PLATEFORMES VACCINALES

FRÉDÉRIC TANGY

CSO OF ONCOVITA INSTITUT PASTEUR, PARIS

FORMER DIRECTOR OF RESEARCH CNRS AND PROFESSOR INSTITUT PASTEUR
FORMER HEAD OF G2V AND INNOVATIVE VACCINES LABORATORY

Journées inter-DES sur la vaccination
16 octobre 2025

Vaccines : the legacy of Jenner and Pasteur

- ✓ Understand the disease, its transmission, its protection
- ✓ Isolate the responsible agent
- ✓ Conceive a biological product safe, efficacious, easy to manufacture and to deliver at low cost

Jenner, the doctor who empirically inoculated vaccinia virus to humans

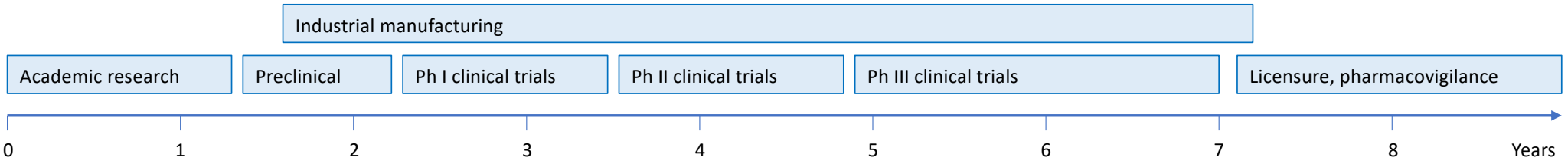
Pasteur, the chemist who revolutionized medicine by inactivating microbes

Antiviral vaccines

Live-attenuated viruses	Inactivated-killed viruses	Pseudo-particles	New technologies
Smallpox Yellow fever Polio Measles Mumps Rubeola Varicella, zona Dengue Rotavirus	Rabies Influenza Polio Hepatitis A JEV, TBE	HBV HPV	DNA/mRNA Viral vectors Adjuvants, Proteins

Defiance

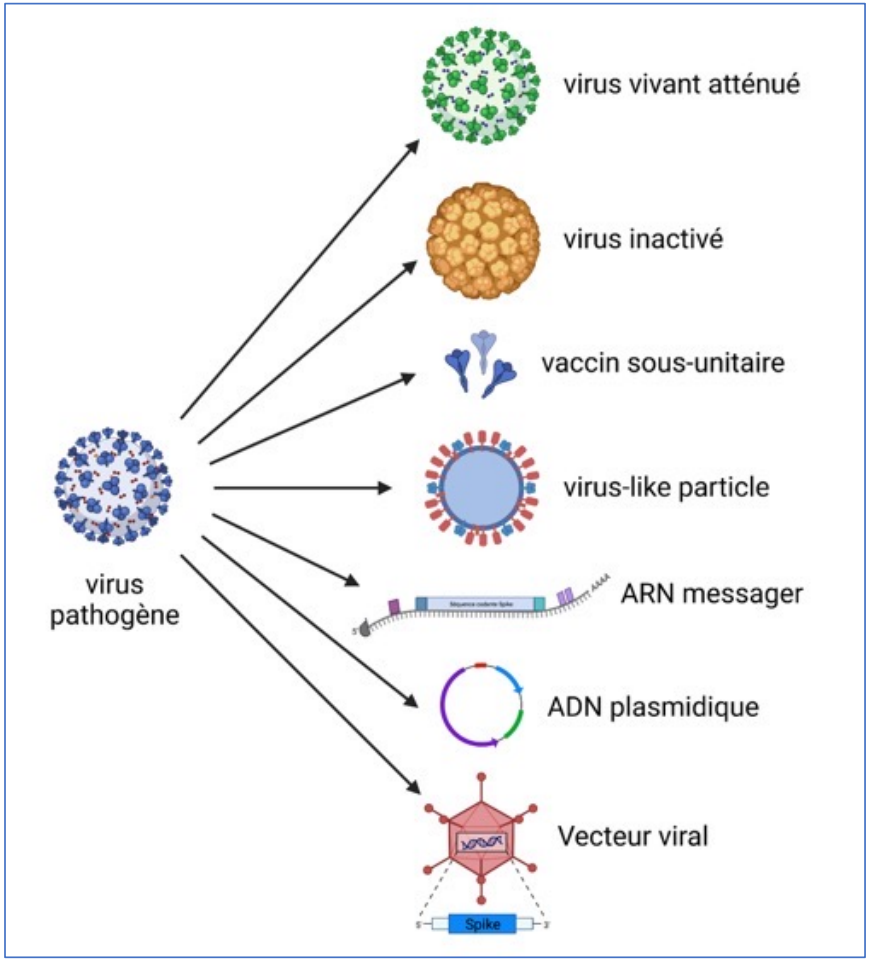
Usual steps to develop a vaccine (mean durations)



200 years to develop new vaccines

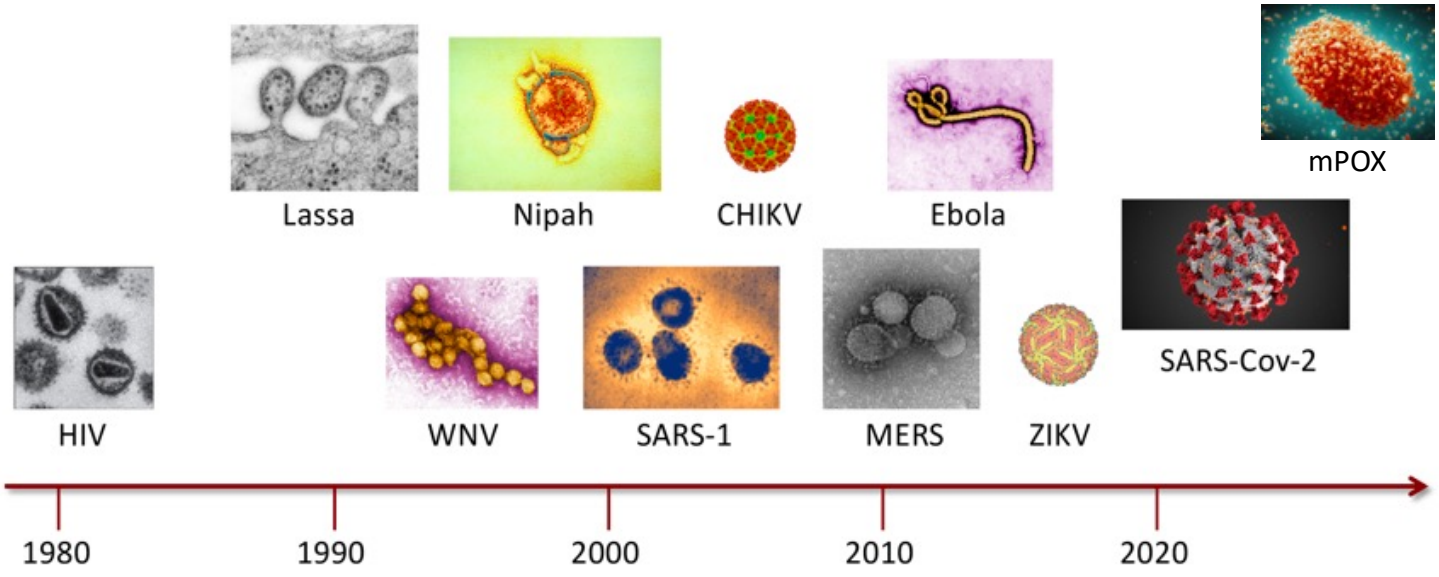
1796	Variole	1964	Rougeole
1879	Choléra	1967	Oreillons
1882	Rage	1970	Rubéole
1890	Tétanos, diphthérie	1974	Varicelle
1897	Peste	1978	Méningite
1926	Coqueluche	1981	Hépatite B
1927	Tuberculose	1985	Méningite bactérienne
1932	Fièvre jaune	1992	Hépatite A
1945	Grippe	1998	Maladie de Lyme
1952	Poliomyélite	2004	Papillomavirus (HPV)

2020 COVID-19 (SARS-CoV-2)



Emerging or re-emerging lethal viral infections threaten humans since ever

Globalization, increasing population, travels, warming

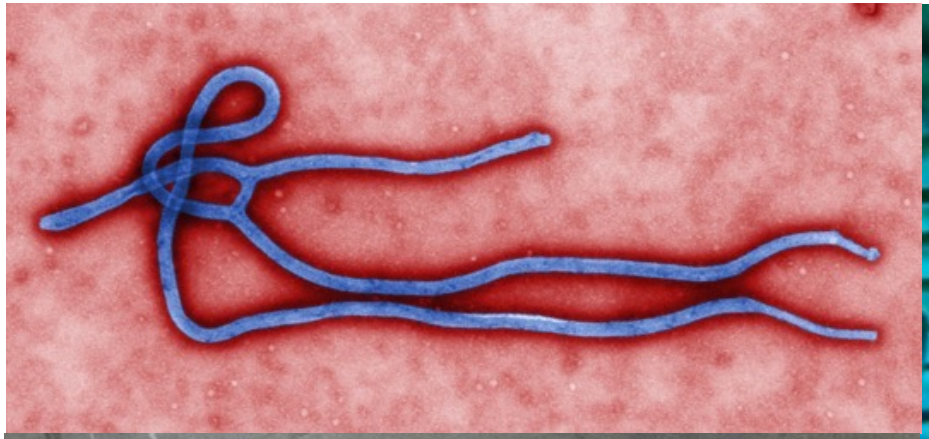


New human respiratory viruses (1997-2013)

Virus	Family	Year
H5N1	Influenza virus	1997
Hendra-Nipah	Paramyxovirus	2000
hMPV	Paramyxovirus	2001
SARS-CoV	Coronavirus	2003
H7N7	Influenza virus	2003
HCoV-NL63	Coronavirus	2004
HCoV-HKU1	Coronavirus	2005
HBoV	Parvovirus	2005
KI/WU-PyV	Polyomavirus	2007
MeIV (Kam V)	Orthoreovirus	2007
H1N1v	Influenza virus	2009
HPBV	Picobimavirus	2010
H3N2 porcine	Influenza virus	2011
HCoV-EMC	Coronavirus	2012
H7N9	Influenza virus	2013
MERS-CoV	Coronavirus	2012

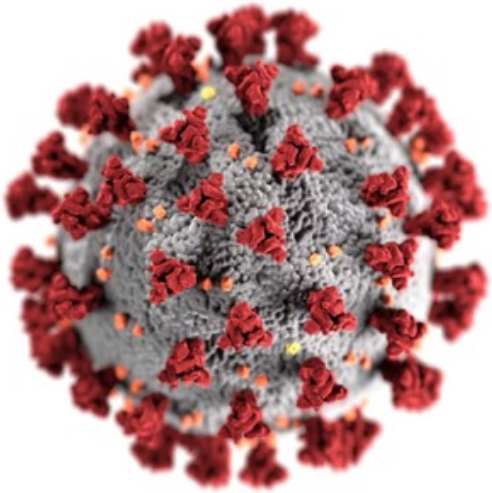
The loss due to Covid for the world Gross Domestic Product (GDP) estimated to be 3 – 82 trillion dollars in 5 years (1 trillion = 10^{18})
https://www.jbs.cam.ac.uk/faculty-research/centres/risk/

Ebola recurrent outbreaks



Zika virus mother to child transmission

2019 Covid-19 pandemic



mPOX comes back

Vaccines are a public health medicine

They need to elicit long-term memory and herd immunity

Memory is essential

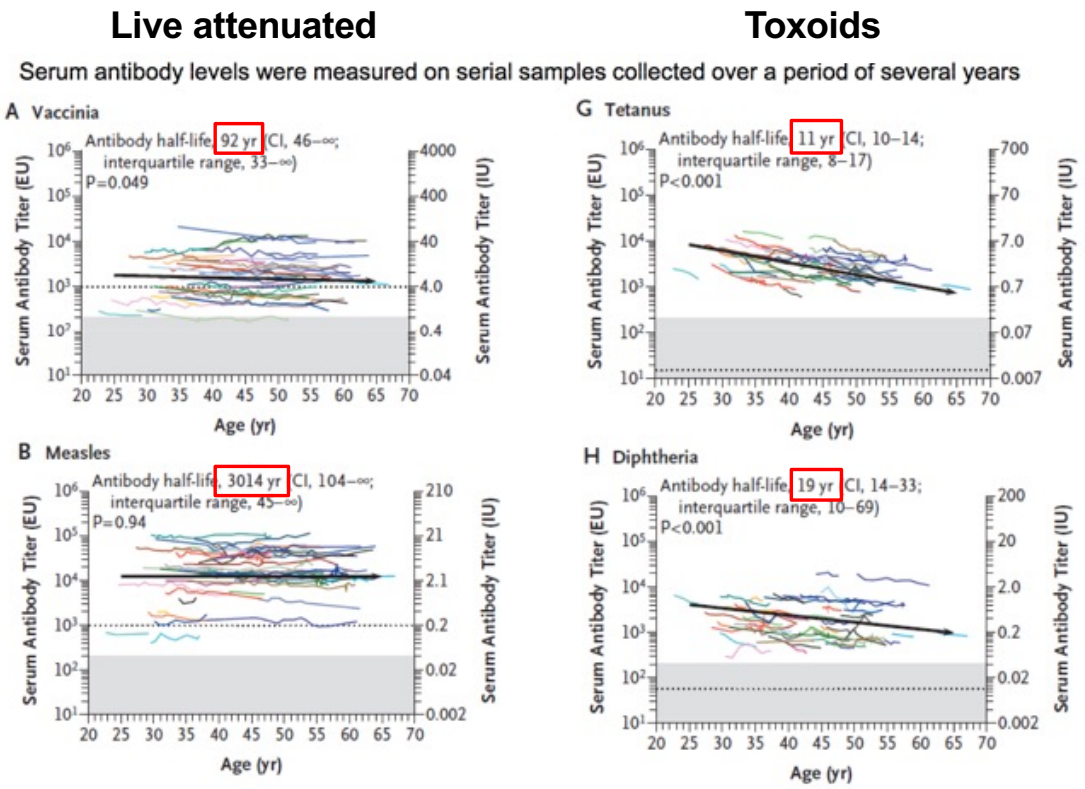
Live attenuated vaccines

- Smallpox (eradicated)
- Poliomyelitis (95-100% morbidity reduction)
- Measles (95-100% morbidity reduction)
- Mumps (95-100% morbidity reduction)
- Rubella (95-100% morbidity reduction)
- Yellow fever (95-100% efficacy)
- Varicella (70-80% morbidity reduction)

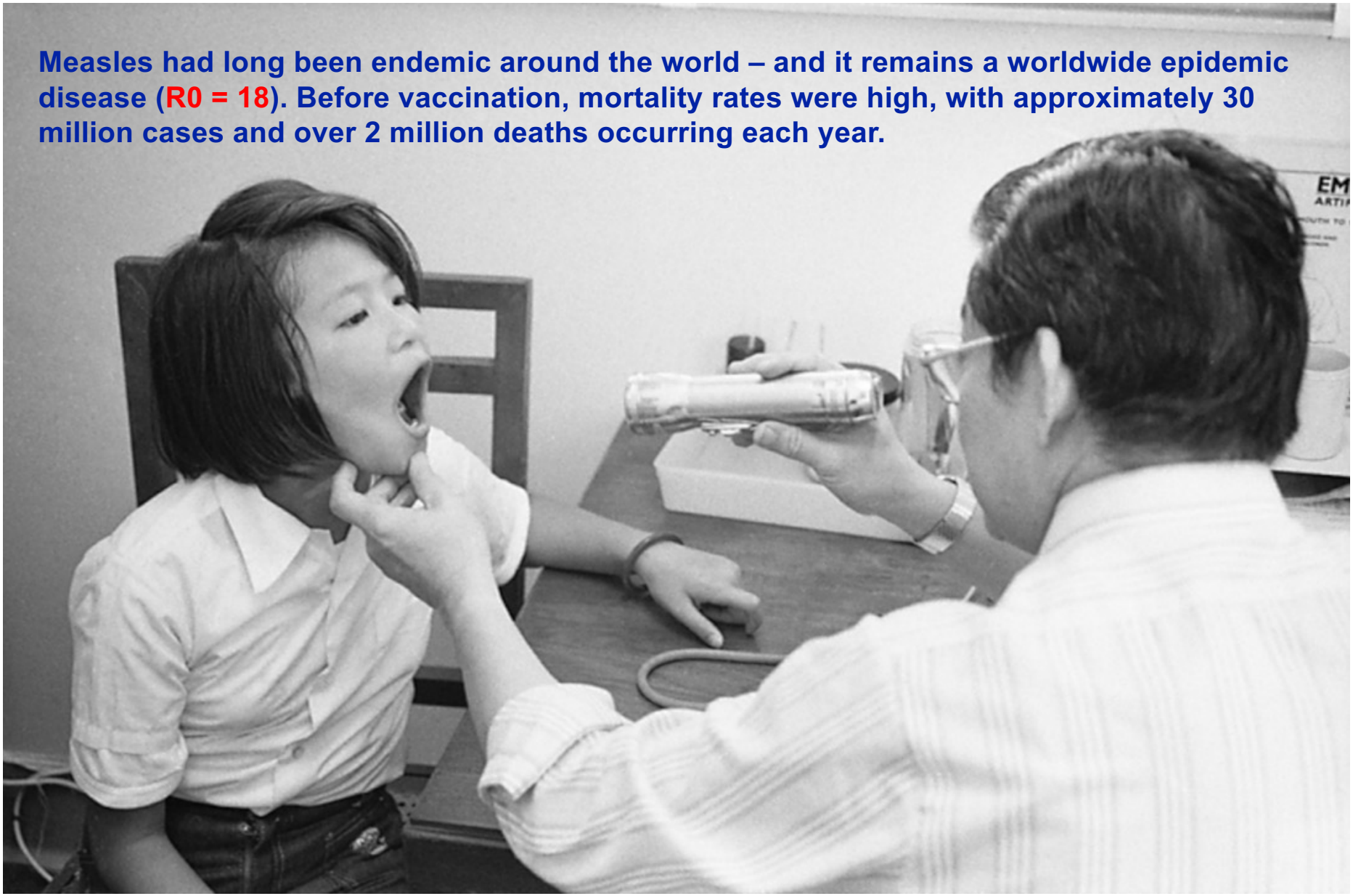
Practical needs

- Pediatric vaccines/adolescents
- 1 or 2 administrations
- Absolute safety
- Humoral and cellular immunity
- Long-term memory
- Low cost and large-scale manufacturing

Vaccine memory



Amanna et al, N Engl J Med 2007;357:1903-15.


Measles had long been endemic around the world – and it remains a worldwide epidemic disease (R0 = 18). Before vaccination, mortality rates were high, with approximately 30 million cases and over 2 million deaths occurring each year.

