


VACCINE RESEARCH CENTER
Dele and Betty Bumpers
 National Institute of Allergy and Infectious Diseases
 National Institutes of Health
 Department of Health and Human Services



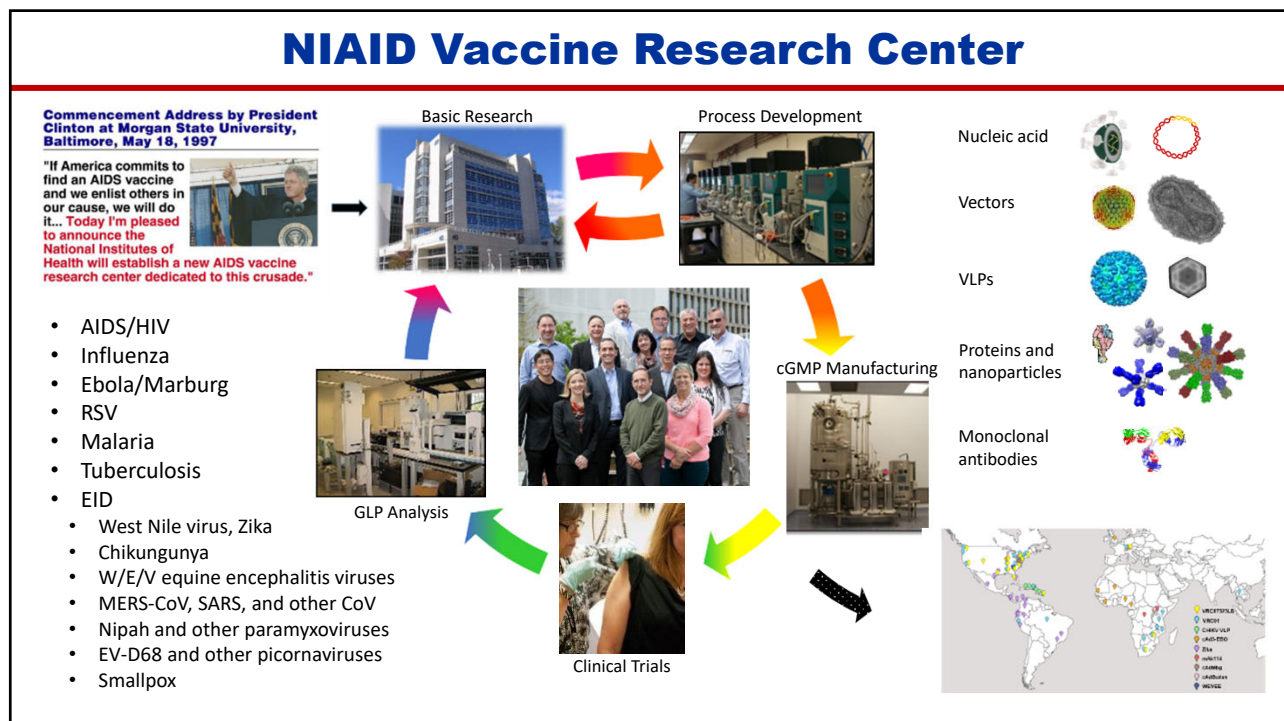
National Institute of
Allergy and
Infectious Diseases

RAPID (AND PRECISE) COVID-19 VACCINE DEVELOPMENT

One Year Living with SARS-CoV-2: Progress on Prevention and Treatment
Indonesia Research Partnership on Infectious Disease (INA-RESPOND)
National Institute of Health Research and Development, Ministry of Health,
Indonesia,
April 10, 2021

Barney S. Graham, MD, PhD
@BarneyGrahamMD
Deputy Director
Vaccine Research Center, NIAID, NIH

1



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Public health burden of re-emerging & emerging viruses

Vaccine Challenges

- Vaccines for unmet needs
- Emerging viruses
- Improved licensed vaccines



Traditional Approaches

- Licensed vaccines/antibiotics
- Passive surveillance
- Contact tracing
- Quarantine

