

# Transforming Vaccinology in the Era of Artificial Intelligence

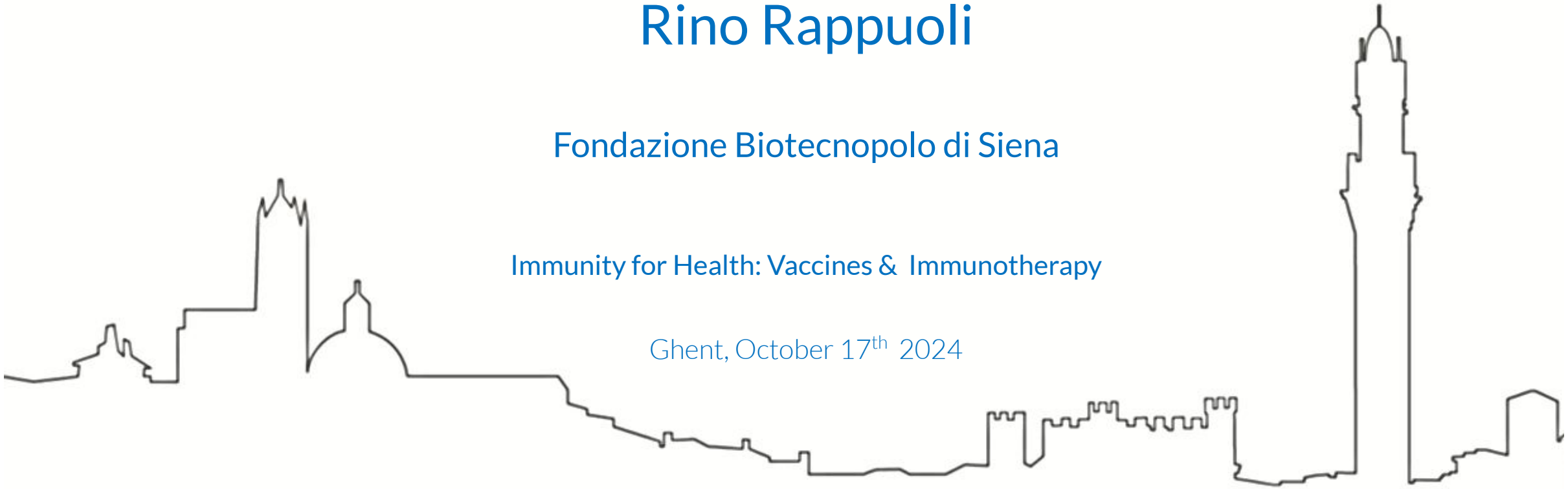
The next frontiers in Biotechnology

Rino Rappuoli

Fondazione Biotechnopolo di Siena

Immunity for Health: Vaccines & Immunotherapy

Ghent, October 17<sup>th</sup> 2024



# The Nobel Prize in Chemistry 2024



Ill. Niklas Elmehed © Nobel Prize  
Outreach  
David Baker

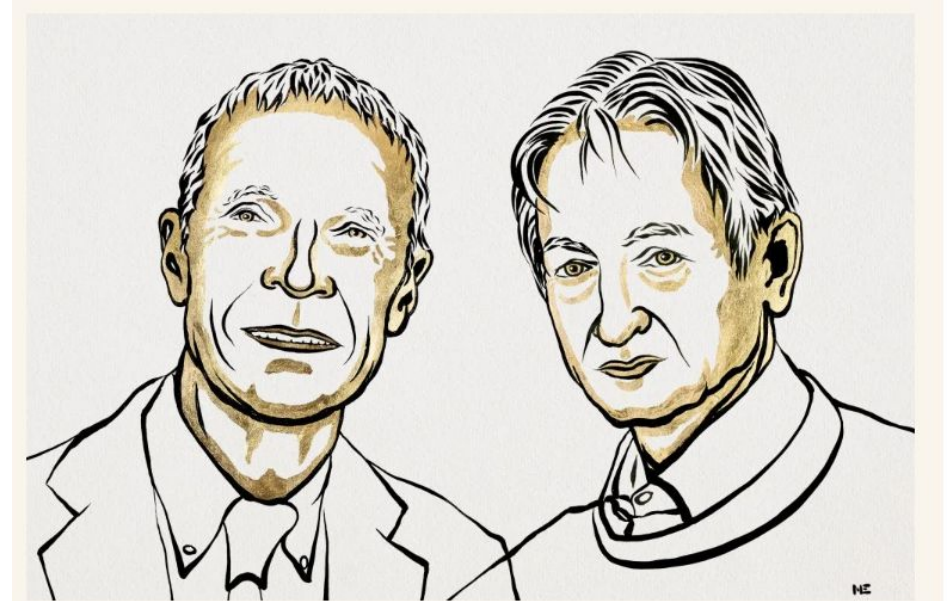


Ill. Niklas Elmehed © Nobel Prize  
Outreach  
Demis Hassabis



Ill. Niklas Elmehed © Nobel Prize  
Outreach  
John M. Jumper

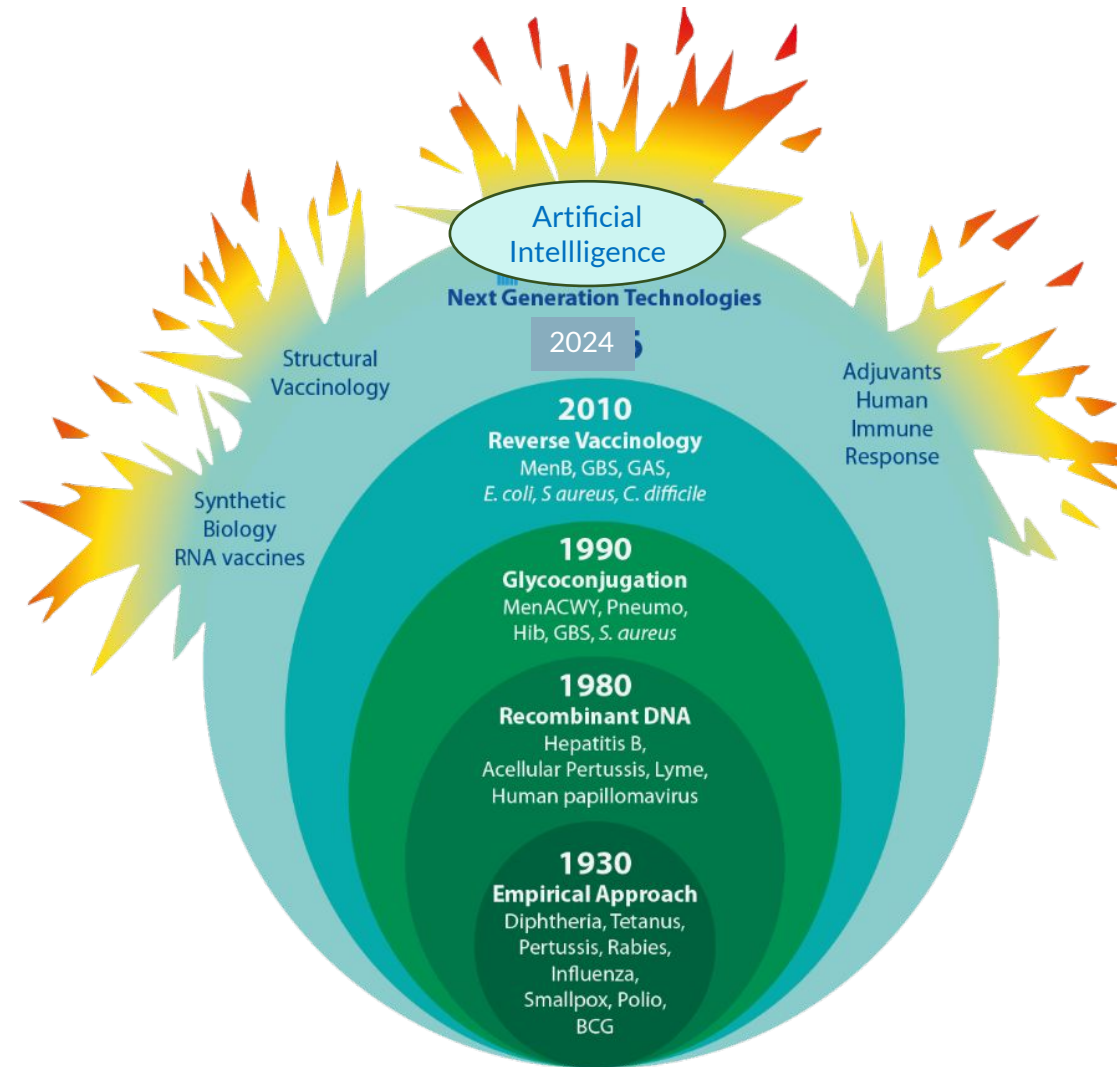
# The 2024 physics laureates



Jeffrey Hinton

Niklas Elmehed

# Transformative Vaccine Technologies





# The Nobel Prize in Chemistry 2024



NOBELPRISET I KEMI 2024  
THE NOBEL PRIZE IN CHEMISTRY 2024



KUNGL.  
VETENSKAPS-  
AKADEMIEN  
THE ROYAL SWEDISH ACADEMY OF SCIENCES



**David Baker**  
University of Washington  
USA



**Demis Hassabis**  
Google DeepMind  
United Kingdom



**John M. Jumper**  
Google DeepMind  
United Kingdom

# The vaccine field has been transformed

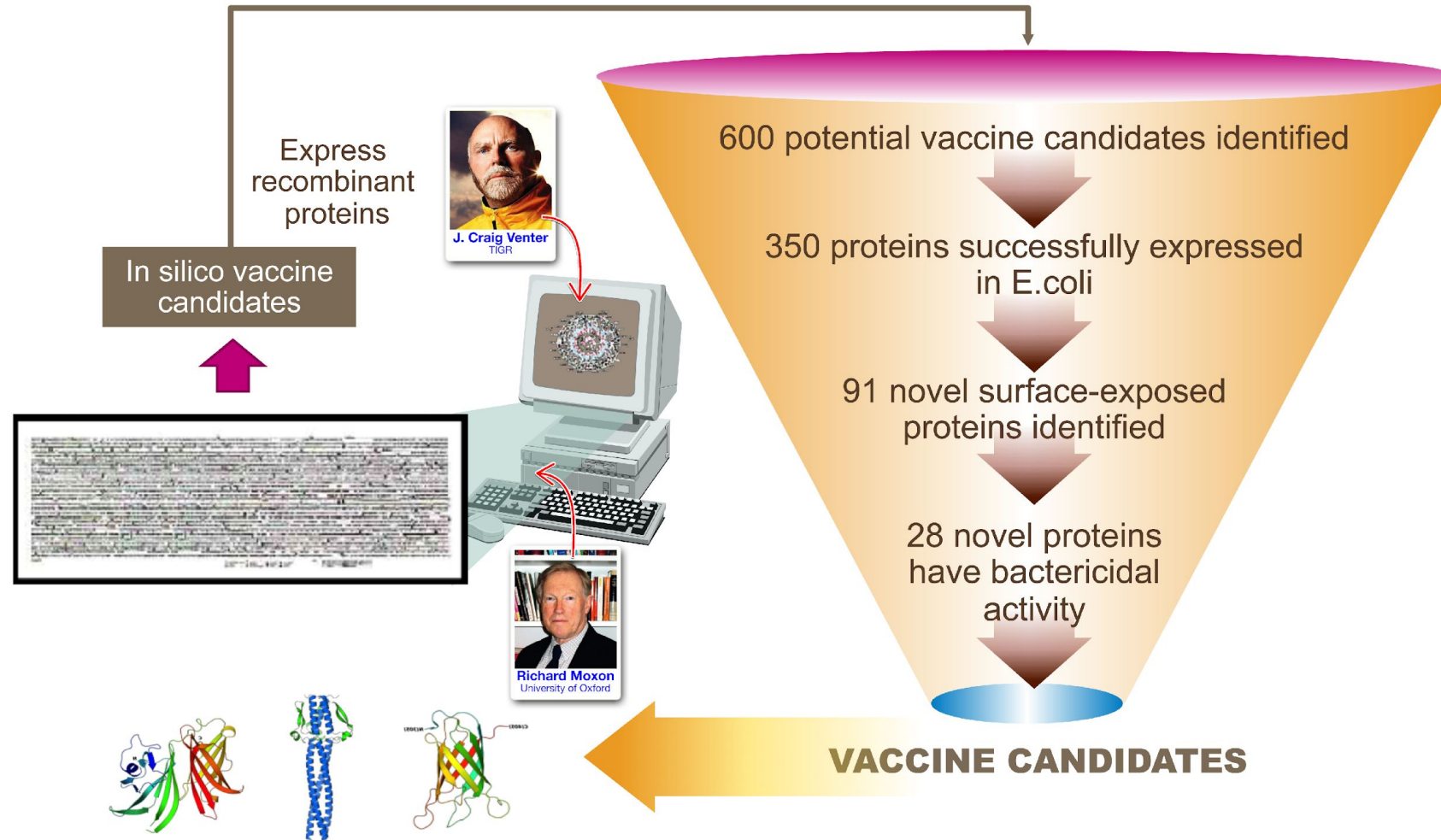
- Reverse Vaccinology
- Structural Vaccinology
- Synthetic biology & Digital Vaccines
- Artificial Intelligence

# Reverse Vaccinology

the beginning of **big data** and high throughput

# Reverse Vaccinology

genomics, the new technology (**big data**) made the meningococcus B vaccine possible



