

Baylor  
College of  
Medicine



Texas Children's  
Hospital<sup>®</sup>



HAGLER INSTITUTE  
FOR ADVANCED STUDY  
*at Texas A&M University*



RICE UNIVERSITY'S  
BAKER INSTITUTE  
FOR PUBLIC POLICY

# ***COVID-19 Meets the Antivaccine Movement***

Peter Hotez MD PhD

Texas Children's Hospital Endowed  
Chair in Tropical Pediatrics

Dean, National School of Tropical Medicine  
at Baylor College of Medicine

University Professor, Baylor University

Hagler Institute of Advanced Studies, Texas  
A&M University

**@PeterHotez**

# Under 5 Child Deaths 2000-2017

## GBD 2017

Sebastiao Salgado

### 2000

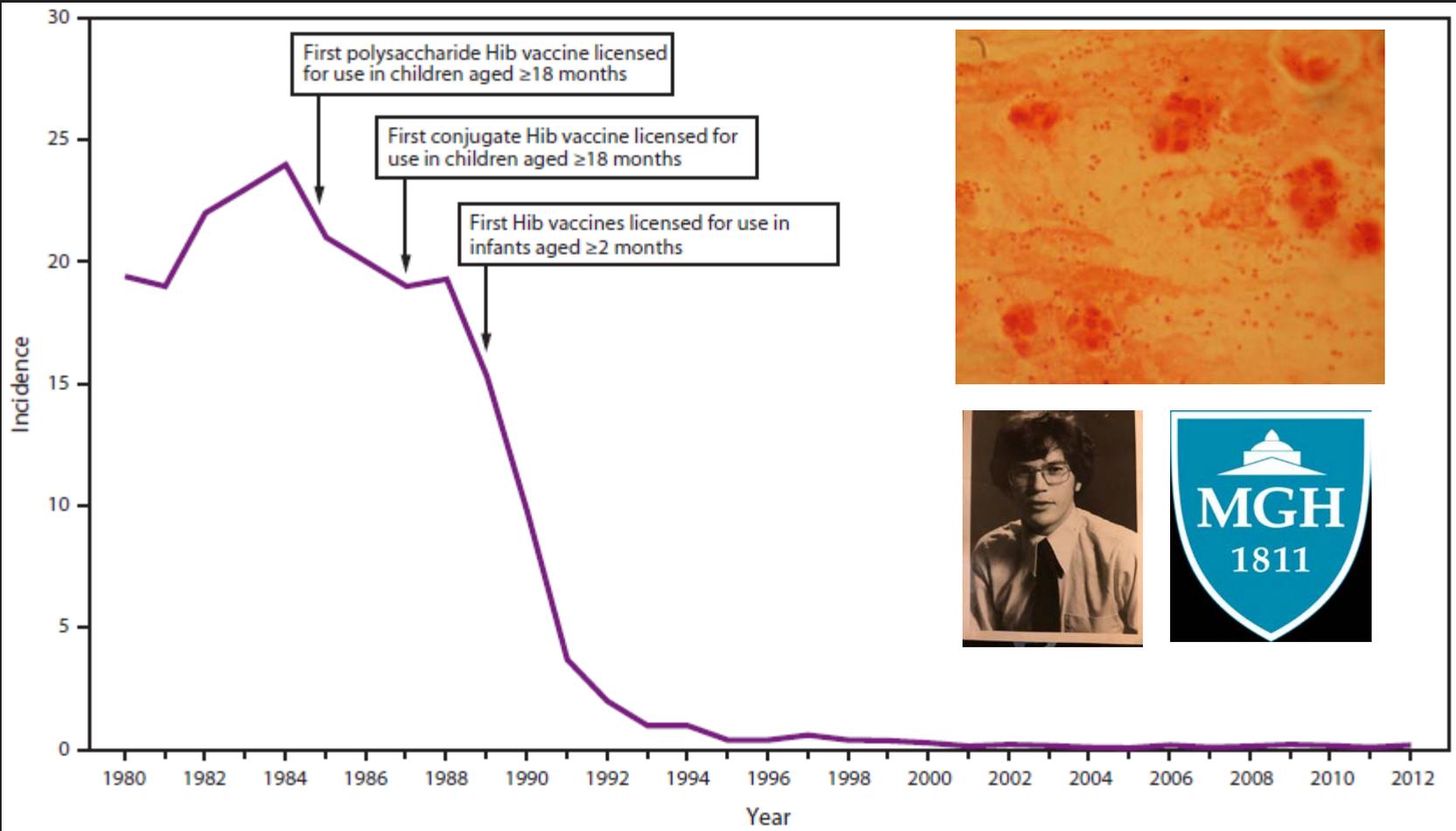
- Measles 478,727
- Pertussis 138,048
- Tetanus 105,333
- H. flu 86,104
- Diphtheria 10,413

### 2017

- Measles 83,438 (-83%)
- Pertussis 86,091 (-38%)
- Tetanus 18,623 (-82%)
- H.flu 36,185 (-58%)
- Diphtheria 2,914 (-72%)



# Incidence of Hib in USA



# New Global “Hot Zones” of Vaccine-Preventable & Neglected Tropical Diseases NTDs

*Where political instability combines with climate change, urbanization, deforestation, or antiscience*



# War, Political Collapse, Climate Change, Urbanization

- Arabian Peninsula

- Venezuela

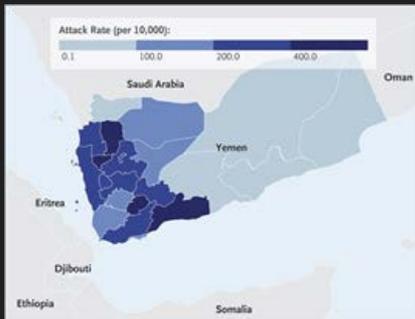
“Aleppo Evil”



Syria and Iraq



Cholera in Yemen



The return of measles to South America



The “malaria mines”



The Yanomami and other indigenous people

# War, Political Collapse, Climate Change, Urbanization

- Africa Un-Wars

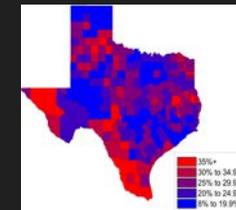
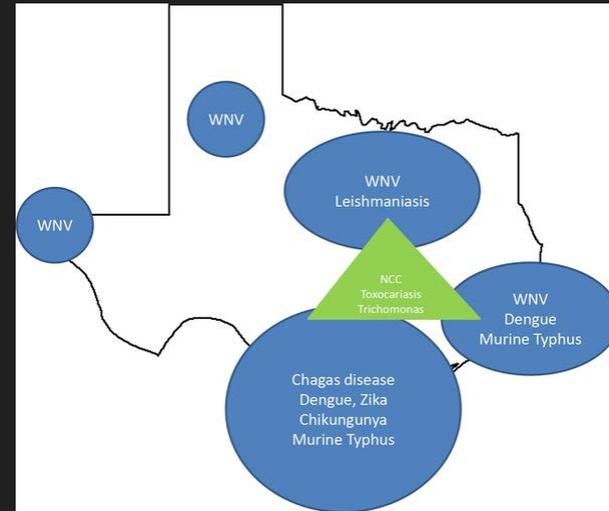


Boko Haram



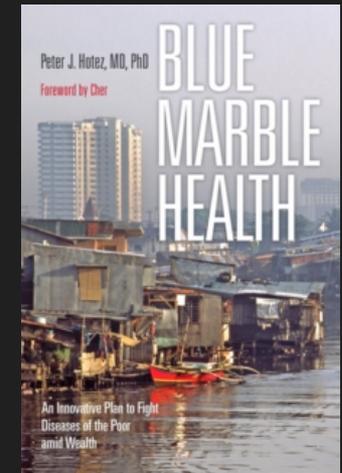
DR Congo

- Texas + Gulf Coast



# SHIFTING POVERTY: “Blue Marble Health”

- Neglected diseases of the poor living amidst wealth
- The “poorest of the rich”
- A new framework for global science policy and the poverty-related diseases



# COVID19 and the G20 Nations

Soon 20 million cases

United States

Brazil

Russia

India

UK

Spain

Italy



POVERTY and the IMPACT  
OF COVID-19:

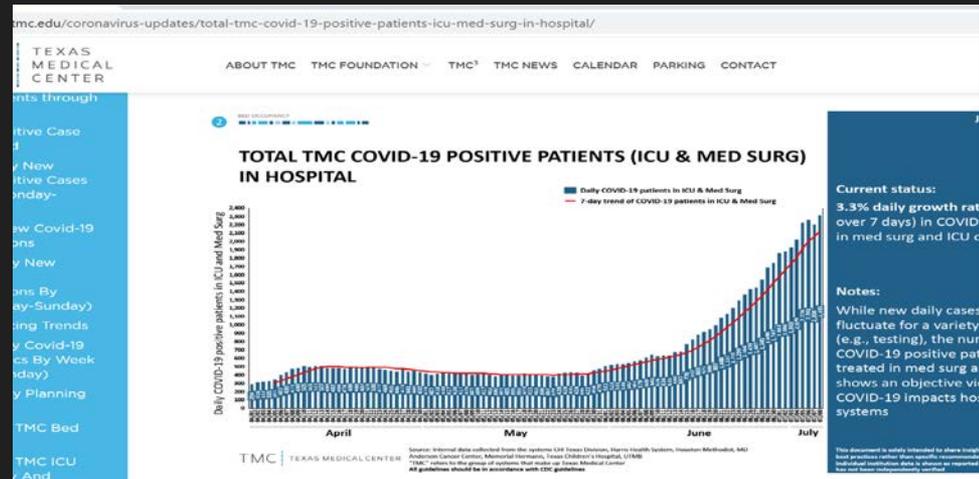
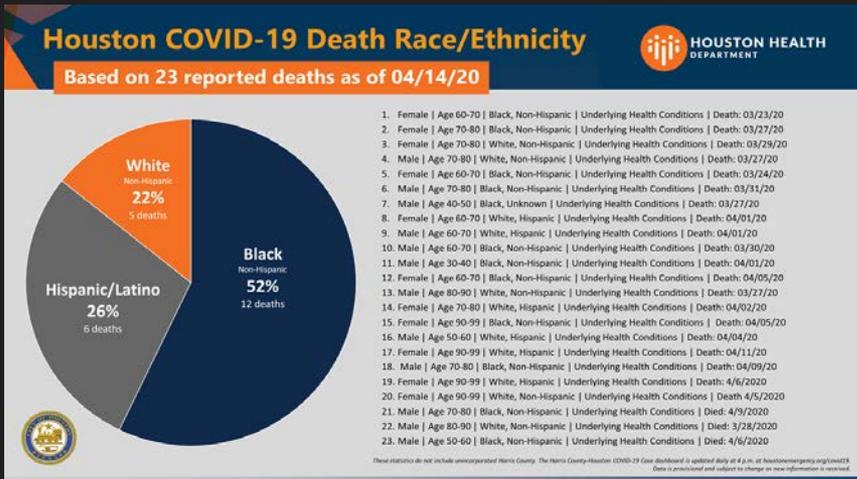
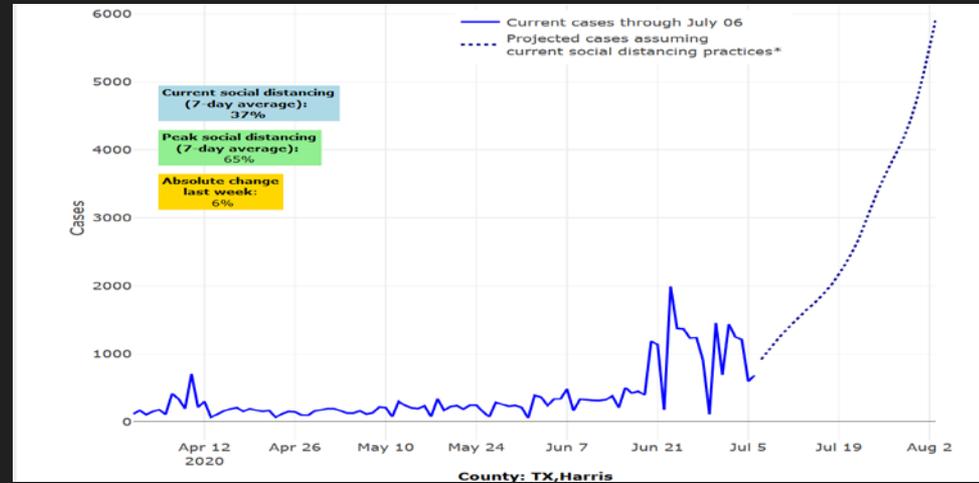
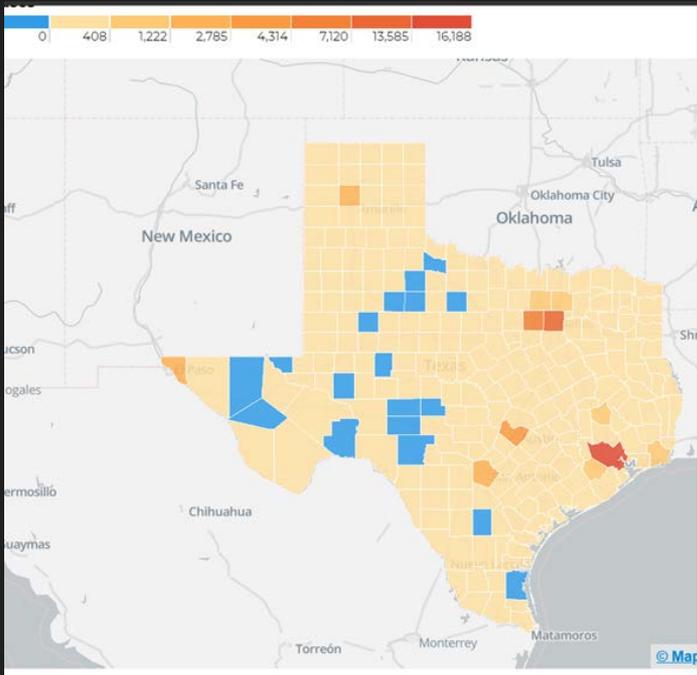
*The Blue-Marble Health Approach*