3

3

New Technologies Facilitate an Engineering Approach

Vaccine Challenges

- Vaccines for unmet needs
- Emerging viruses
- Improved licensed vaccines



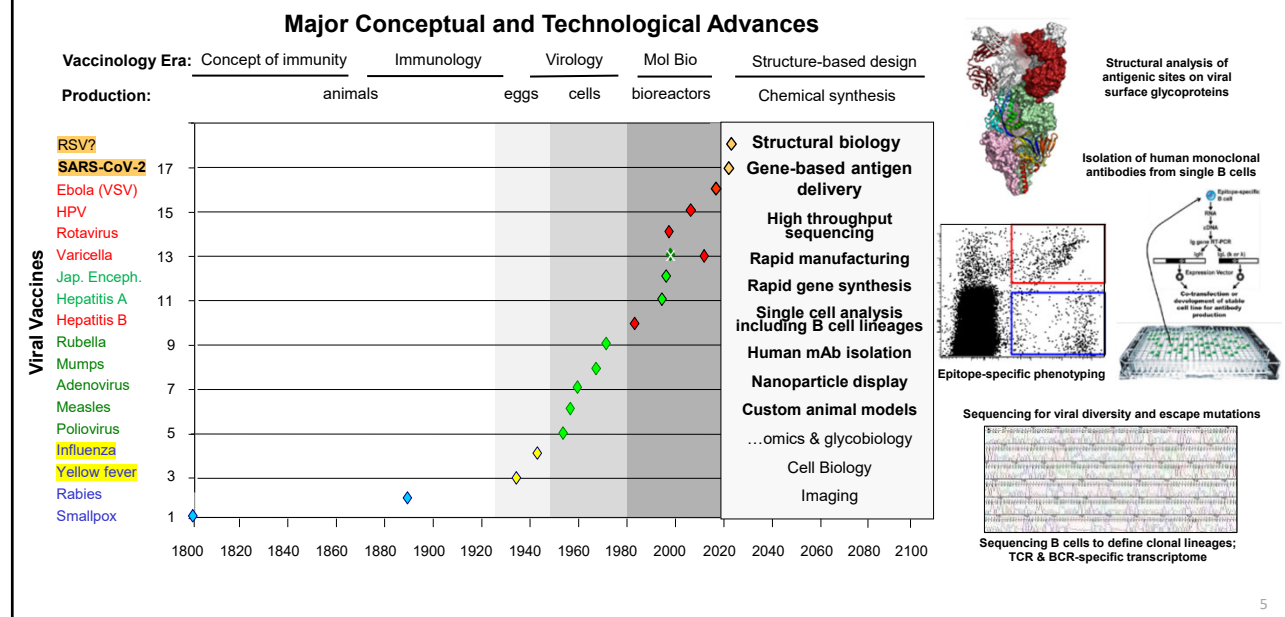
New Technologies

- Structural biology
- Protein engineering
- Single cell sorting and analysis
- High throughput sequencing
- Rapid isolation of human mAbs
- Antibody lineage analysis
- Rapid diagnostic tools
- Systems biology
- Gene-based delivery
- Rapid gene synthesis
- Platform manufacturing

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Technology Advances Make New Vaccines Possible



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New Technologies are Transforming Vaccinology

- Structure-based vaccine design
- Single-cell sorting, sequencing, and bioinformatics
 - Rapid isolation of human mAbs
 - Definition of antibody lineages
 - Analysis of immune responses
- Protein engineering of self-assembling nanoparticles
- Rapid DNA synthesis
- Recombinant DNA and genetic engineering technology
 - Rapid cell line development
 - Animal model development
- Nucleic acid and vector-based delivery of vaccine antigen