# Structural Vaccinology

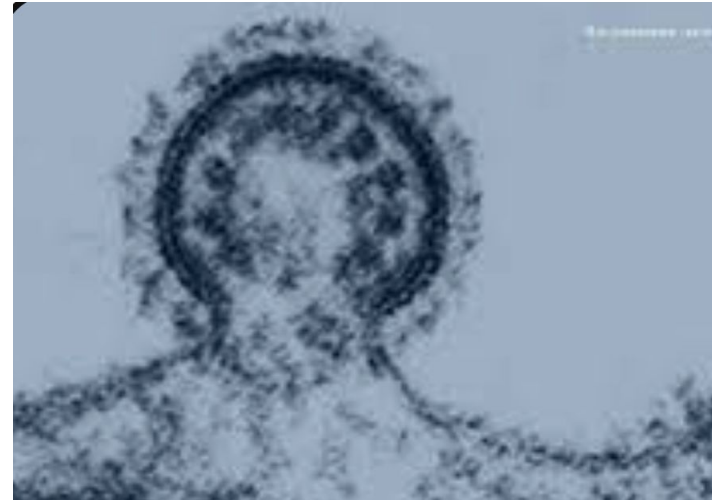
high throughput structure biology



# Structural Vaccinology

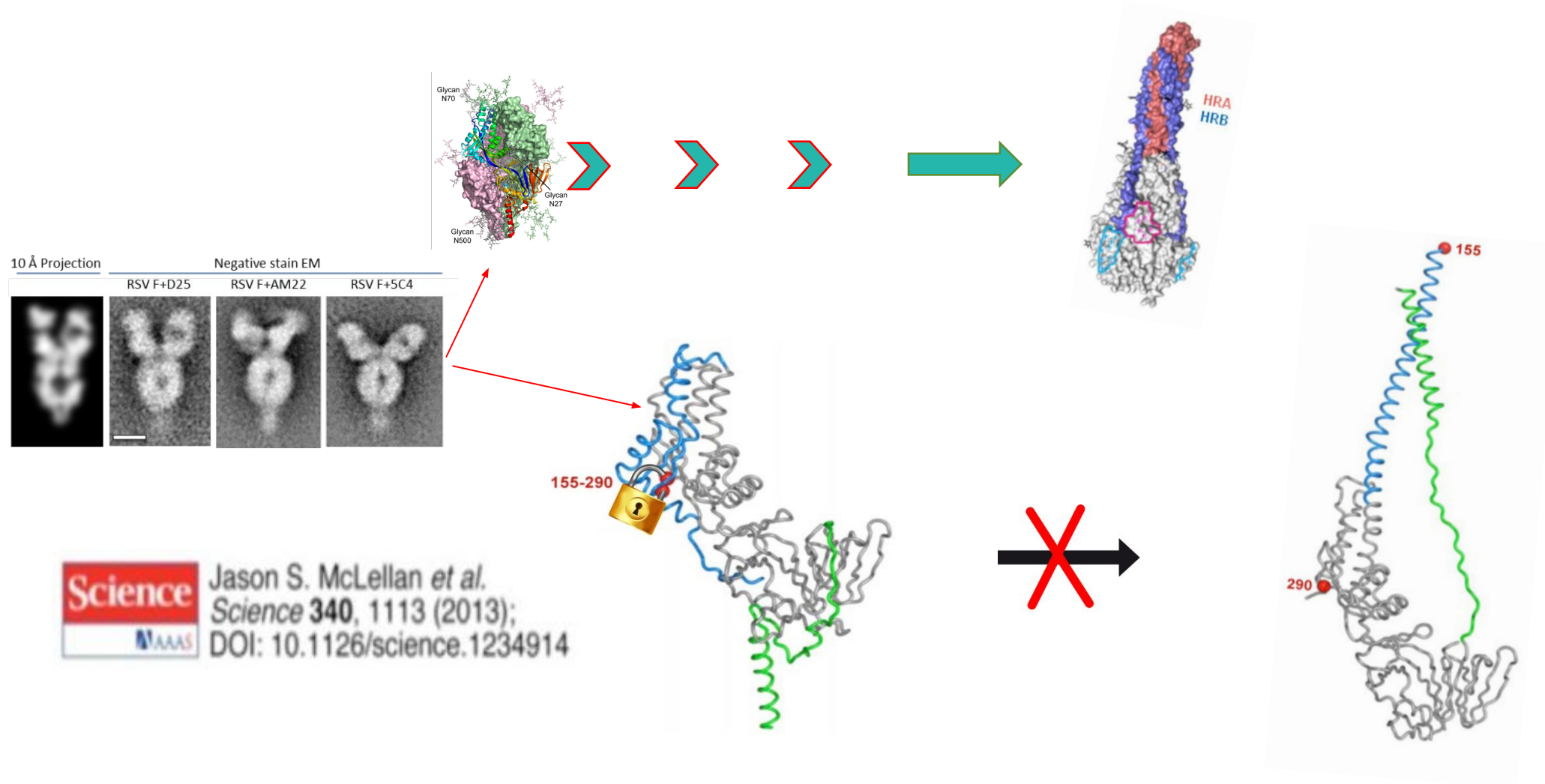
Respiratory Syncytial virus

RSV



# Structural Vaccinology

*in the case of RSV allowed the development of an impossible vaccine*



# 2023 the year of RSV

2 vaccines approved  
for 60 years and older

FDA NEWS RELEASE

## **FDA Approves First Respiratory Syncytial Virus (RSV) Vaccine**

*for Individuals 60 Years of Age and Older*

1 vaccine approved  
for pregnant women

FDA NEWS RELEASE

## **FDA Approves First Vaccine for Pregnant Individuals to Prevent RSV in Infants**

1 monoclonal antibody  
Approved for babies

FDA NEWS RELEASE

## **FDA Approves New Drug to Prevent RSV in Babies and Toddlers**

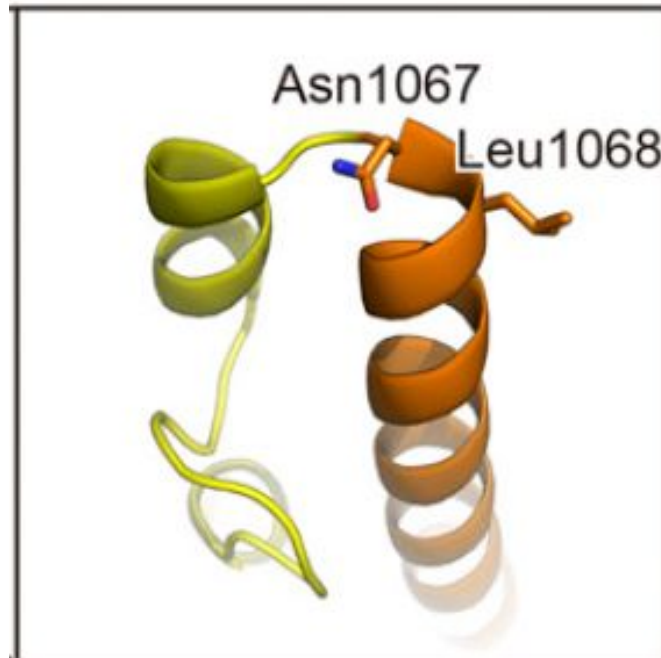
Return to  
Passive immunization



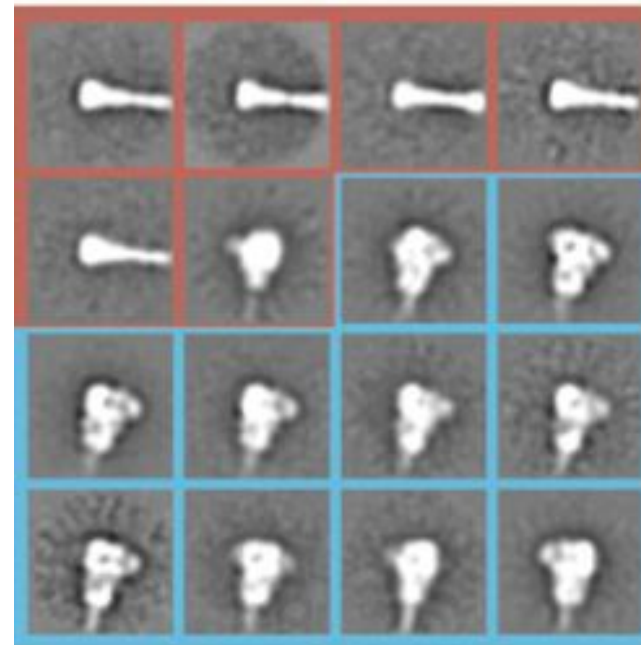
# Stabilizing the prefusion spike protein of MERS in 2017 the prototype of SARS-CoV-2 vaccine

## Immunogenicity and structures of a rationally designed prefusion MERS-CoV spike antigen

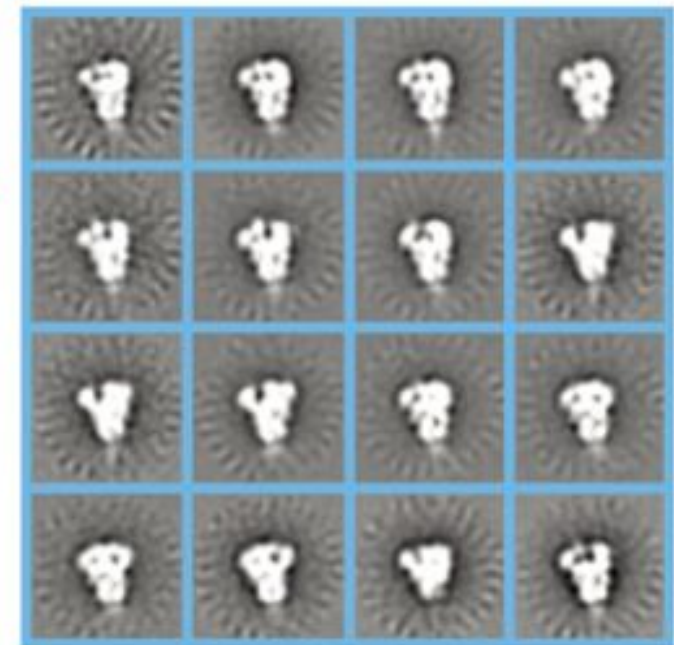
Jesper Pallesen<sup>a,1</sup>, Nianshuang Wang<sup>b,1,2</sup>, Kizzmekia S. Corbett<sup>c,1</sup>, Daniel Wrapp<sup>b</sup>, Robert N. Kirchdoerfer<sup>a</sup>, Hannah L. Turner<sup>a</sup>, Christopher A. Cottrell<sup>a</sup>, Michelle M. Becker<sup>d</sup>, Lingshu Wang<sup>e</sup>, Wei Shi<sup>e</sup>, Wing-Pui Kong<sup>e</sup>, Erica L. Andres<sup>d</sup>, Arminja N. Kettenbach<sup>b,f</sup>, Mark R. Denison<sup>d,g</sup>, James D. Chappell<sup>d</sup>, Barney S. Graham<sup>c</sup>, Andrew B. Ward<sup>a,2</sup>, and Jason S. McLellan<sup>b,2</sup>



→ P



MERS S-WT



MERS S-2P

from

# Reverse Vaccinology

to

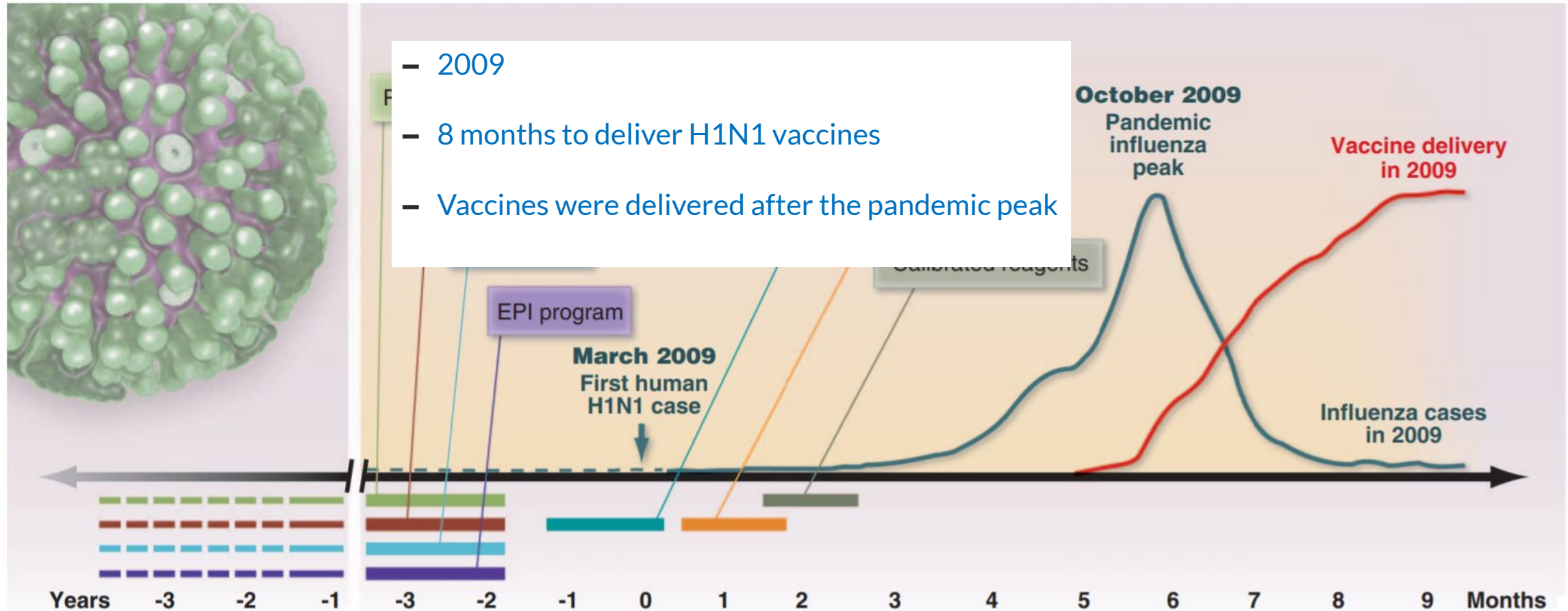
# Synthetic Biology

and

# Digital Vaccinology



# 2009 Swine Influenza Pandemic



## Sunday March 31<sup>st</sup> 2013 Easter day

- Chinese CDC postes the sequence of an H7N9 avian influenza virus
- The virus had already killed 3 people, high risk of influenza pandemic
- Race for vaccine developement starts
- Virus had to be sent from China to CDC in Atlanta