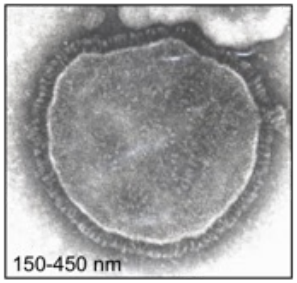
Measles live attenuated vaccine

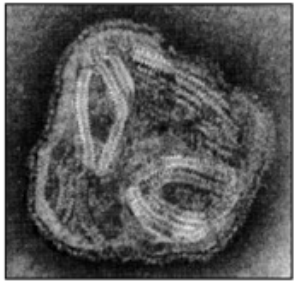
Edmonston strain
Wildtype pathogenic

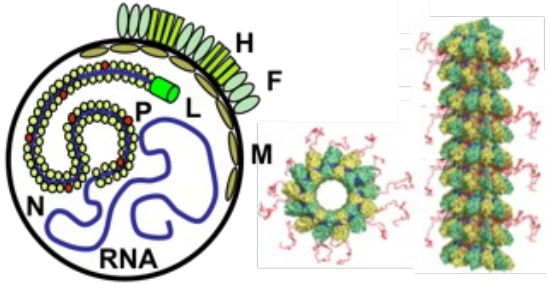
156 passages

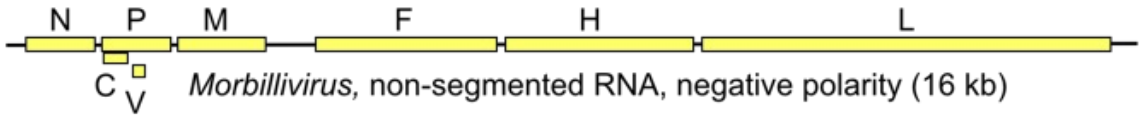
Schwarz strain
Attenuated non-pathogenic

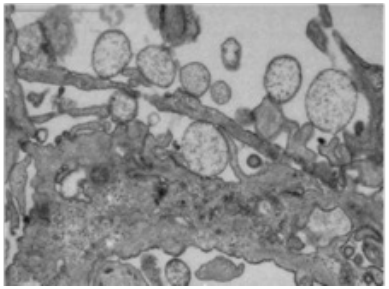
- One low-dose injection
- Life-long protective immunity
- Safety / efficacy track record over 2 billion children
- High genetic stability
- Established manufacturing

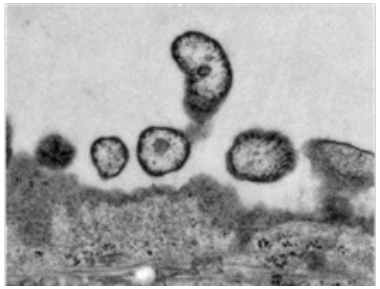


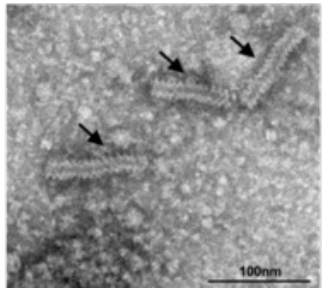






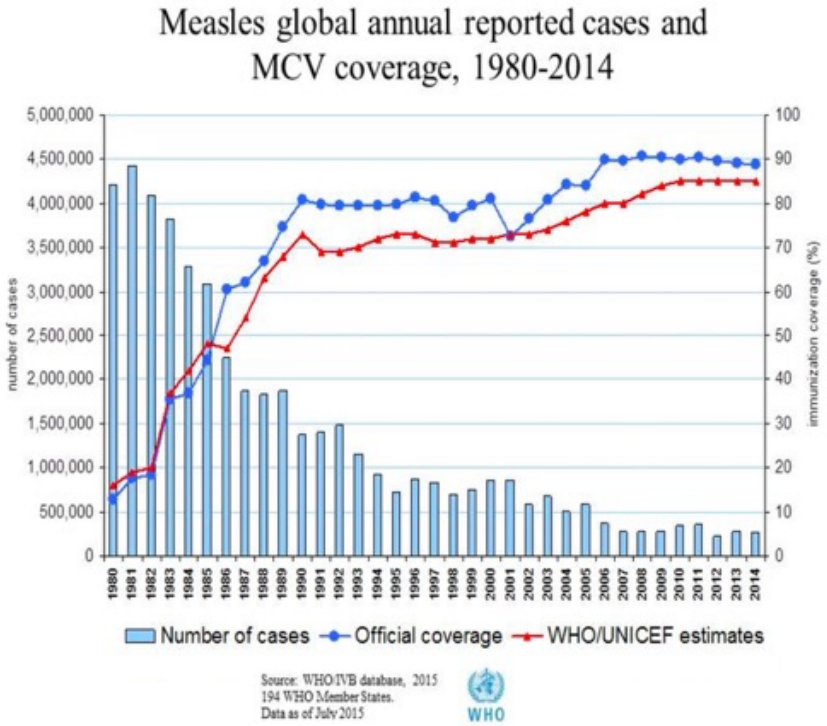






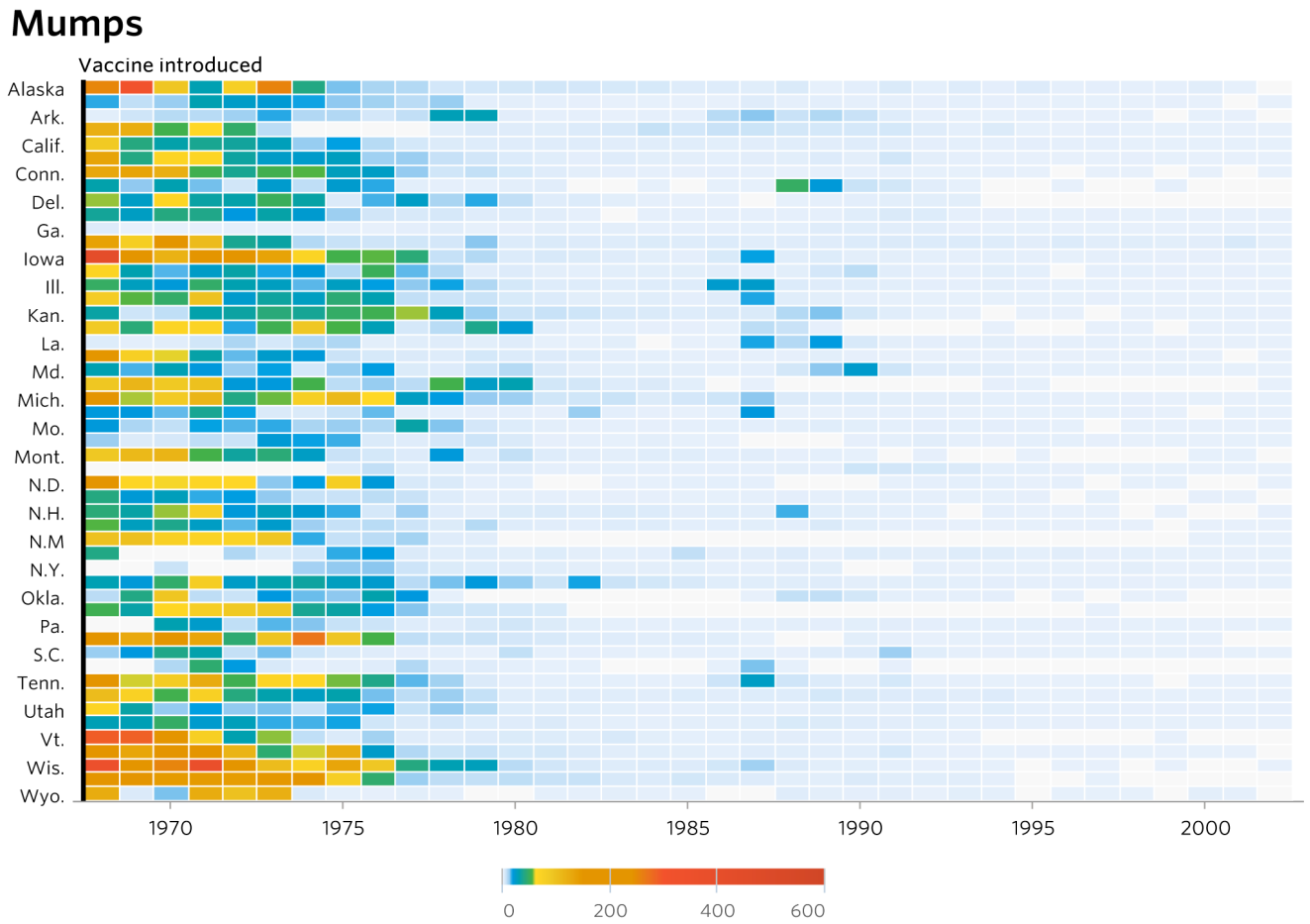
Measles live attenuated vaccine is very efficient

Measles reported cases in USA, 1930 – 2013
Vaccine introduction 1964



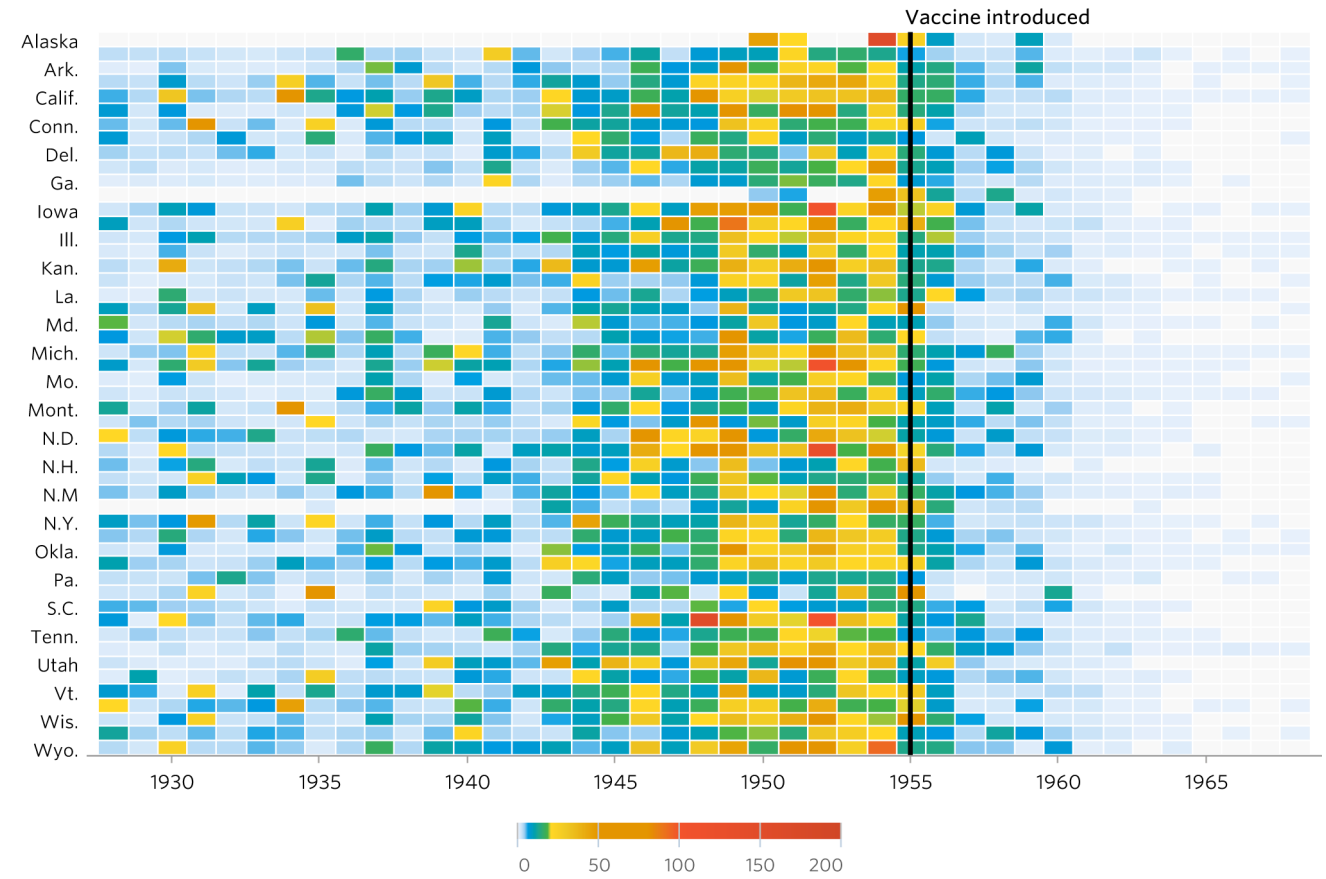
Mumps control in USA

Heat maps showing the number of infected people measures over 70 years in USA
(Tynan DeBold & Doc Friedman)

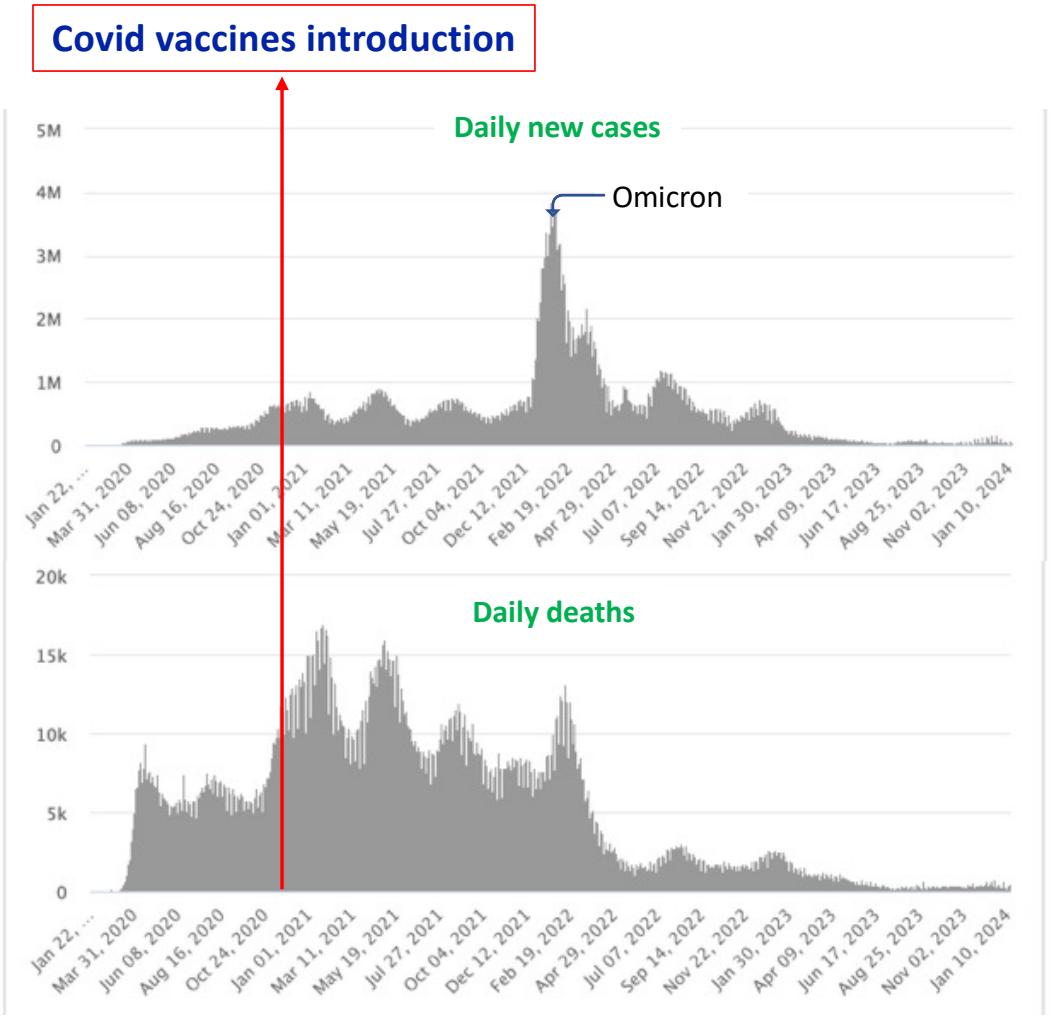


Polio control in USA

Heat maps showing the number of infected people measures over 70 years in USA
(Tynan DeBold & Doc Friedman)



Did SARS-CoV-2 vaccines control the COVID-19 pandemic?



World Covid-19 numbers, Jan 2024

Covid-19 Cases: **> 705 million**

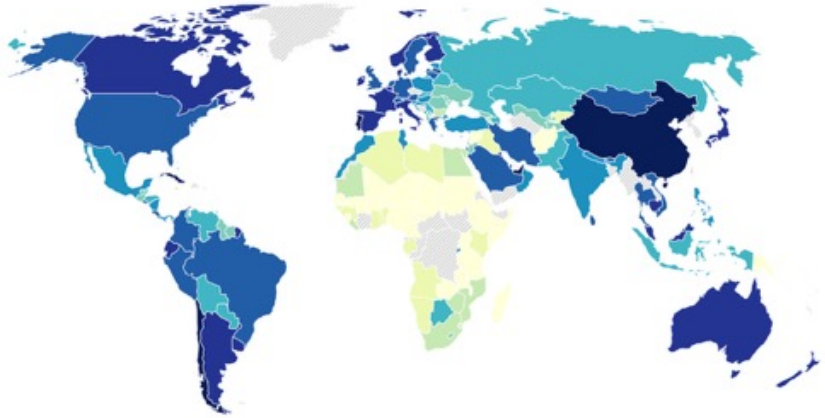
Deaths: **> 7 million**

Recovered: **> 675 million**

Vaccine doses administered: > **10 billion**
(including 5.7 billion doses in China and India)

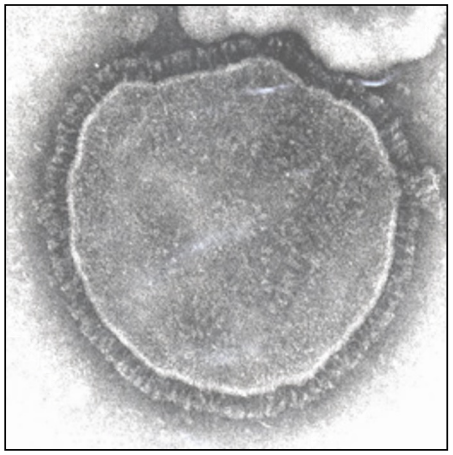
World population: **7.9 billion**

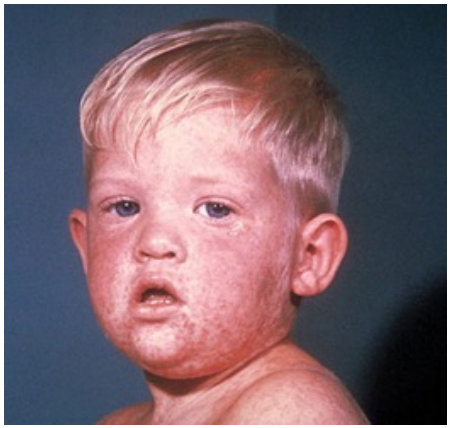
World Covid-19 vaccine coverage



Is polio eliminated ?

Measles elimination ?



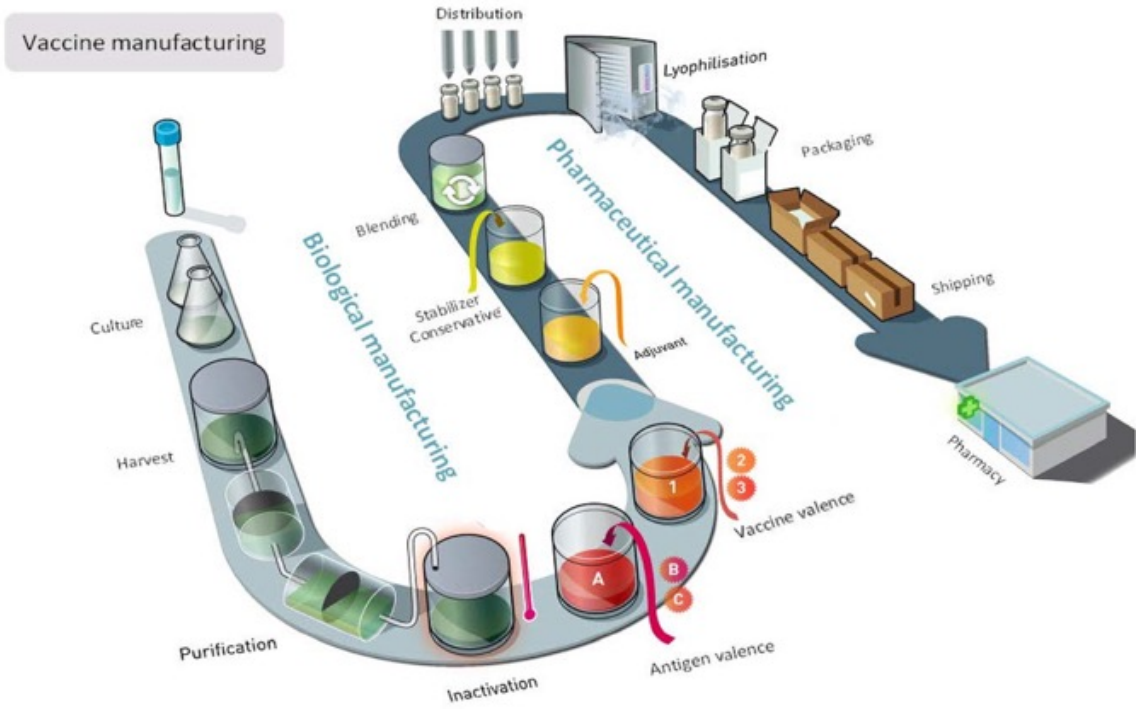


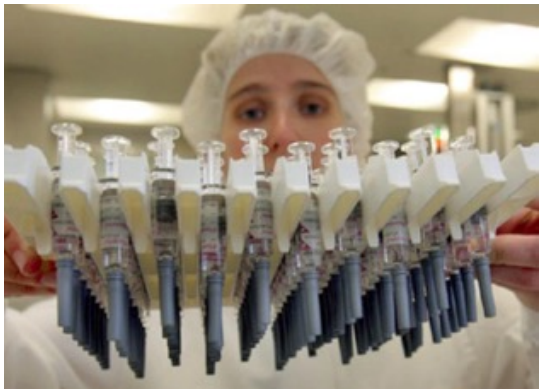
Expanded Program of Immunization (WHO)

EPI: current programme (AFRO)

Vaccines	Period/Age	Number doses	
BCG	Birth	01	Dose-1
DTP	6 weeks 10 weeks 14 weeks	03	Dose-1 Dose-2 Dose-3
Polio	Birth 6 weeks 10 weeks 14 weeks	04	Dose-1 Dose-2 Dose-3 Dose-4
Measles	09 months	01	Dose-1
ATV (pregnant women)	1st contact latest 15days before delivery	02	Dose-1 Dose-2
Yellow fever	09 months	01	Dose-1
Hepatitis B	6 weeks 10 weeks 14 weeks	03	Dose-1 Dose-2 Dose-3
Hib	6 weeks 10 weeks 14 weeks	03	Dose-1 Dose-2 Dose-3