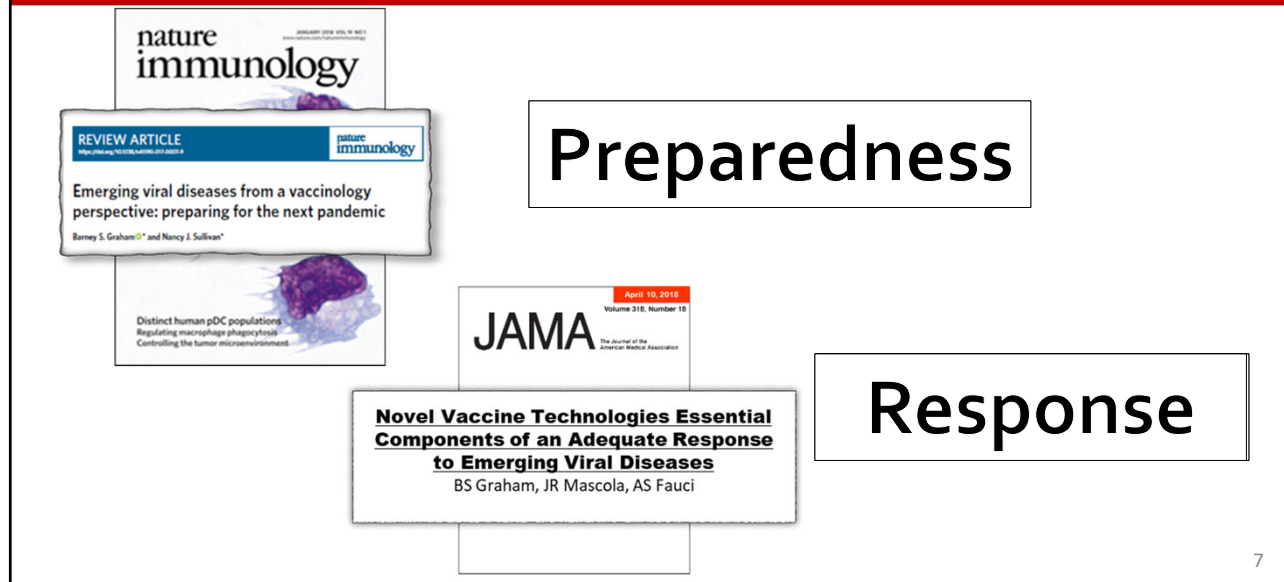
Precision

Speed

Sequencing B cells to define clonal lineages; TCR & BCR-specific transcriptome

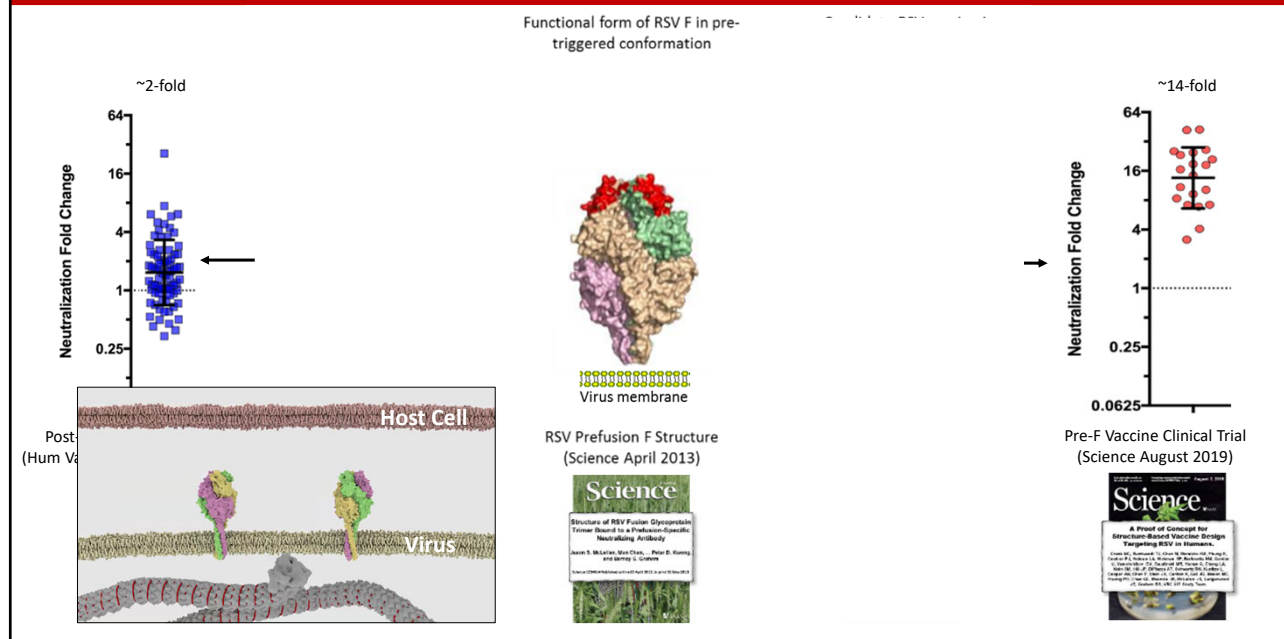
6

... and Provide New Options for Pandemic Preparedness and Response



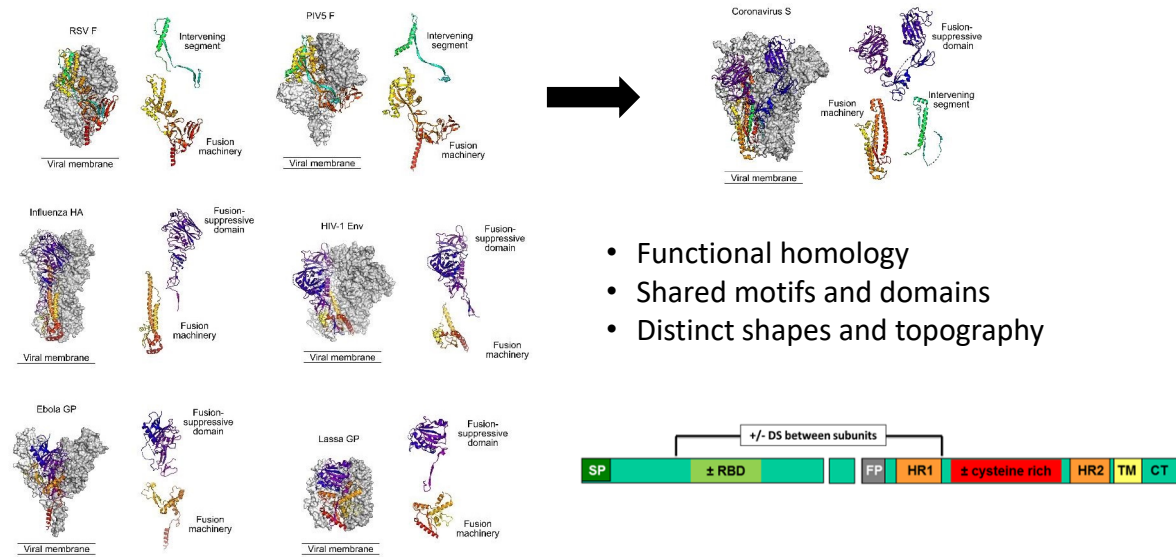
7

Preserving Apical Epitopes Improves Immunogenicity



8

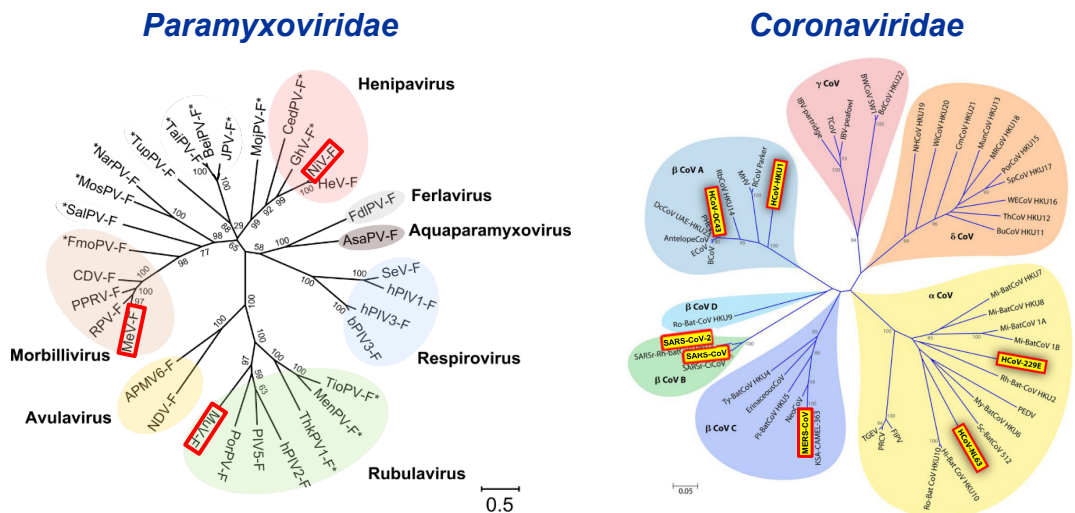
Class I Fusion Glycoproteins



Graham, Gilman, McLellan, Annual Review of Medicine 2019 9

