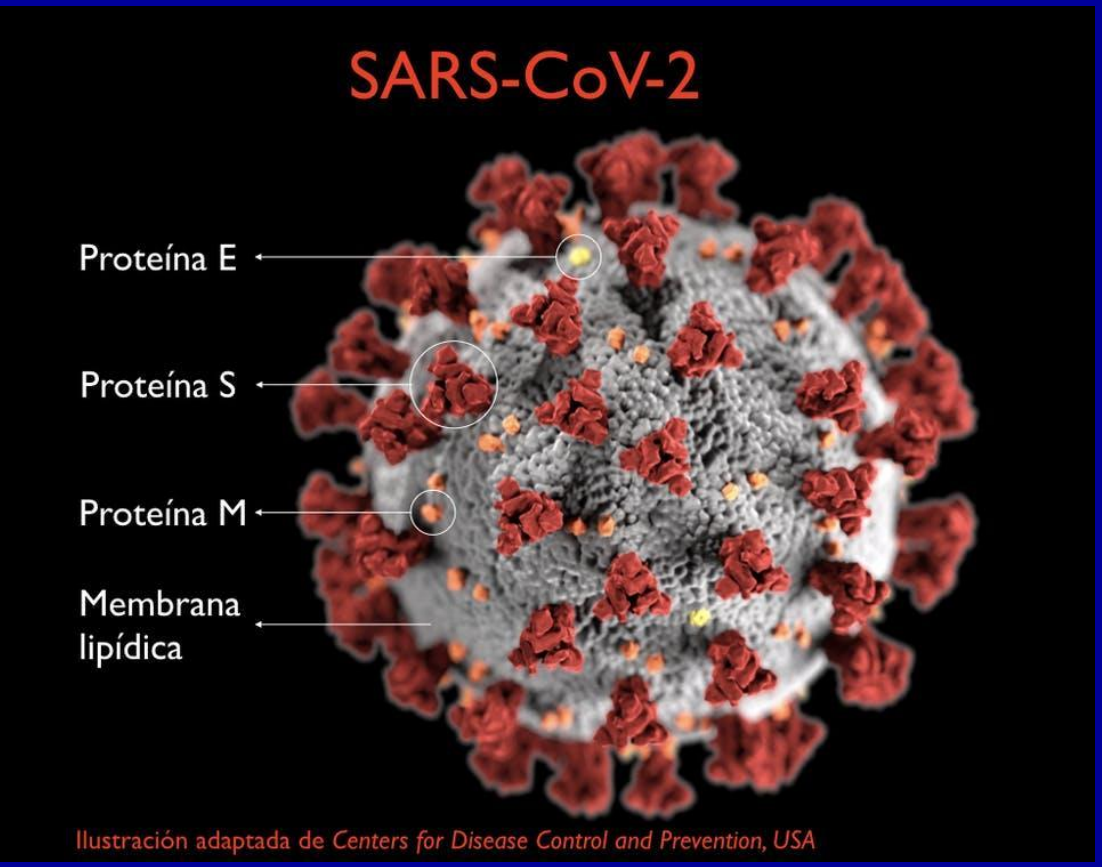
Immunity against SARS-CoV-2 VACCINES candidates Lecture 7



Andronovskaya I.B.