Industrial manufacture

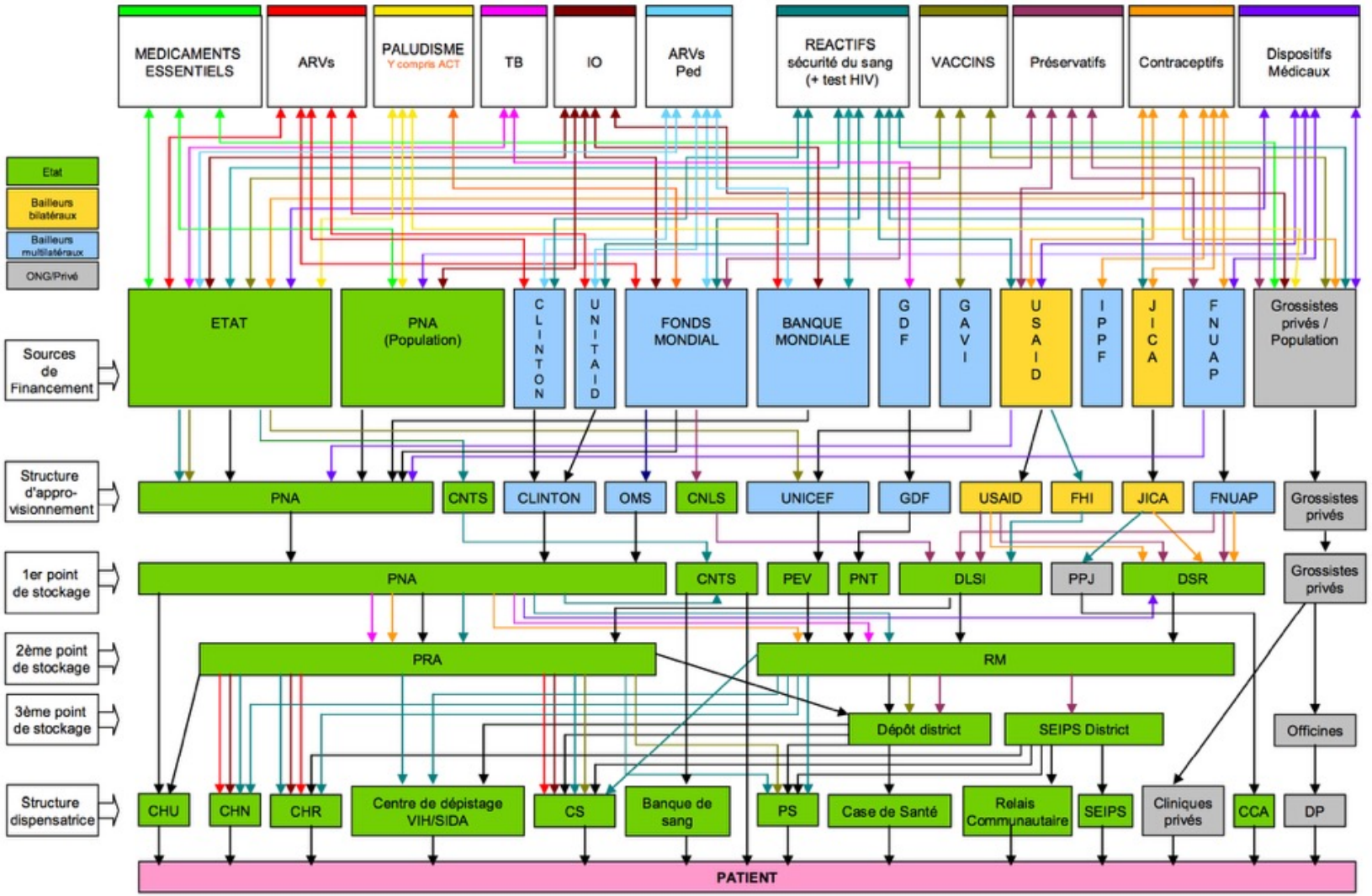




Systèmes d'approvisionnement des produits pharmaceutiques au SENEGAL. Avril 2008

Ministère de la Santé et de la Prévention Médicale

Organisation mondiale de la Santé

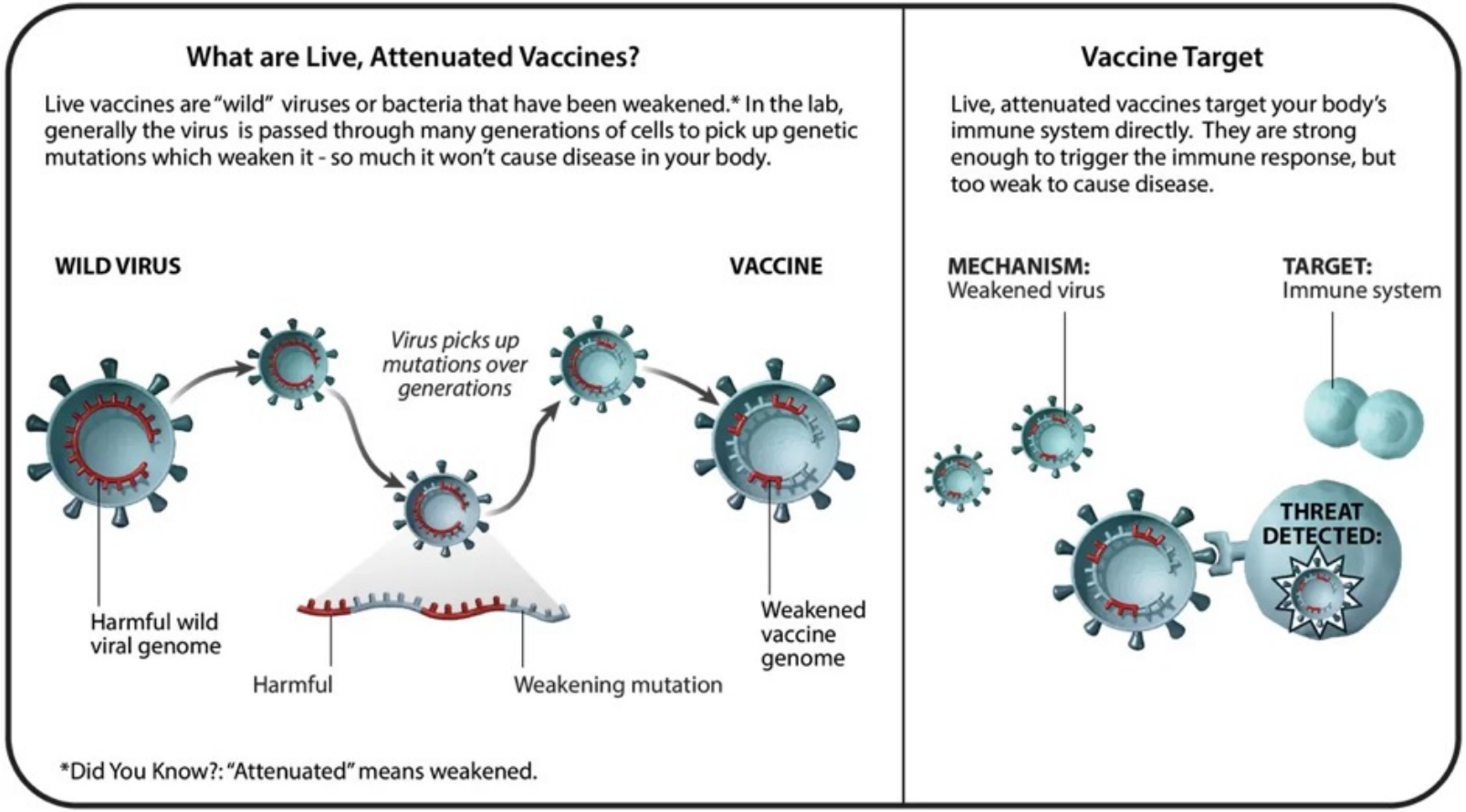


Distribution of vaccines

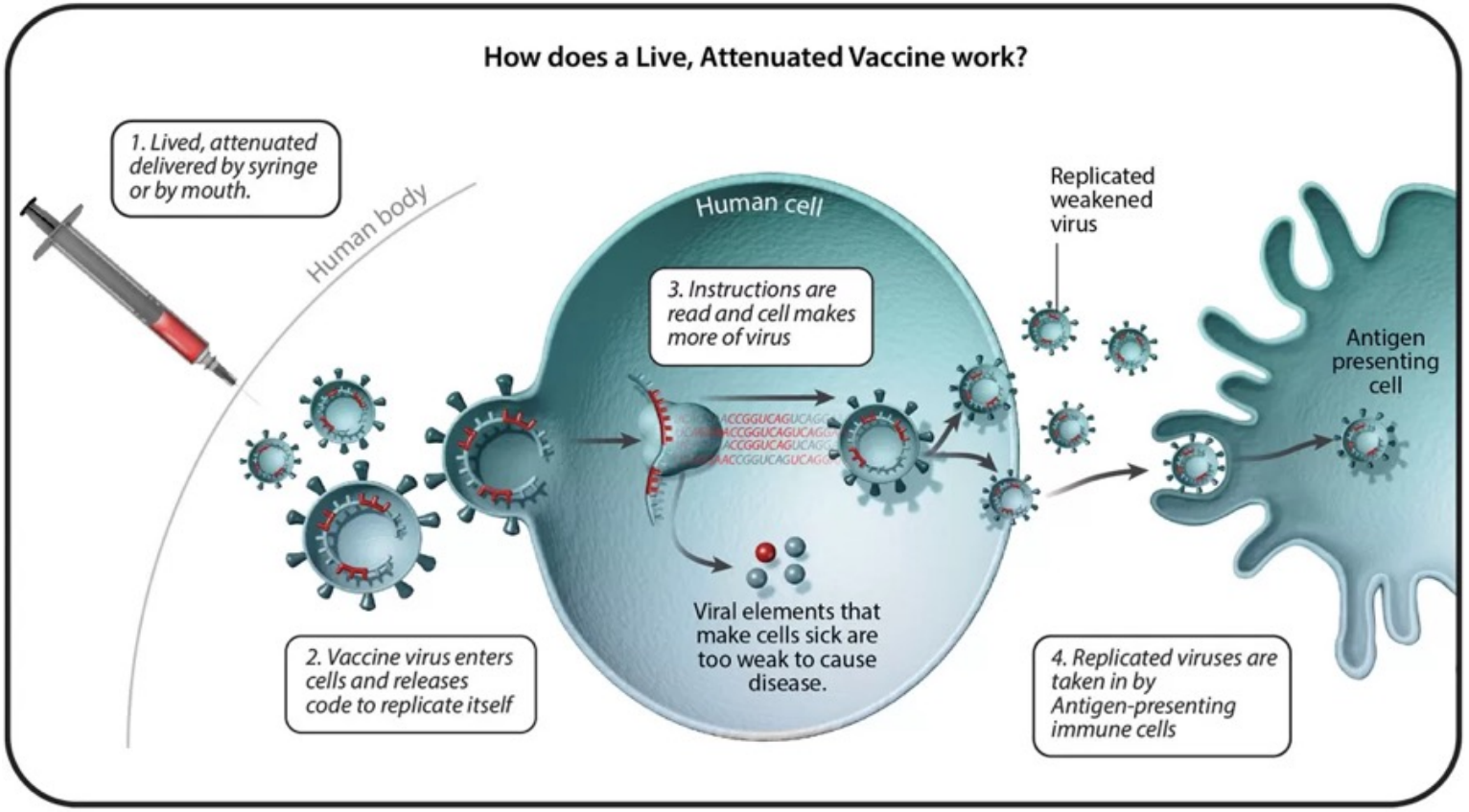
Campaigns (Polio, Measles, YF, MenA and TT) further increase the pressure on already challenged systems

