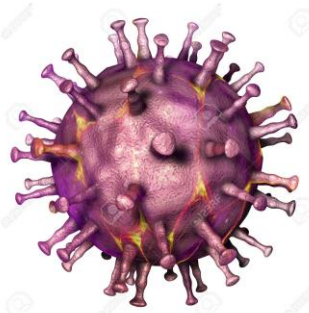
UNIWERSYTET MEDYCZNY
IM. PIASTÓW ŚLĄSKICH WE WROCŁAWIU






Subject: Faculty Lectures of Virology
Topic: Prophylaxis of Viral Infections

Academic Year 2024/2025

Faculty: Medicine
Field of study: Virology
Level of study (uniform MA):
Form of study (full time):
Year of study: III

Academic title/professional title: professor
Name, last name of the lecturer: Beata Sobieszczańska
Position of person conducting classes: teacher
Wroclaw Medical University

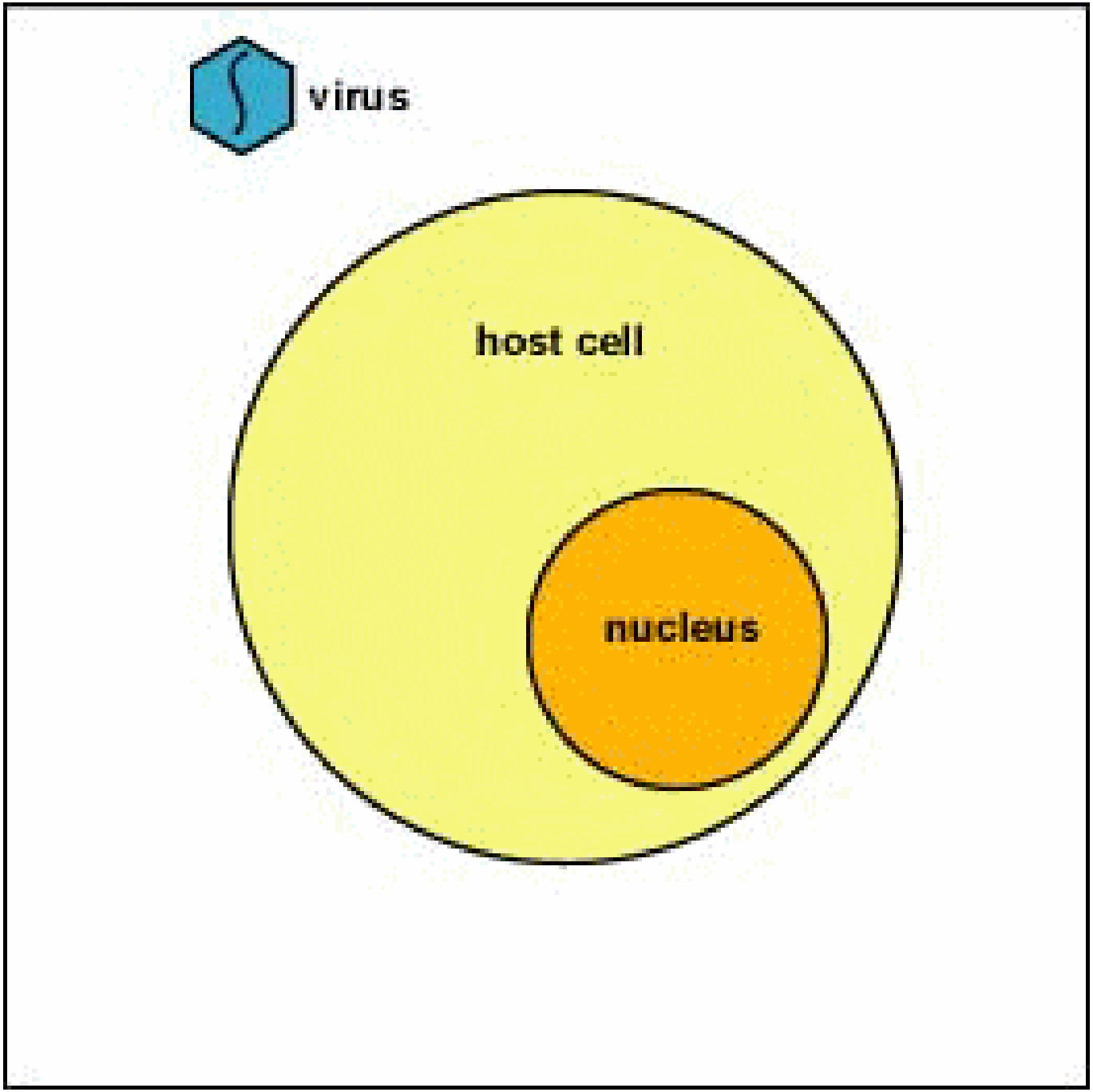
HOST DEFENSE AGAINST VIRAL INFECTION

Table 14.5 The interferons: antiviral cytokines

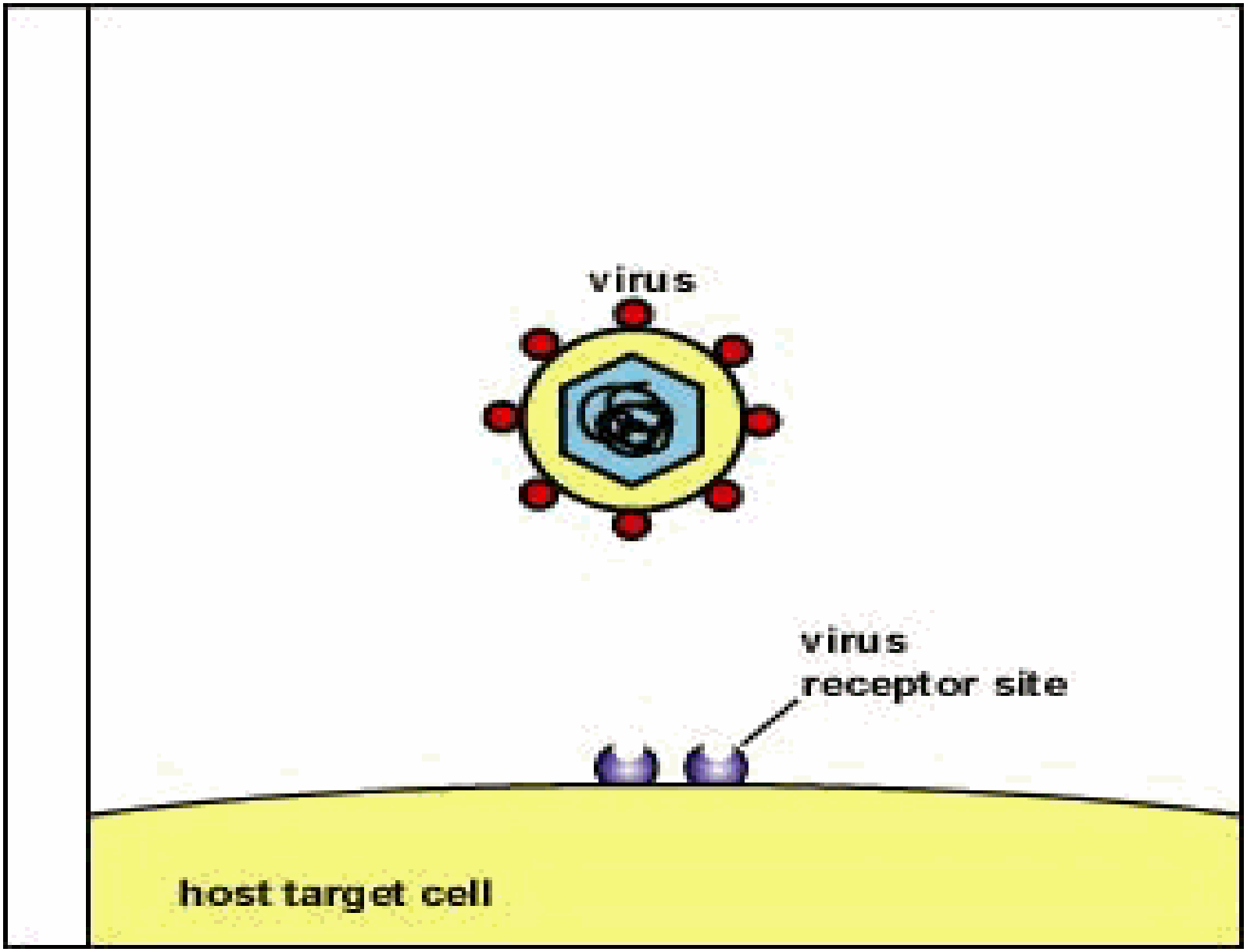
Interferon[a]	Producer cells	Inducers
Ifn-α	Leukocytes	Virus infection, dsRNA
Ifn-β	Fibroblasts, epithelial cells	Virus infection, dsRNA
Ifn-γ	T cells, NK cells	Antigens, mitogens, Il-2, Il-12

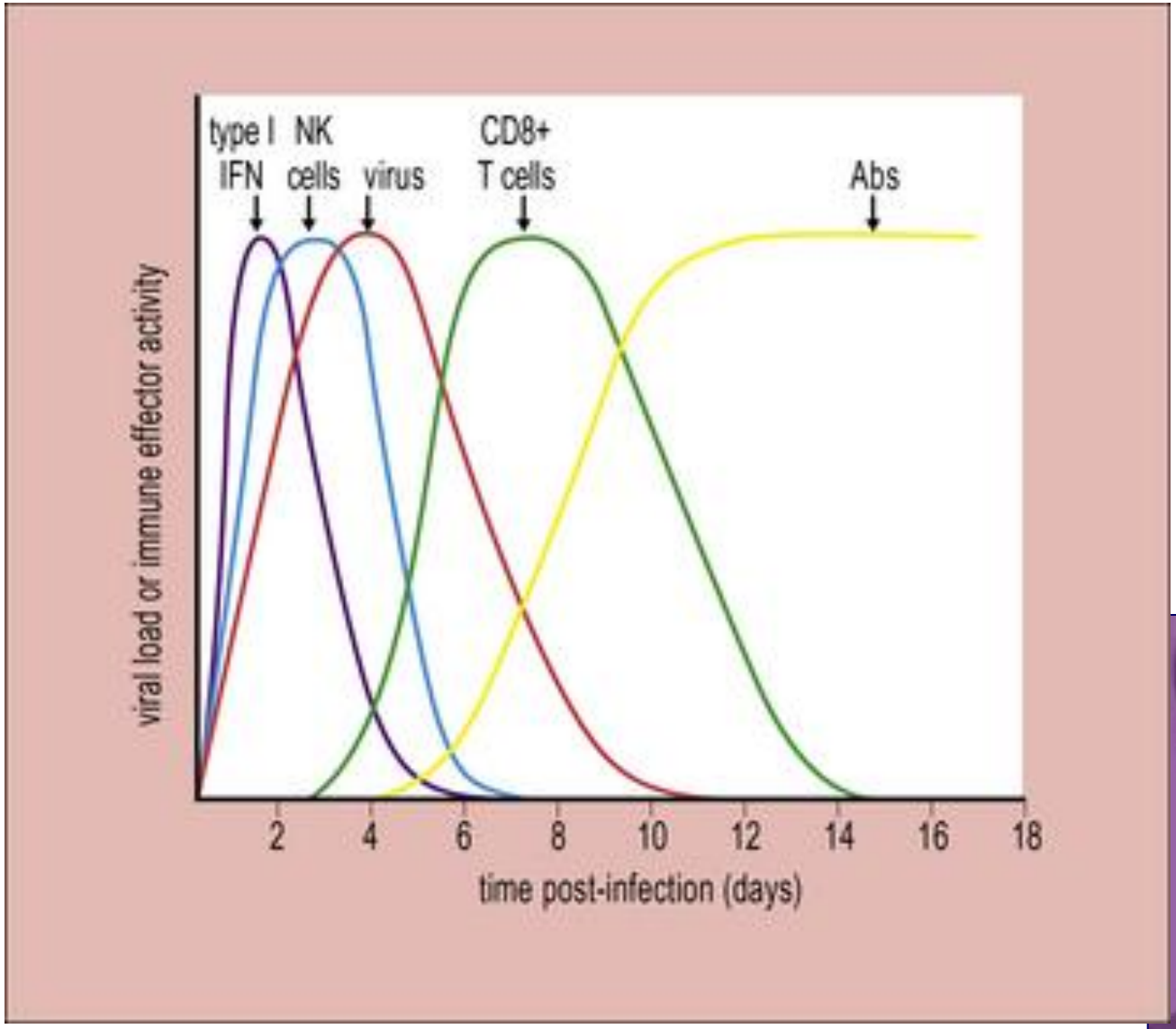
IFNγ is induced only when certain lymphocytes are stimulated to replicate and divide after binding a foreign antigen

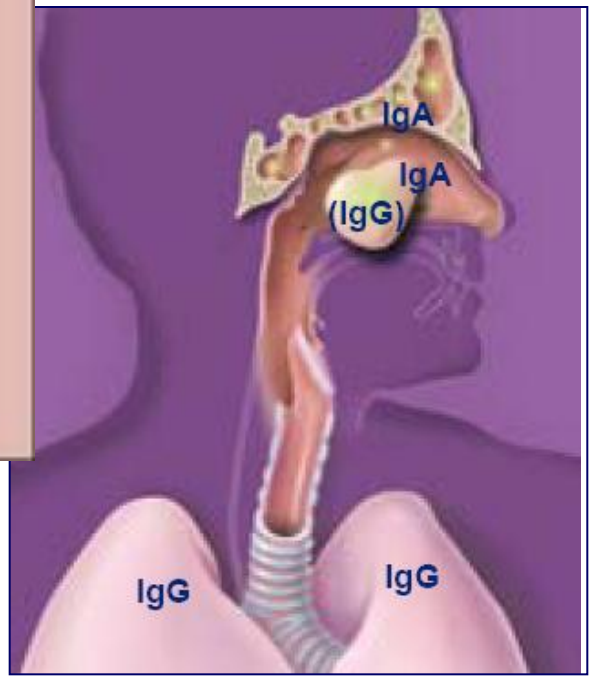
IFNα and IFNβ are induced by viral infection of any cell type


virus
host cell
nucleus

ANTIBODIES




type I IFN
NK cells
virus
CD8+ T cells
Abs
viral load or immune effector activity
2
4
6
8
10
12
14
16
18
time post-infection (days)


IgA
IgA
(IgG)
IgG
IgG

A vaccine is a substance that teaches the body to recognize and defend itself against bacteria and viruses that cause disease

A vaccine induces an immune response, preparing the body's immune system to fight and also to remember how to fight if exposed to a specific infection

A vaccine is not a cure, rather, it prevents infection or slows disease progression

Vaccines

Immunity to viral infections depends on the development of an immune response to:

- Antigens on the virus surface
- Antigens on the virus-infected cell

Vaccines establish immunity and memory without the pathologic effects that normally accompany infection

Immune memory = the presence of specifically dedicated T and B lymphocytes that remain after an infection (or following immunization) and maintain a heightened ability to respond further challenge

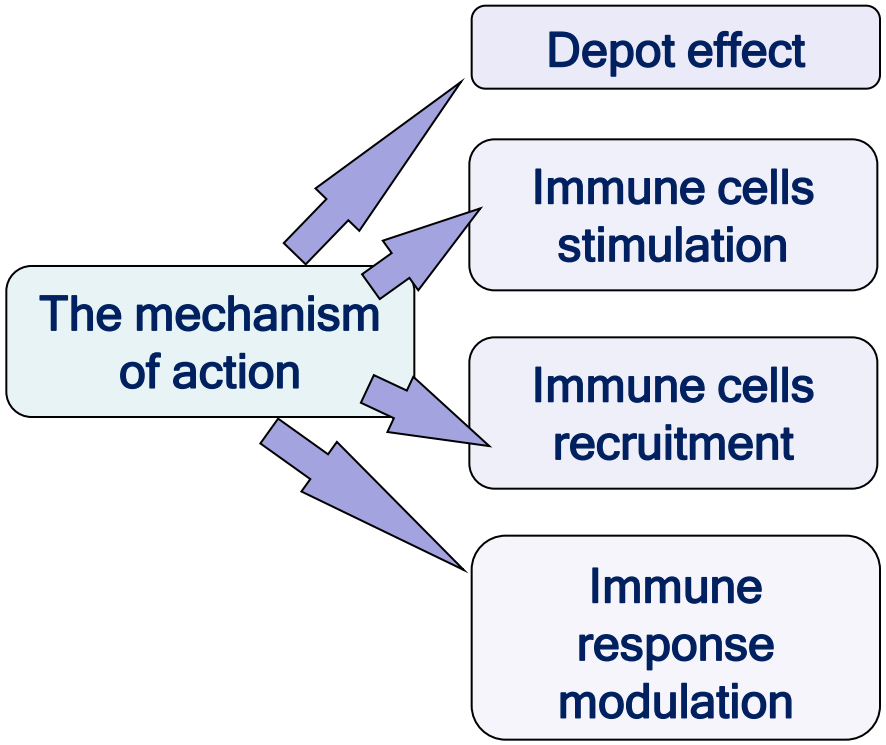
Adjuvants

Indispensable components of the vaccines that potentiate the immune response to the antigen and/or modulate it toward the desired immune response

Adjuvants increase vaccine efficacy

Examples: PLGA, polymers, nanoparticles, nanosomes, and other

Improve immune responses in weaker populations: infants, the elderly, and immunocompromised patients



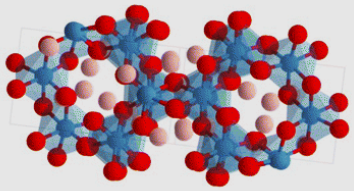
Slow release, prolonged exposure to the antigen