Peter J. Hotez, MD, PhD.

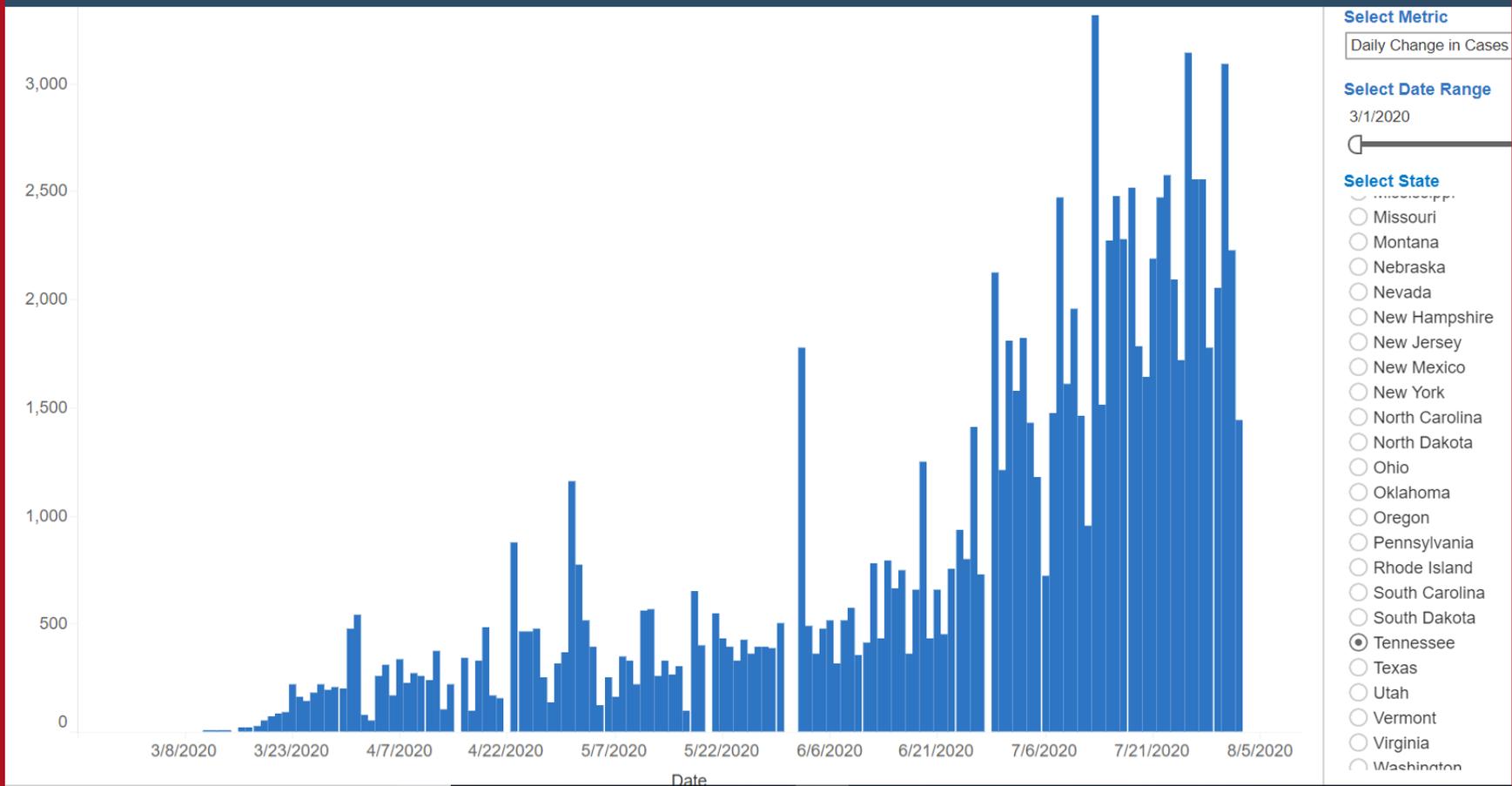
 JOHNS HOPKINS  
UNIVERSITY PRESS

PROJECT  
MUSE 

# Houston Texas, Summer 2020 COVID19 as a Health Disparity



# Tennessee



Select Metric

Daily Change in Cases

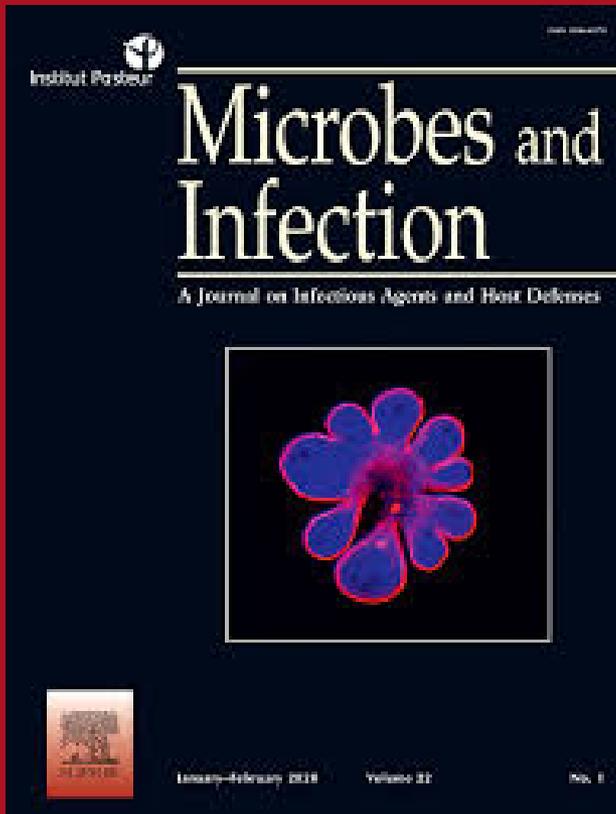
Select Date Range

3/1/2020

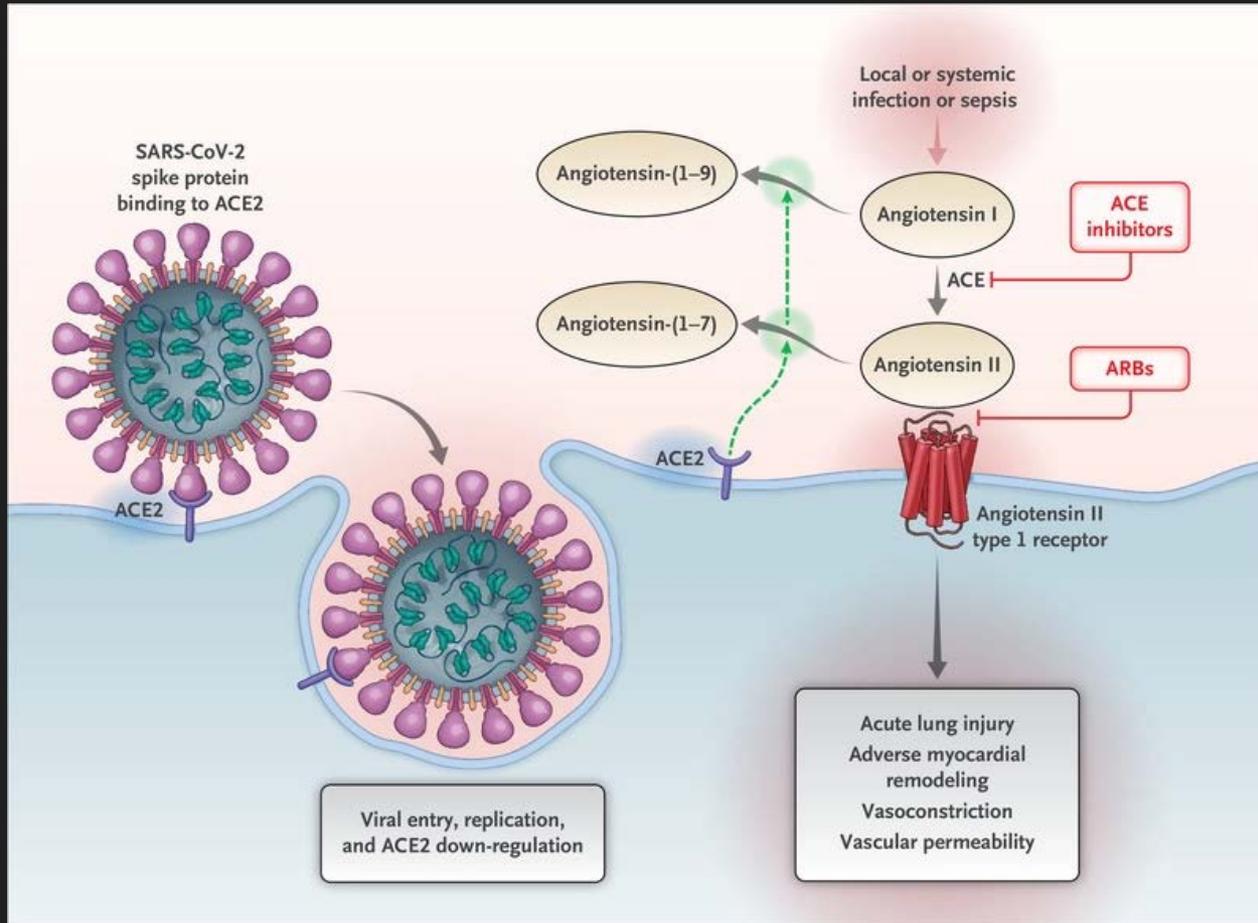
Select State

- Mississippi
- Missouri
- Montana
- Nebraska
- Nevada
- New Hampshire
- New Jersey
- New Mexico
- New York
- North Carolina
- North Dakota
- Ohio
- Oklahoma
- Oregon
- Pennsylvania
- Rhode Island
- South Carolina
- South Dakota
- Tennessee
- Texas
- Utah
- Vermont
- Virginia
- Washington

