RIETI
Research Institute of Economy, Trade & Industry, IAA

FPJ, IPJO, IFRJ-MFJ, RIETI, Kyoto University Seminar

Handout

"Socio-Life Science Interdisciplinary Seminar : Stakes of COVID-19 vaccination"

July 3, 2021

Christiane GERKE

https://www.rieti.go.jp/jp/index.html

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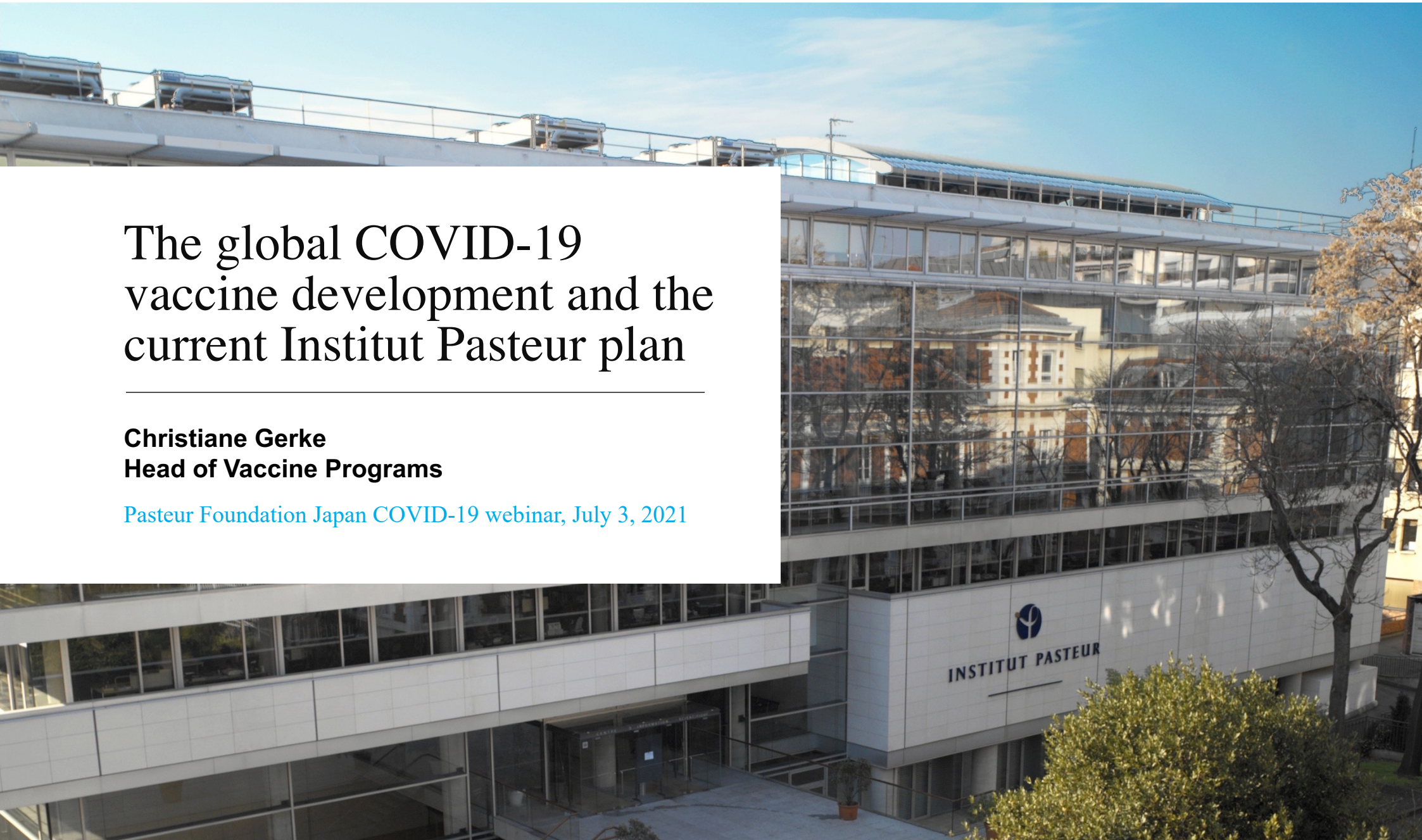
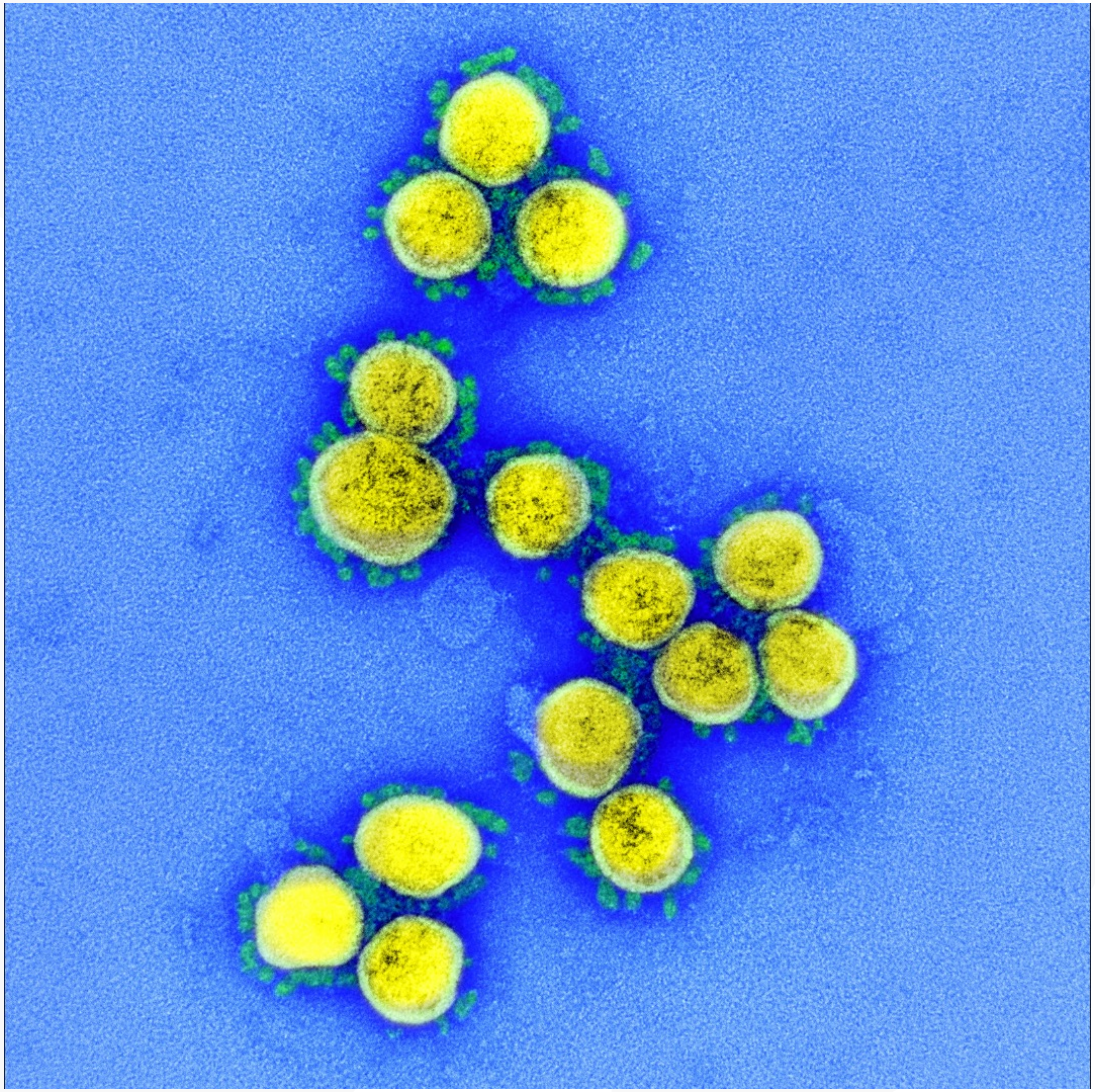


The global COVID-19 vaccine development and the current Institut Pasteur plan

Christiane Gerke
Head of Vaccine Programs

Pasteur Foundation Japan COVID-19 webinar, July 3, 2021

SARS-CoV-2



SARS-CoV-2 causes COVID-19 disease, first detected in Wuhan, China, in December 2019.

