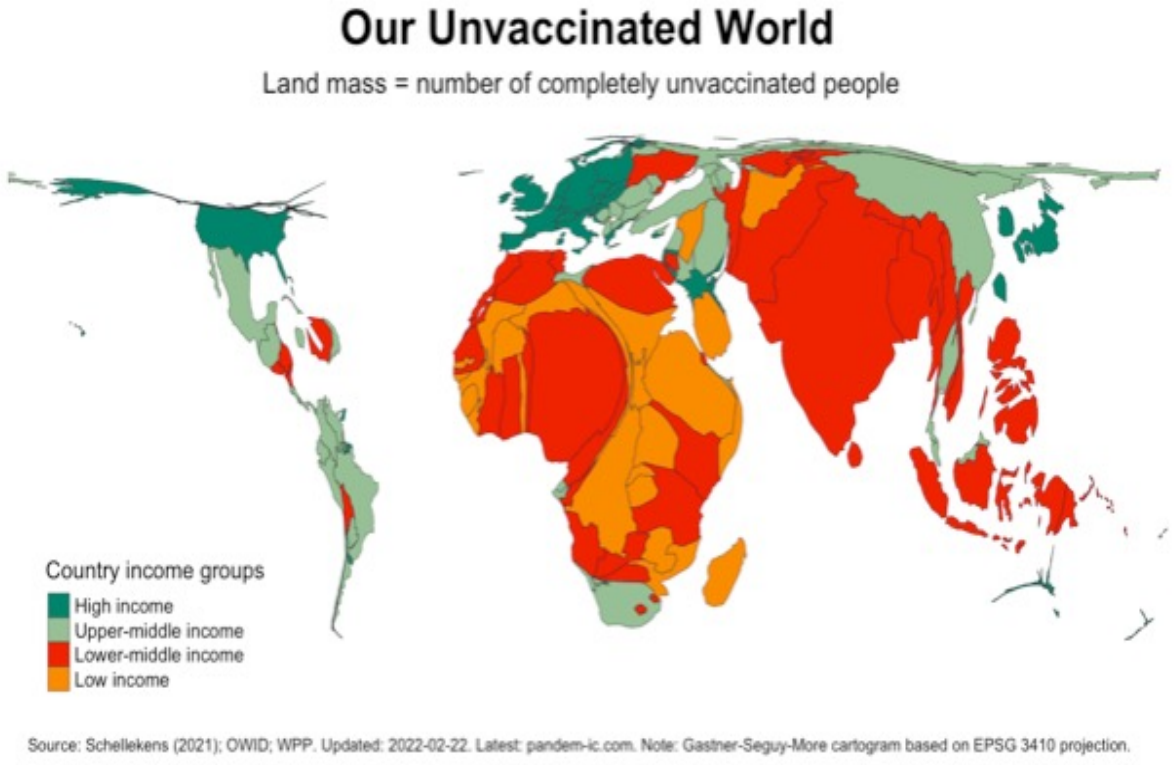
Published: April 10, 2020 • https://doi.org/10.1371/journal.pntd.0008271