# An October 1 Recovery Plan



# SARS CoV and SARS CoV2 Bind to ACE2 Receptors



# SARS CoV2-COVID19 Vaccine Approaches

## 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

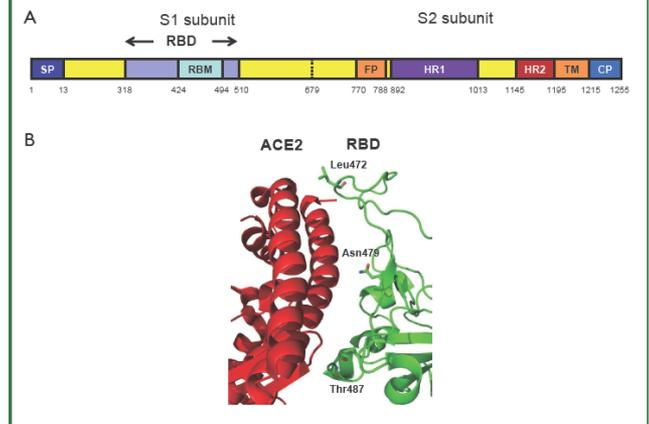
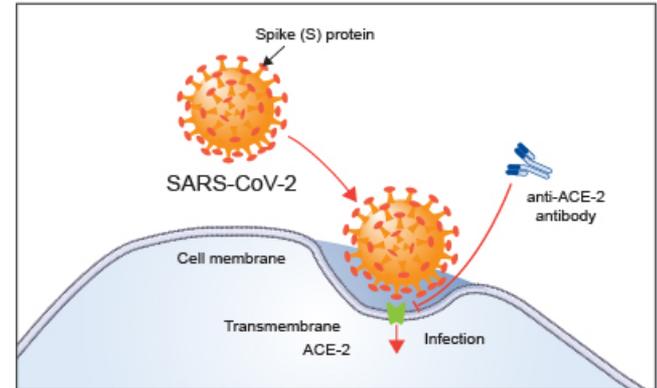


Nanoparticle  
(viral protein on particle)  
Novavax



Live attenuated  
Codagenix

Selected development programs





Texas Children's Hospital®

# Global Coronavirus Vaccine Initiative



Baylor College of Medicine  
NATIONAL SCHOOL OF TROPICAL MEDICINE



# Texas Children's CVD

- Low Cost
- Global Health Vaccines
  - Recombinant protein vaccines
  - Technology transfer to LMICs
  - Building vaccine development capacity in LMICs



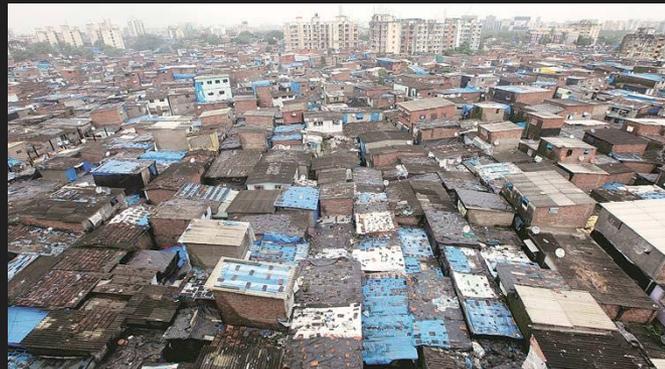
- Our Portfolio
  - Schistosomiasis
  - Hookworm
  - Onchocerciasis
  - Leishmaniasis
  - Chagas disease
  - Coronavirus infections
    - SARS and SARS 2
    - MERS

# COVID-19 in Latin America, India, Africa



**IN ECUADOR**

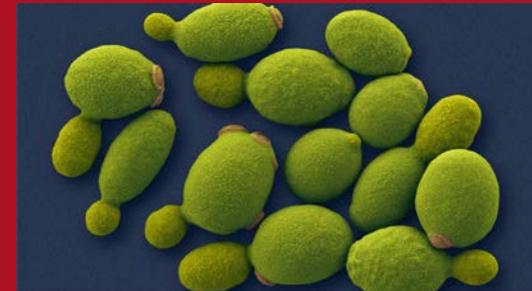
**CORPSES PILE  
ON STREETS,,,**



# Developing Low-Cost COVID19 Vaccines

## YEAST: *Pichia Pastoris*

Yeast Hepatitis B Vaccine:  
Bangladesh, Brazil, Cuba,  
India, Indonesia



SARS CoV RBD  
RBD219-N1

- cGMP Manufactured in 2016
- "Shovel ready" start of phase 1 clinical trial Q3 2020
- Investigational vaccine recommended for outbreak use in 2021

SARS CoV2 RBD

- cGMP manufacture targeted for Q3 2020
- Start of phase 1 clinical trial 2021
- Investigational vaccine recommended for outbreak use in 2022, possibly earlier

# CoV RBD219-N1 triggers a strong IgG and neutralizing antibody response

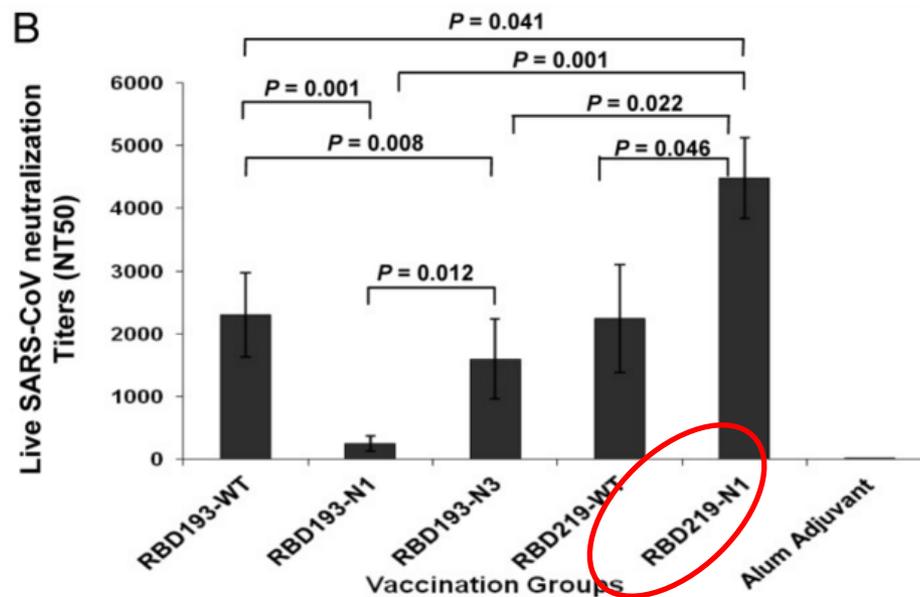
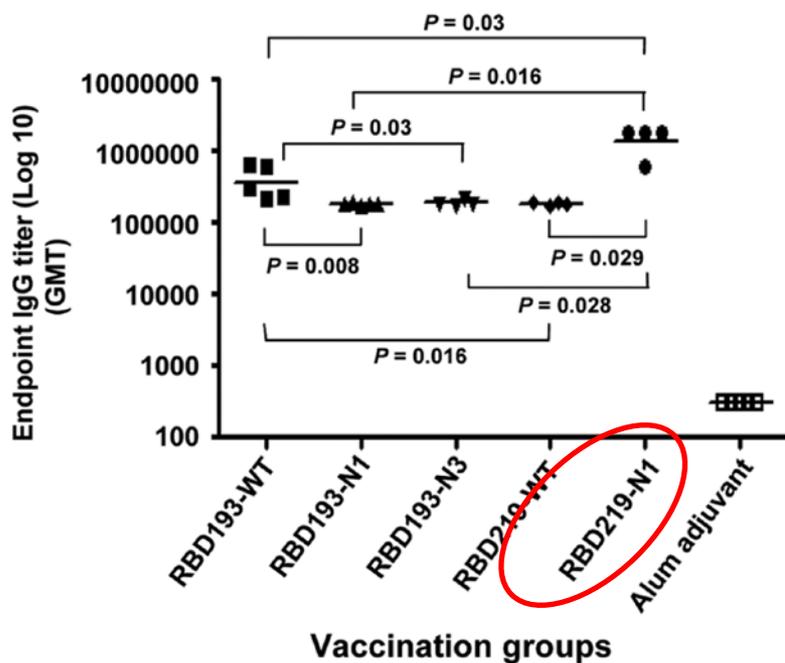


Route: s.c.

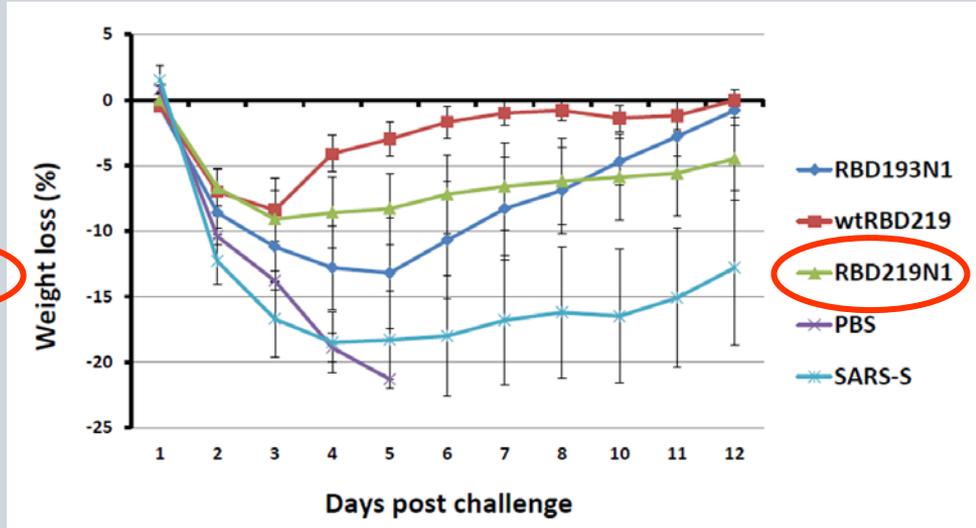
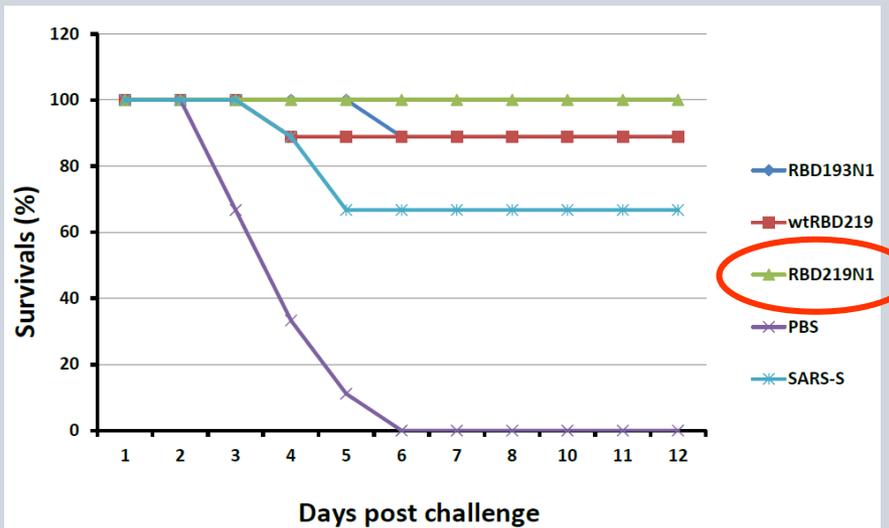
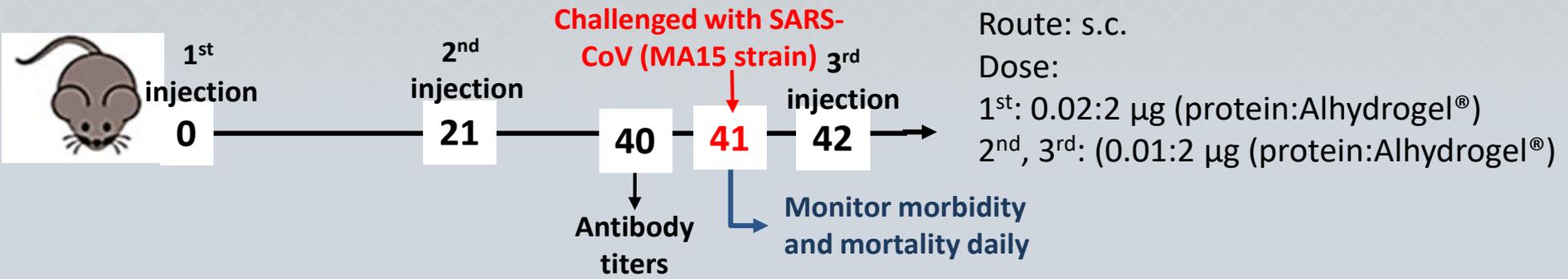
Dose:

1<sup>st</sup>: 0.02:2 μg (protein:Alhydrogel®)

2<sup>nd</sup>, 3<sup>rd</sup>: (0.01:2 μg (protein:Alhydrogel®))

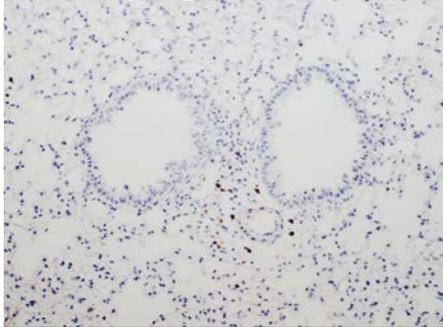


# Mice immunized with CoV RBD219-N1/Alhydrogel<sup>®</sup> showed 100% survival rate and less than 10% weight loss

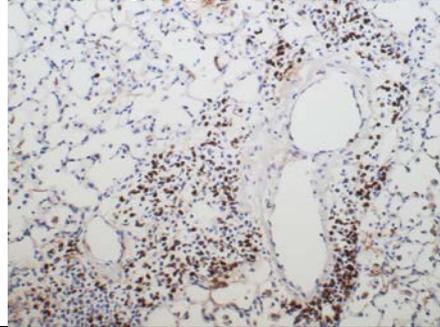


# CoV RBD219-N1/Alhydrogel<sup>®</sup> does not induce Eosinophilic Immune Enhancement

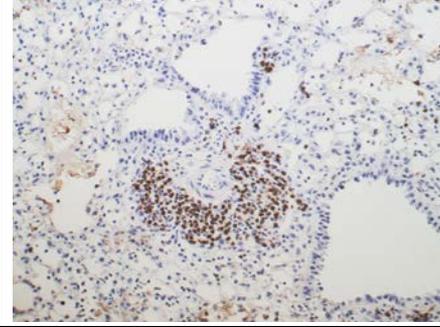
**A. Group 1 RBD (20,10,10);  
(RBD: Alhydrogel = 1:25)**



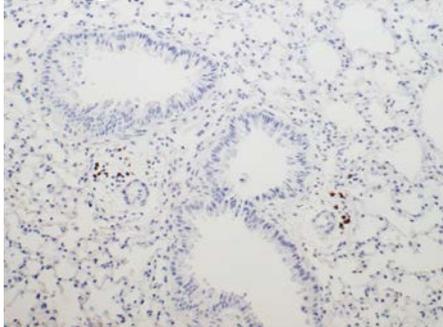
**B. Group 2 RBD (20,10,10);  
(RBD: Alhydrogel = 1:8)**



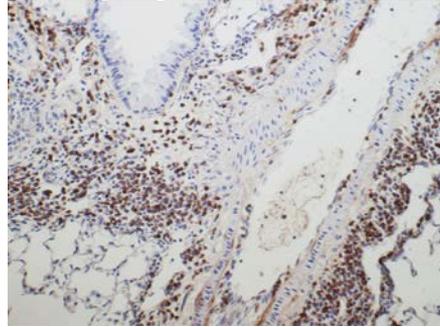
**C. Group 3 RBD (10,10,10);  
(RBD: Alhydrogel = 1:8)**



**D. Group 4 Alhydrogel alone**



**E. Group 5 Spike**



**Figure 7** Photomicrographs of lung tissue from BALB/c mice after challenge with SARS-CoV. (A) In group 1, a formulation of 0.2 mg/mL RBD in 5 mg/mL Alhydrogel<sup>®</sup> with the dose of 20 µg/10 µg/10 µg RBD for prime/1st boost/2nd boost was used for immunization, respectively. (B) In group 2, a formulation of 0.2 mg/mL RBD in 1.6 mg/mL Alhydrogel<sup>®</sup> was tested with a dosing regimen of 10 µg/10 µg/10 µg RBD for prime/1st boost/2nd boost. In group 3, 10 µg RBD were used for all three immunizations. (D) Alhydrogel<sup>®</sup> alone in group 4 was used as a negative control while (E) adjuvanted preformulated SARS-S protein (3 µg) in group 5 was used as a positive control.

# Developing Low-Cost COVID19 Vaccines

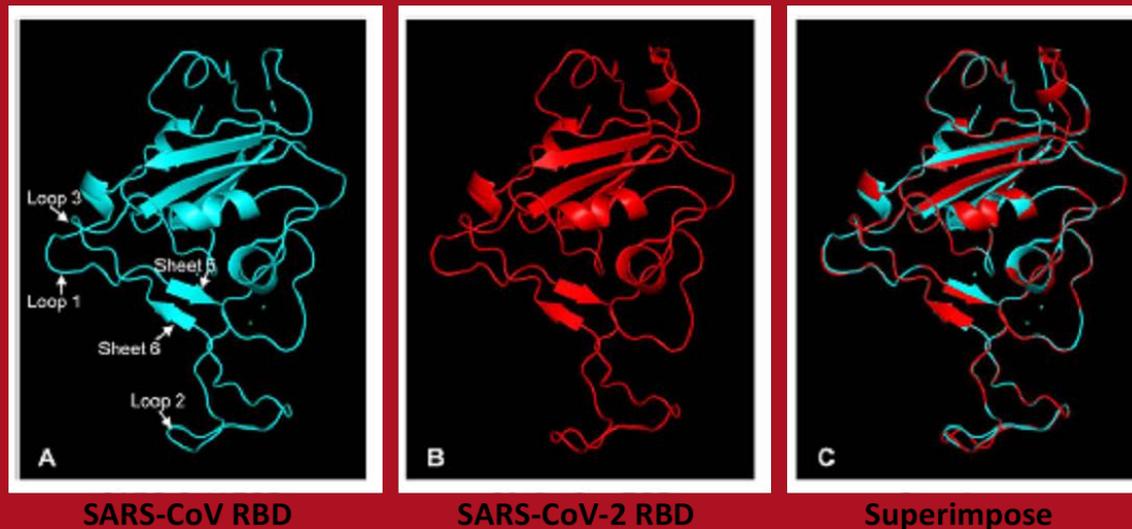
Receptor Binding Domain of Spike Protein

Induce high titer neutralizing antibodies

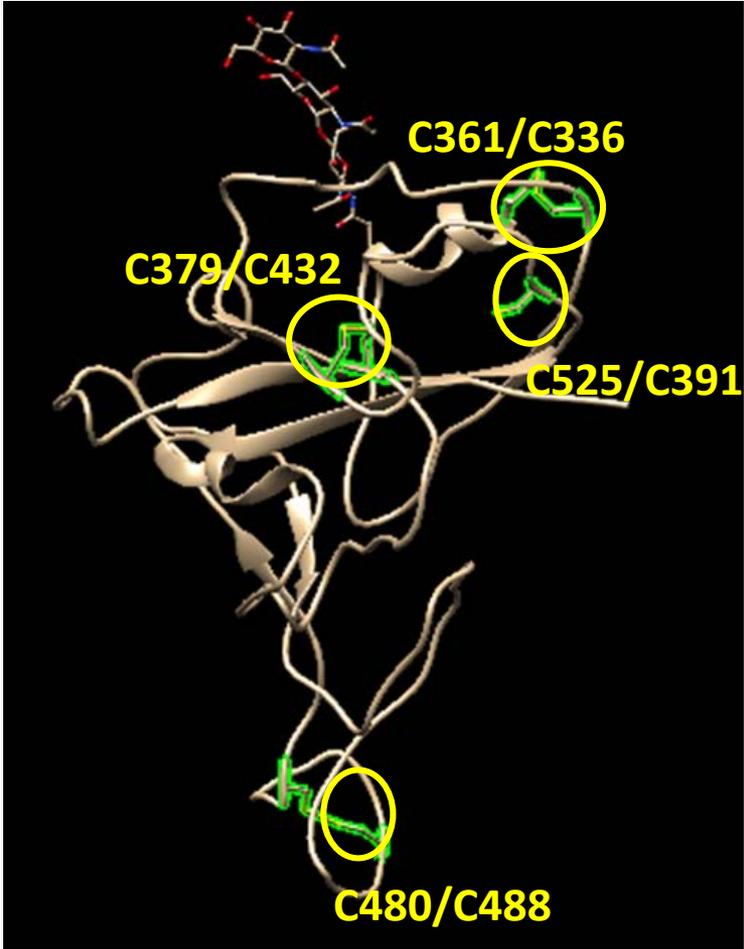
Removal of “immune enhancing” Spike (S) protein epitopes

Yeast expression system used for recombinant hepatitis B vaccine produced in Brazil, India

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 (C).

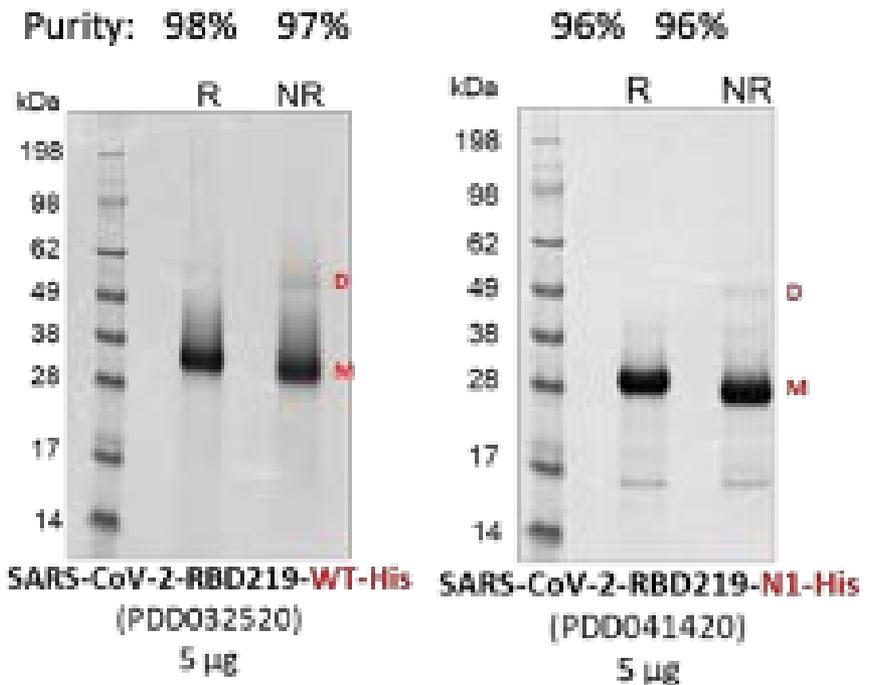


# Cloning and expression strategy for CoV-2 RBD219



NITNLCPFGVEVFNATRFASVYAWNRRKRISNCVADYSVLYNSASFSTFKCYGVSPTKLNDLCFITNVYADSFVIRGDEVQRQIAPGQTGKIADYNYKLPDDFTGCVIAWNSNNLDSKVGGNYNLYRLFRKSNLKPFERDISTEIIYQAGSTPCNGVEGFNCYFPLQSYGFQPTNGVGYQPYRVVVLSEFELLHAPATVCGPKKSTNLVKNKCVNFNFNGLTGT

C361/C336    C525/C391    C379/C432    C480/C488  
 C538/C590

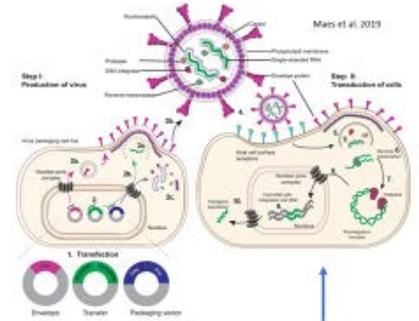
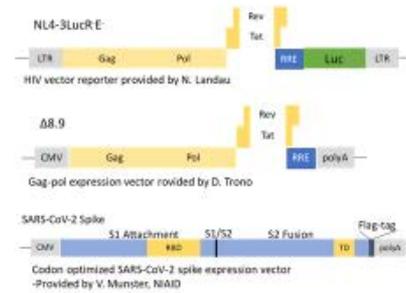