### **Synthetic Generation of Influenza Vaccine Viruses for Rapid Response to Pandemics**

Philip R. Dormitzer *et al.*

*Sci Transl Med* **5**, 185ra68 (2013);

DOI: 10.1126/scitranslmed.3006368

**Emerging Microbes and Infections (2013) 2**, e52; doi:10.1038/emi.2013.54

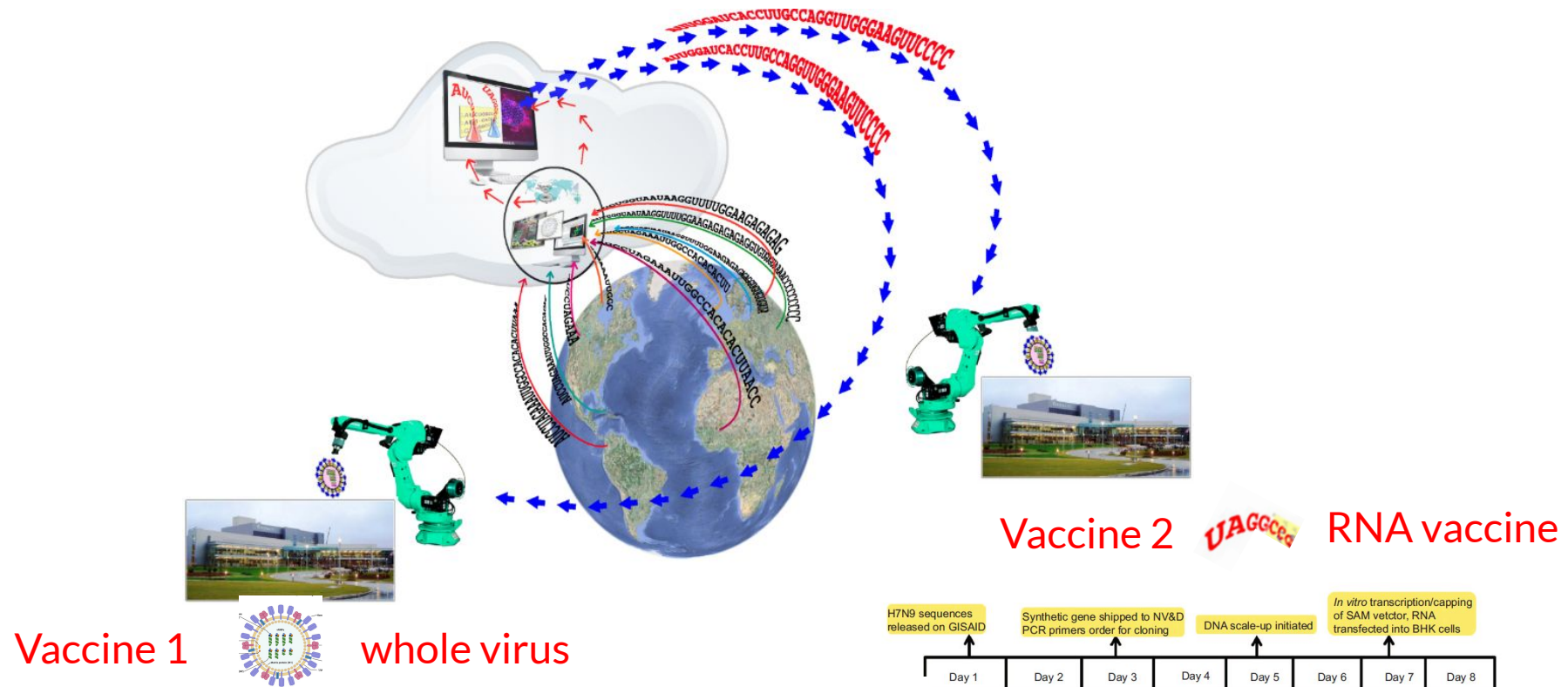
© 2013 SSCC. All rights reserved 2222-1751/13

[www.nature.com/emi](http://www.nature.com/emi)



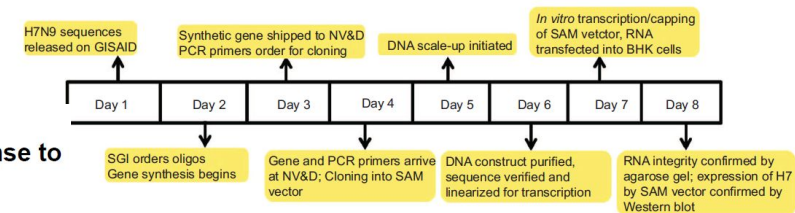
# 2013: Internet & Synthetic Biology-based Vaccines in One Week

In 2013 an RNA vaccine and a virus seed in one week  
using information teleported by internet



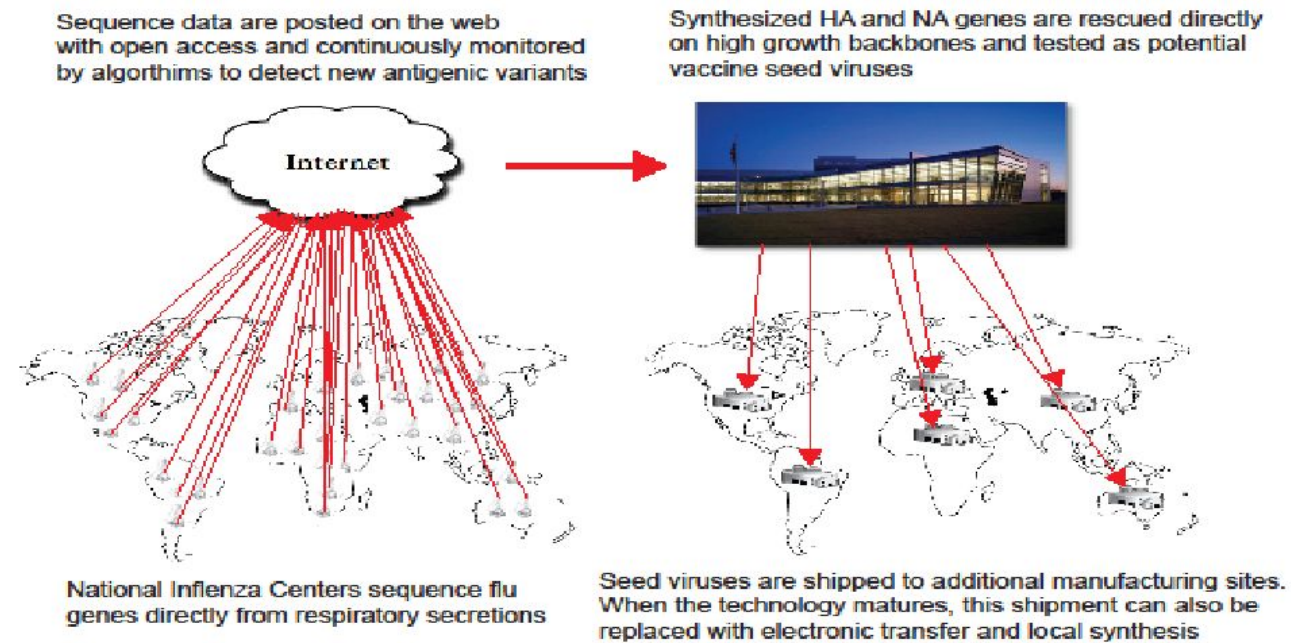
## Synthetic Generation of Influenza Vaccine Viruses for Rapid Response to Pandemics

