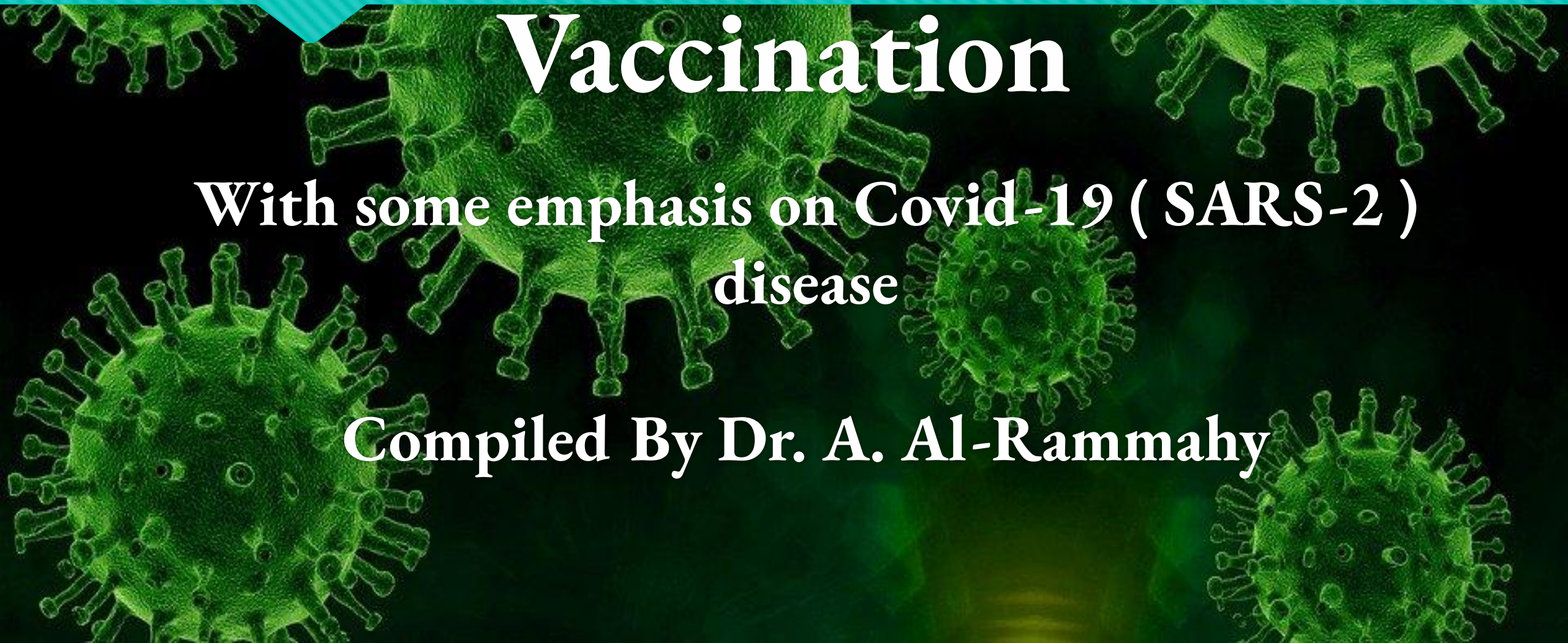
Immunity, Vaccines , and Vaccination



With some emphasis on Covid-19 (SARS-2) disease

Compiled By Dr. A. Al-Rammahy

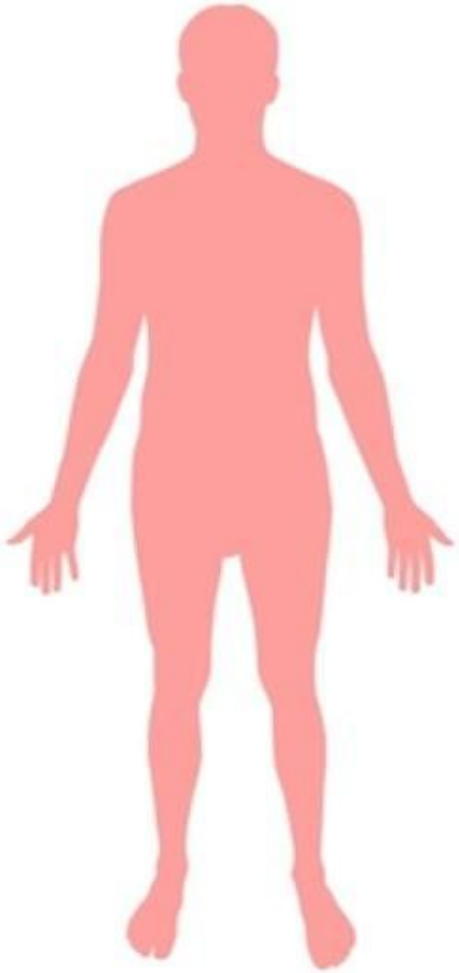
Innate Defense System

external membranes

- skin
- mucous membranes

internal defenses

- antimicrobial proteins
- phagocytes



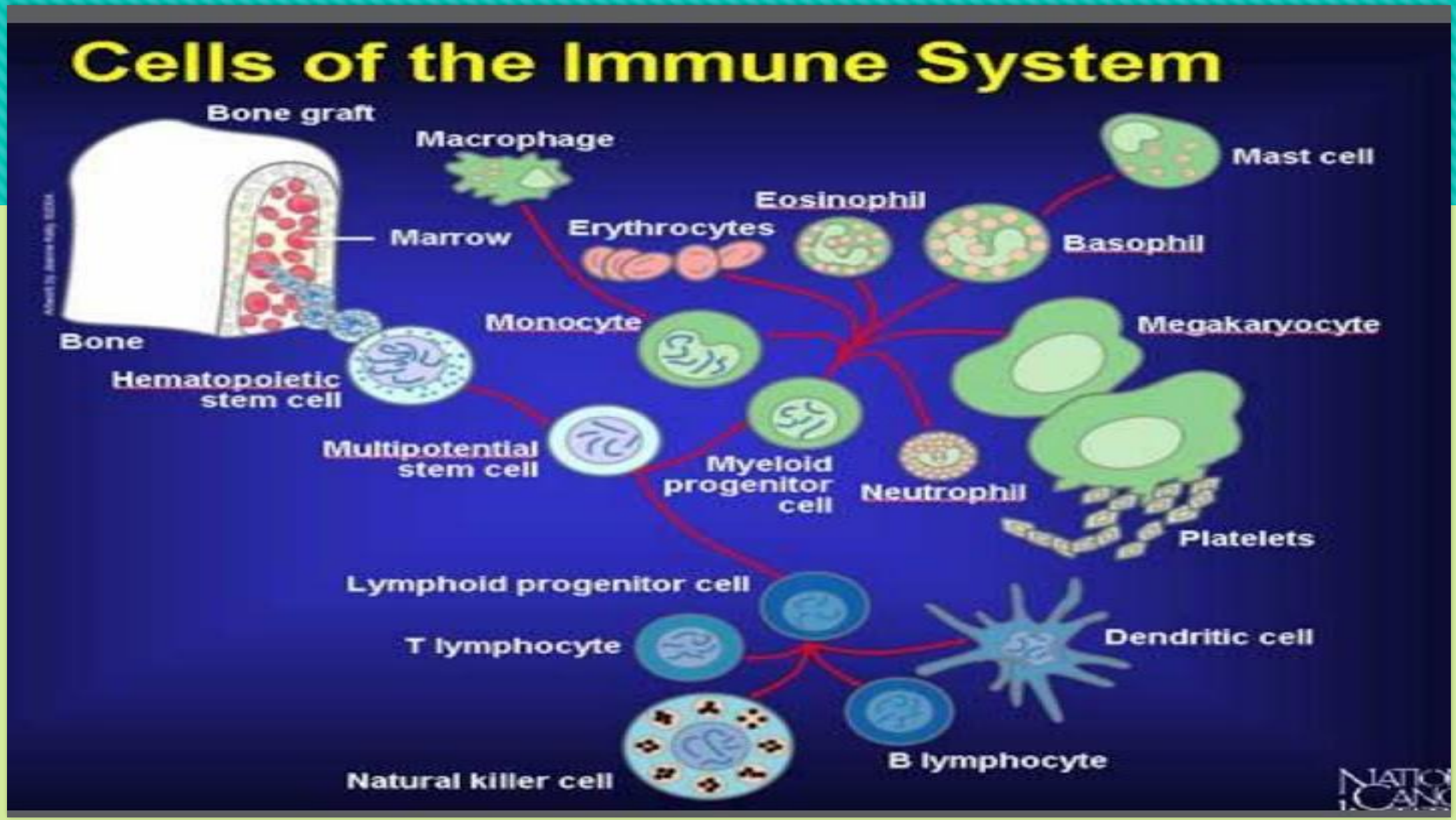
Adaptive Defense System

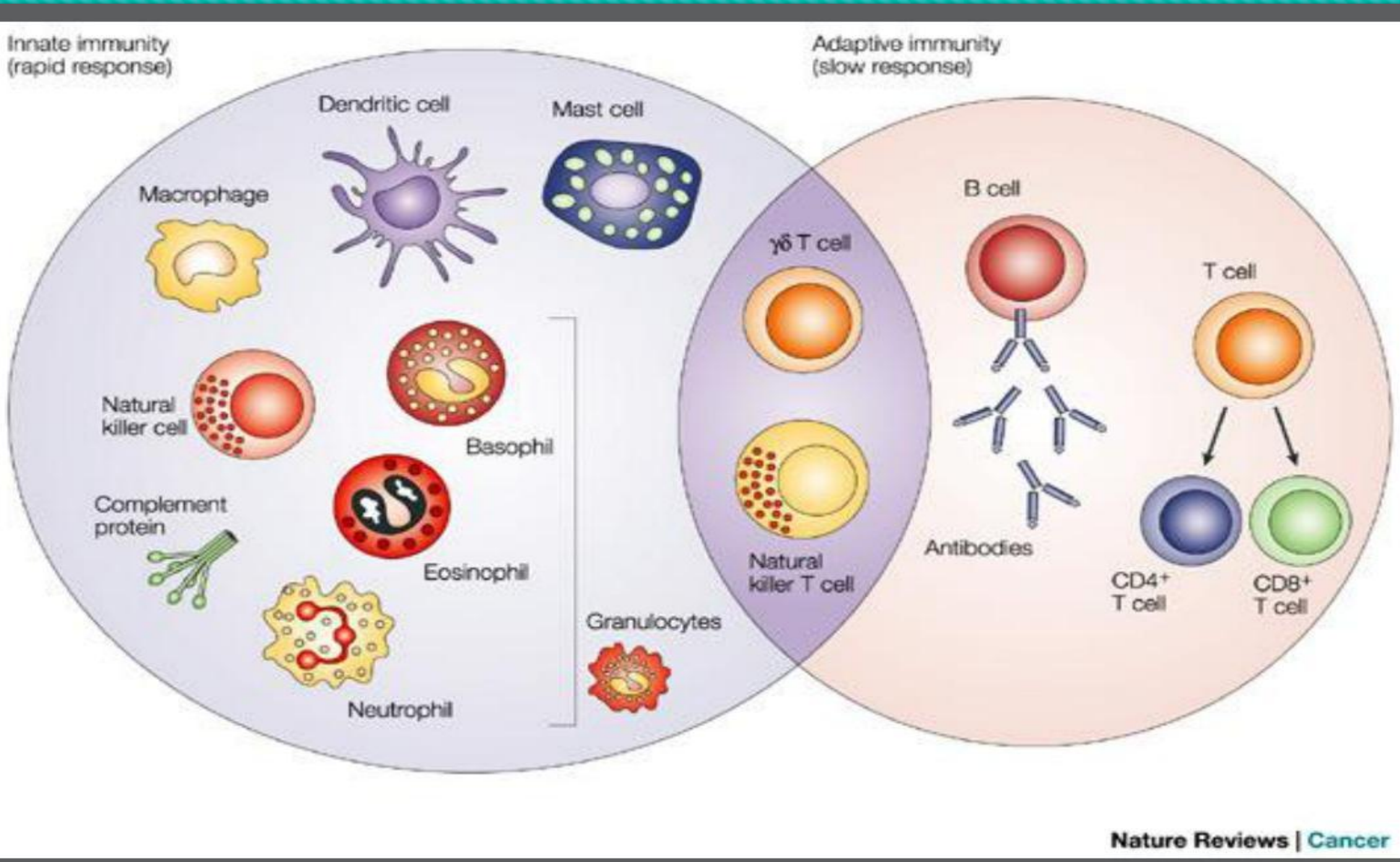
specific response for a specific type of invader

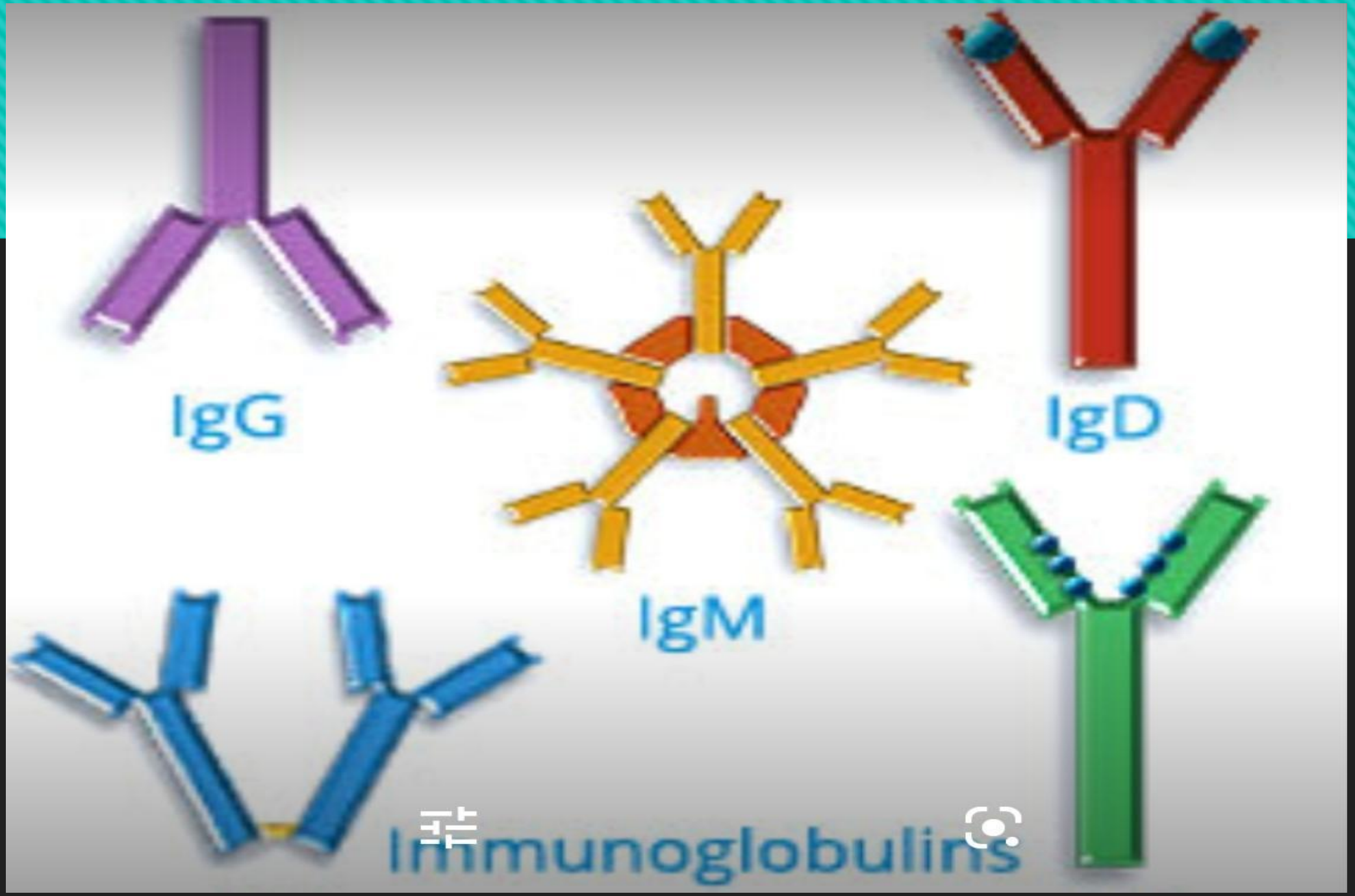
antibody

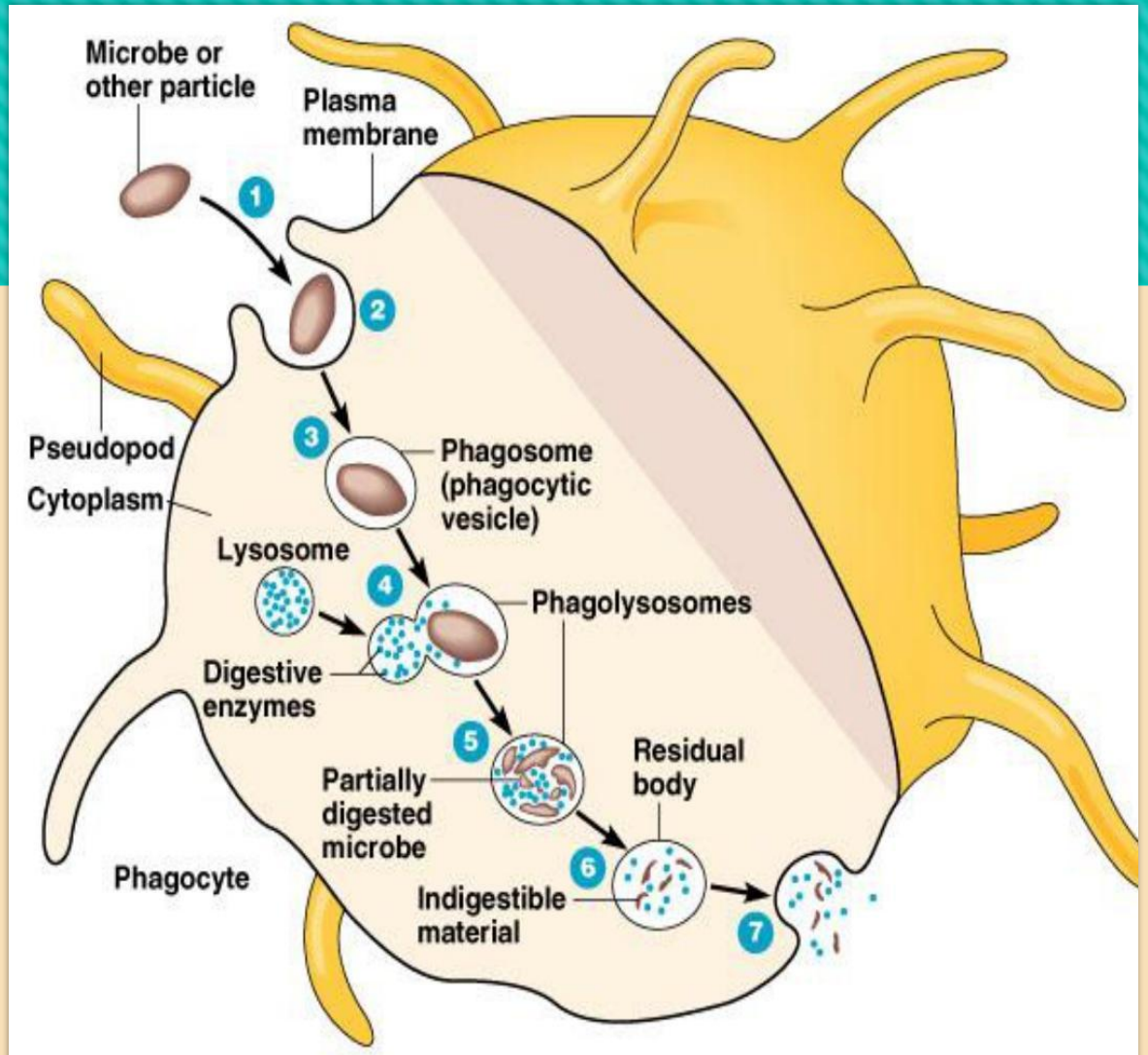
humoral immunity

cellular immunity


Cells of the Immune System
Bone graft
Macrophage
Mast cell
Eosinophil
Erythrocytes
Basophil
Marrow
Monocyte
Megakaryocyte
Bone
Hematopoietic stem cell
Multipotential stem cell
Myeloid progenitor cell
Neutrophil
Platelets
Lymphoid progenitor cell
T lymphocyte
Dendritic cell
B lymphocyte
Natural killer cell


Innate immunity
(rapid response)
Adaptive immunity
(slow response)
Dendritic cell
Mast cell
Macrophage
γδ T cell
B cell
T cell
Natural
killer cell
Basophil
Complement
protein
Eosinophil
Natural
killer T cell
Antibodies
CD4+
T cell
CD8+
T cell
Granulocytes
Neutrophil
Nature Reviews | Cancer