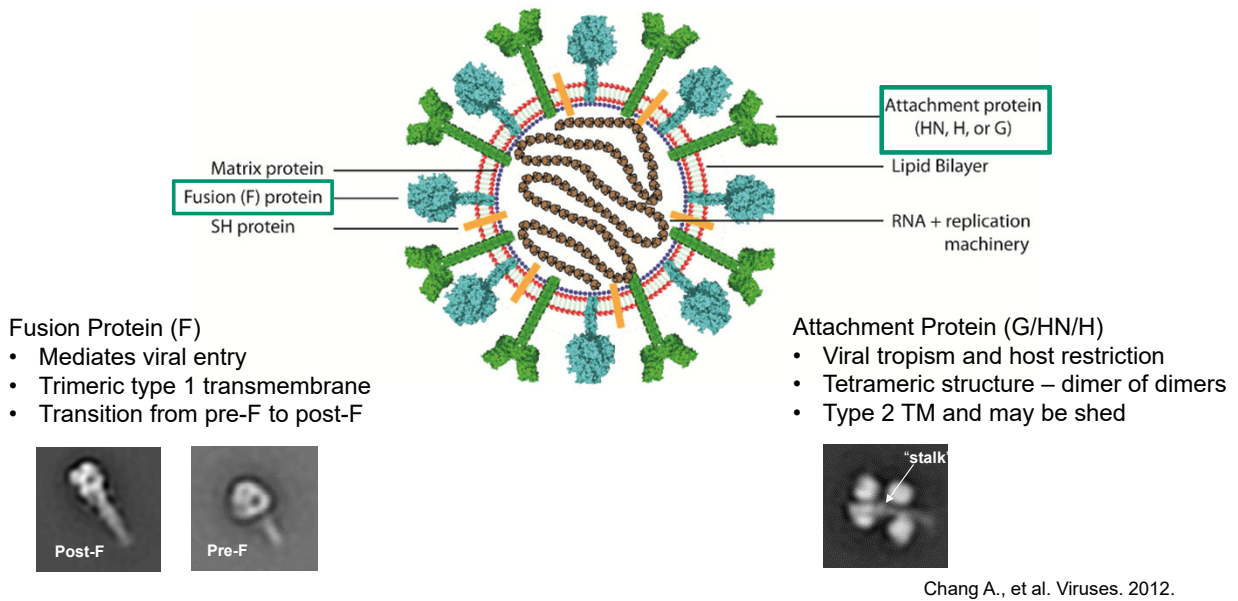
9

Two Viral Families with Extensive Zoonotic Reservoirs



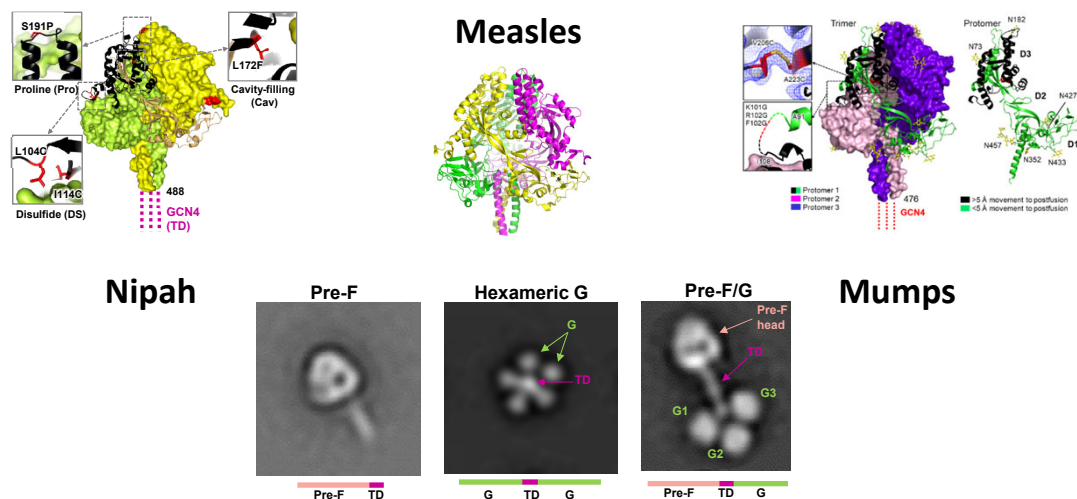
10

Paramyxovirus Surface Proteins



11

Stabilizing Paramyxovirus Pre-F Preserves NT-sensitive Epitopes and Improves Protein Expression

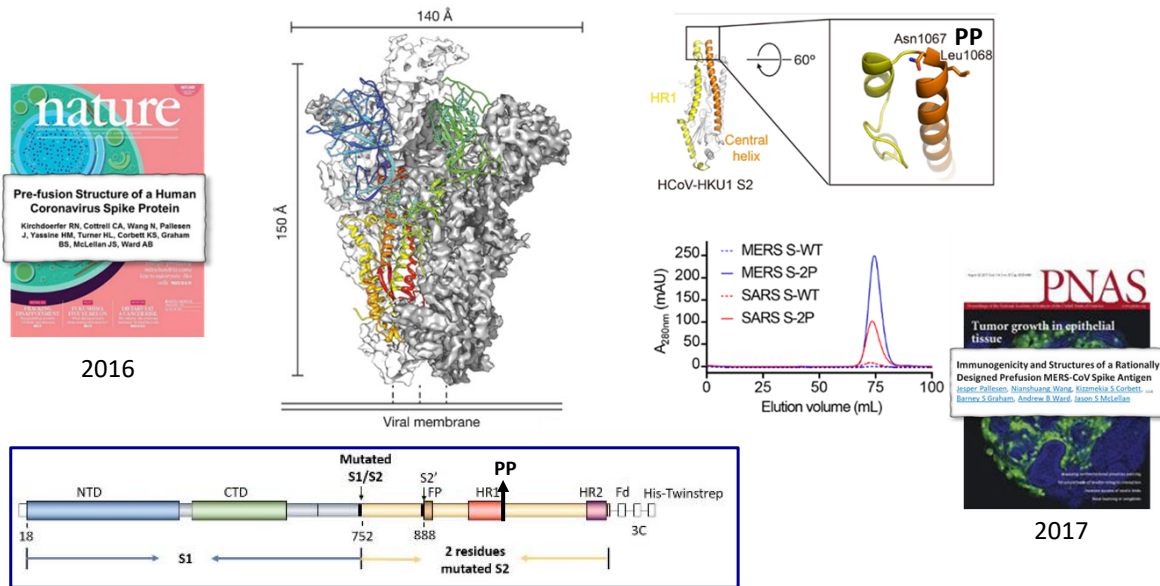


Guillaume Stewart-Jones, Rebecca Loomis et al. Frontiers Immunology 2020 Jun 11;11:842. doi: 10.3389/fimmu.2020.00842.