WHO declared the outbreak a pandemic on March 11, 2020

June 30, 2021 6:09 pm CEST (WHO site):
181,521,067 cases
3,937,437 deaths

2,915,585,482 vaccine doses administered

NIAID-RML

https://www.flickr.com/photos/niaid/49645120251/in/album-72157712914621487/

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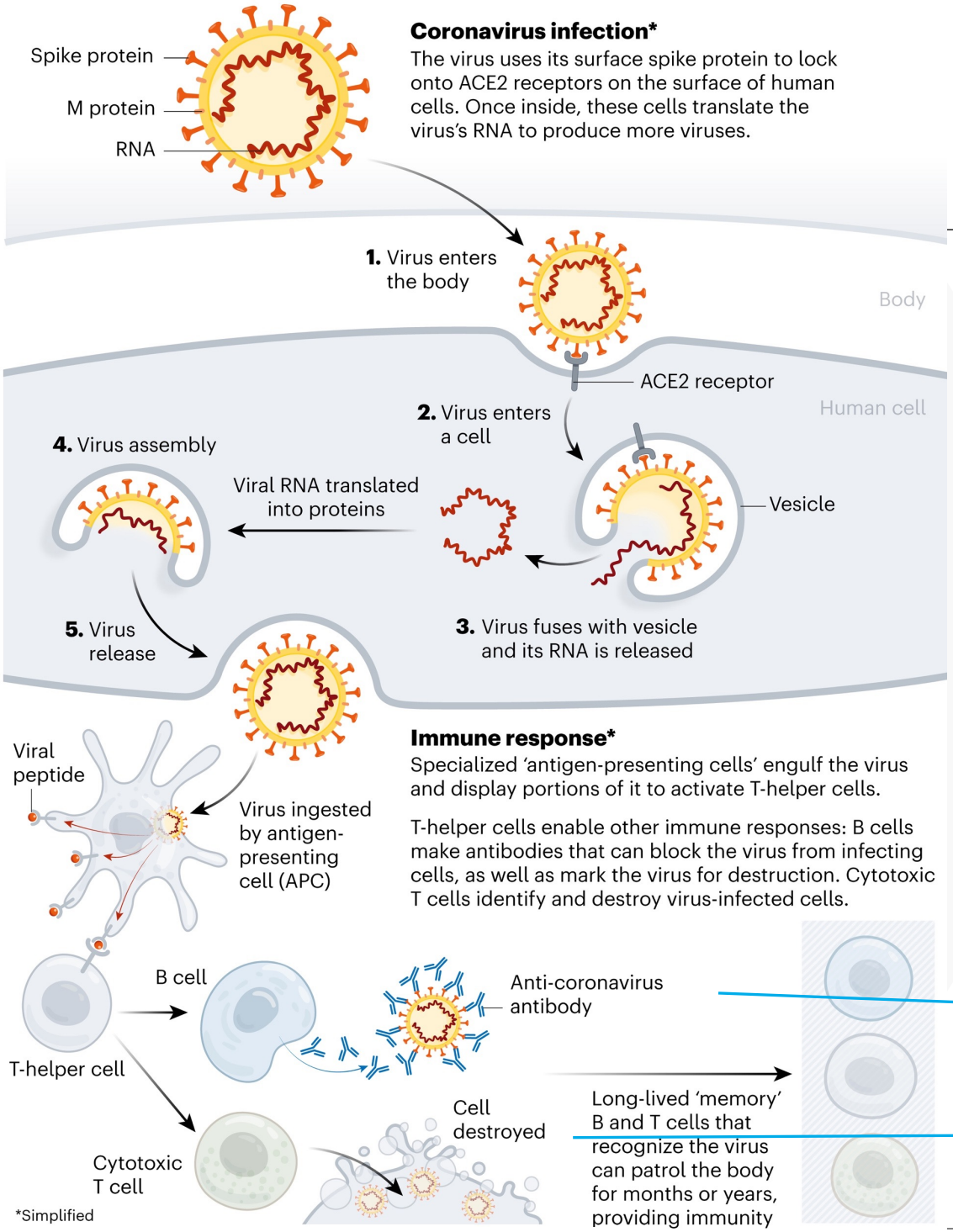
Immune response to SARS-CoV-2 infection



Callaway and Spencer, 2020, Nature

Assumed to be important for protection:

Neutralizing antibodies

T cell responses / Th1 response

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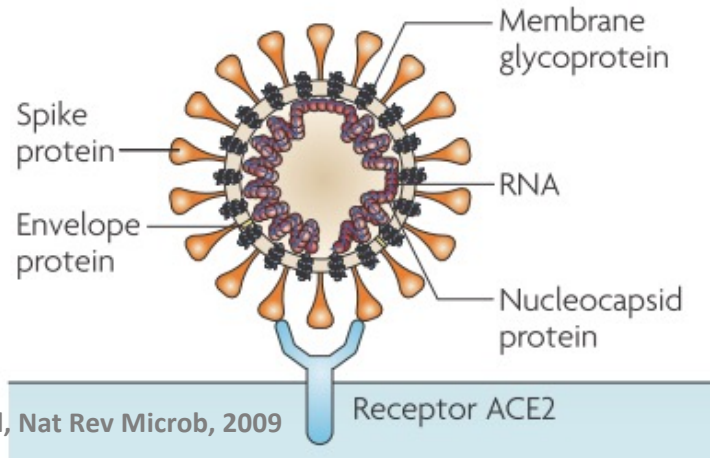
Vaccine Target

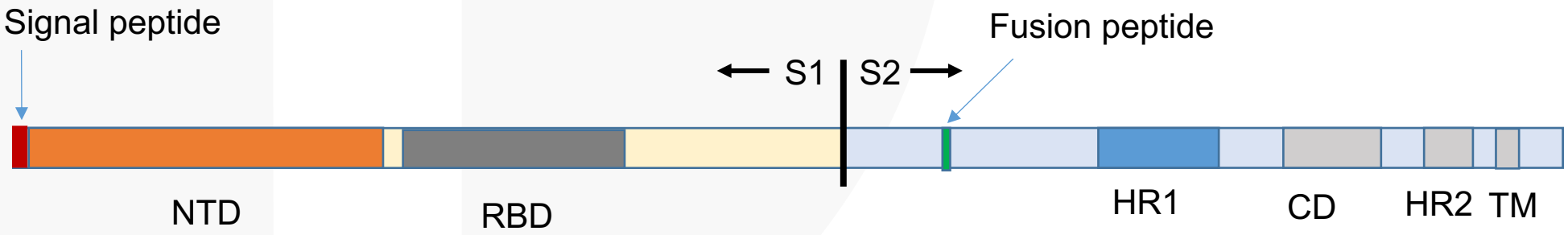
Spike protein as key antigen for current engineered vaccines

Spike = Main antigen
to elicit neutralizing antibodies

Main antigen used as a whole or in part by many of the approaches.
Different modifications used to optimize performance.