RBD219-WT; RBD219-WT-C1  
 RBD219-N1; RBD219-N1-C1  
 RBD196-WT; RBD196-N1

# Antibody to SARs CoV2 RBD219N1C1N expressed in yeast neutralizes pseudovirus



## Spike/Lentiviral SARS-CoV2 Pseudotyped Virions

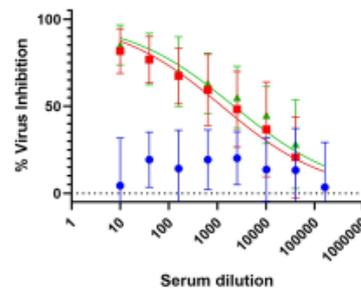


Target cell for these assays:  
293T cells transiently transfected  
With human ACE2 construct

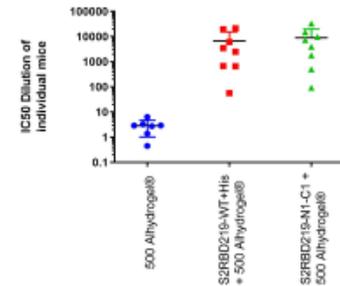
### Pseudovirus assay: Individual mouse samples from groups 1, 2 and 3

(Alum=Alhydrogel)

#### Neutralizing Pseudovirus Assay



- Group1: 500µg Alum IC50: N/A
- group2: 500µg Alum/25µg S2RBD219-wt IC50: 1:1253
- group3: 500µg Alum/25µg S2RBD219-N1C1 IC50: 1:2220



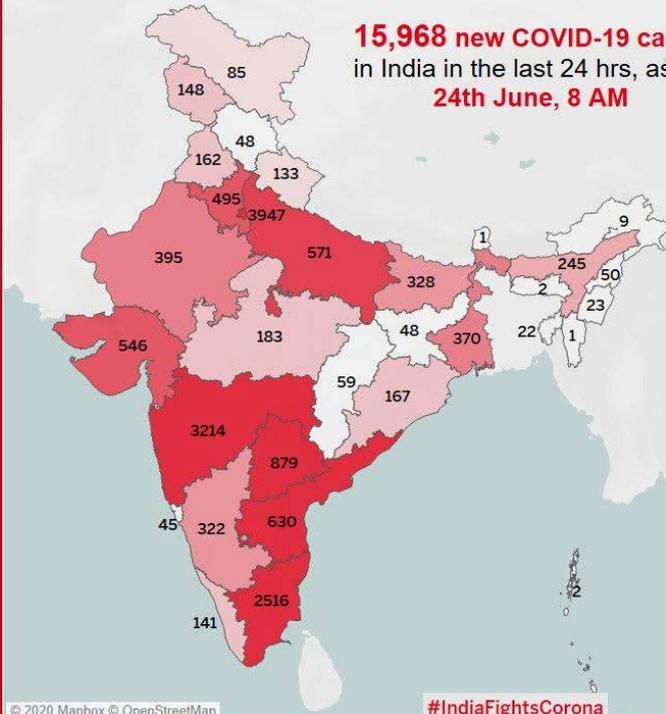
- IC50: The half maximal inhibitory concentration
- A measure of the effectiveness of a substance in inhibiting **a specific biological function.**

Jeroen Pollet  
Leroy Versteeg

# India COVID-19

## New COVID-19 Cases in India

**15,968 new COVID-19 cases**  
in India in the last 24 hrs, as on  
**24th June, 8 AM**



### States with Most Active Cases

Maharashtra	62,848
Tamil Nadu	28,431
Delhi	24,988
UP	6,189
Gujarat	6,148
AP	5,284
Telangana	5,109
W. Bengal	4,930
Haryana	4,844
Karnataka	3,567
Rajasthan	3,049
J&K	2,507
MP	2,401
Assam	2,060
Bihar	1,993
Kerala	1,620
Odisha	1,465
Punjab	1,245
Uttarakhand	903
Chhattisgarh	797
Ladakh	783
Goa	703
Manipur	663
Jharkhand	654

© 2020 Mapbox © OpenStreetMap

#IndiaFightsCorona

@COVIDNewsByMIB



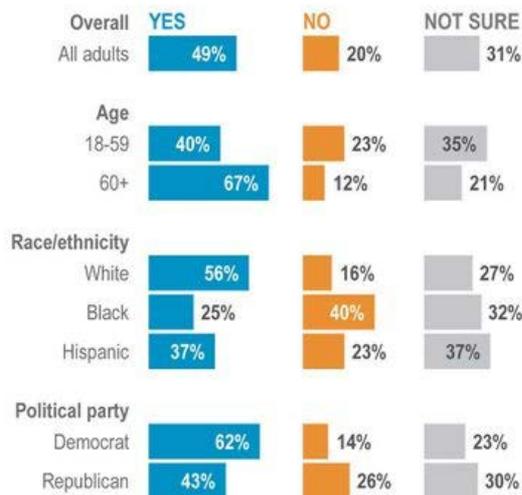
# COVID19 “Operation Warp Speed” Meets the Antivaccine Movement



## About half of Americans say they would get a coronavirus vaccine

A new AP-NORC poll finds that roughly half of Americans say they would get vaccinated for COVID-19, but many are uncertain or would refuse to do so. African Americans, Hispanics, young adults and Republicans are less likely than others to say they would get vaccinated.

If a vaccine against the coronavirus becomes available, do you plan to get vaccinated?



Results based on interviews with 1,056 U.S. adults conducted May 14–18. The margin of error is ±4.2 percentage points for the full sample.

SOURCE: AP-NORC Center for Public Affairs Research



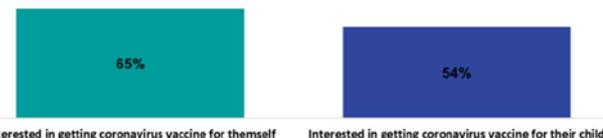
ALL ADULT AMERICANS

## Interest in Coronavirus Vaccine

How interested would you be in getting a coronavirus/COVID-19 vaccine, if at all?

How interested would you be in getting your children a coronavirus/COVID-19 vaccine, if at all? (asked of parents)

% Very/Somewhat interested



11 - Ipsos



11alive.com



## NEW POLL

49% PLAN TO GET VACCINATED  
 20% WILL NOT GET VACCINATED  
 31% NOT SURE

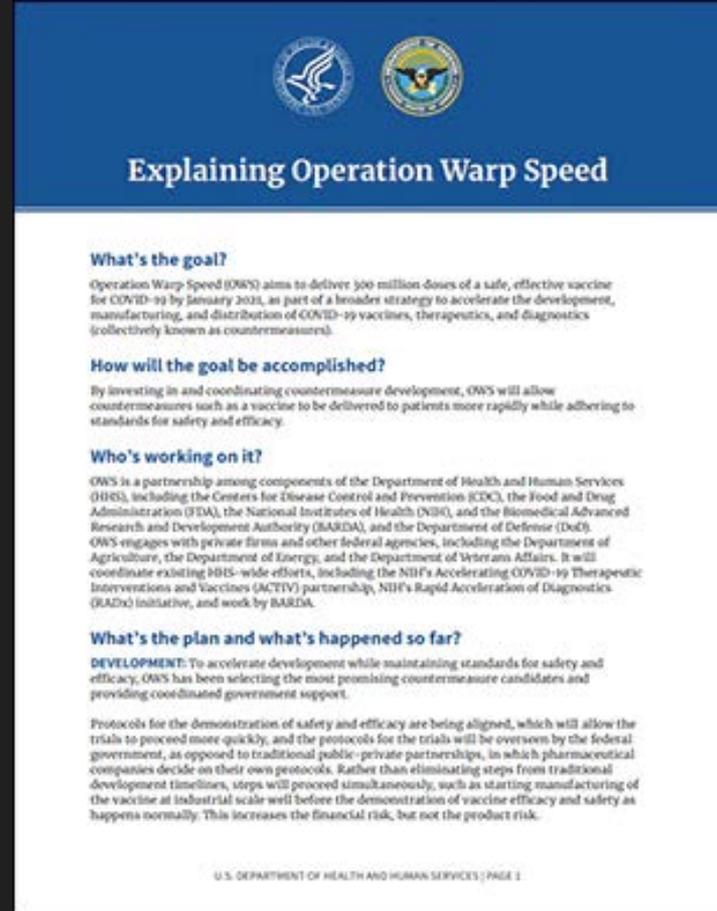
ASSOCIATED PRESS-NORC CENTER FOR PUBLIC AFFAIRS RESEARCH

<https://www.reuters.com/article/us-health-coronavirus-vaccine-poll-exclu/exclusive-a-quarter-of-americans-are-hesitant-about-a-coronavirus-vaccine-reuters-ipsos-poll-idUSKBN22X19G>

<https://apnews.com/dacdc8bc428dd4df6511bfa259cfec44>

# COVID-19 Meets the American Antivaccine Movement

- Antivaccine Tenets
  - Vaccines are rushed
  - Vaccines not tested for safety
  - Pharma and US Govt conflicts
  - “Health Freedom”
  - Vaccines cause autism, other chronic illnesses



**Explaining Operation Warp Speed**

**What's the goal?**  
Operation Warp Speed (OWS) aims to deliver 300 million doses of a safe, effective vaccine for COVID-19 by January 2021, as part of a broader strategy to accelerate the development, manufacturing, and distribution of COVID-19 vaccines, therapeutics, and diagnostics (collectively known as countermeasures).

**How will the goal be accomplished?**  
By investing in and coordinating countermeasure development, OWS will allow countermeasures such as a vaccine to be delivered to patients more rapidly while adhering to standards for safety and efficacy.

**Who's working on it?**  
OWS is a partnership among components of the Department of Health and Human Services (HHS), including the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA), the National Institutes of Health (NIH), and the Biomedical Advanced Research and Development Authority (BARDA), and the Department of Defense (DoD). OWS engages with private firms and other federal agencies, including the Department of Agriculture, the Department of Energy, and the Department of Veterans Affairs. It will coordinate existing HHS-wide efforts, including the NIH's Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) partnership, NIH's Rapid Acceleration of Diagnostics (RADx) initiative, and work by BARDA.

**What's the plan and what's happened so far?**  
**DEVELOPMENT:** To accelerate development while maintaining standards for safety and efficacy, OWS has been selecting the most promising countermeasure candidates and providing coordinated government support.  
  
Protocols for the demonstration of safety and efficacy are being aligned, which will allow the trials to proceed more quickly, and the protocols for the trials will be overseen by the federal government, as opposed to traditional public-private partnerships, in which pharmaceutical companies decide on their own protocols. Rather than eliminating steps from traditional development timelines, steps will proceed simultaneously, such as starting manufacturing of the vaccine at industrial scale well before the demonstration of vaccine efficacy and safety as happens normally. This increases the financial risk, but not the product risk.

