

# SARS-CoV-2

## Preventive measures and Vaccination

***Dr. Fateme Rajabi***

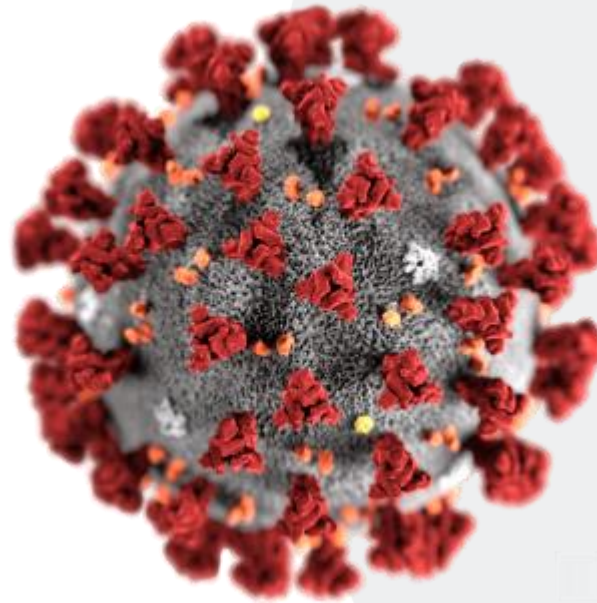
***Center for Research and Training in Skin diseases and Leprosy***

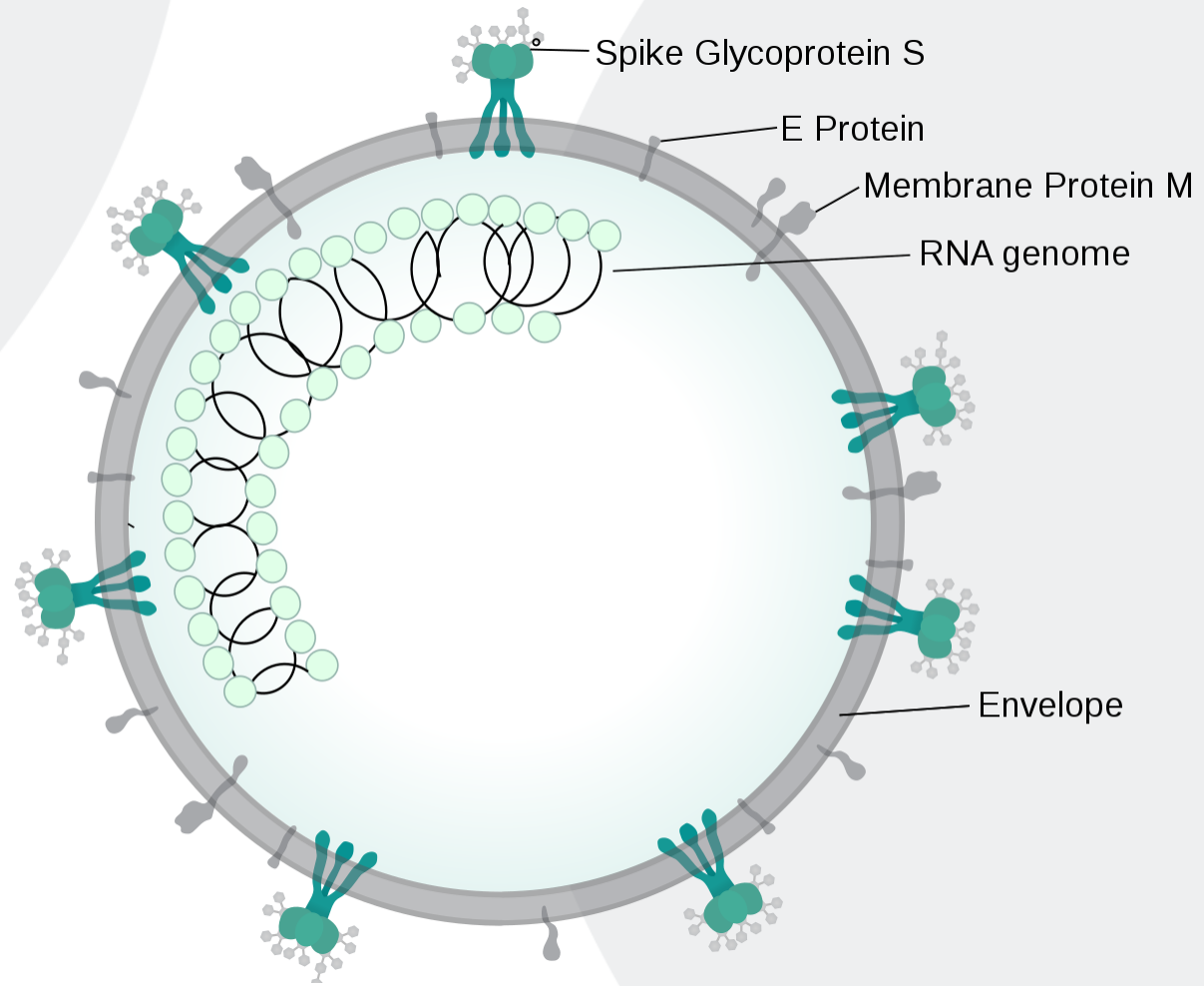


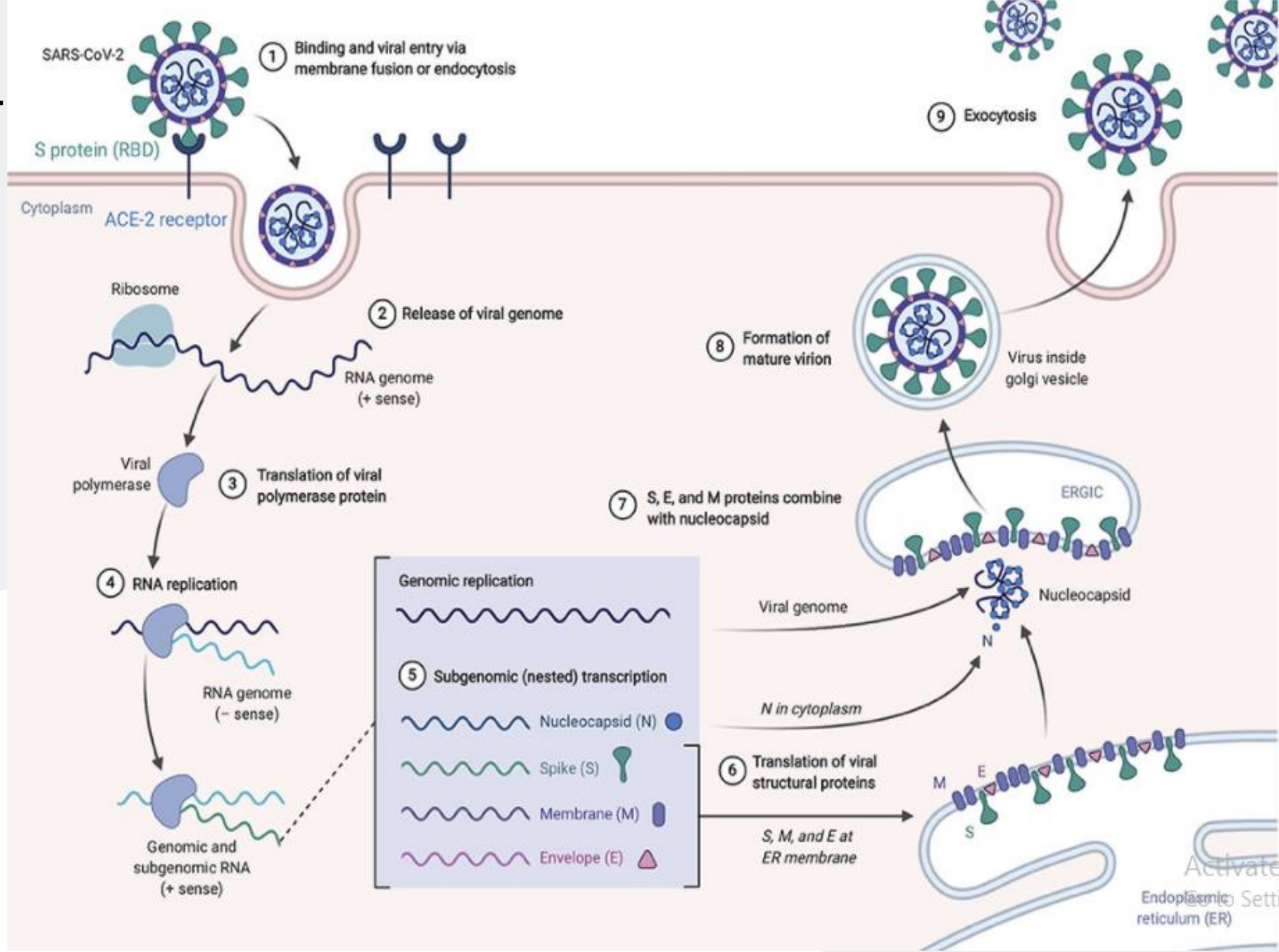
TEHRAN UNIVERSITY  
OF  
MEDICAL SCIENCES



# The life cycle of SARS-CoV-2







# Vaccines





## Classical platforms

### Whole-inactivated virus

Example: Polio vaccine  
COVID-19:  
PiCoVacc in phase 1  
clinical trials



### Live-attenuated virus

Example: MMR vaccine  
COVID-19:  
in preclinical stage



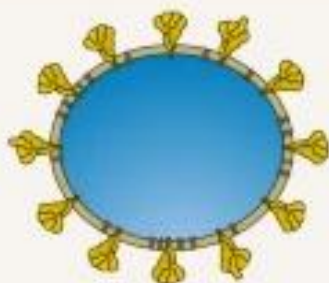
### Protein subunit

Example: Seasonal  
influenza vaccine  
COVID-19:  
NVX-CoV2373 in  
phase 1/2 clinical trials



### Virus-like particle

Example: Human  
papillomavirus vaccine  
COVID-19:  
in preclinical stage



## Next-generation platforms

### Viral vector

Example:  
VSV-Ebola vaccine  
COVID-19:  
AZD1222, Ad5-nCoV  
in phase 1/2/3 clinical trials



### DNA

Example:  
Not currently licensed  
COVID-19:  
INO-4800 in phase 1  
clinical trials



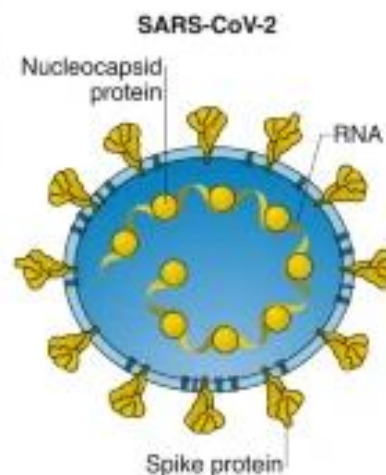
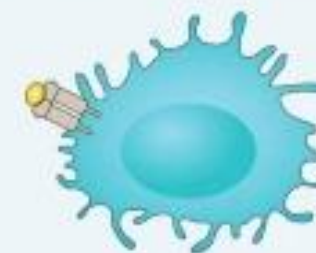
### RNA

Example:  
Not currently licensed  
COVID-19:  
mRNA-1273, BNT162  
in phase 1/2 clinical trials