Triggering immune cells to activate = a stronger immune response

Attract immune cells to the site of introduction

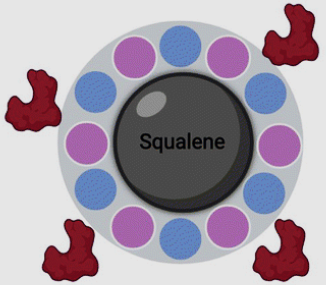
The impact on the type of immune response: humoral (B cells), cell-mediated (T cells)

a) **Aluminum salts**
(aluminum oxyhydroxide, aluminum phosphate)



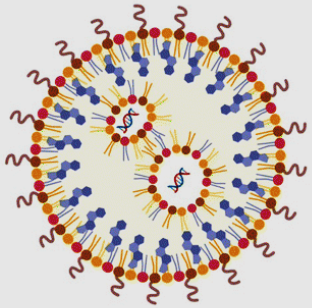
b) **Inorganic nanoparticles**
(nano-aluminum, silica, nanodiamond)

c) **Emulsions**
(MF59, AS03, AF03, SE)

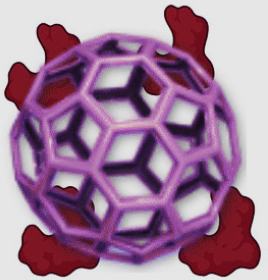


d) **TLR agonist-based**
(CpG-ODN, AS04)

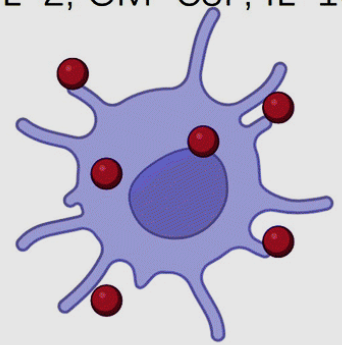
e) **Lipid-based**
(GLA-SE, GLA-AF)



f) **Saponin**
(Matrix M™, AS02)

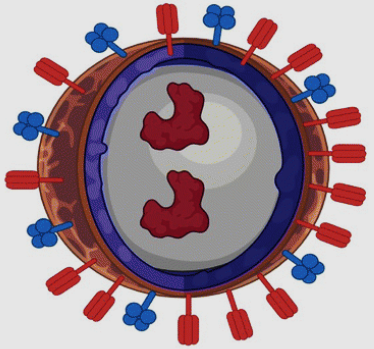


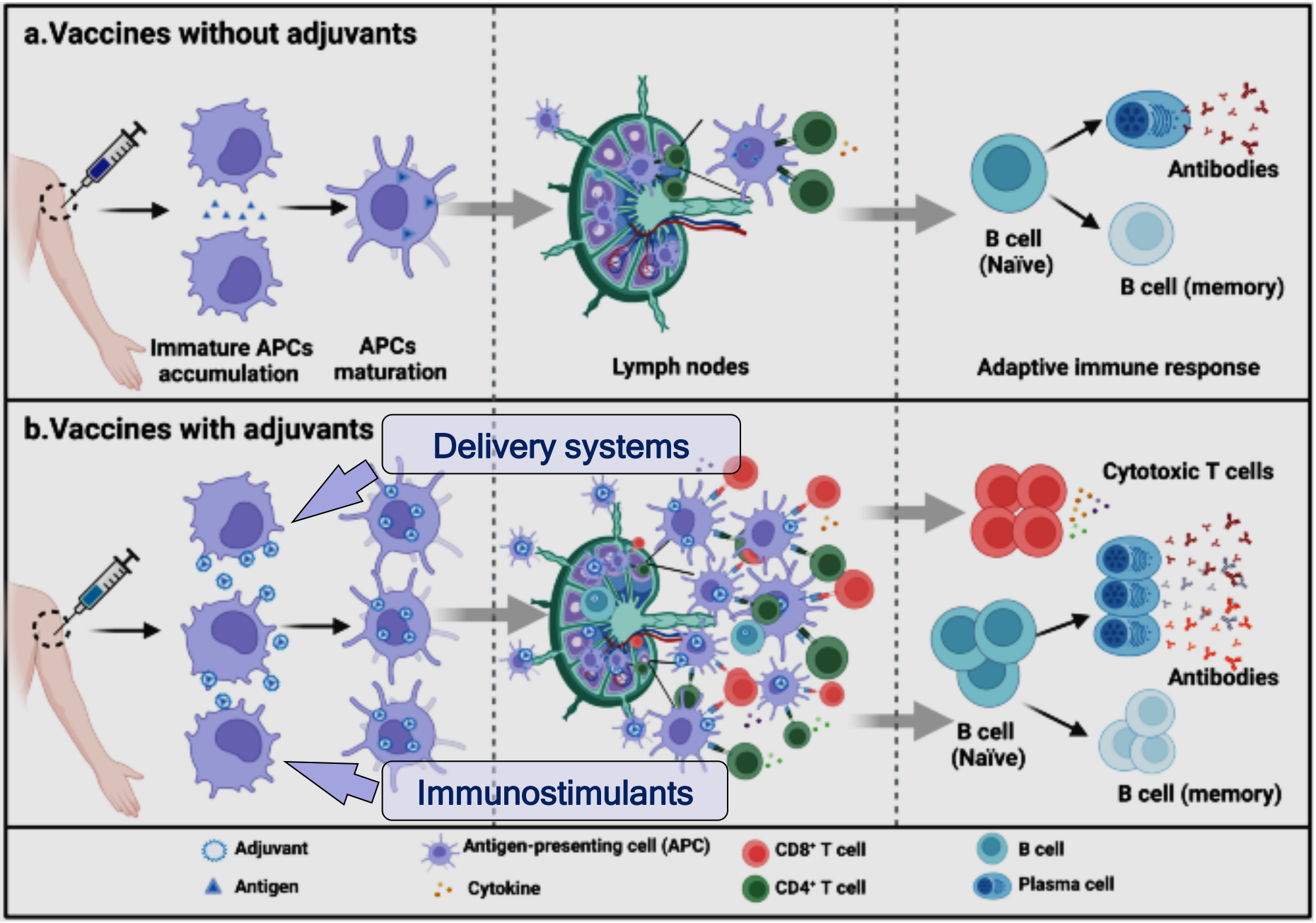
g) **Cytokines**
(IL-2, GM-CSF, IL-15)

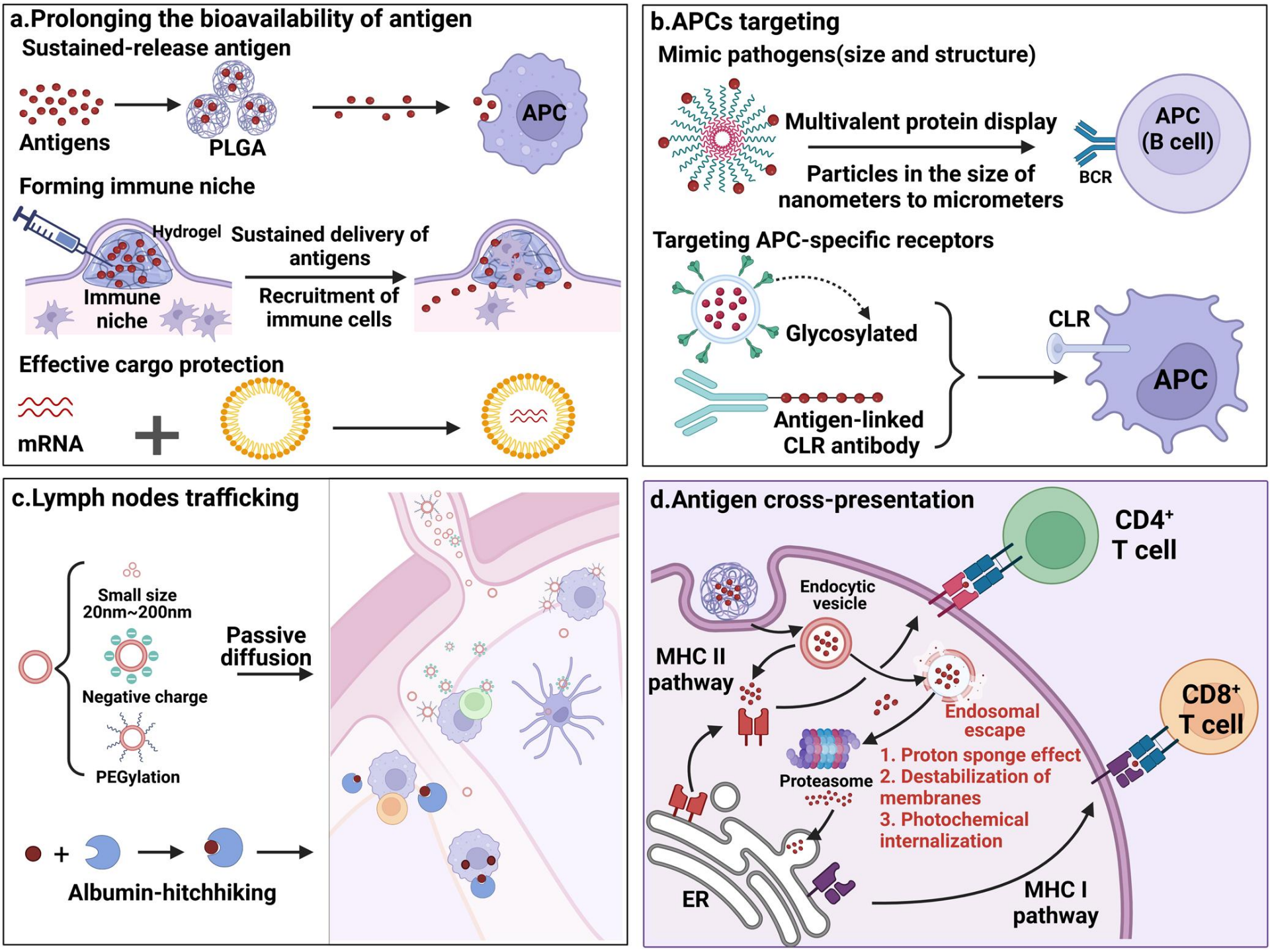


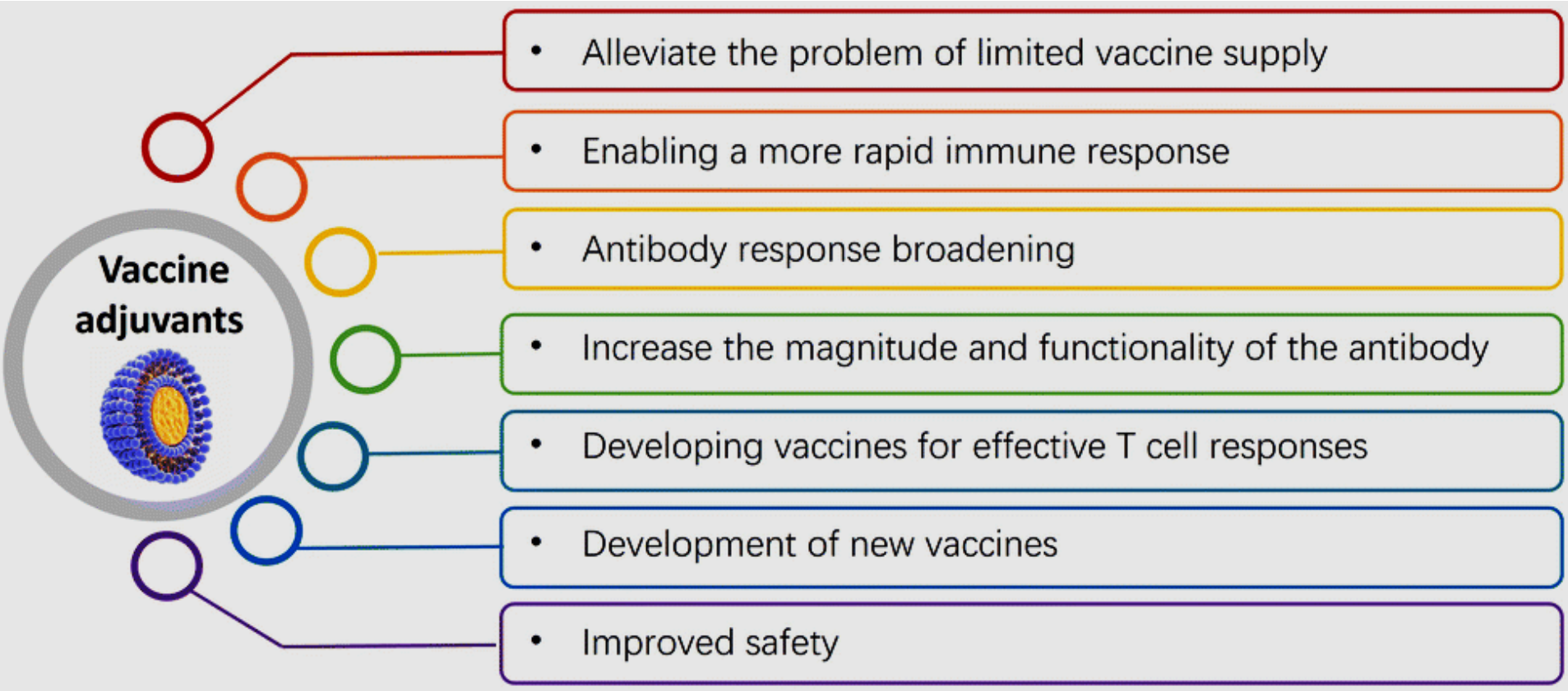
h) **Nucleotide**
(dsRNA, IL-12 DNA)

i) **Virosomes**

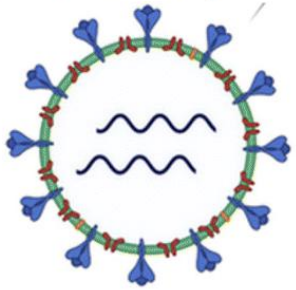



a.Vaccines without adjuvants
Immature APCs accumulation
APCs maturation
Lymph nodes
Antibodies
B cell (Naïve)
B cell (memory)
Adaptive immune response
b.Vaccines with adjuvants
Delivery systems
Immunostimulants
Cytotoxic T cells
Antibodies
B cell (Naïve)
B cell (memory)
Adjuvant
Antigen
Antigen-presenting cell (APC)
Cytokine
CD8⁺ T cell
CD4⁺ T cell
B cell
Plasma cell

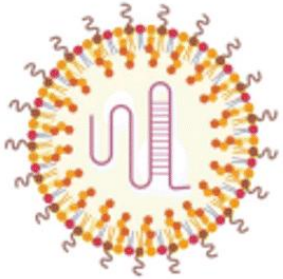

a.Prolonging the bioavailability of antigen
Sustained-release antigen
Antigens
PLGA
APC
Forming immune niche
Hydrogel
Immune niche
Sustained delivery of antigens
Recruitment of immune cells
Effective cargo protection
mRNA
b.APCs targeting
Mimic pathogens(size and structure)
Multivalent protein display
Particles in the size of nanometers to micrometers
APC (B cell)
BCR
Targeting APC-specific receptors
Glycosylated
Antigen-linked CLR antibody
CLR
APC
c.Lymph nodes trafficking
Small size 20nm~200nm
Negative charge
PEGylation
Passive diffusion
Albumin-hitchhiking
d.Antigen cross-presentation
CD4+ T cell
Endocytic vesicle
MHC II pathway
Endosomal escape
1. Proton sponge effect
2. Destabilization of membranes
3. Photochemical internalization
CD8+ T cell
Proteasome
ER
MHC I pathway


Vaccine adjuvants
• Alleviate the problem of limited vaccine supply
• Enabling a more rapid immune response
• Antibody response broadening
• Increase the magnitude and functionality of the antibody
• Developing vaccines for effective T cell responses
• Development of new vaccines
• Improved safety

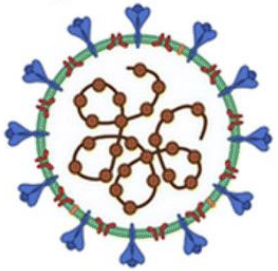
a) Inactivated vaccine
(Sinovac, Sinopharm)



g) mRNA vaccine
(Moderna, BioNTech)

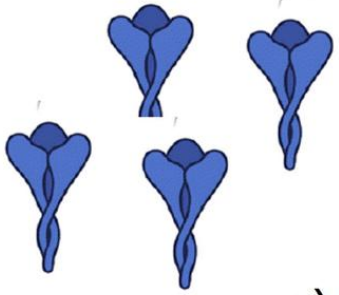


b) Live attenuated vaccine
(Codagenix, Ankara)

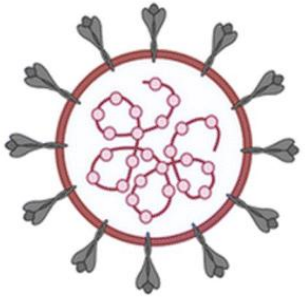


Vaccine

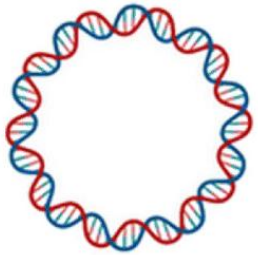
f) Recombinant subunit vaccine
(Novavax, Vaxine)



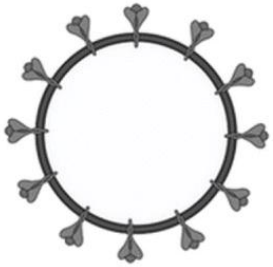
c) Viral vector vaccine
(Oxford, CanSino)