Du et al, Nat Rev Microb, 2009



Adapted from Wrapp et al. Science 2020

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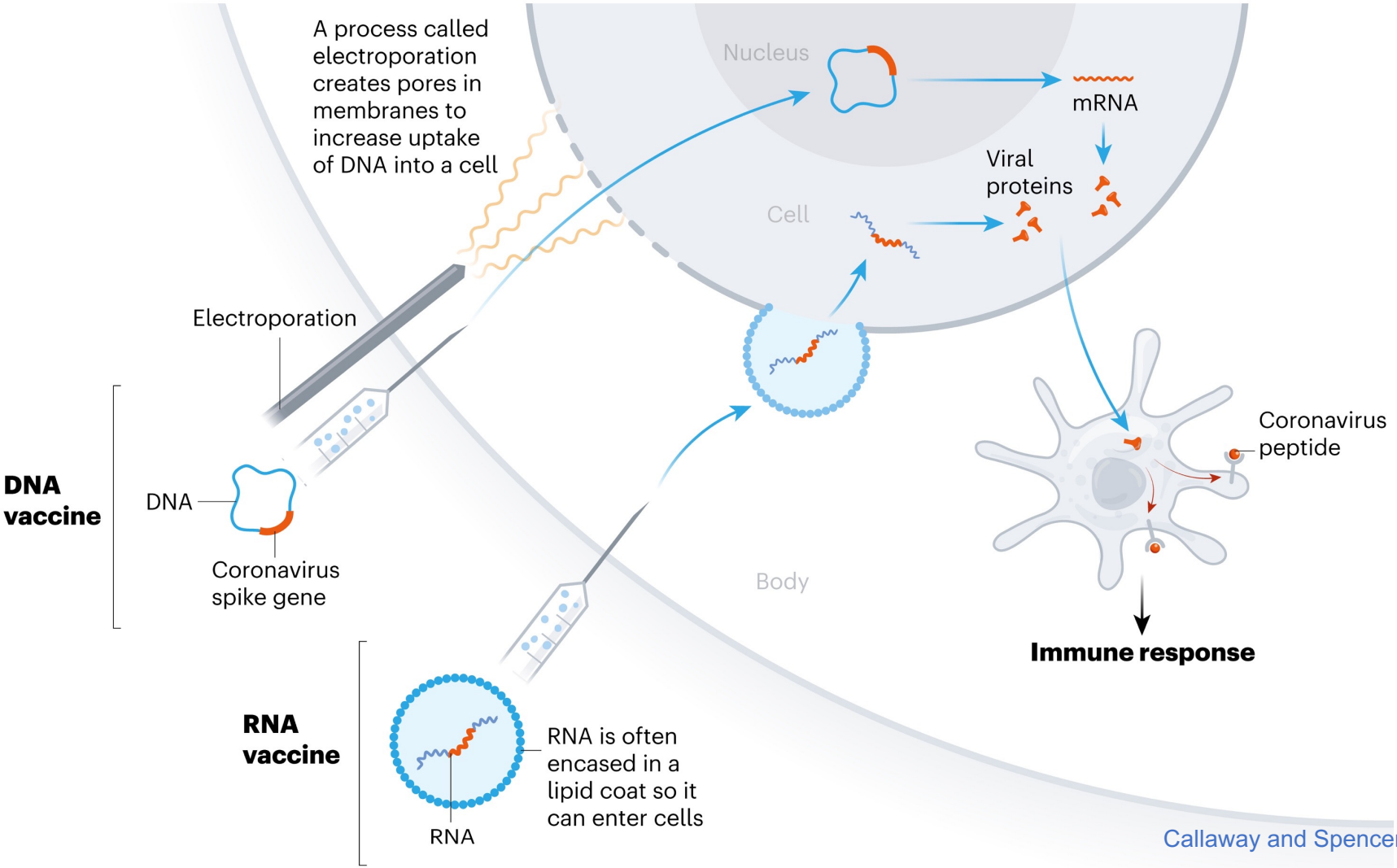
Vaccine Technologies (1/2)

Nucleic Acid Vaccines



Callaway and Spencer, 2020, Nature

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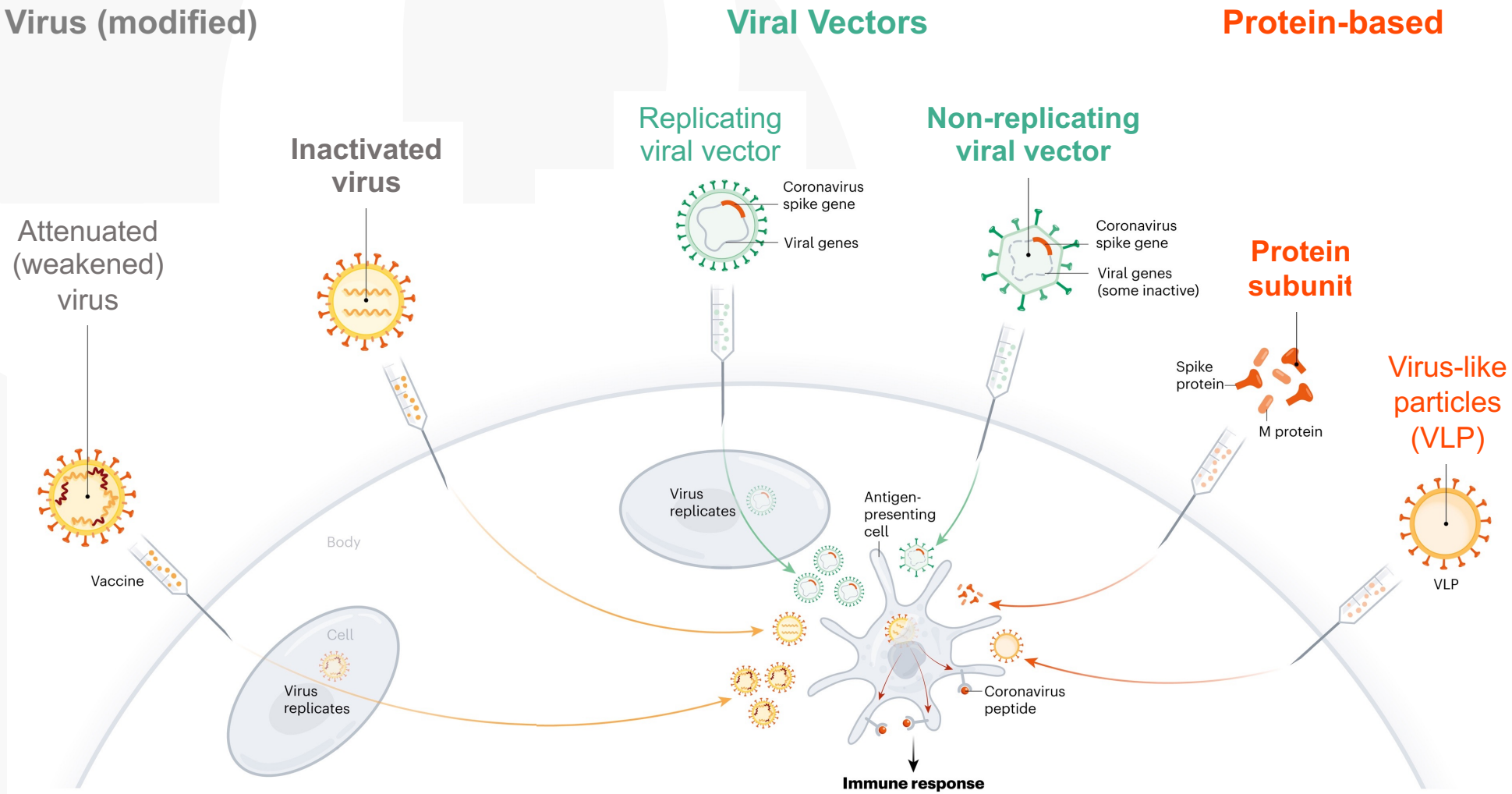
Vaccine Technologies (2/2)