World Health Organization

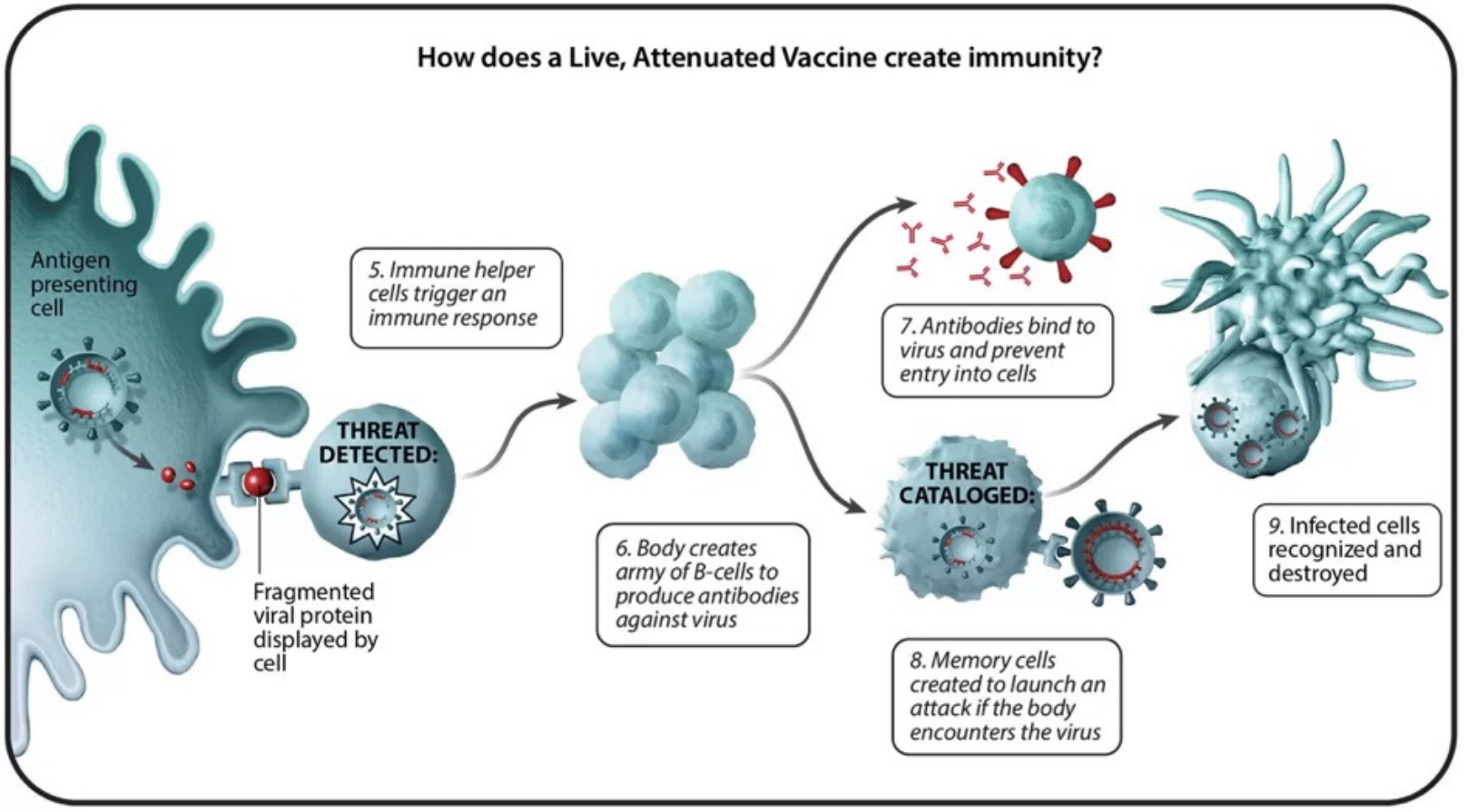
Live attenuated vaccines



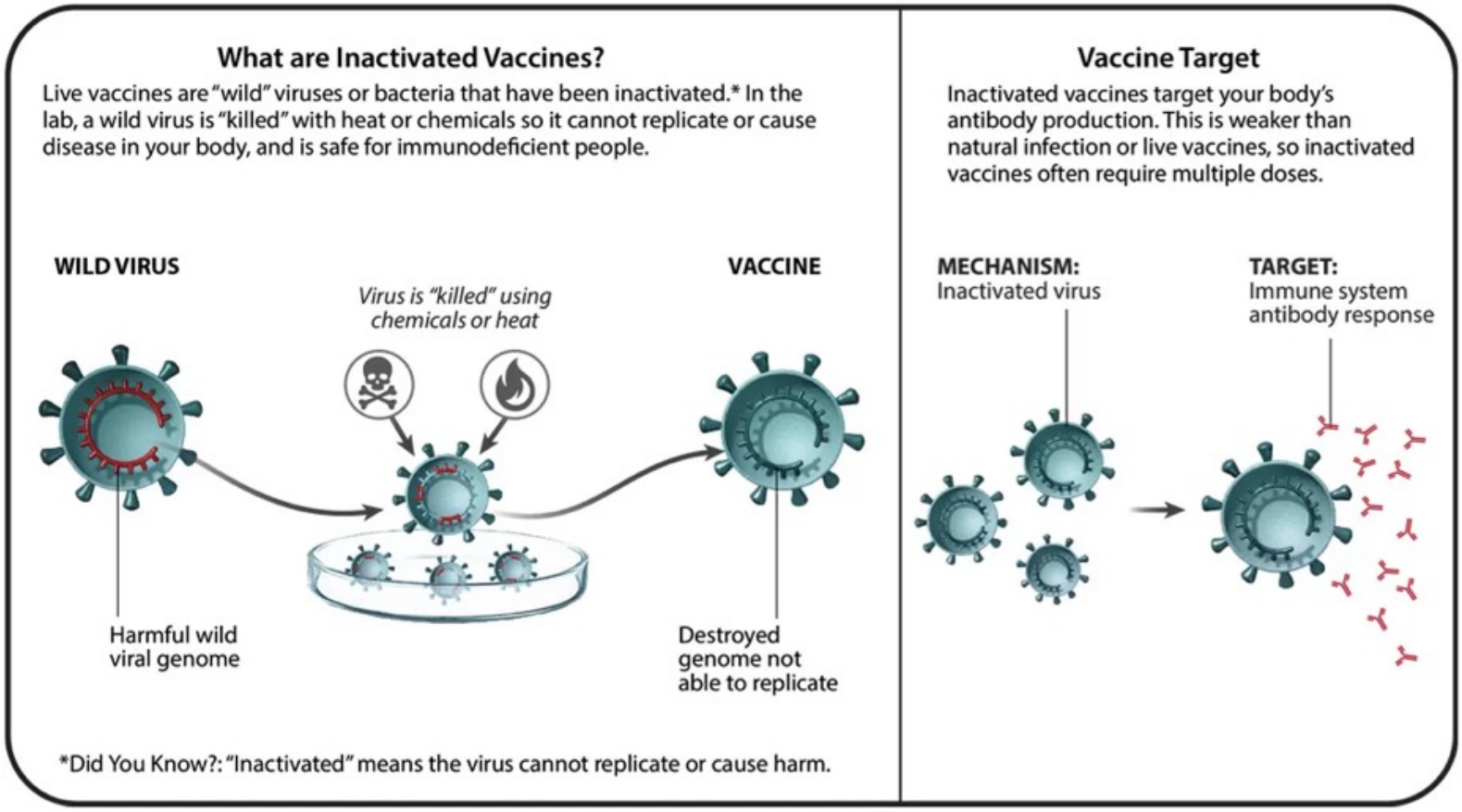
Live attenuated vaccines



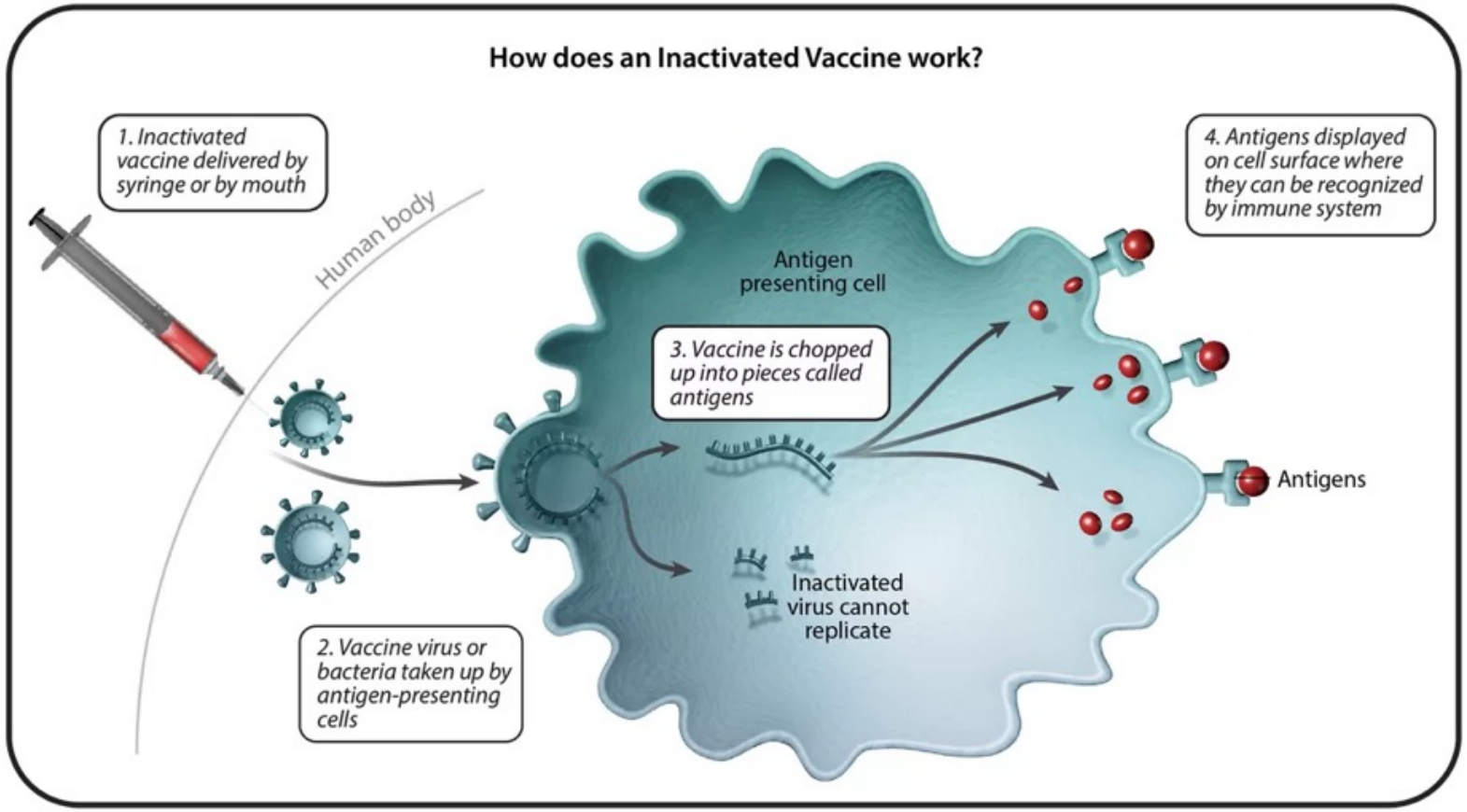
Live attenuated vaccines



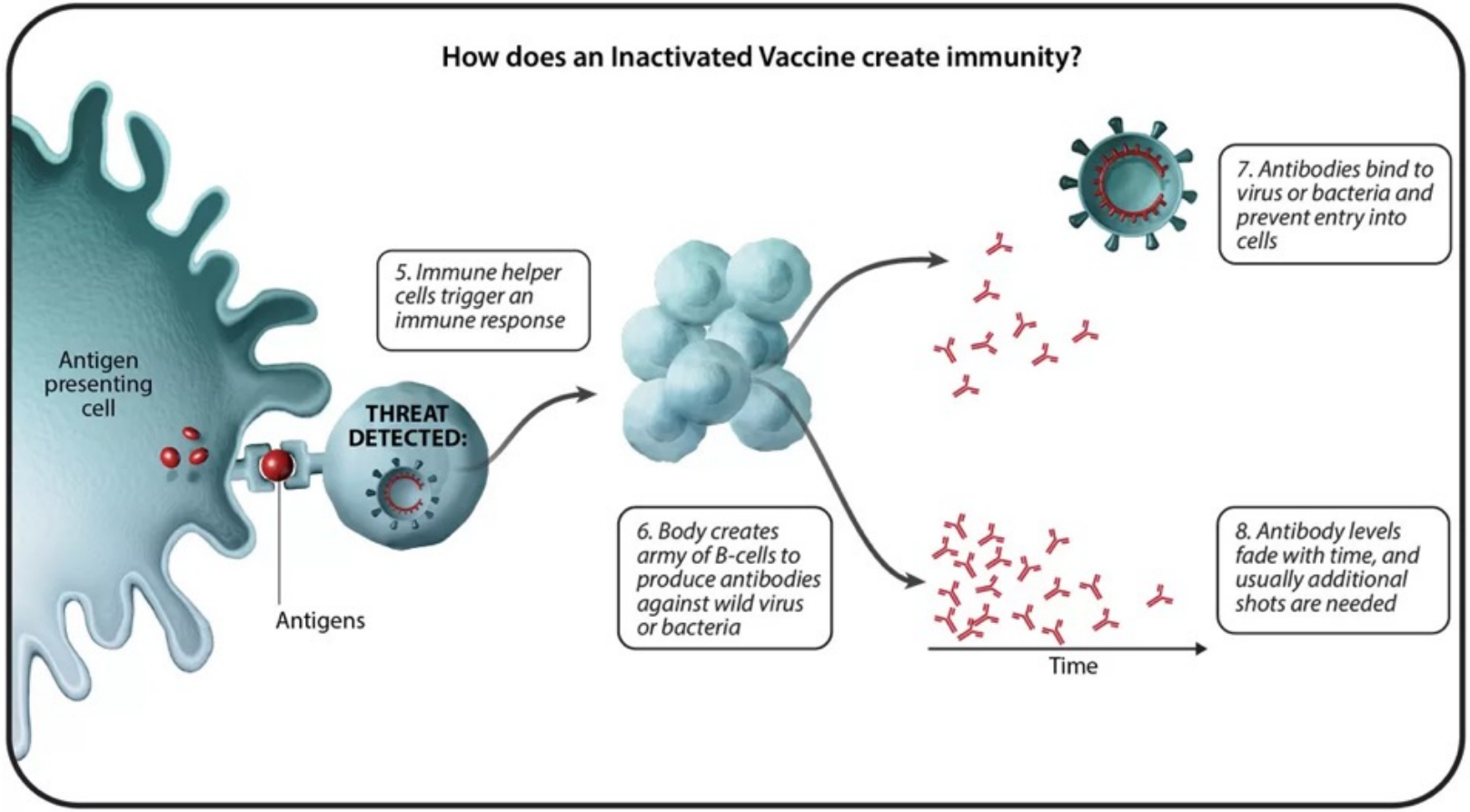
Inactivated vaccines



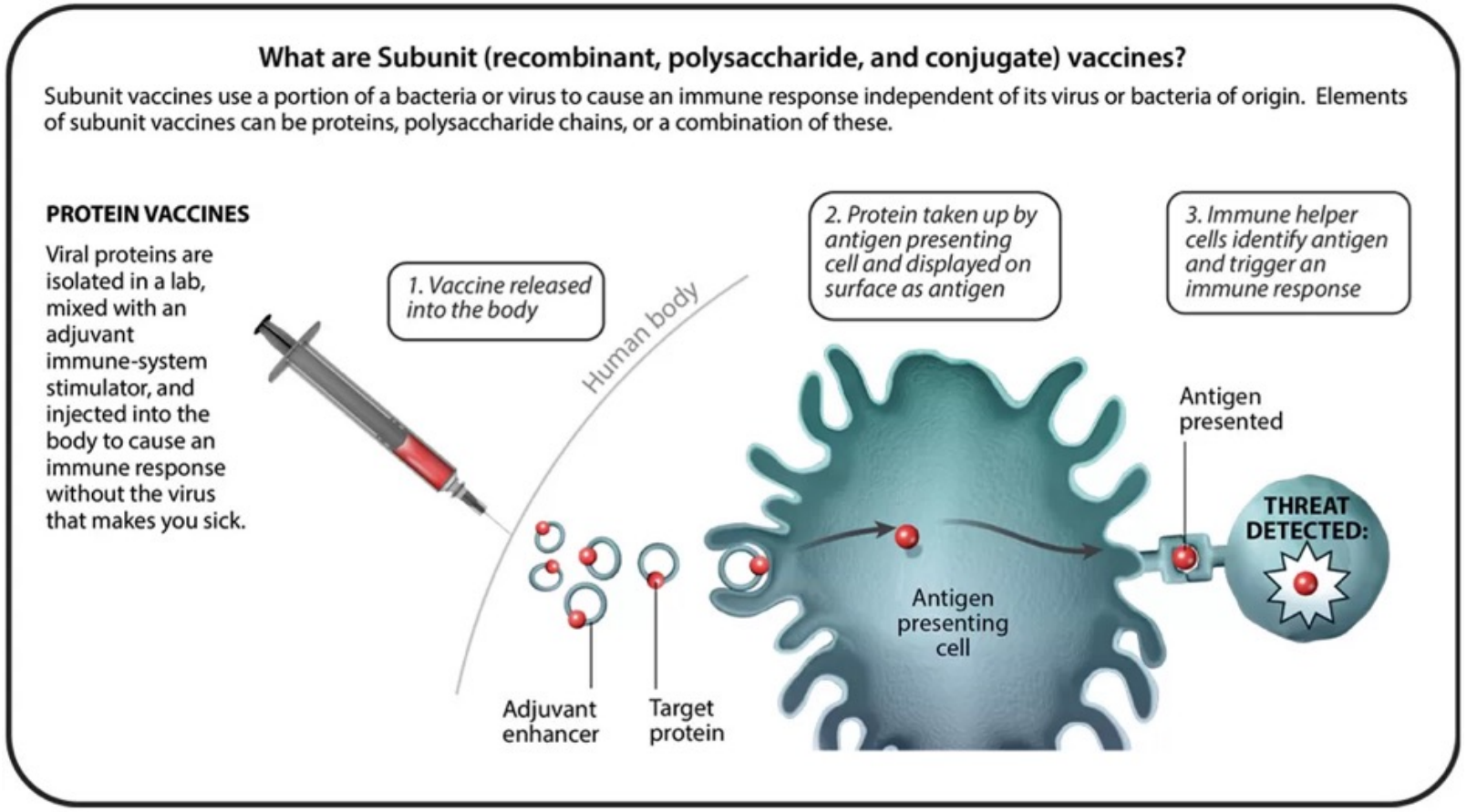
Inactivated vaccines



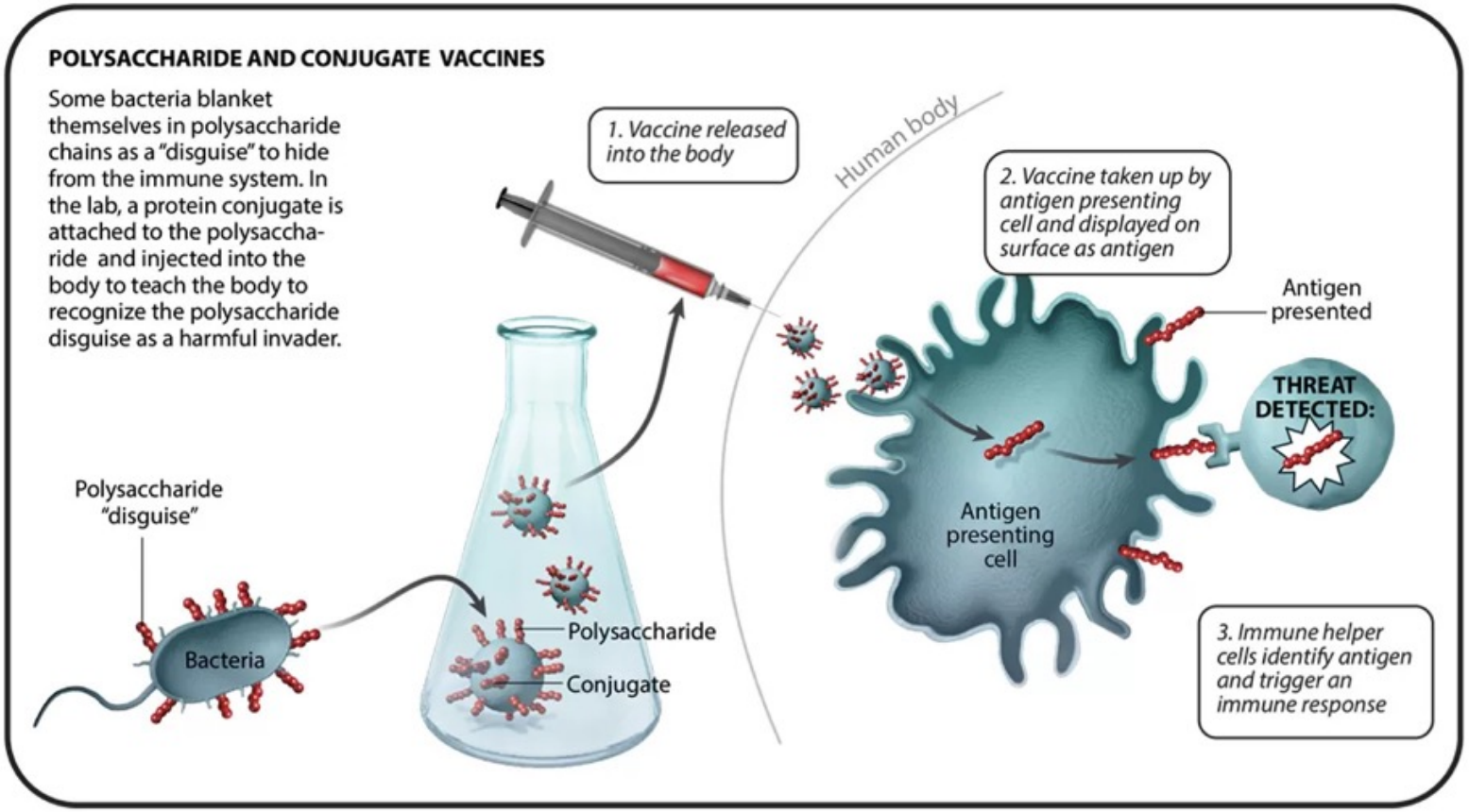
Inactivated vaccines



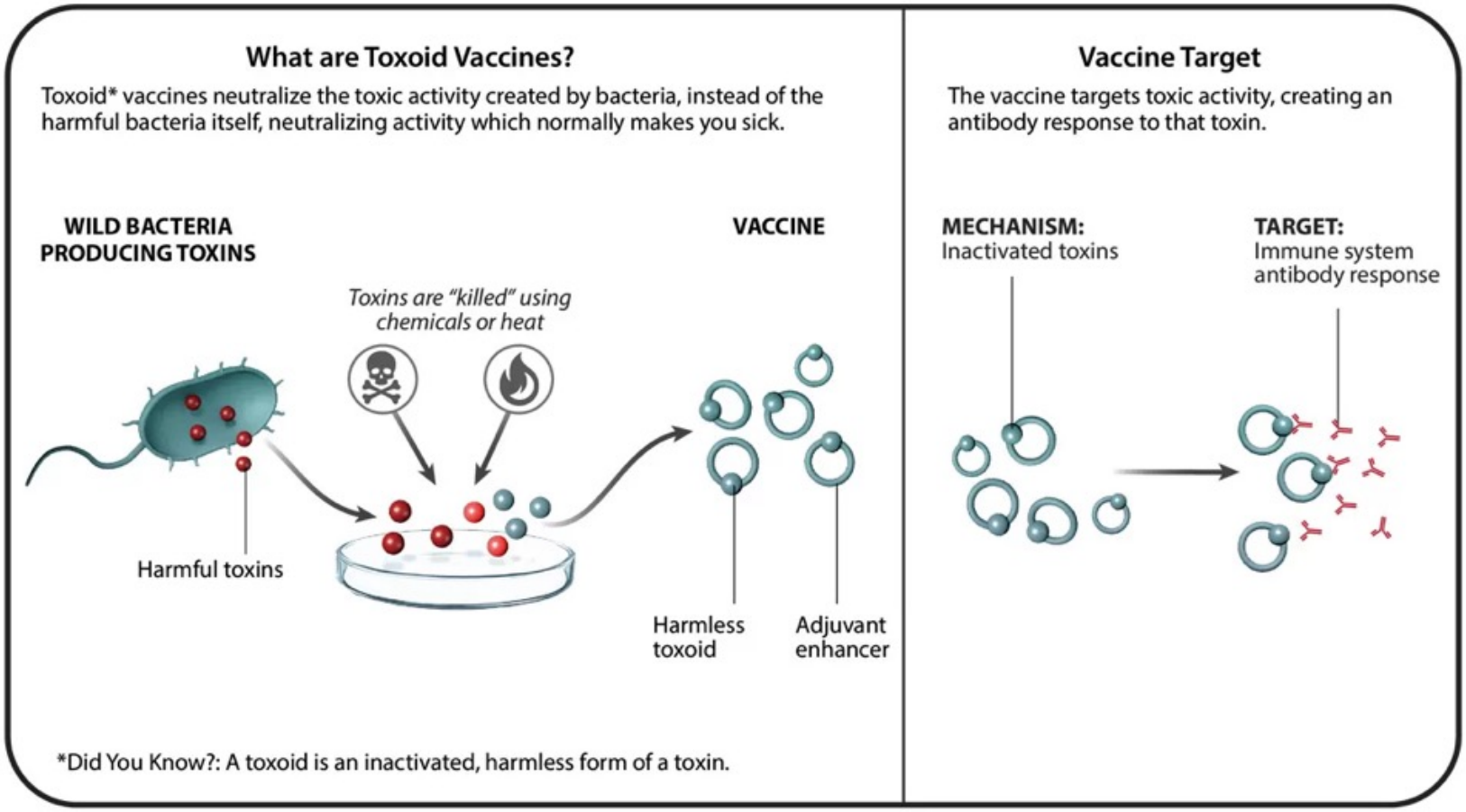
Subunit vaccines



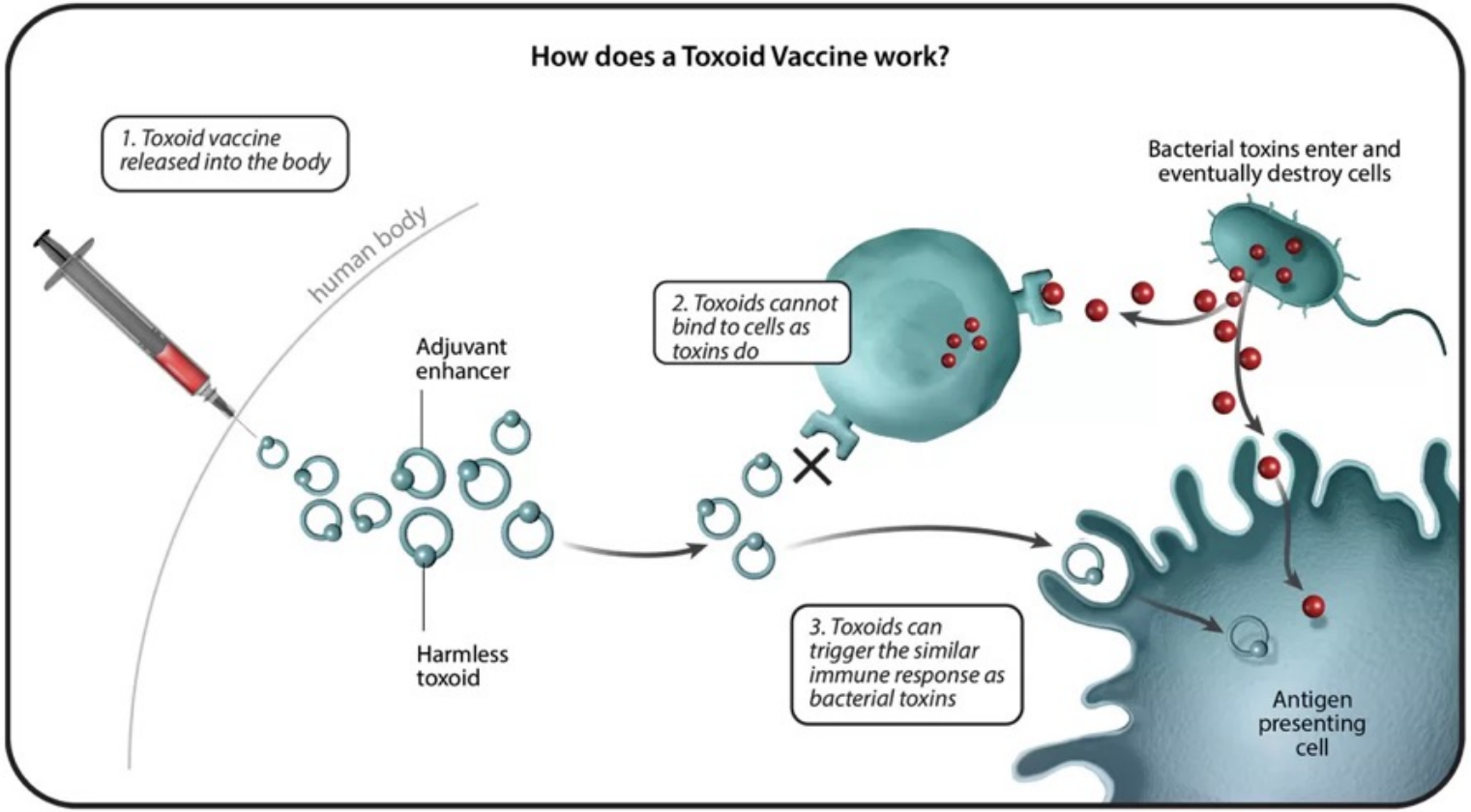
Subunit vaccines



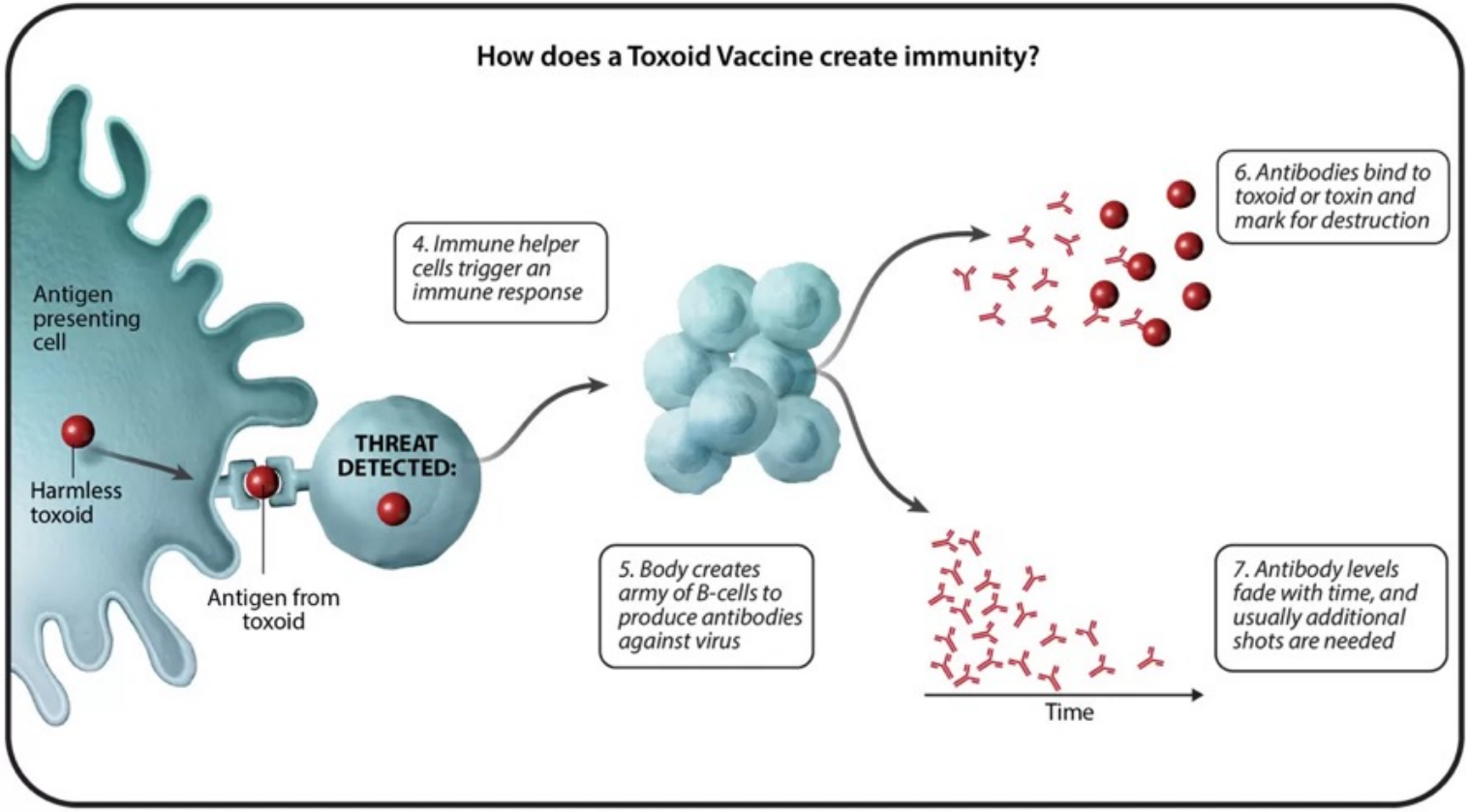
Subunit vaccines



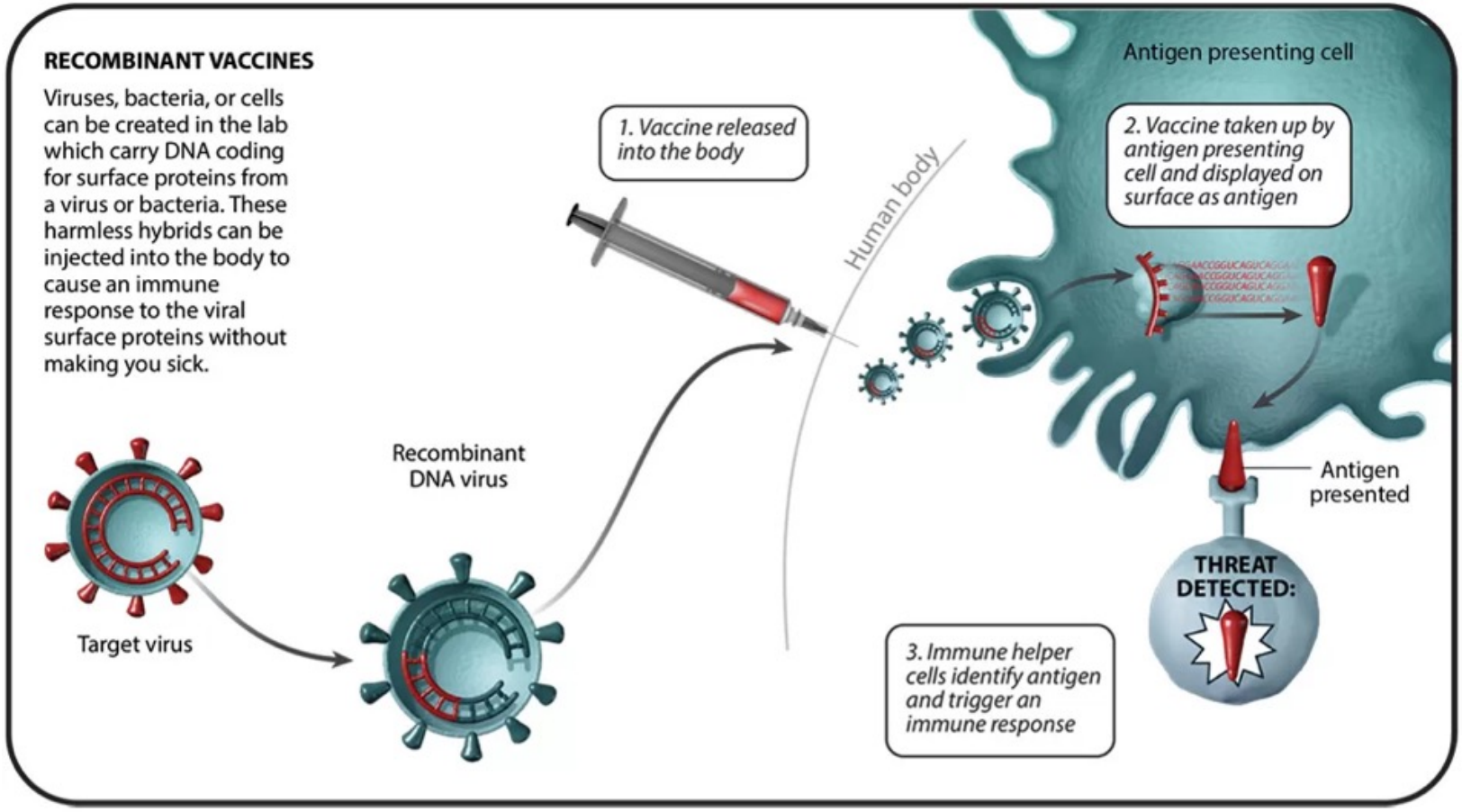
Subunit vaccines



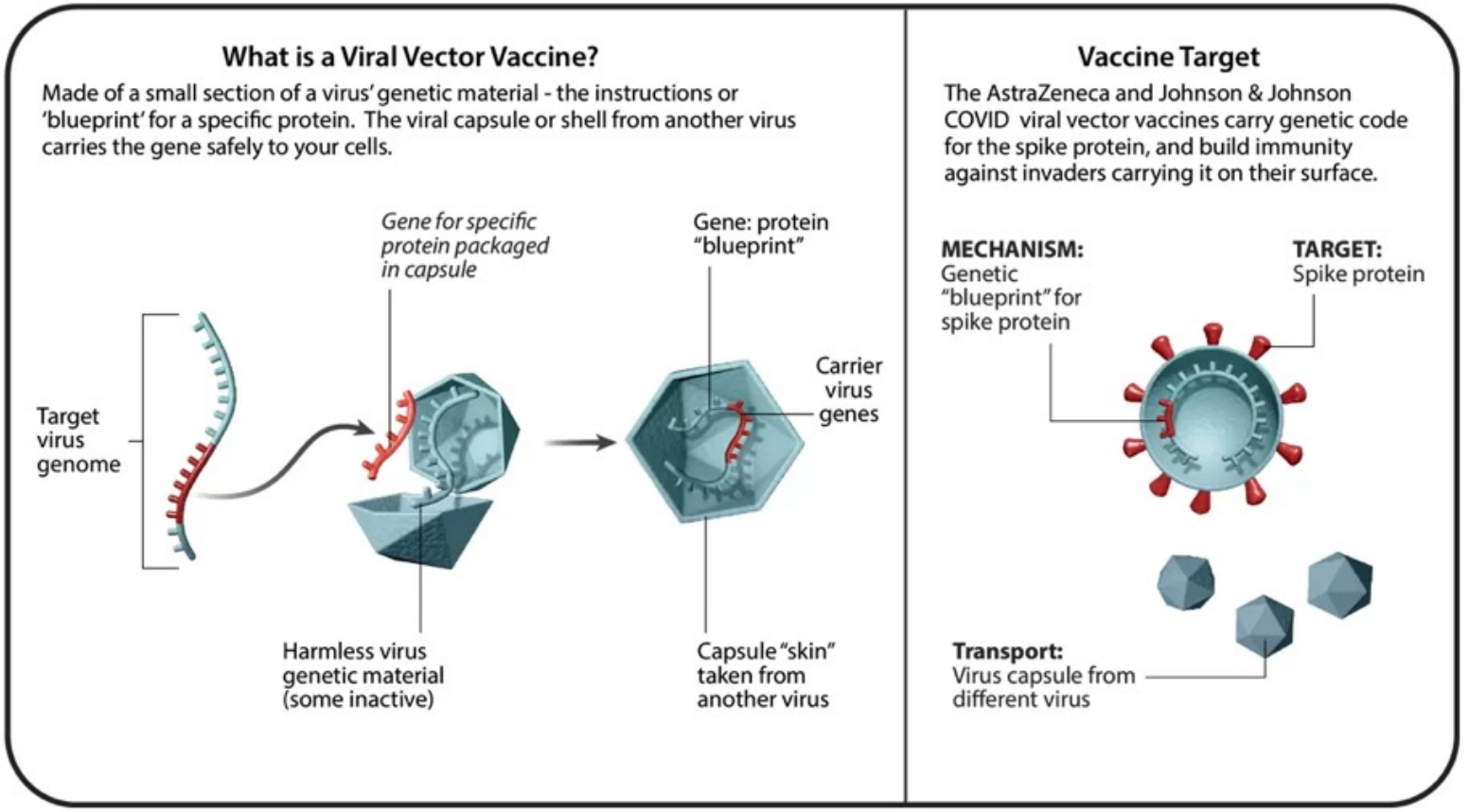
Subunit vaccines



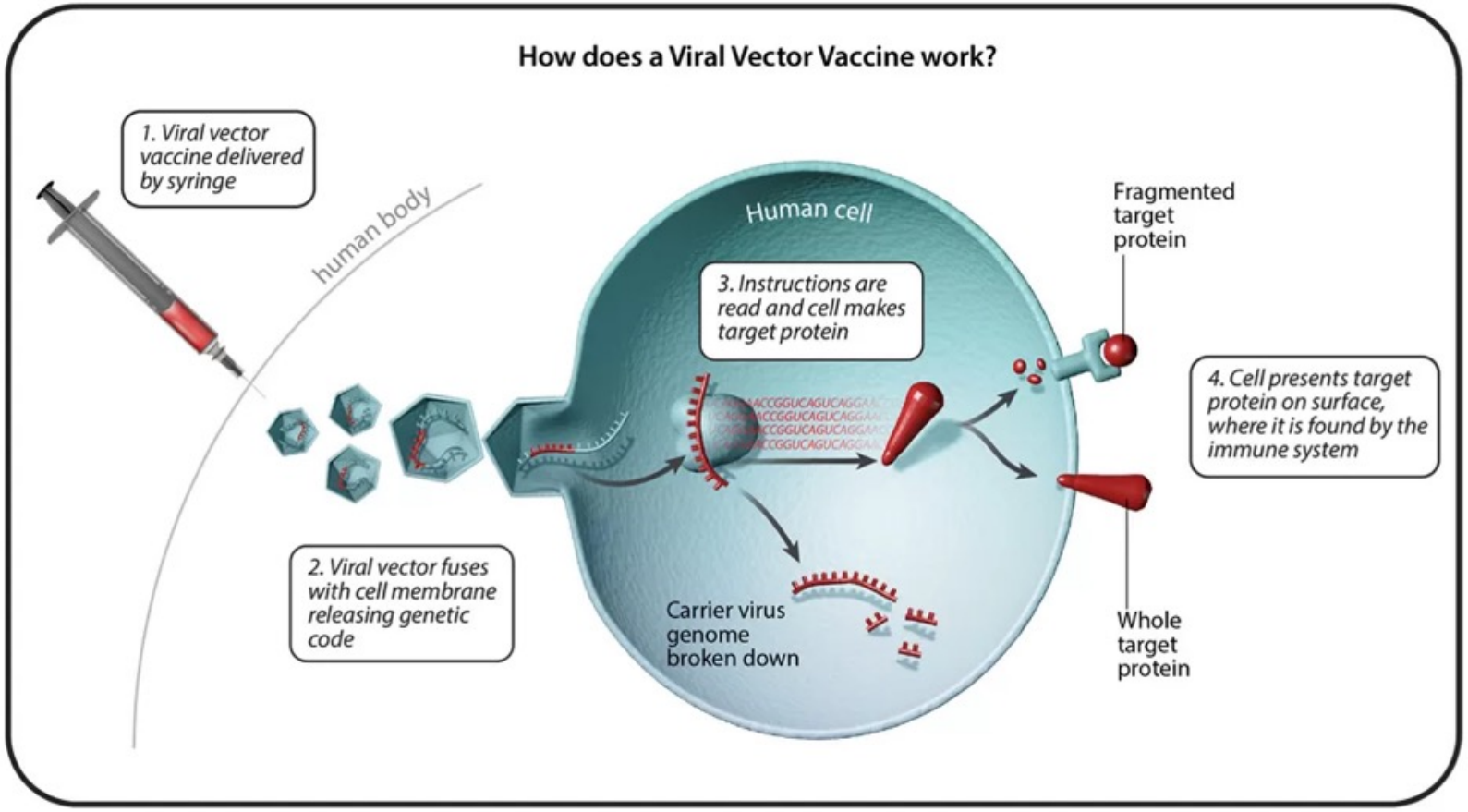
Genetic vaccines



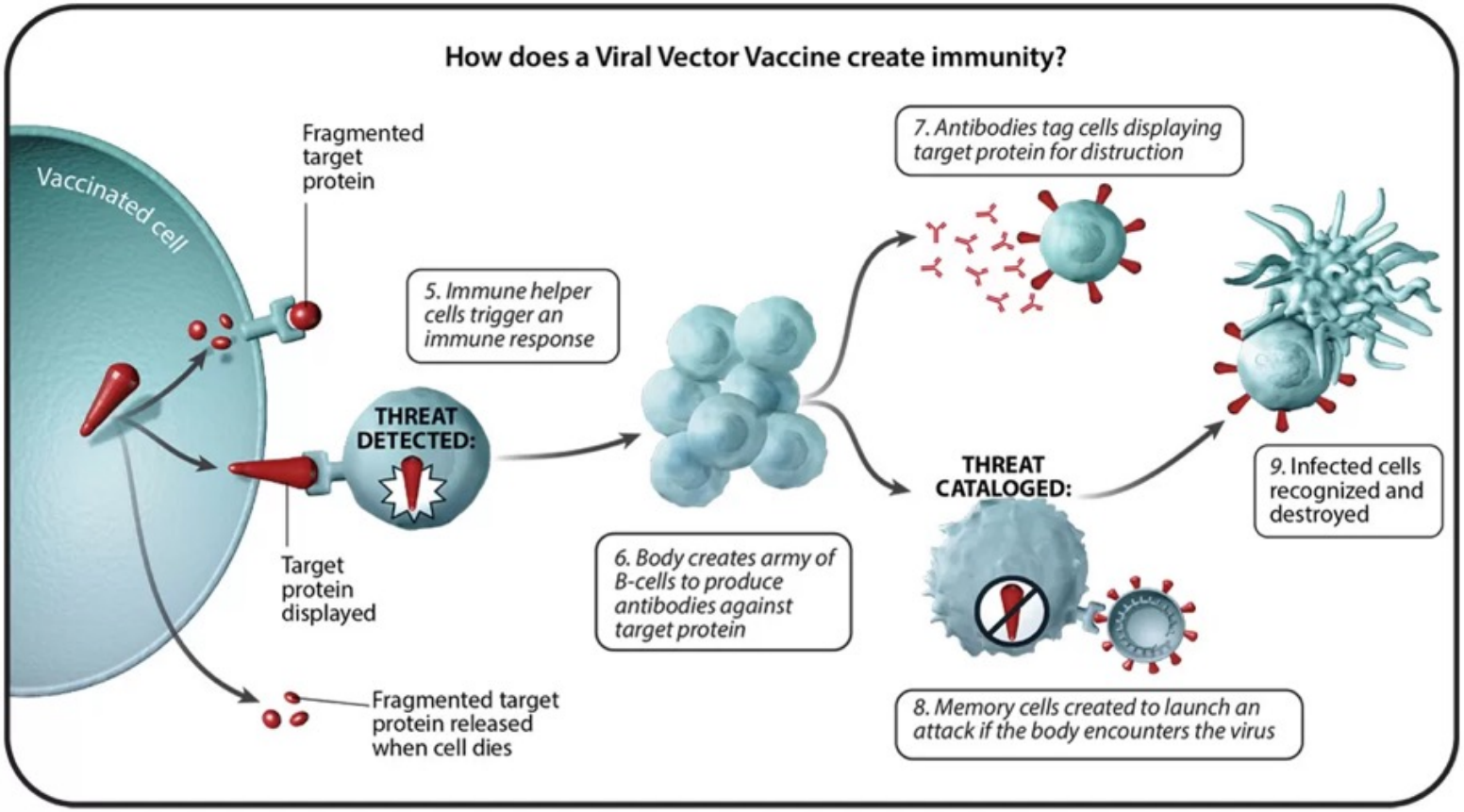
Viral vector vaccines



Viral vector vaccines

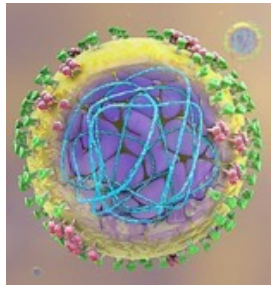