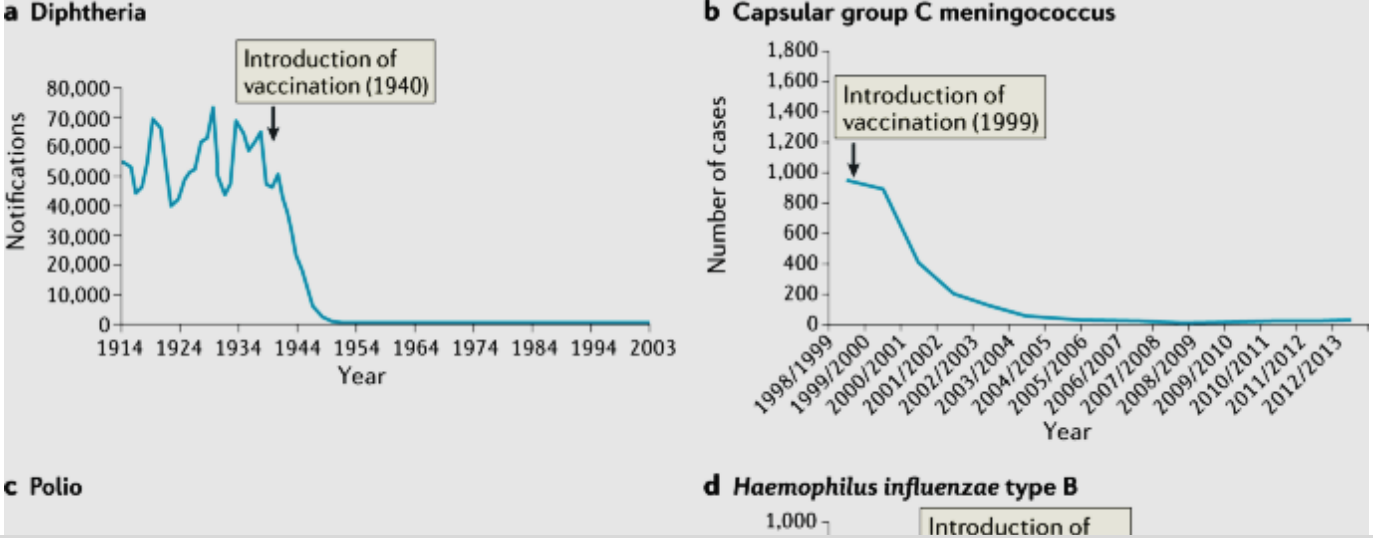
e) DNA vaccine
(Inovio, Zydus Cadila)



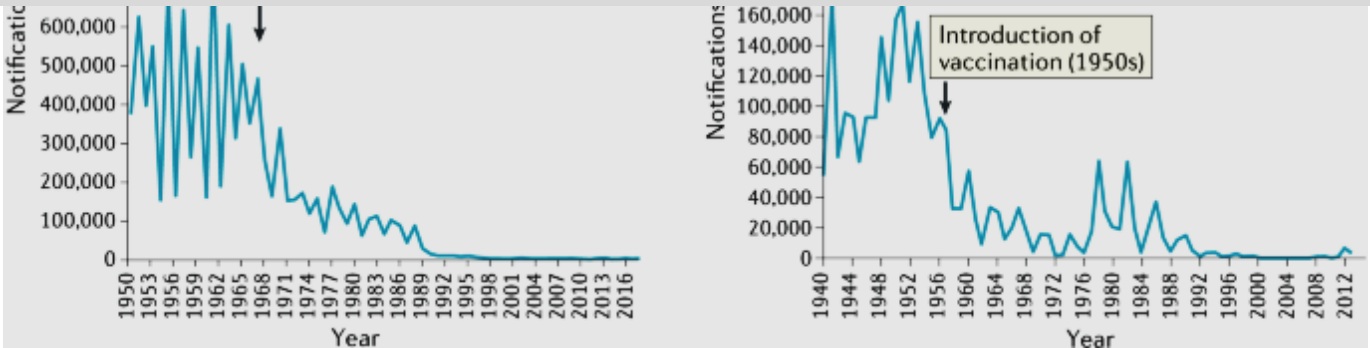
d) Virus-like particles vaccine
(Oxford, CanSino)



Vaccinia, the first-ever vaccine which protects against smallpox, is actually where we get the term ‘vaccination’ from



2-3 million lives are saved each year by current immunization programmes, contributing to the marked reduction in mortality of children less than 5 years of age globally from 93 deaths per 1,000 live births in 1990 to 39 deaths per 1,000 live births in 2018



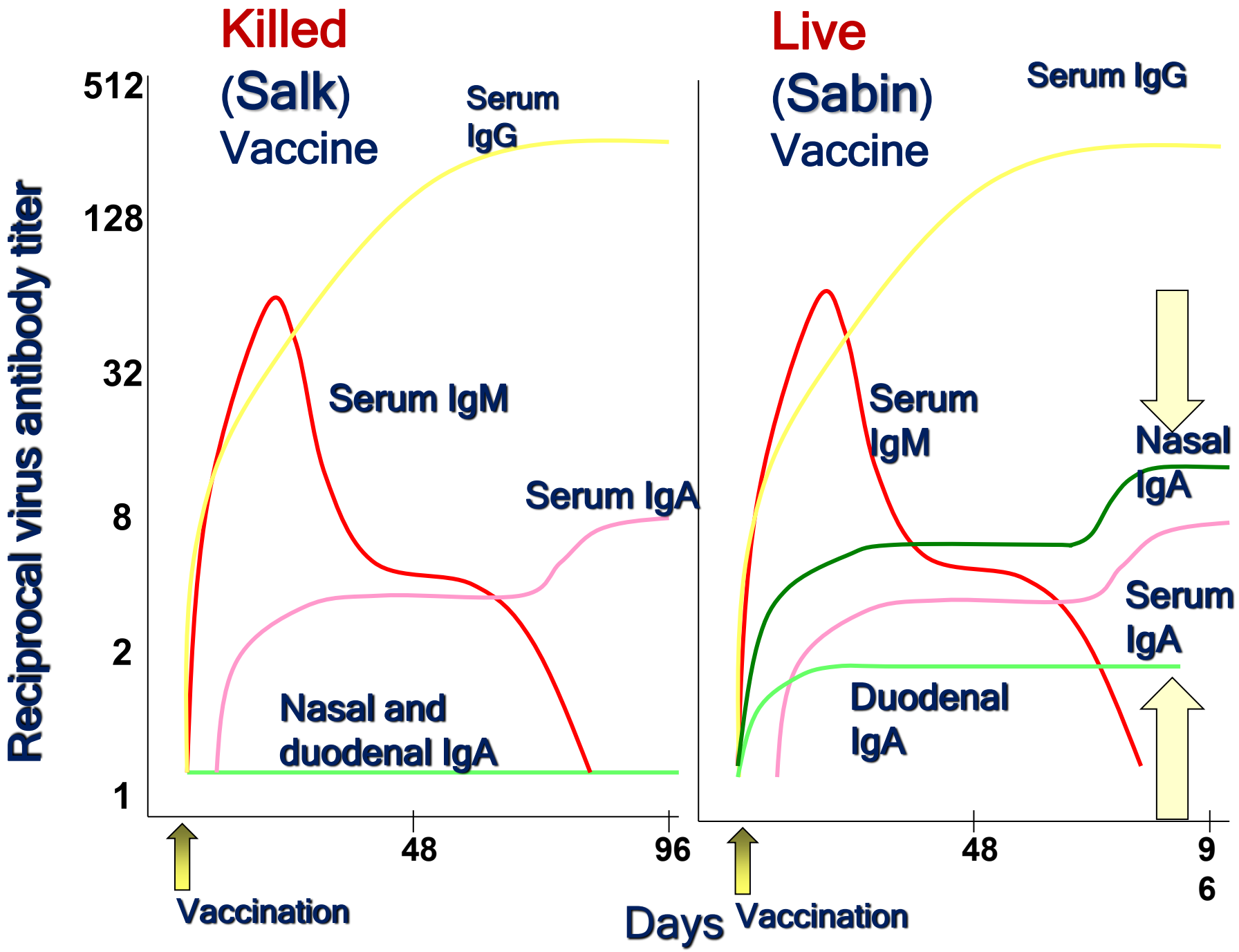
Inactivated vs attenuated vaccines

Inactivated (killed):

- stable
- safe
- cannot revert to the virulent form
- often do not require refrigeration (practical in use in developing countries)
- most stimulate relatively weak responses and so must be given more than once
- usually do not stimulate robust cellular immune responses (important in controlling disease)

Live, attenuated:

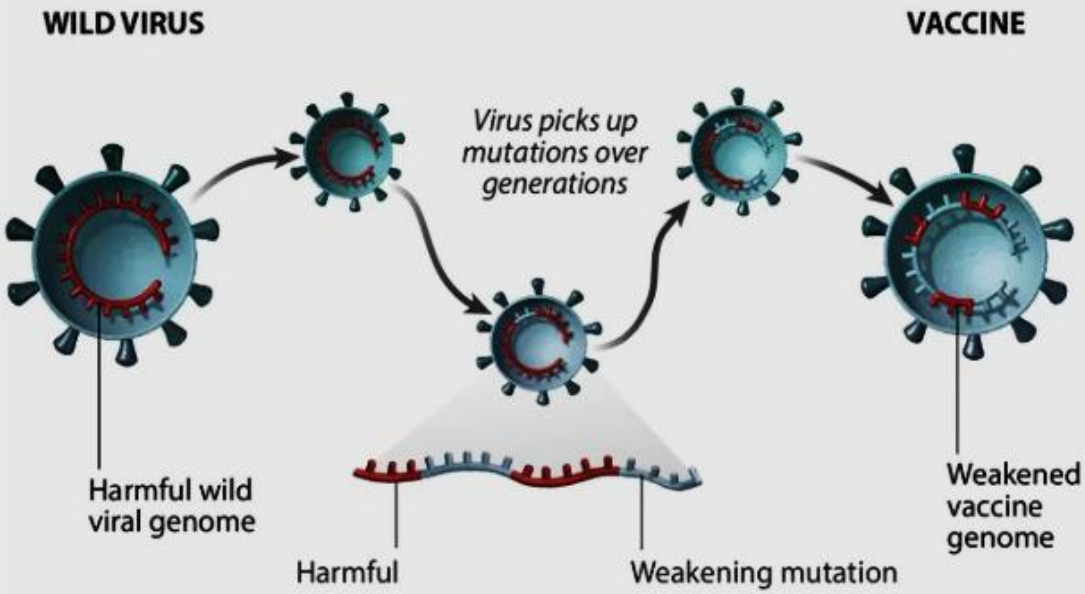
- can stimulate robust T and B cell responses
- mimic natural infection
- usually require special handling and storage
- can mutate in a way that restores wild-type virulence


Killed
(Salk)
Vaccine
Live
(Sabin)
Vaccine
Reciprocal virus antibody titer
512
128
32
8
2
1
Serum IgG
Serum IgM
Serum IgA
Nasal and duodenal IgA
Serum IgG
Serum IgM
Nasal IgA
Serum IgA
Duodenal IgA
48
96
48
96
Vaccination
Vaccination
Days

Live attenuated vaccines

What are Live, Attenuated Vaccines?

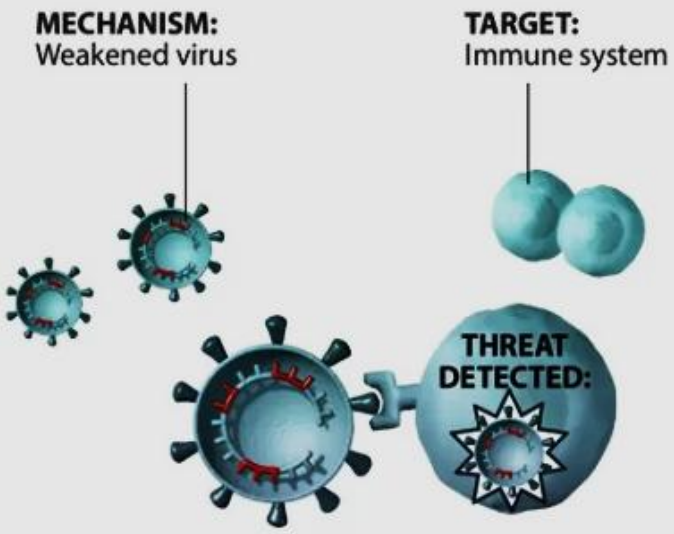
Live vaccines are "wild" viruses or bacteria that have been weakened.* In the lab, generally the virus is passed through many generations of cells to pick up genetic mutations which weaken it - so much it won't cause disease in your body.



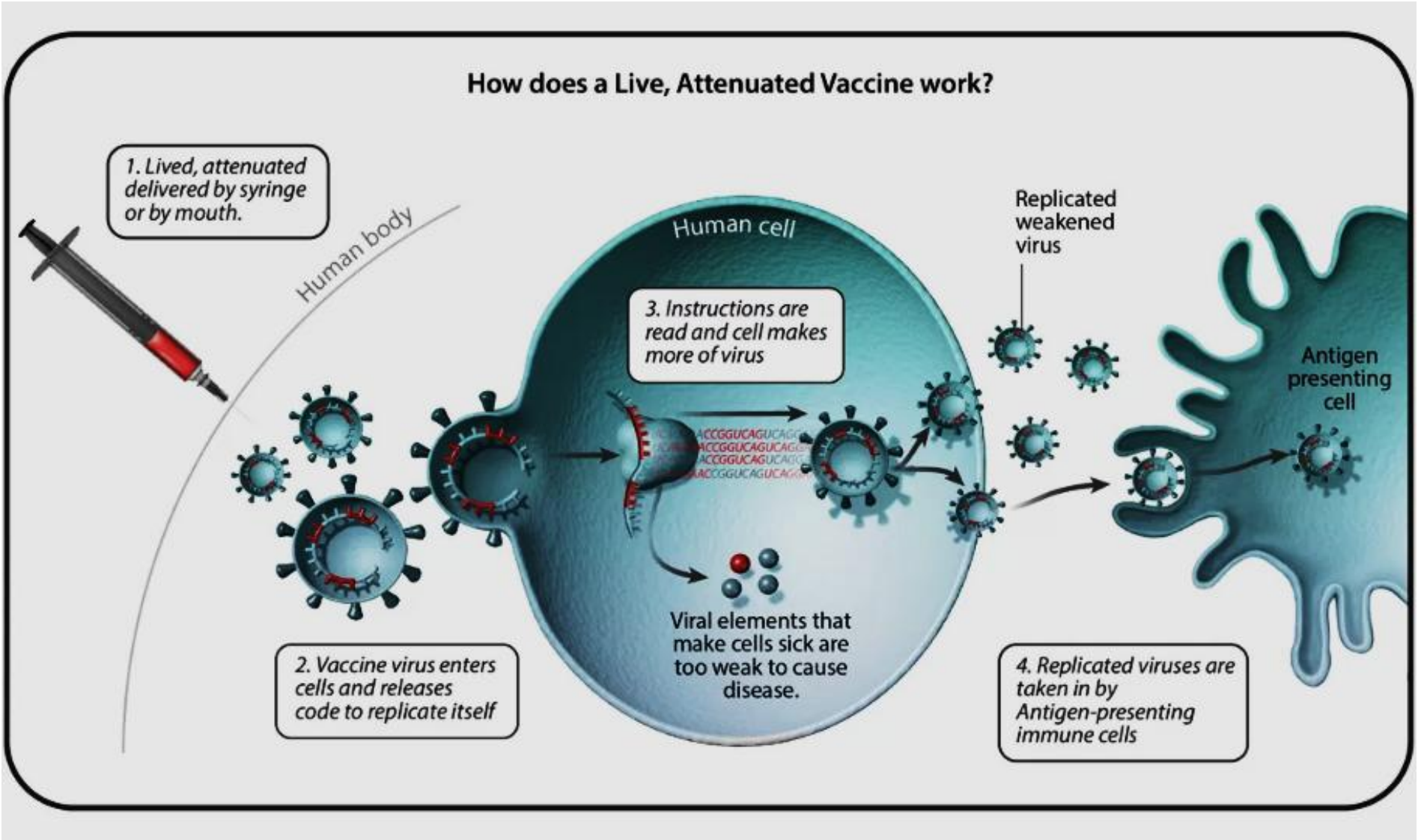
*Did You Know?: "Attenuated" means weakened.