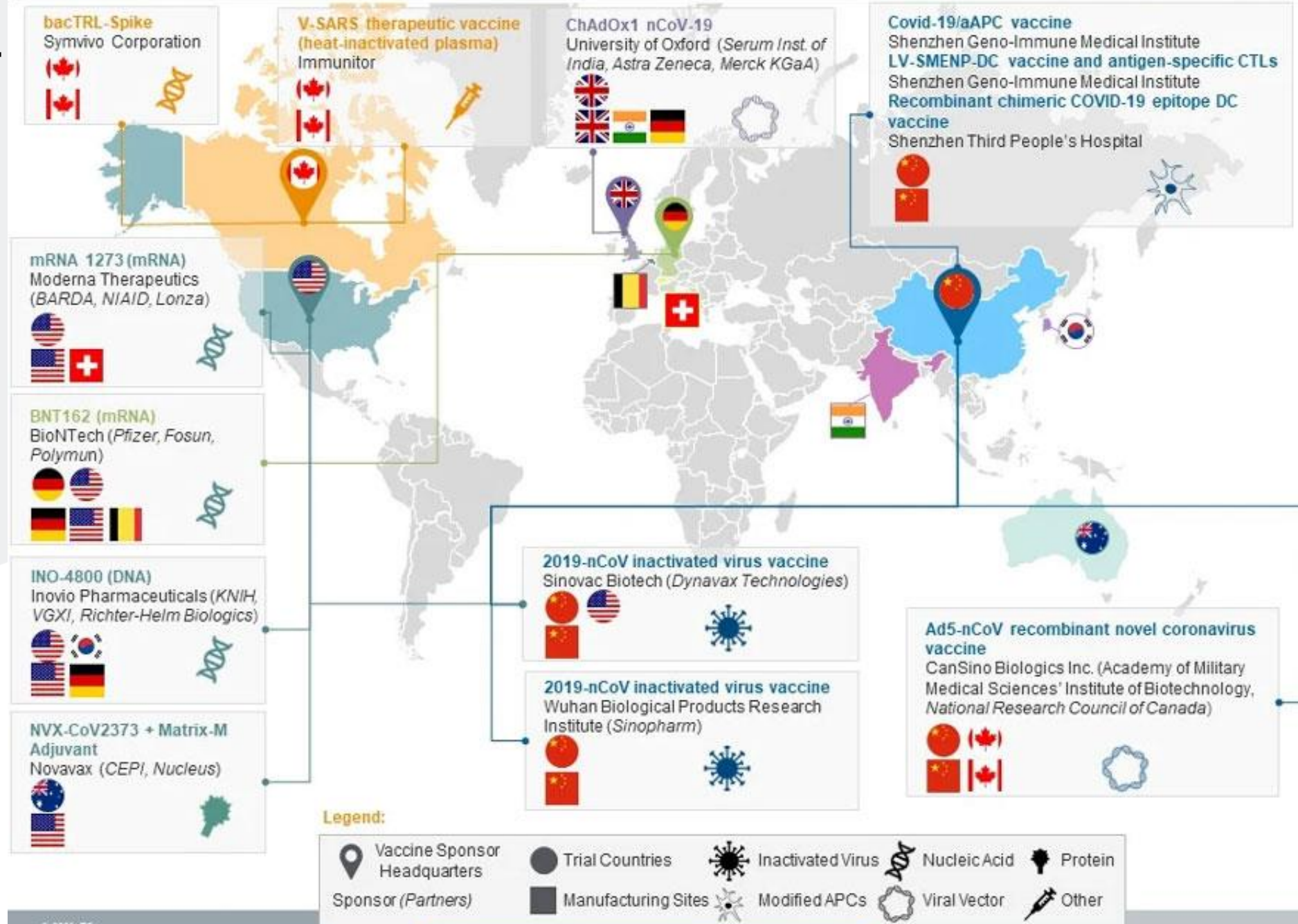


### Antigen-presenting cells

Example:  
Not currently licensed  
COVID-19:  
LV-SMENP-DC,  
COVID-19/αAPC  
in phase 1/2 clinical trials



# COVID-19 Vaccine Candidates: Sponsor, Trial and Manufacturing Sites By Country





# Coronavirus Vaccine Tracker

By [Carl Zimmer](#), [Jonathan Corum](#) and [Sui-Lee Wee](#) Updated July 12, 2021














<https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html>





## Leading vaccines

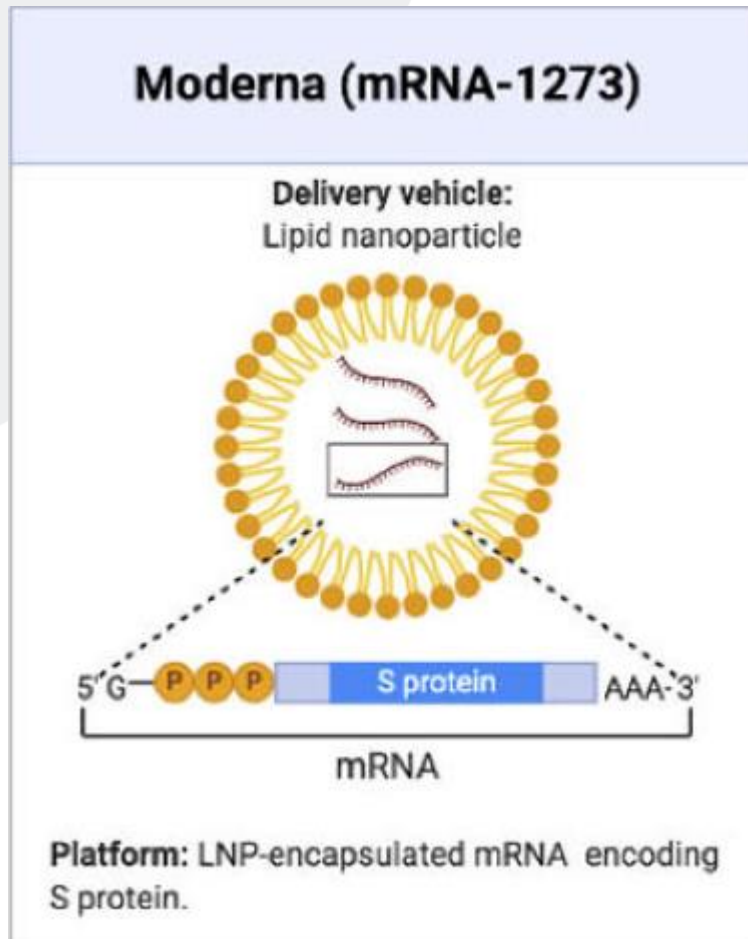
Developer	Type	Phase	Status
 Pfizer-BioNTech	mRNA	<b>2</b> <b>3</b>	Approved in Canada and other countries. Emergency use in U.S. and other countries.
 Moderna	mRNA	<b>3</b>	Approved in Canada. Emergency use in U.S.
 Gamaleya	Adenovirus	<b>3</b>	Early use in Russia. Emergency use in Belarus, Argentina.
 CanSino	Adenovirus	<b>3</b>	Limited use in China.
 Johnson & Johnson	Adenovirus	<b>3</b>	
 Oxford-AstraZeneca	Adenovirus	<b>2</b> <b>3</b>	
 Vector Institute	Protein	<b>3</b>	Early use in Russia.
 Novavax	Protein	<b>3</b>	
 Sinovac	Inactivated	<b>3</b>	Limited use in China.
 Sinopharm-Beijing	Inactivated	<b>3</b>	Approved in U.A.E., Bahrain. Limited use in China.
 Sinopharm-Wuhan	Inactivated	<b>3</b>	Limited use in China, U.A.E.





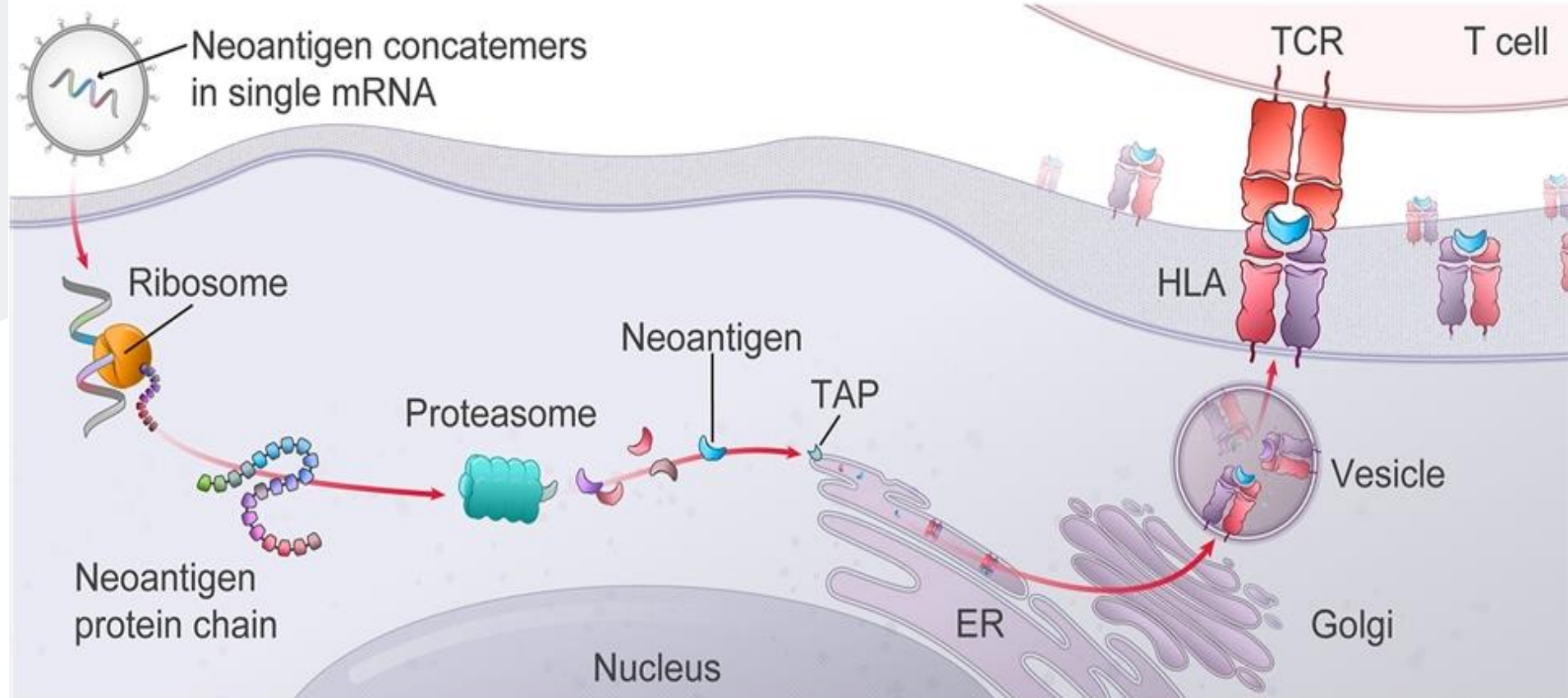
# RNA vaccines

# Moderna (RNA-1273 )



- Contains an mRNA that encode the S protein of that is translated by host cells
- Encapsulated within lipid nanoparticles (LNPs) composed of ionizable lipid, distearoyl phosphatidylcholine, cholesterol, and polyethylene glycol lipid.

## Moderna's mRNA vaccines elicit T cell activation for curative intent cancer therapy





# Moderna (RNA-1273 )

## Advantages:

- Formulation within an LNP improves immunogenicity, protecting the mRNA from enzymatic degradation, and facilitating efficient uptake by target cells.
- rapid discovery and design for a quicker respond to emerging pandemic threats
- Previously deployed in vaccines against CMV, Zika virus, H7N9, and RSV.