IgG
IgD
IgM
Immunoglobulins

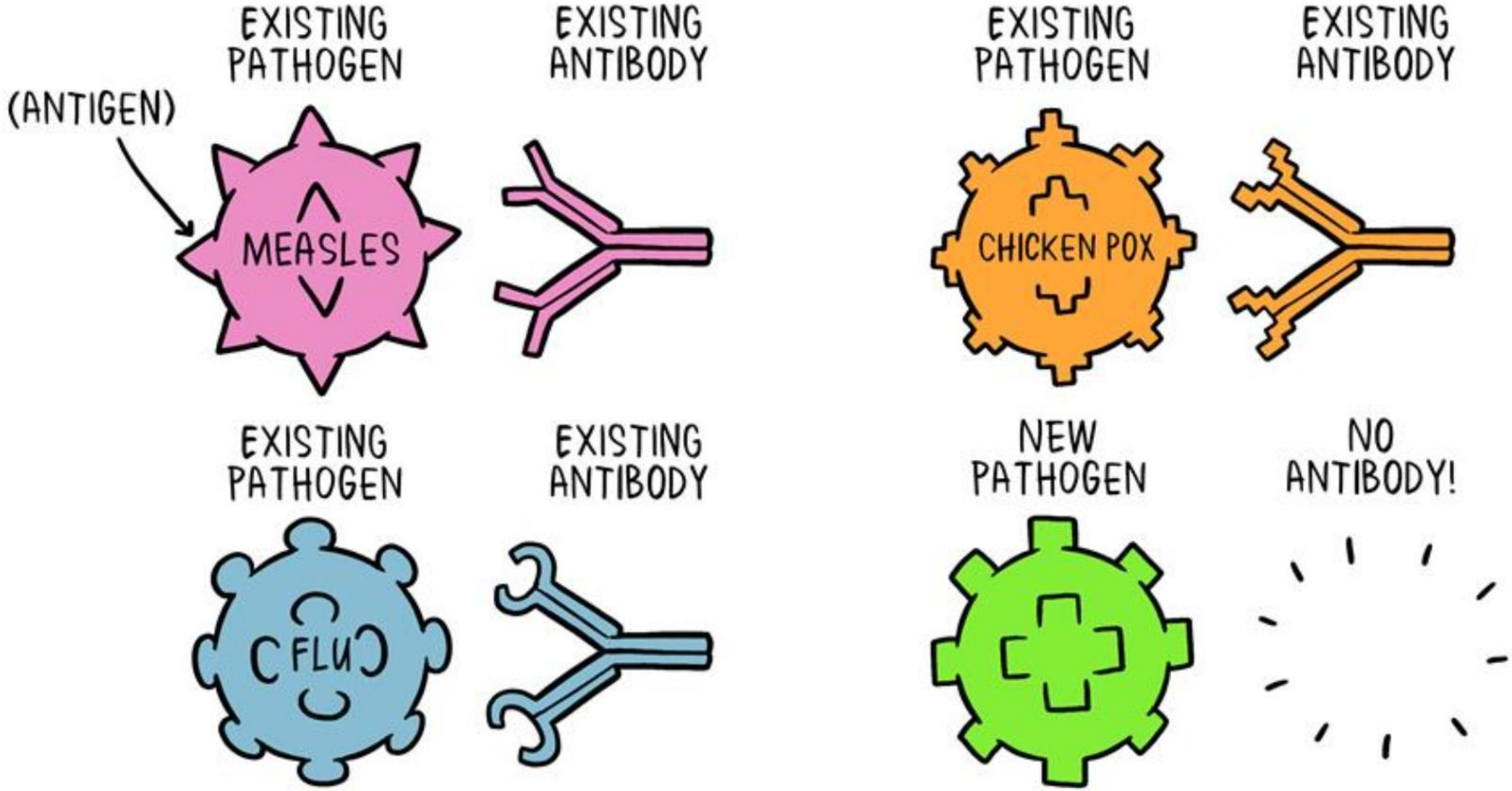


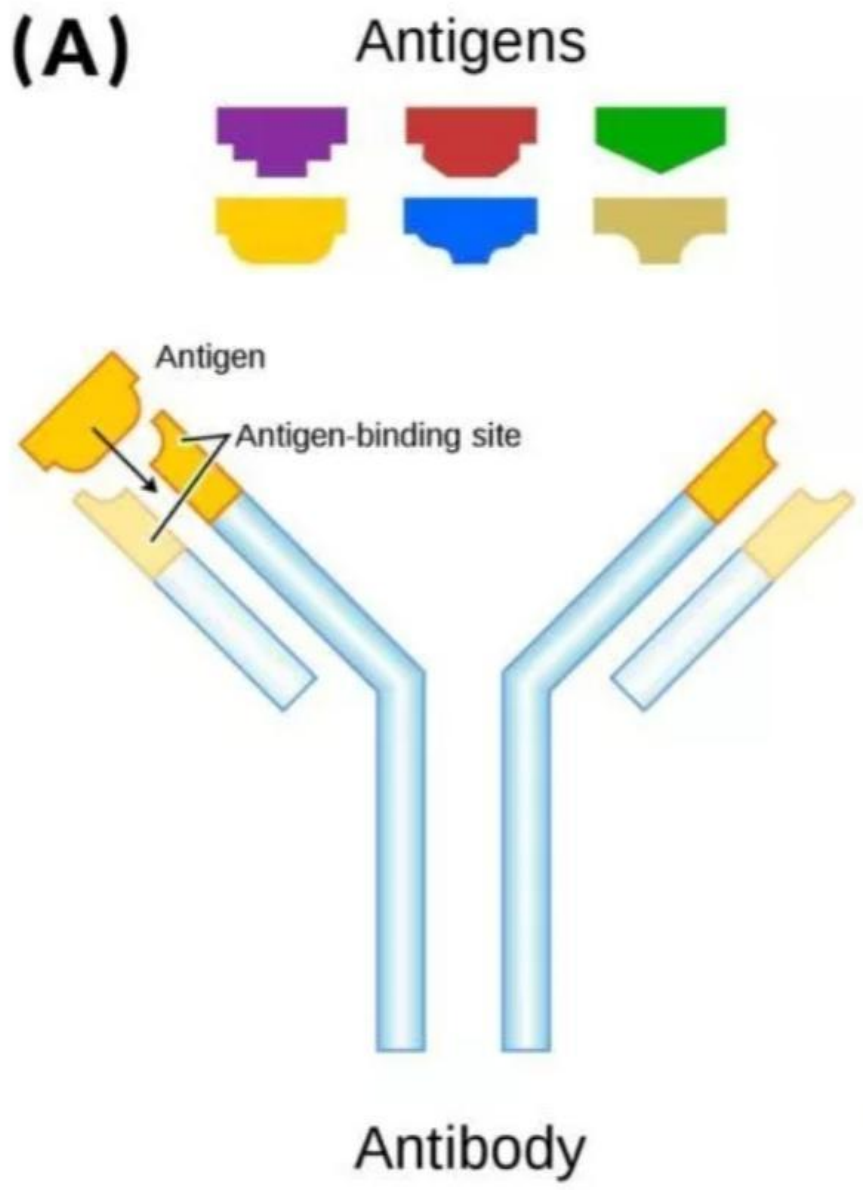
(a) Phases of phagocytosis

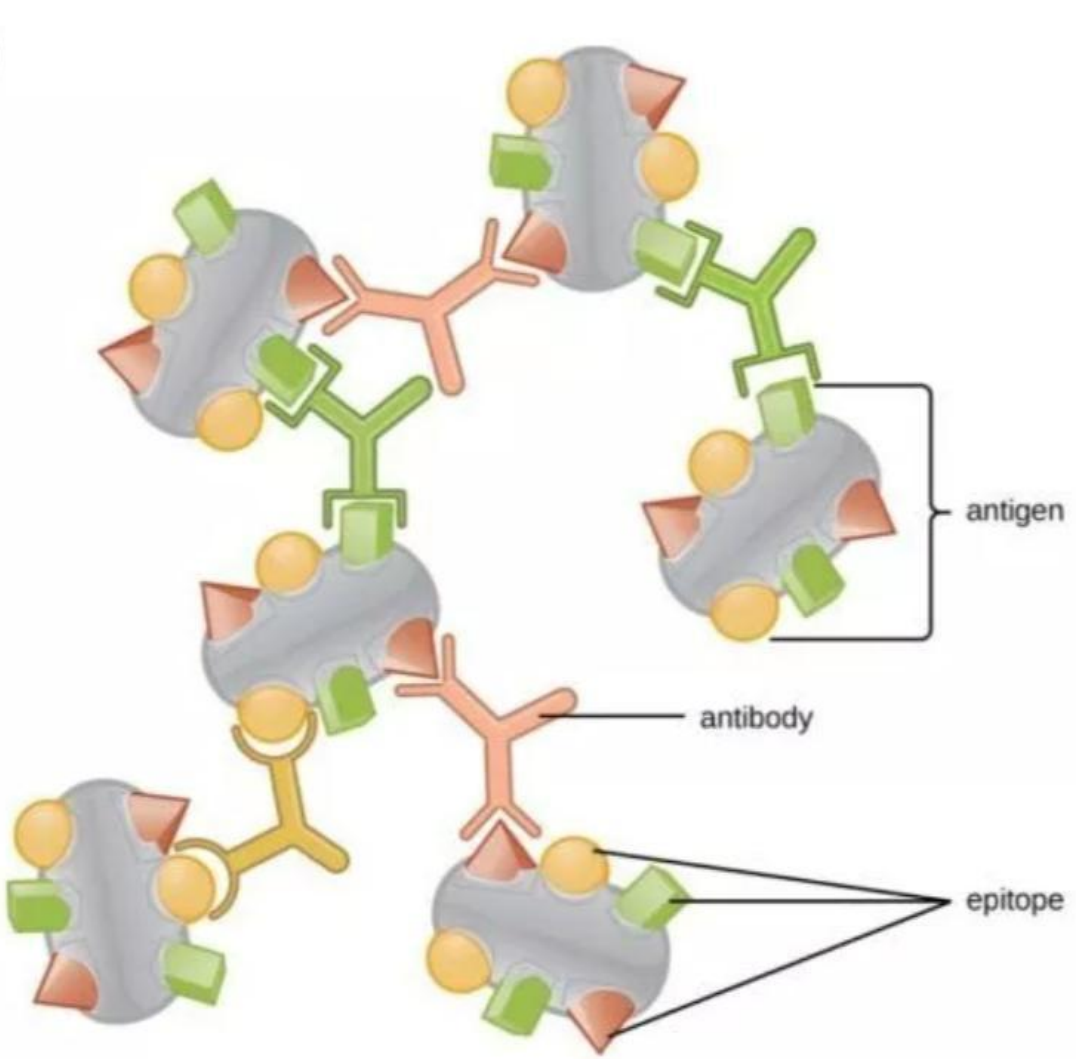
types of adaptive immune response

humoral
immune response

cellular
immune response

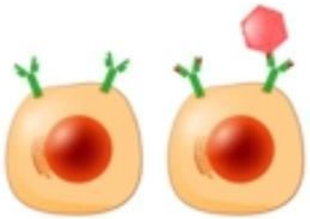

EXISTING PATHOGEN
EXISTING ANTIBODY
(ANTIGEN)
MEASLES
EXISTING PATHOGEN
EXISTING ANTIBODY
CHICKEN POX
EXISTING PATHOGEN
EXISTING ANTIBODY
FLU
NEW PATHOGEN
NO ANTIBODY!