Vaccine Target

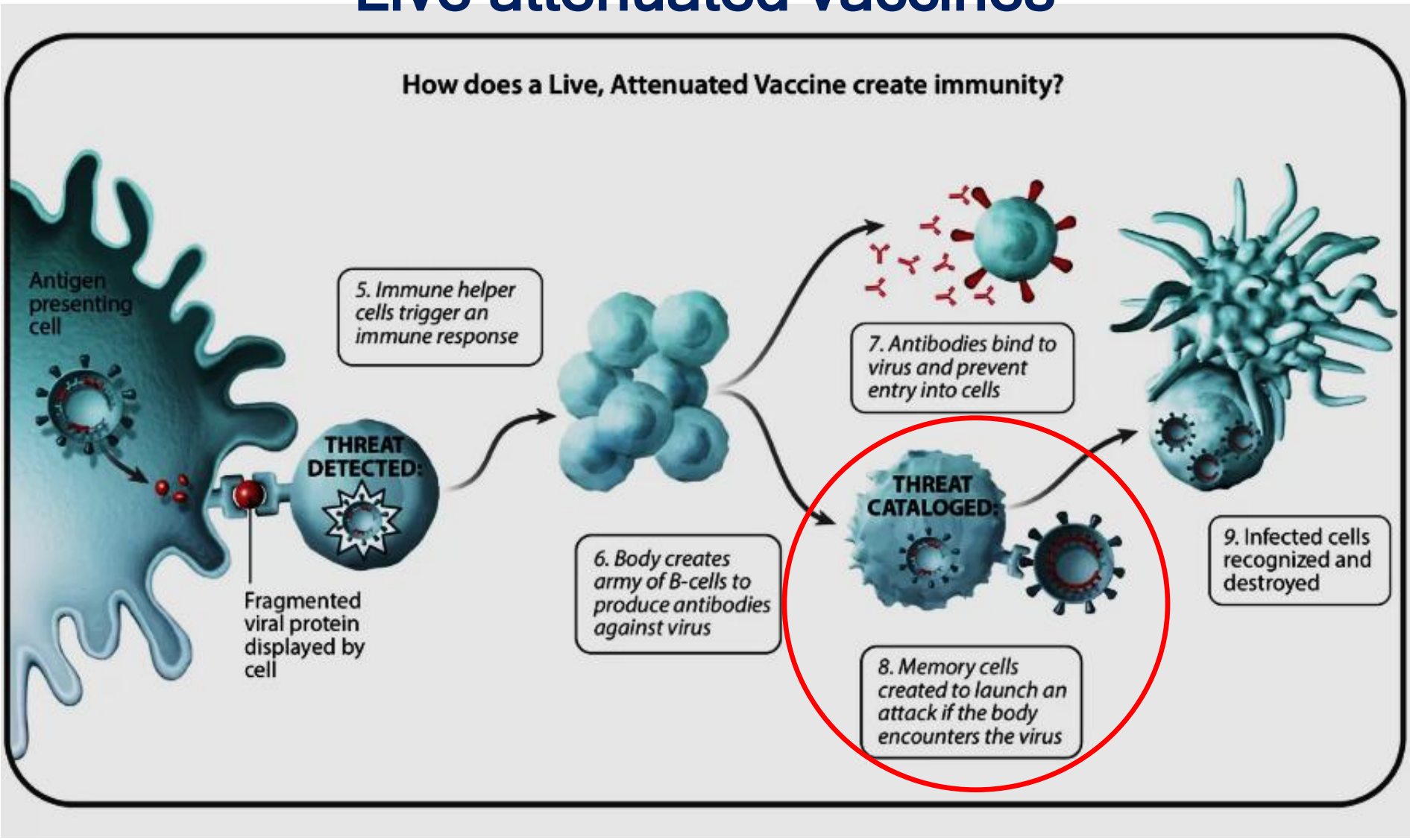
Live, attenuated vaccines target your body's immune system directly. They are strong enough to trigger the immune response, but too weak to cause disease.



Live attenuated vaccines



Live attenuated vaccines

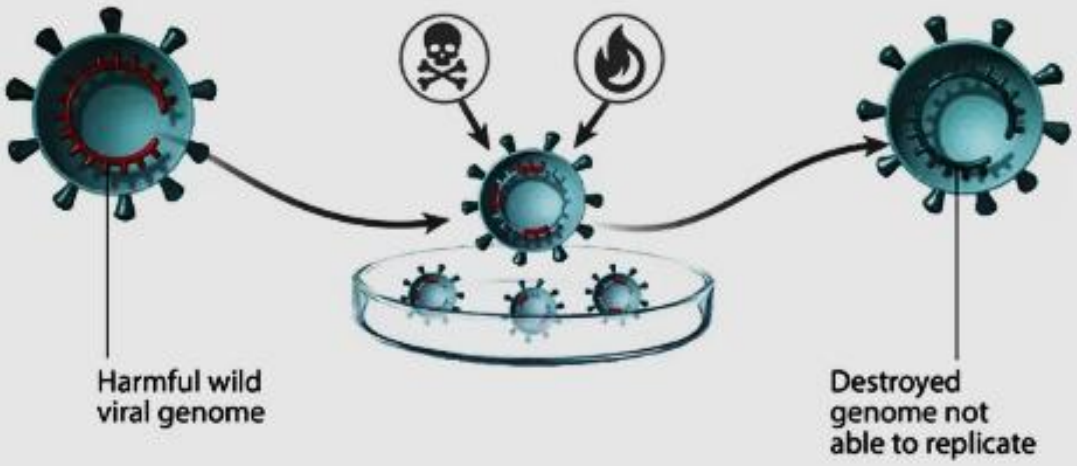


Examples: Measles, mumps, and rubella (MMR), varicella (chickenpox), flu, yellow fever, oral polio, Japanese encephalitis vaccines

Inactivated vaccines

What are Inactivated Vaccines?

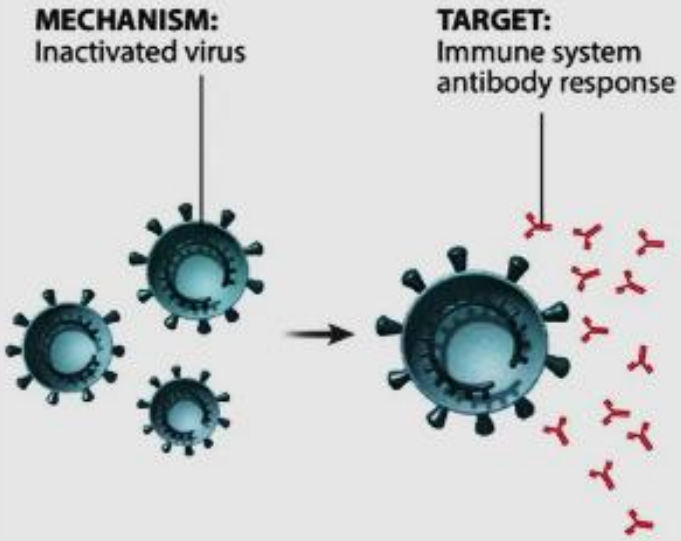
Live vaccines are "wild" viruses or bacteria that have been inactivated.* In the lab, a wild virus is "killed" with heat or chemicals so it cannot replicate or cause disease in your body, and is safe for immunodeficient people.



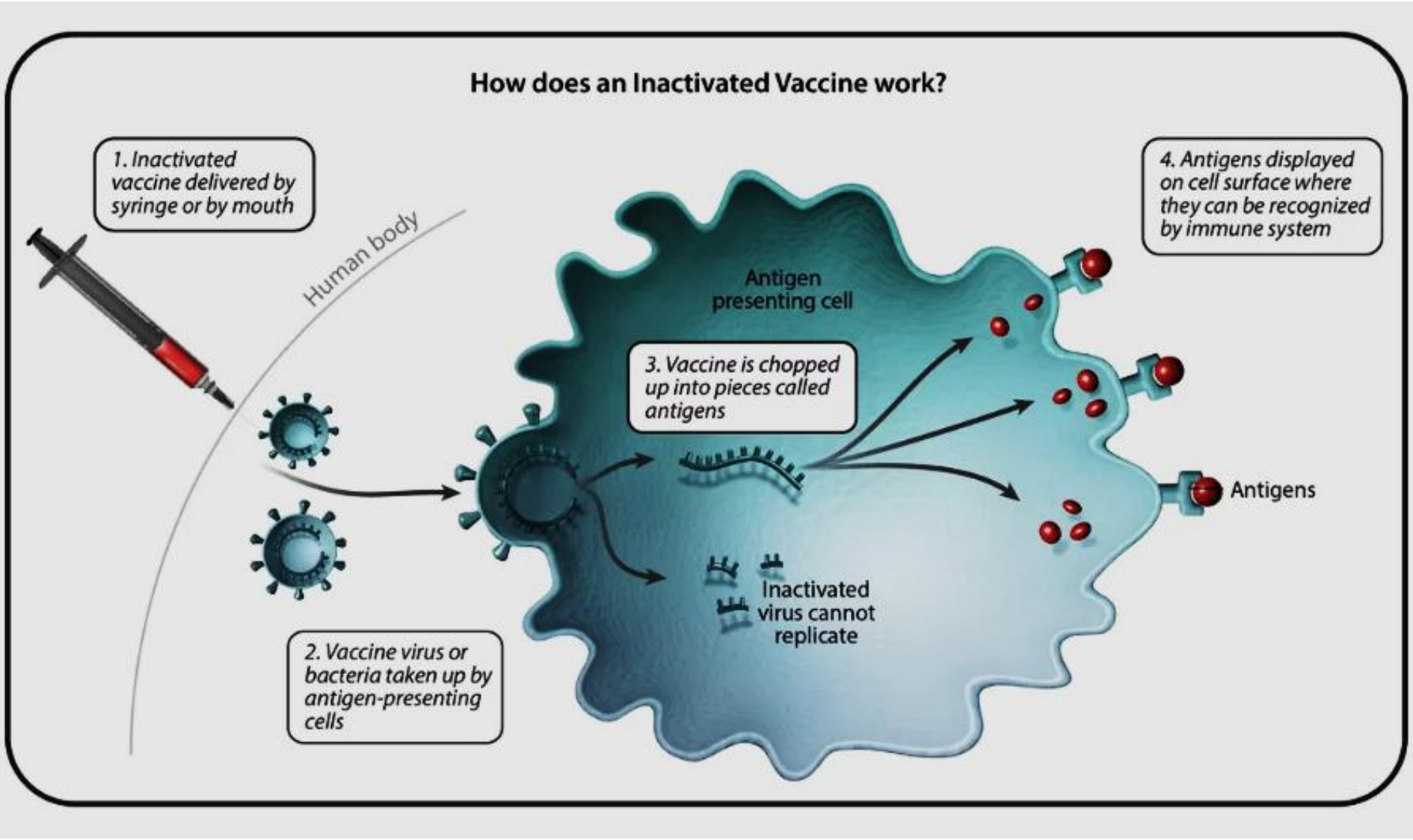
*Did You Know?: "Inactivated" means the virus cannot replicate or cause harm.

Vaccine Target

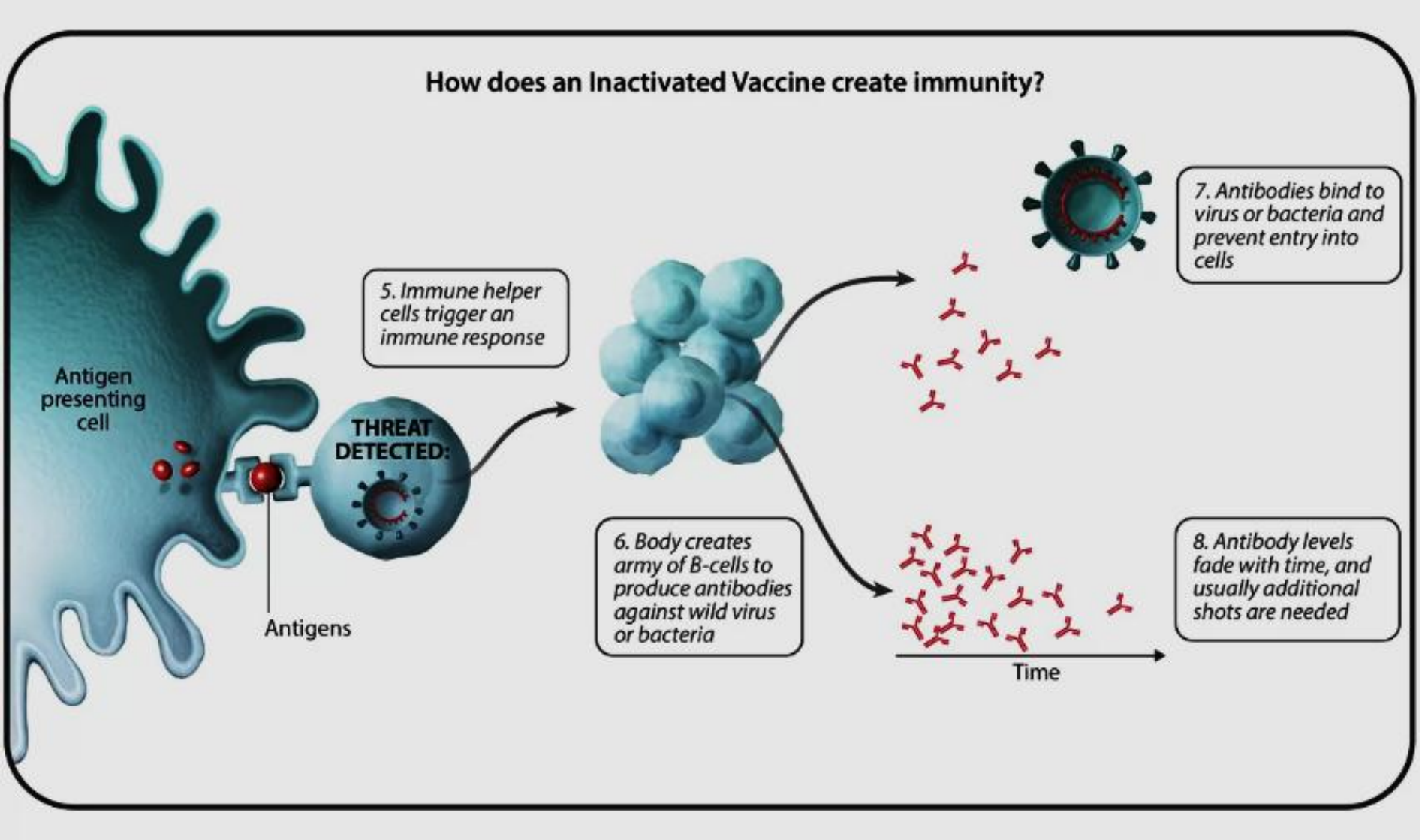
Inactivated vaccines target your body's antibody production. This is weaker than natural infection or live vaccines, so inactivated vaccines often require multiple doses.