12

12

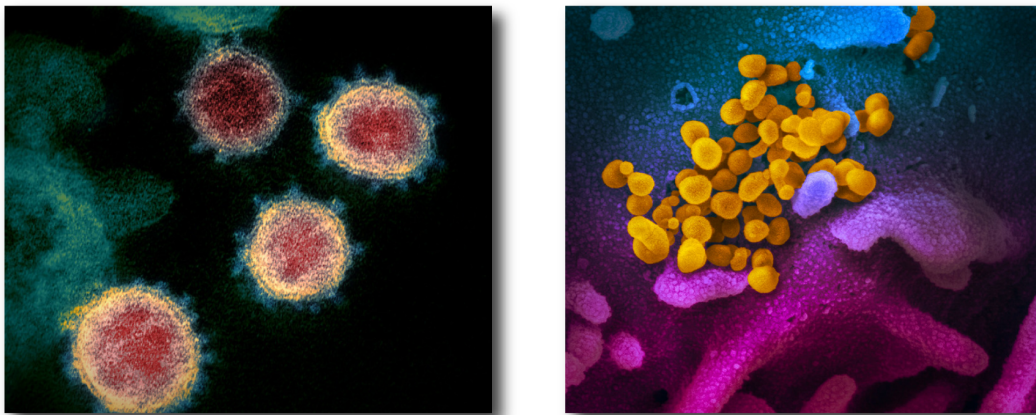
Structure-guided Stabilization of HKU1 CoV Spike



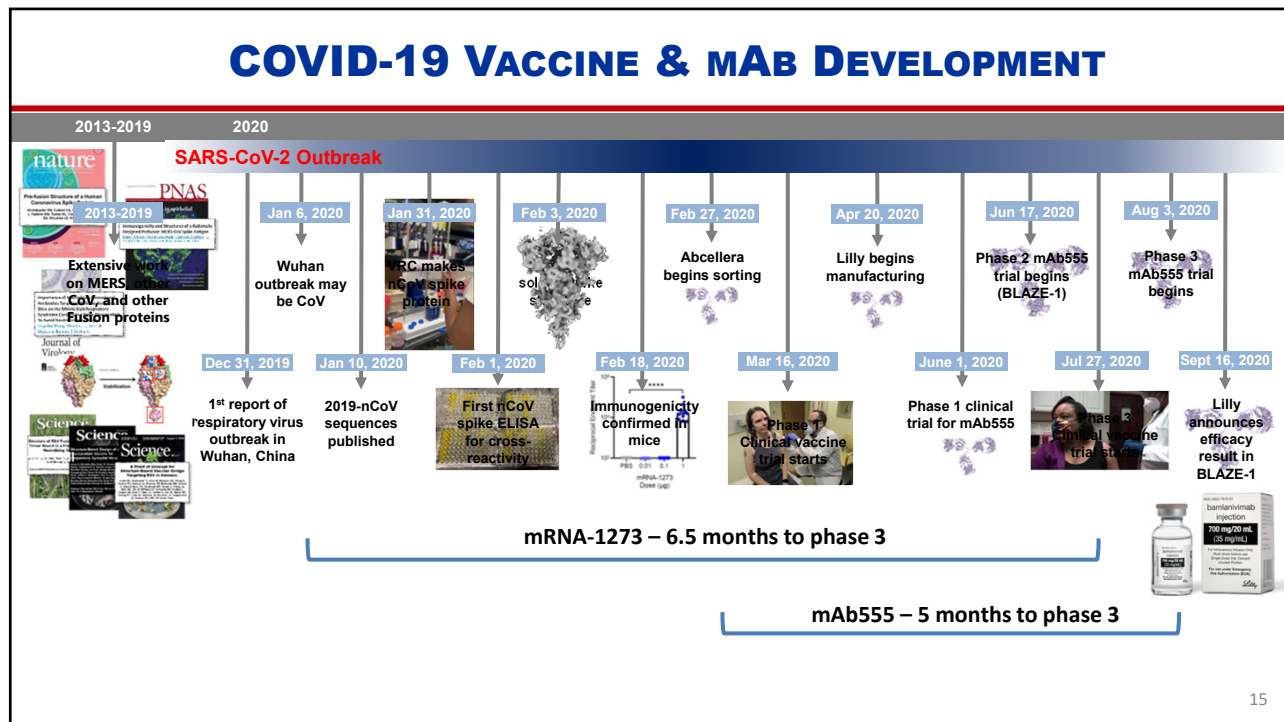
13

Coronavirus Disease 2019 (COVID-19) (December 2019 – Present)