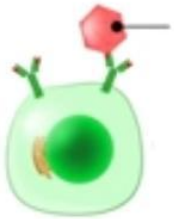


Biology Online

humoral immune response

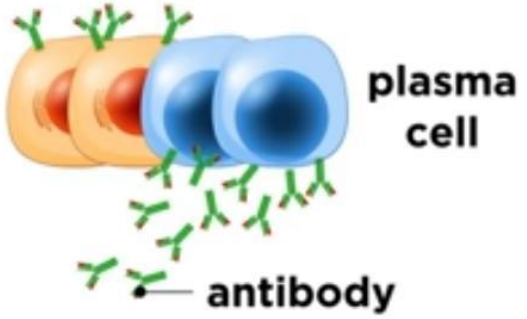


antigen binding

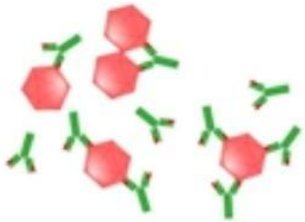


activation

replication or
proliferation



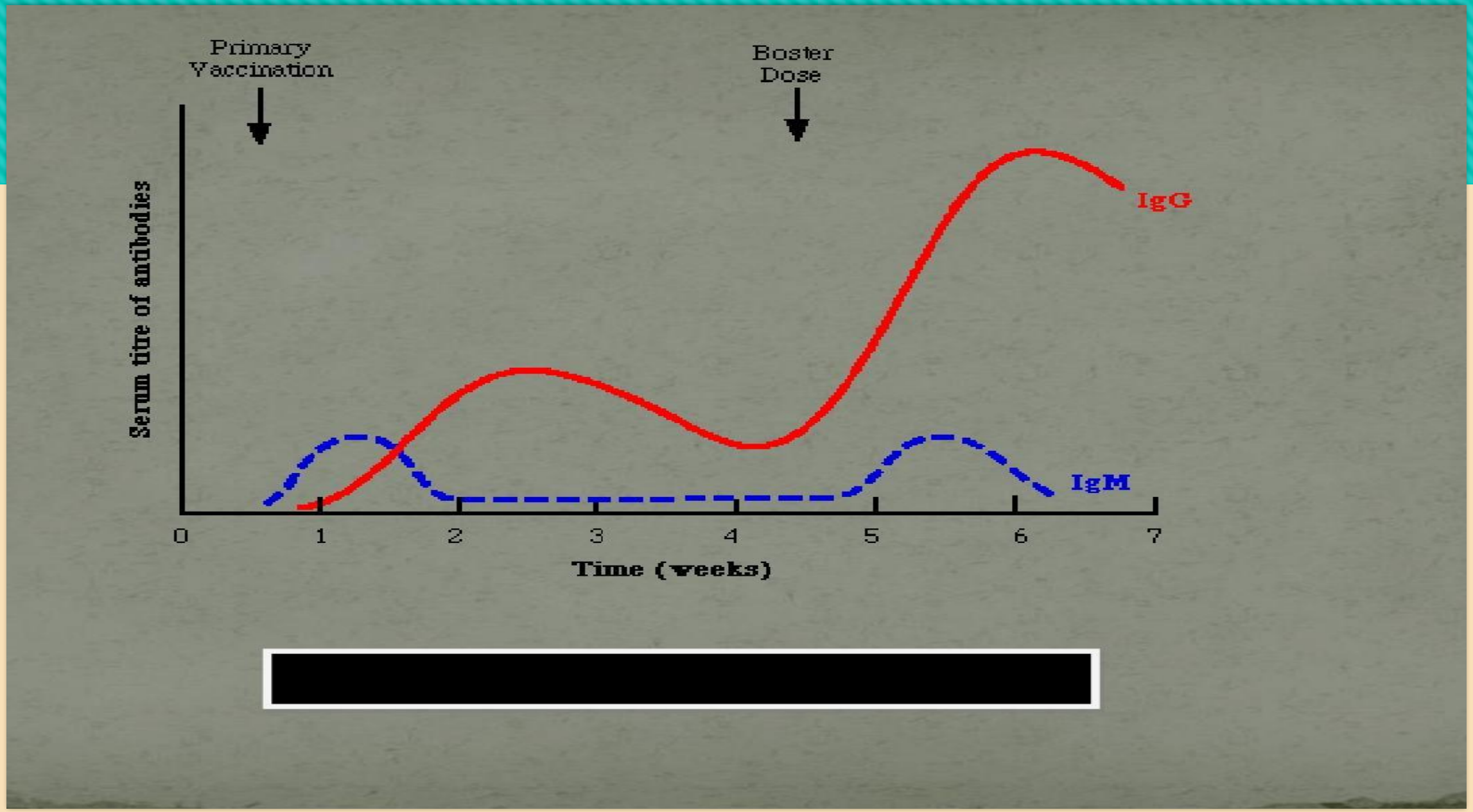
differentiation

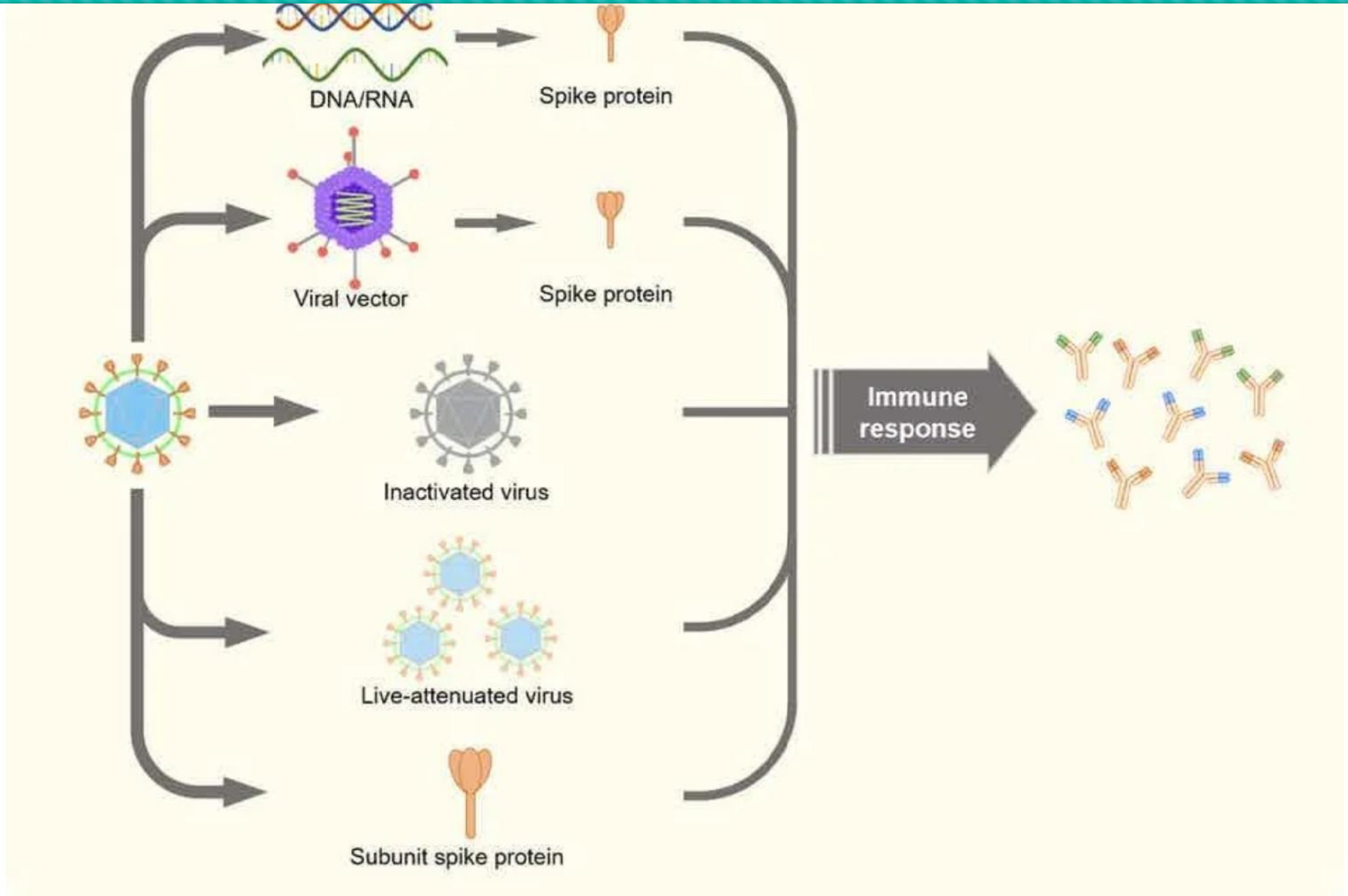


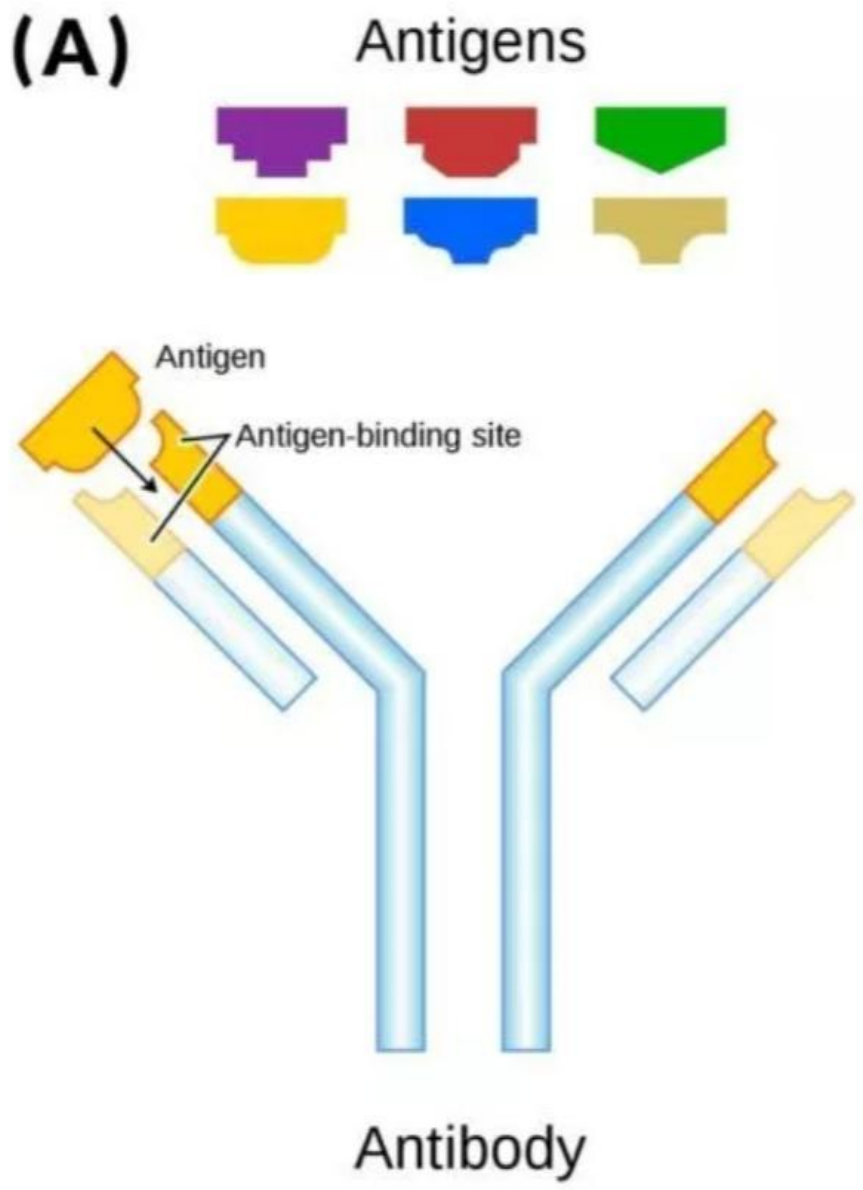
antibodies that
bind that antigen

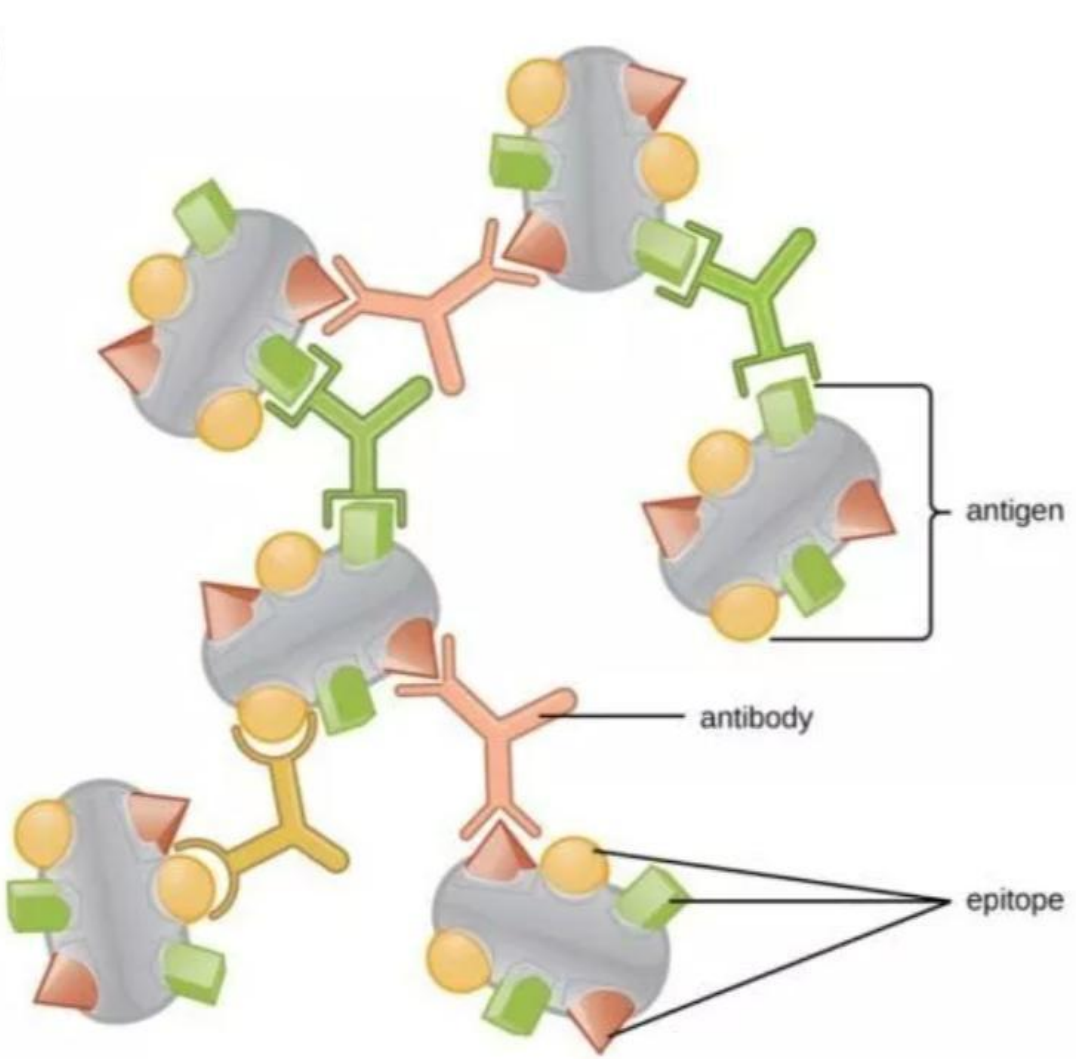
primary immune response

(takes a few days)

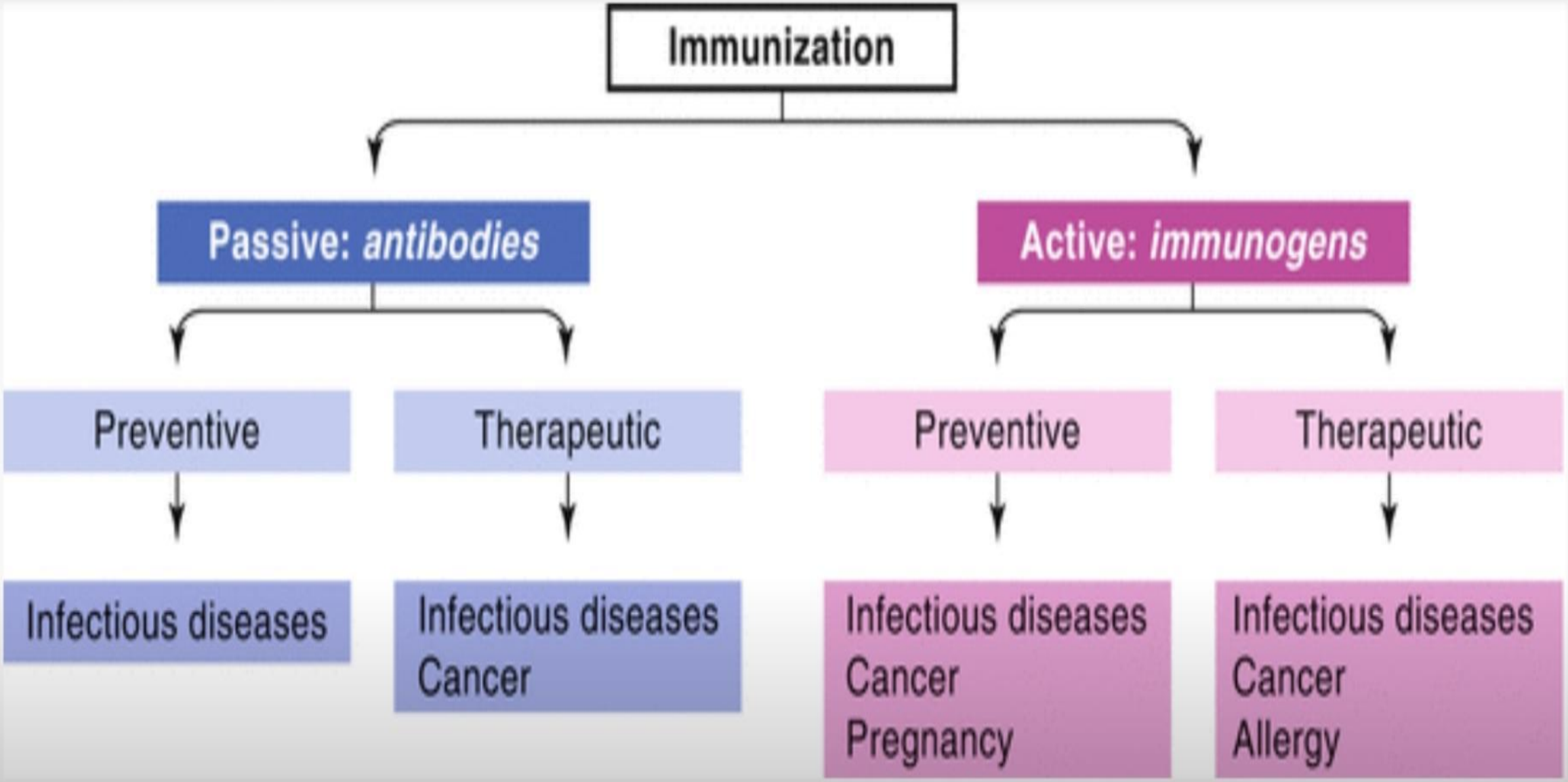

Primary Vaccination
Boster Dose
Serum titre of antibodies
IgG
IgM
0
1
2
3
4
5
6
7
Time (weeks)


DNA/RNA
Spike protein
Viral vector
Spike protein
Inactivated virus
Live-attenuated virus
Subunit spike protein
Immune response





Biology Online


Immunization
Passive: antibodies
Active: immunogens
Preventive
Therapeutic
Preventive
Therapeutic
Infectious diseases
Infectious diseases
Cancer
Infectious diseases
Cancer
Pregnancy
Infectious diseases
Cancer
Allergy

Coronavirus Disease 2019 (COVID-19)

What you need to know

Version 8.0

Disclaimer: This presentation has been developed for educational purposes only. It is not a substitute for professional medical advice. Should you have questions or concerns about any topic described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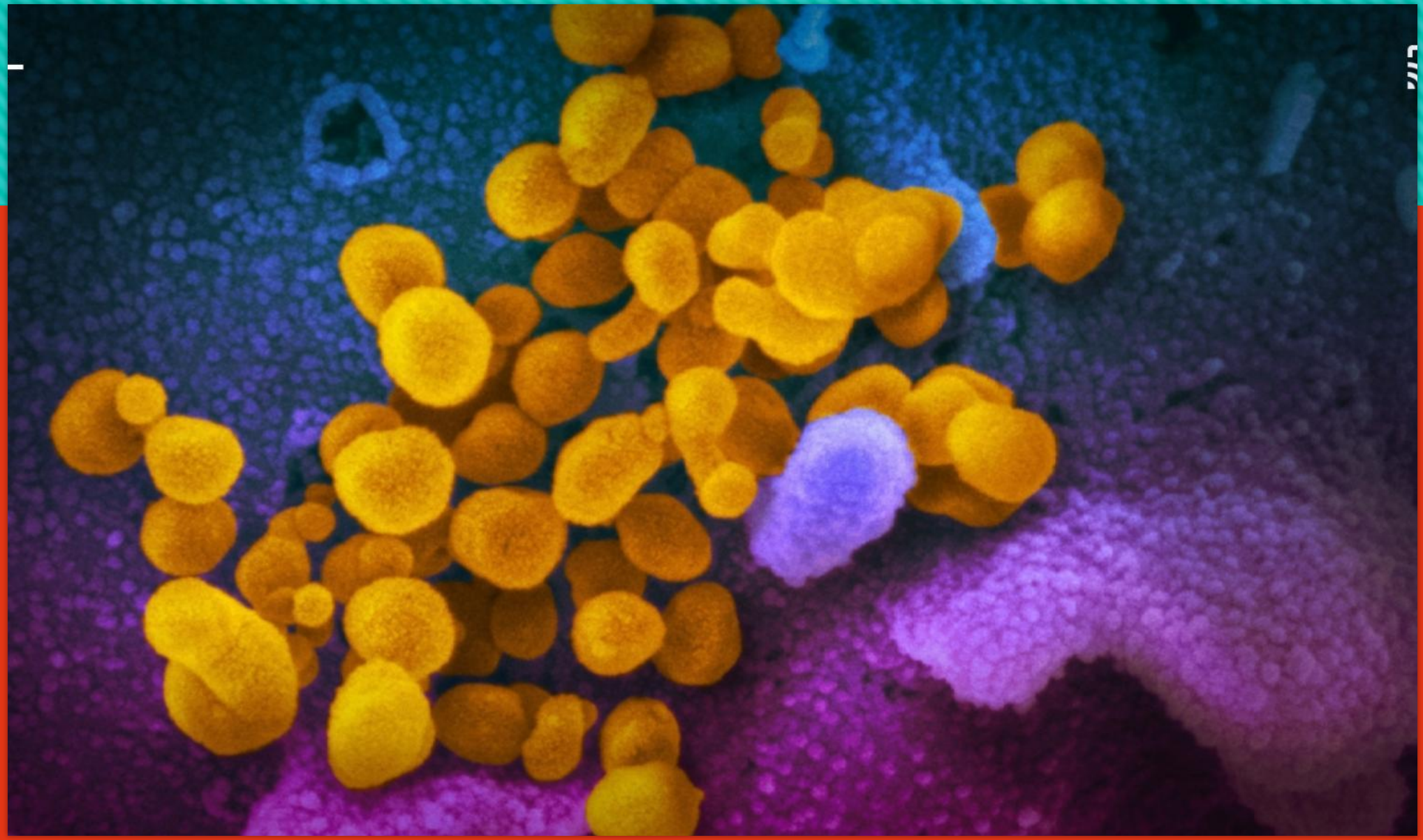