Inactivated vaccines



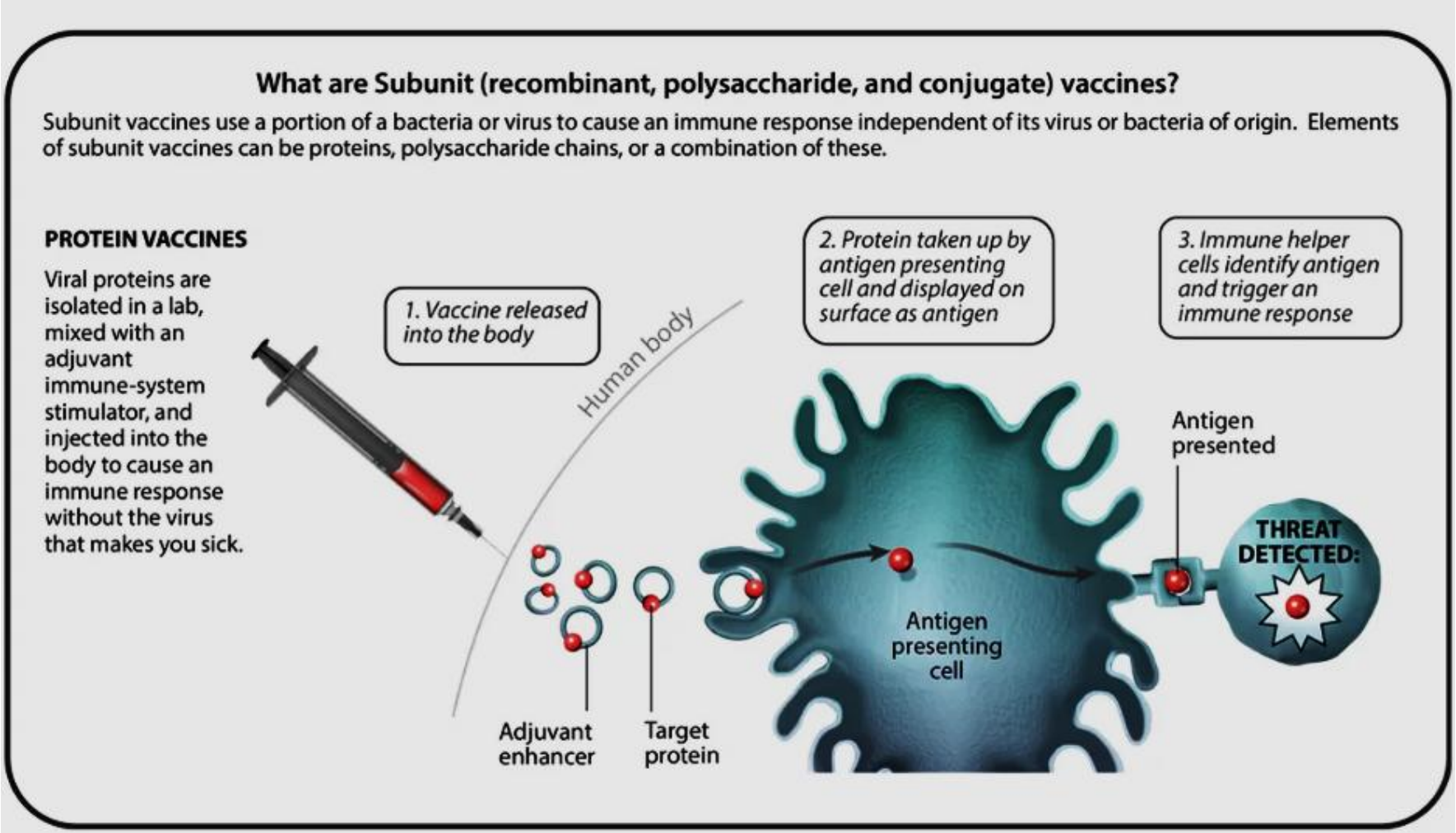
Inactivated vaccines



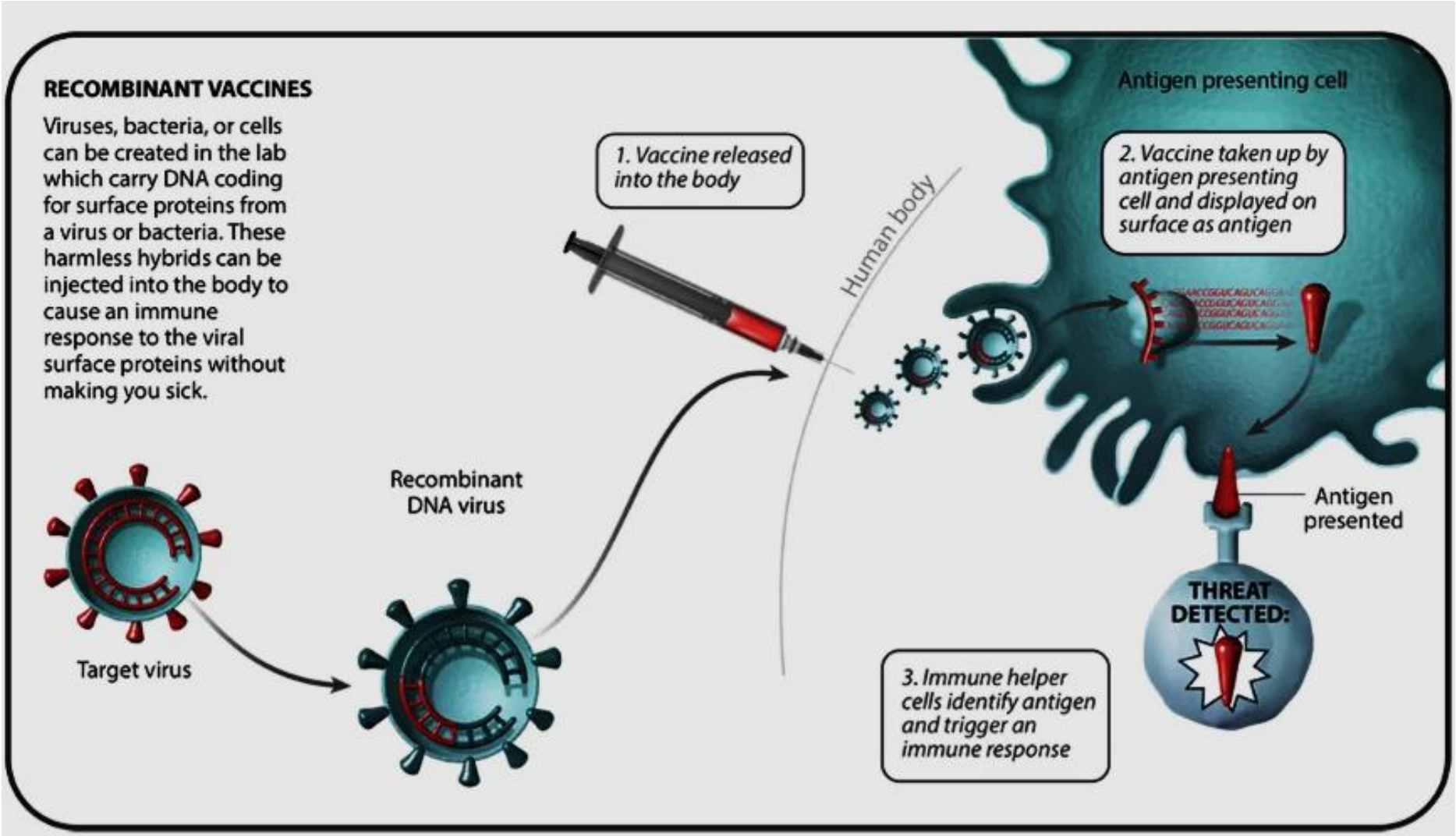
Examples: Polio vaccine, influenza, Japanese encephalitis, HAV, rabies vaccines

Subunits vaccines

Subunit vaccines only contain pieces of a pathogen, not the whole organism, so they cannot cause infection - suitable for people who should not receive “live” vaccines, such as young children, older people, and immunocompromised individuals

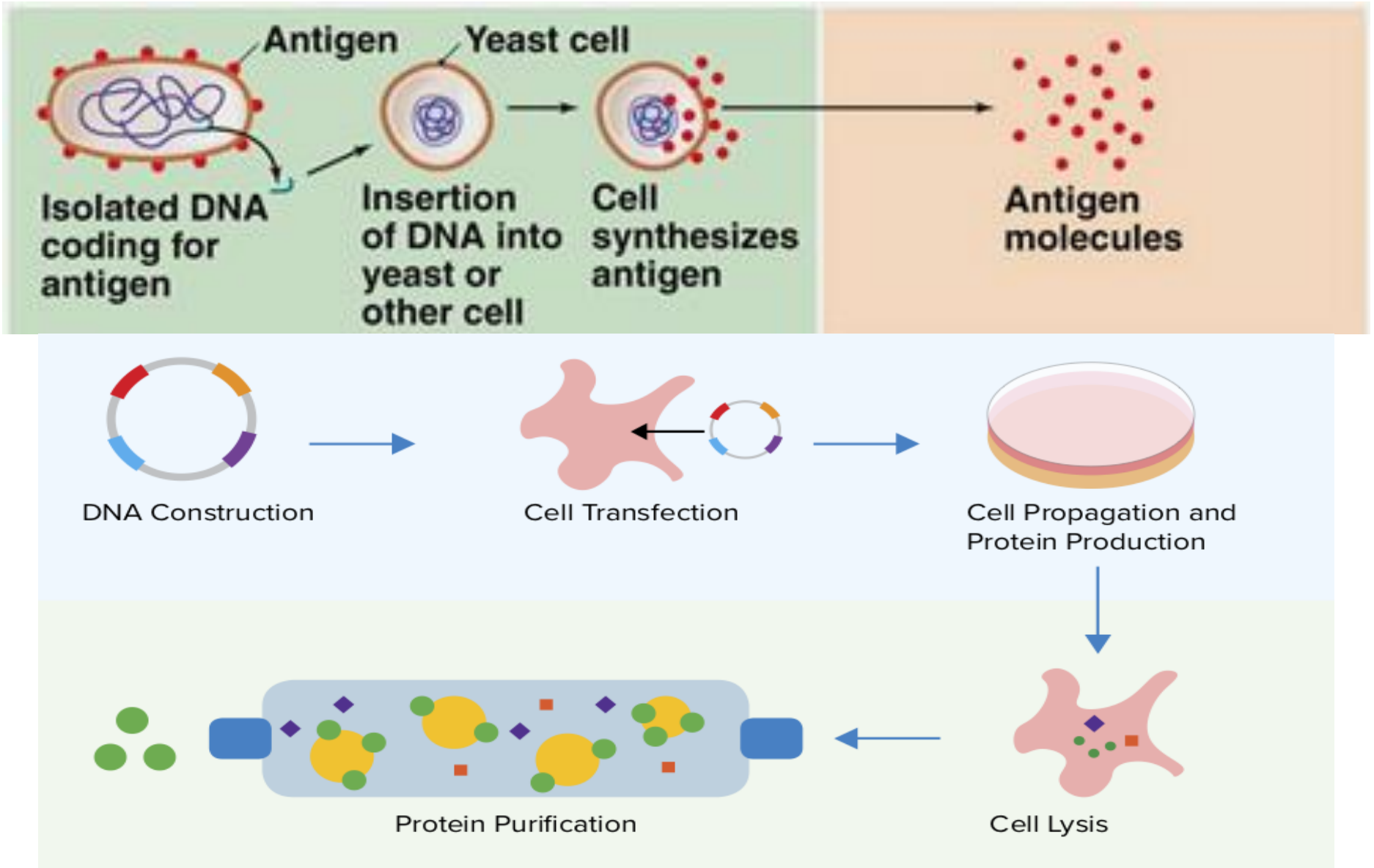


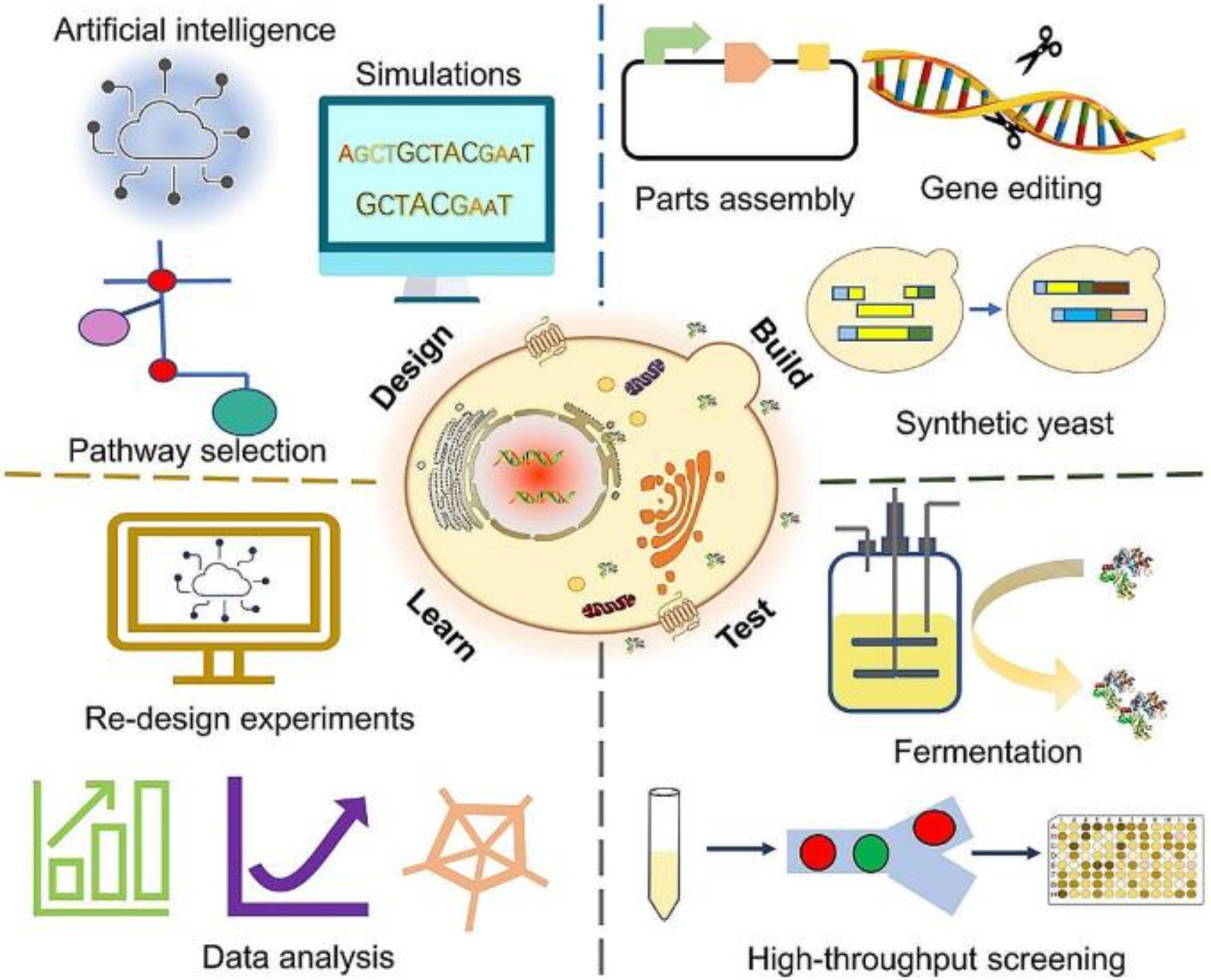
Subunits vaccines



Examples: shingles vaccine (recombinant protein), HBV, HAV (recombinant protein), flu, and many antibacterial vaccines

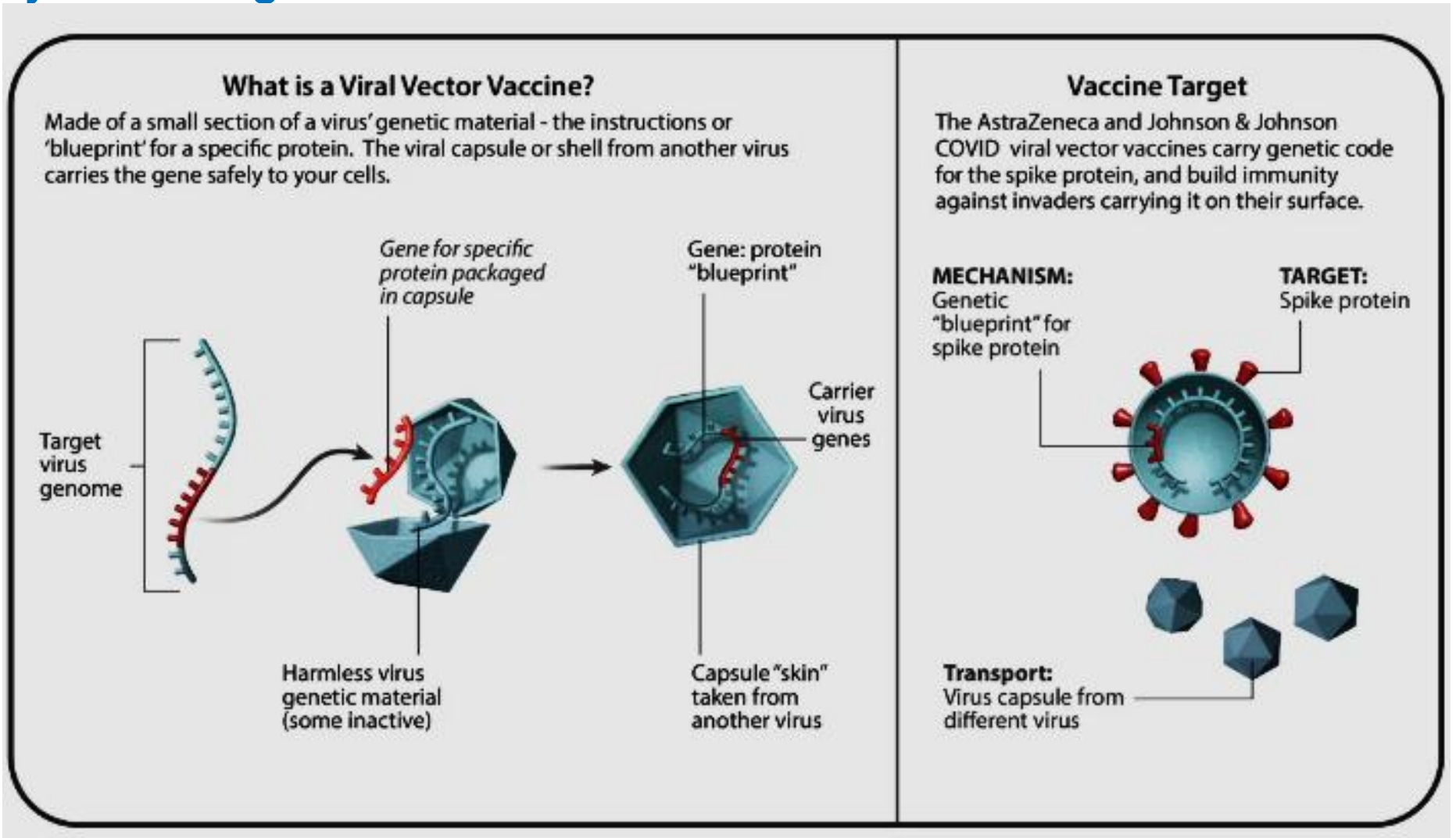
Recombinant DNA



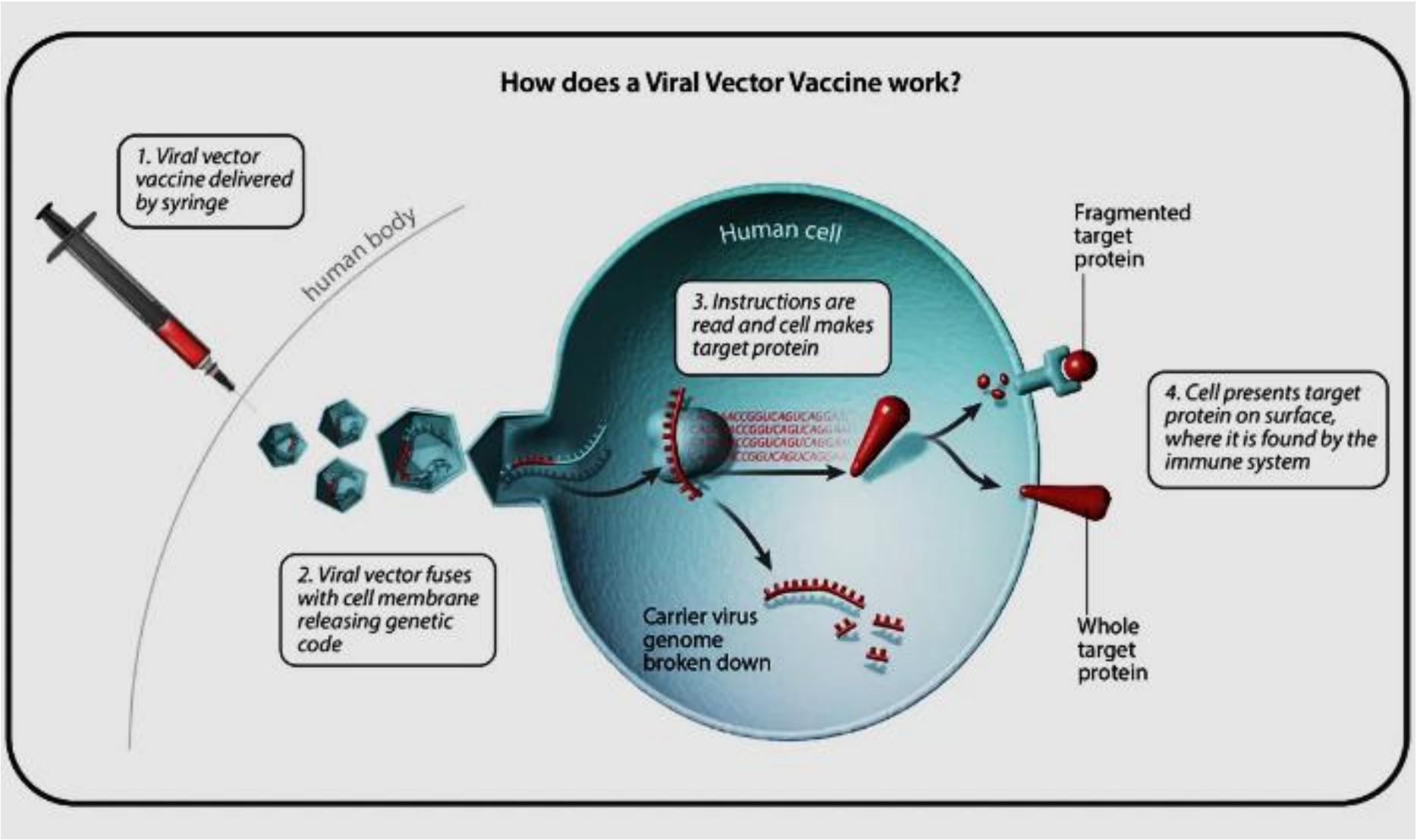

Artificial intelligence
Simulations
AGCTGCTACGAAT
GCTACGAAT
Parts assembly
Gene editing
Pathway selection
Design
Build
Learn
Test
Synthetic yeast
Re-design experiments
Fermentation
Data analysis
High-throughput screening