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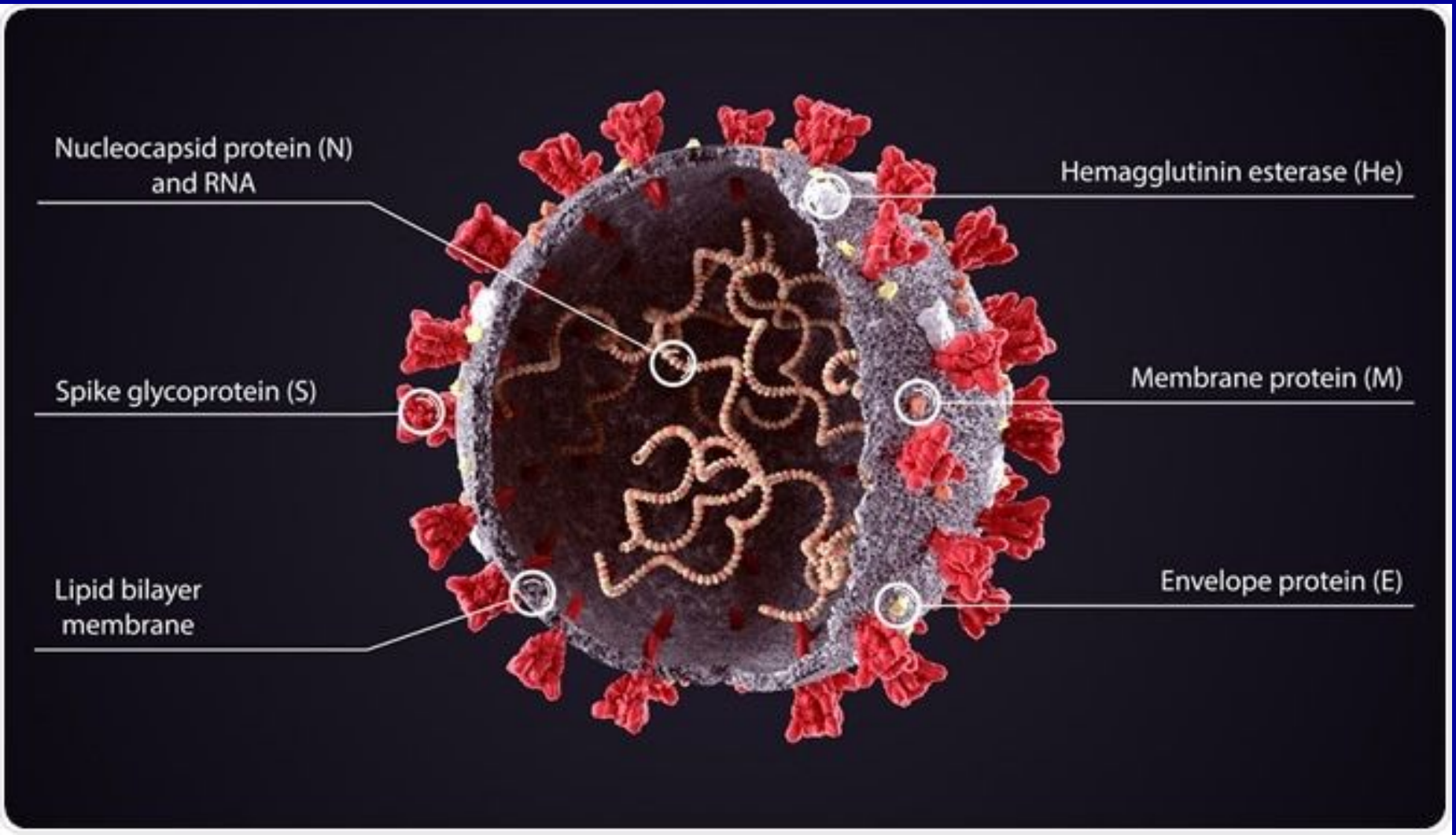
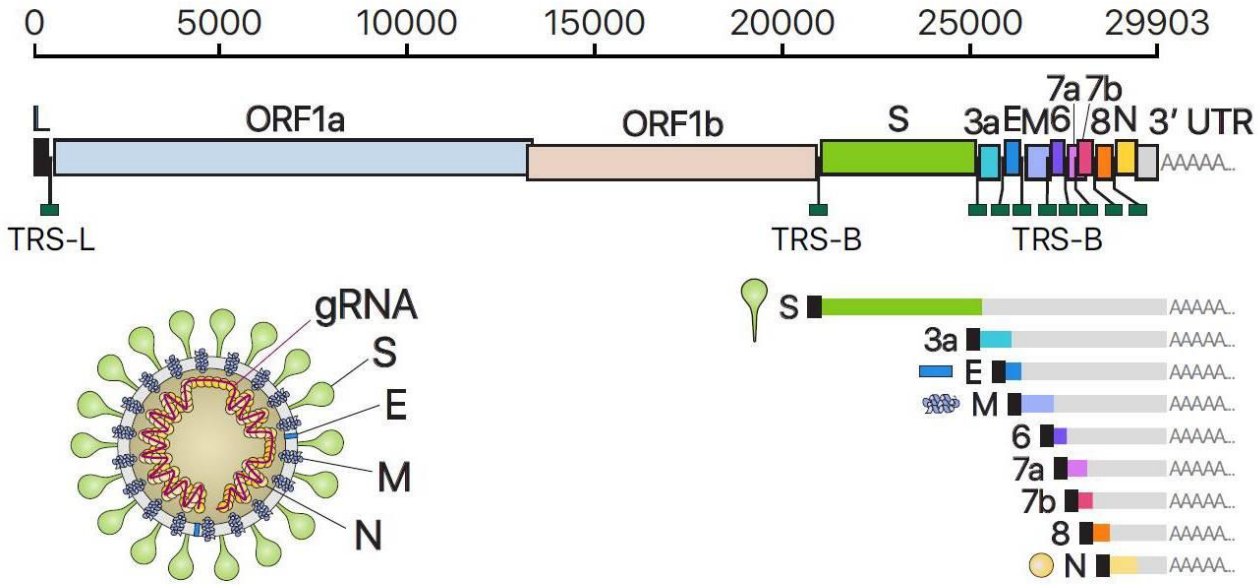
2020

SARS-CoV-2 structure (Type IV according to Baltimore classification)



SARS-CoV-2 genome



Genome: single stranded RNA messenger 29.9kb long, encoding 13 ORFs.

Coronavirus genomes have the longuest RNA virus genome known..