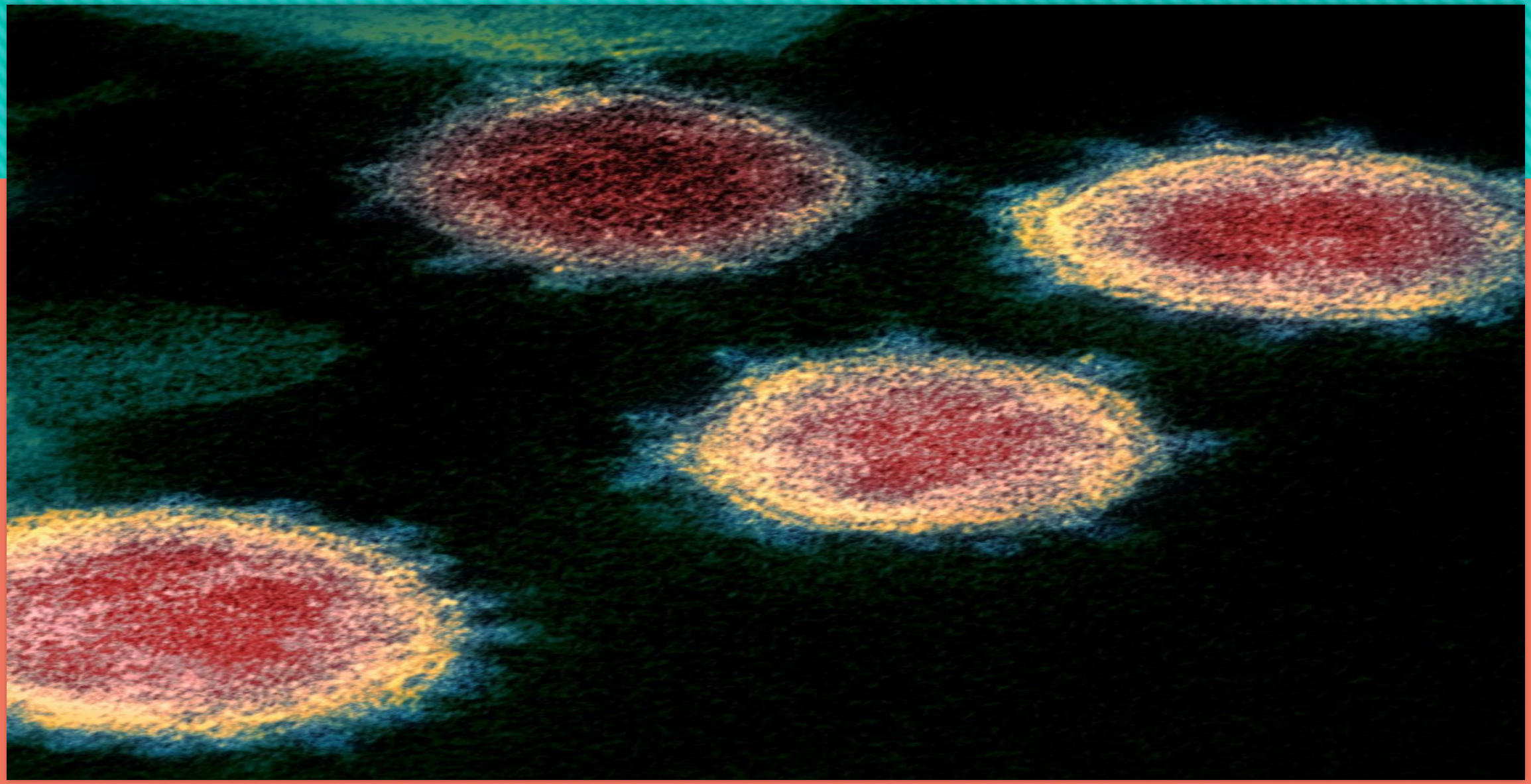

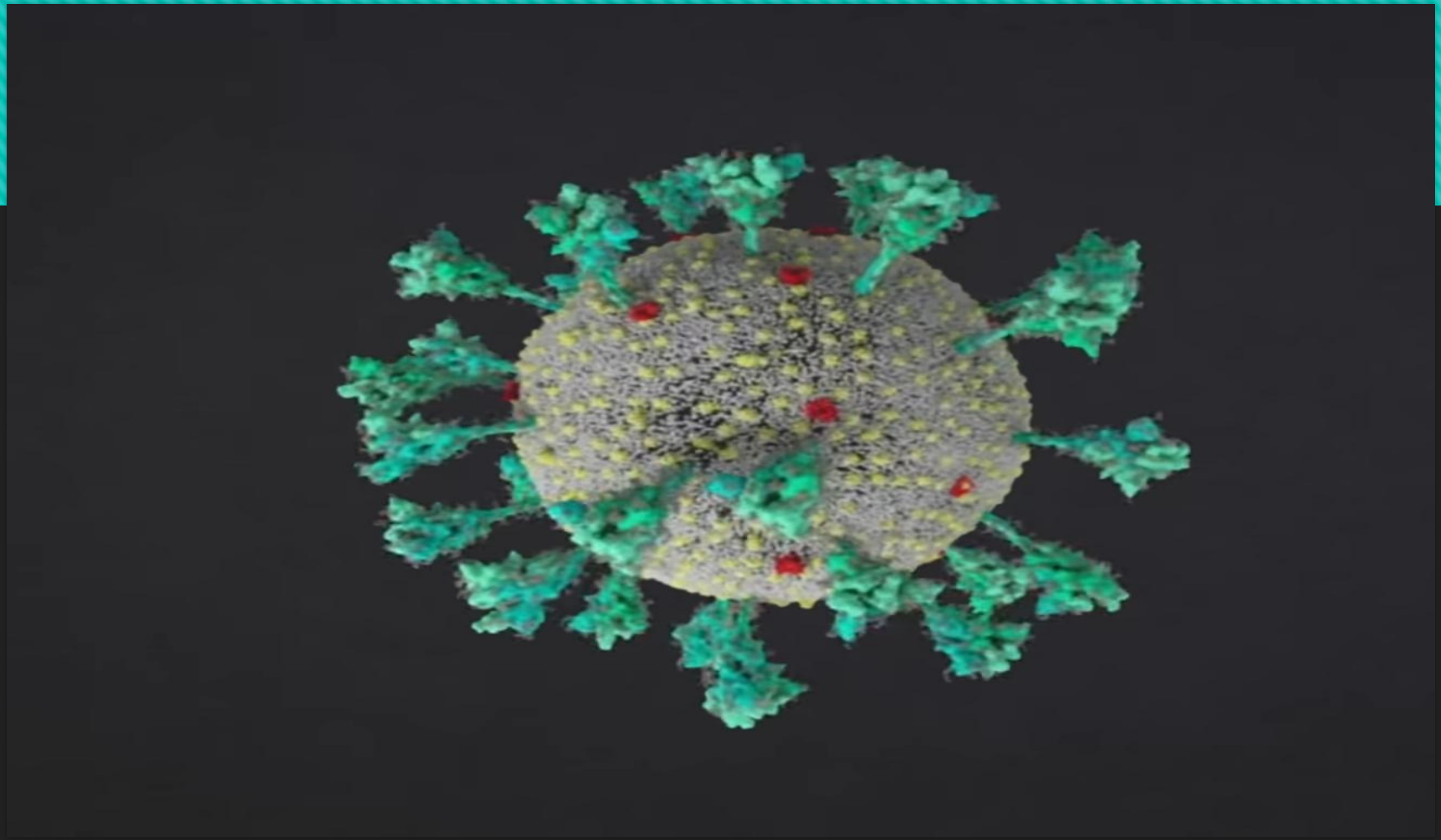

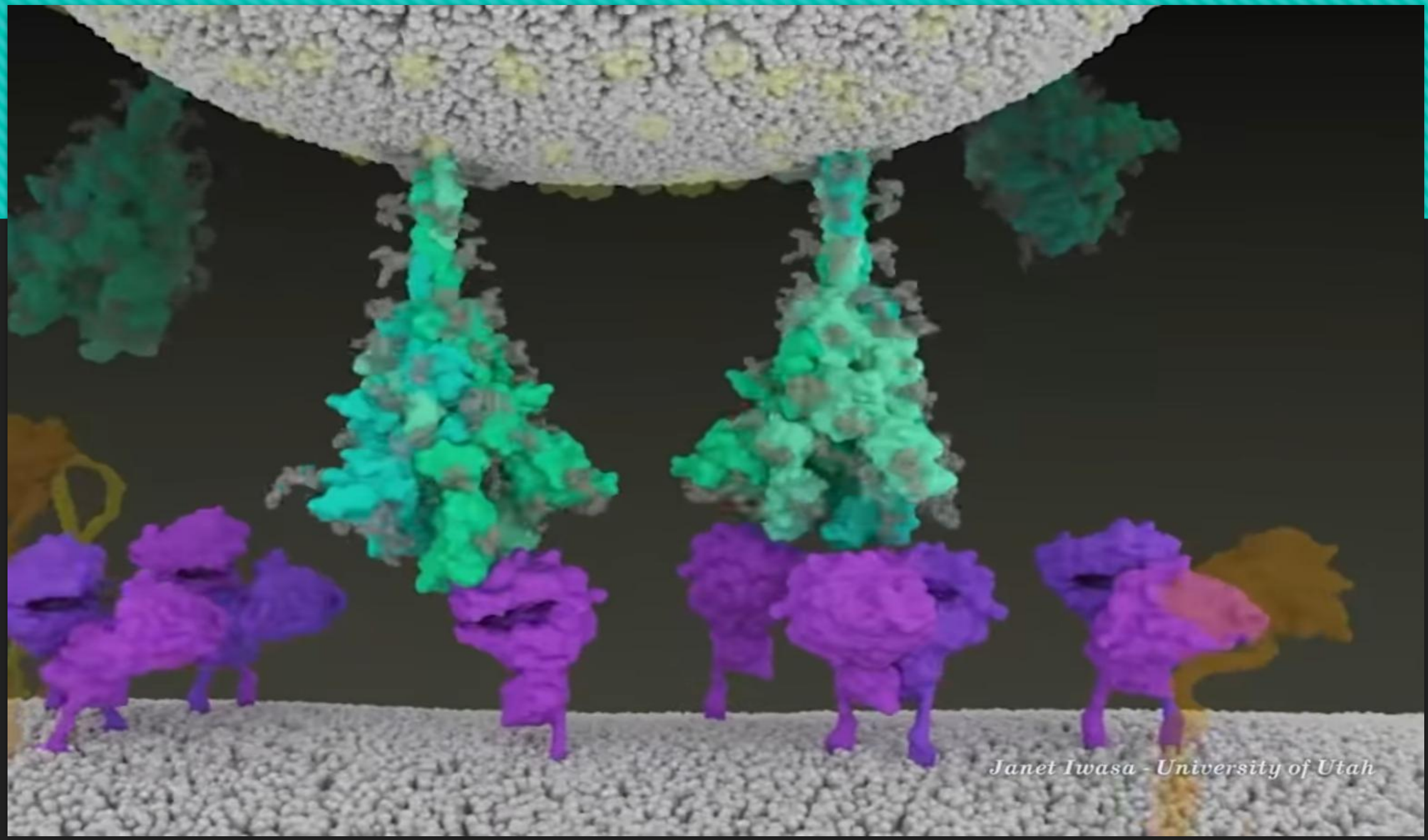
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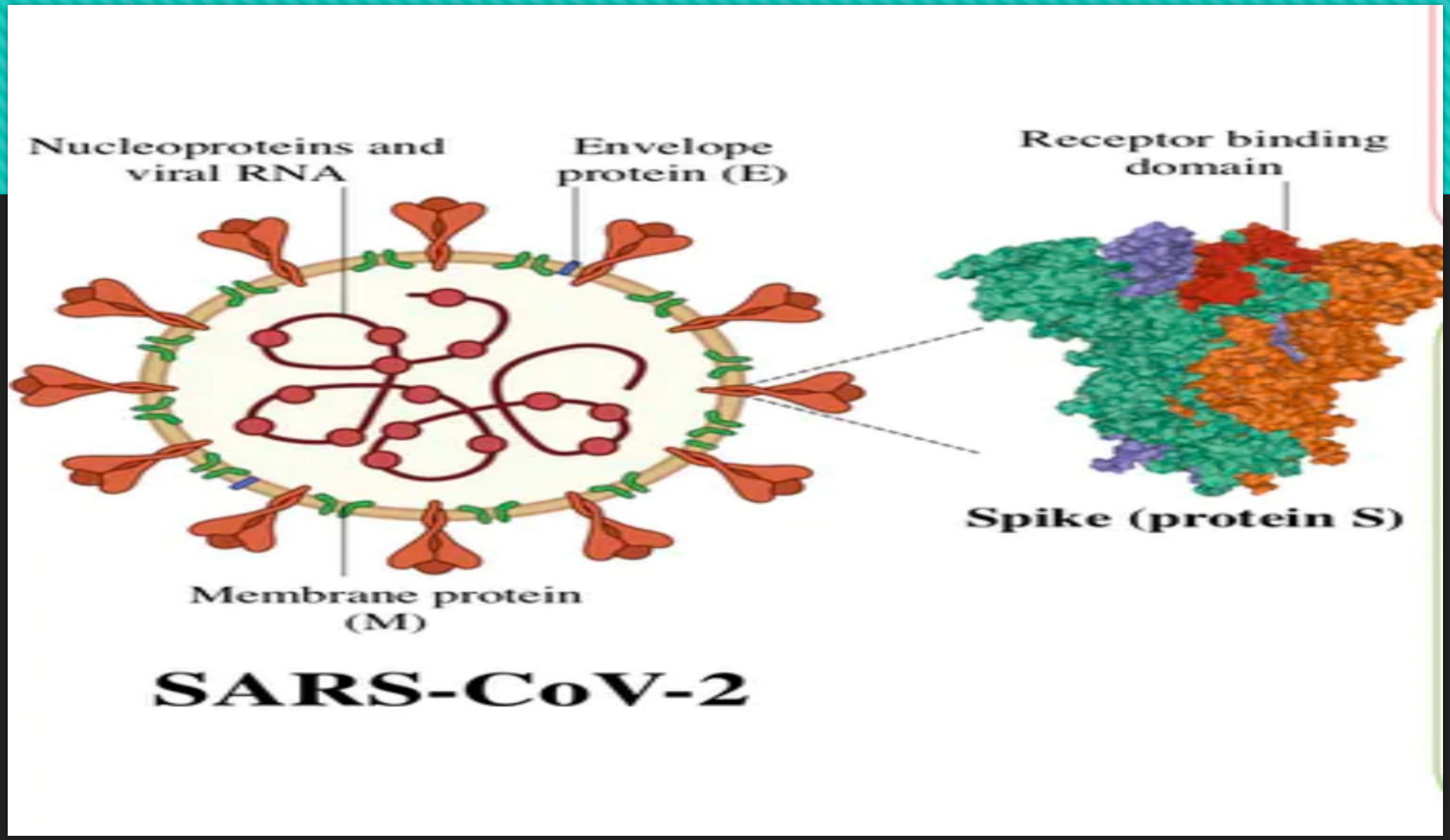
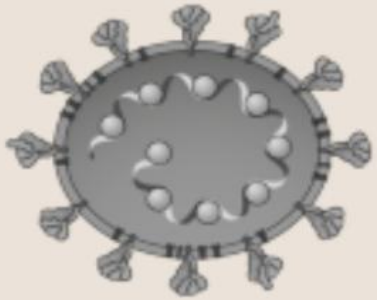
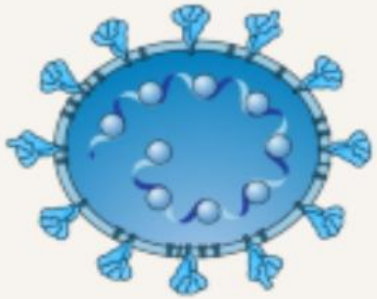
CORONAVIRUS


Nucleoproteins and viral RNA
Envelope protein (E)
Receptor binding domain
Spike (protein S)
Membrane protein (M)
SARS-CoV-2

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

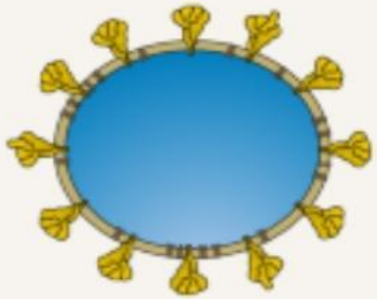


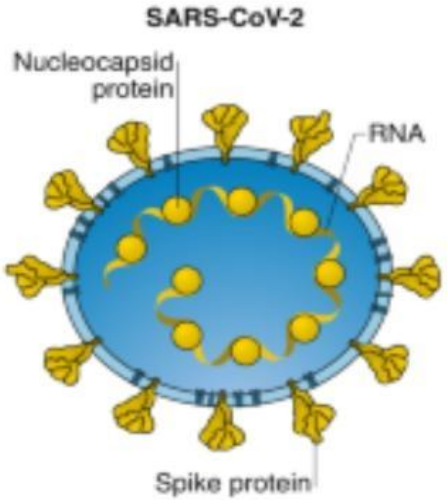
Live-attenuated virus
Example: MMR vaccine
COVID-19:
in preclinical stage



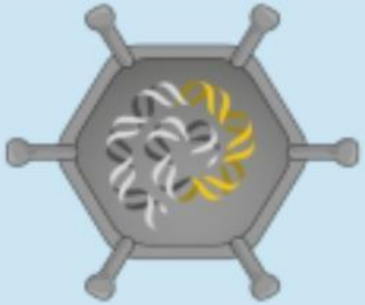
Protein subunit
Example: Seasonal
influenza vaccine
COVID-19:
NVX-CoV2373 in
phase 1/2 clinical trials

Virus-like particle
Example: Human
papillomavirus vaccine
COVID-19:
in preclinical stage





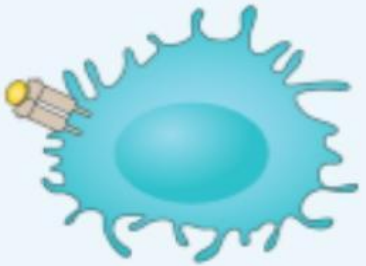
Viral vector
Example:
VSV-Ebola vaccine
COVID-19:
AZD1222, Ad5-nCoV
in phase 1/2/3 clinical trials



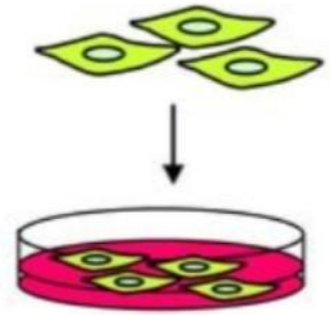
DNA
Example:
Not currently licensed
COVID-19:
INO-4800 in phase 1
clinical trials

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/aAPC
in phase 1/2 clinical trials

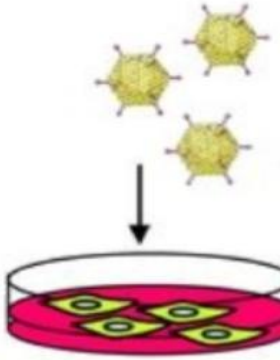


How to produce Vaccine?



cell

Cell culture

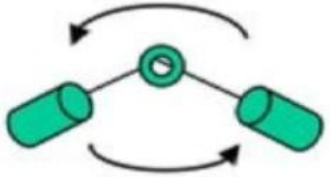


virus (production seed)

Inoculation

Harvest

Bulk



centrifugation

Filtering / Dialysis
Chromatography

Purification

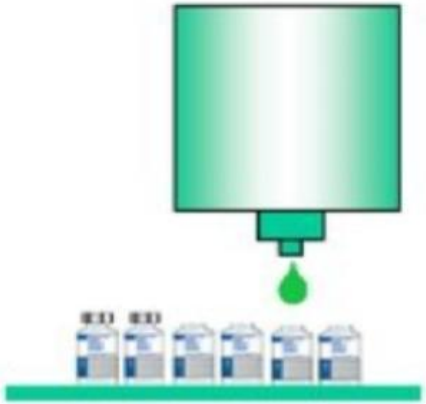
Add

Bulking agent

Adjuvant | Stabilizer

Preservative

Formulation

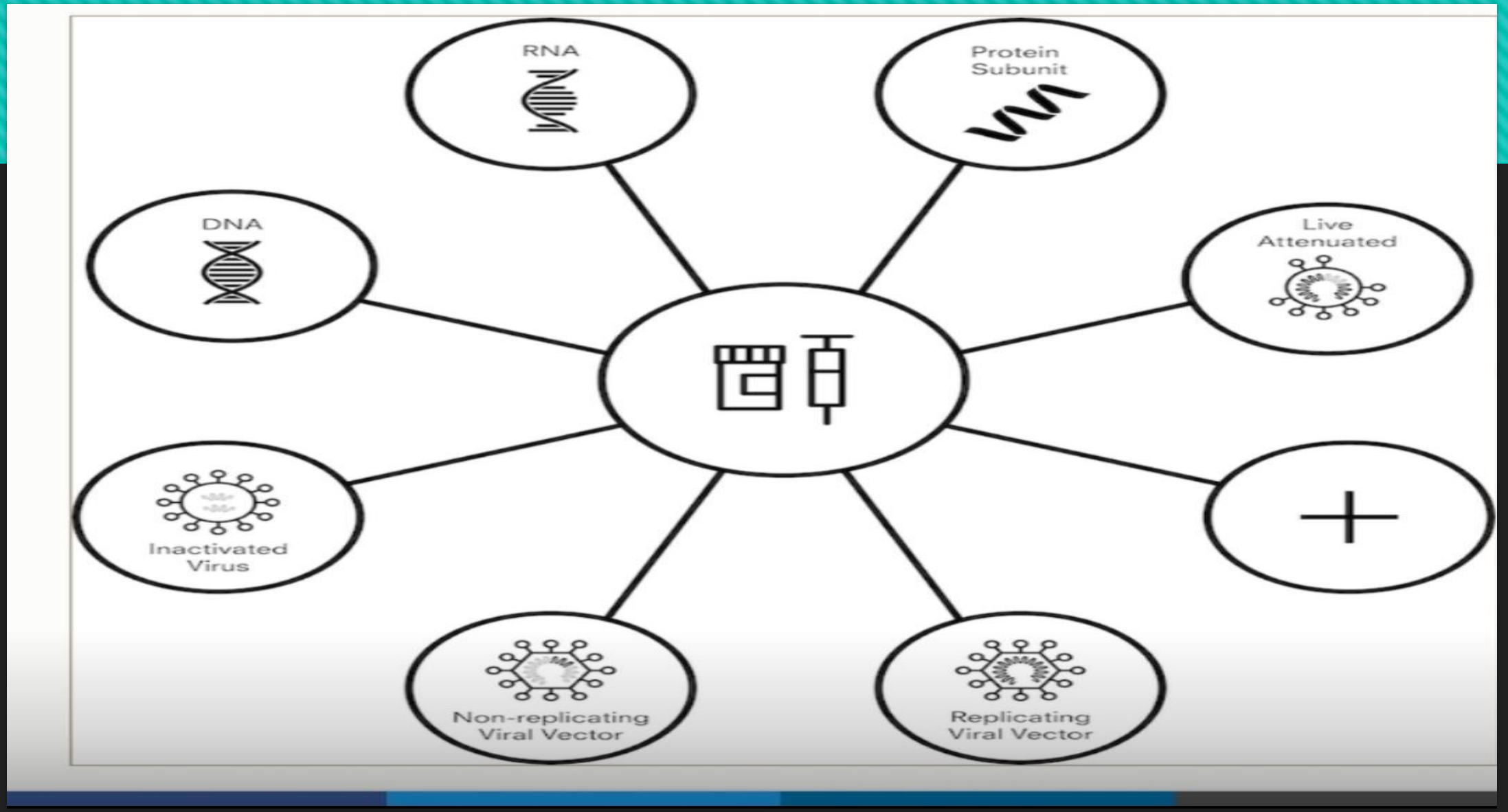


Filling

Inspection

Labeling

Packaging


RNA
Protein Subunit
DNA
Live Attenuated
Inactivated Virus
+
Non-replicating Viral Vector
Replicating Viral Vector

DNA vaccine	Good safety record in human studies. Theoretical risks of integration of the vector. Unable to revert to a pathogenic form.

Live attenuated virus vaccine	Theoretical risk of recombination with circulating wild-type influenza viruses. Risks of hospitalization and wheezing were increased in children younger than 2 years of age.

Vaccine Platform against Influenza Virus	Safety
mRNA vaccine	No risks of infection or integration of the vector Controllable in vivo activity and degradation of mRNA by natural cellular processes. More human data is required to evaluate safety.

Vaccine Platform against Influenza Virus	Safety
Inactivated virus vaccine	May require adjuvants (for example vaccines for avian strains) that can cause significant reactogenicity.