Viral vector vaccines = a gene delivery system

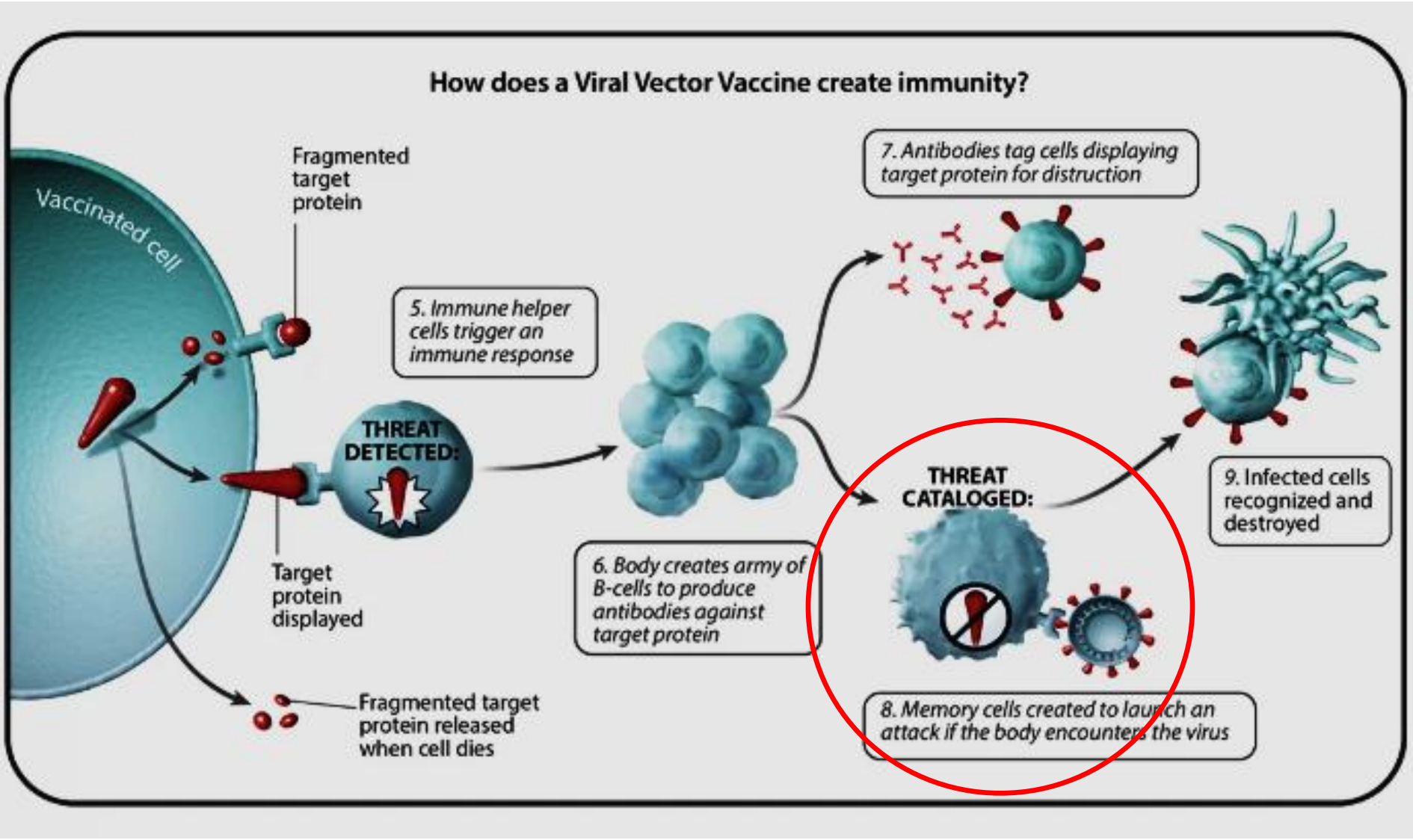
Viral vector vaccines use a harmless virus to deliver to the host's cells the genetic code of the antigen, stimulating the immune system to fight



Viral vector vaccines = a gene delivery system



Viral vector vaccines = a gene delivery system

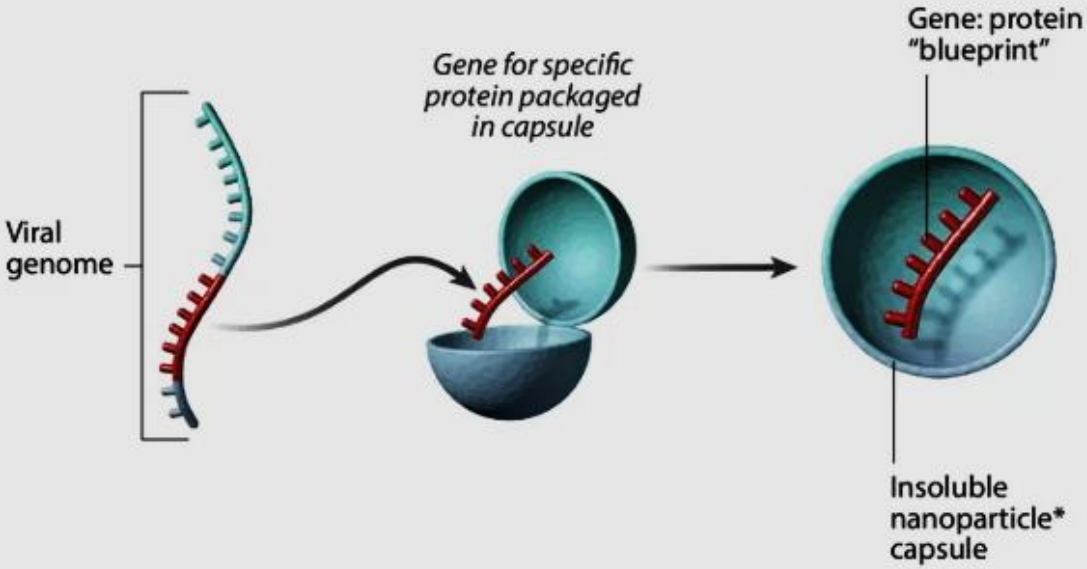


Examples: Ebola vaccine, COVID-19 vaccine

Messenger RNA (mRNA) vaccines = use the pathogen's genetic code

What is the Messenger RNA (mRNA) vaccine?

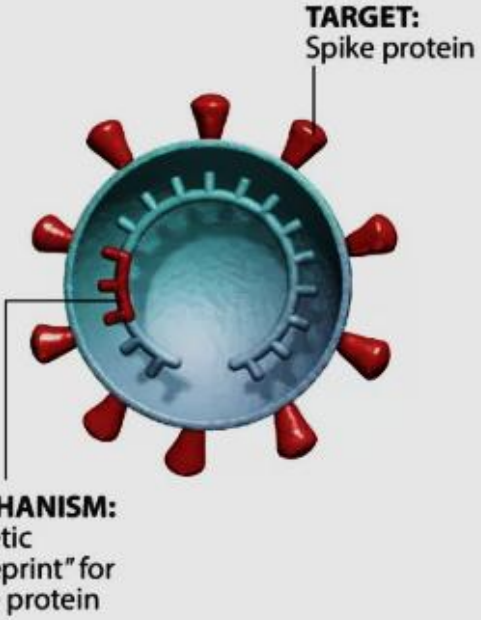
Made of a small section of a virus' genetic material - the instructions or 'blueprint' for a specific protein. A insoluble nanoparticle* capsule carries the gene safely to your cells.



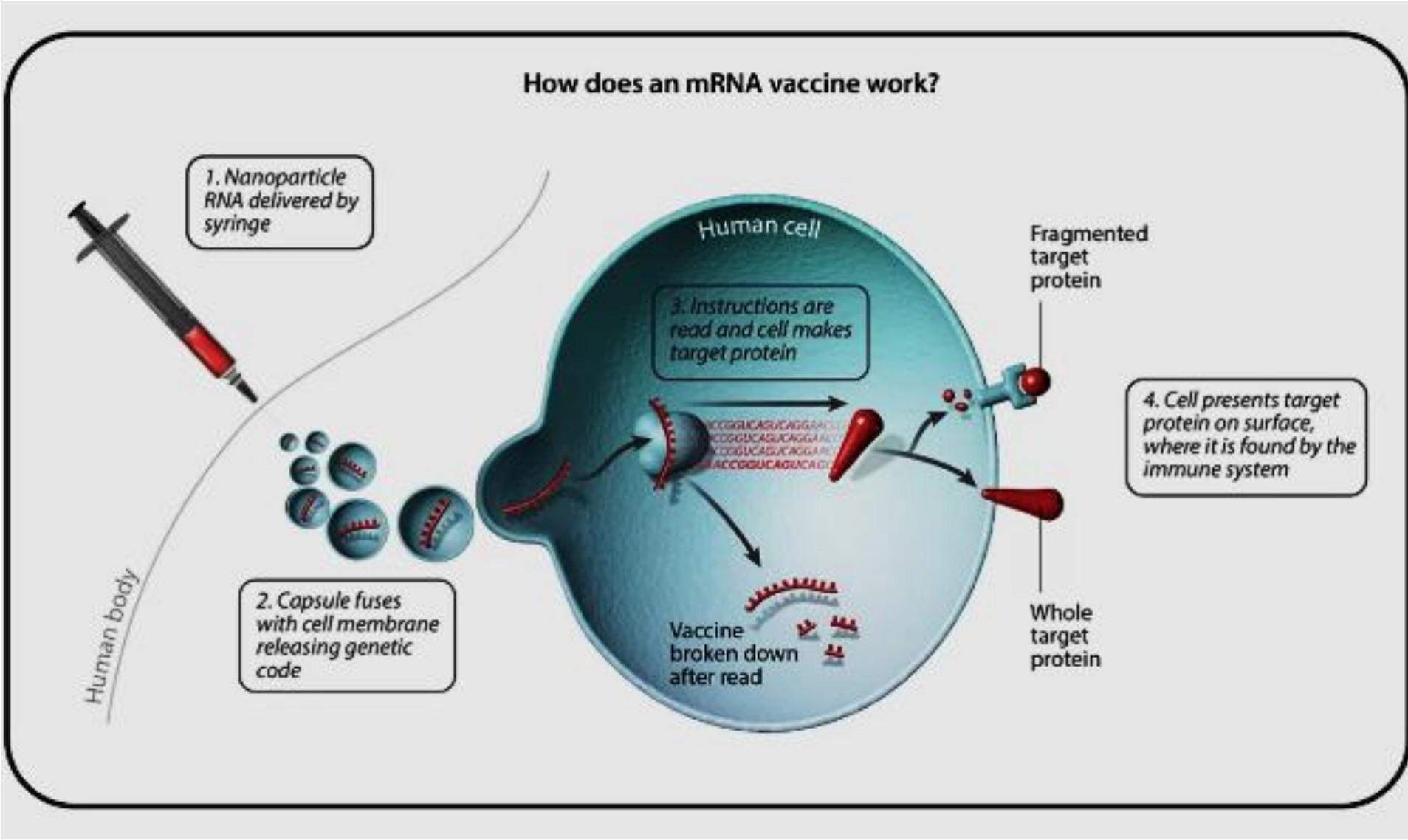
*Did You Know?: "Nano" means small.

Vaccine Target

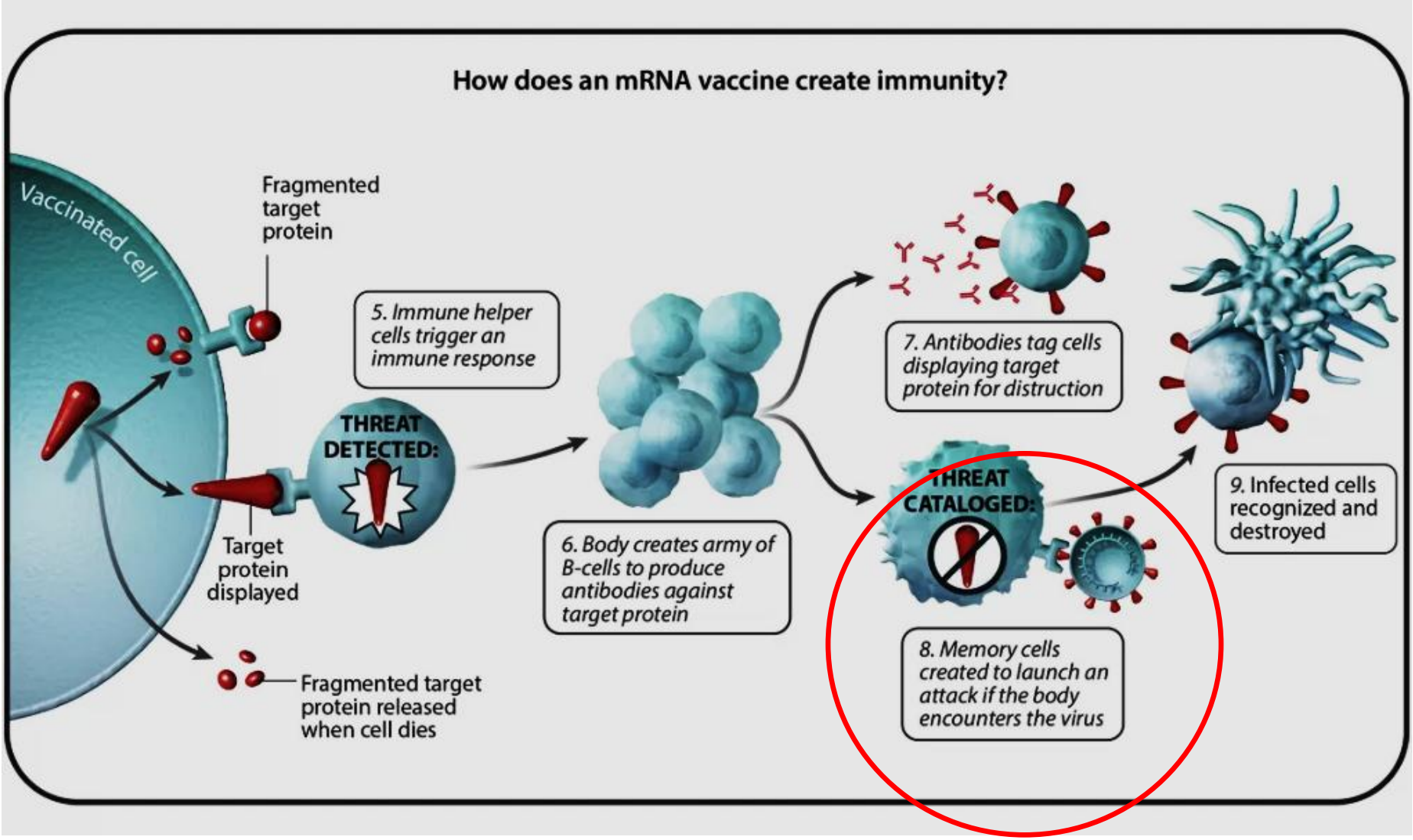
Pfizer's mRNA COVID vaccine carries the genetic blueprint for the spike protein. Your body will make this protein and build immunity against any invaders carrying it on their surface.