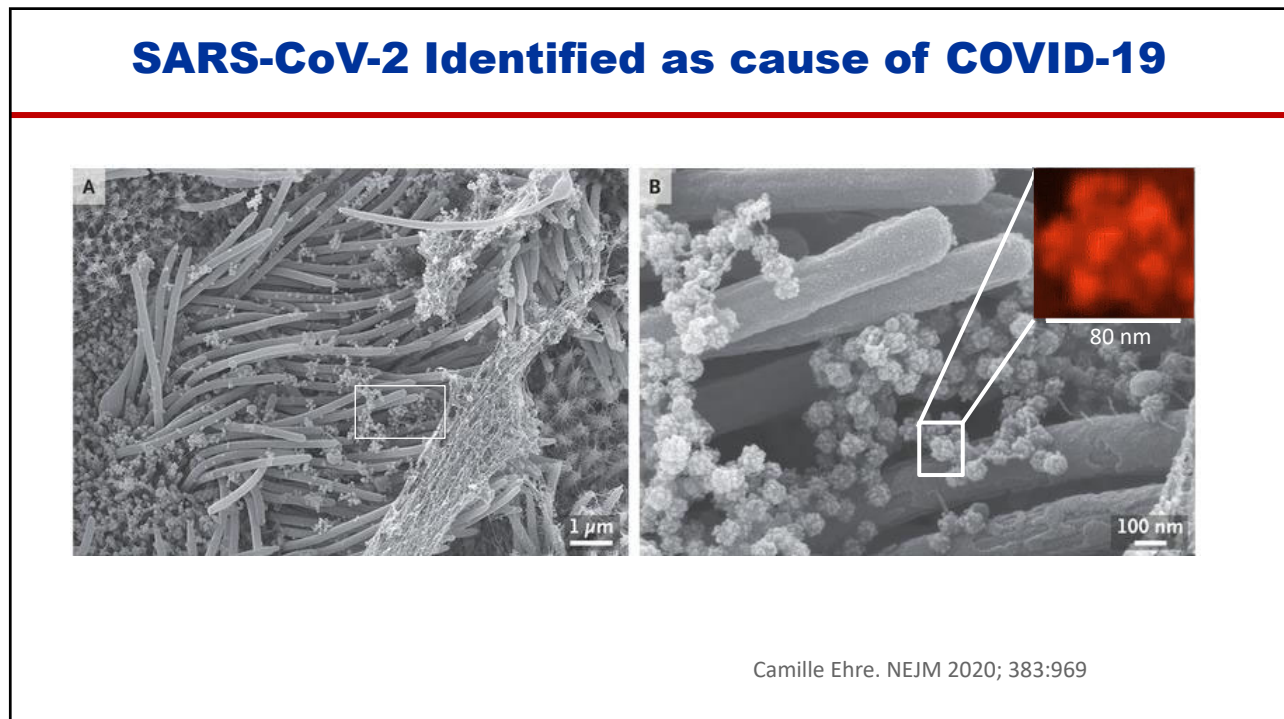
- **COVID-19** is the name of the disease caused by the novel coronavirus **SARS-CoV-2**



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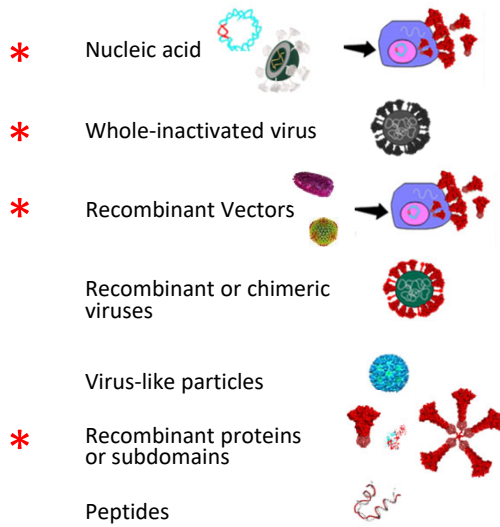
15



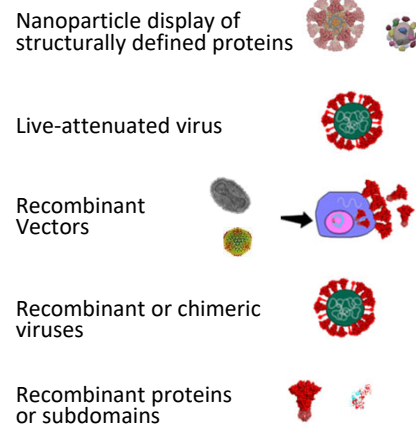
16

Global COVID-19 Vaccine Landscape

85 Vaccine Candidates in Clinical Evaluation
(11 Phase 3 registered)



184 Vaccine Candidates
in Pre-clinical Evaluation



Source: WHO 6 April 2021

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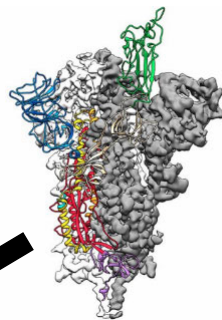
17

High Quality Protein is the Beginning for Everything

Therapy



Diagnostics



The NEW ENGLAND
JOURNAL of MEDICINE

An mRNA Vaccine against SARS-CoV-2 — Preliminary Report
Evaluation of the mRNA-1273 Vaccine against SARS-CoV-2 in
Nonhuman Primates
Safety and Immunogenicity of SARS-CoV-2 mRNA-1273
Vaccine in Older Adults