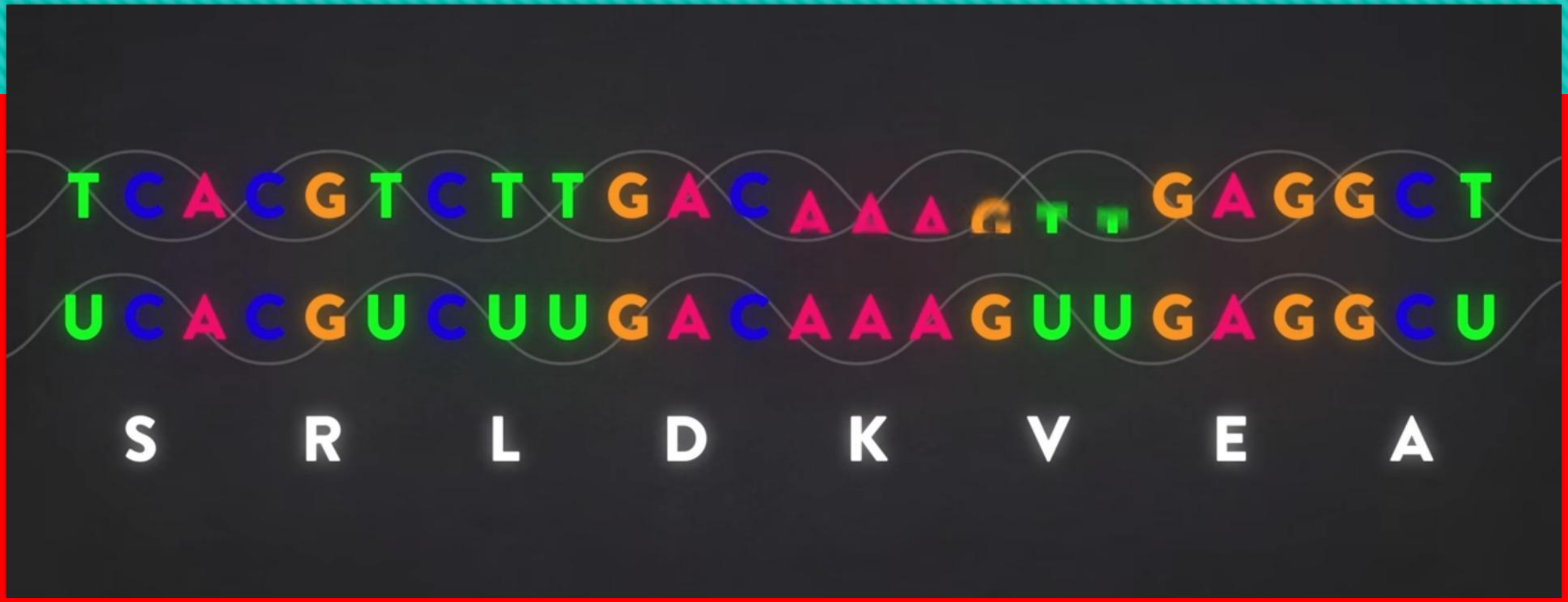
COMMON VACCINES

- Chickenpox vaccine
- DTaP immunization (vaccine)
- Hepatitis A vaccine
- Hepatitis B vaccine
- Hib vaccine
- HPV vaccine
- Influenza vaccine
- Meningococcal vaccine
- MMR vaccine
- Pneumococcal conjugate vaccine
- Pneumococcal polysaccharide vaccine
- Polio immunization (vaccine)
- Rotavirus vaccine
- Shingles vaccine
- Tdap vaccine
- Tetanus vaccine


CHINESE SCIENTISTS DISCOVER NEW VIRUS
ST KE VIRUS SICKENS DOZENS WITH PNEUMONIA IN WUHAN IN CENTRAL CHINA
JAN 9, 2020
CBSN

Date	Milestone
Dec 1	Covid-19 illness documented (unpublicized Nov 17th)
Jan 10	SARS-CoV-2 virus sequenced
Jan 15	NIH designs mRNA vaccine in collaboration with Moderna
Mar 16	Moderna Phase 1l2 trial begins
May 2	Pfizer/BioNTech Phase 1l2 trial begins
July 14	Moderna Phase 1l2 trial published in NEJM
July 27, 28	Moderna and Pfizer/BioNTech Phase 3 trial begins
Aug 12	Pfizer/BioNTech Phase 1l2 published in Nature
October 22,27	Enrollment in both Phase 3 trials complete; >74,000 participants
Nov 9	Pfizer/BioNTech announces interim analysis efficacy > 90%
Nov 16	Moderna announces interim analysis efficacy 94.5%
Nov 18	Pfizer/BioNTech announces 95% efficacy as final result
Nov 20	1st EUA submitted by Pfizer/BioNTech
Nov 27	Distribution of vaccine by UAL charter flights throughout US
Dec 10	FDA External review of Pfizer/BioNTech EUA
Dec 11	Phase 1a Vaccination begins for health care professionals*

*Provisional on positive external review


TCACGTCTTGACAAAGTTGAGGCT
UCACGUCUUGACAAAGUUGAGGCU
S R L D K V E A

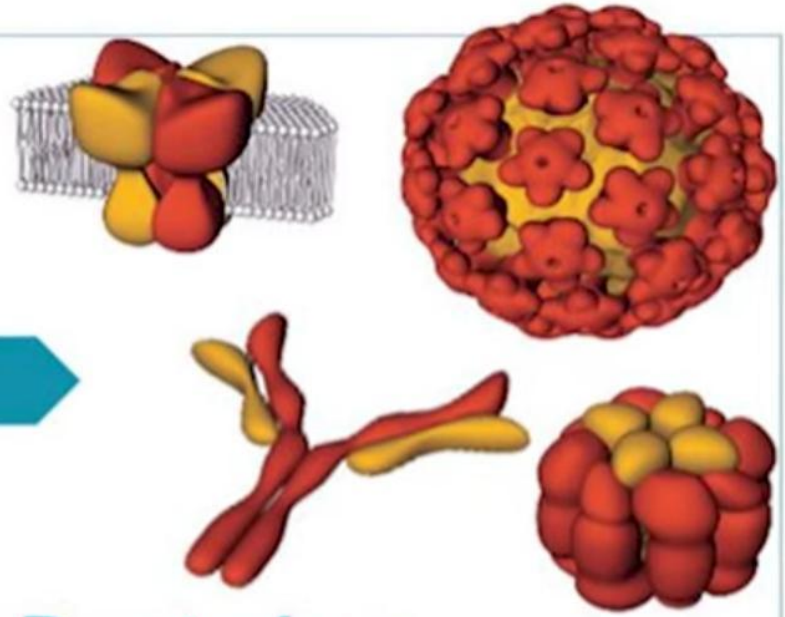
scription

mRNA

Data carrier of code

Carries target-specific instructions for making a protein from a gene to the site of translation

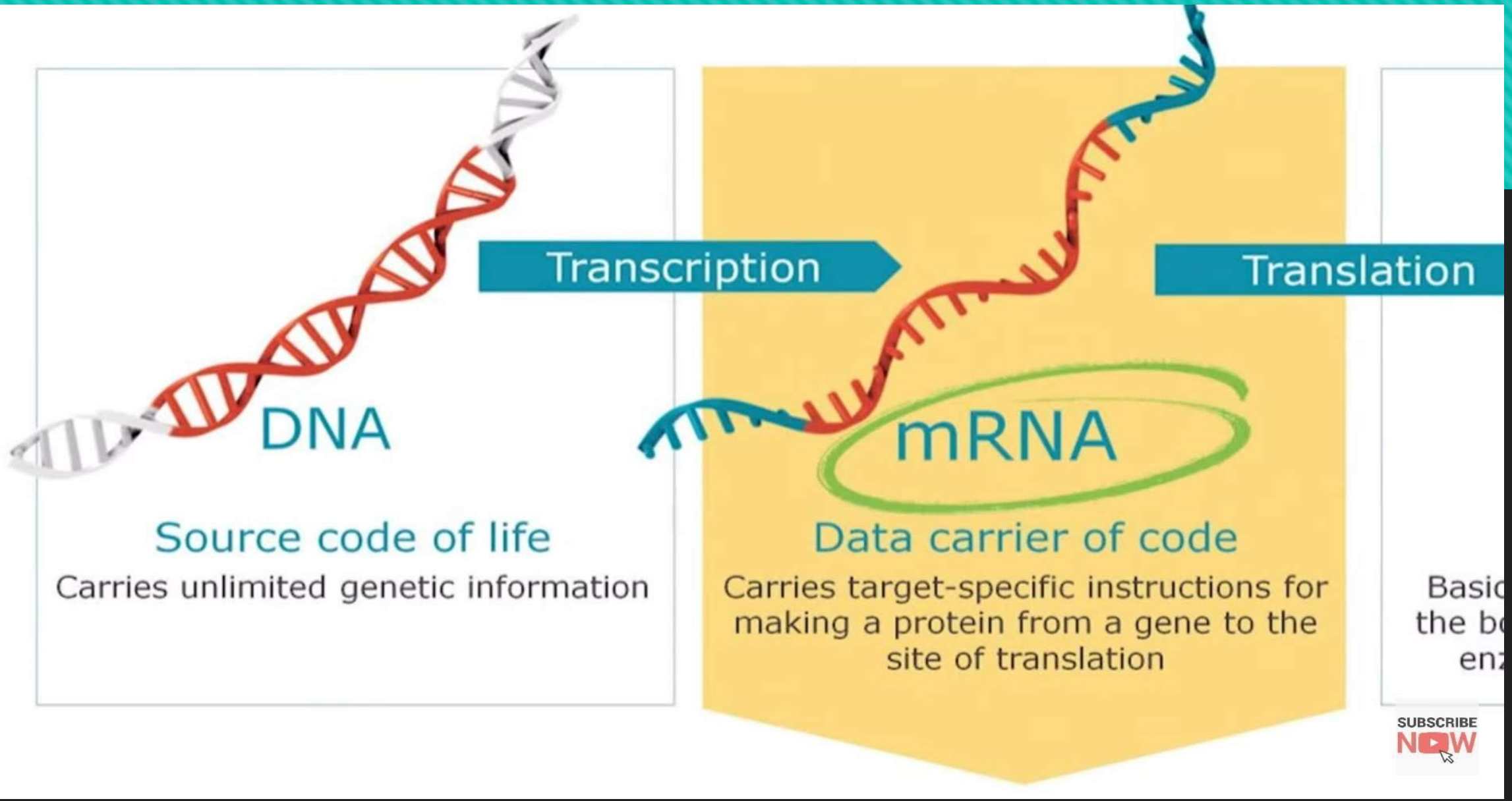
Translation



Proteins

Functional targets

Basic building blocks of all cells in the body – antibodies, hormones & enzymes are central to health


DNA
Transcription
mRNA
Translation
Source code of life
Carries unlimited genetic information
Data carrier of code
Carries target-specific instructions for making a protein from a gene to the site of translation
Basic
the b
enz
SUBSCRIBE
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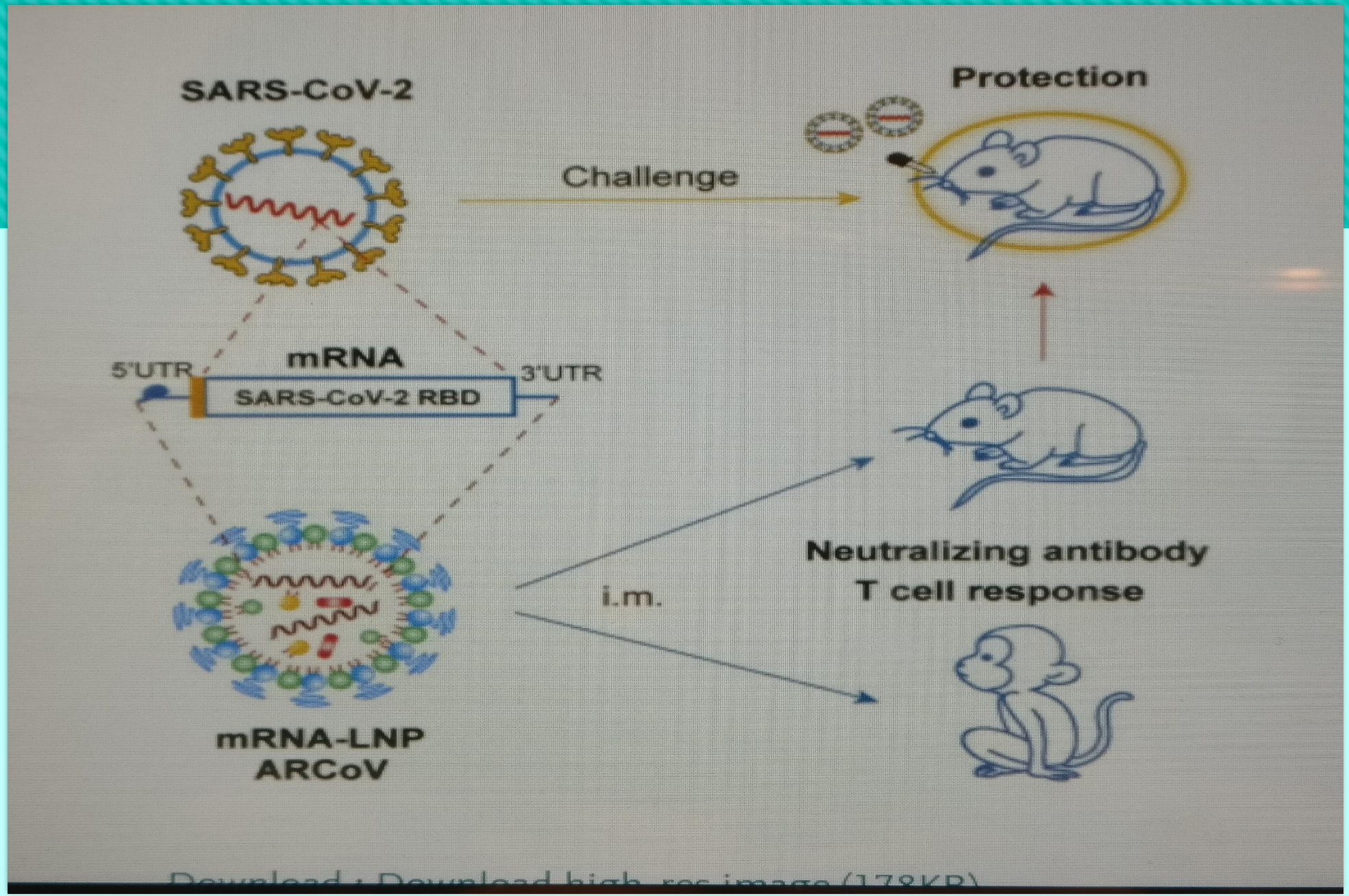
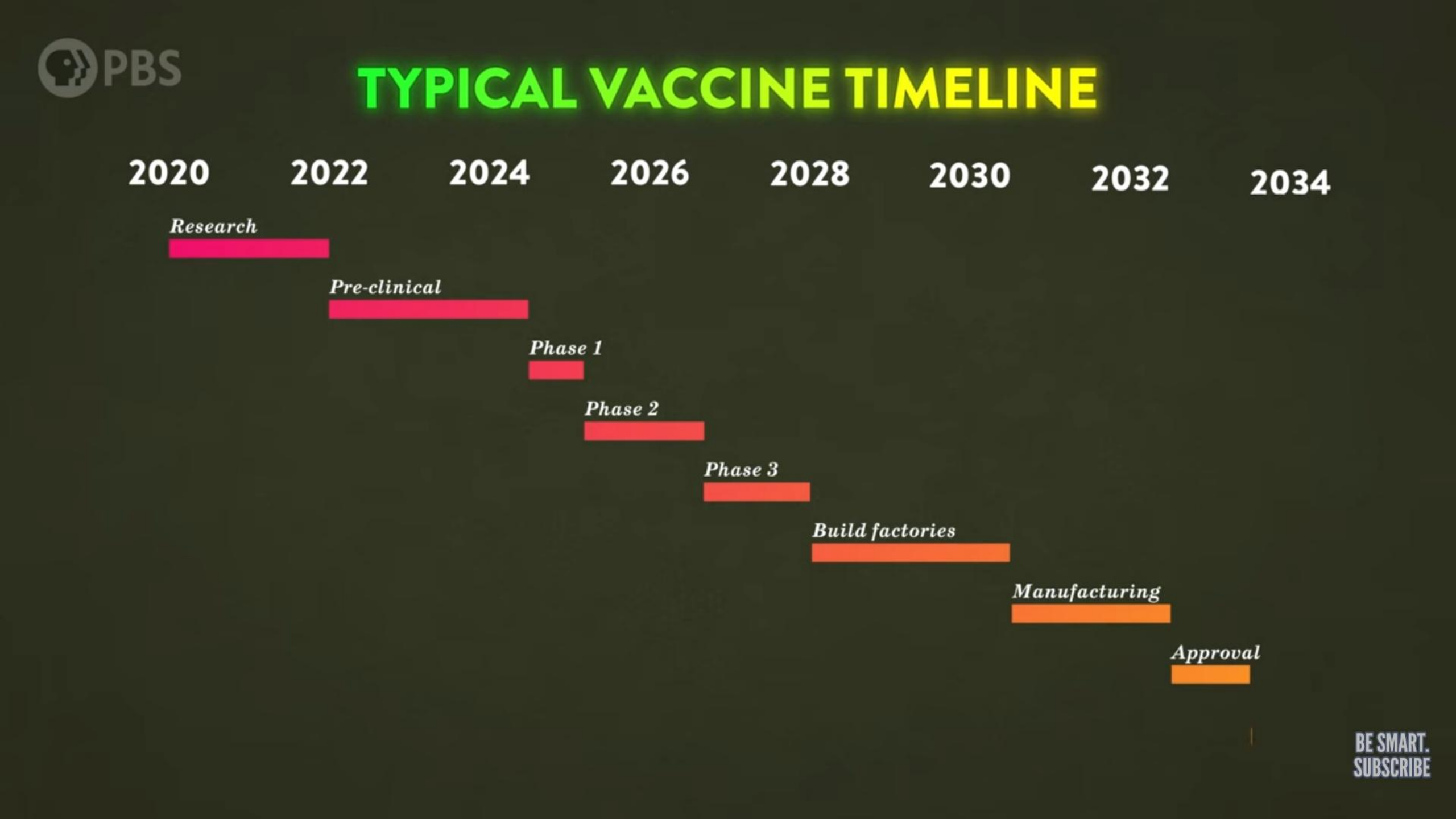
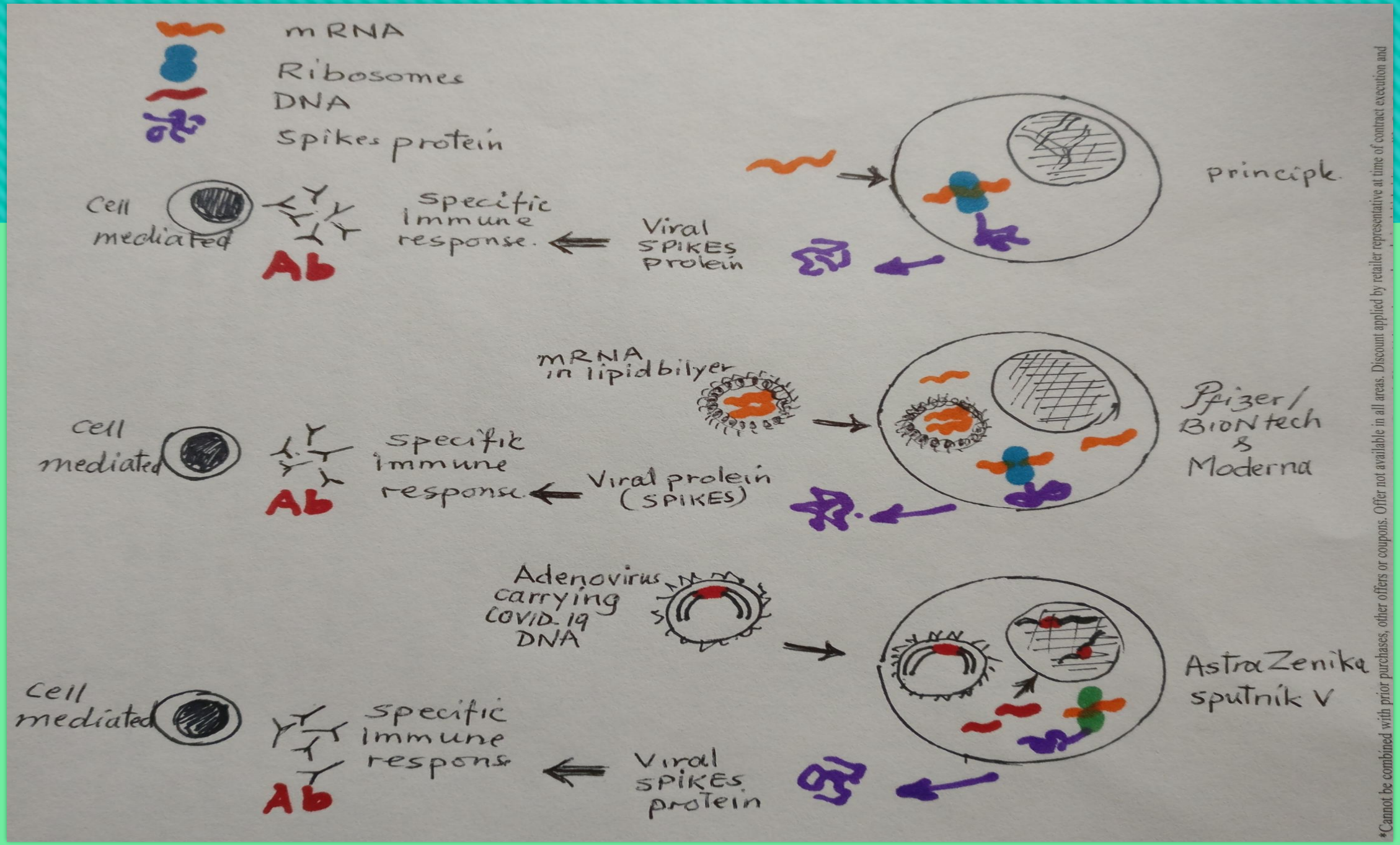
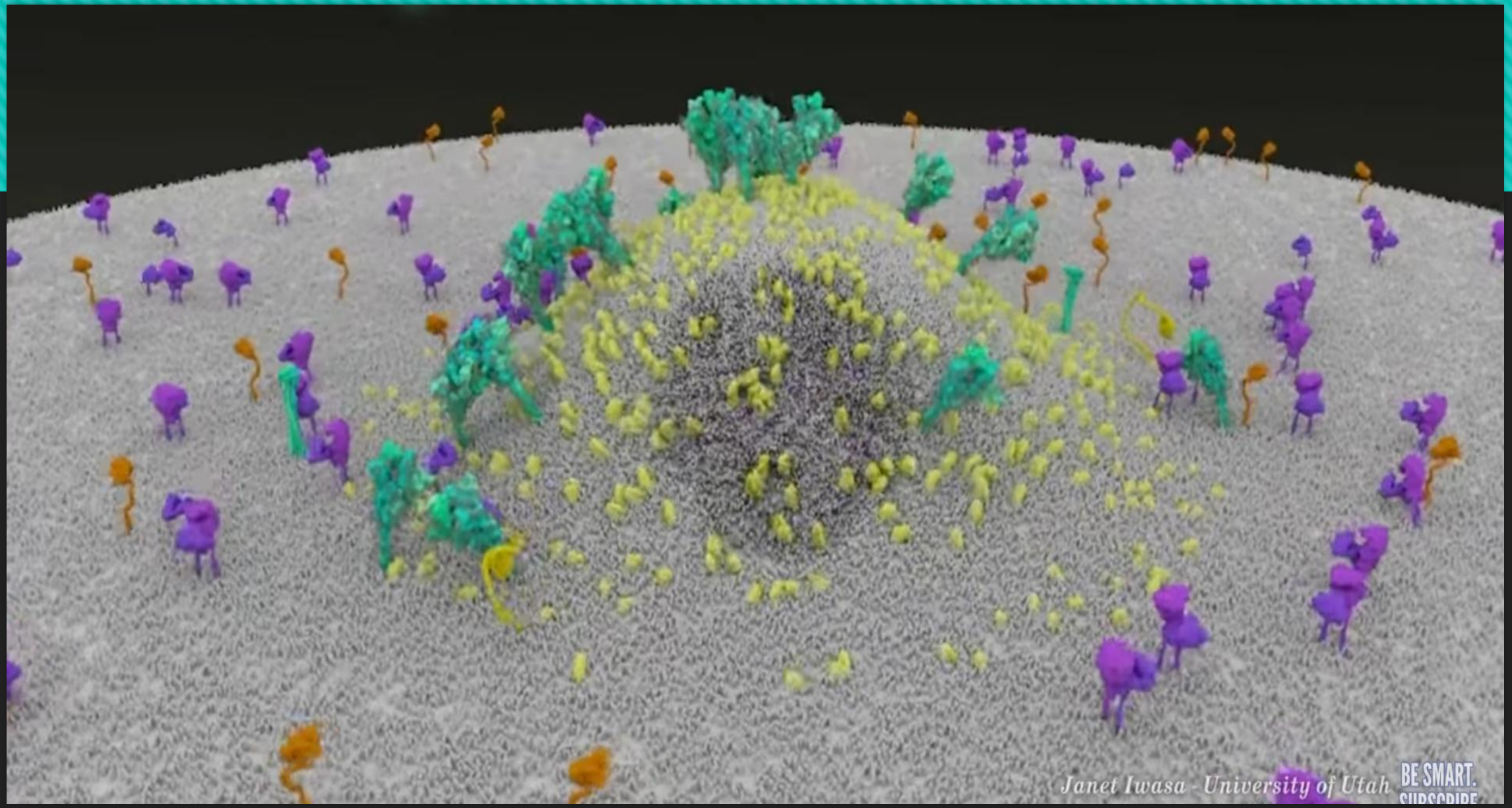