Viral vector vaccines



Viral vaccine vectors

- Non-pathogenic DNA or RNA viruses
  - Enveloped or non-enveloped
  - Replicative or non-replicative
  - Live attenuated human viruses or viruses from other species
- Deliver heterologous antigens to host APC
- Elicit broad immune responses (Innate, Ab, CD4, CD8)
- Intrinsic adjuvant properties
- Easy to prepare thanks to viral genomics, reverse genetics and cell culture
- Based on known viruses with safety/efficacy and manufacturing track record



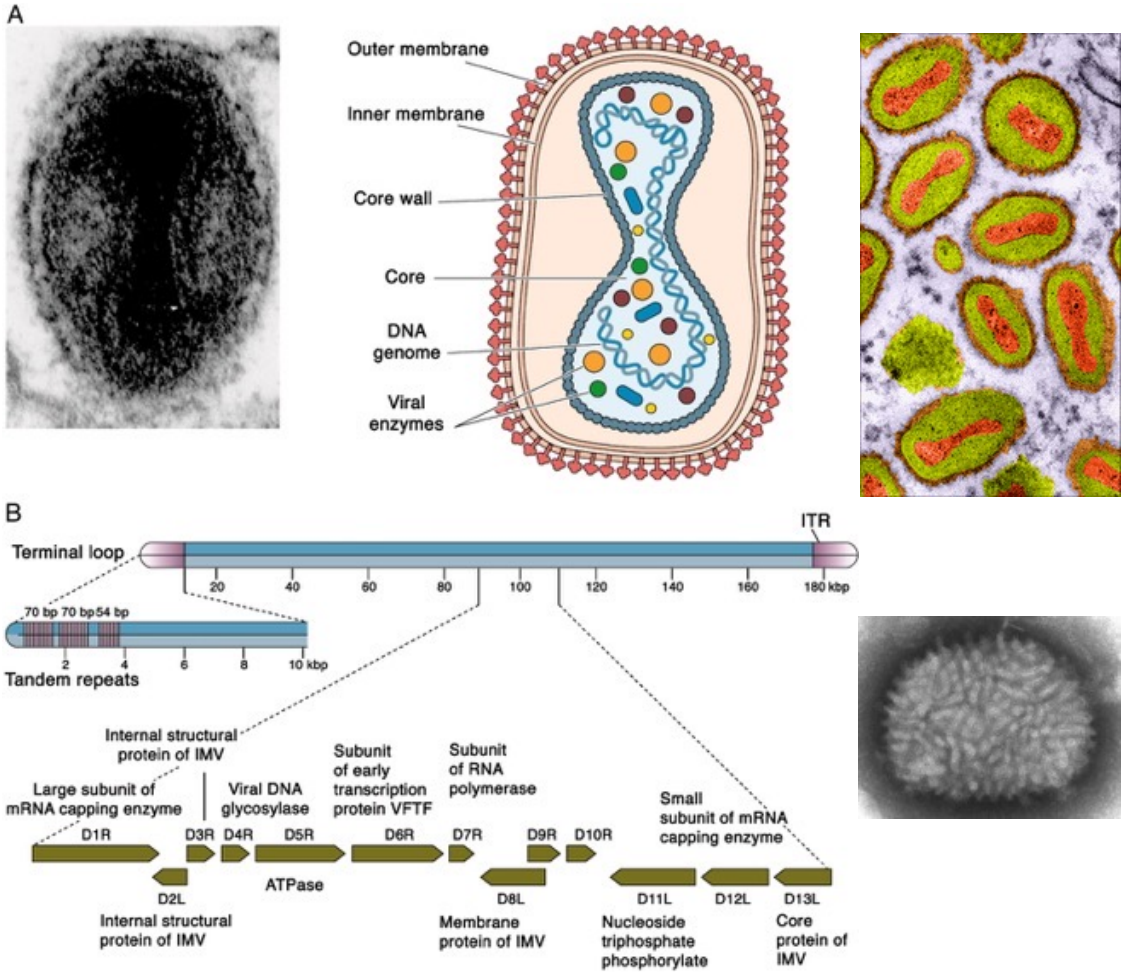
Licensed vectors

- Sanofi IMOJEV, Japanese encephalitis vaccine based on YFV17D live attenuated vaccine
- Sanofi Dengvaxia, ChimeriVax-Dengue vaccine
- GSK RTSS vaccine against malaria based on HBS particles
- Merck Ebola vaccine VSV-Zebov
- Covid-19 vaccines: Oxford/AstraZeneca chimp adenovirus vector and Jansenn (J&J) or Sputnik based on Ad5 and Ad26