Vaccines

moderna *

Pfizer
BIONTECH *

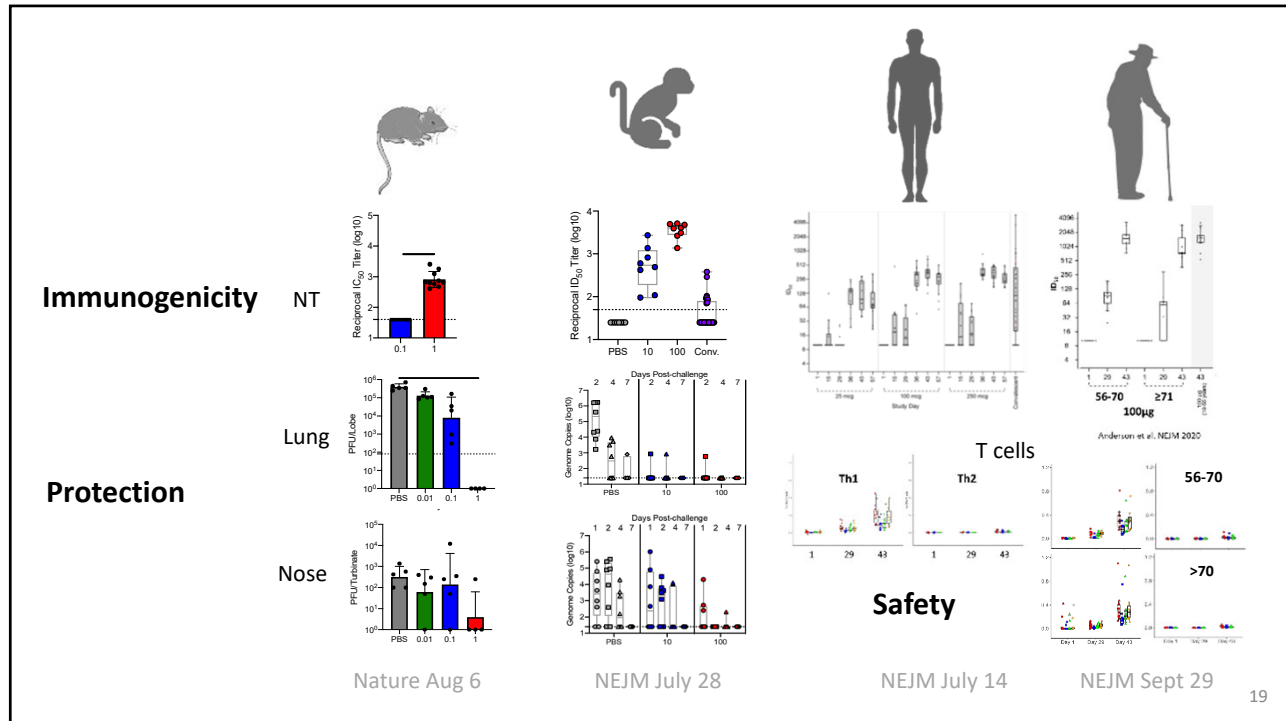
AstraZeneca X

NOVAVAX *

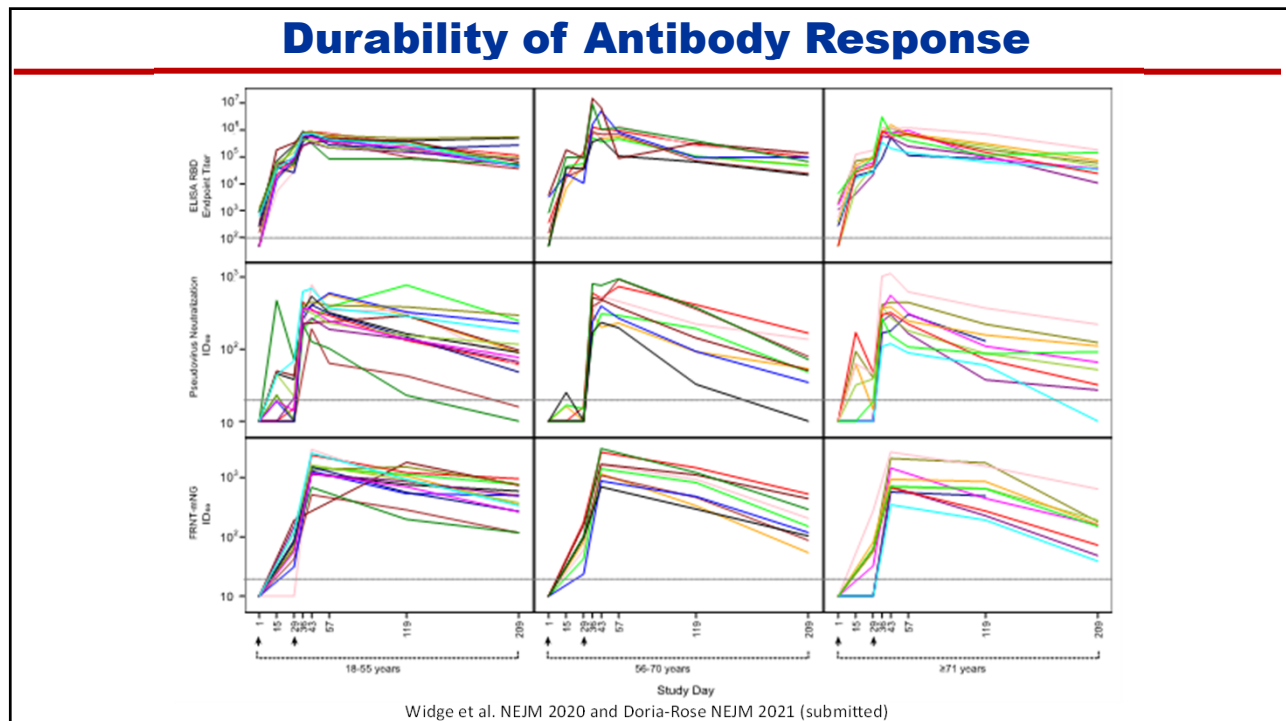
Janssen Johnson & Johnson *

gsk SANOFI *

18



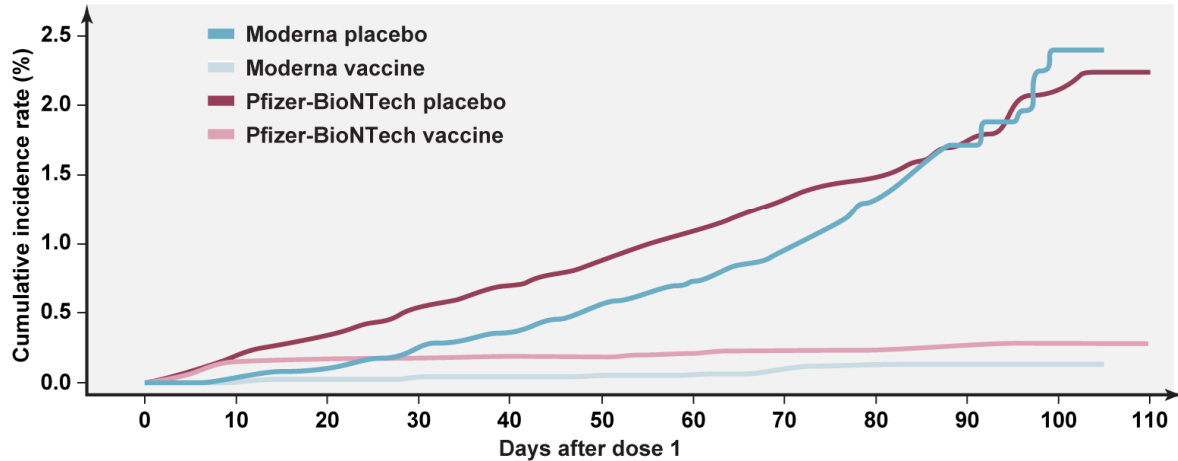
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Messenger RNA Vaccines Against SARS-CoV-2

