Global Vaccine and Immunization Research Forum 2021

Vaccinology in the Context of Pandemic Preparedness: The COVID-19 Experience

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Vaccinology in the Context of Pandemic Preparedness

- "Decade of Vaccines": much accomplished – much to do
- Vaccinology in 2021
- Pandemic preparedness and response
- Challenges for the next decade

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A "Decade of Vaccines" 2011-2020

- Progress towards goals for TB, malaria, and HIV
- Increased clinical trial capacities
- New vaccine technologies
  - Novel genetic approaches
  - Structure-based immunogen design
  - New vaccine platforms

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Goals of the "Decade of Vaccines" (2011-2020)

- Achieve a world free of poliomyelitis
- Meet global and regional elimination targets
- Meet vaccination coverage targets in every region, country and community
- Develop and introduce new and improved vaccines and technologies
- Exceed the Millennium Development Goal 4 target for reducing child mortality (MDG4)

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Vaccinology in 2021: Applying New Science to an Old Discipline

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Vaccinology in 2021: Applying New Science to an Old Discipline

- **Rapid genetic sequencing** for identification of new pathogens and genes encoding structural proteins that can form the basis for vaccine immunogens
- **Delineation of atomic-level structures of viral proteins** for structure-enabled immunogen design and protein engineering
- **Cell sorting and sequencing technologies** for single-cell analysis of immune responses
- **Genetic knock-in technologies** to develop animal models with human antibody genes for vaccine testing

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Vaccinology in 2021: Applying New Science to an Old Discipline (cont.)

- **New vaccine platforms** (e.g. DNA and RNA vaccines; vector expression; nanoparticles)
- **Adjuvants** to improve immune responses to vaccine antigens
- **Reverse vaccinology** (1.0, 2.0)

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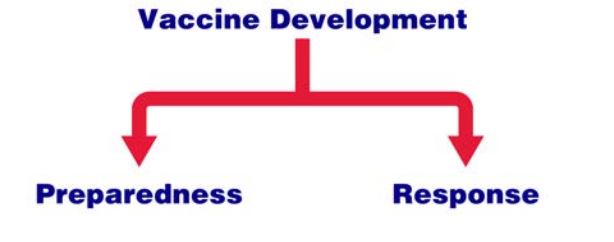
Vaccinology and Emerging Infectious Diseases



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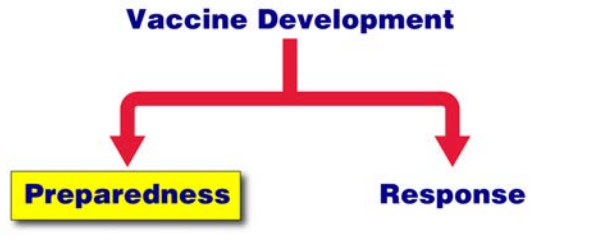

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Vaccine Development for Emerging Infectious Disease Threats: A 21st Century Approach

- Priority-Pathogen Approach
- Platform Approach
- Prototype-Pathogen Approach

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Vaccine Development for Emerging Infectious Disease Threats: A 21st Century Approach

- **Priority-Pathogen Approach**
- Platform Approach
- Prototype-Pathogen Approach

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WHO R&D Blueprint: Priority Diseases, 2020

Ebola virus disease and Marburg virus disease	Lassa fever	Crimean-Congo haemorrhagic fever (CCHF)
Nipah and henipaviral diseases	Rift Valley fever (RVF)	Zika
Middle East respiratory syndrome coronavirus (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS)	Disease X	COVID-19

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Source: WHO

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Vaccine Development for Emerging Infectious Disease Threats: A 21st Century Approach

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- Prototype-Pathogen Approach

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Vaccine Platform Technologies

Genetic immunization (DNA and RNA vaccines)
SARS, MERS, West Nile, Zika, RSV

Nanoparticles (viral protein on particle)
Influenza, Malaria, RSV

Viral vector (e.g., VSV, adenovirus)
Ebola, Marburg, Zika

Virus-like particle (VLP) (no RNA or DNA; non-infectious)
Chikungunya, Zika, WEVEE

Recombinant protein
Influenza, RSV

Adjuvants (e.g., AS01, MF59)

Selected Examples

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Vaccine Development for Emerging Infectious Disease Threats: A 21st Century Approach

- Priority-Pathogen Approach
- Platform Approach
- **Prototype-Pathogen Approach**