DNA
- Poxvirus: Vaccinia, MVA, ALVAC, NYVAC
- Adenovirus (Ad5, Ad26, ChAd)
- HBV: HBs VLP particles

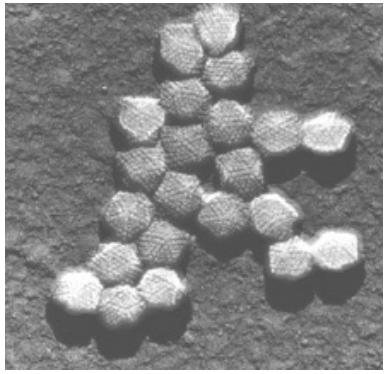
RNA
- Flavivirus: 17-D Yellow Fever vaccine, Dengue 4
- Negative RNA virus: Measles, VSV

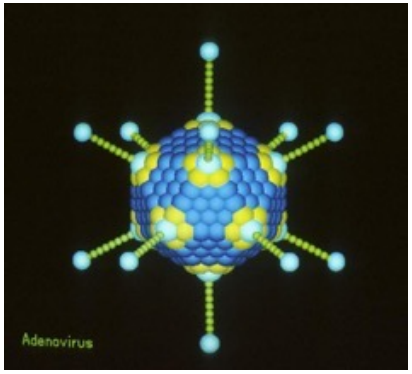
Vaccinia virus Ankara strain (vecteur MVA)

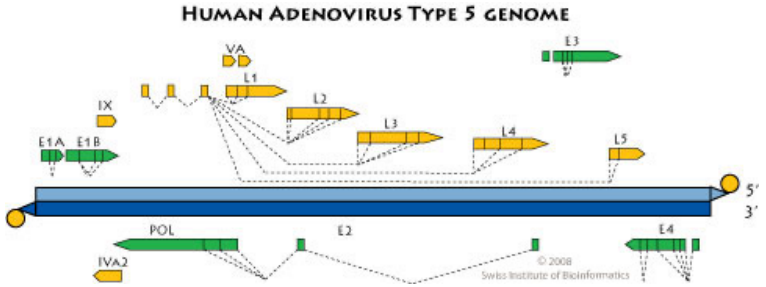


- Modified Vaccinia virus Ankara is licensed as a third-generation vaccine against smallpox
- Attenuated by 570 serial culture passage in primary CEF
- Fails to replicate in most mammalian cells
- Large packaging capacity for heterologous DNA
- Lack of virus persistence in the host
- Recombinant MVA safely tested in numerous clinical trials (doses between 5 x 10^7 and 2 x 10^8 pfu)
  - Malaria, HIV, Influenza, TB, SARS, MERS, H5N1, Ebola, WNV
- Induction of antibodies and moderate CD4 and CD8 T-cell responses when used as a booster

Human adenovirus vectors (HuAd)

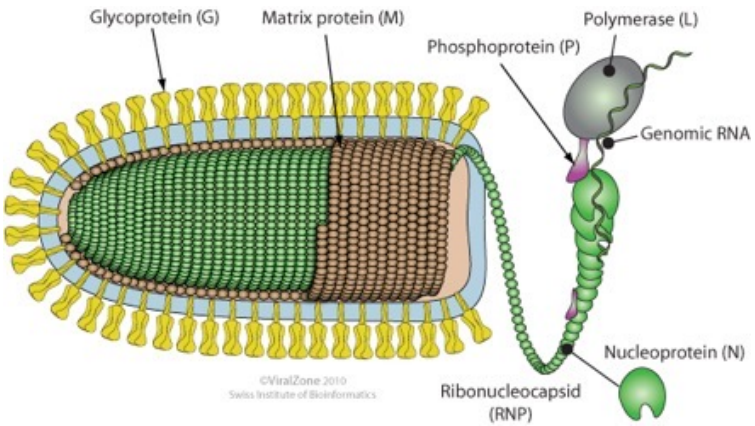




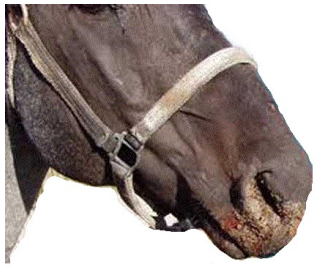


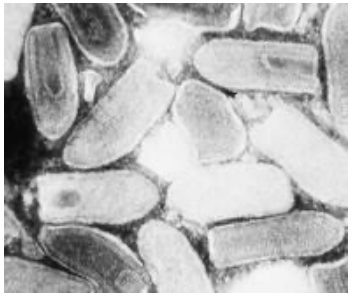
- Small non-enveloped DNA viruses (> 30 kb) icosahedric capsid
- Hundred types (40 infect humans), 52 serotypes
- Broad tropism (CAR receptor)
- Pharyngitis, conjunctivitis, pneumonia, gastro-enteritis
- Repeated infections
- Replication incompetent vectors, early genes deletion
  - 35% of adults living in the USA have neutralizing antibodies to Ad5 and over 90% in individuals living in Côte d'Ivoire
  - Antibodies to the so-called rare Ad26 are below 20% in the USA and Europe but above 90% in South Africa
- CAR is not expressed on dendritic cells and stimulation of T cells largely depends on cross-priming
- Stimulation of strong CD8 T cell response
- Stimulation of vigorous innate immune responses
- High doses are necessary (10^{10} pfu) -> toxicity
- Hundreds of clinical trials have been performed, few efficacy trials (against Malaria, HIV, Influenza, TB, Ebola, Influenza)
- Last year, several Ad SARS-CoV-2

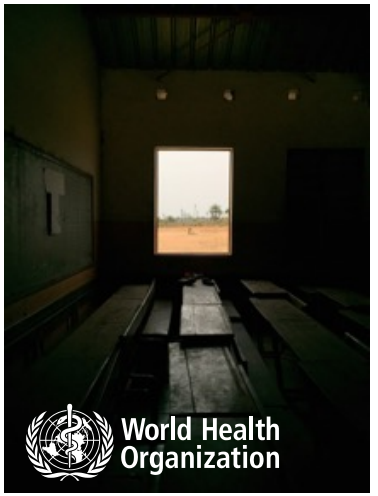
Vesicular stomatitis virus (VSV)



- Rhabdoviridae, mononegavirales
- Transmitted by sandfly
- Infects cattle, horses, pigs
- Zoonosis in humans

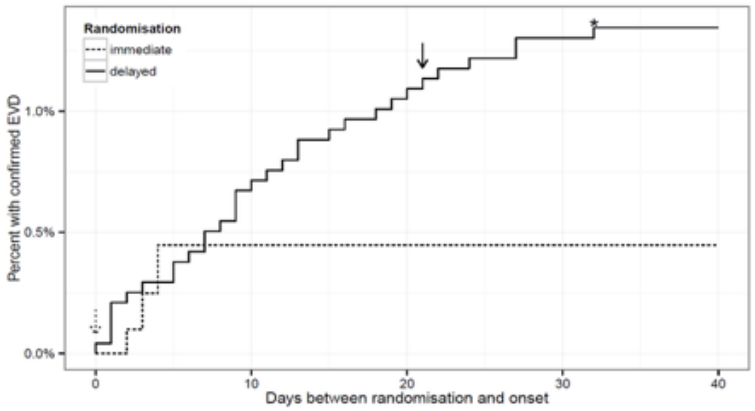




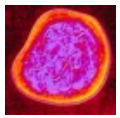


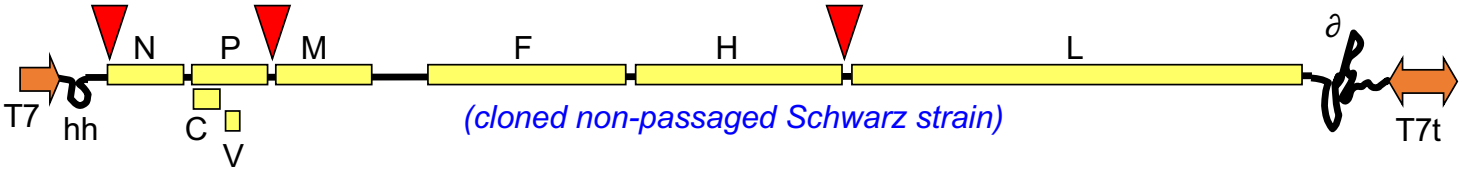
"Ebola ça suffit"

Ring vaccination efficacy trial of rVSV-ZEBOV candidate Ebola vaccine in Guinea, July 2015

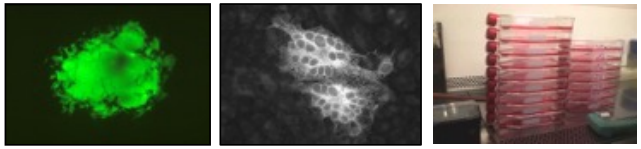


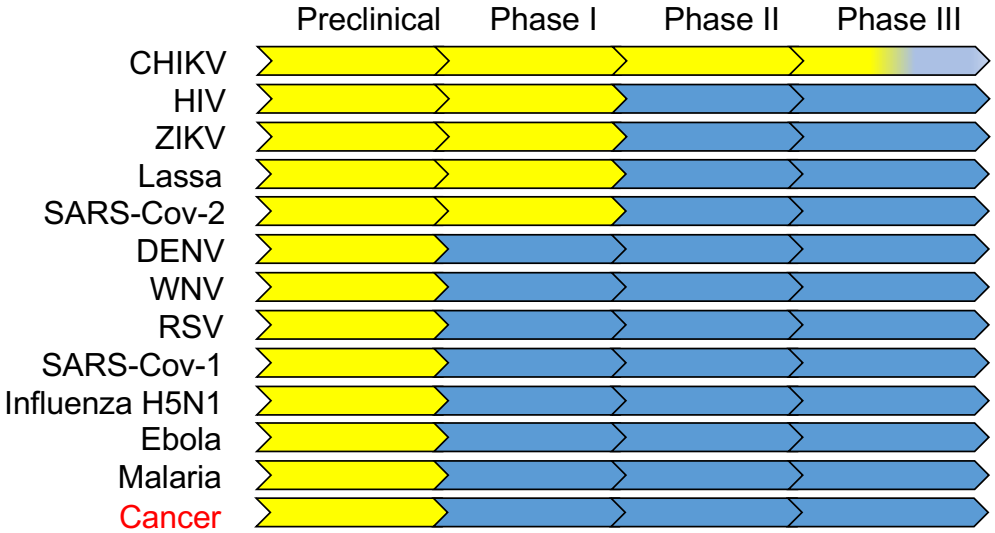
Recombinant measles vaccine platform





- Cloning
- Reverse genetics
- Amplification
- Characterization





This vaccine platform has demonstrated its safety and immunogenicity in numerous preclinical and clinical trials in presence of preexisting anti-measles immunity.

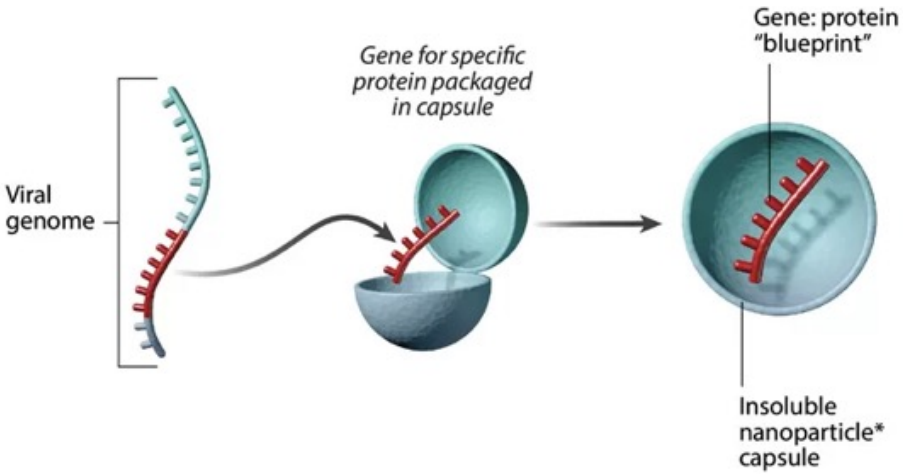
Institut Pasteur

THEMIS

mRNA vaccines

What is the Messenger RNA (mRNA) vaccine?

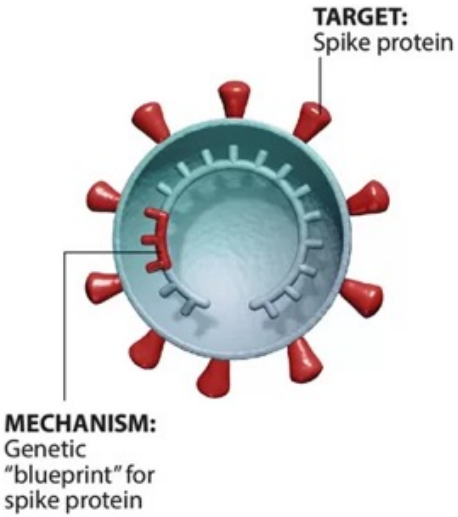
Made of a small section of a virus' genetic material - the instructions or 'blueprint' for a specific protein. A insoluble nanoparticle* capsule carries the gene safely to your cells.



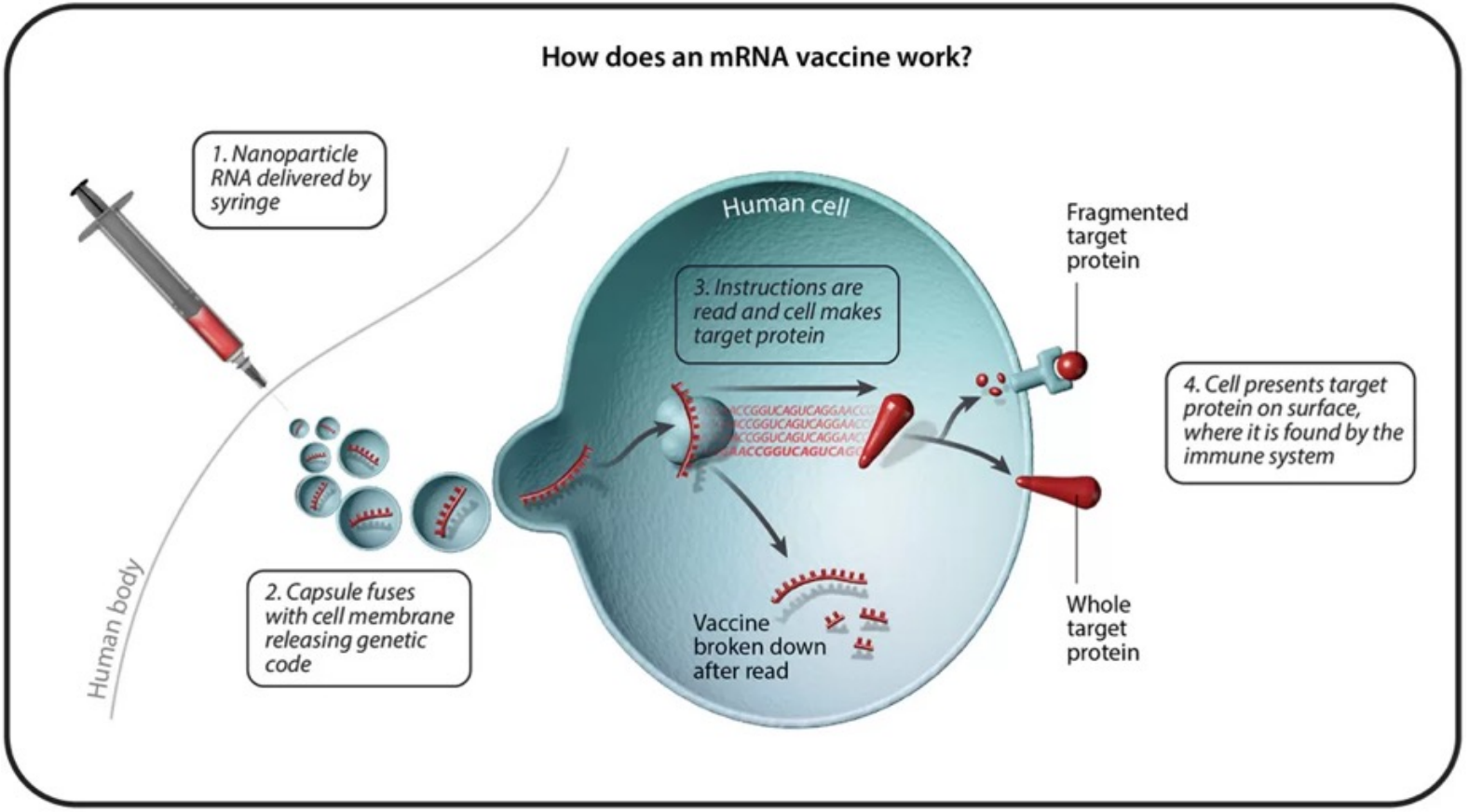
*Did You Know?: "Nano" means small.