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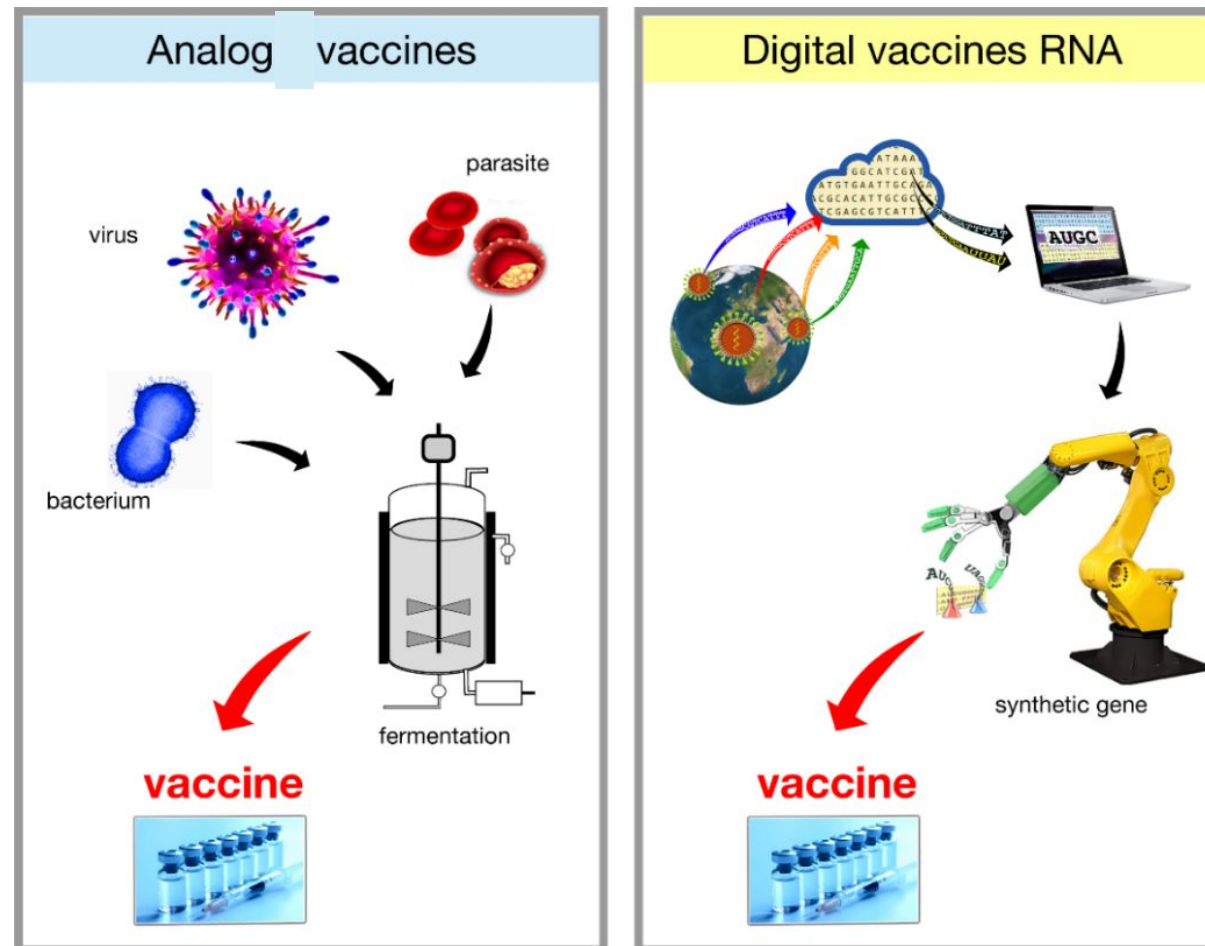
Timeline from electronic gene sequence posting to production of RNA prior to formulation with the LNP delivery system. GISAID, Global Initiative for Sharing Data; PCR, polymerase chain reaction.