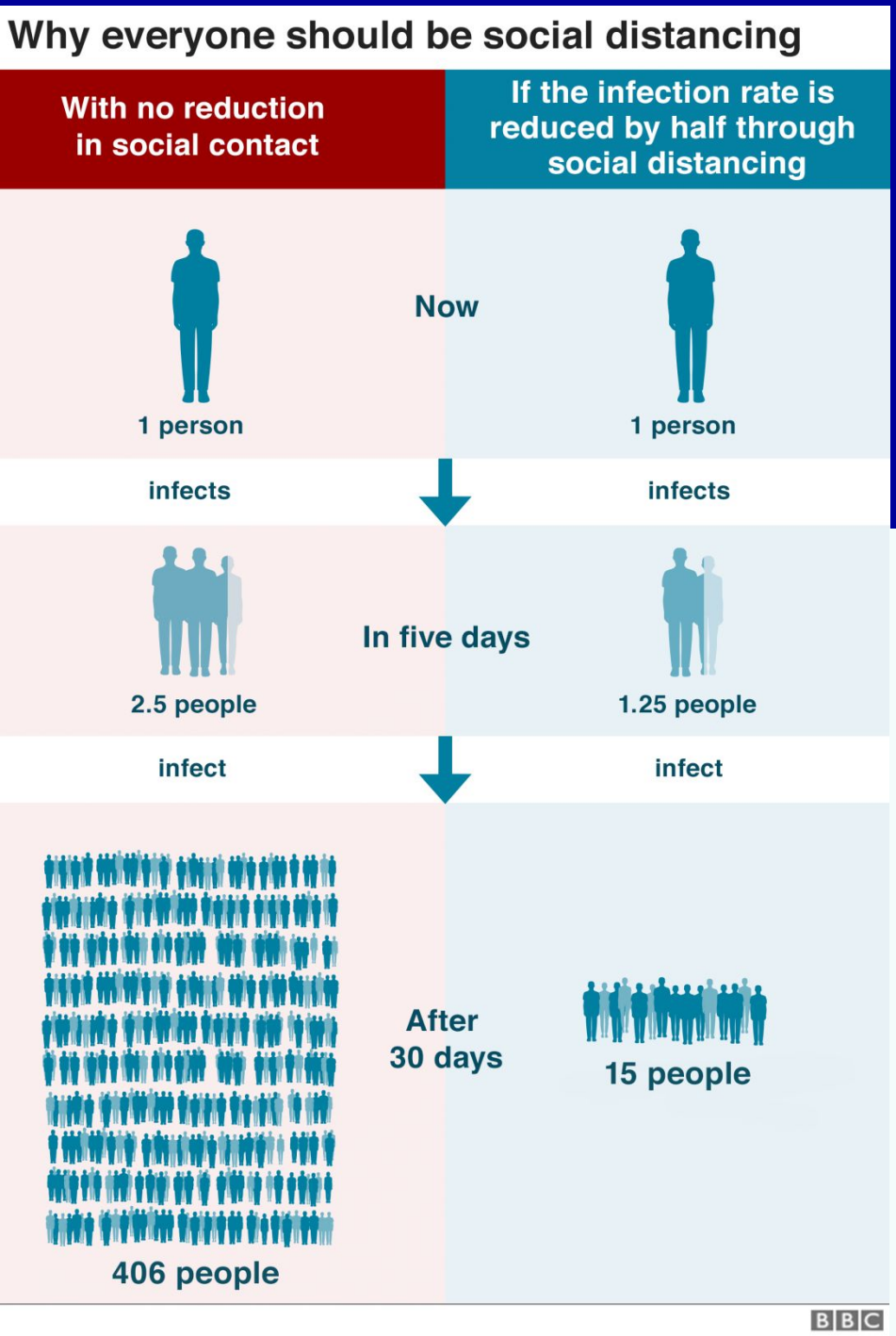
The proteins are expressed by two ways: primary translation of polyprotein that initiates the infection, and after some replication, subgenomic mRNA expression which produces all structural proteins

SARS-CoV-2 causes an infectious causes COVID-19

- Most people infected with the COVID-19 virus will experience mild to moderate respiratory illness and recover without requiring special treatment. Older people, some children and those with underlying medical problems like cardiovascular disease, diabetes, chronic respiratory disease, and cancer are more likely to develop serious illness.

There are basically three ways to stop the Covid-19 disease

1. Extraordinary restrictions on free movement and assembly, as well as aggressive testing, to interrupt its transmission entirely;
2. Just wait until enough people get infected and develop NATURAL ACQUIRED ACTIVE immunity (herd immunity);
3. A vaccine that could protect everyone by developing ARTIFICIAL ACQUIRED ACTIVE immunity (also herd immunity)



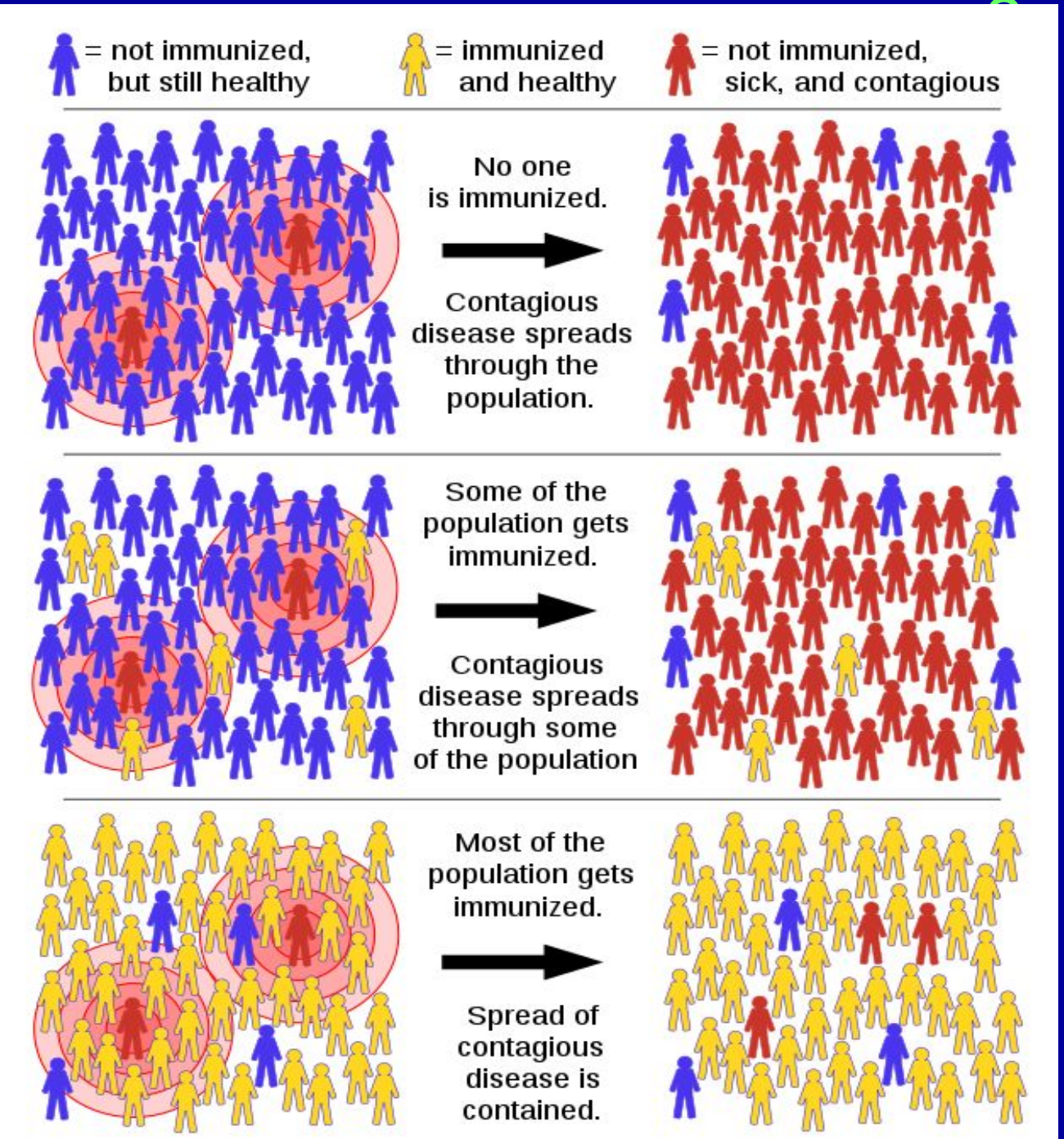
1. Restrictions measures interrupt transmission entirely (immunity is not developed)