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES | PAGE 1

# Texas “Health Freedom” Antiscience

## Health Freedom Protests

- Vaccines
- Social Distancing
- Contact Tracing
- Masks



<https://www.freedomfortexas.com/>



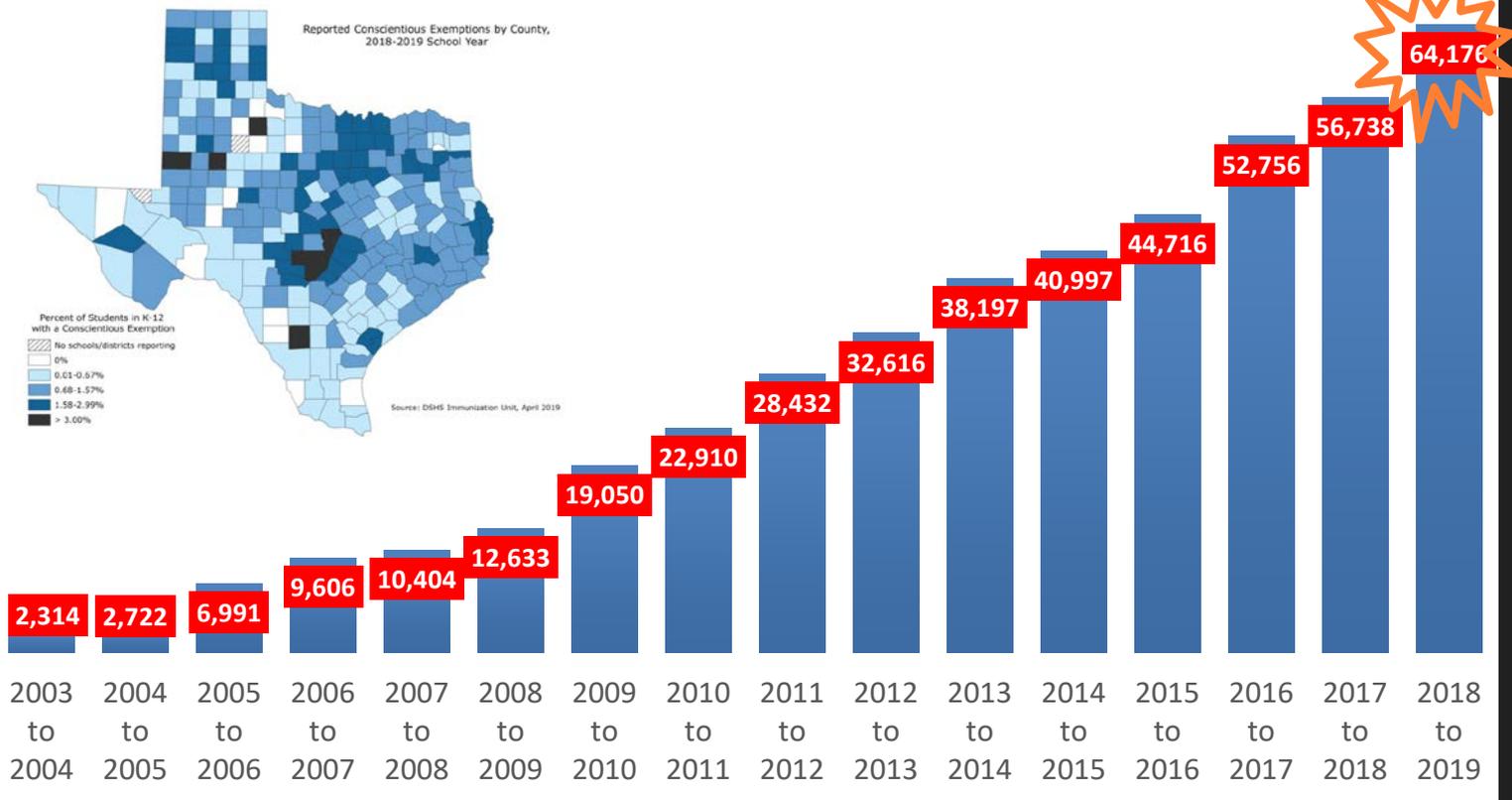
<https://www.nytimes.com/2020/04/18/us/texas-protests-stay-at-home.html>



<https://www.nbcnews.com/news/us-news/europe-s-coronavirus-death-toll-nears-100-000-lockdown-protests-n1187301>

# TEXAS NON-MEDICAL VACCINE EXEMPTIONS (2003-2019)

Figure 1. Percent of Students in Kindergarten through 12th Grade with a Conscientious Exemption on file for at least one vaccine



# Texas “Health Freedom” Antiscience

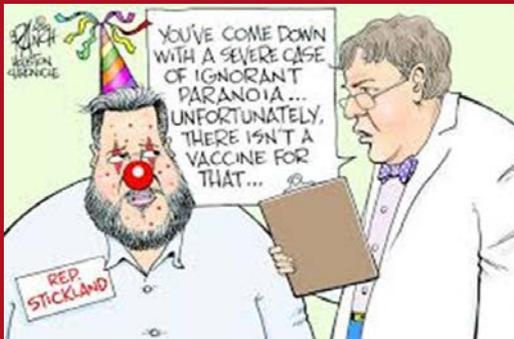


 **Jonathan Stickland**  
@RepStickland Follow

Replying to @PeterHotez @TexasDSHS

You are bought and paid for by the biggest special interest in politics. Do our state a favor and mind your own business. Parental rights mean more to us than your self enriching “science.” #txlege

11:52 PM - 7 May 2019

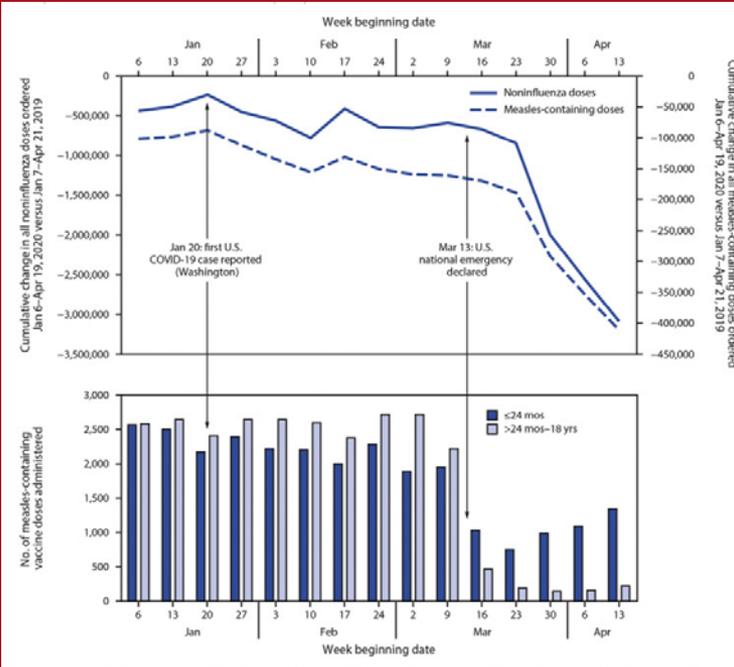


<http://digital.olivesoftware.com/olive/ODN/HoustonChronicle/shared/ShowArticle.aspx?doc=HHC%2F2019%2F05%2F12&entity=Pc03006&mode=image&sk=1ABAC59B>

<https://www.independent.co.uk/news/world/americas/alex-jones-coronavirus-lockdown-protest-texas-anthony-fauci-fire-a9472611.html>

# The Autumn of 2020

## A Time of Instability in America



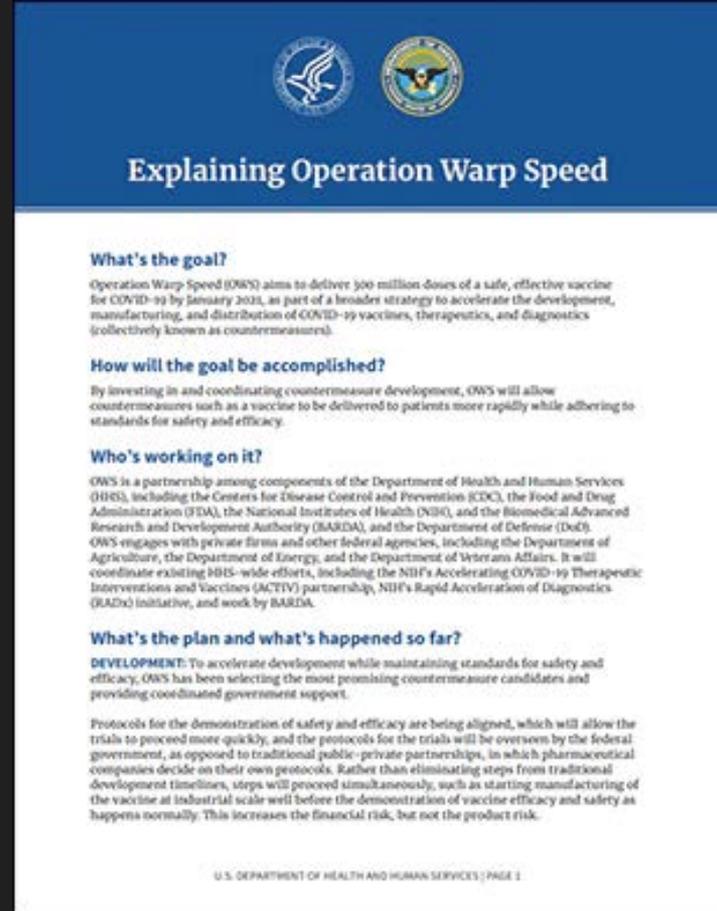
Declines in MMR  
Vaccine in US 2020

<https://www.cdc.gov/mmwr/volumes/69/wr/mm6919e2.htm>

<https://news.sky.com/story/coronavirus-armed-michigan-residents-protest-against-stay-at-home-order-calling-it-tyranny-11973905>

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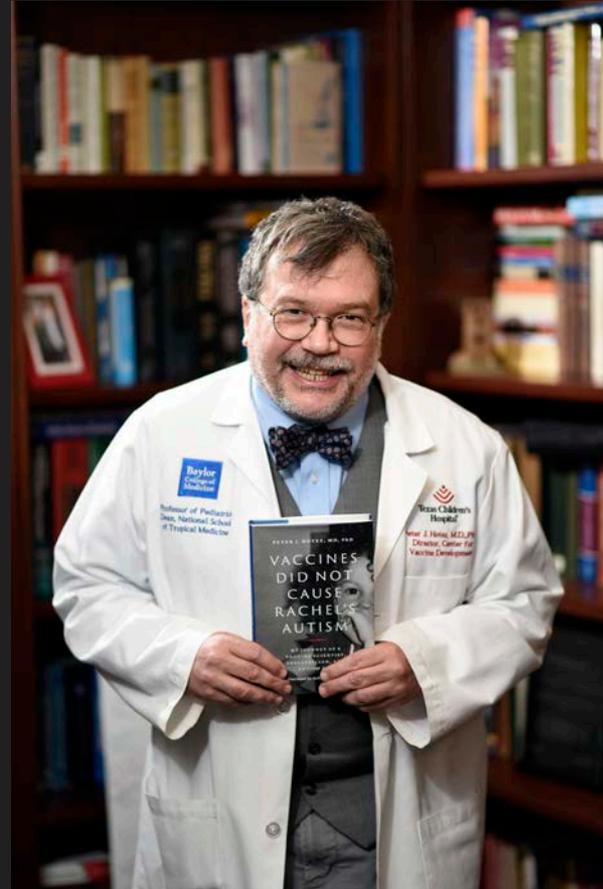
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**What's the plan and what's happened so far?**  
**DEVELOPMENT:** To accelerate development while maintaining standards for safety and efficacy, OWS has been selecting the most promising countermeasure candidates and providing coordinated government support.  
Protocols for the demonstration of safety and efficacy are being aligned, which will allow the trials to proceed more quickly, and the protocols for the trials will be overseen by the federal government, as opposed to traditional public-private partnerships, in which pharmaceutical companies decide on their own protocols. Rather than eliminating steps from traditional development timelines, steps will proceed simultaneously, such as starting manufacturing of the vaccine at industrial scale well before the demonstration of vaccine efficacy and safety as happens normally. This increases the financial risk, but not the product risk.

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES | PAGE 1

# Vaccine Scientist, Pediatrician, Autism Dad



# Autism Genes: Early Fetal Brain Development

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

## Patches of Disorganization in the Neocortex of Children with Autism

Rich Stoner, Ph.D., Maggie L. Chow, Ph.D., Maureen P. Boyle, Ph.D.,  
Susan M. Sunkin, Ph.D., Peter R. Mouton, Ph.D., Subhojit Roy, M.D., Ph.D.,  
Anthony Wynshaw-Boris, M.D., Ph.D., Sophia A. Colamarino, Ph.D.,  
Ed S. Lein, Ph.D., and Eric Courchesne, Ph.D.