# Shipping **Information** Instead of **Viruses**





# 2013 marked the transition from Analog to Digital Vaccines



SCIENCE TRANSLATIONAL MEDICINE | VIEWPOINT

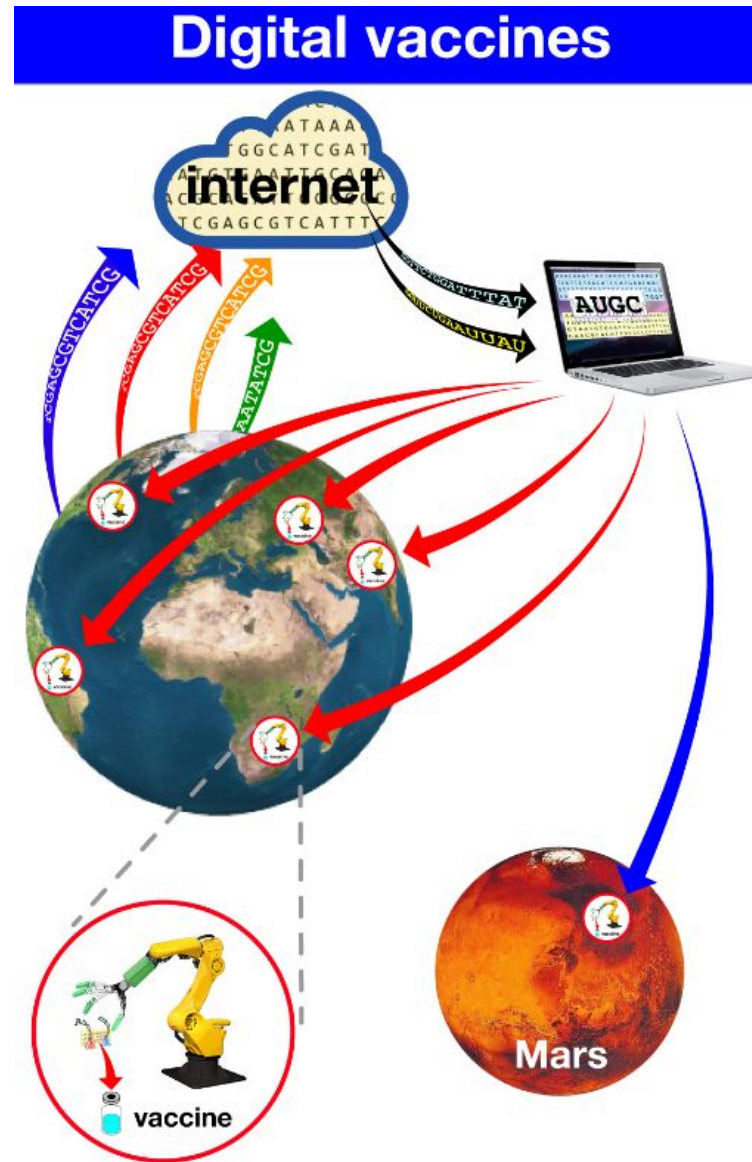
CORONAVIRUS

## Vaccines 2020: The era of the digital vaccine is here

Mariagrazia Pizza, Simone Pecetta, Rino Rappuoli\*

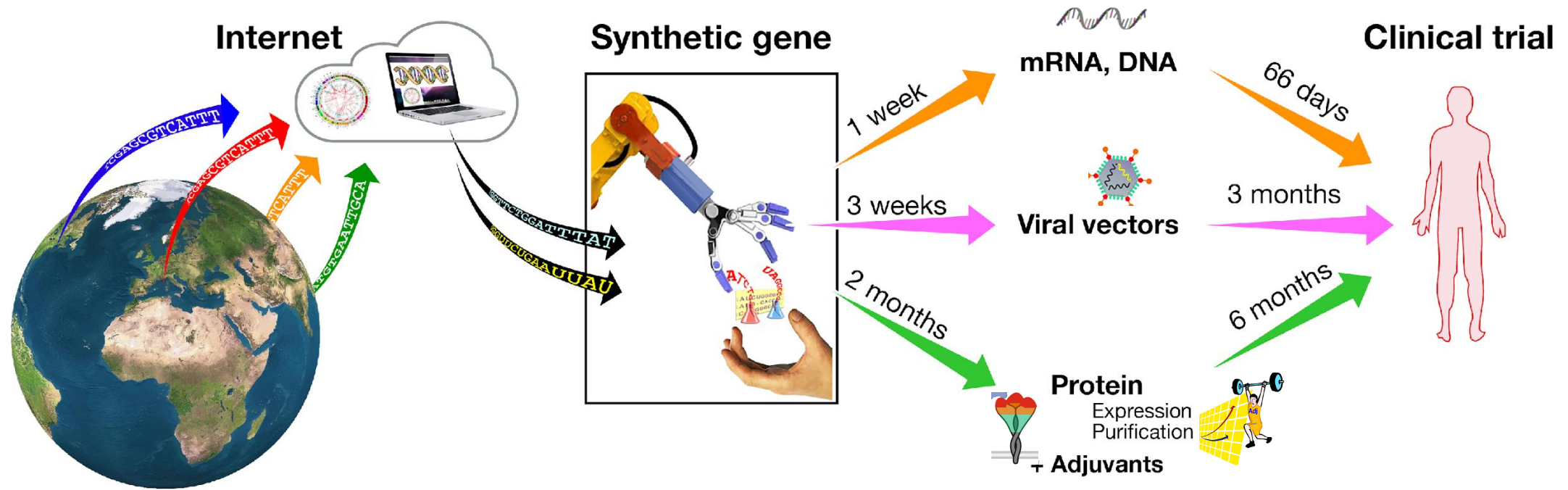


# Accessible Vaccines Globally and even in Mars

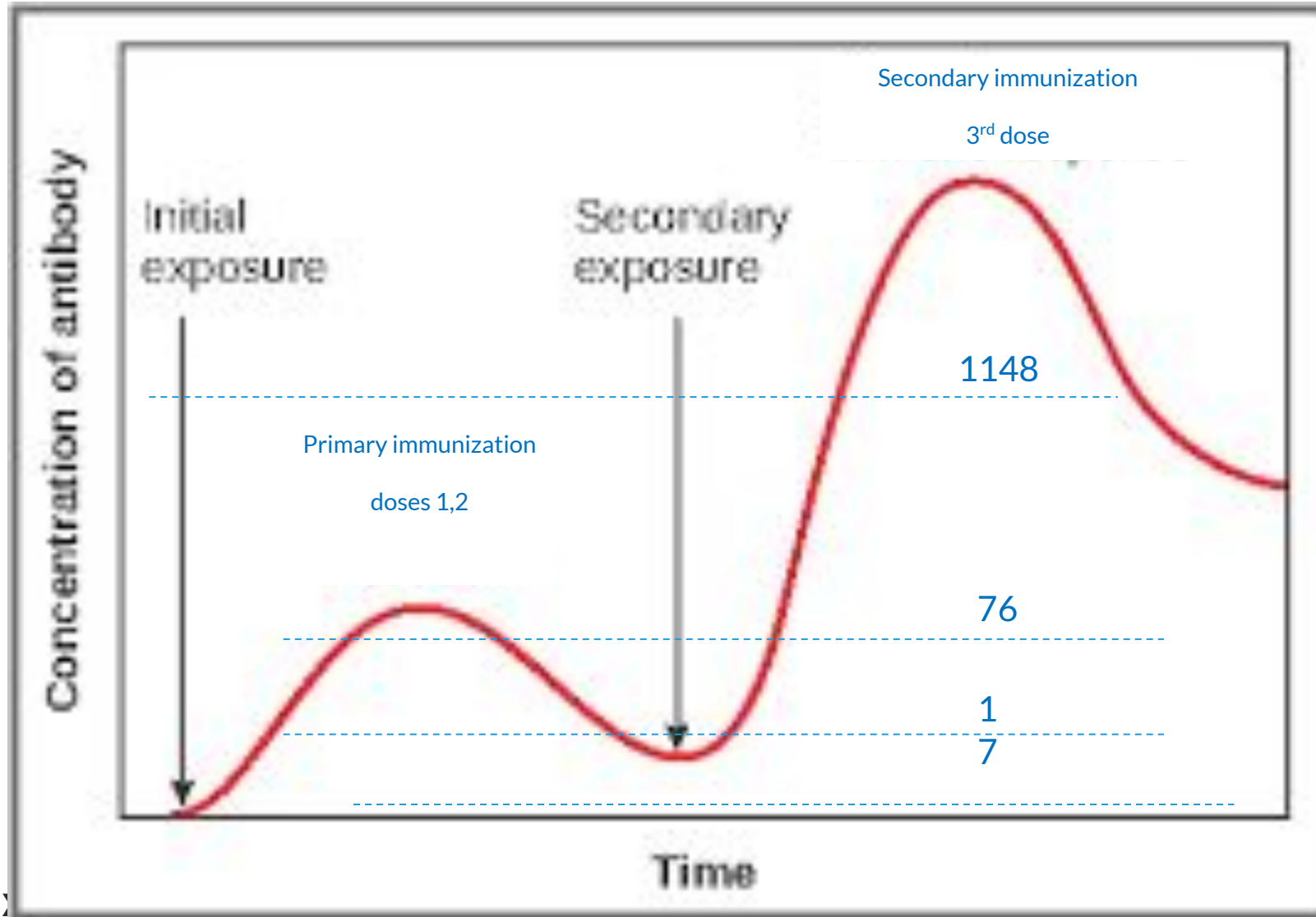


# January 10<sup>th</sup> 2020 SARS-CoV-2 Sequence Posted in Internet

350 labs worldwide used the sequence to make synthetic genes



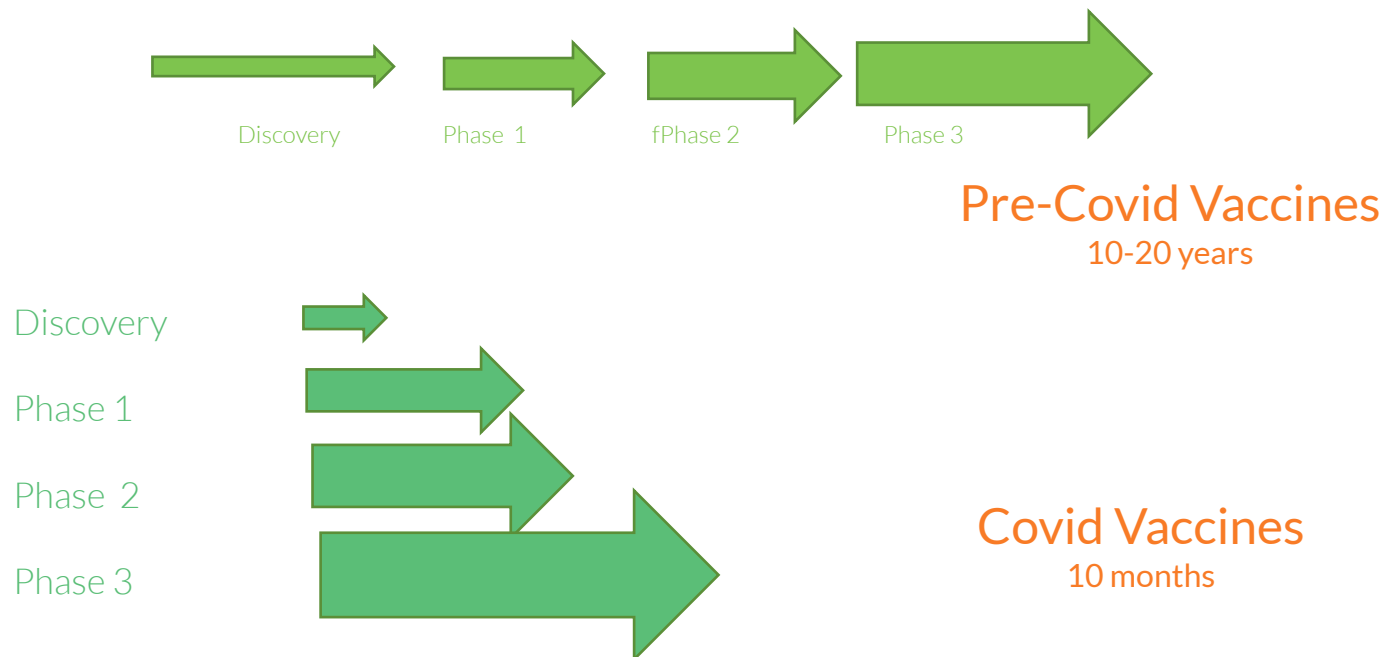
# Vaccines protect well from Covid-19 disease they do not protect well from infection



# Unprecedented Acceleration of Vaccine Development



**Investment > 15 billion** investment from the public sector (>10 billion USA alone) in vaccine Development and Manufacturing allowed at risk development (parallel investment in discovery, early and late development)



## Conclusions

- Investment accelerated development