The LMICs are Left Behind

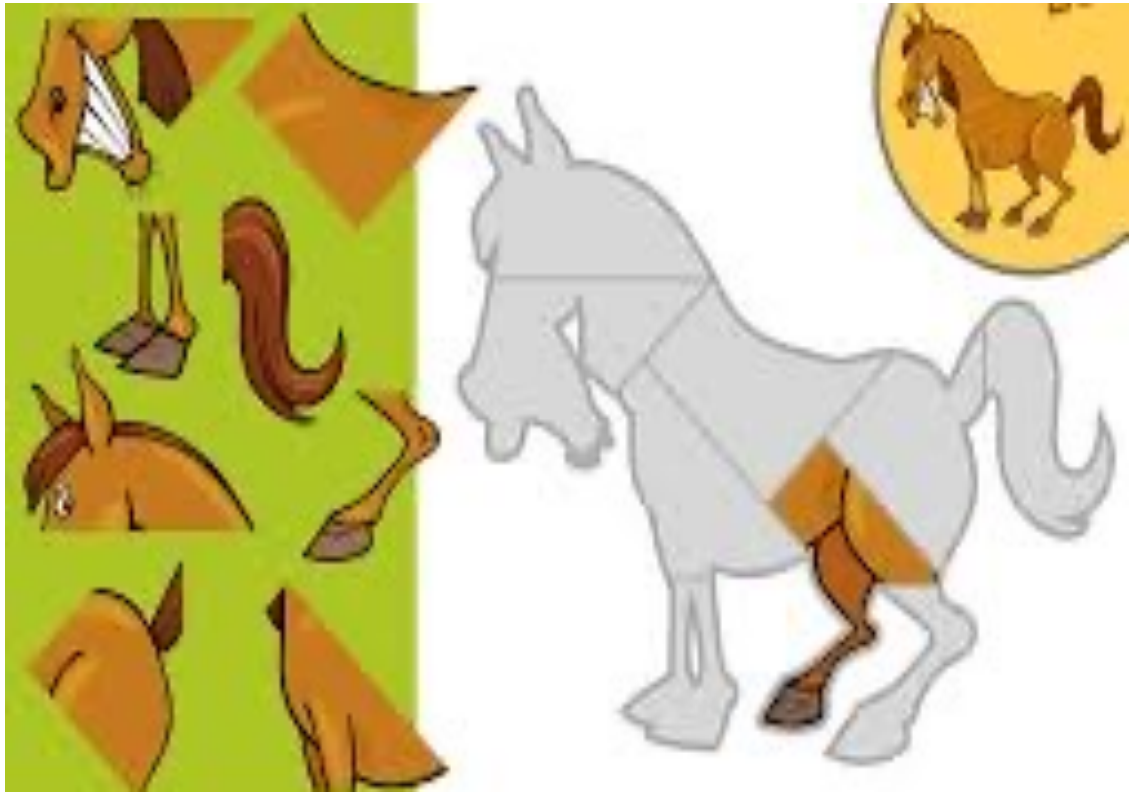
https://launchandscalefaster.org/covid-19/vaccineprocurement

Today 2.9 billion people have yet to receive their first vaccine shot against COVID-19. The chart below shows where they live.



https://pandem-ic.com/mapping-our-unvaccinated-world/

A COVID-19 Vaccine for Global Access



PHASE 3 | EMERGENCY USE IN INDIA, BOTSWANA

Baylor College of Medicine

Texas Children's Hospital

BE Biological E. Limited
Celebrating Life Every Day

DYNAVAX
INNOVATING IMMUNOLOGY

VACCINE NAME: Corbevax

EFFICACY: Over 90%

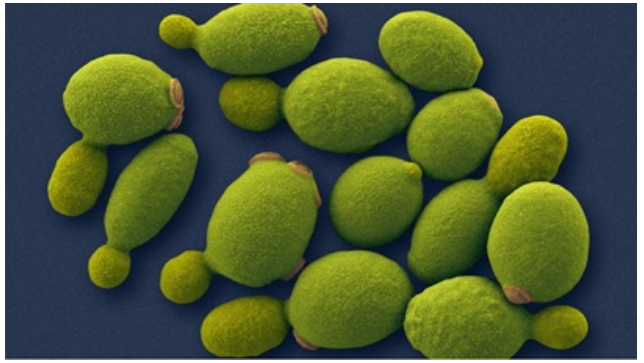
The World's COVID-19 Vaccine

Texas Children's Hospital

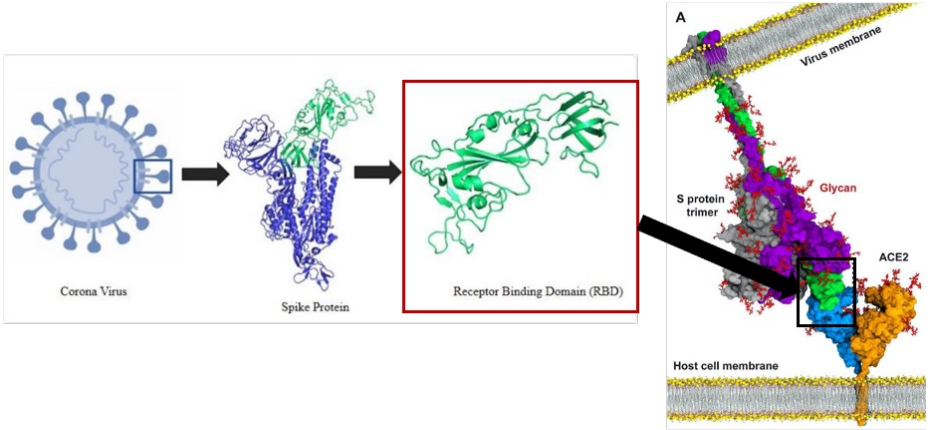
Target the SARS CoV-2 Receptor Binding Domain