2. **Get infected -** another way for a herd immunity, aside from vaccines. Some die, and the rest develop antibodies and/or cell-mediated immunity.

There have been two killer coronaviruses before:

- **SARS-CoV** infected only 8,000 people, killing 774 (about 10%), and was contained in 7½ months.
- **MERS** has never stopped but is rare. Since arising in 2012 it's infected 2,519 people, killing 35% of them (866 deaths so far).

A novel SARS-CoV-2 by now infects more than 5,6 mln people, kills more then 351,000 of them, and is not going to stop.



Herd immunity is an epidemiological concept that describes the state where a population is sufficiently immune to a disease that the infection will not spread within that group.

2. How many people should be infected to develop herd immunity?

- For mumps, 92 percent of the population should be immune for the disease to stop spreading entirely. This is what's known as the herd immunity threshold.
- COVID-19 is less infectious than mumps, with the proportion of people who need to be infected is lower but still high, sitting at around 70 percent of the entire population.

And what happens if 70 percent of an entire population gets sick, and due to fatality rate around 0,5-1% , how many of them will die?

It is a catastrophic outcome, and is a nonsense, but not preventive measure.

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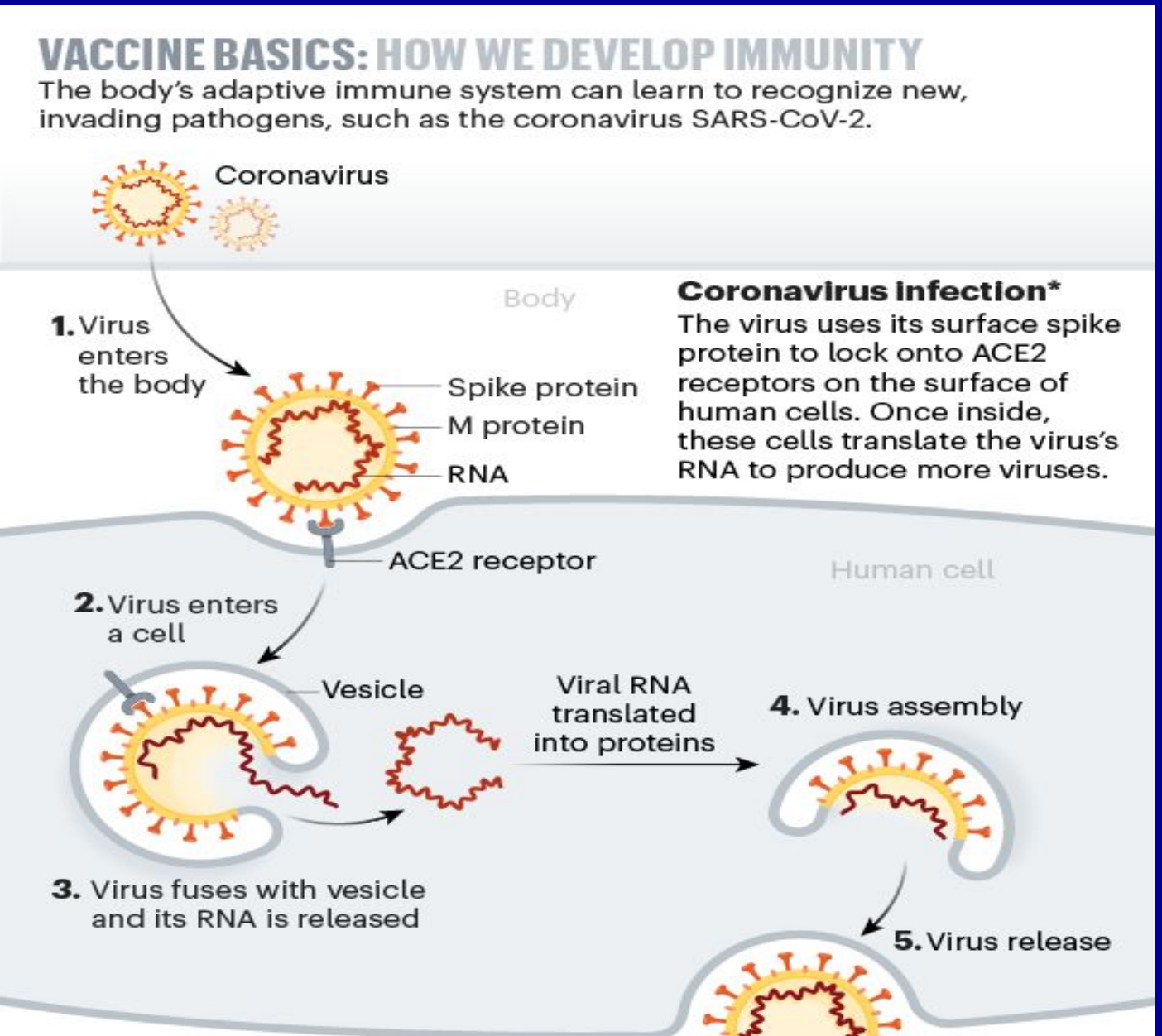
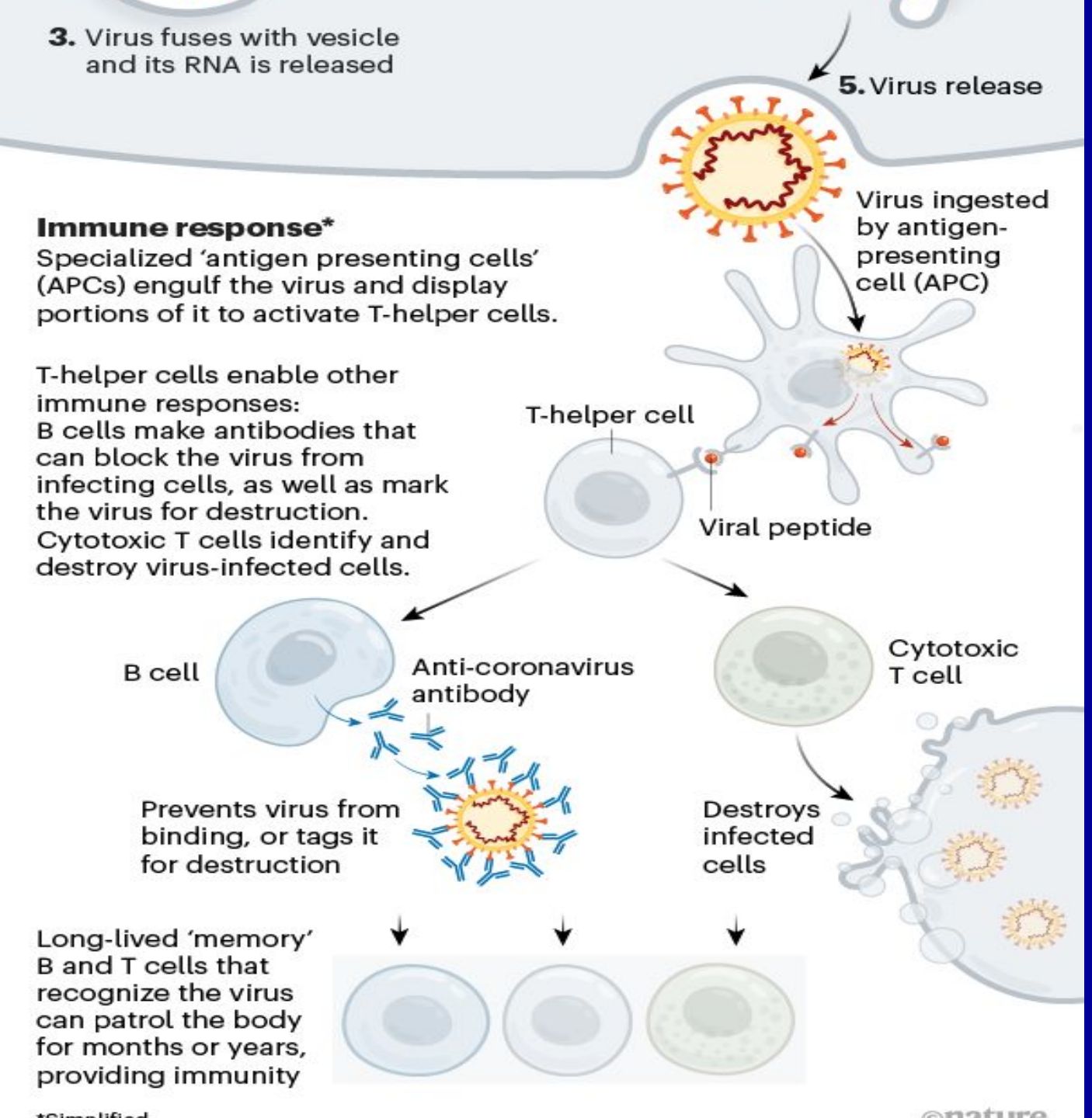
3. Vaccination-the only way for the herd immunity.