  - No risk taken on safety and efficacy
  - Financial risk taken by public sector
- Investment pay back: 12 hours

Combining  
Reverse Vaccinology & Digital Vaccinology  
to Cure Cancer



# First efficacious Cancer Vaccine reported

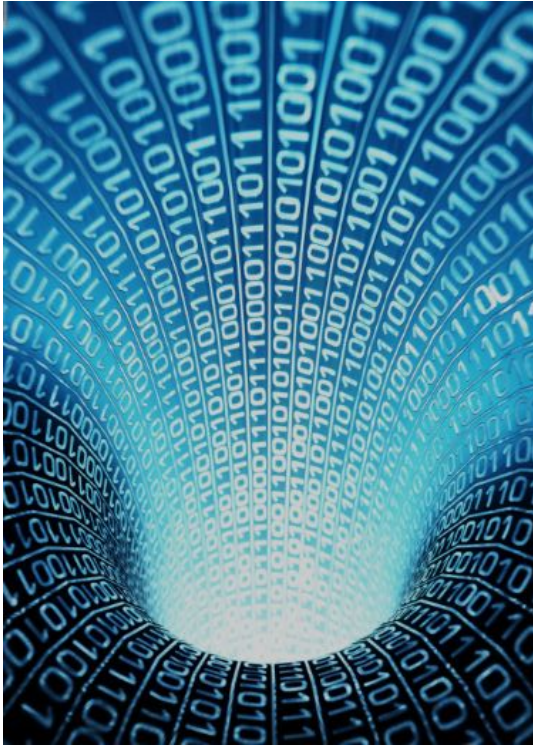
(press release from Merck/Moderna)

- People with melanoma stage 3 or 4 of the disease
  - 157 patients with surgically removed cancer
    - 50% of patients treated with checkpoint inhibitor
    - 50% of patients treated with checkpoint inhibitor + *personalized mRNA vaccine containing 34 epitopes derived from the genome of the tumor of each patient*
- **Cancer vaccine reduced the risk of recurrences or death 65%**



# The vaccines of the future

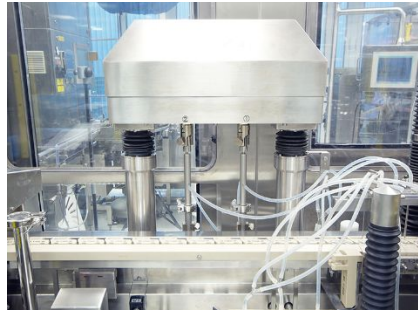
## Digital/designed by AI



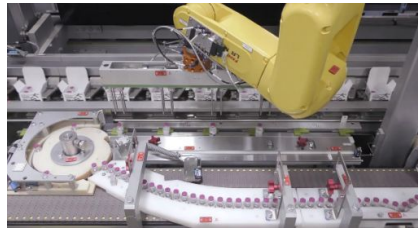
- structure/epitope
- Stability
- Formulation