What we do:

- Engineer yeast-produced recombinant RBD vaccine antigens – **THE STARTER KITS**
  - Production of seeds and cell banks fully characterized for ancestral & variants strains
- Process development, formulation and preclinical testing: scale-up to 10L production, purification design – **THE RECIPES**
- Develop and qualify analytical (biochemical/biophysical) and functional release and stability indicating assays - **THE ASSAYS FOR QUALITY AND STABILITY**
- Technology transfer to pilot and/or industrial manufacturers – **WE SHARE WIDELY – NO PATENTS**



Pichia pastoris



US-India partnership for a COVID-19 People's Vaccine

Technology Transfer

Biological E. Limited
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The TCH/Baylor/BioE Vaccine:
Receptor-binding domain (RBD) SARS-CoV2 spike protein expressed in yeast (*Pichia pastoris*)

INDIAN EXPRESS N. D. 5/6/2021

SIMPLY PUT

How Corbevax is different

India has placed an advance order for 300 million doses of Corbevax. How does this Covid-19 vaccine work, and how does it differ from others? What could the order mean for India's vaccination programme?

PRABHA RAGHAVAN
NEW DELHI, JUNE 4

INDIA HAS placed an advance order to block 300 million doses of a new Covid-19 vaccine, Corbevax, from Hyderabad-based company Biological E. What is this vaccine, and why is it important for India?

How it works

Corbevax is a "recombinant protein subunit" vaccine, which means it is made up of a specific part of SARS-CoV-2 — the spike protein on the virus's surface.

The spike protein allows the virus to enter the cells in the body so that it can replicate and cause disease. However, when this protein is alone is given to the body, it is not expected to be harmful as the rest of the virus is absent. The body is expected to develop an immune response against the injected spike protein. Therefore, when the real virus attempts to infect the body, it will already have an immune response ready that will make it unlikely for the person to fall severely ill.

Although this technology has been used for decades to make hepatitis B vaccines, Corbevax will be among the first Covid-19 vaccines to use this platform. Novavax has also developed a protein-based vaccine, which is still waiting for emergency use authorisation from various regulators.

How it was made

While it is indigenously produced, Corbevax's beginnings can be traced to the Baylor College of Medicine's National School of Tropical Medicine. The School had been working on recombinant protein vaccines for coronaviruses SARS and MERS for a decade.

"We knew all the techniques required to produce a recombinant protein/vaccine for coronaviruses at high levels of efficiency and integrity," said Dr Peter Hotez, Professor and Dean at the School.

When the genetic sequence for SARS-CoV-2 was made available in February 2020, researchers at the School pulled out the sequence for the gene for the spike protein, and worked on cloning and engineering it. The gene was then put into yeast, so that it could manufacture and release copies of the protein. "It's actually similar to the production of beer. Instead of releasing alcohol, in this case, the yeast is releasing the recombinant protein," Dr Hotez said.

After this, the protein was purified to remove any remnants of the yeast "to make it pristine". Then, the vaccine was formulated using an adjuvant to better stimulate the immune response.

Most of these ingredients are cheap and easy to find.

THE MANUFACTURER

BIOLOGICAL E, headquartered in Hyderabad, was founded by Dr D V K Raju in 1953 as a biological products company that pioneered the production of heparin in India. By 1962, it forayed into the vaccines space, producing DPT vaccines on a large-scale. Today, it is among the major vaccine makers in India and, by its own claim, the "largest" tetanus vaccine producer in the world.

It has seven WHO-prequalified shots, including a five-in-one vaccine against diphtheria, tetanus, pertussis, hepatitis B and haemophilus influenza type-b infection. Its vaccines are supplied to over 100 countries and it has supplied more than two billion doses in the last 10 years alone.

Since 2013, the company has been under the management of Mahima Datla — the third generation of the founding family. During her time as managing director, the company has received WHO prequalification of its Japanese encephalitis, DTwP and Td as well as measles and rubella vaccines and also commenced commercial operations in the US.