# Moderna (RNA-1273 )

## Trial:

- 0.5 ml of 25 or 100 µg IM day 0 and 29
- All participants achieved seroconversion.
- Antibody levels reached or exceeded convalescent sera after the second dose.
- Immunogenicity increased in a dose-dependent manner
- Viral challenge in mice showed complete protection against viral replication in their lungs .
- Only few grade 3 adverse events such as erythema around the injection site



PHASE 3

APPROVED IN CANADA

EMERGENCY USE IN U.S.

moderna



National Institutes of Health  
Turning Discovery Into Health

VACCINE NAME: mRNA-1273

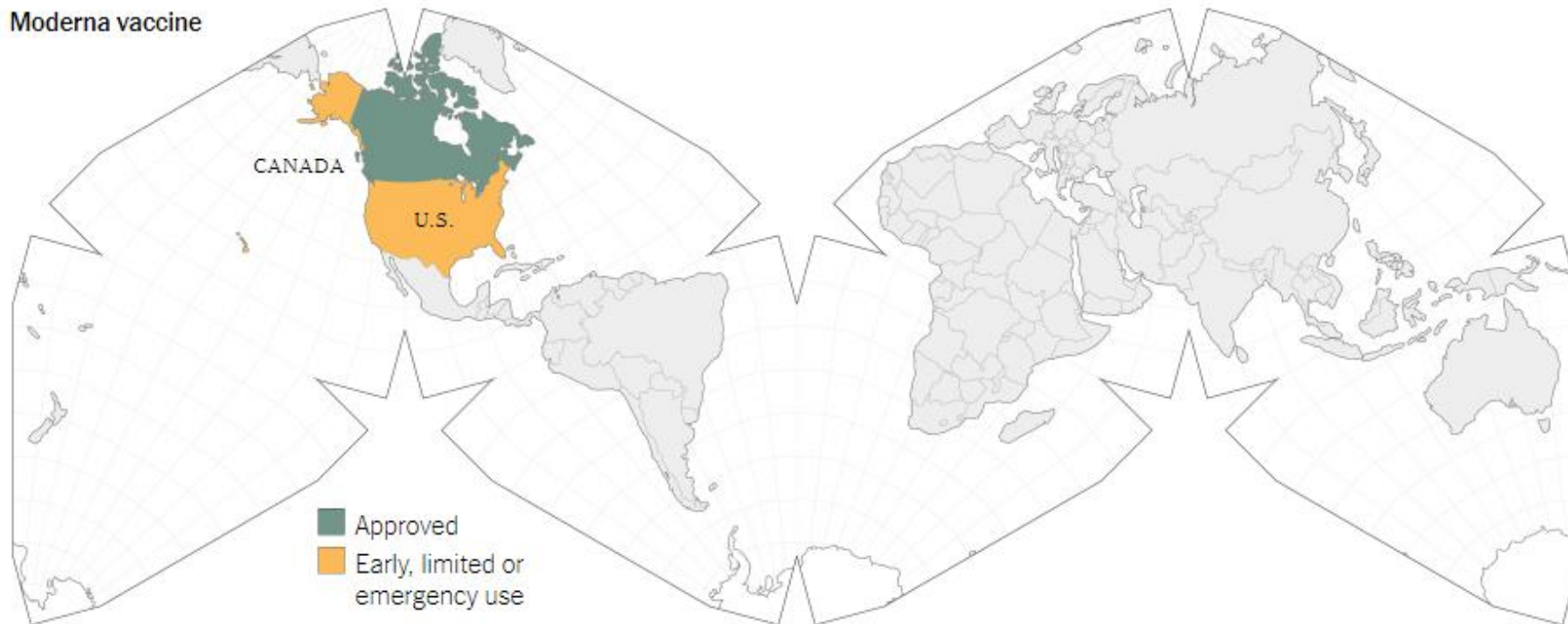
EFFICACY: 94.5%

DOSE: 2 doses, 4 weeks apart

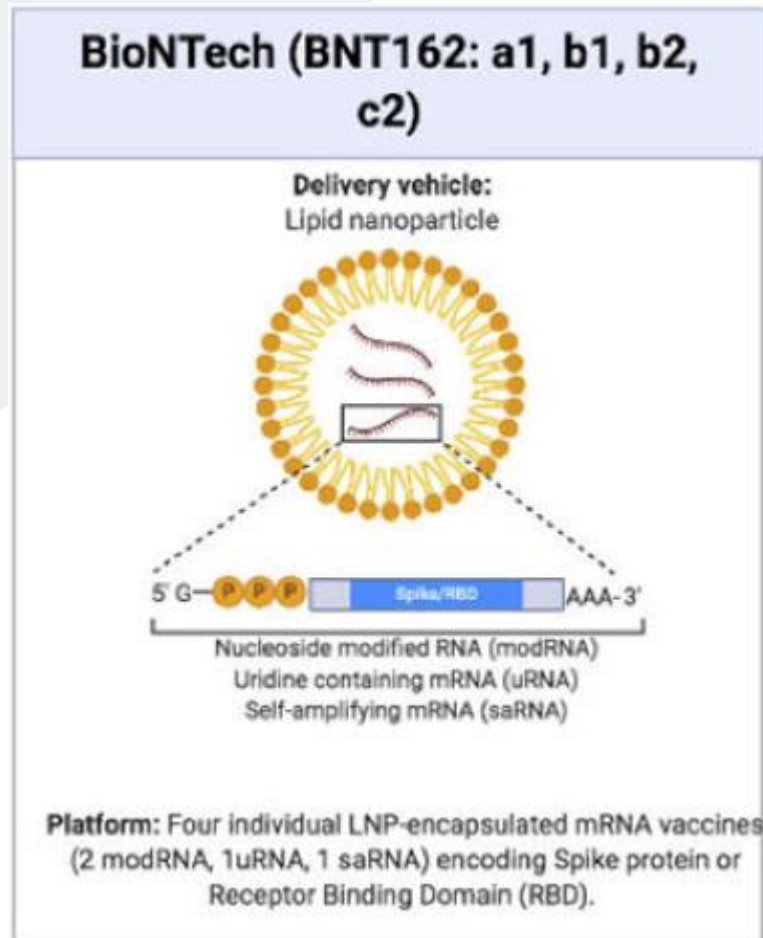
TYPE: Muscle injection

STORAGE: 30 days with refrigeration, 6 months at  $-4^{\circ}\text{F}$  ( $-20^{\circ}\text{C}$ )

Moderna vaccine



# BioNTech-Pfizer



- A lipid nanoparticle encapsulating mRNA encoding for SARS-CoV-2 protein S antigen. Four vaccine candidates, each of them demonstrating a different combination of mRNA format and target antigen.

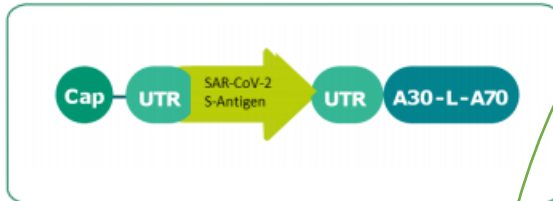




# BNT162 mRNA vaccine technologies

a1

## Uridine mRNA (uRNA)<sup>1</sup>

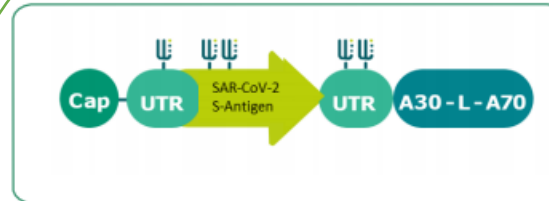


### Rationale

- Prime / boost
- Strong adjuvant effect
- Active at low doses
- Strong antibody response
- CD8 T-Cells > CD4 T-Cells

b1 b2

## Nucleoside-modified mRNA (modRNA)<sup>2</sup>



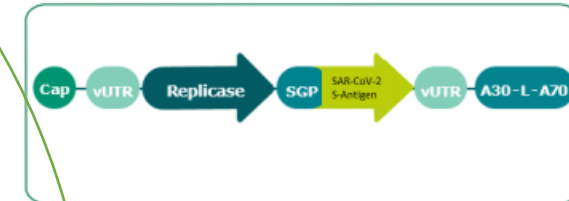
### Rationale

- Prime / boost
- Moderate adjuvant effect
- Very strong antibody response
- CD4 T-Cells > CD8 T-Cells

Chemically modified nucleosides, such as 2'-O methyl nucleoside dramatically suppress TLR-mediated immune activation.

c1

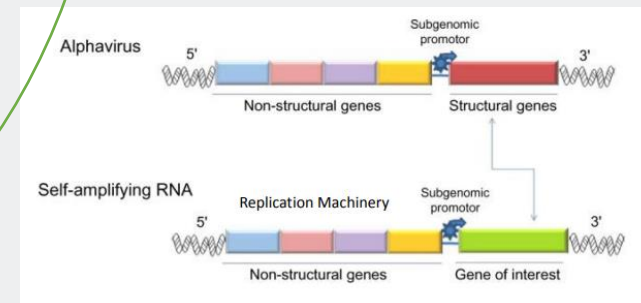
## Self-amplifying mRNA (saRNA)<sup>3</sup>



### Rationale

- Prime (1x injection)
- Long-term activity
- Very strong antibody response
- Very strong T-Cell response (CD8 and CD4)
- Potent immune protection at low doses (approx. 60x lower dosages required to induce immunity vs. uRNA observed in preclinical models)

The sequence contains no uridine residues; it is replaced by 1-methyl-3'-pseudouridine.



PHASE 2

PHASE 3

COMBINED PHASES

APPROVED IN SEVERAL COUNTRIES

EMERGENCY USE IN U.S., ELSEWHERE



BIONTECH

VACCINE NAME: Comirnaty (also known as tozinameran or BNT162b2 )