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Prototype Pathogen Approach To Vaccine Development

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Build on Prior Experiences

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Applying Strategies and Tools from One Virus to Inform Vaccine Design for Related Viruses

- Basic virology (e.g., neutralization mechanisms)
- Assays for preclinical and clinical settings
- Animal models
- Antigenic targets
- Optimal platforms
- Potential immune correlates
- Manufacturing strategies

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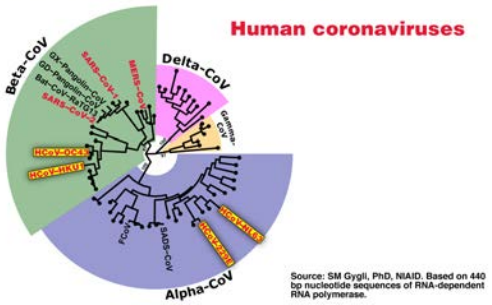
Coronavirus Phylogenetic Tree



Source: SM Gygli, PhD, NIAID. Based on 440 bp nucleotide sequences of RNA-dependent RNA polymerase.

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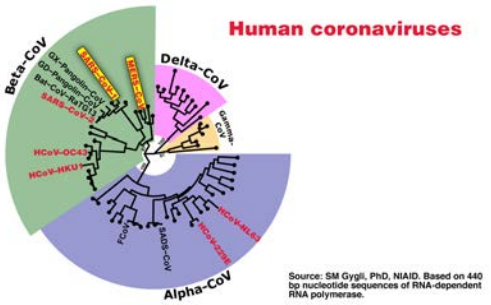

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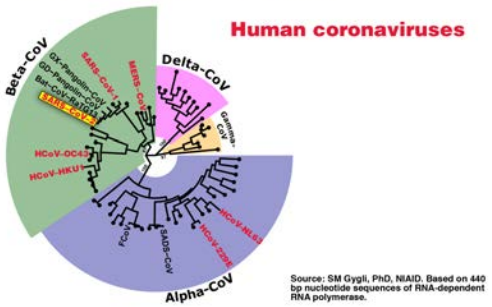

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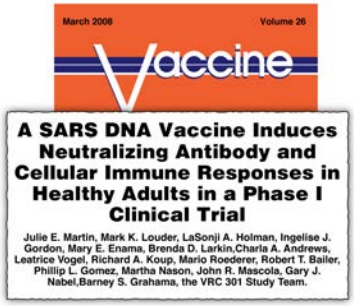
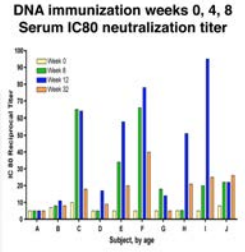
VRC: SARS DNA Vaccine Phase 1 Study





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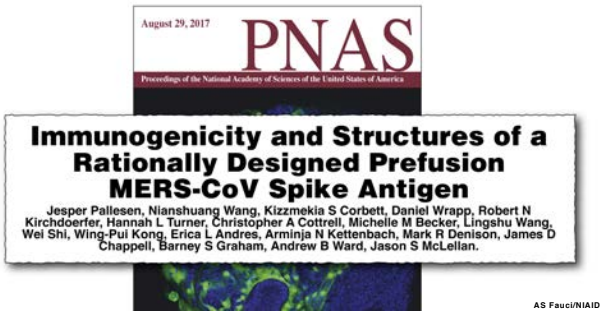
Structure-based Design of MERS Vaccine



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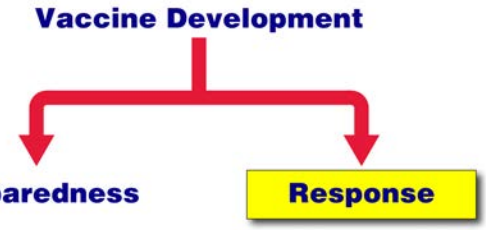

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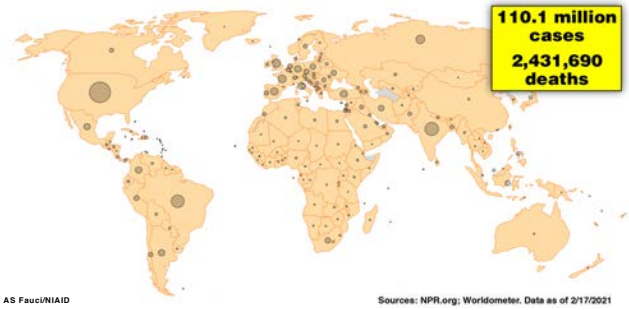
COVID-19 Globally



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Sources: NPR.org; Worldometer. Data as of 2/17/2021

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SARS-CoV-2 mRNA Vaccine Design Enabled by Prototype Pathogen Preparedness

KS Corbett, BS Graham et al.