How we develop immunity against virus



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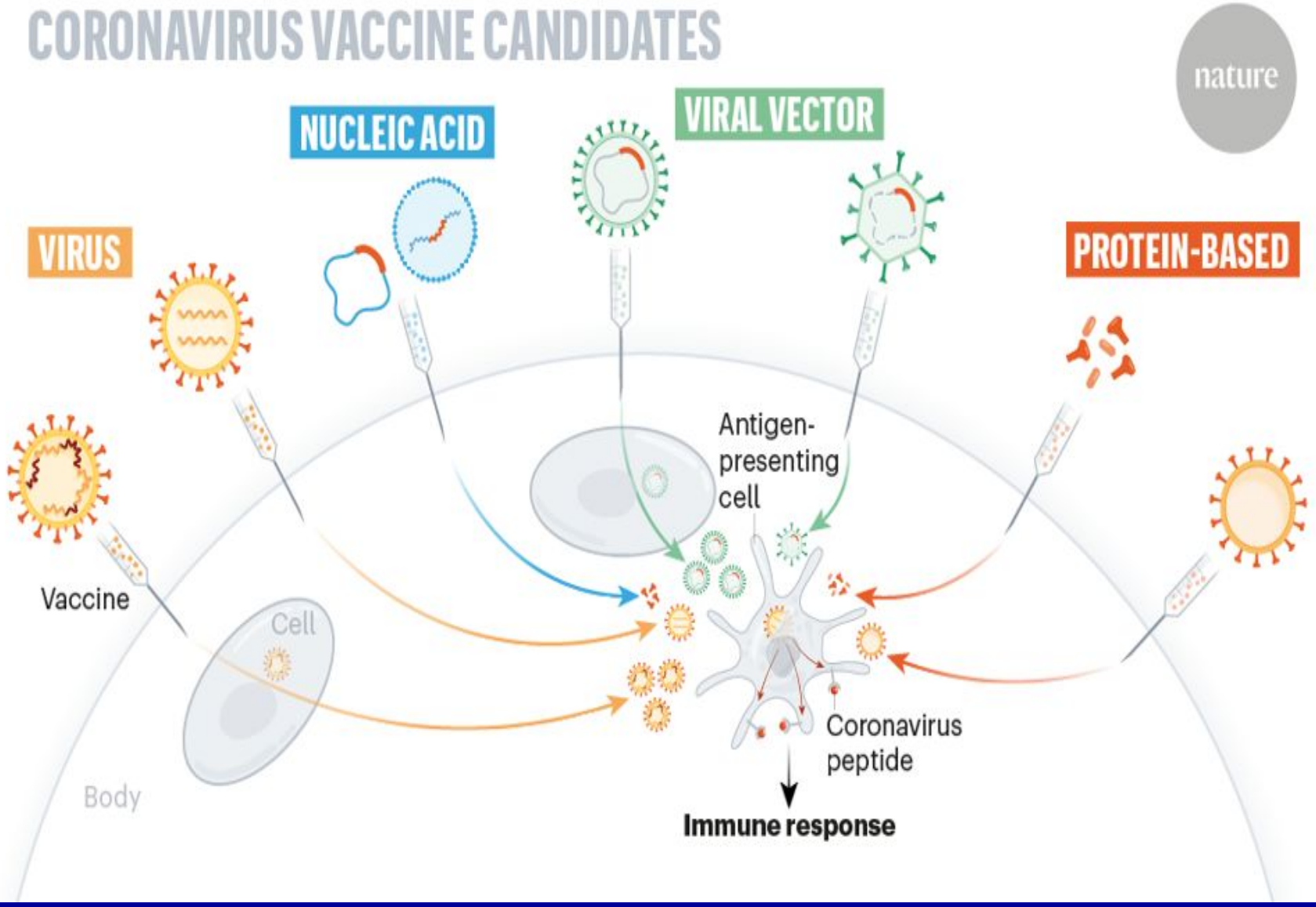
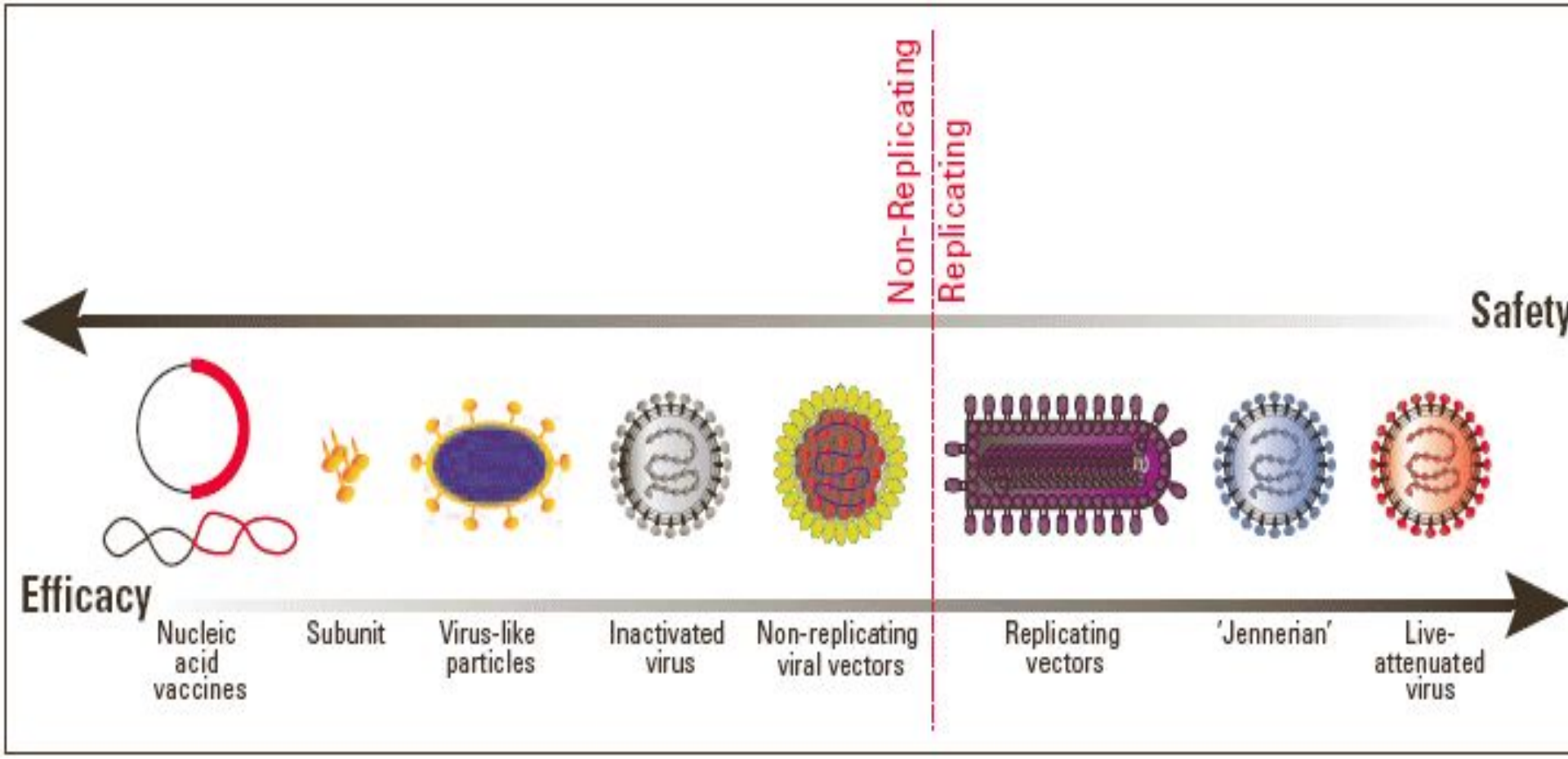
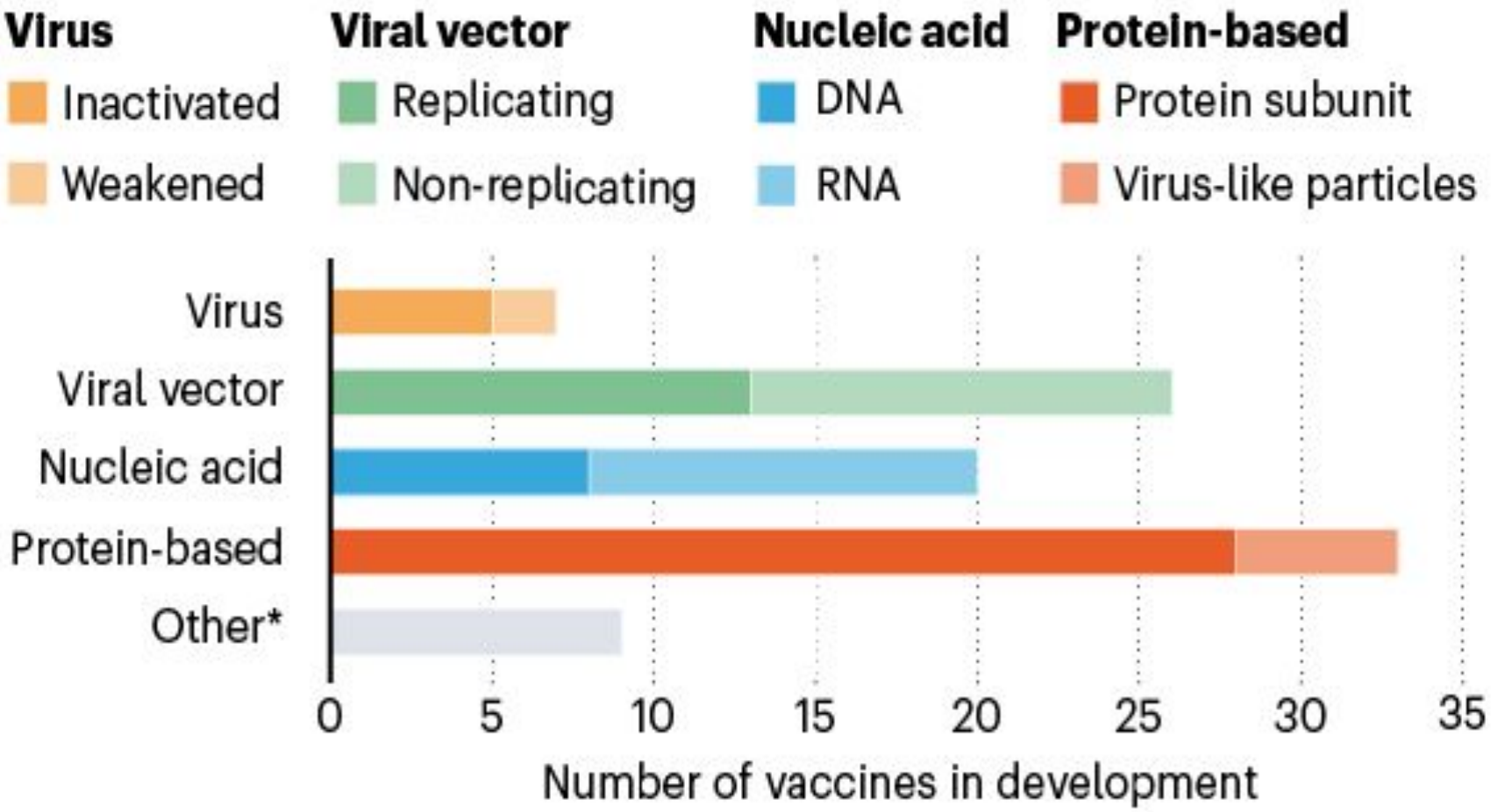