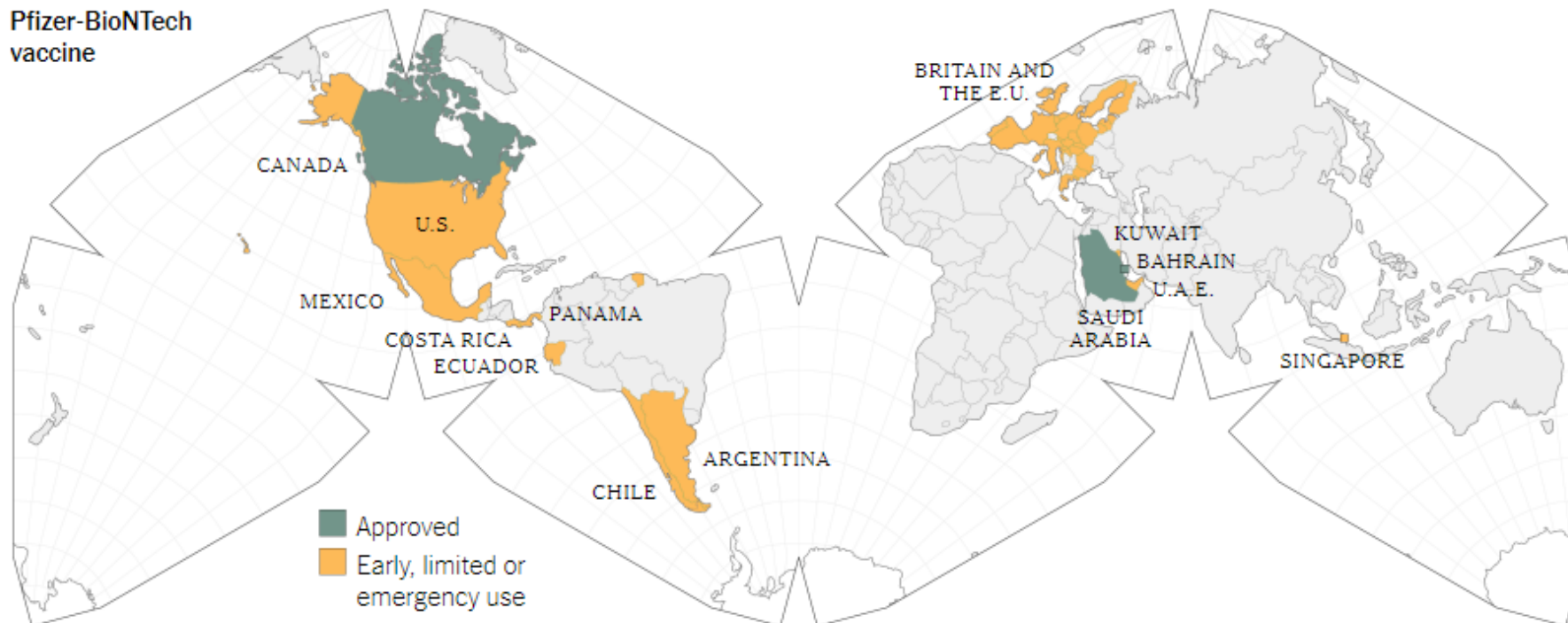
EFFICACY: 95%

DOSE: 2 doses, 3 weeks apart

TYPE: Muscle injection

STORAGE: Freezer storage only at -94°F (-70°C)

Pfizer-BioNTech  
vaccine



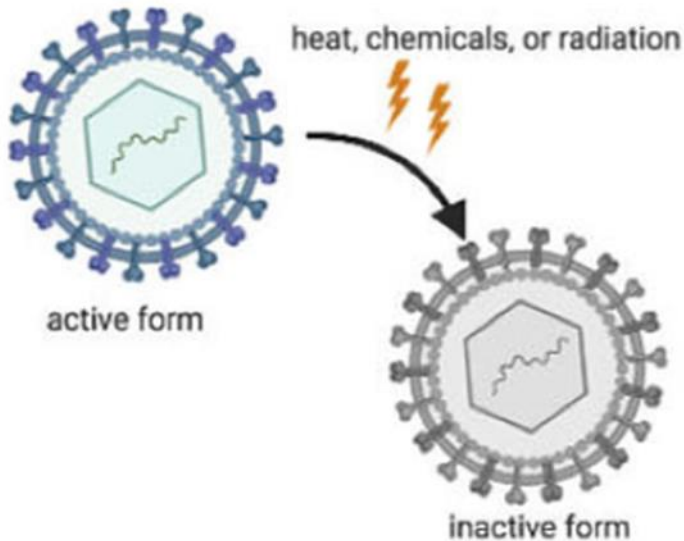


# Inactivated whole virus vaccines

# Chinese Vaccines based inactive virus

## Whole inactivated Vaccine

ex: Sinovac, Beijing Institute of Biological Products and Wuhan Institute of Biological Products



**platform:** inactivating the virus by either heat, formaldehyde or radiation.

- The state-owned Chinese company Sinopharm tested two vaccines:
  - Beijing Institute of Biological Products (BBIBP)
  - Wuhan Institute of Biological Products.
- Vaccines based on inactivated coronaviruses.







VACCINE NAME: **BBIBP-CorV**

EFFICACY: 86%

DOSE: 2 doses, 3 weeks apart

TYPE: Muscle injection

Sinopharm and  
Beijing Institute  
vaccine





武汉生物制品研究所有限责任公司

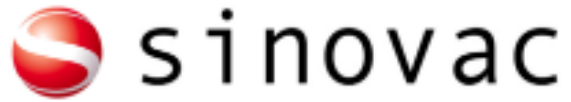
WUHAN INSTITUTE OF BIOLOGICAL PRODUCTS CO.,LTD.

Sinopharm and  
Wuhan Institute  
vaccine



PHASE 3

LIMITED USE IN CHINA



VACCINE NAME: CoronaVac (formerly PiCoVacc)

EFFICACY: Over 50 percent

DOSE: 2 doses, 2 weeks apart

TYPE: Muscle injection

STORAGE: Refrigerated

Sinovac Biotech, a private Chinese company, developed an inactivated vaccine called CoronaVac.

In July, Sinovac launched a Phase 3 trial in Brazil, followed by others in Indonesia and Turkey.

Chinese government gave the Sinovac vaccine an emergency approval for limited use in July.

In October, authorities in the eastern Chinese city of Jiaxing announced they were giving CoronaVac to people in relatively high-risk jobs.



## PHASE 1



At the end of December, Iran launched its first clinical trial of a coronavirus vaccine. Although the government did not name the company that created the vaccine in its announcement, the Iranian pharmaceutical company **Shafa Pharmed Pars** is listed on the World Health Organization's roster of companies developing coronavirus vaccines. It has developed a two-dose inactivated coronavirus vaccine. Iran Press reported that the Phase 1 trial will recruit 56 volunteers.

Updated Dec. 24







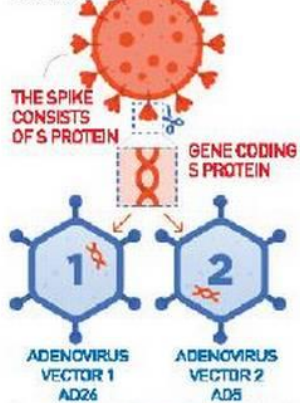
# Adenovirus vaccines

# Gamaleya (Sputnik V)

## Two-vector vaccine against coronavirus

### Vector creation

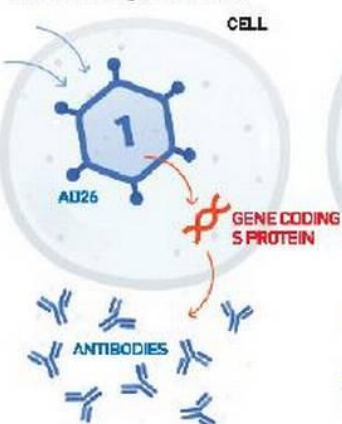
A vector is a virus that lacks a gene responsible for reproduction and is used to transport genetic material from another virus that is being vaccinated against into a cell. The vector does not pose any hazard to the body. The vaccine is based on an adenoviral vector which normally causes acute respiratory viral infections.



A gene coding S protein of SARS-COV-2 spikes is inserted into each vector. The spikes form the "crown" from which the virus gets its name. The SARS-COV-2 virus uses spikes to get into a cell.

### First vaccination

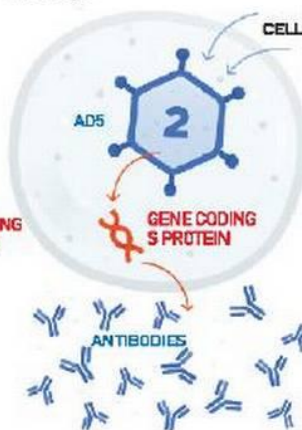
Vector with a gene coding S protein of coronavirus gets into a cell.



The body synthesises S protein in response, the production of immunity begins.

### Second vaccination

Repeated vaccination takes place in 21 days.



The vaccine based on another adenovirus vector unknown to the body boosts the immune response and provides for long-lasting immunity.

Source: Gamaleya Center, RDIF, 2020

- Contains the genetic sequence of the SARS-COV-2 S protein with a transgenic, non-replicating adenovirus-26 and 5.



МИНИСТЕРСТВО  
ЗДРАВООХРАНЕНИЯ  
РОССИЙСКОЙ ФЕДЕРАЦИИ

VACCINE NAME: Sputnik V (formerly Gam-Covid-Vac)

EFFICACY: 91.4%

DOSE: 2 doses, 3 weeks apart

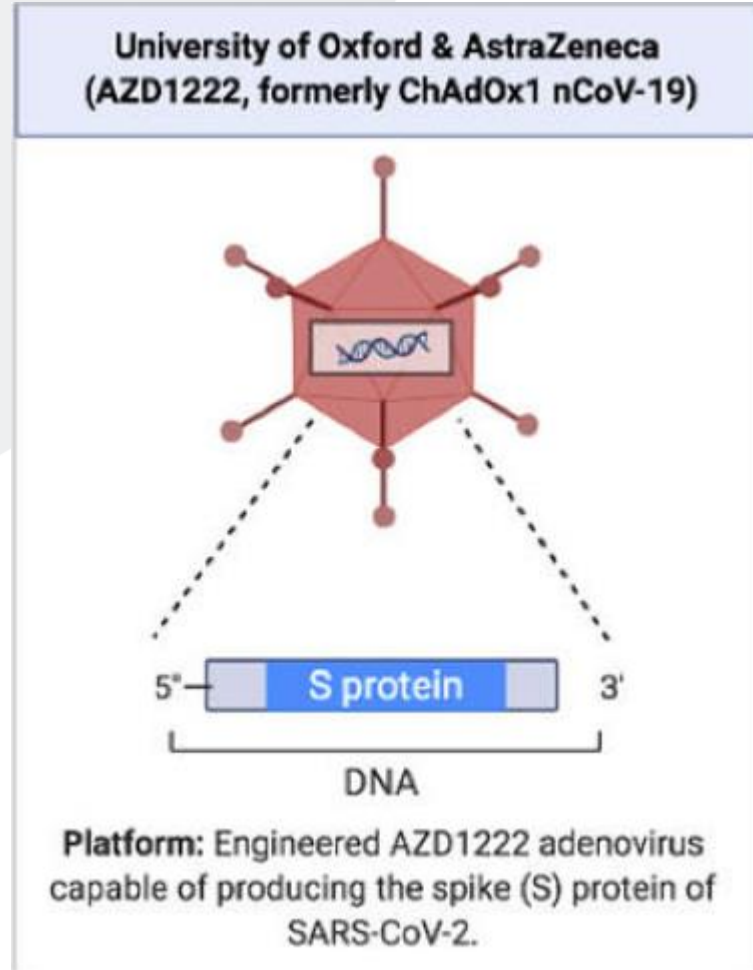
TYPE: Muscle injection

STORAGE: Freezer storage. Developing an alternative formulation that can be refrigerated.

Gamaleya's  
Sputnik V  
vaccine



# University of Oxford (AZD1222)



- Contains the genetic sequence of the SARS-COV-2 S protein with a transgenic, non-replicating chimpanzee adenovirus-based vector.

# University of Oxford (AZD1222)

## Advantages:

- Host cells express the coronavirus S protein thus leading to a robust humoral and T cell-mediated immune response.
- The non-replicating feature of this vaccine makes it relatively safe in the immunocompromised and children.
- This platform has been used successfully for the MERS vaccine.