SARS-CoV-2
Protection
Challenge
mRNA
5'UTR
3'UTR
SARS-CoV-2 RBD
i.m.
Neutralizing antibody
T cell response
mRNA-LNP
ARCoV


PBS
TYPICAL VACCINE TIMELINE
2020
2022
2024
2026
2028
2030
2032
2034
Research
Pre-clinical
Phase 1
Phase 2
Phase 3
Build factories
Manufacturing
Approval
BE SMART.
SUBSCRIBE

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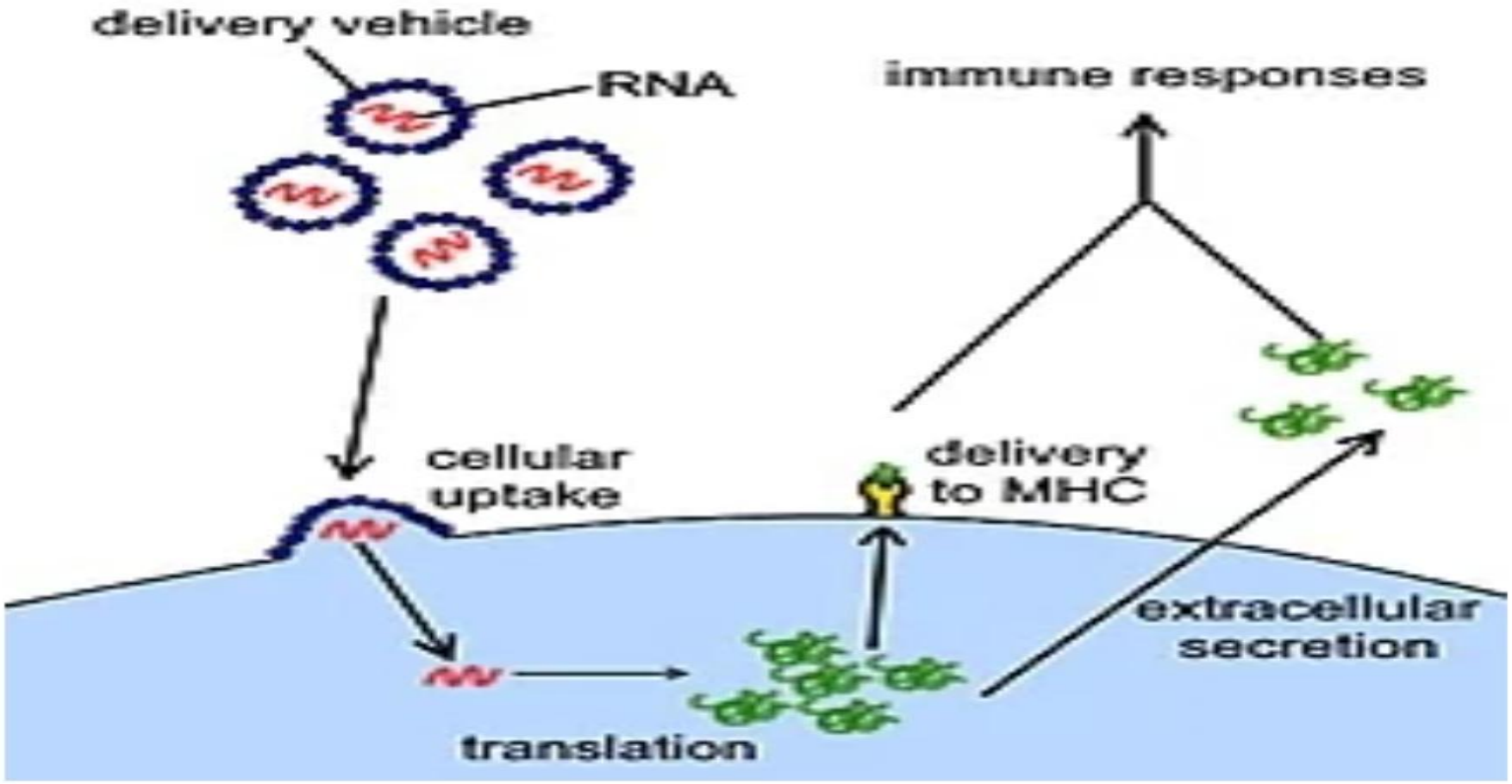
BE SMART.



An illustration of the mechanism of action of the RNA vaccine


VACCINE
10ml


moneycontrol
Pfizer, Moderna, AstraZeneca & Russian
vaccines have all reported mild side effects
SUBSCRIBE
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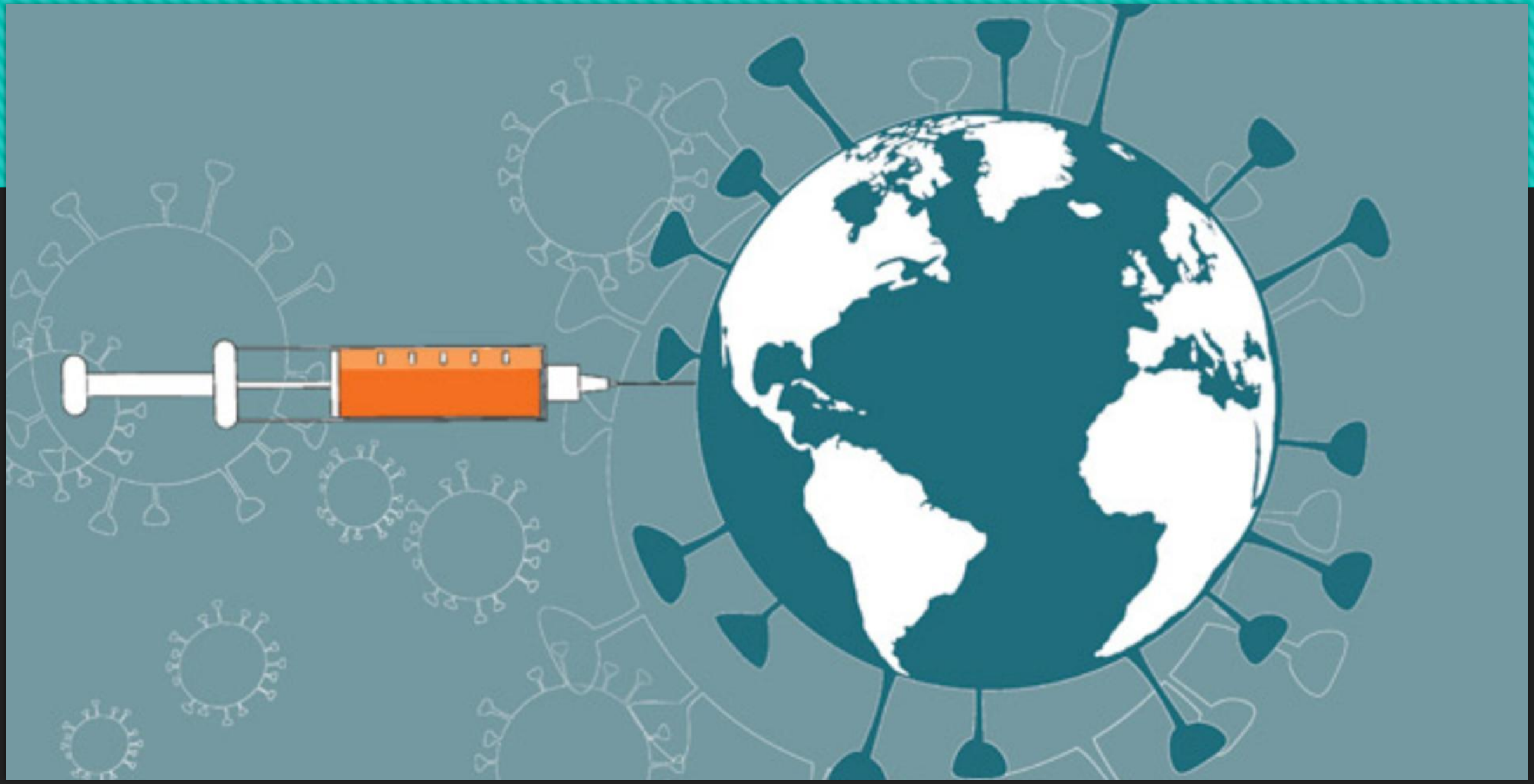
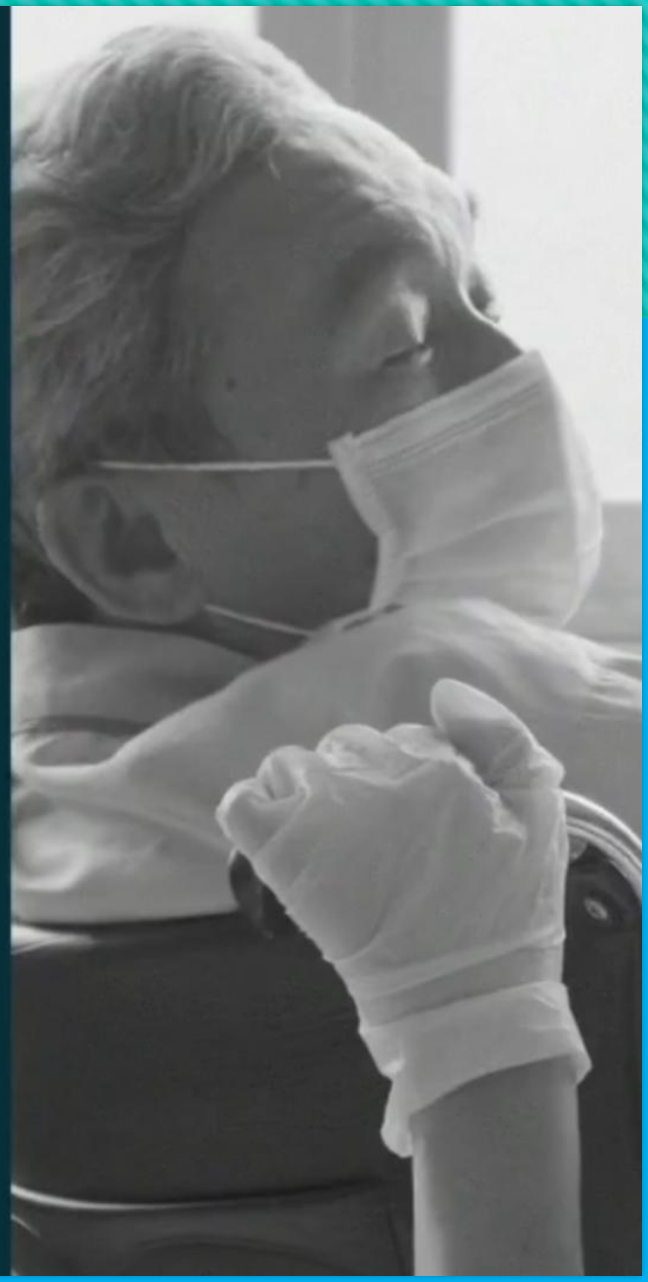


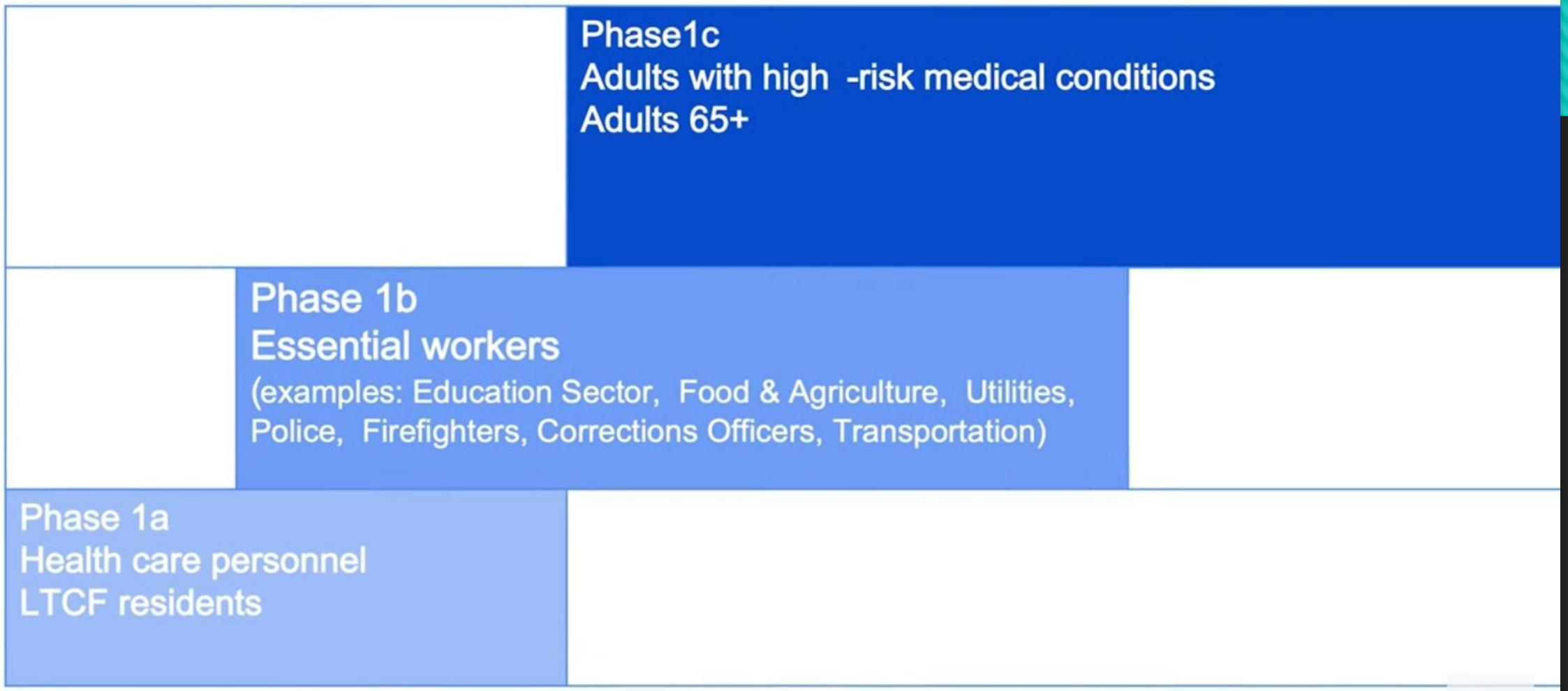

ONE WORLD
PROTECTED
CEPI
Gavi
The Vaccine Alliance
World Health
Organization

HEALTH SYSTEMS ARE READY TO ENSURE DOSES REACH THE PEOPLE THAT NEED THEM THE MOST.




WITH OVER 180 GOVERNMENTS
NOW INVOLVED, COVAX POOLS
FUNDING TO INVEST

Work Group Proposed Interim Phase 1 Sequence



Proposed groups for Phase 1a vaccination

Health care Personnel[1,2] (HCP) (~21million)	Long-Term Care Facility (LTCF) Residents[3] (~3M)
Examples	
• Hospitals • Long-term care facilities • Outpatient clinics • Home health care • Pharmacies • Emergency medical services • Public health	• Skilled nursing facilities (~1.3 M beds) • Assisted living facilities (~0.8 M beds) • Other residential care (~0.9 M beds)

1. https://www.cdc.gov/infectioncontrol/guidelines/healthcare
2. personnel/index.html https://www.cisa.gov/publication/guidance -essential-critical-infrastructure-workforce

HOW LONG DOES THE PROTECTION LAST?

DOES IT PROTECT AGAINST ASYMPTOMATIC DISEASE?

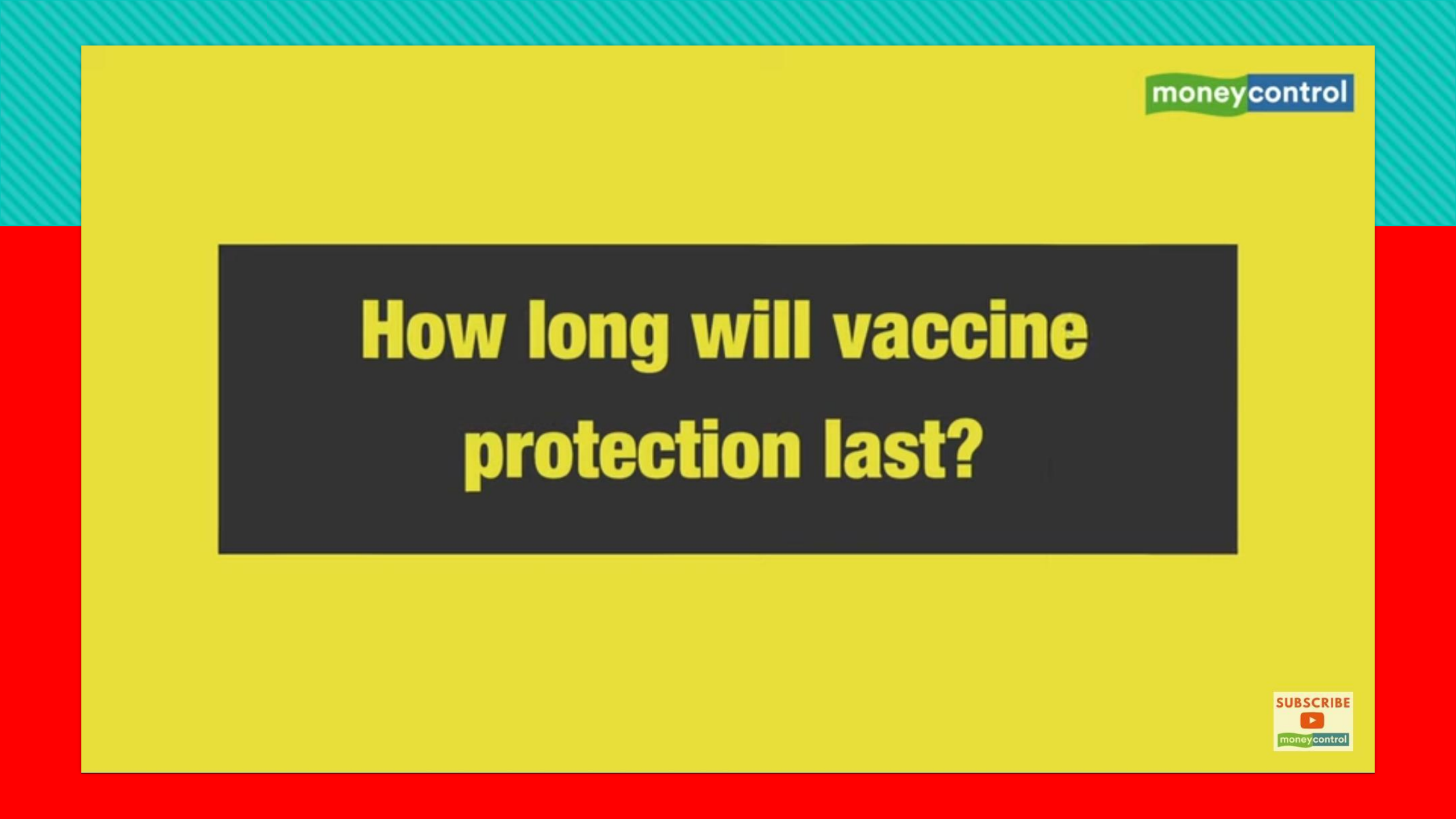
DOES IT PREVENT PEOPLE FROM SPREADING THE VIRUS TO OTHERS?