## Manufactured more and more by AI driven robotics

### Fermentation



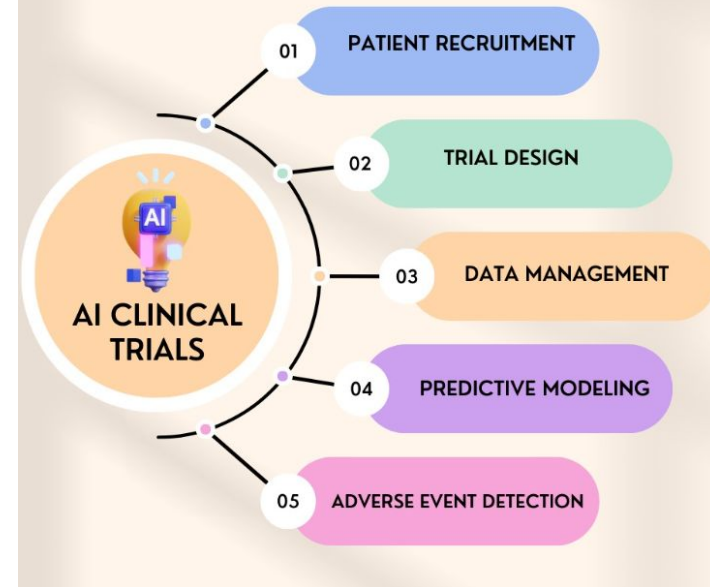
### Filling



- Fermentation
- Filling
- Purification
- Digital twins
- Quality controls

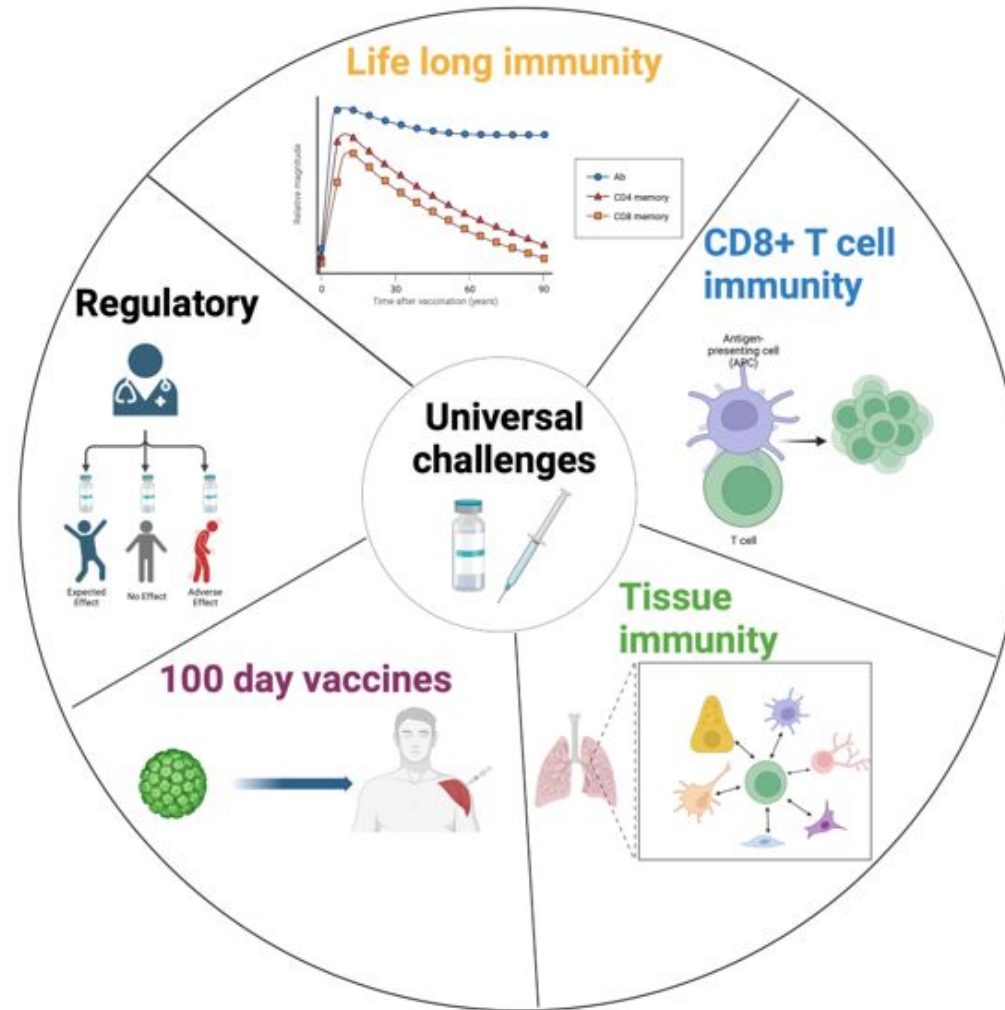
## Clinical/regulatory Help/risks?

### 5 Ways AI Transforms Clinical Trials



- Can they replace established statistics
- They may introduce bias

# The challenges for the vaccines of the future



**Cell**  
Leading Edge

Volume 187, Issue 19, P5171-5194, September 19, 2024

**Transforming vaccinology**

Rino Rappuoli,<sup>1,\*</sup> Galit Alter,<sup>2,\*</sup> and Bali Pulendran<sup>3,4,5,\*</sup>



# Looking at the future

Vaccines to be better prepared

for

**Emerging Infections**

**Antimicrobial Resistance (AMR)**

**Pandemics**

**May 5<sup>th</sup> 2023**

## **COVID-19 pandemic no longer constitutes a public health emergency**

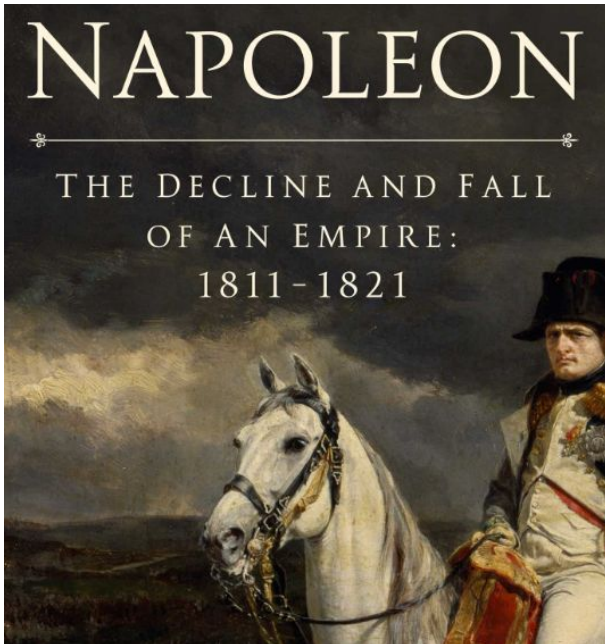


WHO says COVID-19 is no longer a global health emergency



**May 5<sup>th</sup> 1821**

## **Death of Napoleon Bonaparte**



***Manzoni wrote about Napoleon's death***

*Ei fu. Siccome immobile, dato il fatal sospiro, stette la salma immemore orba di tanto spiro.....*