PHASE 2

PHASE 3

COMBINED PHASES



UNIVERSITY OF  
OXFORD

AstraZeneca



VACCINE NAME: AZD1222

EFFICACY: Up to 90%

DOSE: 2 doses, 4 weeks apart

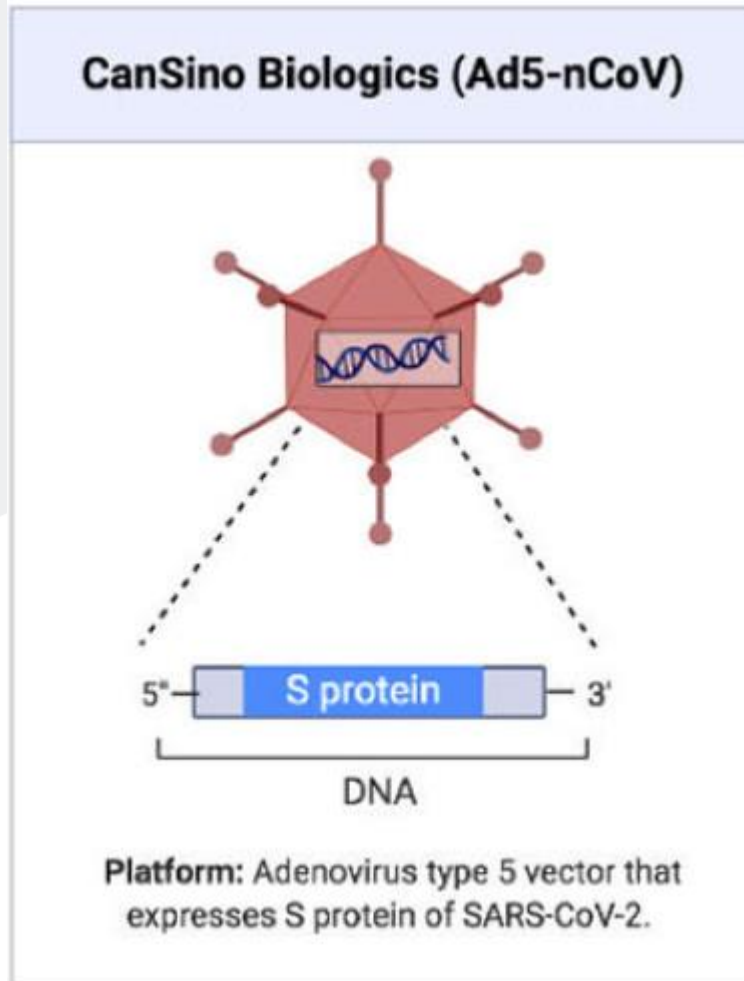
TYPE: Muscle injection

STORAGE: Stable in refrigerator for at least 6 months





# CanSino Biologics (Ad5-nCoV)



- Contains a replication-defective adenovirus type 5 as a vector to express the full-length SARS-CoV-2 S protein
- The first SARS-CoV-2 vaccine to move into Phase II





VACCINE NAME: Convidecia (also known as Ad5-nCoV)

EFFICACY: Unknown

DOSE: Single dose

TYPE: Muscle injection

STORAGE: Refrigerated

### Advantages:

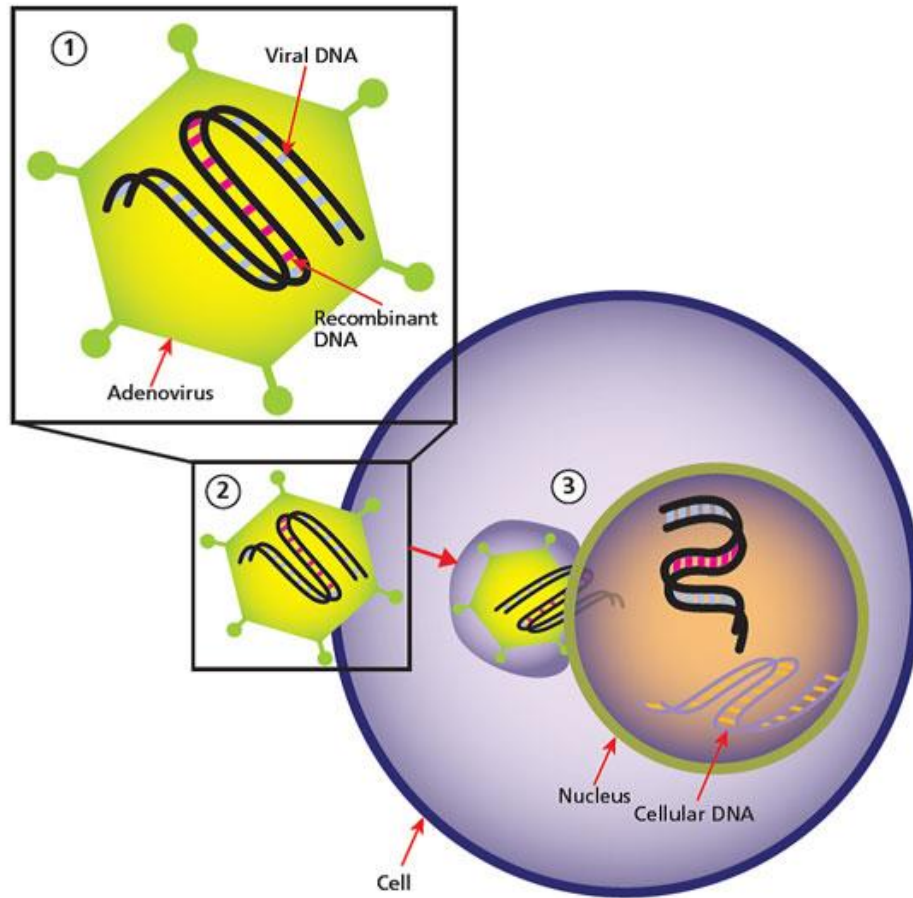
- Single dose.

### Disadvantage:

- presence of pre-existing immunity from natural exposure to Ad5 can dampen cellular immune responses to whatever antigens are encoded



# Ad26.COV2.S (Johnson and Johnson)



- Contains a replication-defective adenovirus type 26 as a vector to express the full-length SARS-CoV-2 S protein
- Johnson & Johnson developed vaccines for Ebola and other diseases with Ad26 and have now made one for the coronavirus.

## PHASE 3

Johnson & Johnson

Beth Israel Lahey Health   
Beth Israel Deaconess Medical Center

VACCINE NAME: Ad26.COV2.S

EFFICACY: Unknown

DOSE: 1 dose

TYPE: Muscle injection

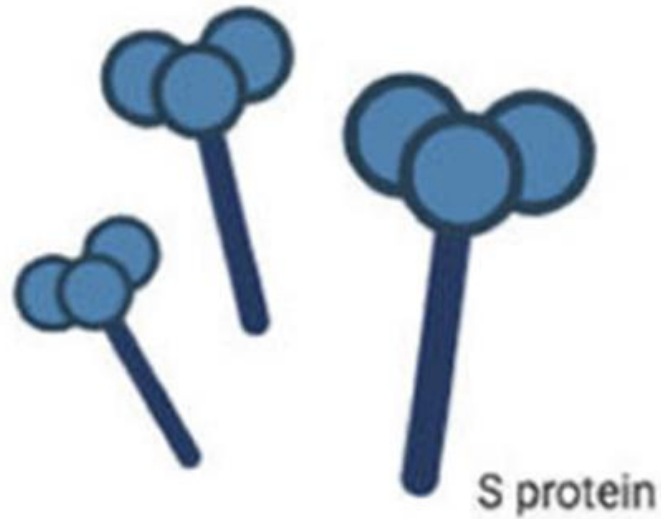
STORAGE: Up to two years frozen at  $-4^{\circ}\text{F}$  ( $-20^{\circ}\text{C}$ ), and up to three months refrigerated at  $36\text{--}46^{\circ}\text{F}$  ( $2\text{--}8^{\circ}\text{C}$ ).





# Protein vaccines

# EpiVacCorona (Vector Institute)



- The vaccine contains small portions of viral proteins, known as peptides.
- The second one to receive that designation after the Gamaleya Institute's Sputnik V vaccine.



**PHASE 3**

**EARLY USE IN RUSSIA**



**BEKTOP**

VACCINE NAME: EpiVacCorona

EFFICACY: Unknown

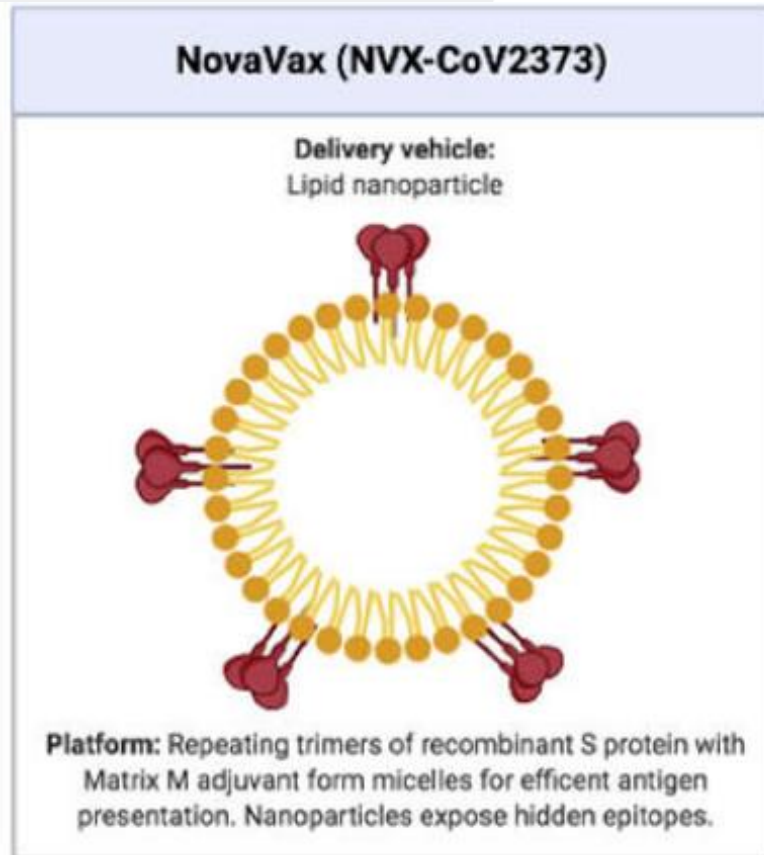
DOSE: 2 doses, 3 weeks apart

TYPE: Muscle injection

STORAGE: Stable in refrigerator for up to two years

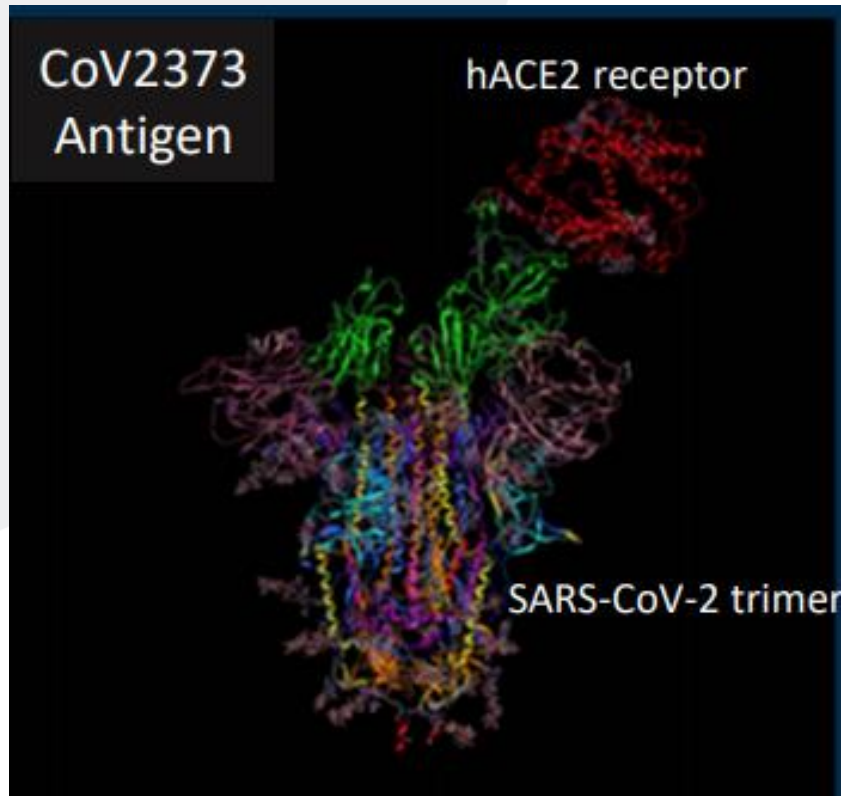


# NovaVax (NVX-CoV2373)



- Contains a recombinant S protein (SARS-CoV-rS) and Novavax's Matrix-M saponin-based adjuvant.
- Matrix-M is a potent inducer of leukocyte migration into the draining lymph nodes (LN) resulting in the increase in T-, B-, NK, and dendritic cells in draining LNs.