- Using established immunogen design, the release of SARS-CoV-2 sequences triggered immediate rapid manufacturing of an mRNA vaccine expressing the prefusion-stabilized SARS-CoV-2 spike trimer.

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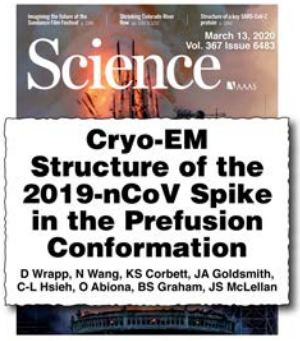

Cryo-EM Structure of the 2019-nCoV Spike in the Prefusion Conformation

D Wrapp, N Wang, KS Corbett, JA Goldsmith, C-L Hsieh, O Abiona, BS Graham, JS McLellan

Atomic-level structure of SARS-CoV-2 spike protein. Receptor binding domain is colored green.

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A Strategic Approach to COVID-19 Vaccine R&D

L Corey, JR Mascola, AS Fauci & FS Collins

- Unprecedented collaboration and resources will be required to research and develop safe and effective vaccines for COVID-19 that can be manufactured and delivered in the scale of billions of doses to people globally.

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Selected COVID-19 Vaccines

Platform	Developer	Status	
Nucleic Acid (mRNA)	moderna	94% efficacy vs. symptomatic disease	→ EUA
	BIONTECH Pfizer	95% efficacy vs. symptomatic disease	→ EUA
Adenovirus Vector	janssen	72% efficacy in U.S. 85% efficacy overall vs. severe disease in U.S., South Africa, Latin America	→ EUA review Feb. 26
	AstraZeneca	63% efficacy vs. symptomatic disease in U.K., Brazil and South Africa	→ EUA TBD
Recombinant Protein and Adjuvant	gsk SANOFI	Phase 2 starts	→ Feb. 2021
	NOVAVAX	89% efficacy vs. symptomatic disease in U.K.	→ EUA TBD

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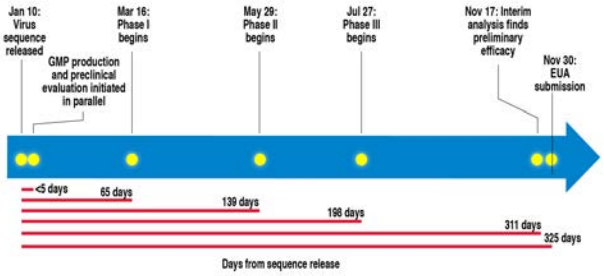
SARS-CoV-2 Vaccine Development: mRNA-1273



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The New York Times
December 11, 2020

F.D.A. Clears Pfizer Vaccine, and Millions of Doses Will Be Shipped Right Away

Efficacy: 95%

The New York Times
December 19, 2020

COVID-19: F.D.A. Authorizes Moderna Vaccine for Emergency Use, Adding Millions of Doses to U.S. Arsenal

Efficacy: 94%

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NOVAVAX

January 28, 2021

Press Release

- UK Phase 3 Results
  - 89.3% effective against symptomatic COVID-19
  - >50% of cases were B.1.1.7 variant
- South Africa Phase 2b Results
  - 49.4% effective against symptomatic COVID-19
  - 92.6% of cases were B.1.351 variant

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Johnson & Johnson

Press Release January 29, 2021

Johnson & Johnson Announces Single-Shot Janssen COVID-19 Vaccine Candidate Met Primary Endpoints in Interim Analysis of its Phase 3 ENSEMBLE Trial

Efficacy:
- 66% overall vs. moderate-to-severe COVID-19
  - 72% in U.S.
  - 66% in Latin America
  - 57% in South Africa
- 85% vs. severe disease across all regions studied
- Protection generally consistent across all age groups

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- Improve existing vaccines
- Develop novel vaccines for potentially vaccine-preventable diseases
- Ensure equitable access

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