ABSTRACT

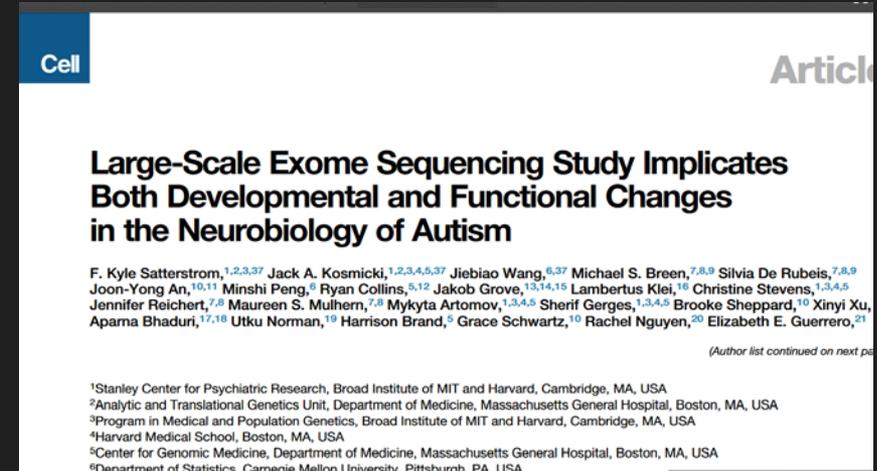
### BACKGROUND

Autism involves early brain overgrowth and dysfunction, which is most strongly evident in the prefrontal cortex. As assessed on pathological analysis, an excess of neurons in the prefrontal cortex among children with autism signals a disturbance in prenatal development and may be concomitant with abnormal cell type and

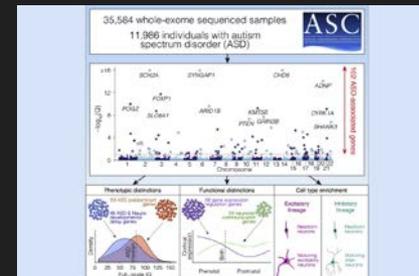


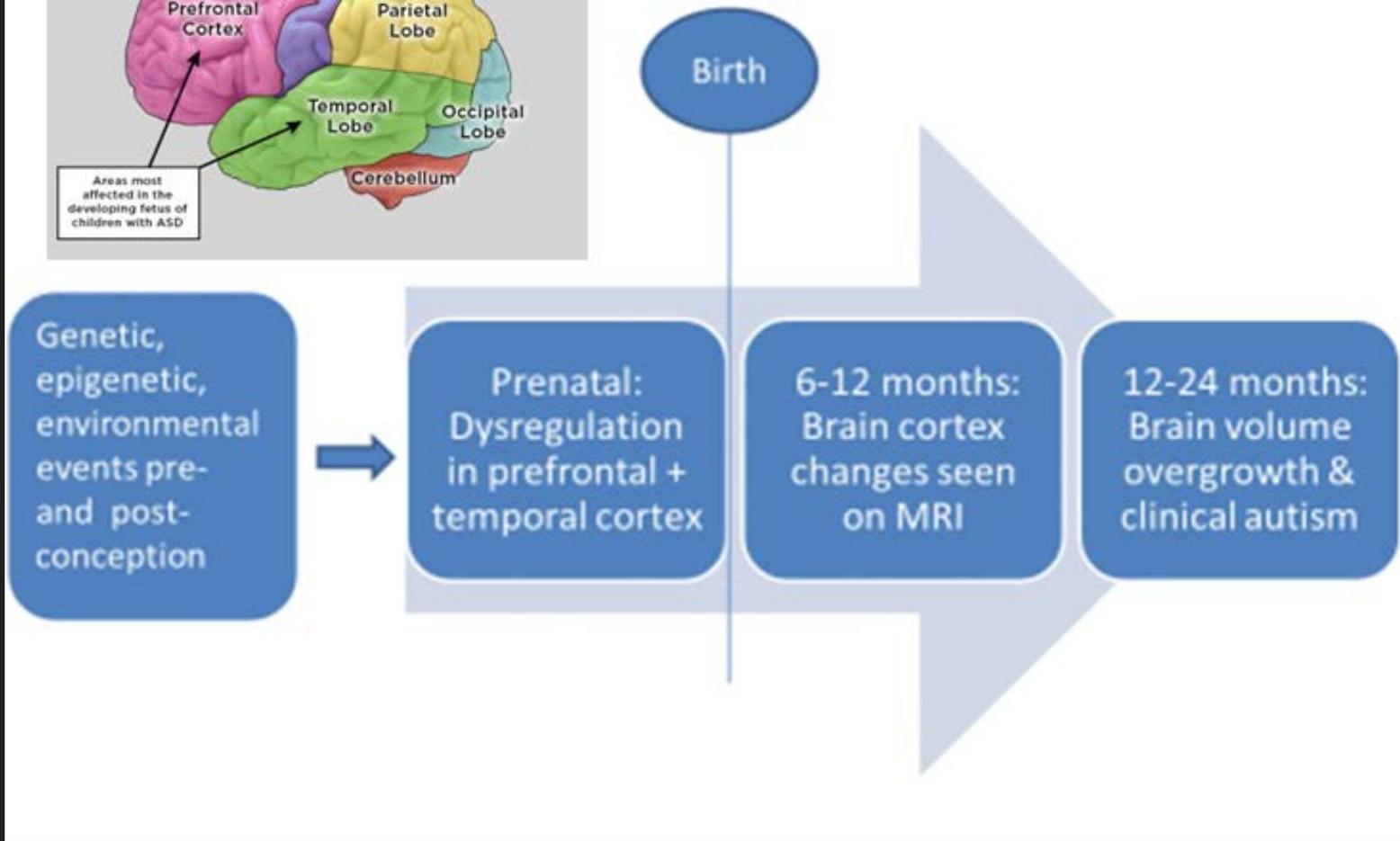
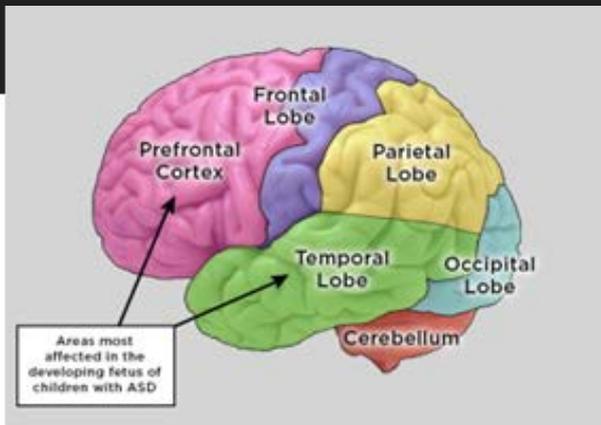
# Early Fetal Brain Development: Large Scale Exome Sequencing and Autism

- 102 genes implicated in risk for autism spectrum disorder
- All but one expressed in the cortex
- Expressed early in brain development
- Regulation of gene expression or neuronal communication
- Most are expressed and enriched early in excitatory and inhibitory neuronal lineages
- Most affect synapses or regulate other genes
- Neuronal cytoskeleton (Biorxiv)
- Some ASD genes alter early development broadly, others appear more specific to ASD



[https://www.cell.com/cell/pdf/S0092-8674\(19\)31398-4.pdf](https://www.cell.com/cell/pdf/S0092-8674(19)31398-4.pdf)





# The Neurobiology of Autism

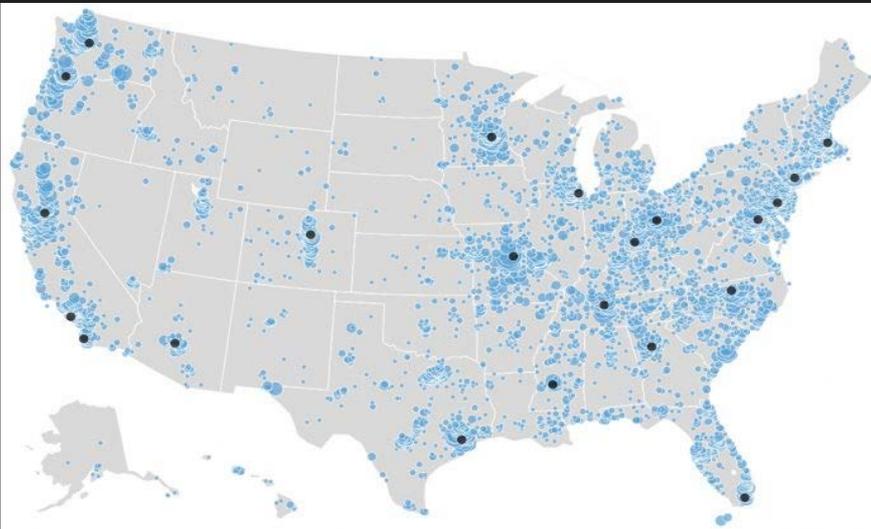
# SPARK Consortium

# SPARK

Simons Powering Autism Research



- SPARK will enable advances in two major ways.
- Having genetic samples from 50,000 families for scientists to analyze will enable far deeper insight into the genetic changes that contribute to autism.
- SPARK families will be available to receive invitations from researchers to participate in other studies, enabling research of all types to get off the ground more quickly.



# SPARK Consortium

## Autism in Dependent Adults

- SPARK Study Finds that More than Two-thirds of Dependent Autistic Adults Have Psychiatric Disorders
- 3,000 autistic adults found that more than two-thirds have psychiatric issues. The most common were anxiety and ADHD, which were both reported in about 4 in 10 participants.
- Almost half of participants in the study had intellectual disability. Almost a third had very limited language as adults. About 4 in 10 had sleep issues, and 3 in 10 had eating problems.

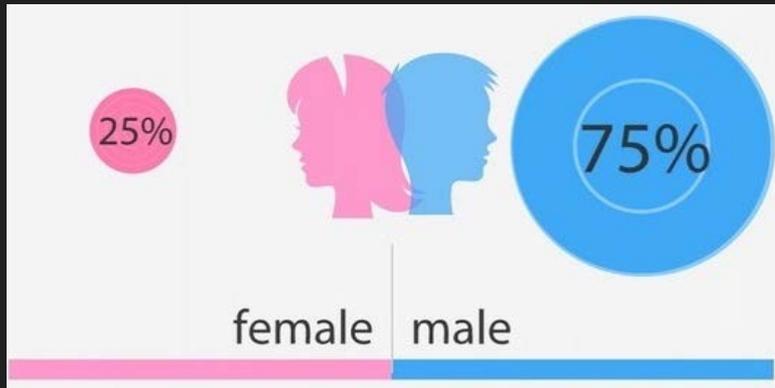


Eric Fombonne, M.D.  
Director, Autism Research Center,  
OHSU Brain Institute  
Professor, Department of Psychiatry

# SPARK Consortium

- One in six caregivers who participate in a national research cohort believe that child immunizations could be a cause of autism in their child.
- Parent social background and child developmental features (regression in second year, poorer language skills, and worse adaptive outcomes) index caregivers who are more likely to harbor these beliefs and could benefit from targeted educational activities.
- Beliefs in Vaccine as Causes of Autism Among SPARK Cohort Caregivers
- Eric Fombonne, Robin P Goin-Kochel, Brian J O'Roak, SPARK Consortium
- <https://pubmed.ncbi.nlm.nih.gov/31924427/>

# Girls vs Boys



Does autism present differently in boys and girls?