In August, BCM transferred its production cell bank for this vaccine to Biological E, so that the Hyderabad-based company could take the candidate through trials. The vaccine has received approval for phase 3 trials, which the government expects will be over by July.

Biological E is also expected to scale up production for the world.

How it's different

Other Covid-19 vaccines approved so far are either mRNA vaccines (Pfizer and Moderna), viral vector vaccines (AstraZeneca-Oxford/Covishield, Johnson & Johnson and Sputnik V) or inactivated vaccines (Covaxin, Sinovac-CoronaVac and Sinopharm's SARS-CoV-2 Vaccine-Vero Cell).

Inactivated vaccines, which include killed particles of the whole SARS-CoV-2 virus, attempt to target the entire structure of the virus. On the other hand, Corbevax, like the mRNA and viral vector Covid-19 vaccines, targets only the spike protein, but in a different way.

Viral vector and mRNA and vaccines use a code to induce our cells to make the spike proteins against which the body have to build immunity. "In this case (Corbevax), we're actually giving the protein," said Dr Hotez.

Like most other Covid-19 vaccines, Corbevax is administered in two doses. However, as it is made using a low-cost platform, it is also expected to be among the cheapest available in the country.

Why it matters

This is the first time the Indian government has placed an order for a vaccine that has not received emergency use authorisation, paying Rs 1,500 crore in advance to block an order that could vaccinate 15 crore Indian citizens. The Centre has provided major preclinical and clinical trial support towards the vaccine's development, including against-risk of Rs 100 crore from the Department of Biotechnology.

A major reason for India placing such a big order is the difficulties it is facing in enhancing vaccine supplies. While the US, UK and the EU had made advance payments and at-risk investments into vaccines like Pfizer, AstraZeneca and Moderna, India waited until after its first two vaccines were approved before placing limited orders. Even after the government eased regulatory requirements for foreign vaccines, it did not receive a speedy response from companies like Pfizer and Moderna. their supplies already blocked through orders from other countries. India is currently in negotiations for a limited supply of Pfizer's vaccine, and expecting to receive up to two billion doses of Covid vaccines by December this year. Given the ease with which it can be mass produced, Corbevax could make up a sizeable portion of this expected supply.

- Scaled up protein production to 1.2 Billion doses
- Formulation capacity of 140 Million vaccine doses per month
- Combined Phase1/2 in 7 India sites
- Phase 3 immuno-bridging superiority trial
- Pediatric and Booster Trials
- EUA Dec 28, 2021

https://doi.org/10.1101/2022.03.08.22271822
https://doi.org/10.1101/2022.03.20.22271891
https://www.medrxiv.org/content/10.1101/2022.04.20.22274076v1

More than 35 million kids vaccinated with CORBEVAX

Biological E. Limited @biological_e · 7h

On #NationalVaccinationDay, Ms Mahima Datla, MD of Biological E. Limited, met with the 13-year-old boy, Harsha Kumar, the first recipient of #TheSureShot by #CORBEVAX, at a Vaccination Centre in Hyderabad on March 16, 2022.

12-14 Years

1st Dose	2nd Dose
3,49,17,732	1,88,71,349
(1,10,292 in last 24 Hours)	(2,57,627 in last 24 Hours)

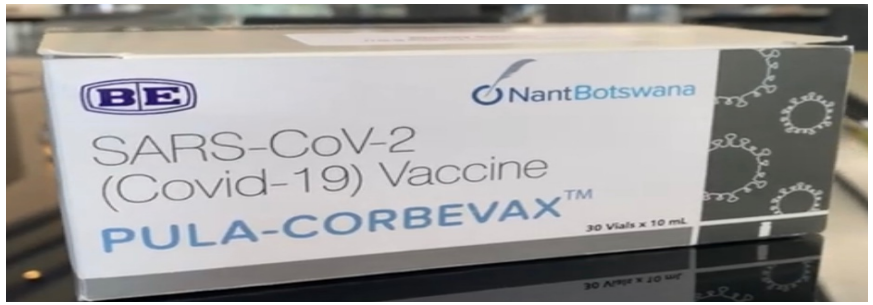
https://www.mohfw.gov.in/pdf/CummulativeCovidVaccinationReport10Jun2022.pdf

HEALTH

DCGI approves Corbevax for children aged 5-12 years, Covaxin for 6-12 years

Botswana Approves Corbevax Covid Vaccine, Plans Local Output

Mbongeni Mguni, Bloomberg News



NEWS / INDIA NEWS / Corbevax Gets Nod As Booster Jab For Covaxin, Covish...