Modified Virus, Vectors, Subunits



Callaway and Spencer, 2020, Nature

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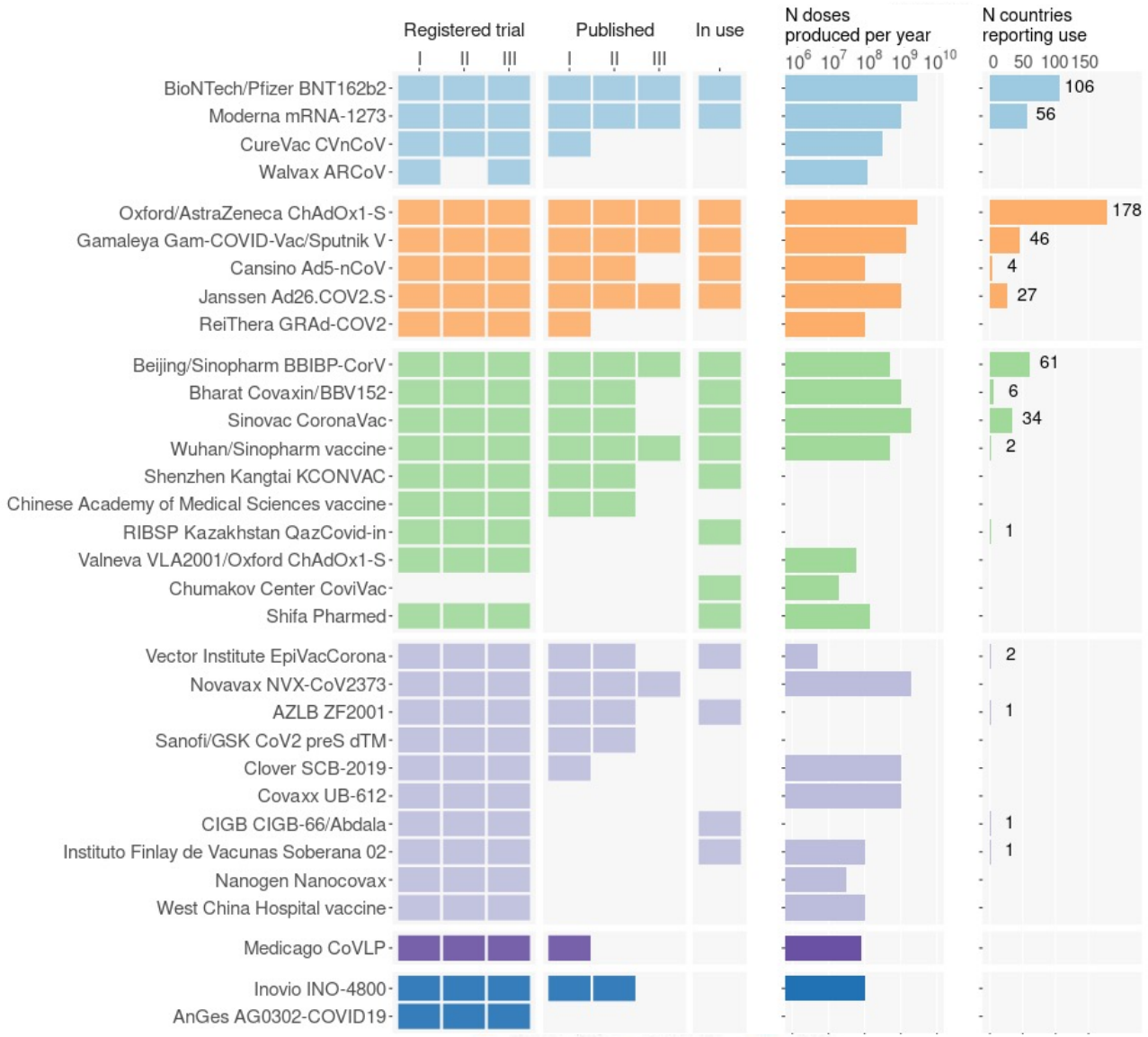
Most advanced vaccines

Interactive website tracking COVID-19 vaccine development



An interactive website tracking COVID-19 vaccine development

Madhumita Shrotri, Tui Swinnen, Beate Kampmann, Edward P K Parker

The Lancet Global Health

Volume 9 Issue 5 Pages e590-e592 (May 2021)

DOI: 10.1016/S2214-109X(21)00043-7

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Overview of vaccine development

Other sources

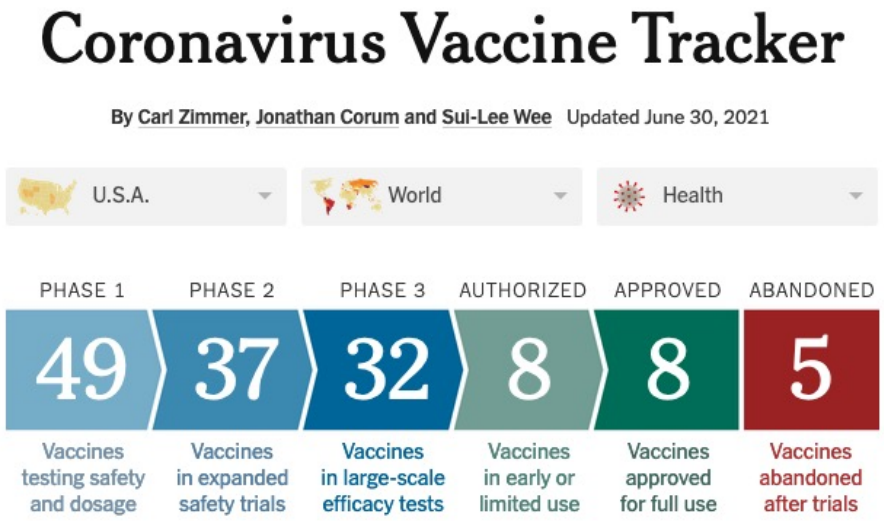
WHO

COVID-19 vaccine tracker and landscape

- Vaccine candidates in development
- Status of COVID-19 Vaccines within WHO EUL/PQ evaluation process

https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines

New York Times



https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html?referringSource=articleShare

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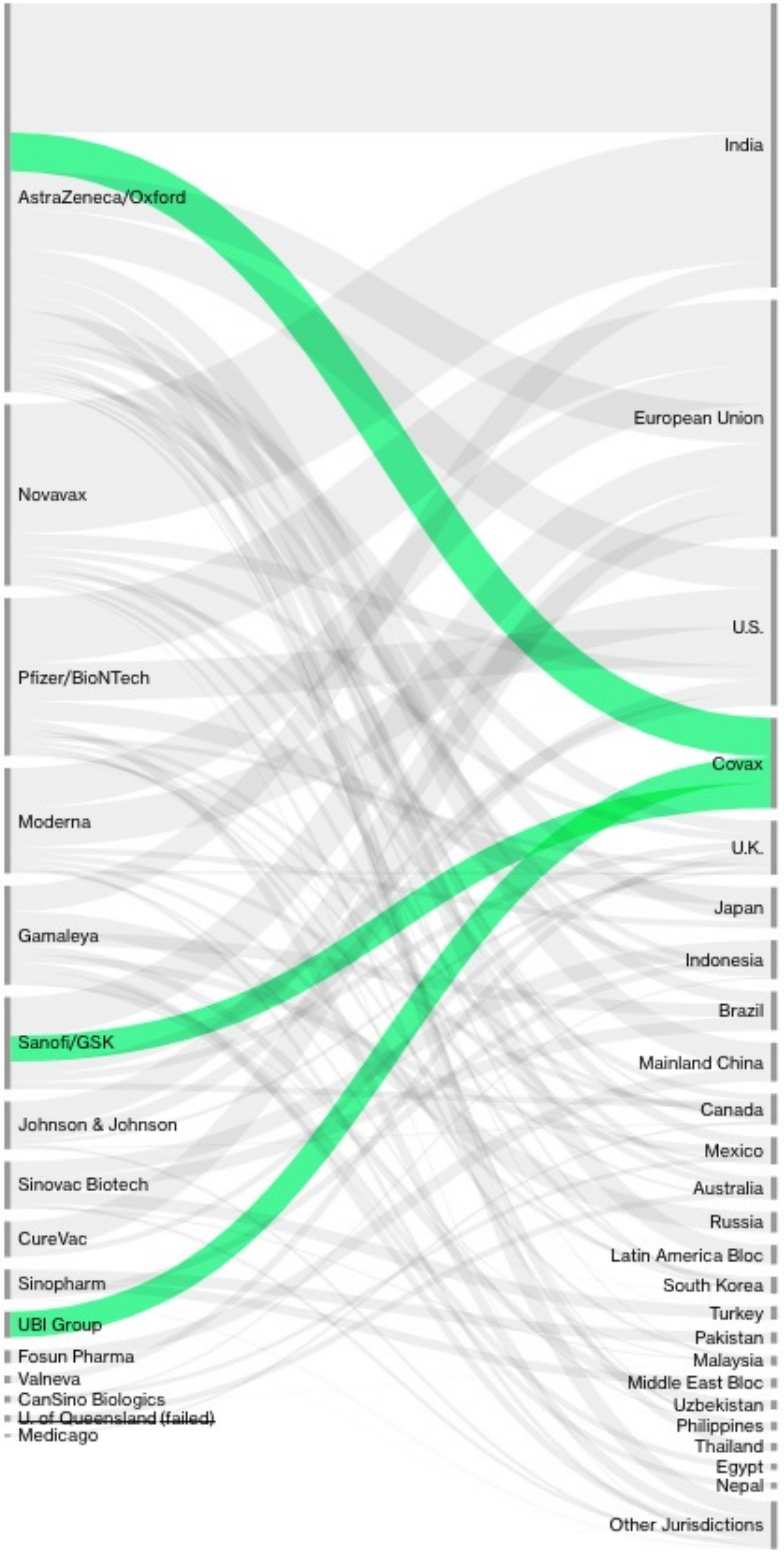