DO I STILL NEED VACCINE IF I HAD COVID?

IS THE VACCINE SAFE FOR ME WITH MY UNDERLYING MEDICAL CONDITION?


How well will they
protect the elderly?


Arctic Ocean
Arctic Ocean
NORTH AMERICA
EUROPE
ASIA
North Atlantic Ocean
North Pacific Ocean
North Pacific Ocean
AFRICA
SOUTH AMERICA
Indian Ocean
AUSTRALIA
South Pacific Ocean
South Atlantic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How long will vaccine protection last?
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What does the immune response look like?

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Memory B cells

Antibodies

Killer T cells (CD8+)

Helper T cells (CD4+)

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Can even better results be achieved?

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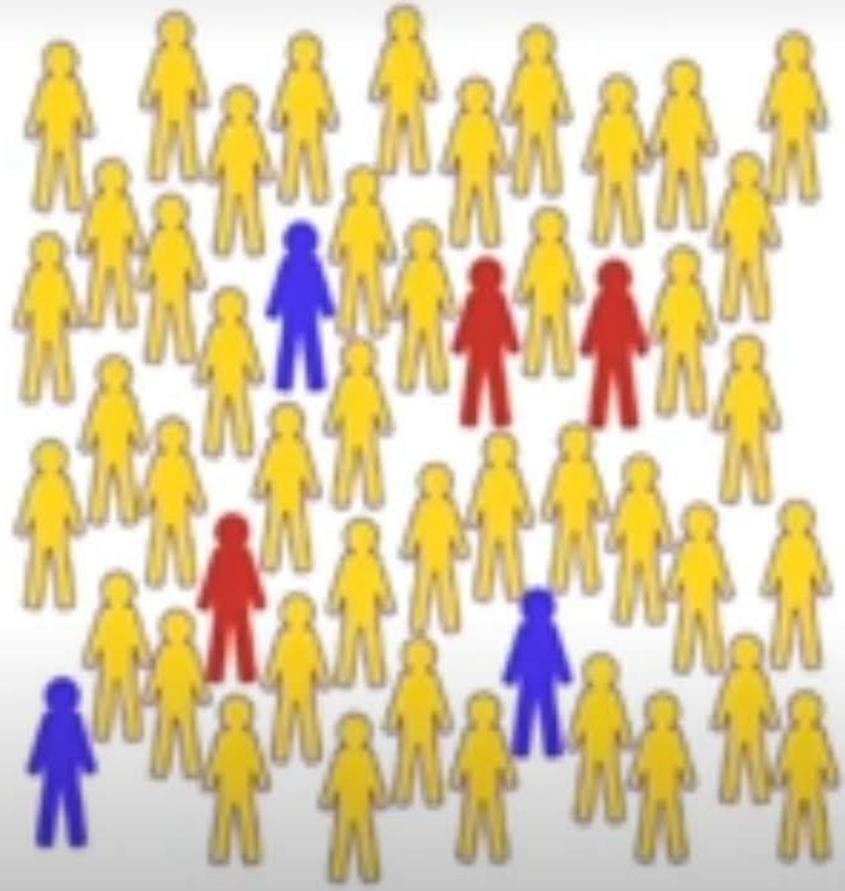
= not immunized, but still healthy

= immunized and healthy

= not immunized, sick, and contagious

Most of the population gets immunized.

Spread of contagious disease is contained.



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What is the B-cells and T-cells component?

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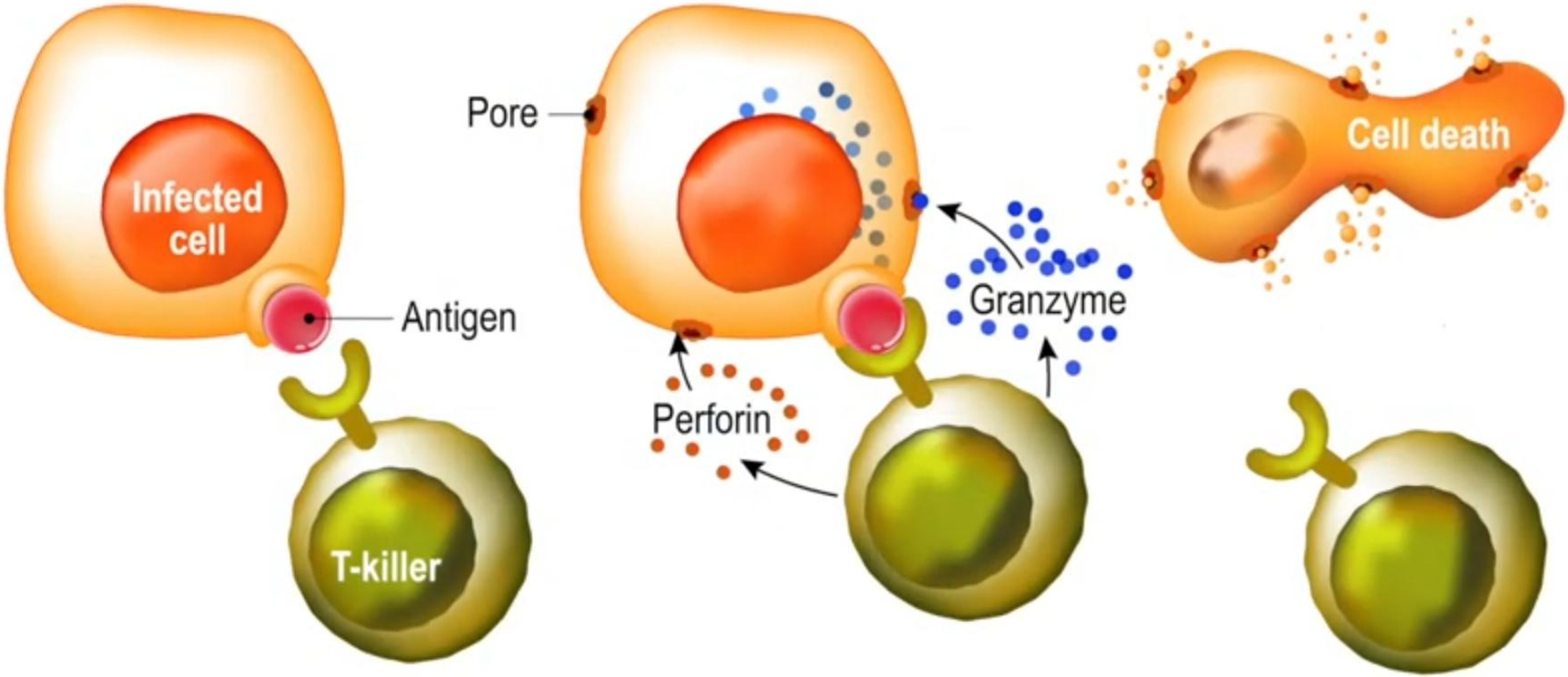

Infected cell
Antigen
T-killer
Pore
Perforin
Granzyme
Cell death

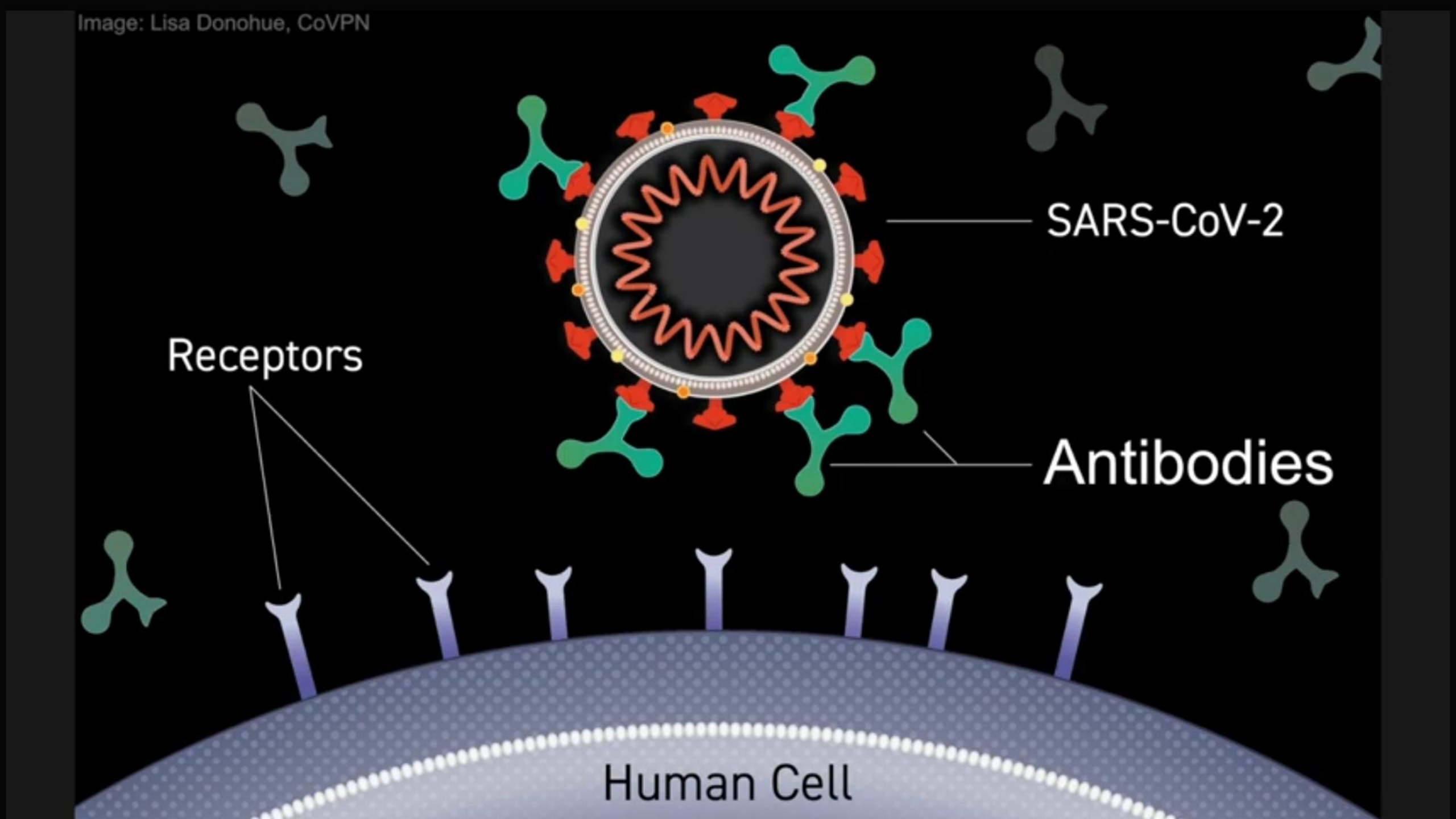
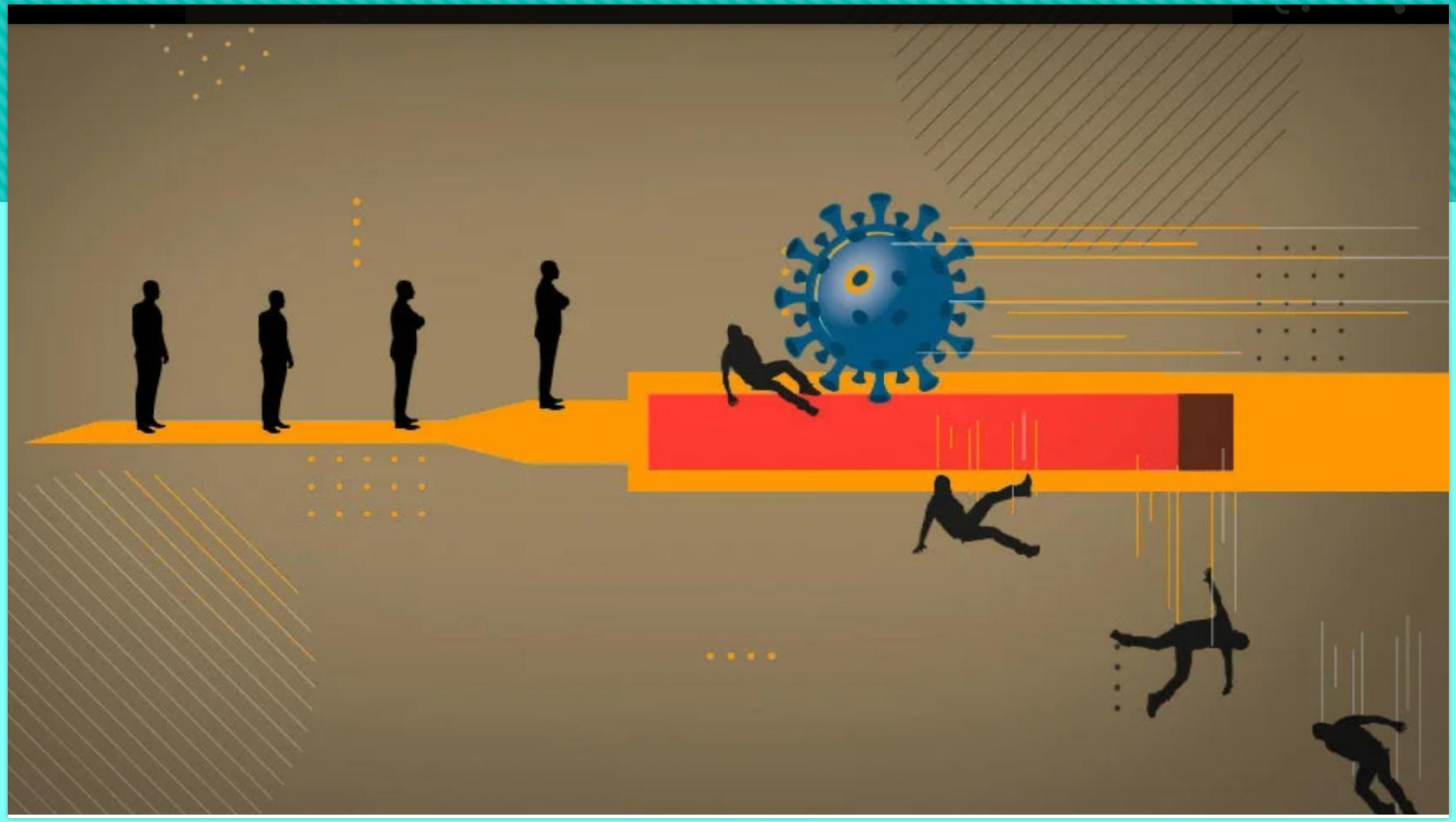
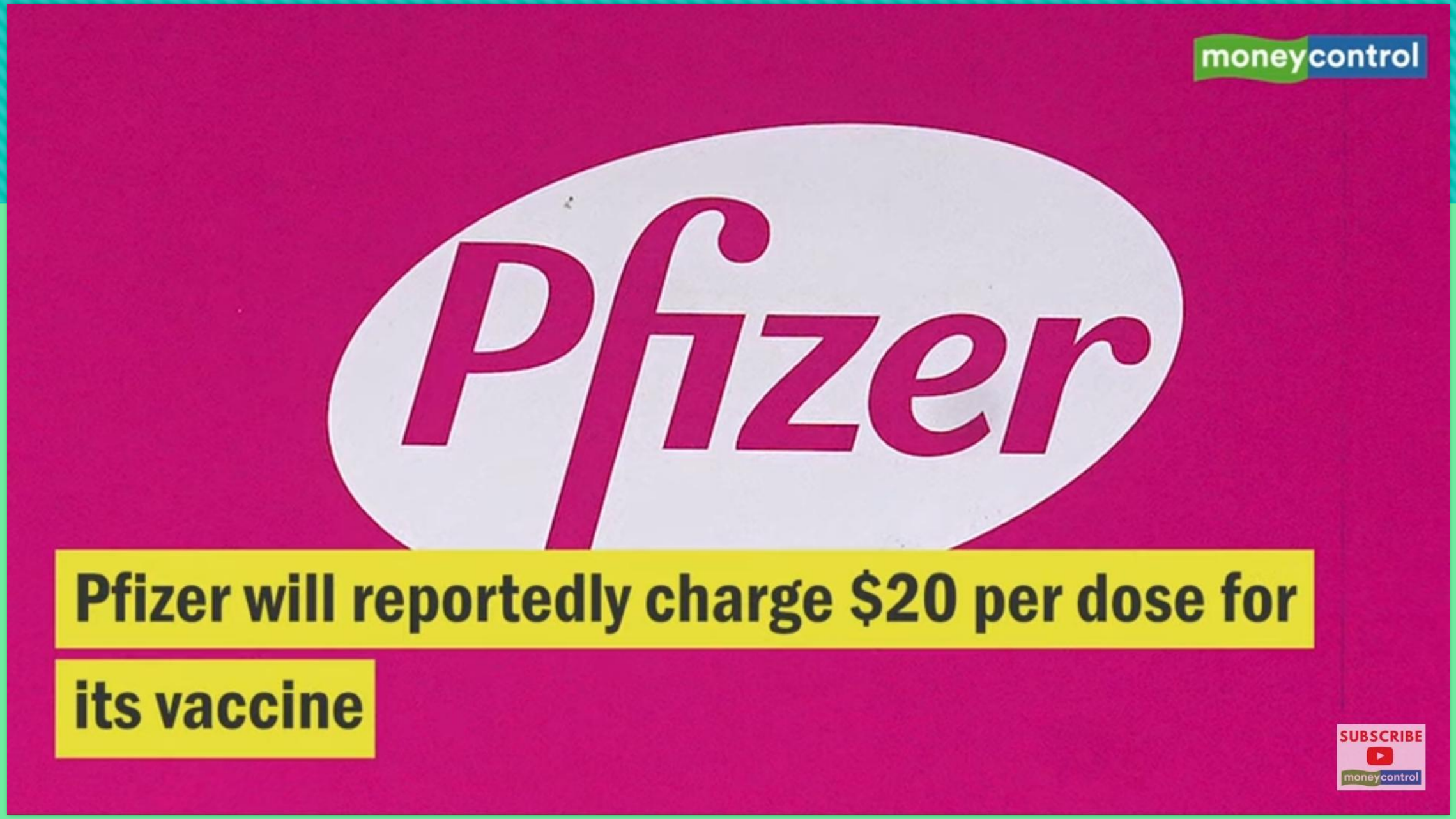


Image: Lisa Donohue, CoVPN
SARS-CoV-2
Receptors
Antibodies
Human Cell

Will it work in people who are immunocompromised?