Vaccine Target

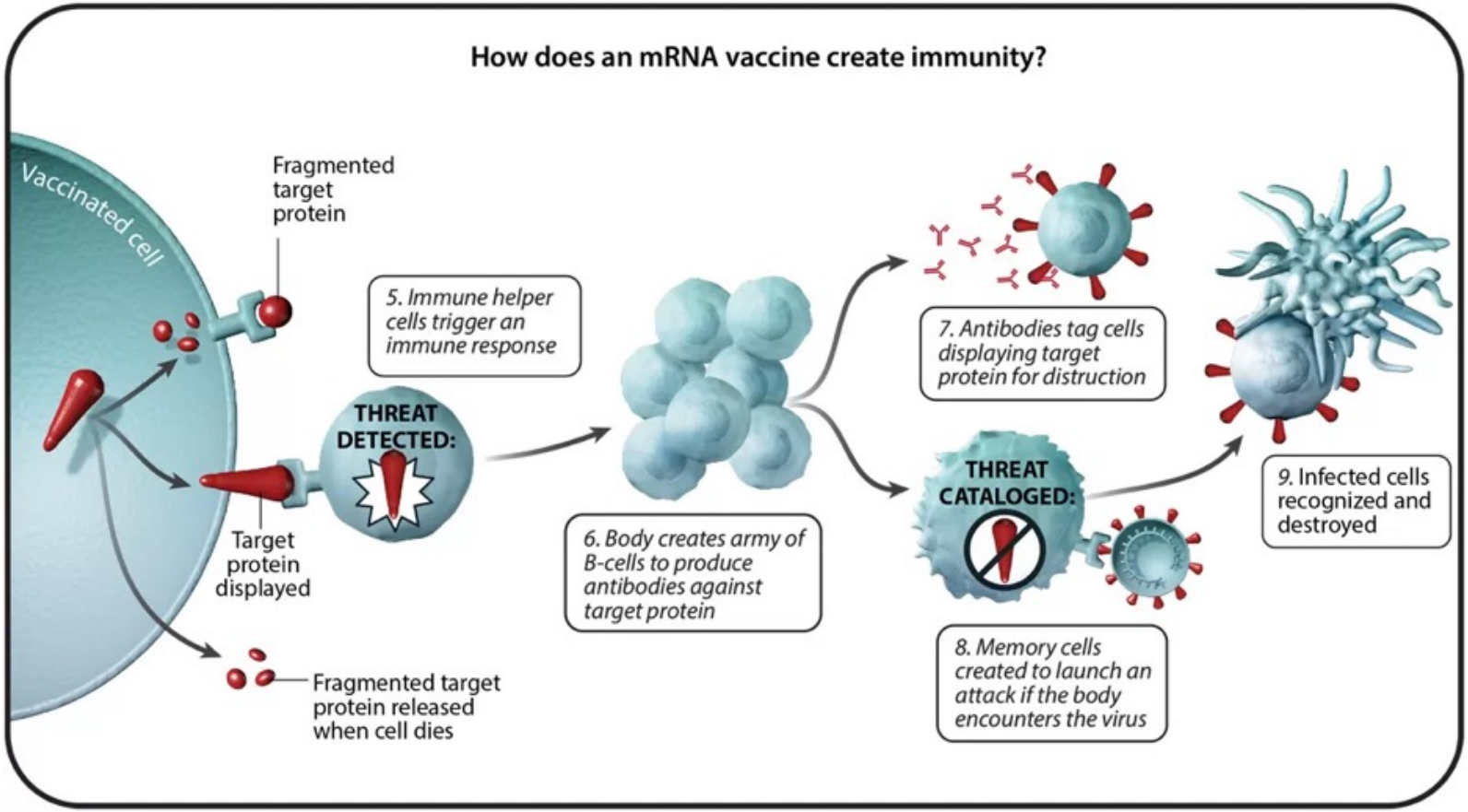
Pfizer's mRNA COVID vaccine carries the genetic blueprint for the spike protein. Your body will make this protein and build immunity against any invaders carrying it on their surface.



mRNA vaccines

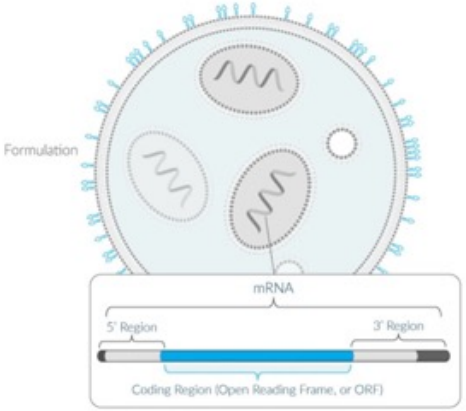


mRNA vaccines

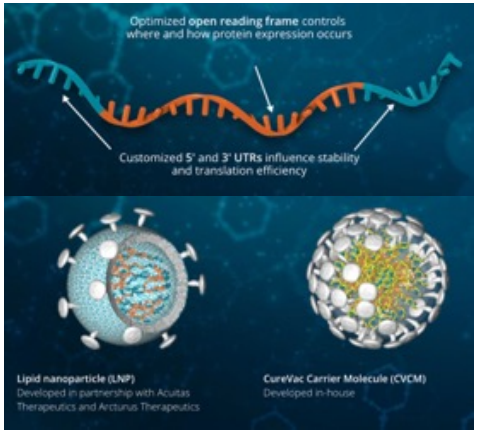


SARS-Cov-2 vaccines have used new technologies

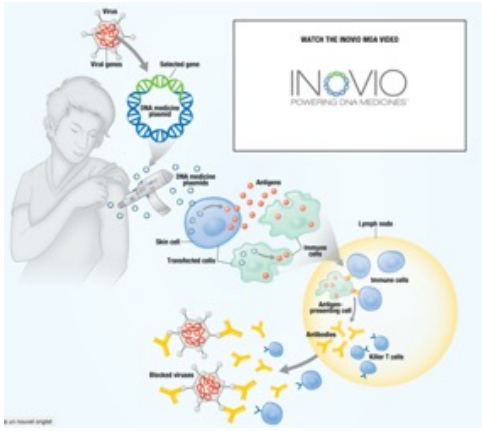
MODERNA (mRNA)



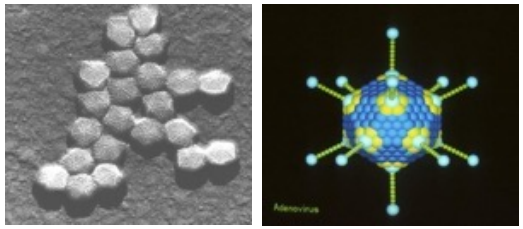
CUREVAC (mRNA)



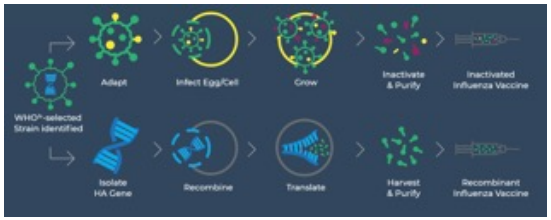
INOVIO (DNA)



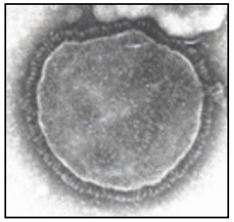
OXFORD
(ChAdOx1)



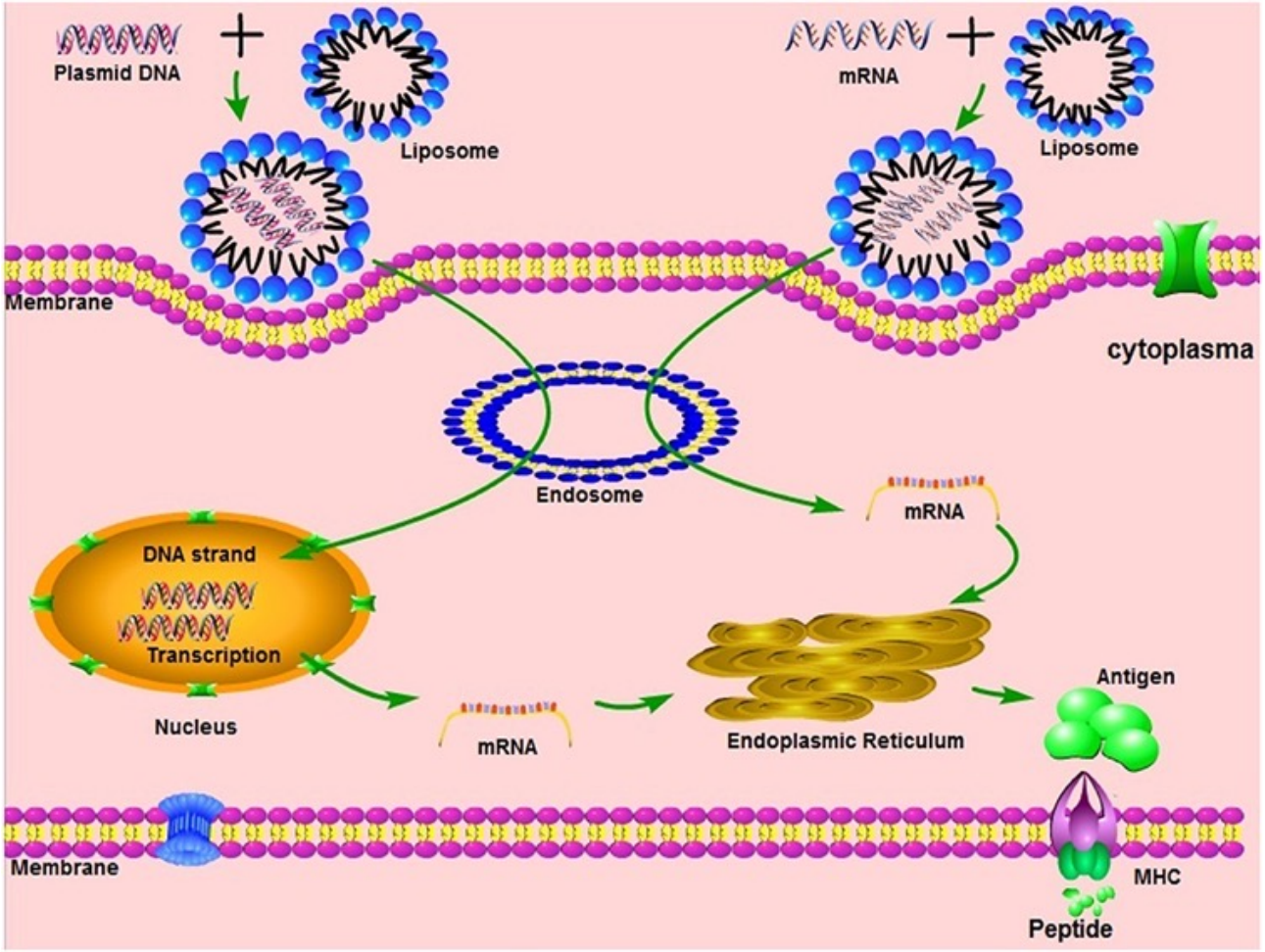
SANOFI
(Baculovirus protein)



INSTITUT PASTEUR
(Measles vector)



Genetic vaccines



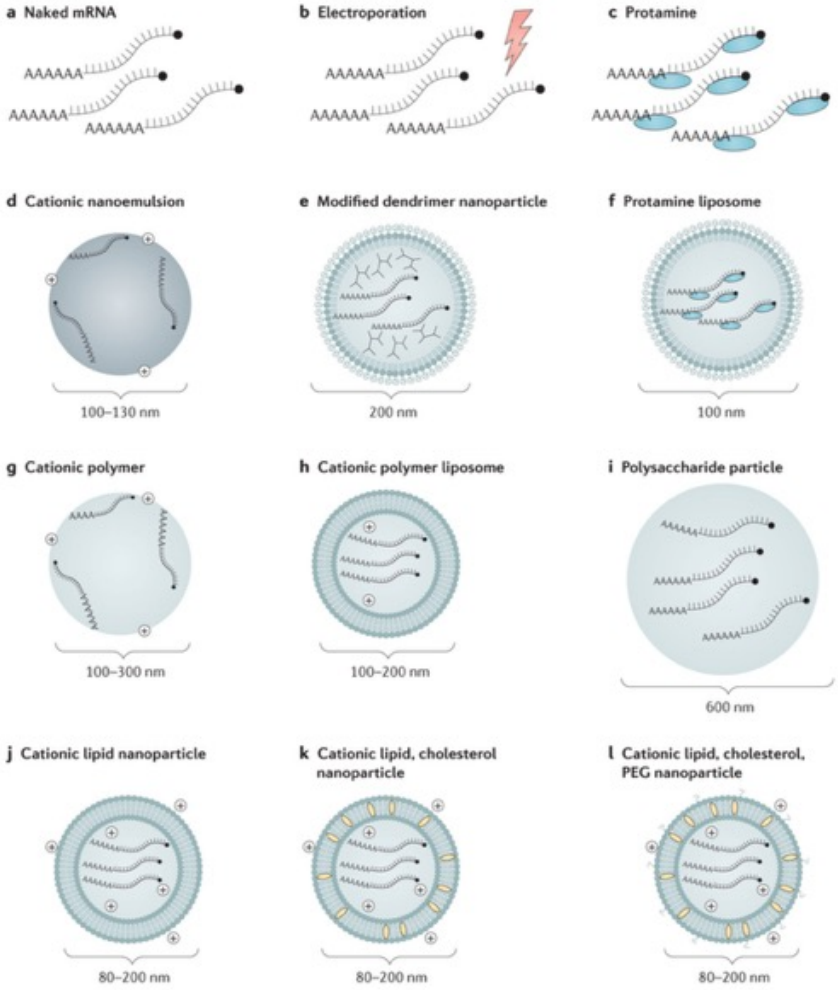
Formulation and delivery methods of mRNA vaccines

Box 1

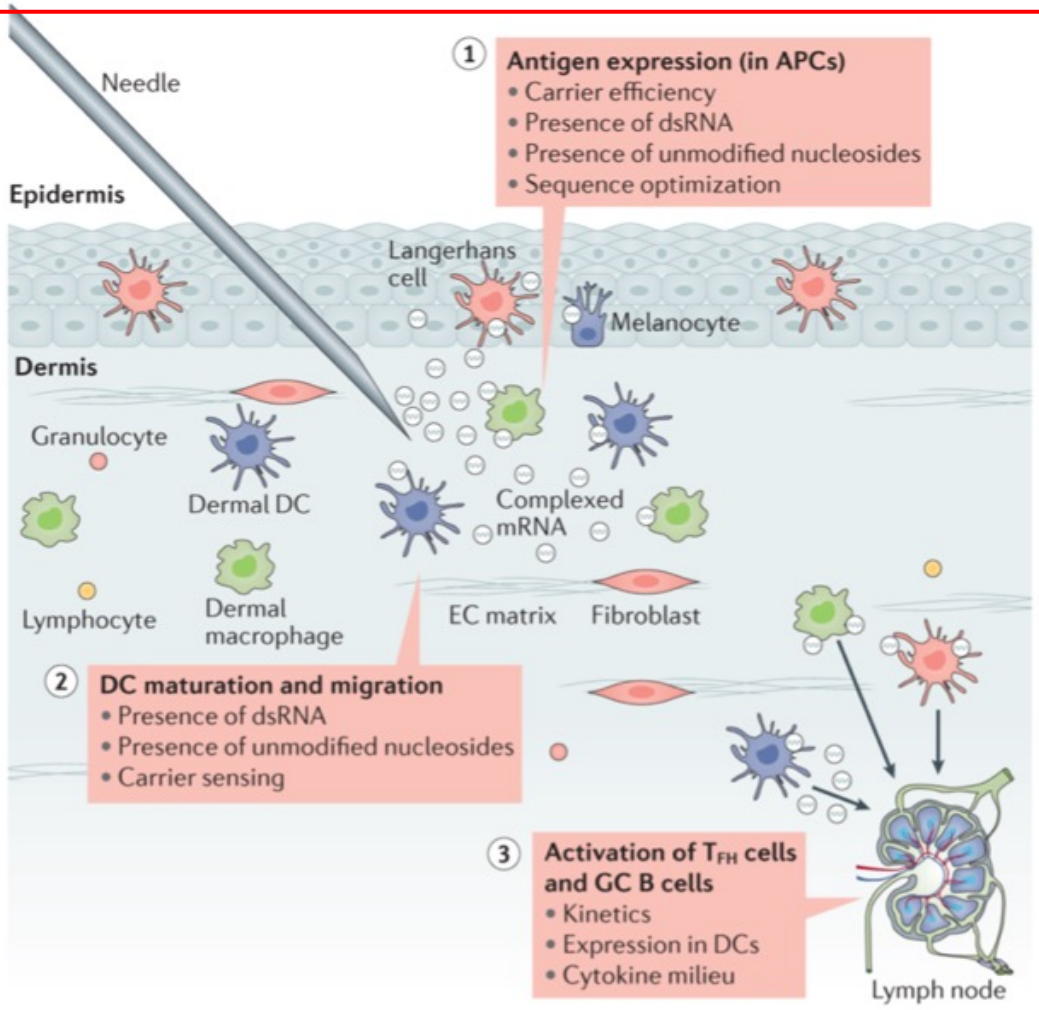
Strategies for optimizing mRNA pharmacology

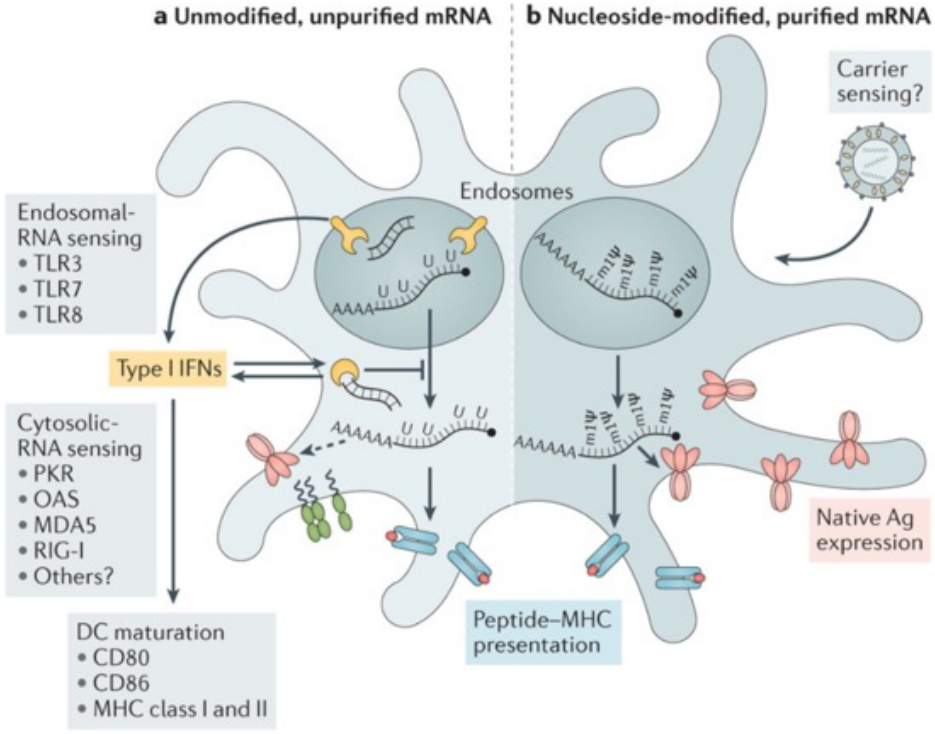
A number of technologies are currently used to improve the pharmacological aspects of mRNA. The various mRNA modifications used and their impact are summarized below.

- Synthetic cap analogues and capping enzymes[26,27] stabilize mRNA and increase protein translation via binding to eukaryotic translation initiation factor 4E (EIF4E)
- Regulatory elements in the 5′-untranslated region (UTR) and the 3′-UTR[23] stabilize mRNA and increase protein translation
- Poly(A) tail[25] stabilizes mRNA and increases protein translation
- Modified nucleosides[9,48] decrease innate immune activation and increase translation
- Separation and/or purification techniques: RNase III treatment (N.P. and D.W., unpublished observations) and fast protein liquid chromatography (FPLC) purification[13] decrease immune activation and increase translation
- Sequence and/or codon optimization[29] increase translation
- Modulation of target cells: co-delivery of translation initiation factors and other methods alters translation and immunogenicity



Mode of immune sensing and activation by mRNA vaccines

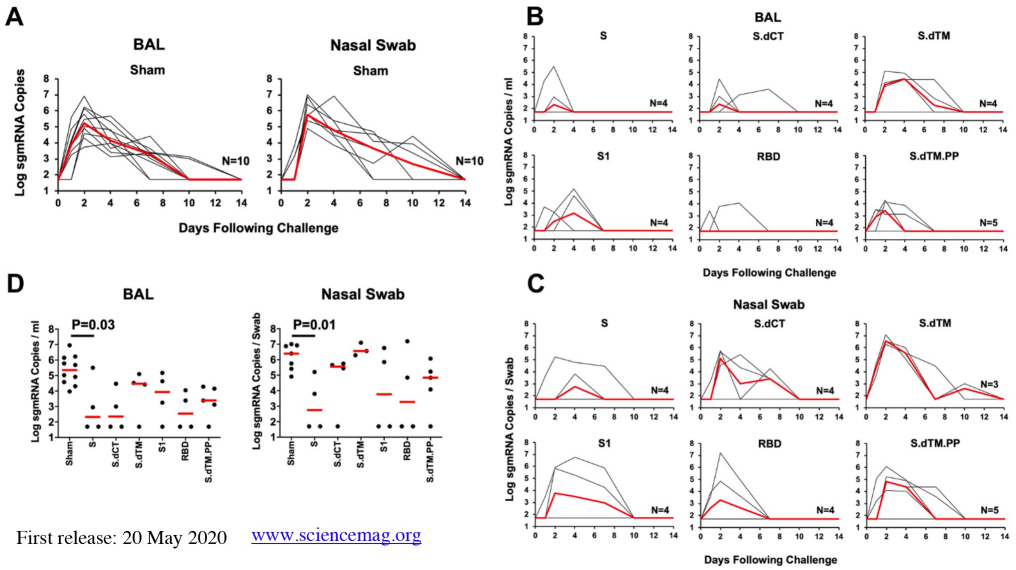




Nat Rev Drug Discov. 2018 April ; 17(4): 261–279. doi:10.1038/nrd.2017.243.