Shots across the Globe

9.6 billion doses already sold as of March 1, 20201

= enough for half of the world's population
(most vaccines use 2 doses)

A global Network of publicly disclosed vaccine deals
https://www.bloomberg.com/graphics/covid-vaccine-tracker-global-distribution/contracts-purchasing-agreements.html

World Map of Vaccination
https://www.bloomberg.com/graphics/covid-vaccine-tracker-global-distribution/

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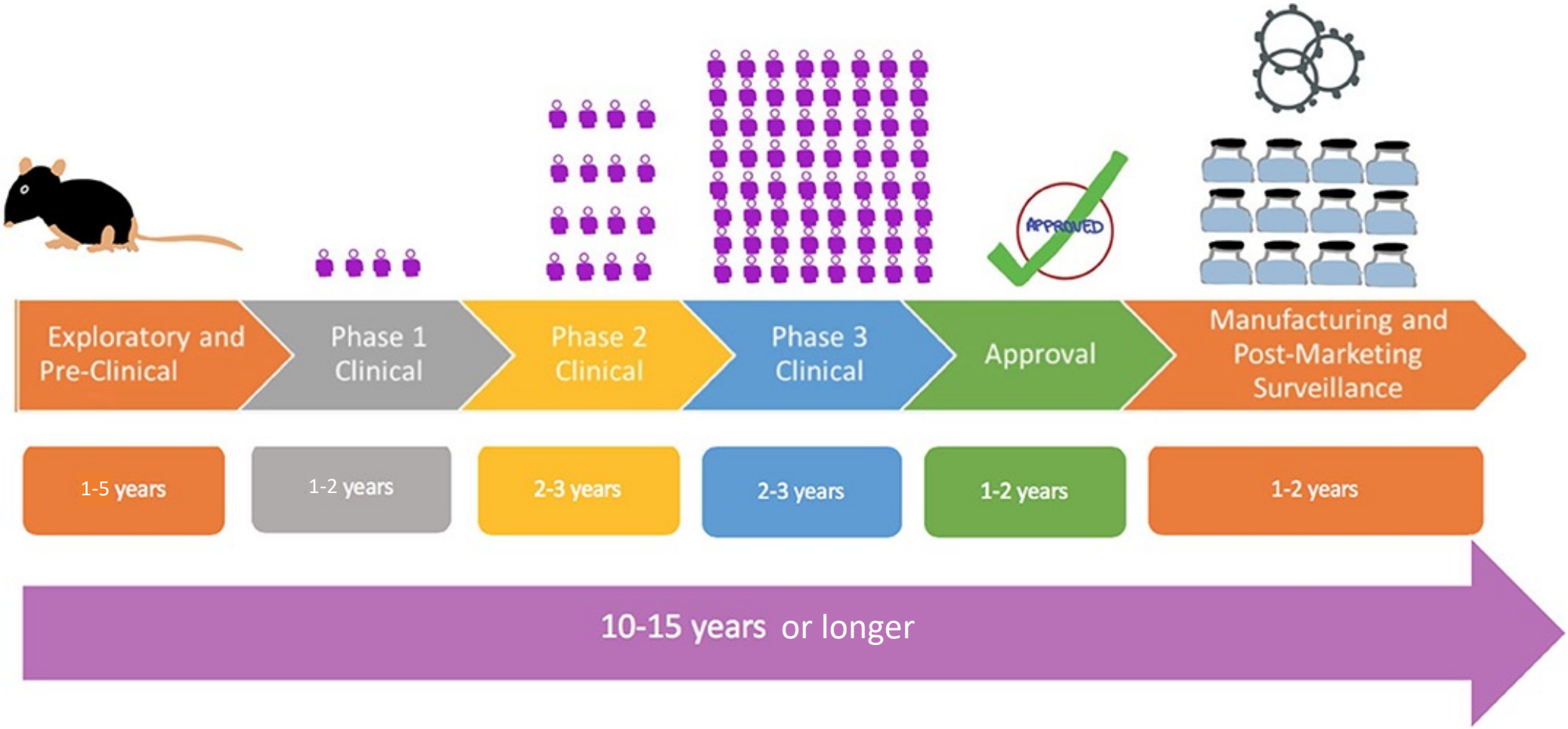
Vaccine development – standard timeline



Adapted from Sharma et al. 2002. Front. Immunol.

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Vaccine development – accelerated schedule

Adapted from Sharma et al. 2002. Front. Immunol.