# NovaVax (NVX-CoV2373)



- In pre-clinical trials, highly immunogenic in animal models. NVX-CoV2373 produced high levels of S protein-specific antibodies that can block ACE-2 human RBD and wild-type SARS-CoV-2 neutralizing antibodies after one dose. After a second dose, the neutralization titers jumped eight-fold



## PHASE 3

# NOVAVAX

Creating Tomorrow's Vaccines Today

VACCINE NAME: NVX-CoV2373

EFFICACY: Unknown

DOSE: 2 doses, 3 weeks apart

TYPE: Muscle injection

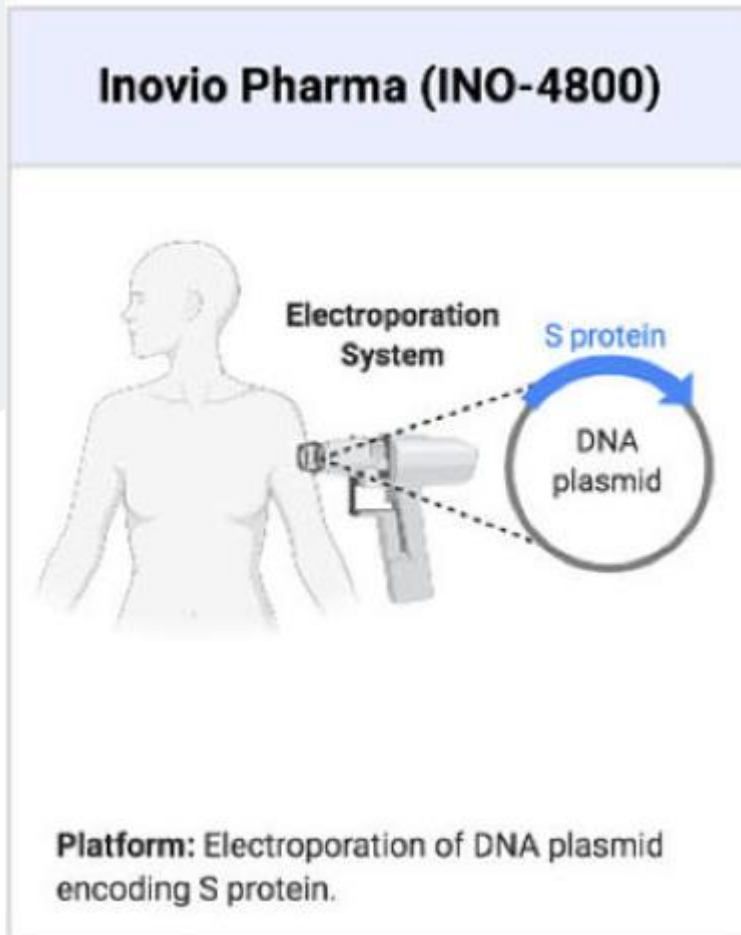
STORAGE: Stable in refrigerator





# Vaccines under development

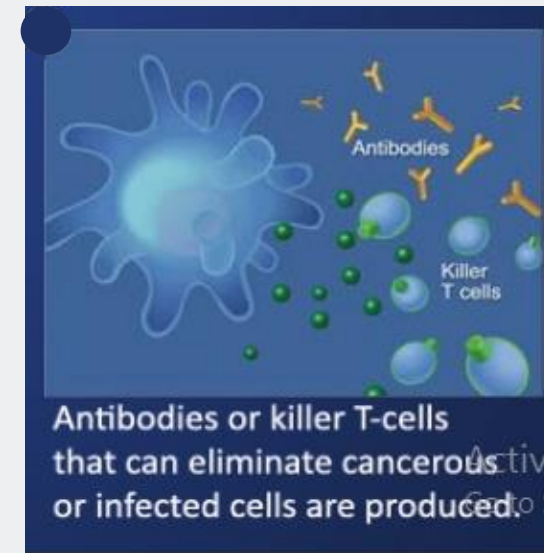
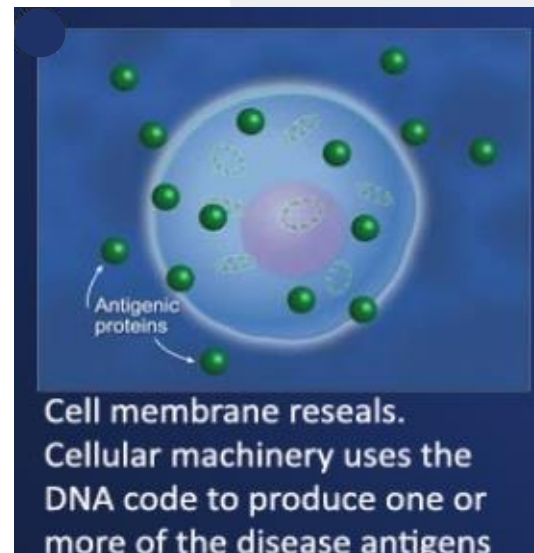
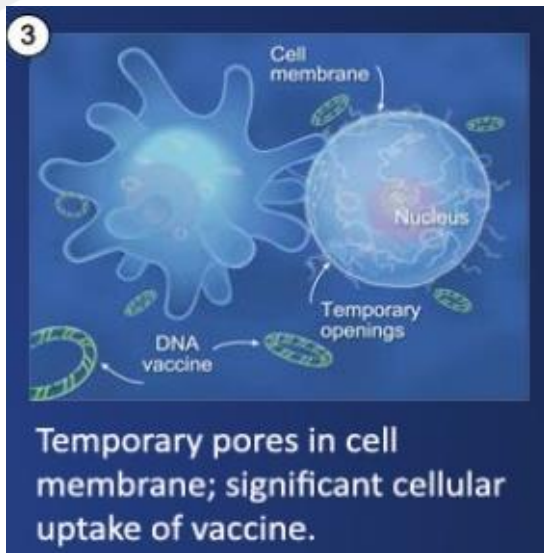
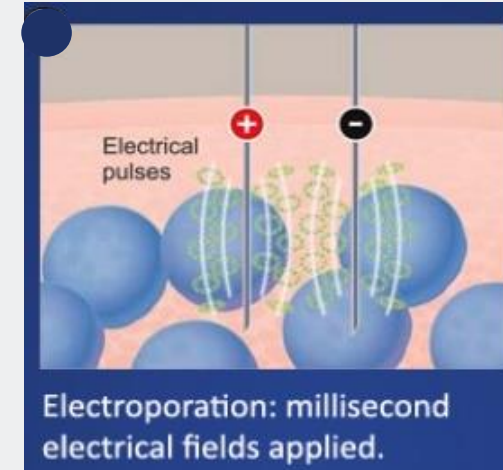
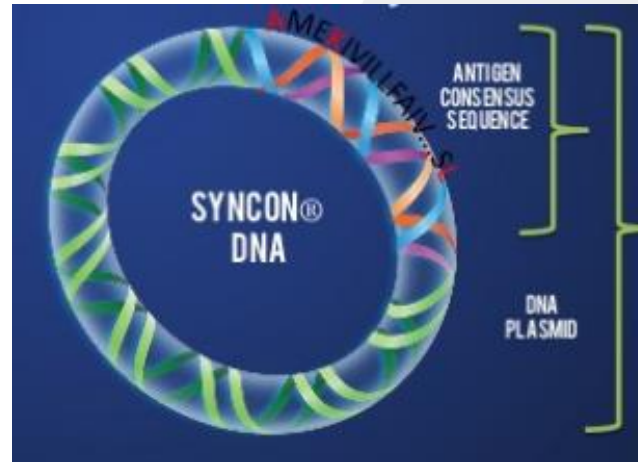
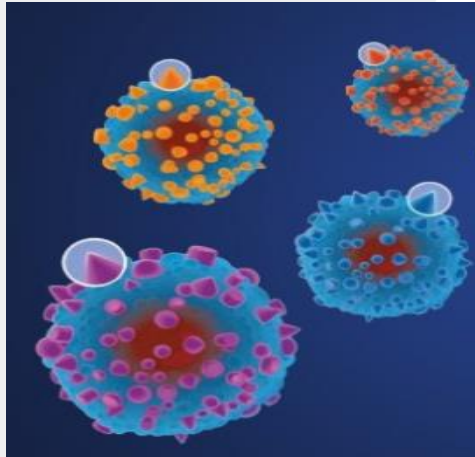
# Invio Pharma (INO4800)



- Synthetic DNA-based vaccine that are delivered into human cells via electroporation (EP) and translated into S proteins to induce an immune response.



# Invio Pharma (INO4800)



# Invio Pharma (INO4800)

## Advantages:

- Accelerated developmental Rapidly designed
- Manufactured in large quantities
- Flexibility in terms of antigen manipulation
- Unable to revert into active forms
- **Cold chain free**
- Strong cellular and humoral responses
- Utilizes a strategy identical to the DNA vaccine for MERS INO-4700.
- INO-4700 clinical tests outcome showed very promising results :92% ability to neutralize the virus and 84% robust T cell response after the third dose.