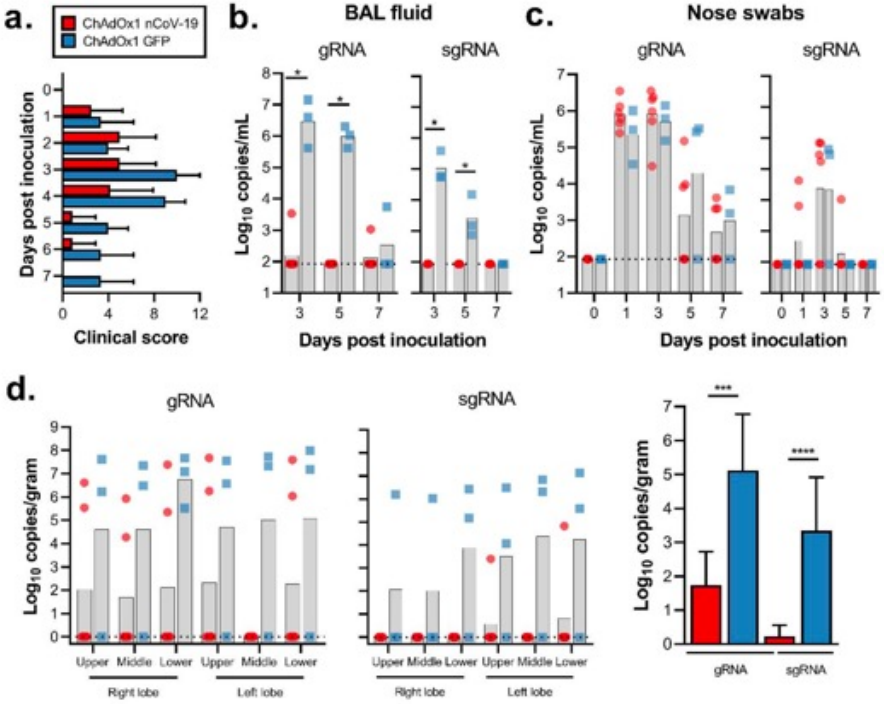
First preclinical results of COVID vaccines showed partial protection

DAN BAROUCH, HARVARD
DNA vaccine



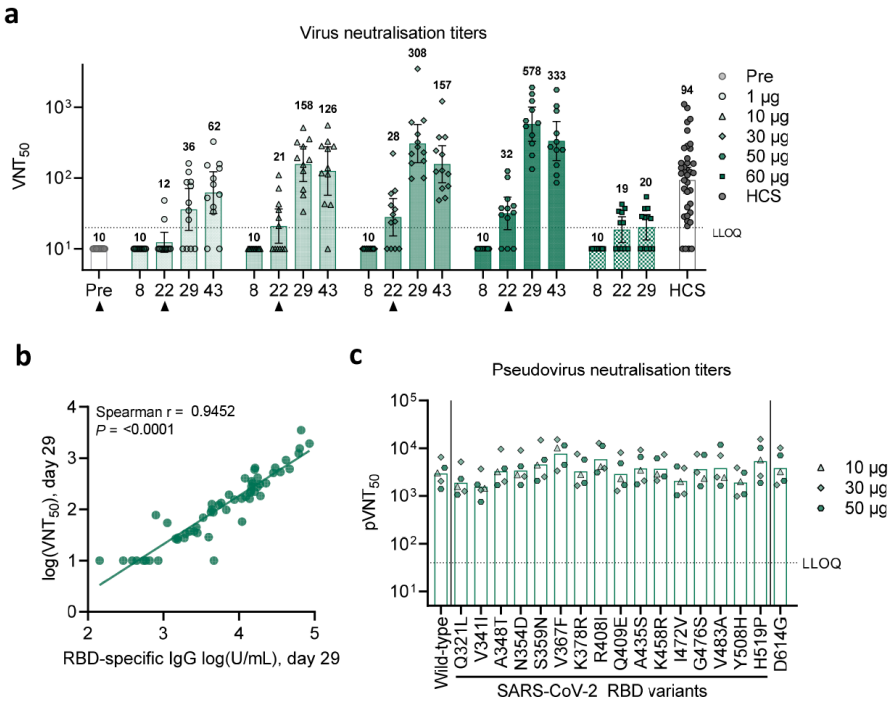
First release: 20 May 2020 www.sciencemag.org

OXFORD
ChAdOx1 nCoV-19

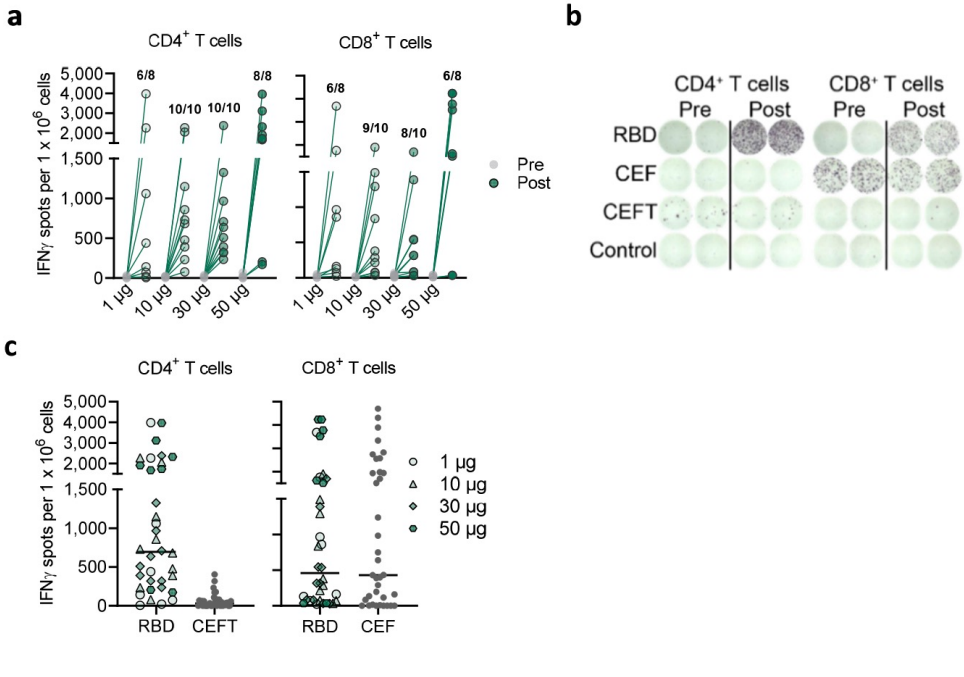


Phase I/II clinical trial results of Biontech/Pfizer mRNA candidate

Antibody response



T cell response

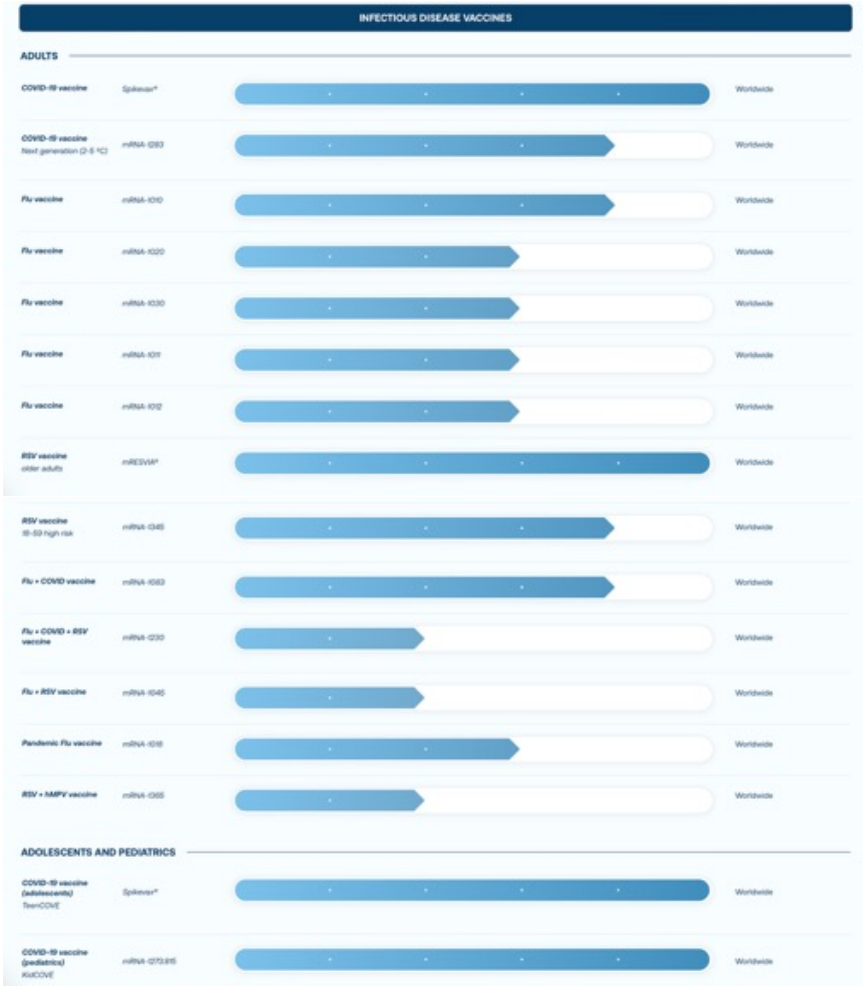


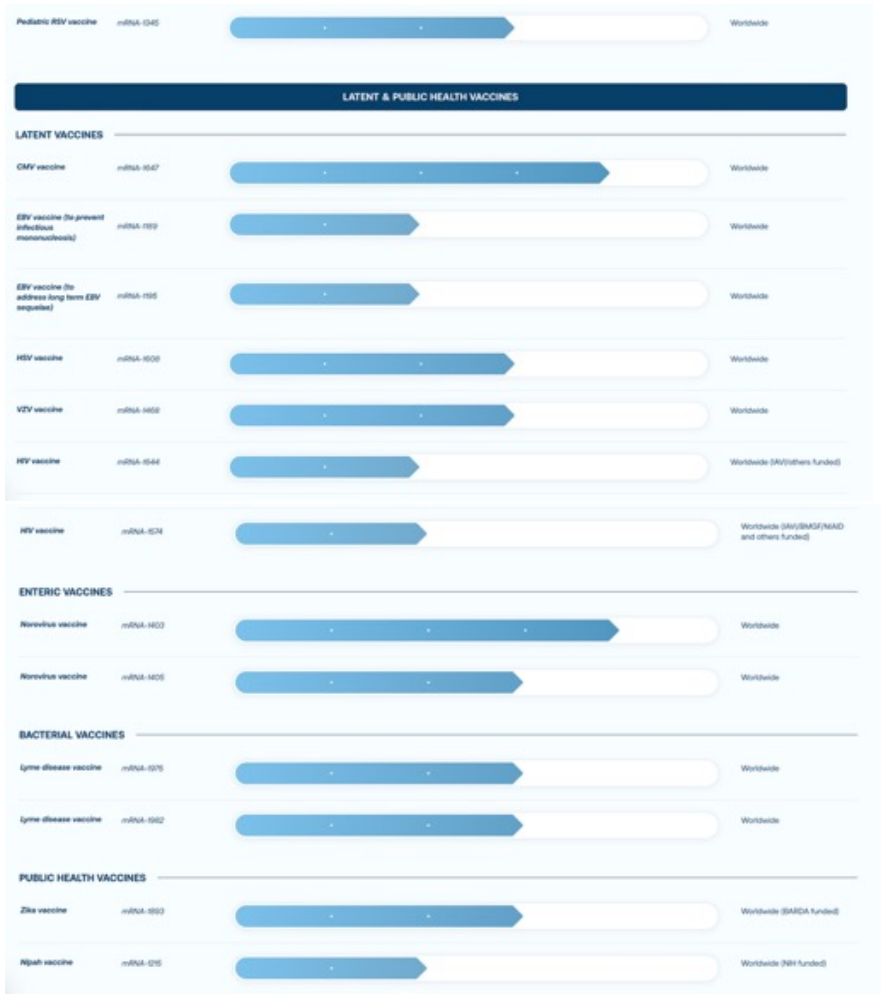
Phase III efficacy clinical trial results of Biontech/Pfizer mRNA candidate

Table 2. Vaccine Efficacy against Covid-19 at Least 7 days after the Second Dose.*

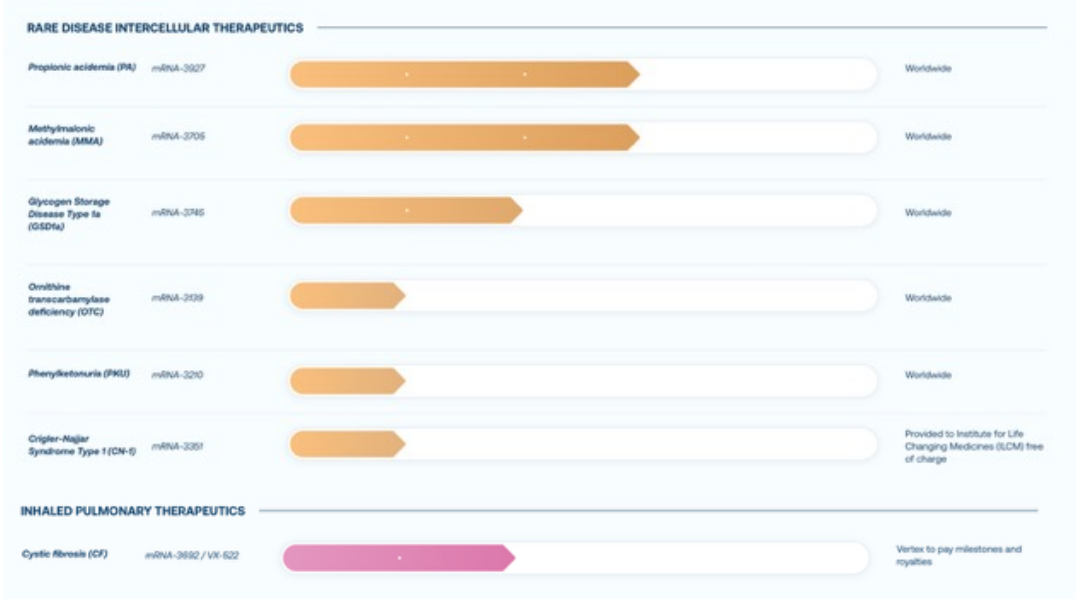
Efficacy End Point	BNT162b2		Placebo		Vaccine Efficacy, % (95% Credible Interval)‡	Posterior Probability (Vaccine Efficacy >30%)§
	No. of Cases	Surveillance Time (n)†	No. of Cases	Surveillance Time (n)†		
		(N=18,198)		(N=18,325)		
Covid-19 occurrence at least 7 days after the second dose in participants without evidence of infection	8	2.214 (1,7411)	162	2.222 (17,511)	95.0 (90.3–97.6)	>0.9999
		(N=19,965)		(N=20,172)		
Covid-19 occurrence at least 7 days after the second dose in participants with and those without evidence of infection	9	2.332 (18,559)	169	2.345 (18,708)	94.6 (89.9–97.3)	>0.9999

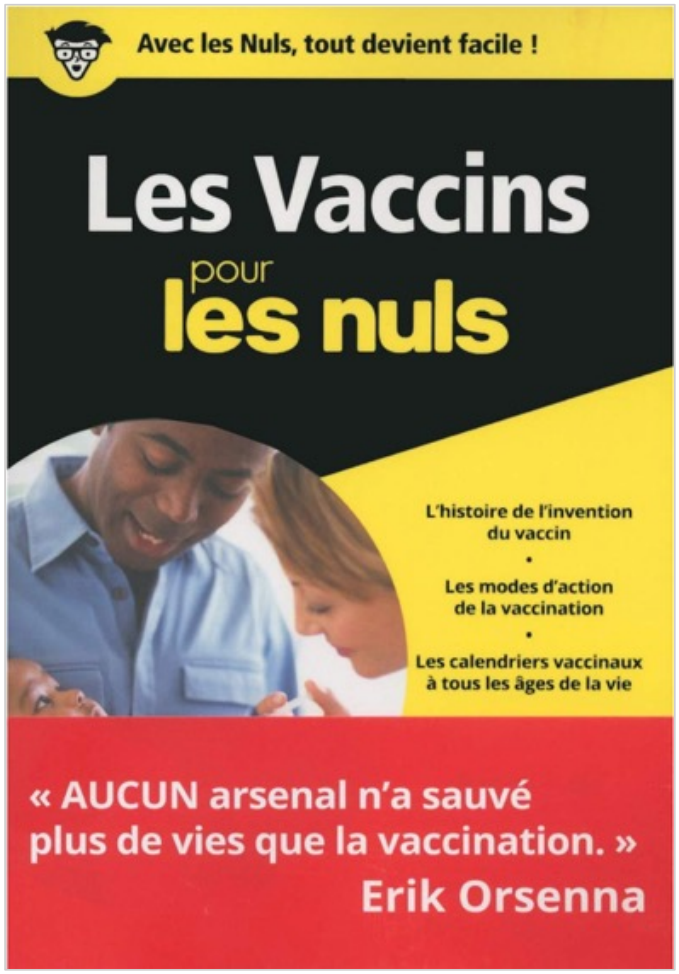
Moderna mRNA vaccines pipeline (49 vaccines)

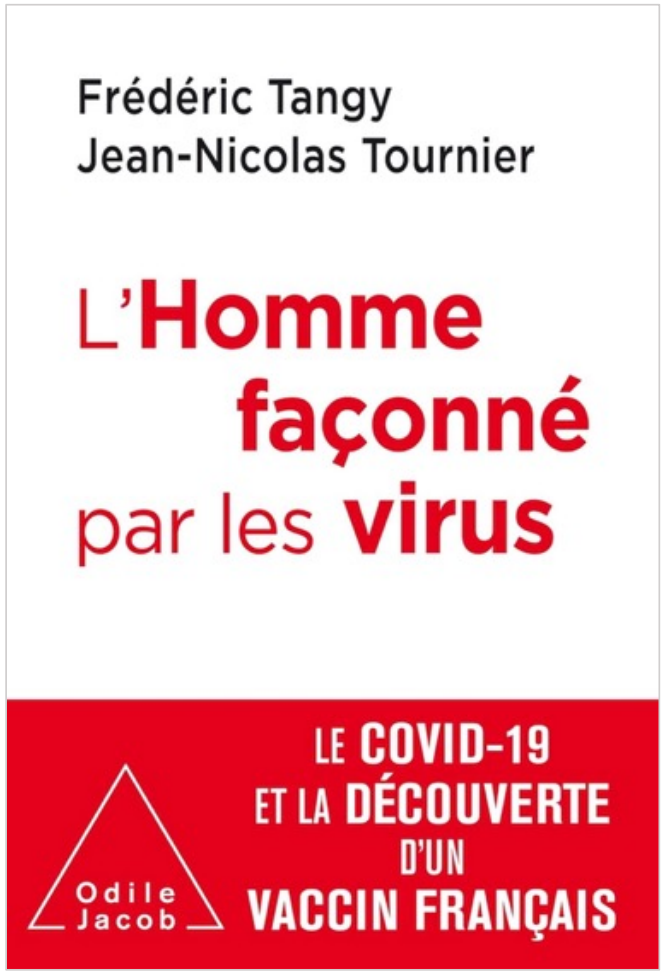


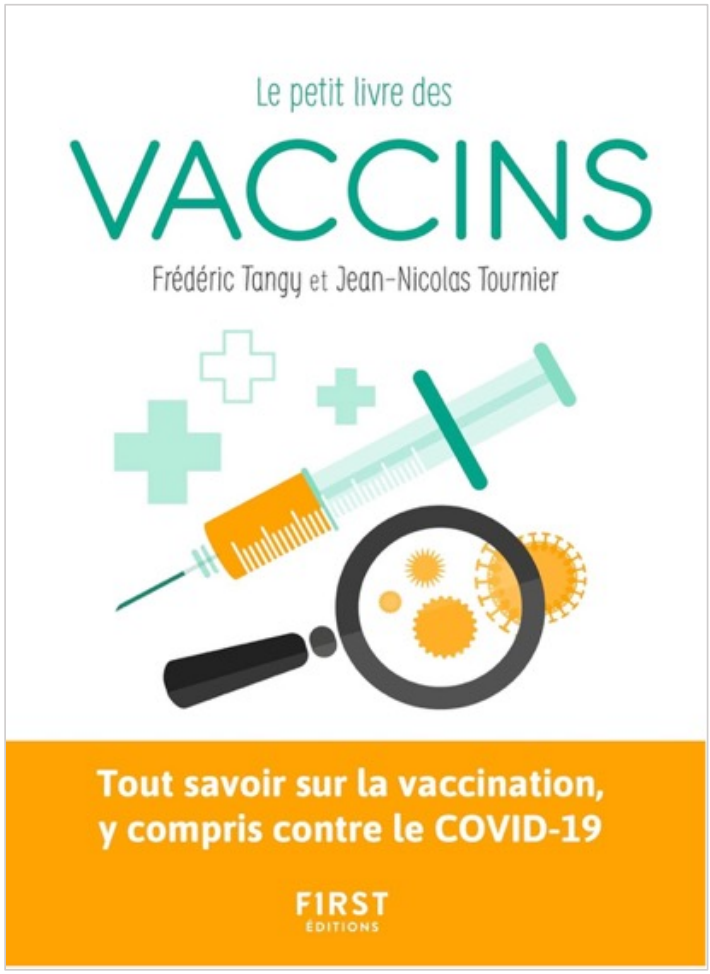


Moderna mRNA vaccines pipeline




Avec les Nuls, tout devient facile !
Les Vaccins
pour
les nuls
L'histoire de l'invention du vaccin
•
Les modes d'action de la vaccination
•
Les calendriers vaccinaux à tous les âges de la vie
« AUCUN arsenal n'a sauvé plus de vies que la vaccination. »
Erik Orsenna


Frédéric Tangy
Jean-Nicolas Tournier
L'Homme façonné par les virus
Odile Jacob
LE COVID-19 ET LA DÉCOUVERTE D'UN VACCIN FRANÇAIS


Le petit livre des
VACCINS
Frédéric Tangy et Jean-Nicolas Tournier
Tout savoir sur la vaccination, y compris contre le COVID-19
FIRST
ÉDITIONS