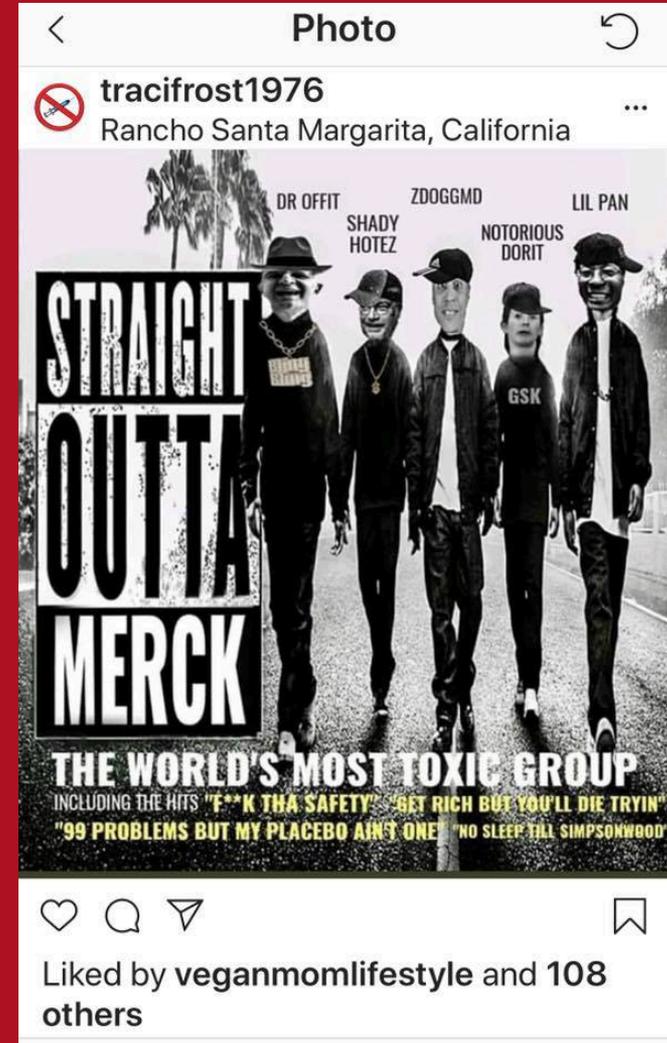
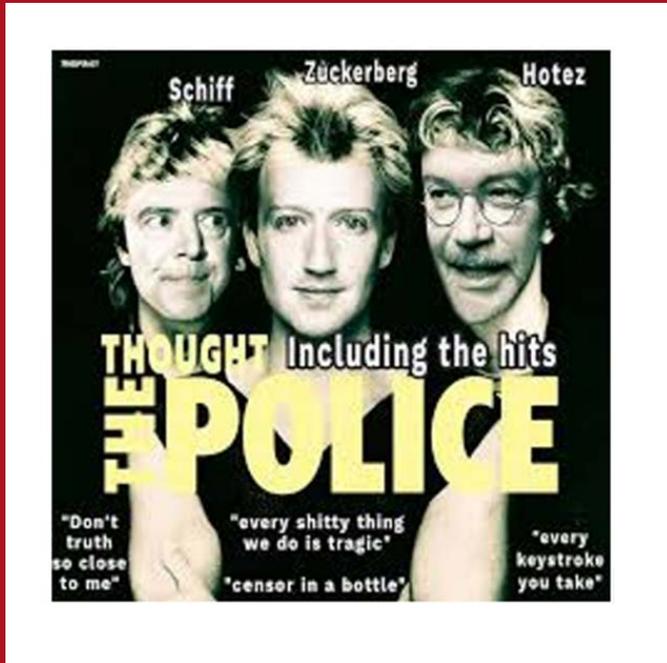
# Autism Science Foundation

## Autism Sisters Project

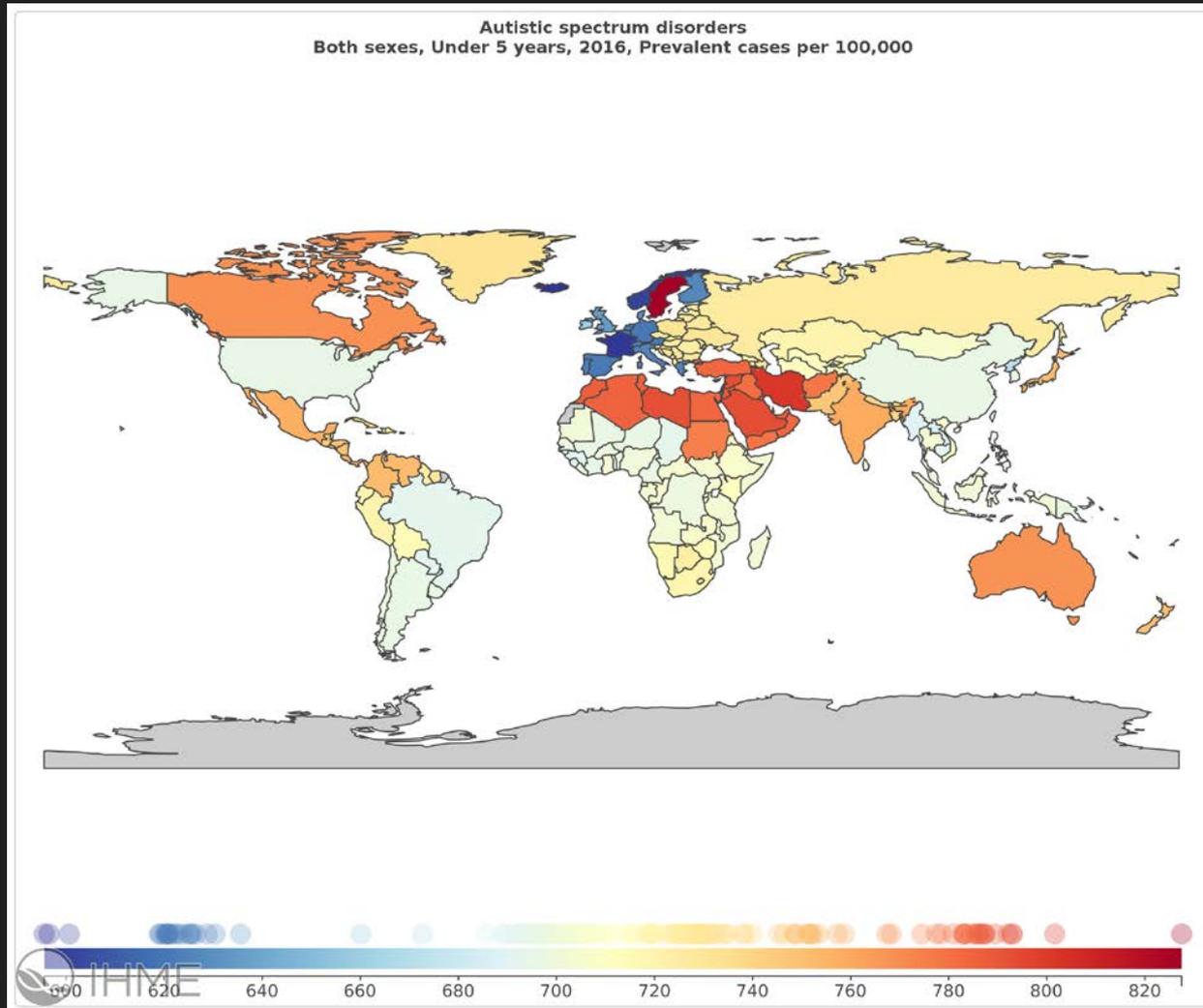
- Almost 4x as many boys are diagnosed with autism compared to girls
- Leading theory behind the male sex bias is that females in a family are protected against a diagnosis in some way.
- Female protective effect—and one of the best ways to study this is to look at undiagnosed sisters.



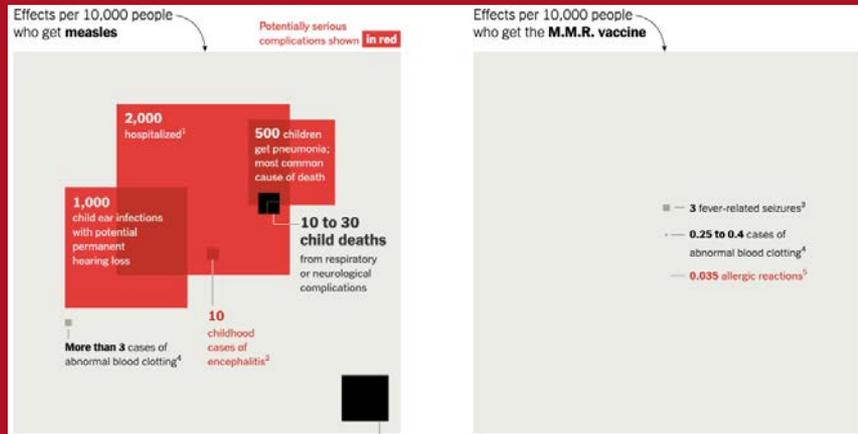
# The Face of the Antivaccine Movement in America



# Global Autism (IHME GBD 2016)



# You Are Unvaccinated and Got Sick. These Are Your Odds



The New York Times

Opinion

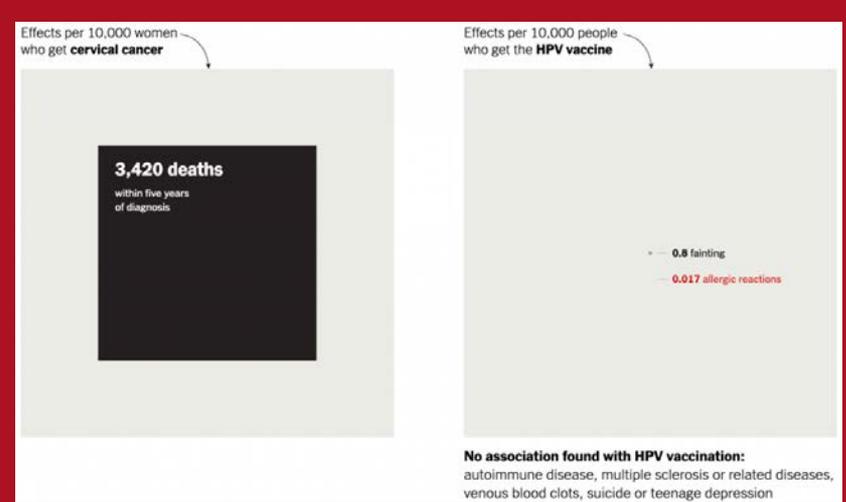
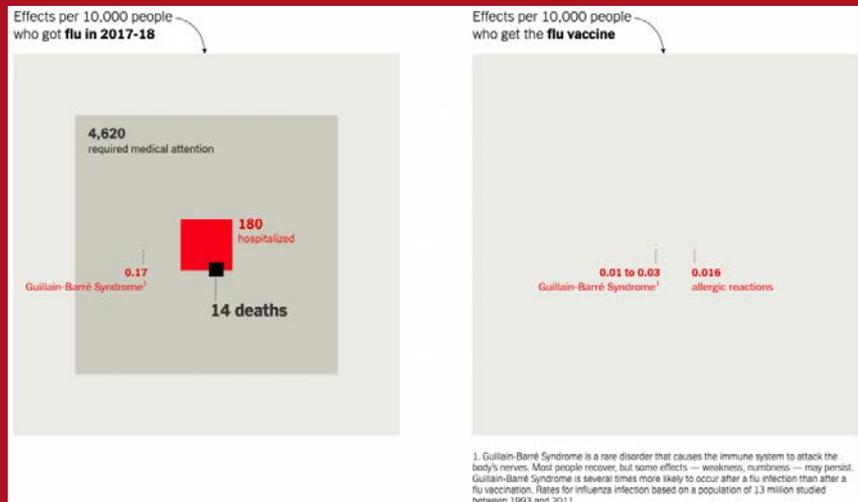
## You Are Unvaccinated and Got Sick. These Are Your Odds.

Comparing the dangerous effects of three diseases with the minimal side effects of their corresponding vaccines.

By Peter J. Hotez Graphics by Bill Marsh  
Dr. Hotez, a vaccine scientist and pediatrician at the Baylor College of Medicine, is the author of "Vaccines Did Not Cause Rachel's Autism."

Jan. 9, 2020

f t e s b 551



# “Vaccinationalism” vs Vaccine Diplomacy



# The Epic Struggle



PETER J. HOTEZ, MD, PhD

*A Science Essay on Stemming the Tide of War,  
Political Collapse, Climate Change, and Anti-science*

## PREVENTING THE NEXT PANDEMIC



*Vaccine Diplomacy  
in a Time of Anti-science*

Vaccines

21<sup>st</sup> Century Forces  
Poverty, Climate Change,  
War, Political Collapse,  
Urbanization, Antiscience