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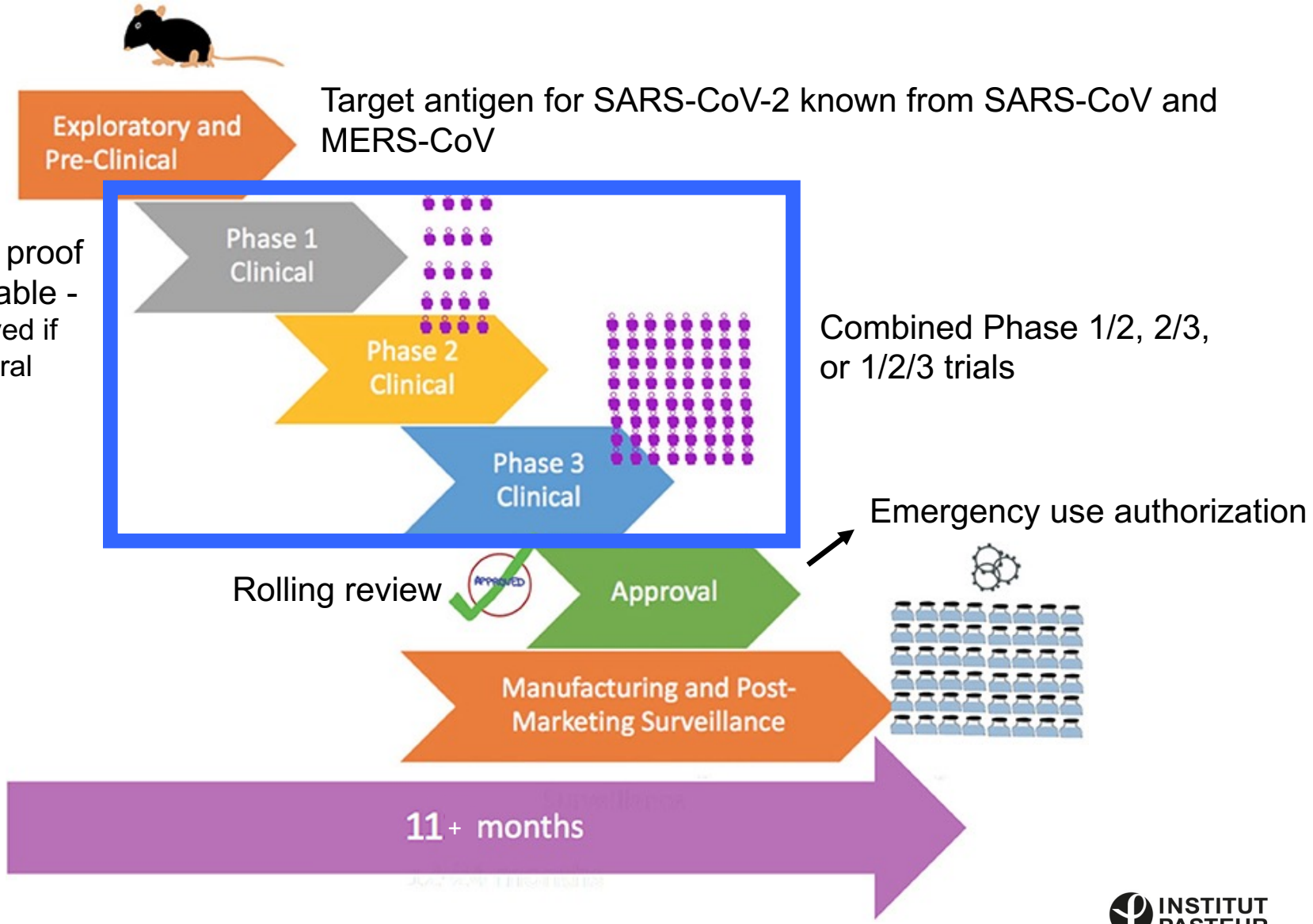
Vaccine development – accelerated schedule

Technologies with previous proof of concept in humans available - pre-clinical toxicity studies waived if technology already tested several times



Adapted from Sharma et al. 2002. Front. Immunol.

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How is efficacy determined?

Example Biontech/Pfizer BNT162b2 – Combined Phase I, II, III

Vaccine:

Lipid nanoparticle-formulated, nucleoside modified mRNA vaccine encoding full-length spike protein

Safety:

Reactogenicity acceptable in all groups

Immunogenicity :

Neutralizing antibody levels higher (18-55y) or similar (65-85y) as in convalescent patients

Efficacy:

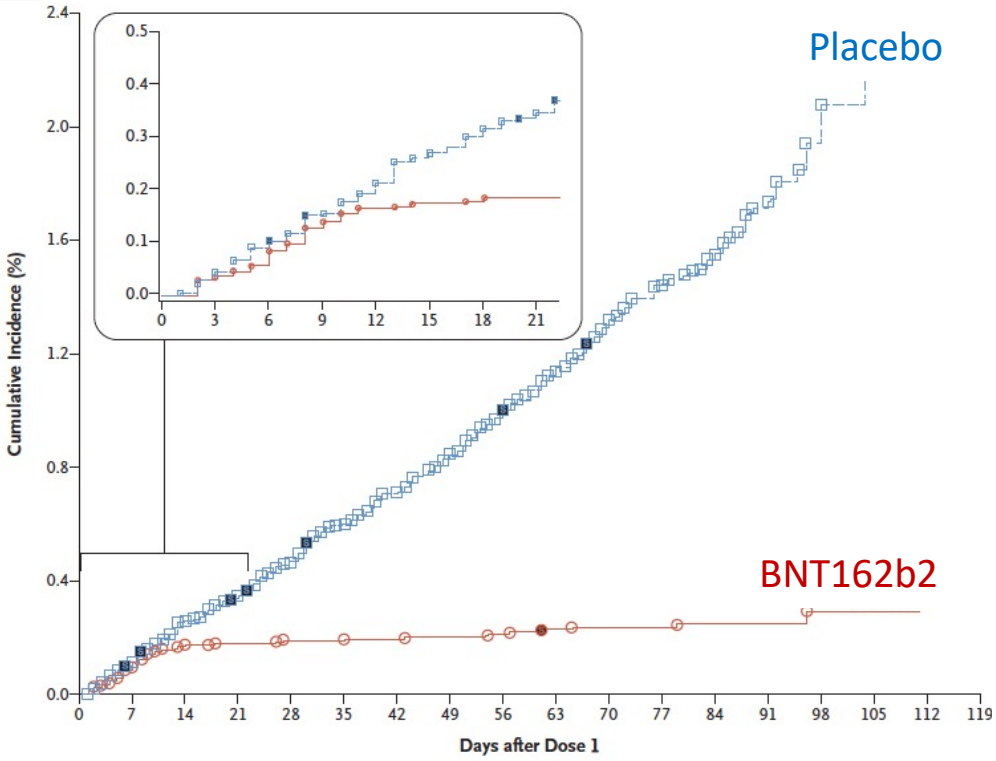
44,338 received 2 injections (36,532 SARS-CoV-2 naïve)

Vaccine recipients : placebo recipients = 1:1

Protection in previously naïve ≥ 7 days after 2nd injection:

170 COVID-19 cases: 8 in vaccinees, 162 in placebo recipients
= 95% efficacy

Efficacy Readout – Cumulative number of cases in vaccine and placebo recipients



Polack et al. N Engl J Med 2020

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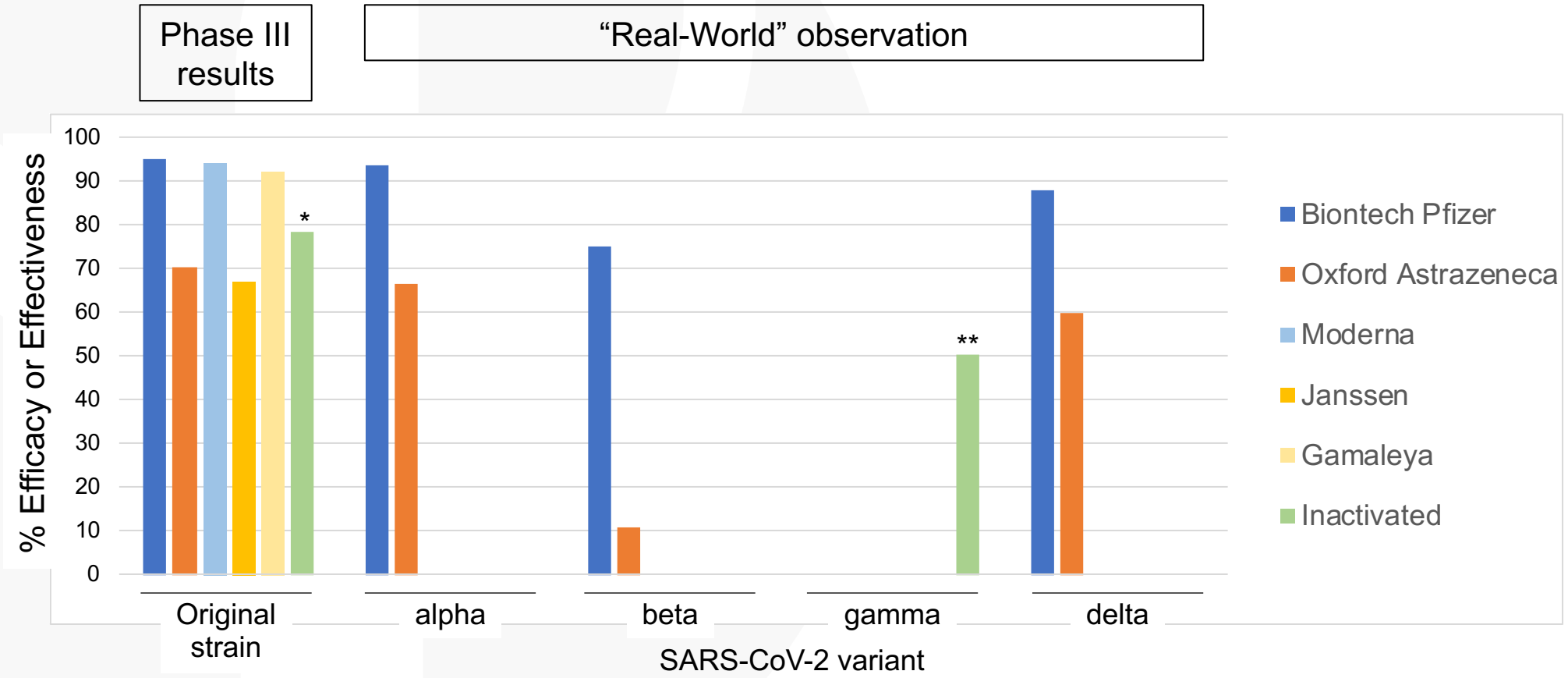
Real-World Effectiveness of Licensed Vaccines