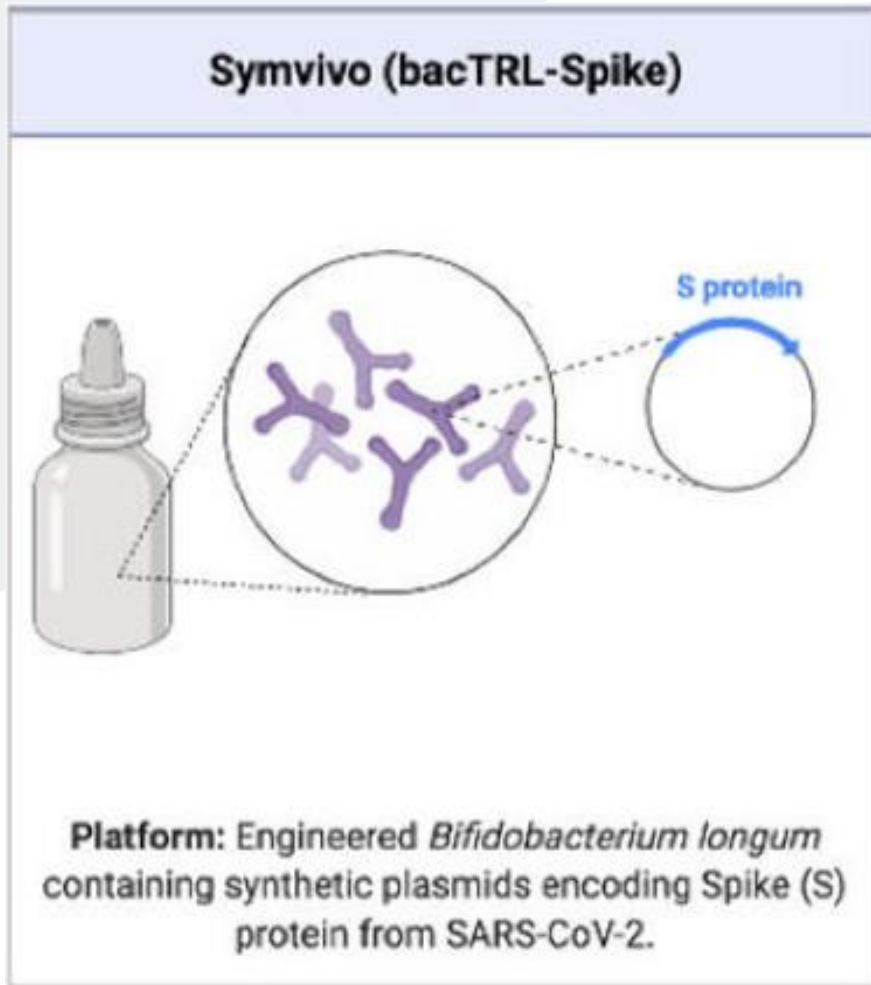
# Invio Pharma (IN04800)

Trial:

- Intradermally (ID) on day 0 and week 4 of 1.0
- Electroporation (EP) using the CELLECTRA<sup>®</sup> 2,000 device



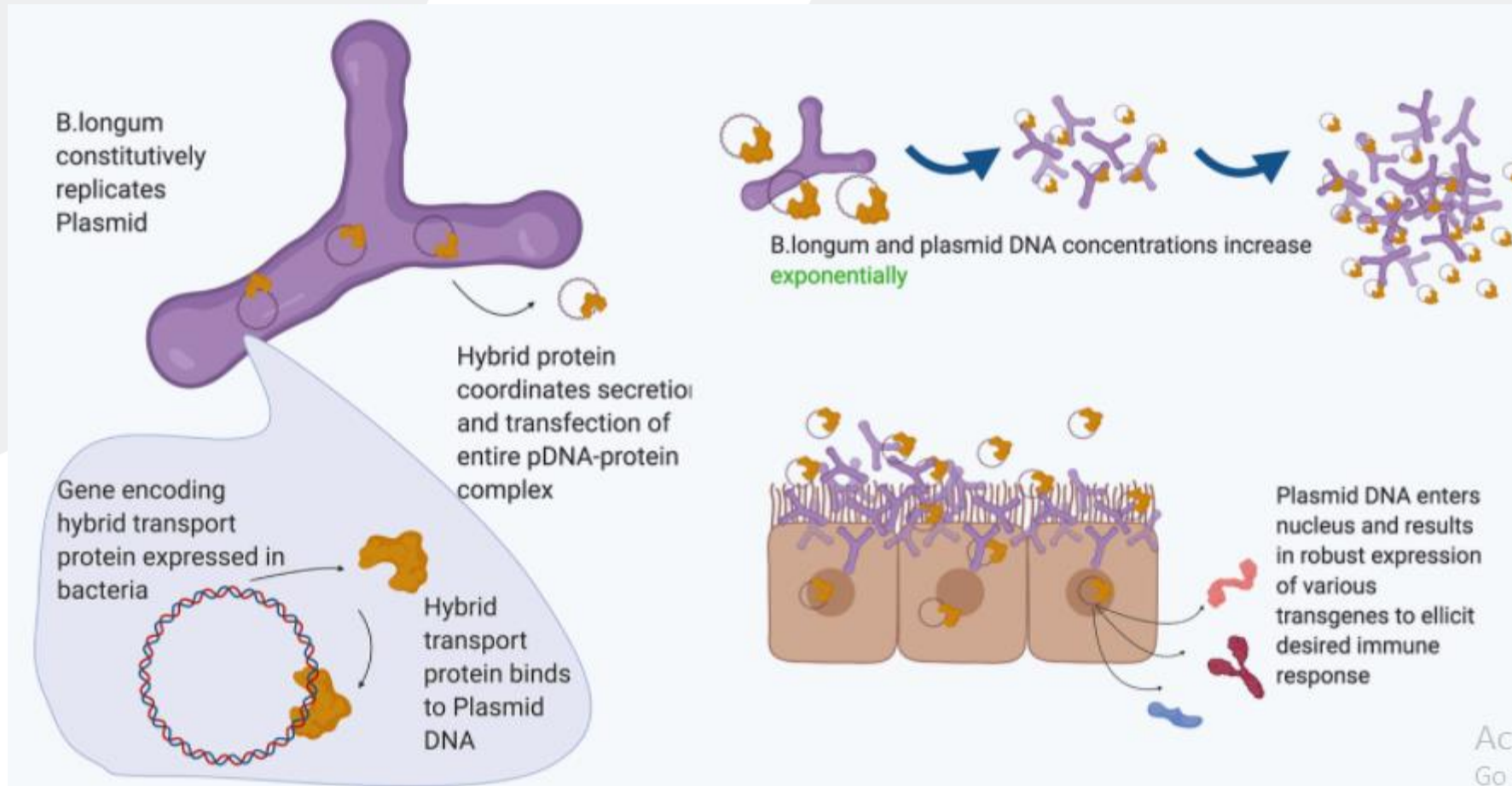
# Symvivo (bacTRL-Spike)



- Orally administered
- Genetically modified probiotic bacteria, *Bifidobacterium longum*, that colonizes the gut, bind to intestinal epithelial cells, replicate, secrete, and deliver plasmids expressing the SARS-CoV-2 spike protein.
- Expected to be sustained throughout the life of the colonized *B. longum*.
- Translation of this plasmid within the gastrointestinal lymphoid tissues initiates a robust mucosal, systemic humoral, and cell-mediated immune response.



# Symvivo (bacTRL-Spike)



# Symvivo (bacTRL-Spike)

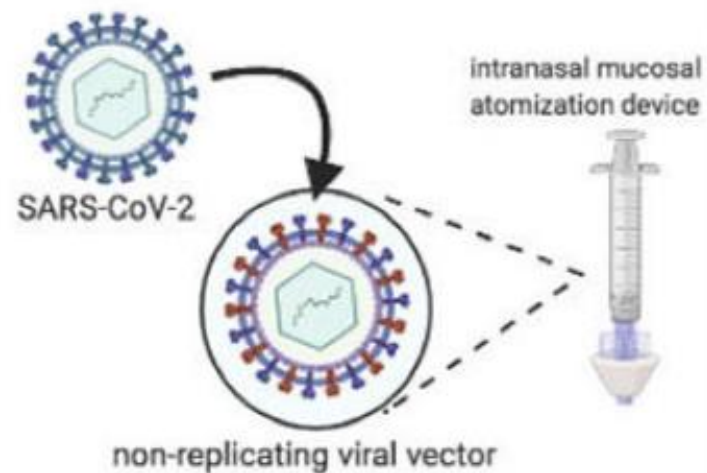
- Orally administered as frozen liquid
- The company is planning to produce lyophilized gel-capsule similar to traditional consumer probiotic supplements
- 1, 3, or 10 billion colony forming units (CFU) of the live, genetically modified *B. longum* alongside.
- **Advantage: Sustained immune response**