Messenger RNA (mRNA) vaccines



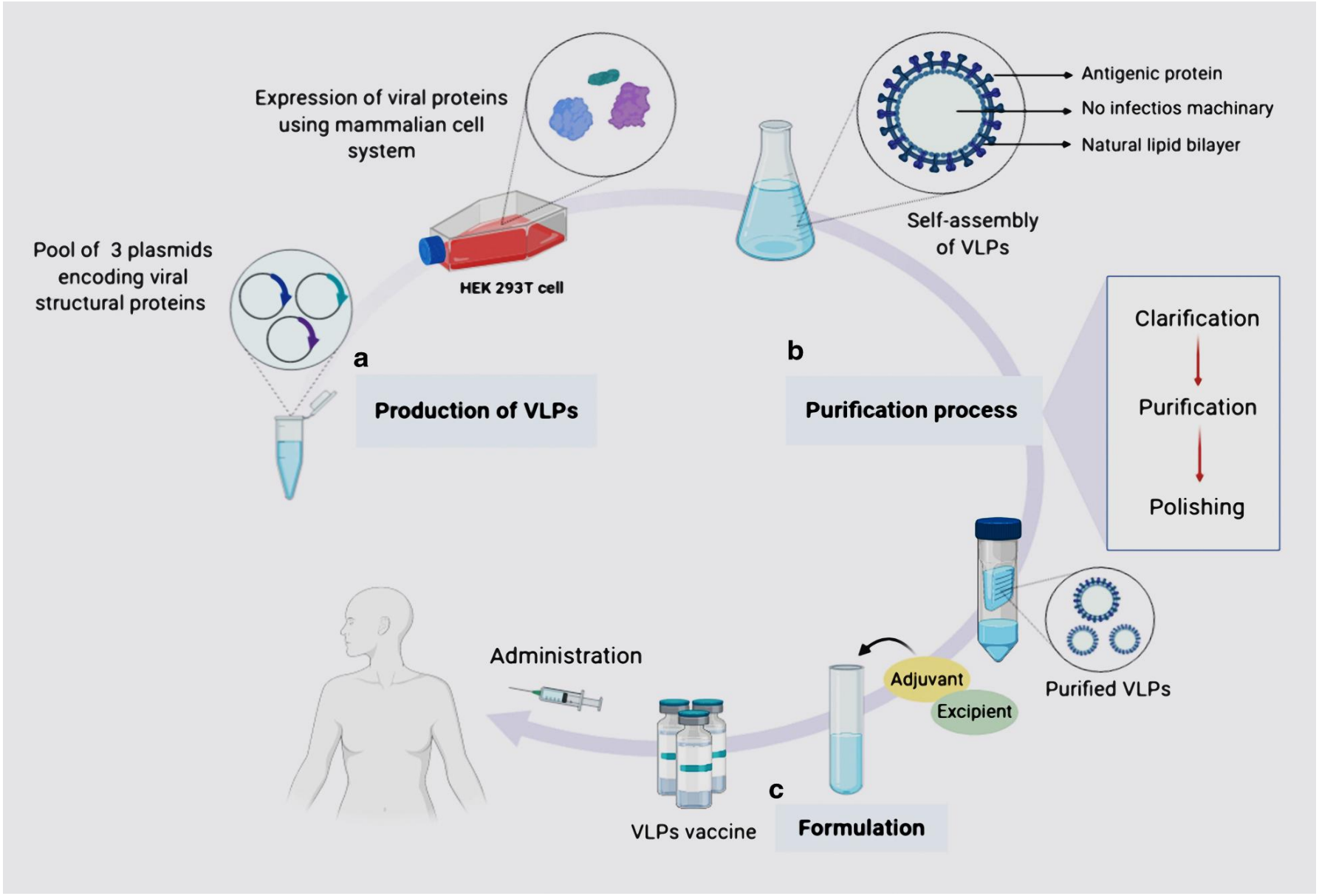
Messenger RNA (mRNA) vaccines



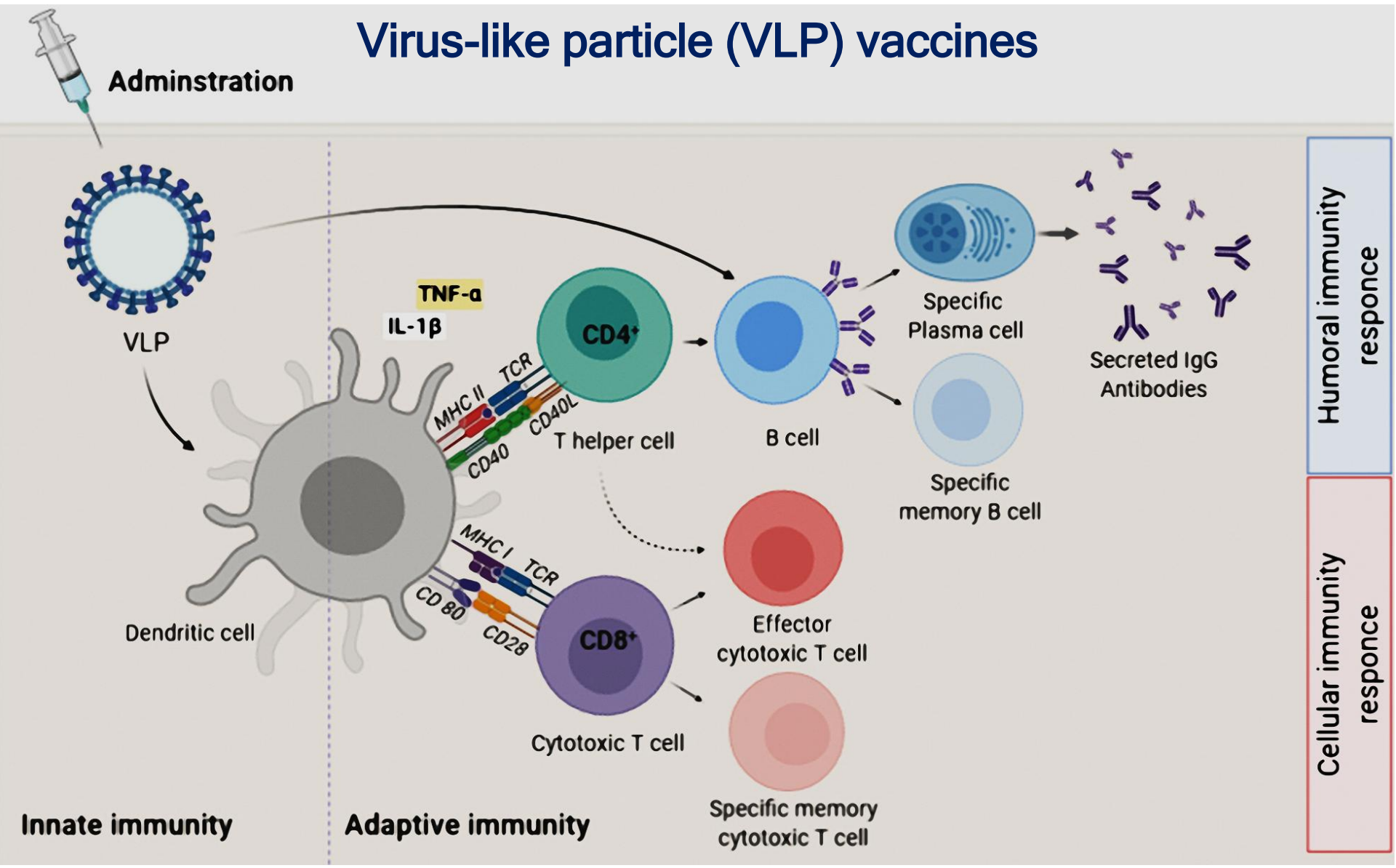
Examples: Sars-CoV-2 vaccine

mRNA vaccines elicit potent in vitro immunity against infectious disease targets in animal models of influenza virus, Zika virus, rabies virus, and others

Virus-like particle (VLP) vaccines = nanovaccines, drug nanocarriers



Virus-like particle (VLP) vaccines



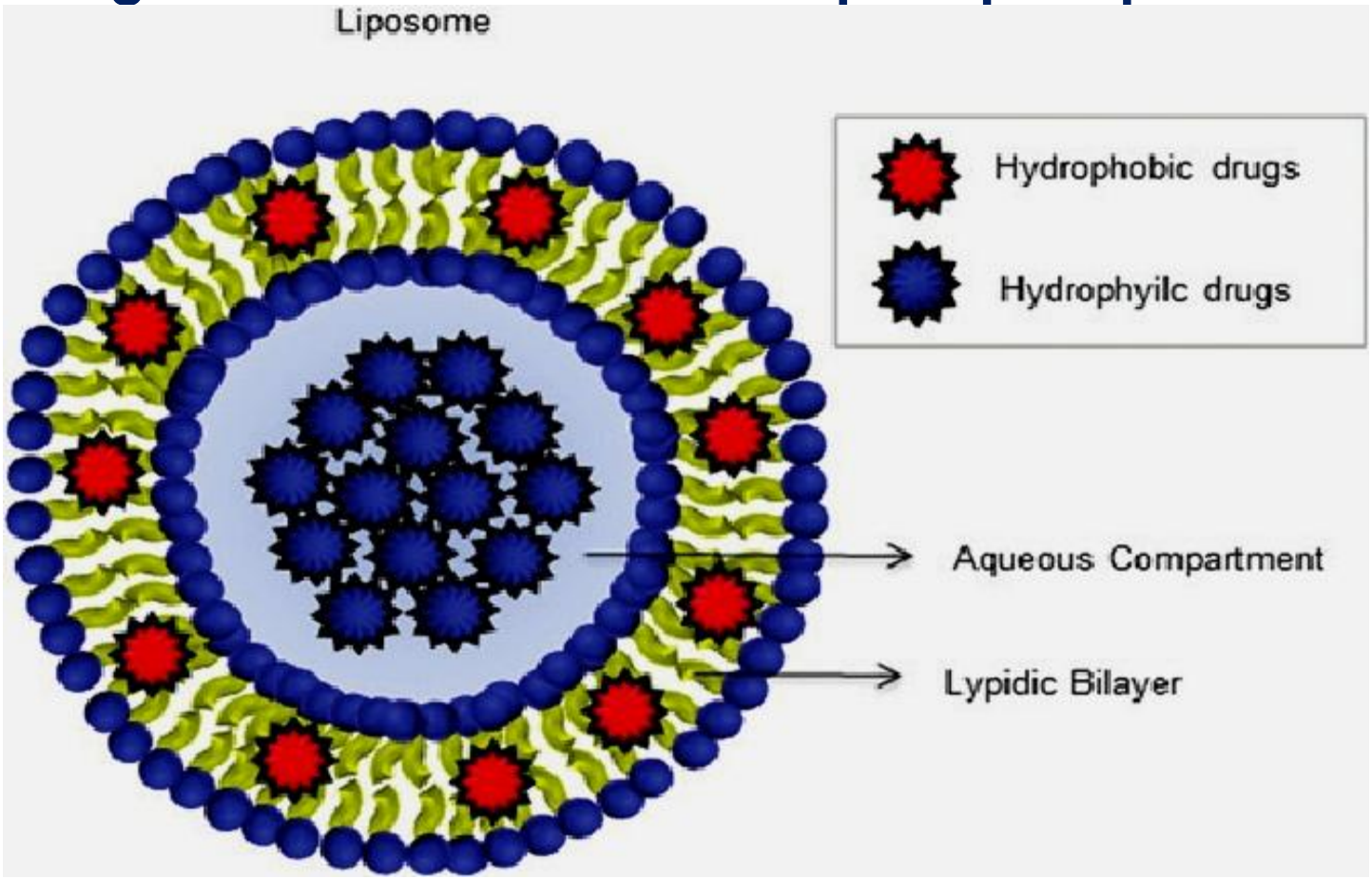
Examples: HPV

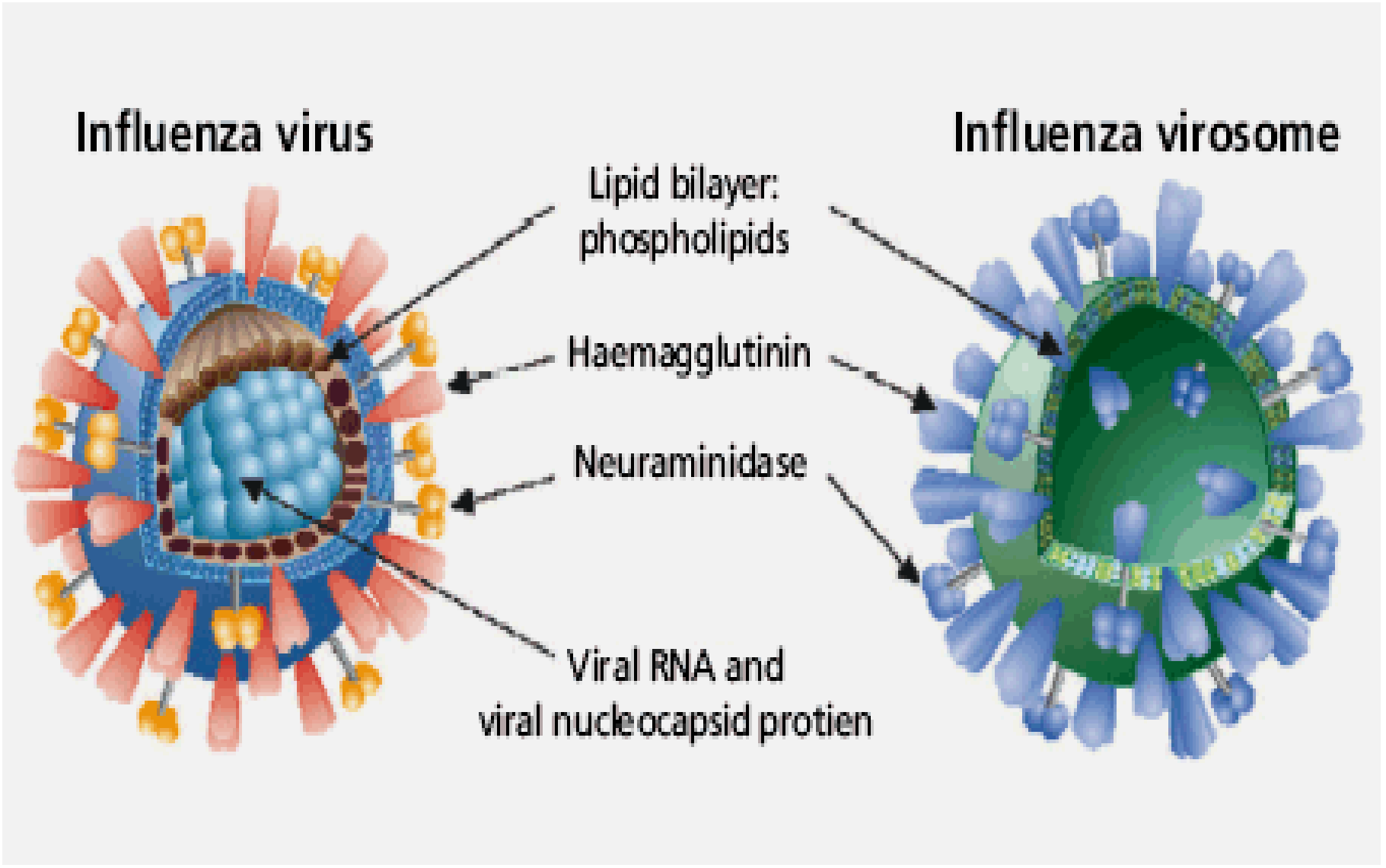
Liposomal (VIROSOMES) vaccines

Based on viral membrane proteins

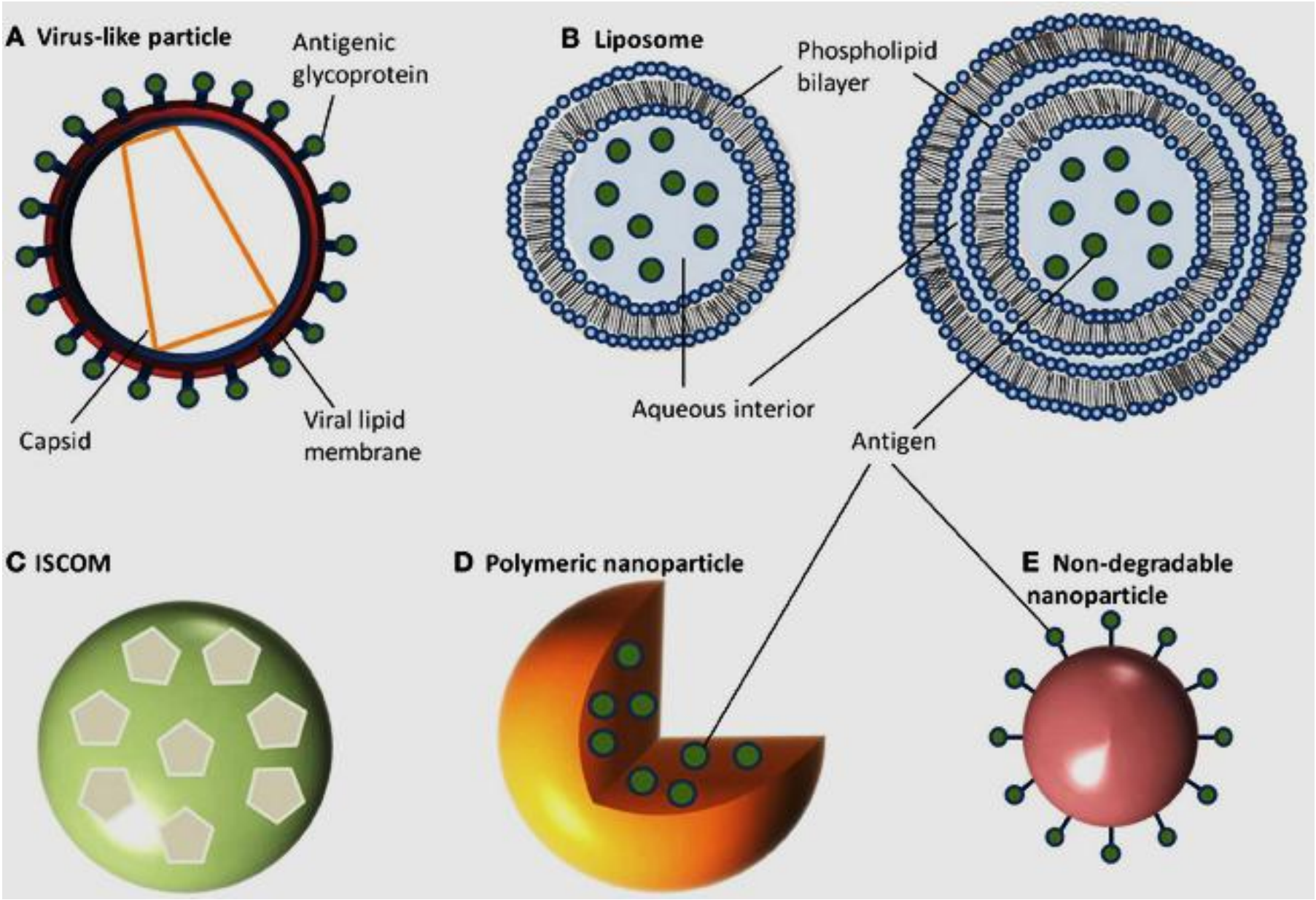
► Virosome – drug or vaccine delivery mechanism:

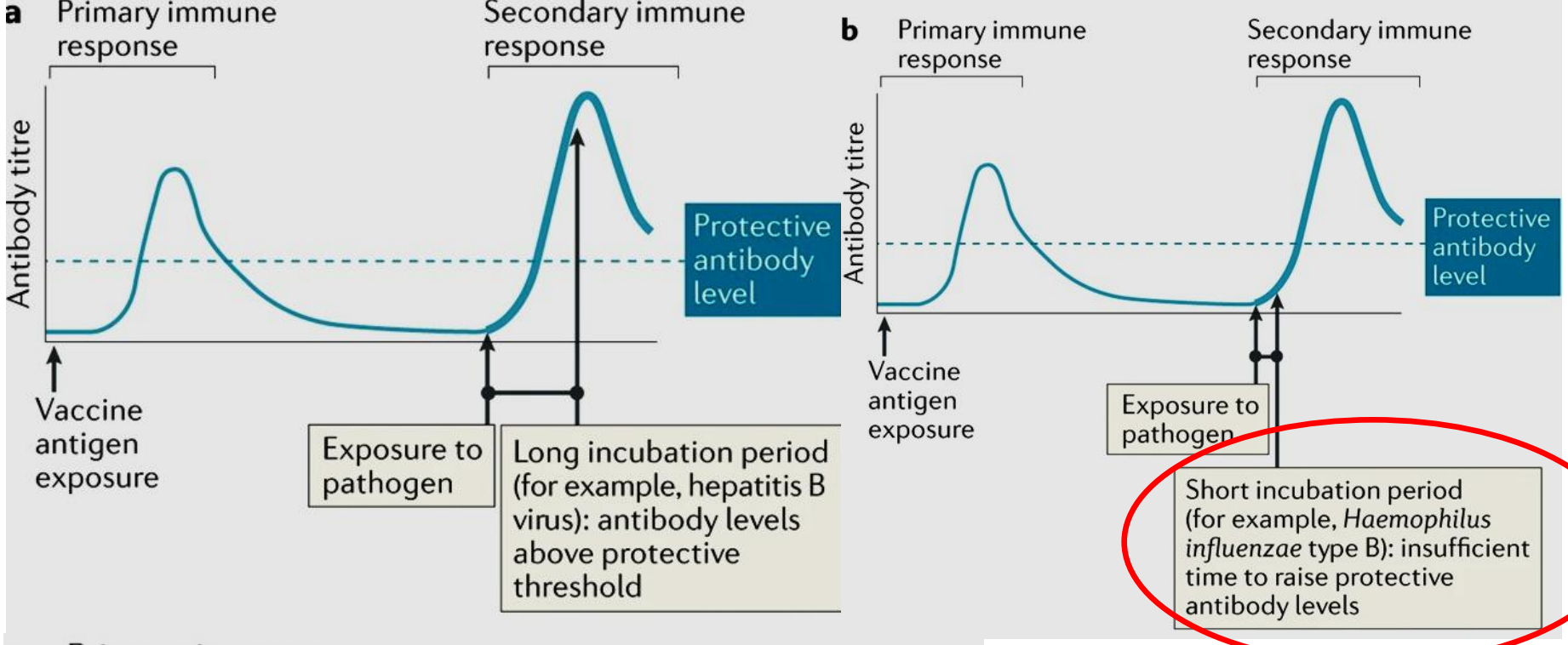
viral antigens are embedded in a phospholipid membrane

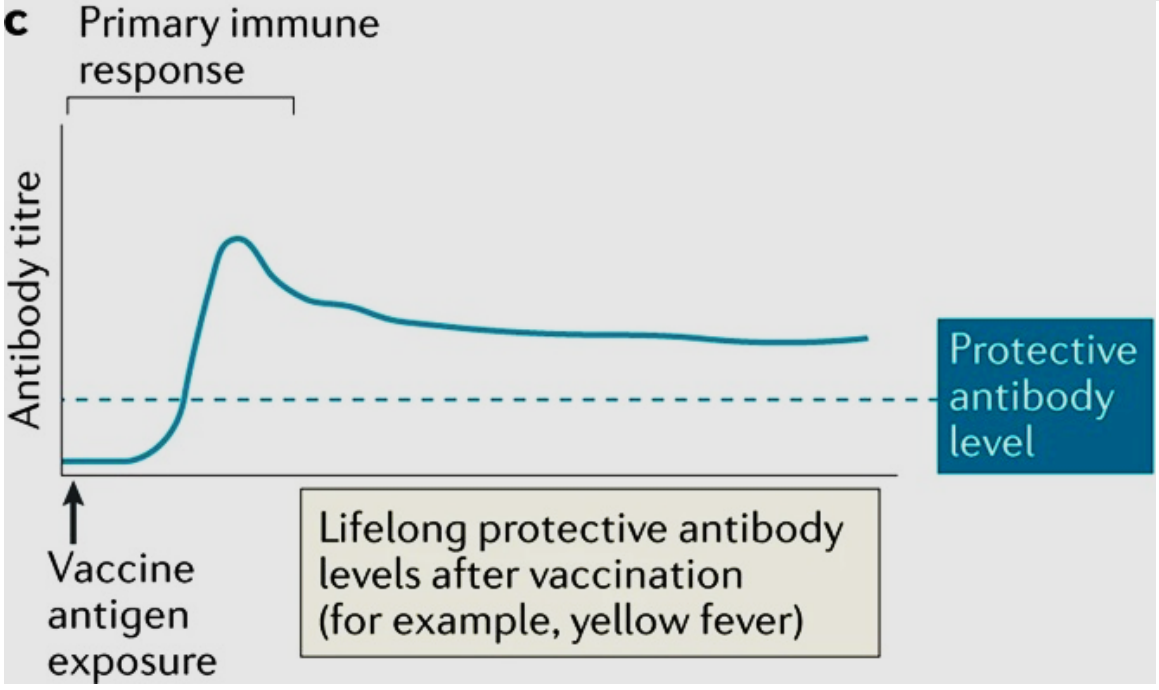



Influenza virus
Influenza virosome
Lipid bilayer:
phospholipids
Haemagglutinin
Neuraminidase
Viral RNA and
viral nucleocapsid protien

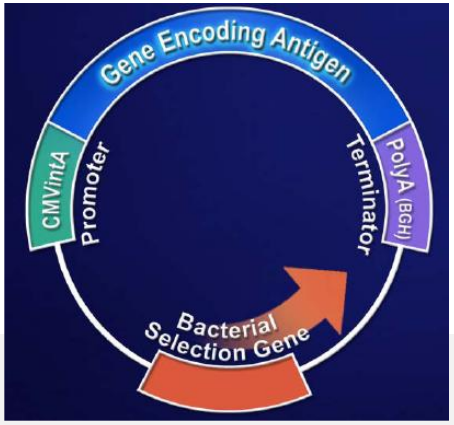
Nanoparticle-based vaccines







The waning of antibody levels depends on:
the age of the vaccine recipient (remarkably fast in infants due to the lack of bone marrow niches for B cell survival),
the nature of the antigen,
the number of booster doses administered



DNA Vaccines

DNA vaccine

Indirect route

Direct route

Vaccine uptake by non-DC at injection site

Vaccine uptake by DC at injection site

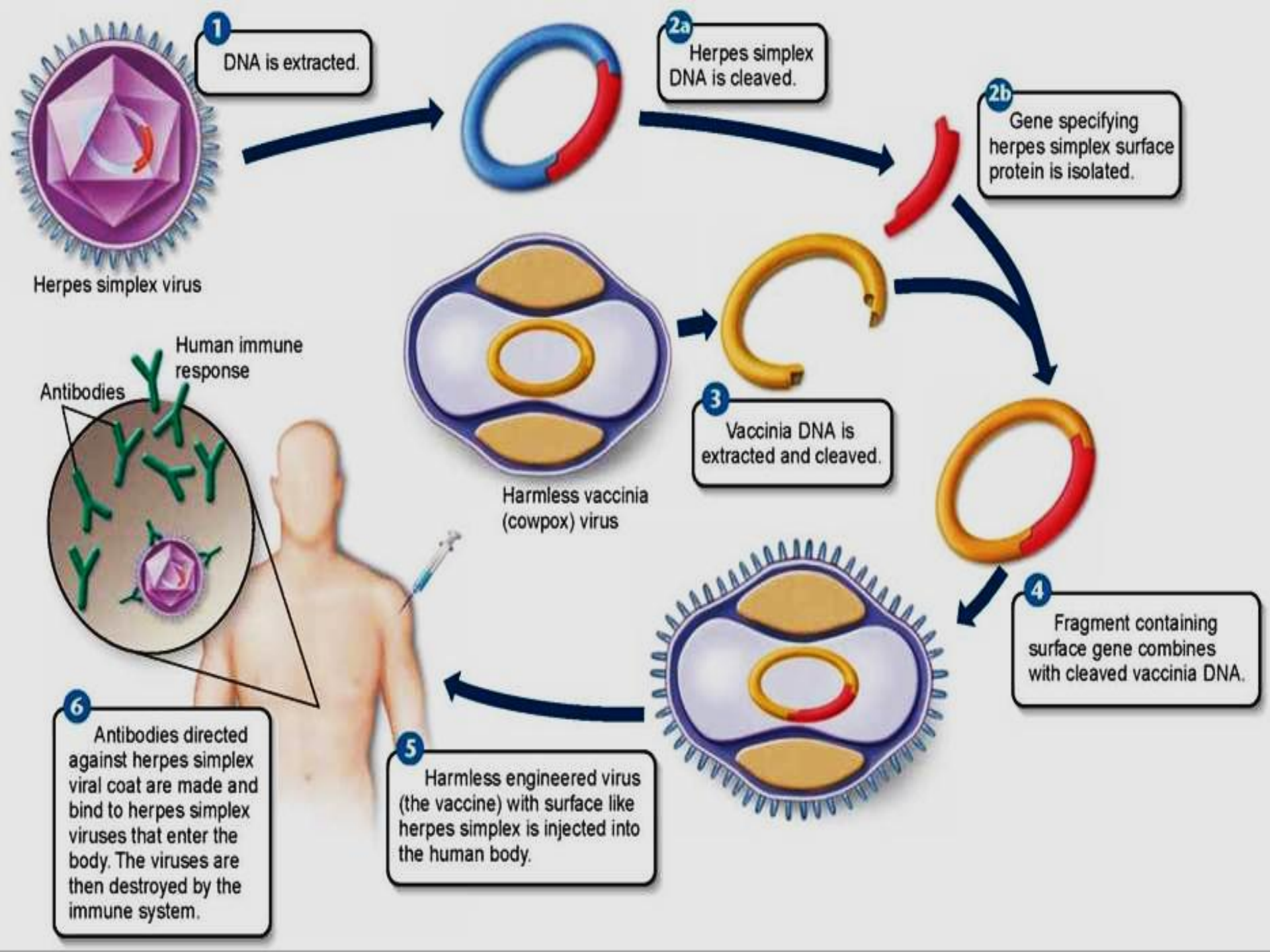
Keratinocyte

Myocyte

Cross-presentation of vaccine-encoded peptides for $CD8^+$ T-cell recognition

DC

Presentation of vaccine-encoded peptides for $CD4^+$ T-cell recognition


1
DNA is extracted.
Herpes simplex virus
2a
Herpes simplex DNA is cleaved.
2b
Gene specifying herpes simplex surface protein is isolated.
Harmless vaccinia (cowpox) virus
3
Vaccinia DNA is extracted and cleaved.
4
Fragment containing surface gene combines with cleaved vaccinia DNA.
5
Harmless engineered virus (the vaccine) with surface like herpes simplex is injected into the human body.
Human immune response
Antibodies
6
Antibodies directed against herpes simplex viral coat are made and bind to herpes simplex viruses that enter the body. The viruses are then destroyed by the immune system.

DNA Vaccines

- Plasmids are easily manufactured in large amounts
- DNA is very stable
- DNA resists temperature extremes so storage and transport are straightforward
- DNA sequence can be changed easily in the laboratory - this means that we can respond to changes in the infectious agent
- By using the plasmid in the vaccine to code for antigen synthesis, the antigenic protein(s) that are produced are processed (post-translationally modified) in the same way as the proteins of the virus against which protection is to be produced - this makes a far better antigen than purifying that protein and using it as an immunogen

DNA Vaccines

- Mixtures of plasmids could be used that encode many protein fragments from a virus/viruses so that a broad-spectrum vaccine could be produced
- The plasmid does not replicate and encodes only the proteins of interest
- No protein component, hence no immune response against the vector itself
- Because of the way the antigen is presented, there is a CTL response that may be directed against any antigen in the pathogen
- A CTL response also offers protection against diseases caused by specific obligate intracellular pathogens (e.g., Mycobacterium tuberculosis)

DNA Vaccines

DNA vaccines produce a situation that reproduces a virus-infected cell

Broad-based immune response

- Long-lasting CTL response
- Advantages of new DNA vaccines for many diseases
- CTL response can be against an internal protein
- In mice, a nucleoprotein DNA vaccine is effective against a range of viruses

Disease Models in Which DNA Vaccines Have Demonstrated Efficacy

Infectious Diseases

Viruses

- HIV
- Influenza
- Rabies
- Hepatitis B,C,D
- Ebola
- Herpes Simplex
- Papilloma
- CMV
- Rota
- Measles
- LCMV
- St. Louis Enceph

Bacteria

- B. Burgdorferi
- C. tetani
- M. Tb
- S. typhi

Parasites/Protozoa

- Malaria
- Mycoplasma
- Leishmania
- Schistosoma
- Taenia ovis
- Toxo. gondii

Cancer

- Breast (Her2/neu)
- Colon
- Prostate
- Myeloma
- Lymphoma
- E7-Induced
- Fibrosarcoma

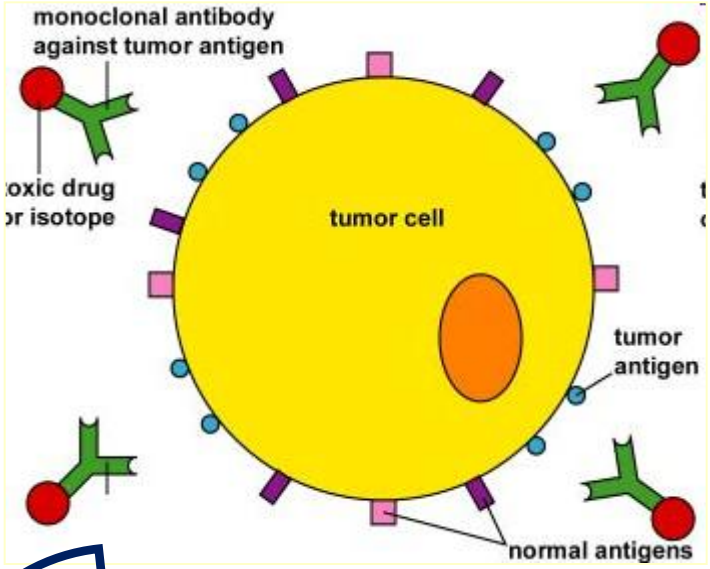
Allergy

- House Dust Mite
- Peanut
- Experimental Airway Hyperresponsiveness

Autoimmune Disease

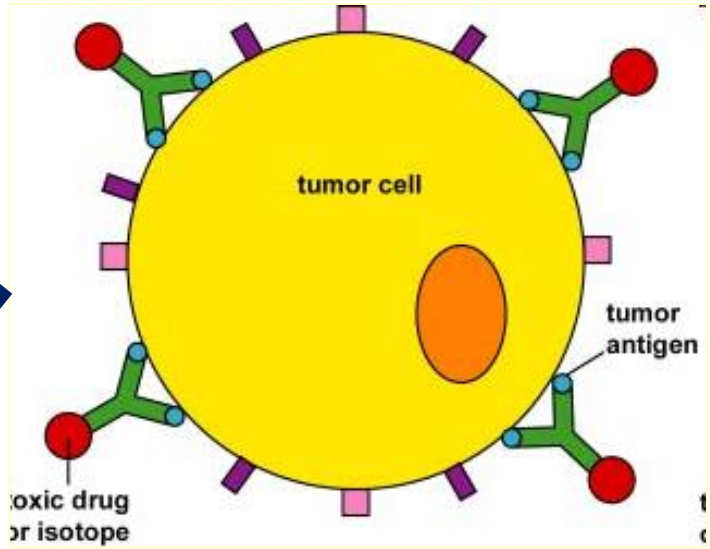
- Diabetes
- EAE (MS model)

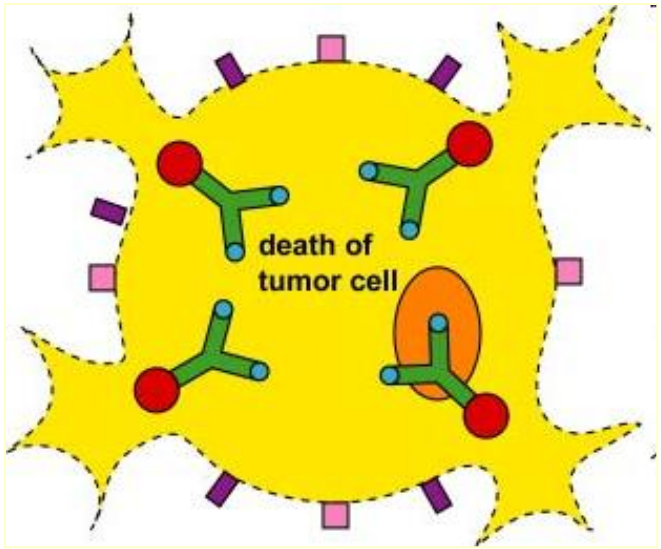
Anti-tumor vaccines



Immunotoxins

(e.g., Pseudomonas aeruginosa exotoxin) conjugated with specific anti-tumor antibody





Questions

1. What is an adjuvant? What is its role in immunization?
2. What types of vaccines against the flu are available?
3. Name the type of vaccine against HPV cancers.
4. Name three advantages of a live attenuated vaccine over the inactivated one.
5. Why will the vaccine not always protect from infection?

UNIWERSYTET MEDYCZNY
IM. PIASTÓW ŚLĄSKICH WE WROCŁAWIU

Thank you for your attention!

To get information on the presented content,
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beata.sobieszczanska@umw.edu.pl