Full vaccine regimen



*Sinopharm (UAE, Bahrain)
** Sinovac (study in Brazil with 75% occurrence of P.1)

Sources: Peer-reviewed publications, pre-prints from PHE, WHO website

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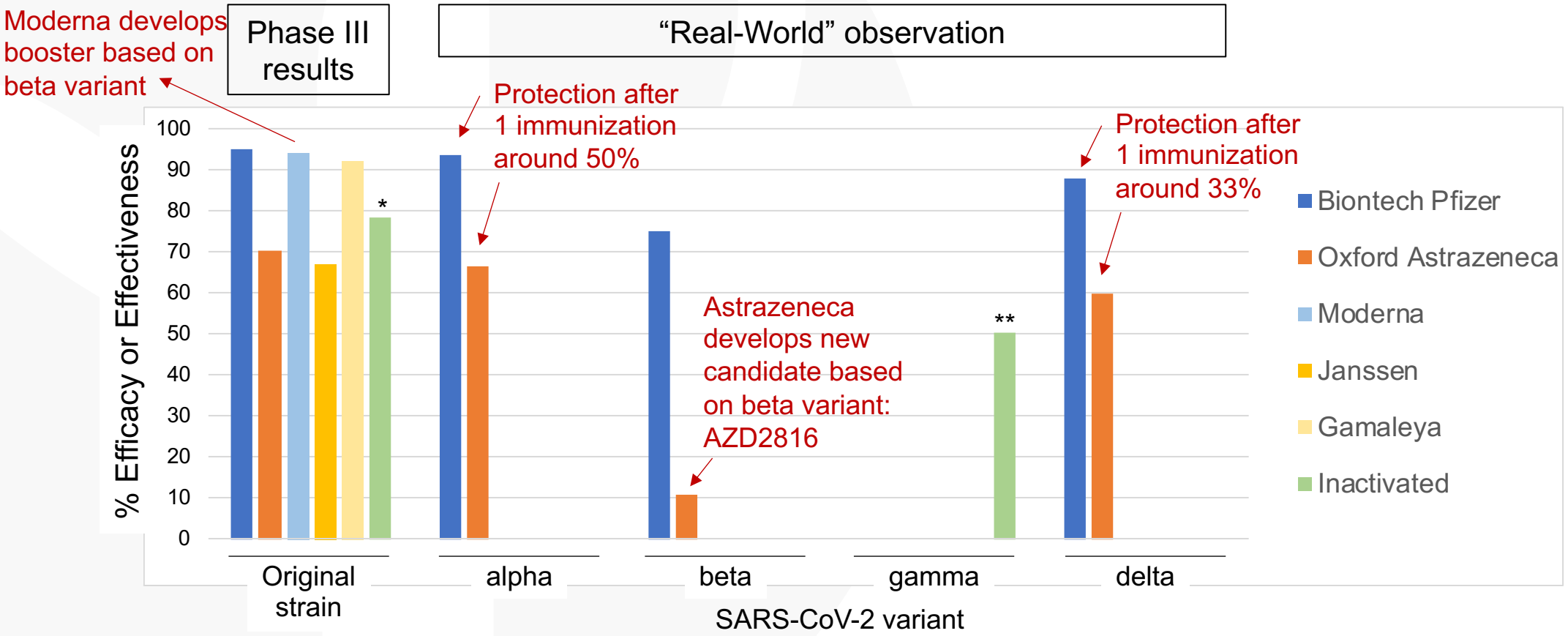
Real-World Effectiveness of Licensed Vaccines

One shot effectiveness and new developments



*Sinopharm (UAE, Bahrain)
** Sinovac (study in Brazil with 75% occurrence of P.1)

Sources: Peer-reviewed publications, pre-prints from PHE, WHO website

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What do we know so far?

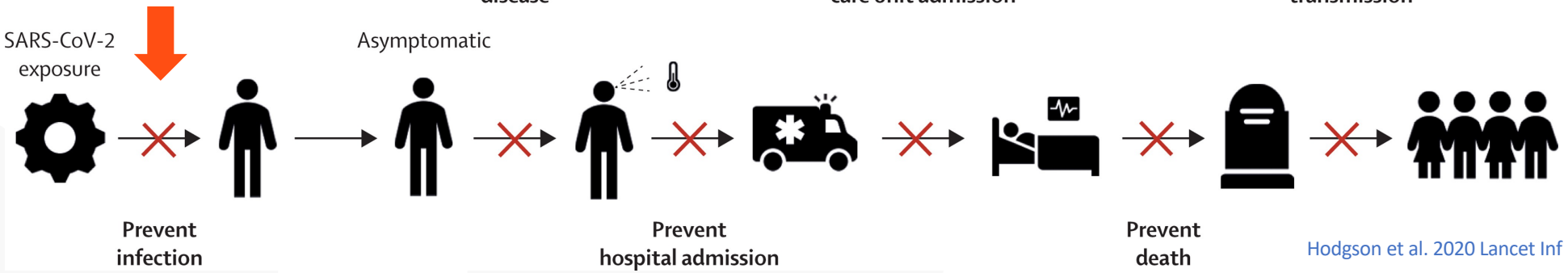
Endpoints of an efficacious vaccine

1. Results of the Phase III trials
+ real world effectiveness data

First data showing prevention of Infection by BNT162b2

> 80% efficacy for mRNA and Chadox / Ad vaccines

First reports of lower viral load after BNT162b2 vaccination



Hodgson et al. 2020 Lancet Inf Dis.

Open questions:

- How long will the protection elicited by the vaccination last?
- To which level will the vaccines prevent transmission of highly transmissible variants?
- Will boosting be implemented? Several boosting studies and new vaccine developments ongoing.