## Replicating/non-replicating viral vector vaccine

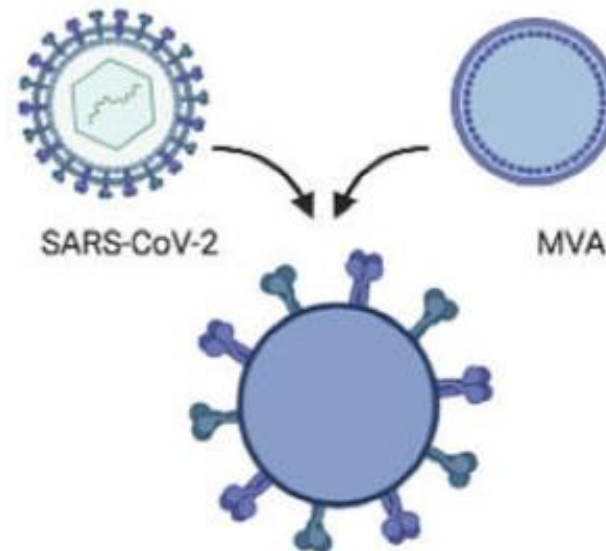
ex: Altimune



**Platform:** Adenovirus based NasoVAX expressing SARS-CoV-2 spike protein (Intranasal vaccine).

## Virus-like particles Vaccine

ex: GeoVax—BravoVax



**Platform:** Modified Vaccinia Ankara combined with Virus Like Particles (MVA-VLP).

## Nucleic acid vaccine

ex: CureVac

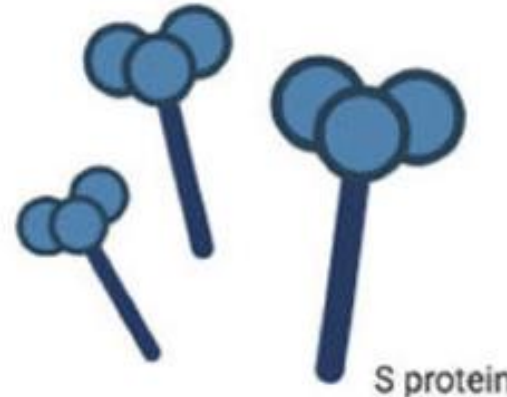


mRNA encoding  
S protein

**Platform:** mRNA based vaccine against COVID-19.

## Recombinant subunit Vaccine

ex: Clover Biopharmaceuticals

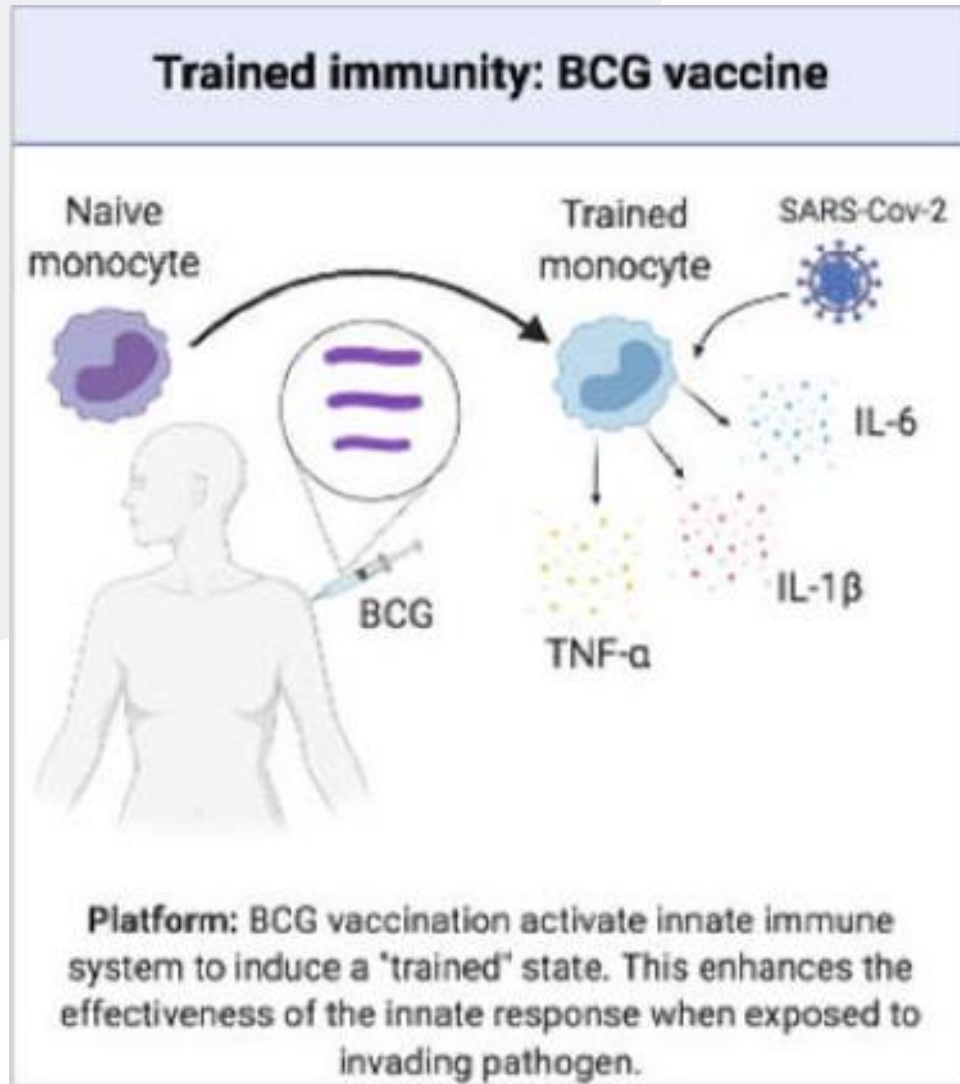


S protein

**Platform:** Construct a 2019-nCoV S protein subunit-trimer vaccine (S-Trimer) utilizing thier Trimer-Tag© technology.



# Trained immunity (BCG vaccine)



- BCG vaccines are being considered to reduce the impact of Covid-19 due to its ability to induce trained immunity.
- Trained immunity involves the induction of metabolic and epigenetic modifications that promote an innate immune response against subsequent infections.
- Through trained immunity, BCG vaccines have been shown to prevent pneumonia and influenza and have also been shown to reduce the severity of yellow fever infection.

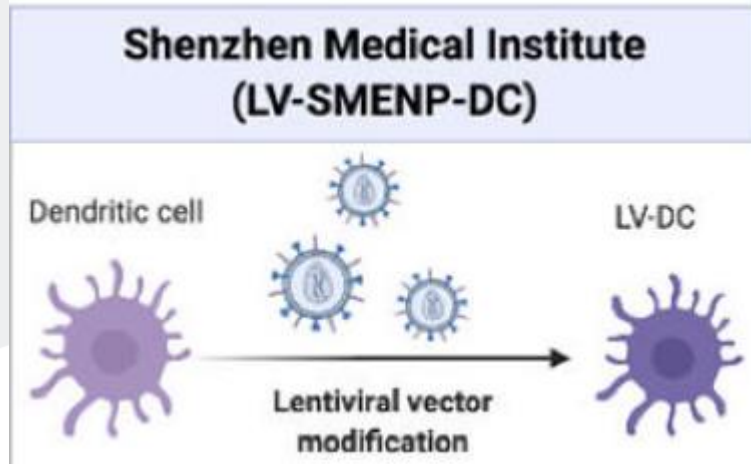
# Trianed immunity (BCG vaccine)

## Trial:

- The only vaccine in the phase III clinical trial.
- The primary and secondary outcomes
  - SARS-CoV-2 Spike protein antibodies
  - COVID-19 symptom duration, disease severity, hospital admittance, and deaths.
- BCG vaccines containing either the TICE, Danish 1331, or Moscow 361-1 strains of live attenuated Mycobacterium bovis.
- Administration will either be intradermal or intracutaneous depending on the trial.
- Study enrollment estimates vary with the lowest including 500 patients and highest including 10,078 patients.
- The soonest estimated completion date of December 1, 2020 and latest of May 2022.



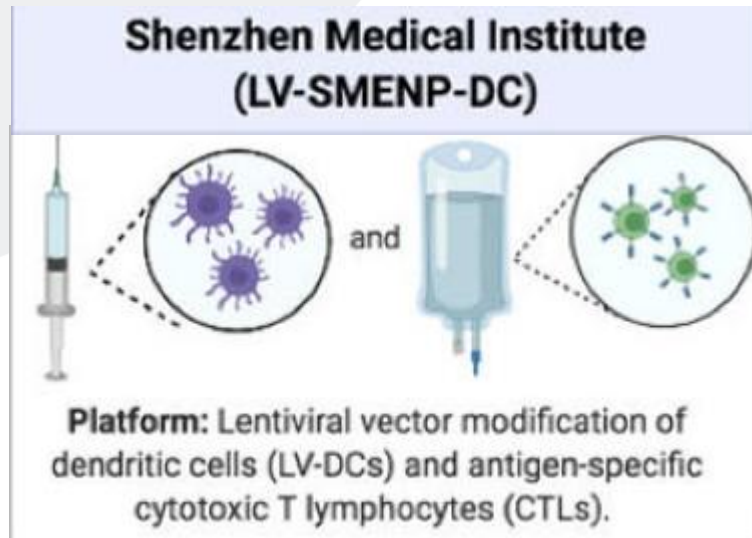
# Shenzhen Medical Institute (LV-SMENP-DC)



- A cellular vaccine:
- Dendritic cells (DC) are exposed to genetically engineered lentivirus vectors (LV) expressing SARS-COV-2 minigene (SMENP).
- The LV-DCs are able to stimulate robust and durable antigen-specific T cell responses



# Shenzhen Medical Institute (LV-SMENP-DC)



- Two methods:
- $5 \times 10^6$  CELLS of LV-DC alone via ID injection
- $5 \times 10^6$  cells of LV-DC vaccine and  $1 \times 10^8$  antigen-specific cytotoxic T lymphocytes (CTLs) via ID injection and IV infusion, respectively

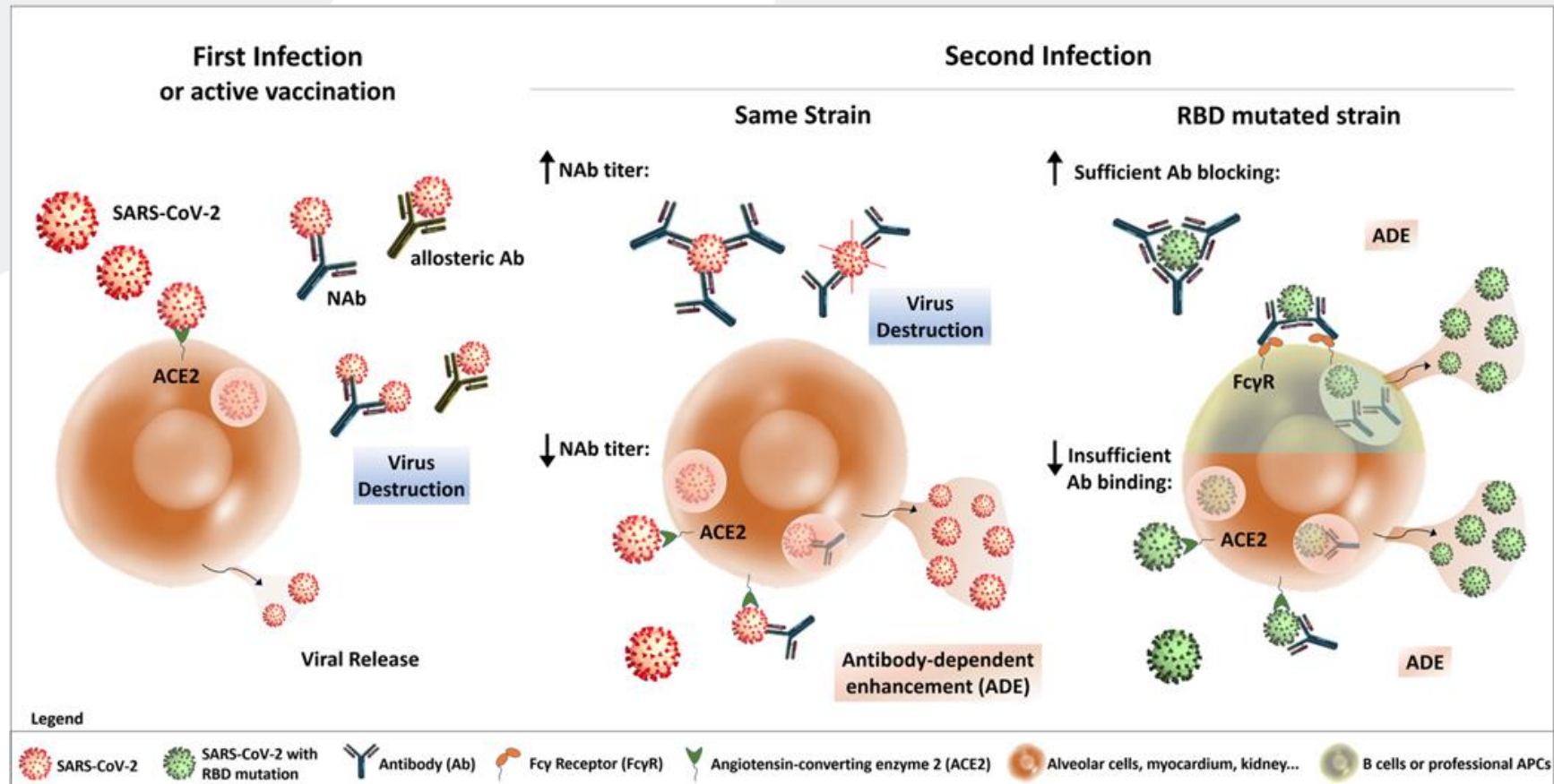




# A Potential Hurdle for Coronavirus Vaccine Development

Antibody Dependent Enhancement (ADE):

Instead of blocking the binding to cells, the pre-existing antiviral Ab could facilitate the entry of the virus to host cells through either interaction with FcR receptors or complement receptors.





# Chemical Prevention



# Pre-Exposure Prophylaxis

- **The COVID-19 Treatment Guidelines Panel (the Panel) recommends against the use of any agents for SARS-CoV-2 pre-exposure prophylaxis except in a clinical trial (AIII).**
- Clinical trials are investigating several agents:
  - Emtricitabine + tenofovir alafenamide/tenofovir disoproxil fumarate (TRUVADA)
  - **Hydroxychloroquine (suspended)**
  - Zinc
  - Vitamin C
  - Vitamin D
- Studies of monoclonal antibodies that target SARS-CoV-2 are in development.



# Post-Exposure Prophylaxis

- **The Panel recommends against the use of any agents for SARS-CoV-2 post-exposure prophylaxis (PEP), except in a clinical trial (AIII).**
- Potential options for PEP that are currently under investigation include: 21 Studies
  - Chloroquine, hydroxychloroquine (did not show efficacy in multiple studies)
  - Lopinavir/ritonavir (Kaletra)
  - Nitazoxanide
  - vitamin super B-complex
  - vitamin D.
- Other post-exposure preventive strategies that are in development include the use of SARS-CoV-2 monoclonal antibodies and convalescent plasma.



# Summary



## STAY HOME. SAVE LIVES.

Help stop coronavirus

- 1 **STAY** home as much as you can
- 2 **KEEP** a safe distance
- 3 **WASH** hands often
- 4 **COVER** your cough
- 5 **SICK?** Call ahead



# THANK YOU FOR YOUR ATTENTION



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