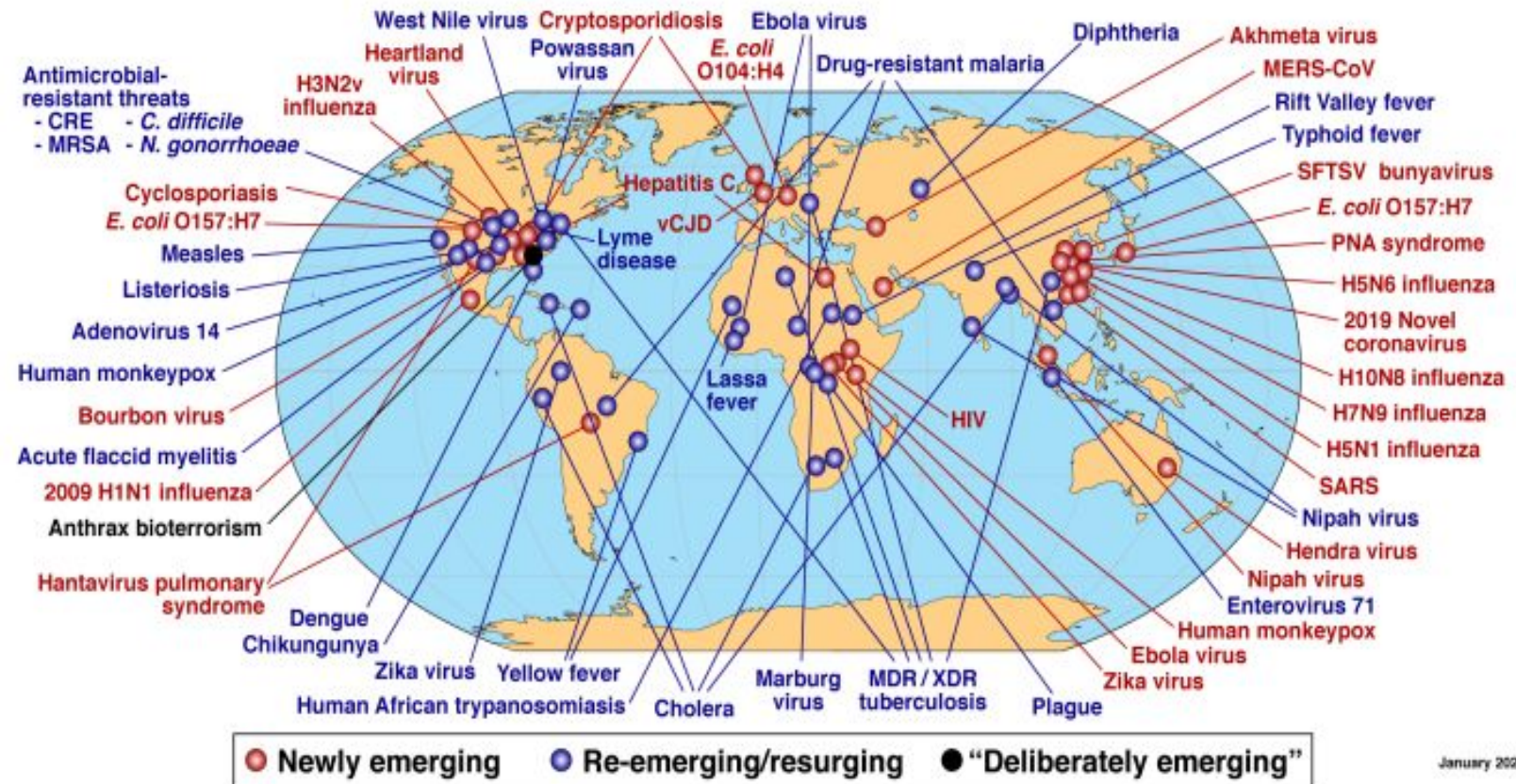
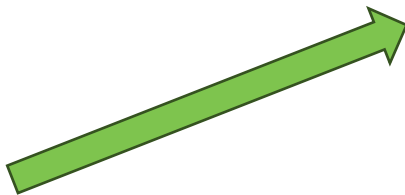
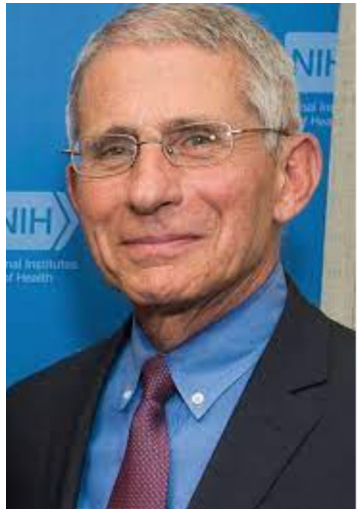
*così percossa, attonita la terra al nunzio sta*

*né sa quando una simile orma di piè mortale la sua cruenta polvere a calpestar verrà.*



# Emerging & Re-emerging Infectious Diseases will happen with increased frequency

- Climate change
- 8 billion people
- Deforestation
- Urbanization
- Travel



Viruses, bacteria and fungi that according to Antony Fauci  
may cause new pandemics



## CEPI, the Coalition for Epidemic Preparedness Innovations, a global partnership

Mission supported by G7, G20, NIH, WHO ....

Negotiating Pandemic Treaty

Prioritize pathogens with pandemic potential ..

Develop vaccines in 100 days

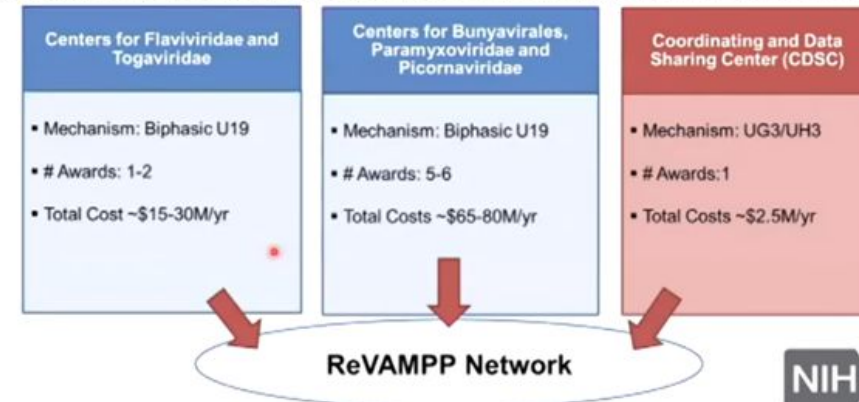
Equity



# ReVAMPP

## FY24 Concept: Research and Development of Vaccines and Monoclonal Antibodies for Pandemic Preparedness (ReVAMPP) Network

- **Objective:** Establish a network of comprehensive, cooperative basic and translational research centers to
  - Develop and validate generalizable approaches for vaccines and mAbs for the prototype viruses and other related family members
  - Advance scientific knowledge for prototype viruses within families with high pandemic potential

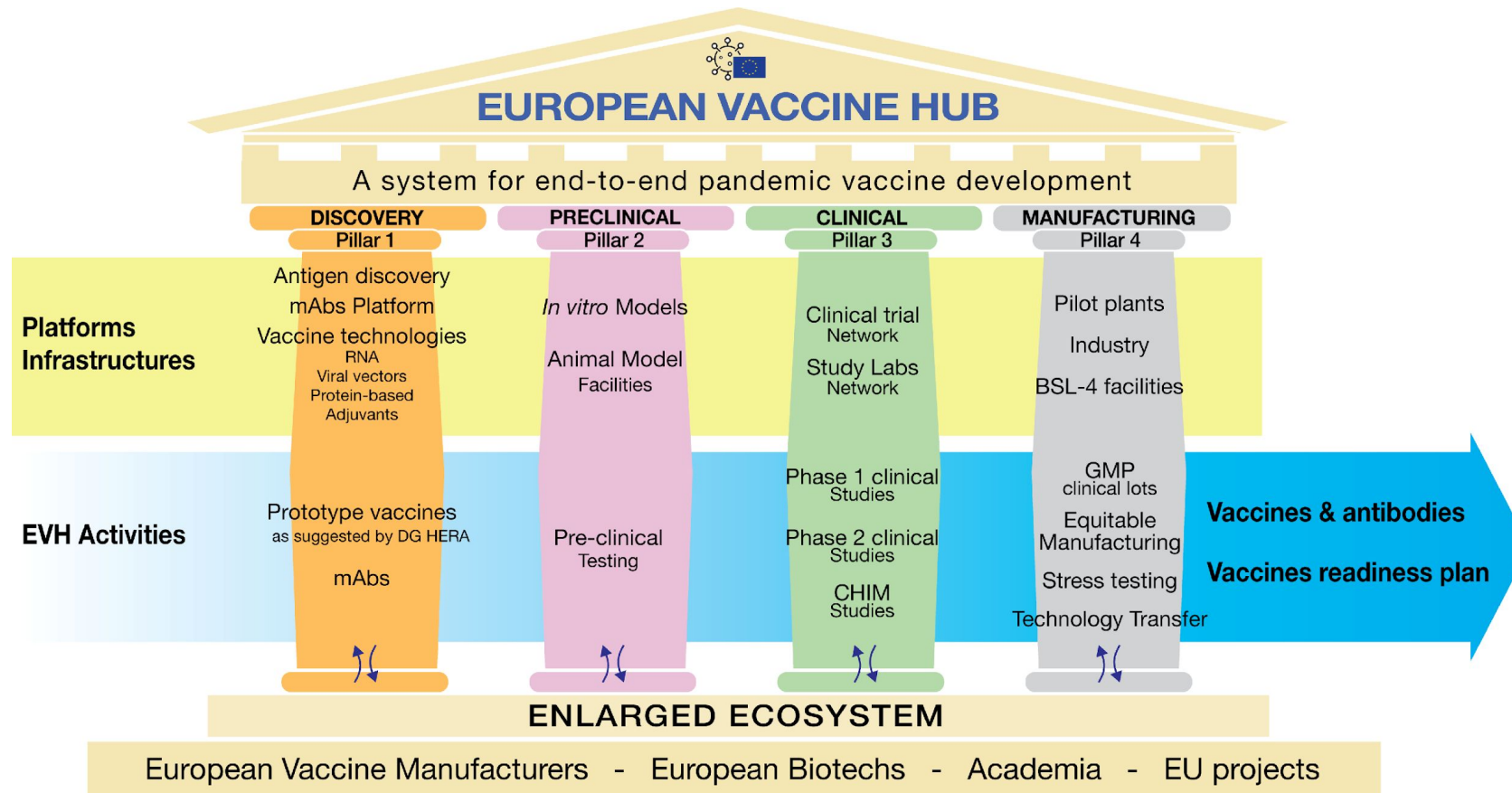




# European Vaccine Hub



**1.1. EU4H-2024-PJ-01-1 (CP-g-24-10) - Call for proposals on the European Hub for vaccine development (HERA)**



Thank you