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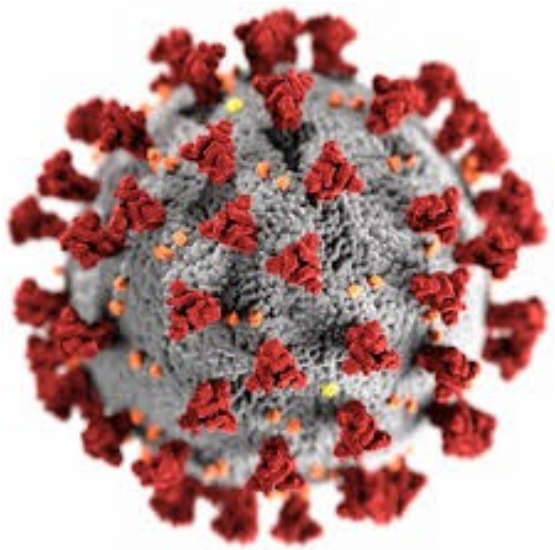
Institut Pasteur and the fight against COVID-19

- Development of the first RT-qPCR test in France, virus isolation, sequencing of multiple isolates and understanding of virus introductions (NRC VRI)
- Development of serology tests and application to seroprevalence studies
  - Community transmission (Crépy-en-Valois)
  - Establishment of humoral responses in different populations and protection
- SARS-CoV-2 biology: key viral and host determinants of infection, neurotropism, immunity, genetics
- **Vaccine development**
  - 5 vaccine candidate projects
  - Rodent models
- Therapeutic approaches
  - Platform for antiviral evaluation (in vitro, in vivo)
  - Identification of drug candidates



450 scientists in 69 research groups
A rapid engagement allowed by Institut Pasteur model and public generosity

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COVID-19 Vaccine Research - Institut Pasteur

5 Vaccine Candidate Projects

Example:

→ **Lentiviral vector - Laleh Majlessi, Pierre Charneau**

Animal models:

hACE2 transiently transgenic mice – Pierre Charneau

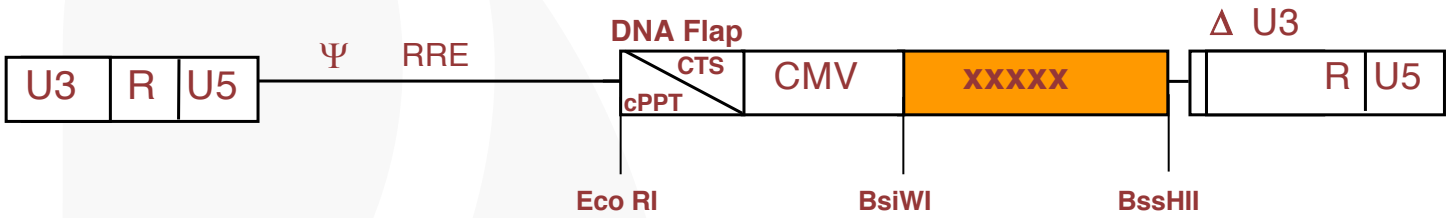
hACE2 transgenic mice – Pierre Charneau

Collaborative cross - Xavier Montagutelli

Lentiviral Vector Technology

Pierre Charneau

Lentiviral vector



LV-**HIV –** Therapeutic candidate

Phase I randomized, placebo-controlled trial 38 HIV-positive patients under HAART
= first-ever lentiviral vector vaccination trial in humans

Interim results:

- good safety profile: absence of any serious adverse events and safety concerns.
- elicited multi-specific and poly-functional CD8 and CD4 T-cell responses in most of the vaccinated patients

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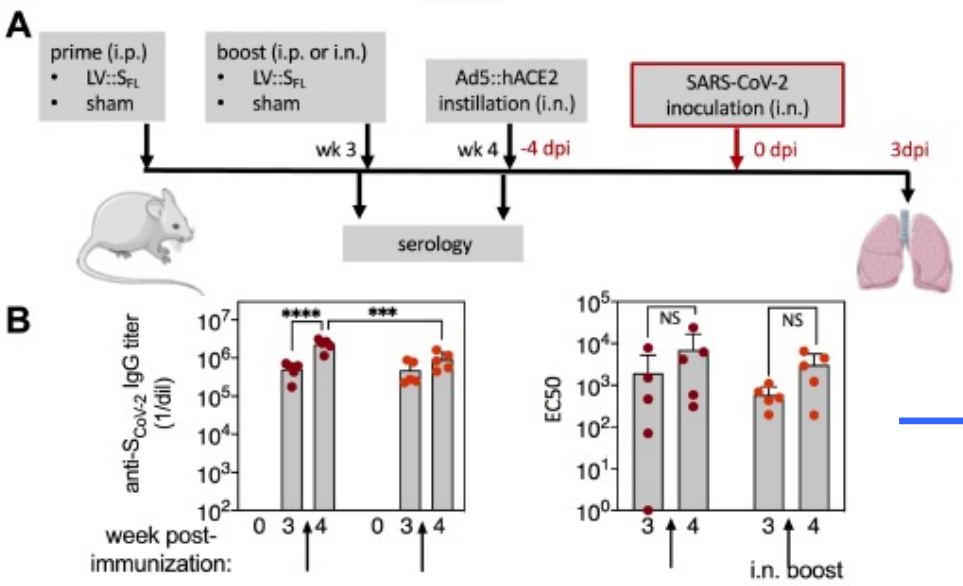
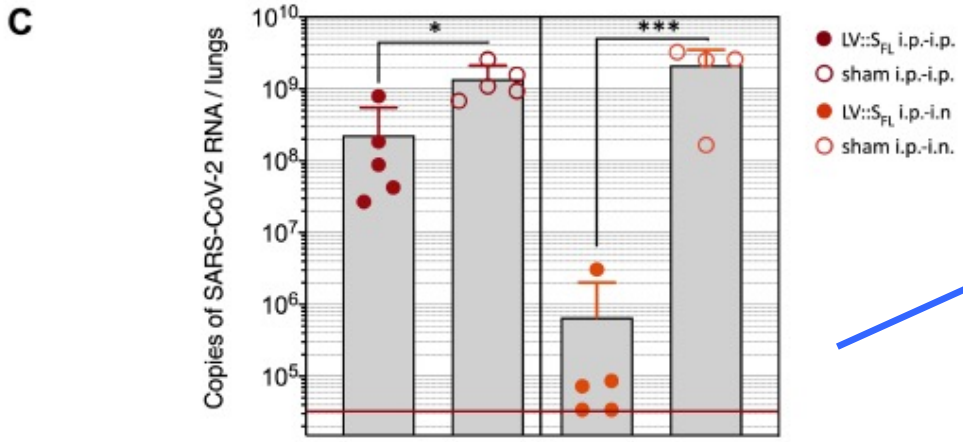
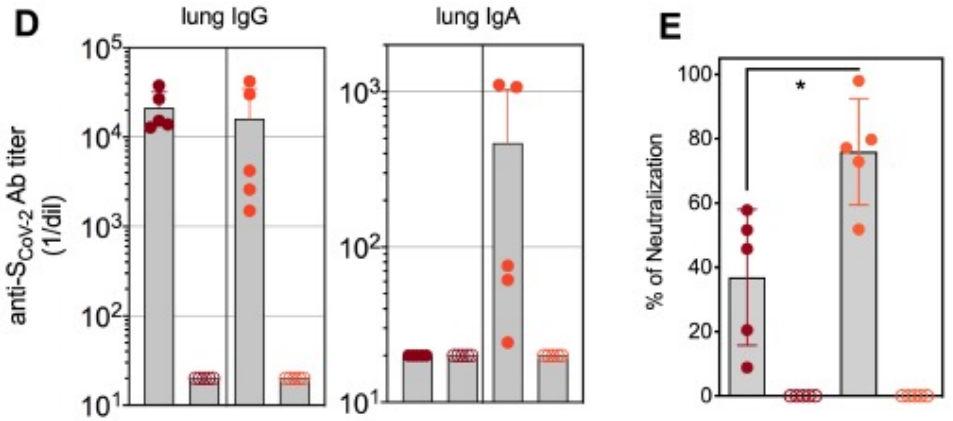
LV vector-based COVID-19 vaccine



Single injection in mice elicits similar levels of neutralizing antibodies as found in recovered COVID-19 patients



Intransal immunization results in much larger reduction of viral RNA in the lungs
"Prime target" immunization



Non-integrative vector for preventive vaccine use

Laboratoire commun Institut Pasteur/ TheraVectys
Laleh Majlessi
Pierre Charneau

Ku at al. Host Cell Microbe
https://doi.org/10.1016/j.chom.2020.12.010

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Thank You