Vaccine efficacy



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Vaccinating Frontline Workers

Week of December 27, 2020



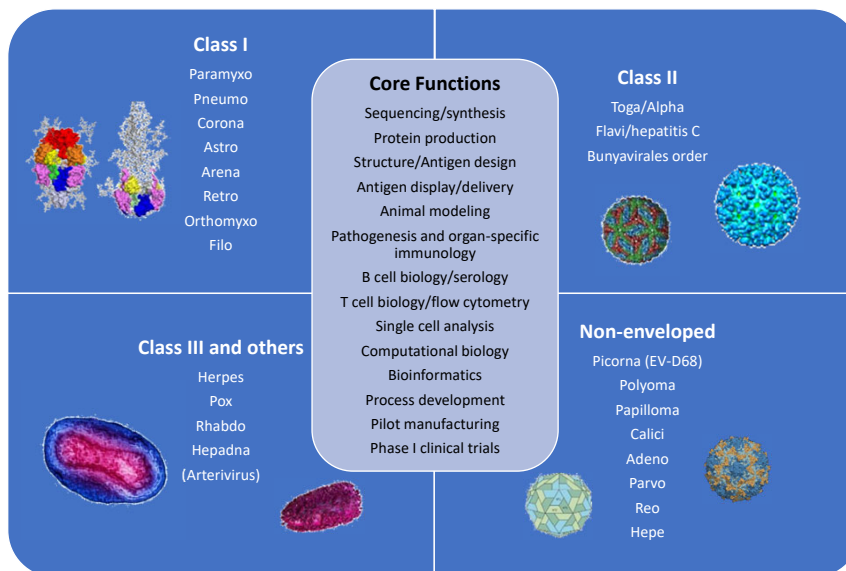
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Celebrating Vaccination



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Organizing for Pandemic Preparedness



Core functions: Intramural programs and extramural contracts connected to intramural and extramural basic research laboratories

Viral Research Groups: Organized by viral fusion protein type; combined resources of intramural and extramural investigators

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Prototype Pathogen Approach for Pandemic Preparedness

26 viral families known to infect humans

~120 viruses from those families known to infect humans with potential for increasing human-to-human transmission and virulence

- Develop vaccines for ~30 prototype viruses and take through phase 1
- Develop vaccine candidates (and reagents) for other ~90 and take through animal testing

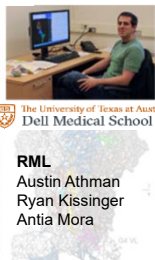
Other prioritization lists

WHO – Lassa, Nipah, MERS/SARS CoV, Rift Valley fever, Crimean Congo Hemorrhagic fever, Zika, Ebola and Marburg, Pathogen X
 CEPI – Lassa, Nipah, MERS-CoV, ...

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Summary and Acknowledgements

- Proof-of-concept for a prototype pathogen approach for pandemic preparedness
- Rapid pandemic response based on:
 - Prior fundamental basic and translational research
 - Both precision and speed
 - Pre-established public-private partnership



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COVID-19 Response: A VRC-wide Effort

Olubukola Abiona	Jason Gall	Rosemarie Mason	Chaim Schramm
Cassandra Almasri	Lucio Gama	Adrian McDermott	Diana Scorpio
Gabriela Alvarado	Rebecca Gillespie	Krishna McKee	Robert Seder
Obrimpong Amoa-Awua	Ingelise Gordon	John Misasi	Wei Shi
David Ambrozak	Barney Graham	Juan Moliva	Erica Smit
Charla Andrews	Martin Gaudinski	Damee Moon	Nancy Sullivan
Sarah Andrews	Christina Harris	Ian Moore	Phillip Swanson
Eli Boritz	Christian Hatcher	Kaitlyn Morabito	Alison Taylor
Seyhan Boyoglu-Barnum	Ashley Heimann	Sandeep Narpala	I-Ting Teng
Evan Cale	Marie Hirsch	Richard Nguyen	John-Paul Todd
Kevin Carlton	Geoffrey Hutchinson	Nadesh Nji	Yaroslav Tsybovsky
Lauren Chang	Masaru Kanekiyo	Amy Noe	Lingshu Wang
Kizzmekia Corbett	Azad Kumar	Laura Novik	Anne Werner
Adrian Crenaga	Peter Kwong	Sarah O'Connell	Alicia Widge
Katie Cunnane	Wing-Pui Kong	Sijy O'Dell	Eun Sung Yang
Marybeth Daucher	Richard Koup	Amarendra Pegu	Christina Yap
Anthony DiPiazza	Evan Lamb	Yuliya Petrova	Baoshan Zhang
Mitzi Donaldson	Julie Ledgerwood	Emily Phung	Yi Zhang
Daniel Douek	Kwanyee Leung	Madhu Prabhakaran	Tongqing Zhou
Naomi Douek	Bob C. Lin	Amy Ransier	Cynthia Ziwawo
Britta Flach	Catherine Liu	Mario Roederer	
Dylan Flebbe	Rebecca Loomis	Tracy Ruckwardt	
Barbara Flynn	Lindsay Longobardi	Noemia Santana Lima	
Katherine Foulds	Mark Louder	Stephen Schmidt	
Joseph Francica	John Mascola	Alec Schrager	