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Pfizer
Pfizer will reportedly charge $20 per dose for its vaccine
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moderna

Moderna has said that their vaccine will cost $37

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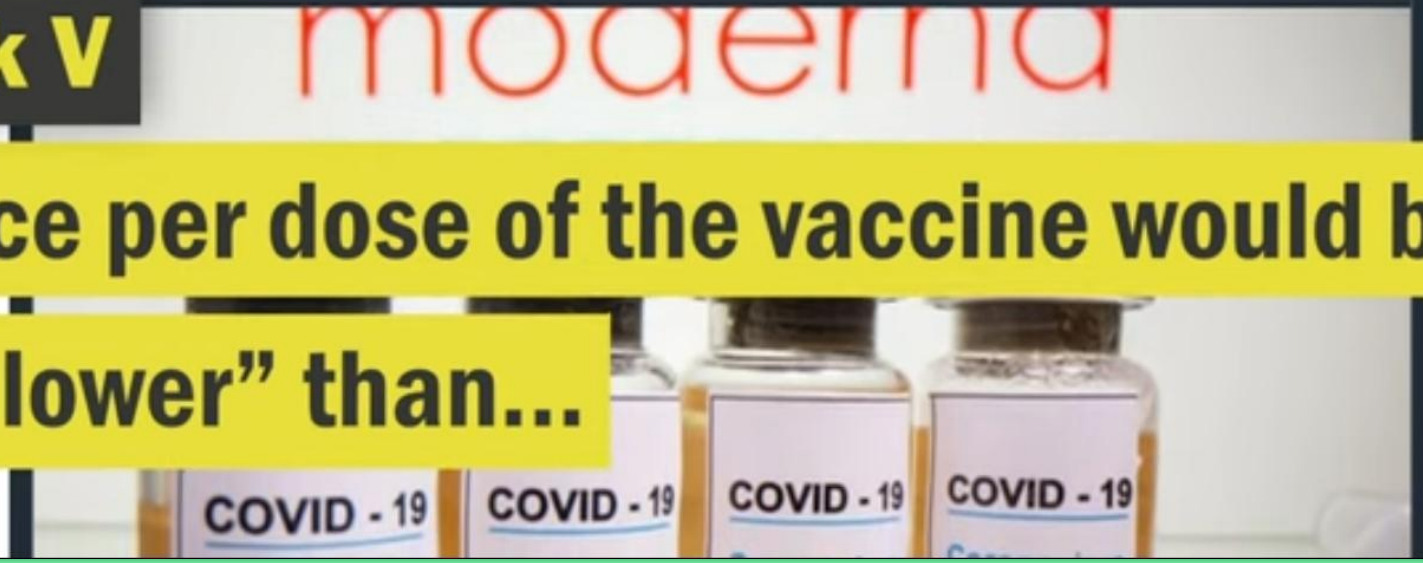
SII

Vaccine will cost between ₹500 and ₹600 per dose for the general public

Translating pharma lingo: the announced price of Pfizer of $19.50 and Moderna of $25-$37 per dose actually means their price of $39 and $50-$74 per person. Two doses are required per person for the Pfizer, Sputnik V and Moderna vaccines. The price of Sputnik V will be much lower.

> **NDTV** @ndtv · Nov 22
> Moderna To Charge $25-$37 Per Dose For Its #COVIDVaccine, Says CEO
> ndtv.com/world-news/mod...



Sputnik V

The price per dose of the vaccine would be "much lower" than...

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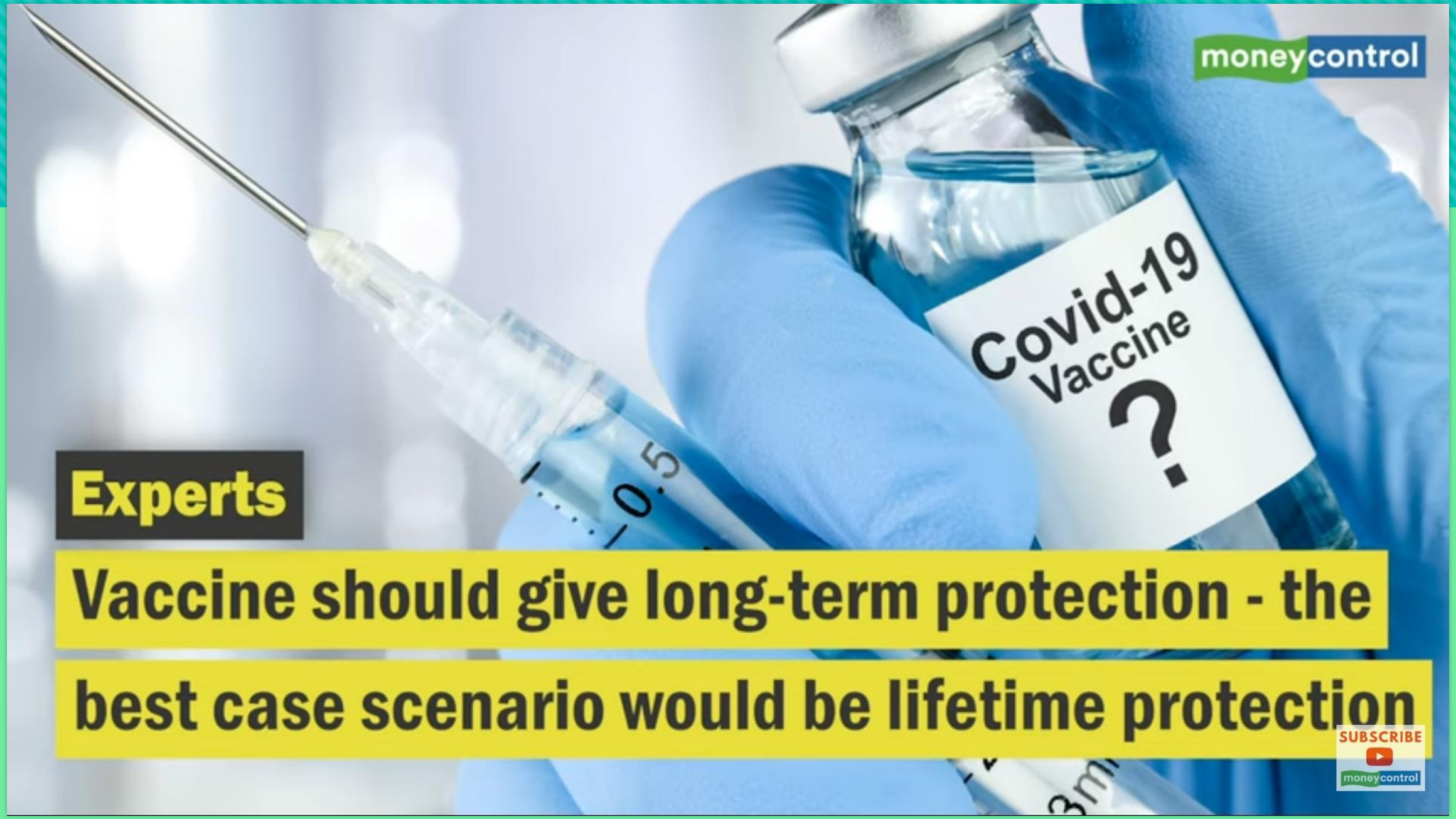
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Covid-19
Vaccine
?
Experts
Vaccine should give long-term protection - the
best case scenario would be lifetime protection
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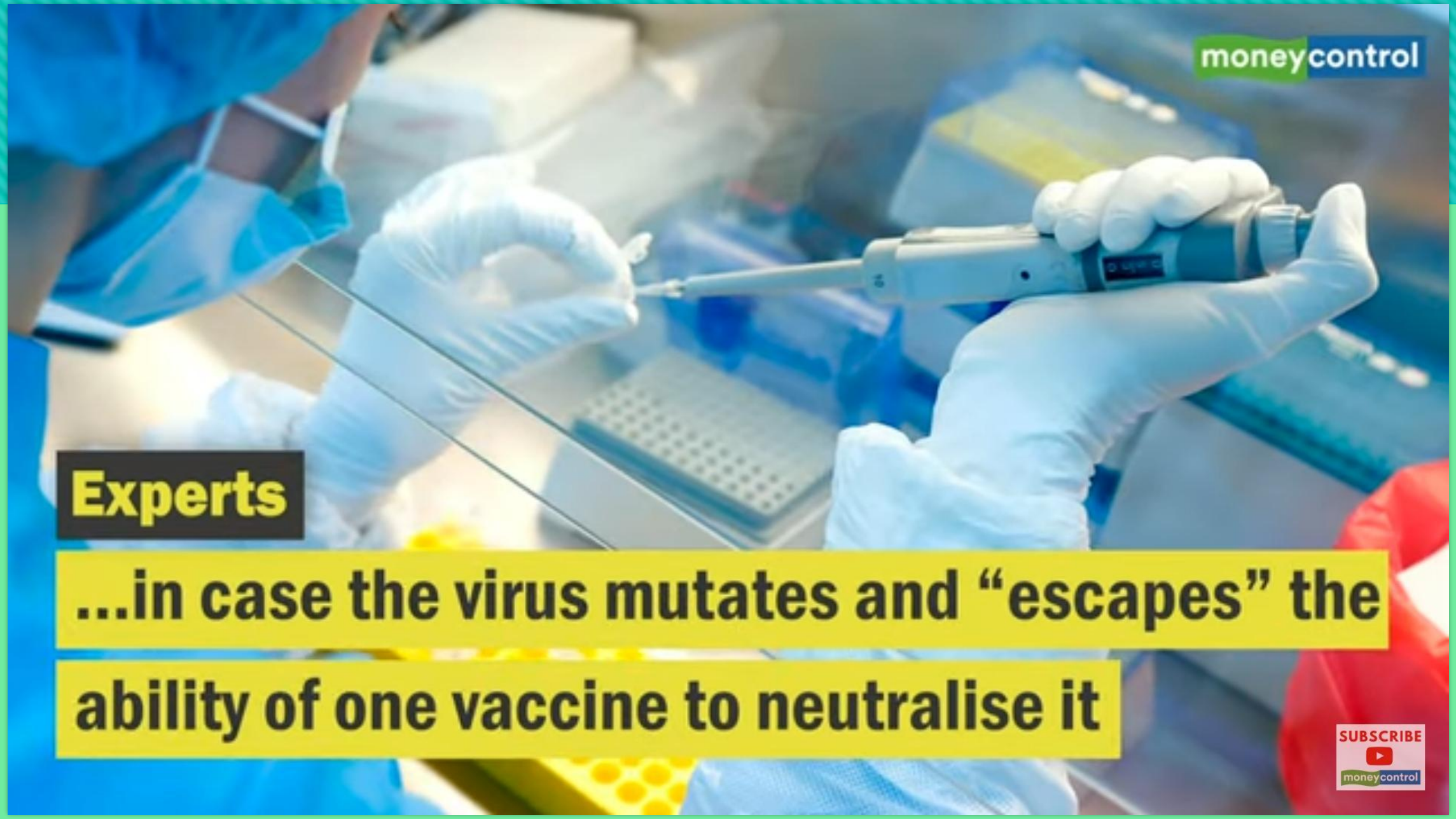
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Experts
...in case the virus mutates and “escapes” the
ability of one vaccine to neutralise it
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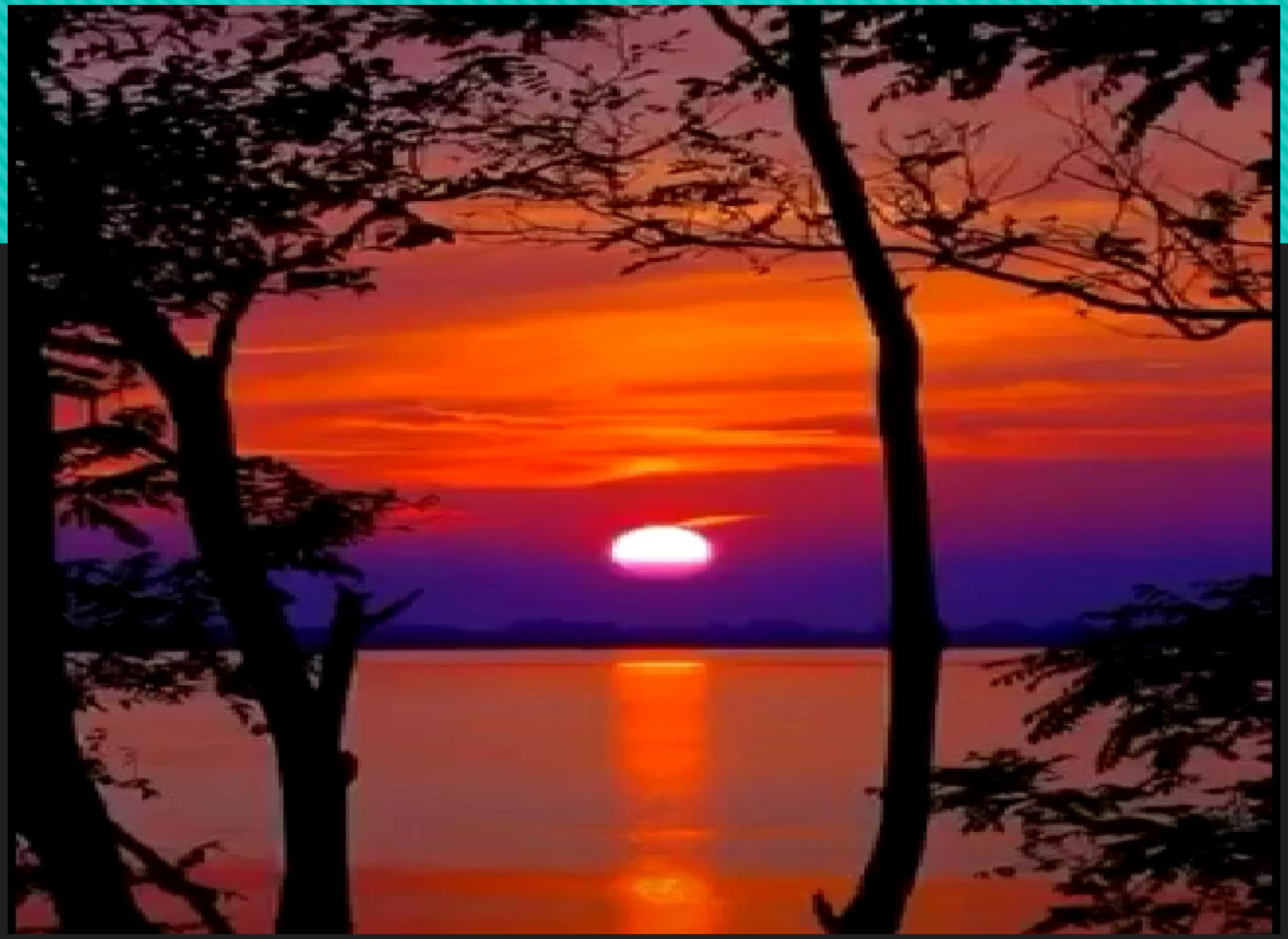
VACCINE
10ml


الإصرار على التفاؤل
قد يصنع ما كان مستحيلاً
@feda
Fado1997.tumblr



- Optimisation of the Vaccines

Reduced or increased/ one or two shots/ boost within 1, 2, or 3 years.

Mutation is possible especially when they infect the animals where they were first developed (bat,, mink) and back to humans.

200 cases reported in Denmark and Netherlands.

- Whether the Vaccines are protective,i.e prevent transmission .

,We don't know .

Some reinfection happened and secreted the virus.

The Vaccines in these trials prevented the occurrence of severe cases.

We need to continue to protect ourselves.

- About 20 trln lost because of Covid-19 compared to 20 bln spent on preparing the Vaccines.
- Duration of protection / don't know
- Safety among certain high risk population:

People with autoimmunity,People with cancer (immunocompromised , about 500000 patients) . Vaccination is important but don't know the degree of protection.These groups were not included in the trial.

- when will the general public receive the vaccine/March or April
- Rapid Ag testing.

Using slide testing like pregnancy test

If you have a gathering or family get together you can test yourself within 10 minutes. Many companies applied for authorization from US authorities (EUA)....????

- PCR could be positive after recovery, Rapid Ag checking for protein (not for RNA) so only positive when it is active infection (protein)
- Is there any more peaks or another pandemic, Yes , we need a contingency plan.

- To reach herd immunity you need to vaccinate 60-70 % of the community.
- Remdesivir(RDV) , it is an antiviral nucleotide analogue (RNA polymerase

Used in ,Ebola , SARS, MERS (not promising
Increase liver enzymes (indication of liver damage.

- Trump's treatment = Vit D , RDV + monoclonal antibodies.
- Covid-19 Vaccines timetable

*Preclinical data (Interim analytical data)... Genome sequencing , identifying the part that code for spike protein, preparing mRNA synthetically , putting mRNA inside nanolipid , add adjuvant....get the approval of FDA to go ahead with human trials. (154)

*Phase 1. Undergo safety tests for healthy people.[21]

*Phase 2. Broader group of people.[13]

*Phase 3. Large international trials to test the vaccine s impact on Covid-19[10]

- WHO/ International Consortium (Gavi/Covax) and Cepi ...to distribute the Vaccines to 190 countries .Many countries will get their Vaccines for free

Cepi (Coalition For Epidemic Preparedness Innovation) founded in Davos , Switzerland.
Headquarter , Oslo/ Norway
Founded and financed by Bill& Melinda Gate foundation, Norway ,India , Wellcome trust.
They have already paid for two billion doses of Vaccines.
They are fighting with high income countries to get their share to distribute to poor countries.

- Gavi/Covax and Cepi 2 bln doses

USA .....2 bln doses
European.....1.5 bln doses
Japan.....300 mil dose

- The advantages of mRNA Vaccines over traditional protein Vaccines.

1) design and production speed
2) low cost production
3) induction of cellular and humoral immunity...but
Required cold chain distribution &
Easy to degrade.

- placebo groups received different injections in Pfizer , Moderna and AstraZenika.
- In their trials ,checking for infection with Covid-19 after vaccination differ .?
- Is it mandatory to vaccinate?

They say NO and it is up to the person.
But , ...? ??

- Covid-19 and ethnic disparities.

In USA/ Black , Latino, then white
In UK /Black , Asian then white.
biomedical , social factors and political aspects.
Minority groups are disproportionately
affected by chronic medical conditions and lower access to health care.
Living and working conditions predisposed them to...

- Blood groups & Covid-19

A or AB are more likely to have severe Covid-19 infection than people of group B or O.

- Active smoking.

In some studies smoking increased resistance to Covid-19 infection but not in old people especially over 70 years old.
Nitrous oxide -- vasodilation
Nicotine is an anti-inflammatory

- It is a vascularity disease

High cases in people with cardiac problems and other vascular system.Massive clots appear in
Autopsies of Covid-19 infected people.

- Activation of immune system (LPS , lipopolysaccharide), or infection will lower Vit.D level. ,So in Covid-19 infection we expect low Vitamin D.
- 14000 subjects , Vit.D was checked prior to checking PCR(10.1% were positive). Vitamin D was less than 30ng/ml.
- Higher infection in 60 years and under but less hospitalization . Lower infection in over 60 years but more hospitalization.
- Affinity of Covid-19 virus to certain receptors. It attaches to(Ace 2 receptors) on the cells of the tongue, alveolar type 2 cells, pharynx and nose.
- When are we going to see the effect of Vaccination? 6-8 months
- does it protect against infection/ we don't know. Many scenarios :

1) it prevents clinically recognized disease.
2) not clinically recognizable but have the virus in nasopharynx./ don't know.
3) infected, no symptoms ---- the immune system doesn't allow the virus to replicate---- so no dissemination of the virus

- Weather and Covid-19

It is thermolabile virus/during cooking (60-70 C)
Avoid raw meat , snakes
*In one study (in cold weather become weak and die under freezing temperatures.
*Others study the virus increase in cold and dry weather.
*In the USA it increases in summer with high humidity.
*In general Respiratory diseases are seasonal but this virus does not circulate long enough to establish any potential seasonal pattern.

- Is there any rare side effects/ NO . phase 3 didn't give any information. With more people vaccinated they will appear
- Vit. D and Covid-19

It can be considered as a therapeutic not only a vitamin. It is like a steroid hormone can go inside the nucleus through a VDR (Vit. D receptor)....
Sun--dermis---previtamin D3----stored in the fat & when needed ---to the kidneys where they will be changed to the active form.
It will bind to the immune cells.
Viral infection increased in the north of 35 parallel .

- inverse relationship of Vit.D and BMI

(Body mass index)
Obese people need more Vit.D
#BMI 25 ---no supplement over the daily dose.
BMI 26-30--1.5 the regular dose
BMI over 30 you need to take three times the daily dose.

- Old age and Vit.D.

- Companies working or producing Covid-19 Vaccines:

Pfizer- Biontech, Moderna, AstraZenika، Johnson & Johnson, Novavax, Sanofi , Glaxosmithkline, Sinofarm, Sinovac,CanSino Biologics , SII, Bharat Biotech

- In an interview Americans say

  60% yes [they will take the vaccine]

  18% unwilling to take (probably they will change).

  22% are pretty sure they won't take Covid-19 vaccine.

- Side effect of the Vaccines during trials :

Arm pain, fatigue ,fever ,chills , nausea, headache .

Lymphadenopathy :

64 in vaccinated

06 in placebo

04 got Bell's palsy (in vaccinated)

You trust us with your penis.

Trust our vaccine.