Corbevax gets nod as booster jab for Covaxin, Covishield recipients

Swati Bharadwaj / TNN / Updated: Jun 5, 2022, 01:24 IST

SHARE AA

India to vaccinate children aged 5-12 as Covid infections surge

Issued on: 01/05/2022 - 15:37

Children attend a class at the Sangharsh Vidya Kendra school at a slum area on the outskirts of Jammu, India. AP - Channi Anand

We are Partners for the World

Biological E. Limited
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ImmunityBio

Incepta Pharmaceuticals Ltd

A health worker holds a syringe during a Covid-19 vaccination program in Tanah Abang market, Central Jakarta on Feb. 17, 2021. (JG Photo/Yudha Baskoro)

BUMN Covid-19 Vaccine Kicks Off Phase 3 Clinical Trial

BY :JAYANTY NADA SHOFA
JUNE 09, 2022

bioFarma

Vegan, scalable, stable technology

Excellent safety profile

Highly immunogenic in humans

Neutralizing Ab GMTs indicative of vaccine effectiveness of >80% based on immunological correlates

Highly durable and long last-lasting virus neutralizing antibodies

EUA based on a Ph 3 superiority trial compared to AstraZeneca vaccine

Works against a broad range of variants of concern

Lowest cost (Rs 250 = $1.90 per dose)

Vaccines for the unvaccinated

Vaccines for additional doses and boosters

Vaccines for pediatric populations

Vaccines with broader and long-term protection

Vaccines for future coronavirus (unknown)

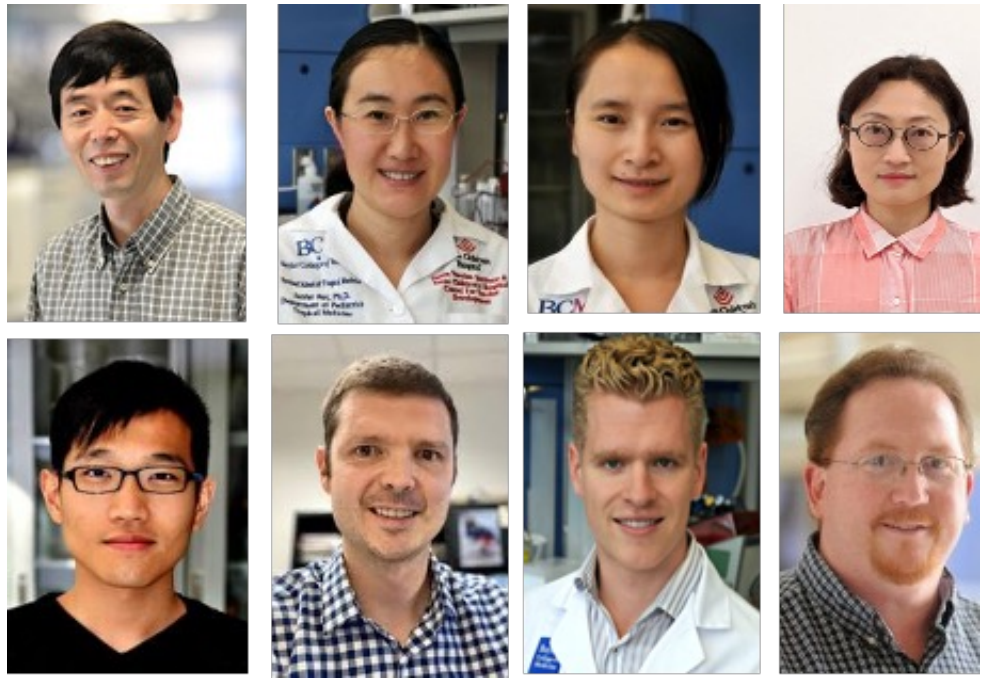
THANK YOU

Maria Elena Bottazzi, PhD
Co-Director
bottazzi@bcm.edu

Peter Hotez, MD, PhD
Co-Director
hotez@bcm.edu

Ulrich Strych, PhD
Strategic Initiatives, Business & Program Development
strych@bcm.edu

Dr. Kimata Lab



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