CORONAVIRUS VACCINE CANDIDATES
nature
NUCLEIC ACID
VIRAL VECTOR
VIRUS
PROTEIN-BASED
Antigen-presenting cell
Vaccine
Cell
Body
Coronavirus peptide
Immune response

Important features of vaccines: Safety and efficiency



AN ARRAY OF VACCINES

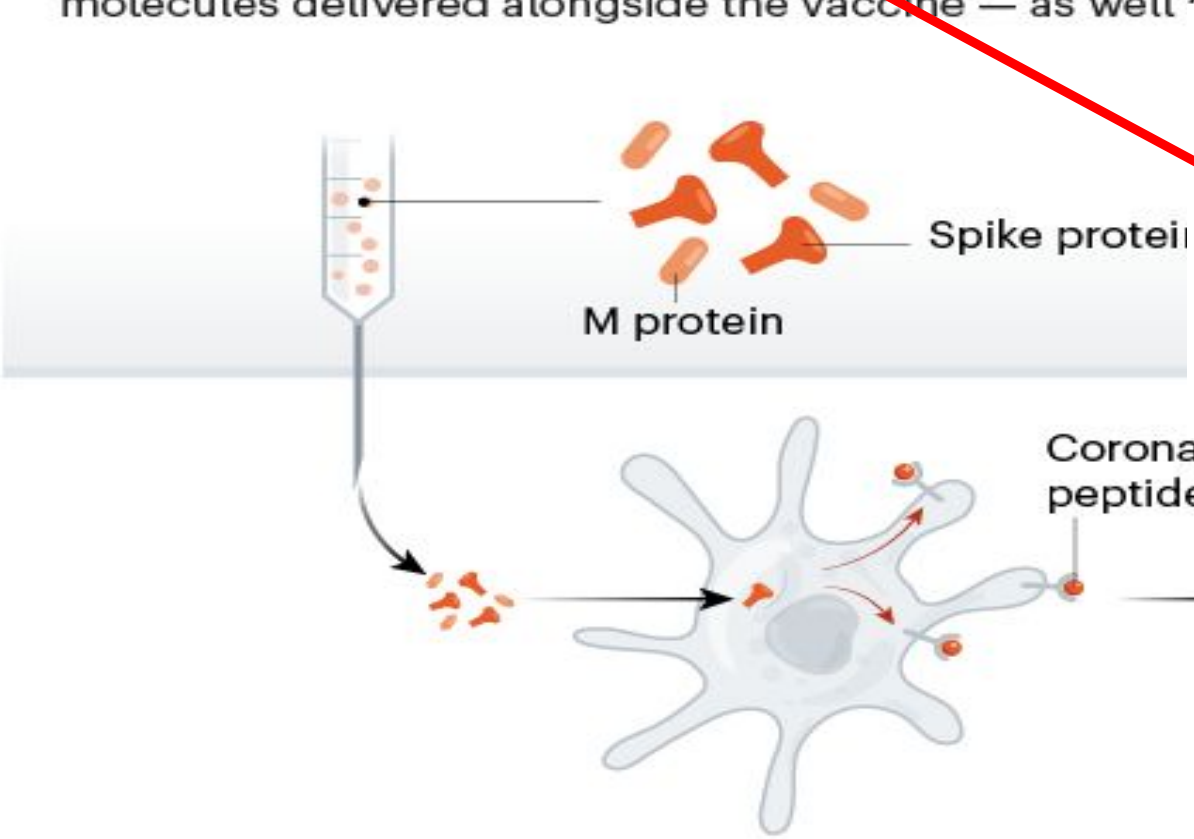


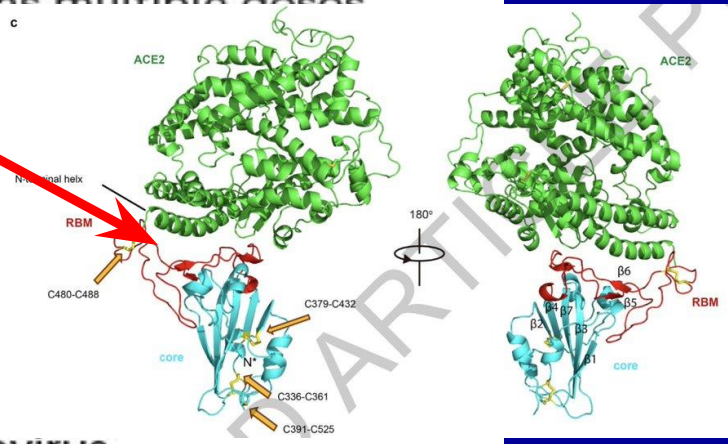
* Other efforts include testing whether existing vaccines against poliovirus or tuberculosis could help to fight SARS-CoV-2 by eliciting a general immune response (rather than specific adaptive immunity), or whether certain immune cells could be genetically modified to target the virus.

PROTEIN-BASED VACCINES

Protein subunits

Twenty-eight teams are working on vaccines with viral protein subunits — most are focusing on the virus's spike protein or a key part of it called the receptor binding domain. Similar vaccines against the SARS virus protected monkeys against infection but haven't been tested in people. To work, these vaccines might require adjuvants — immune-stimulating molecules delivered alongside the vaccine — as well as multiple doses.



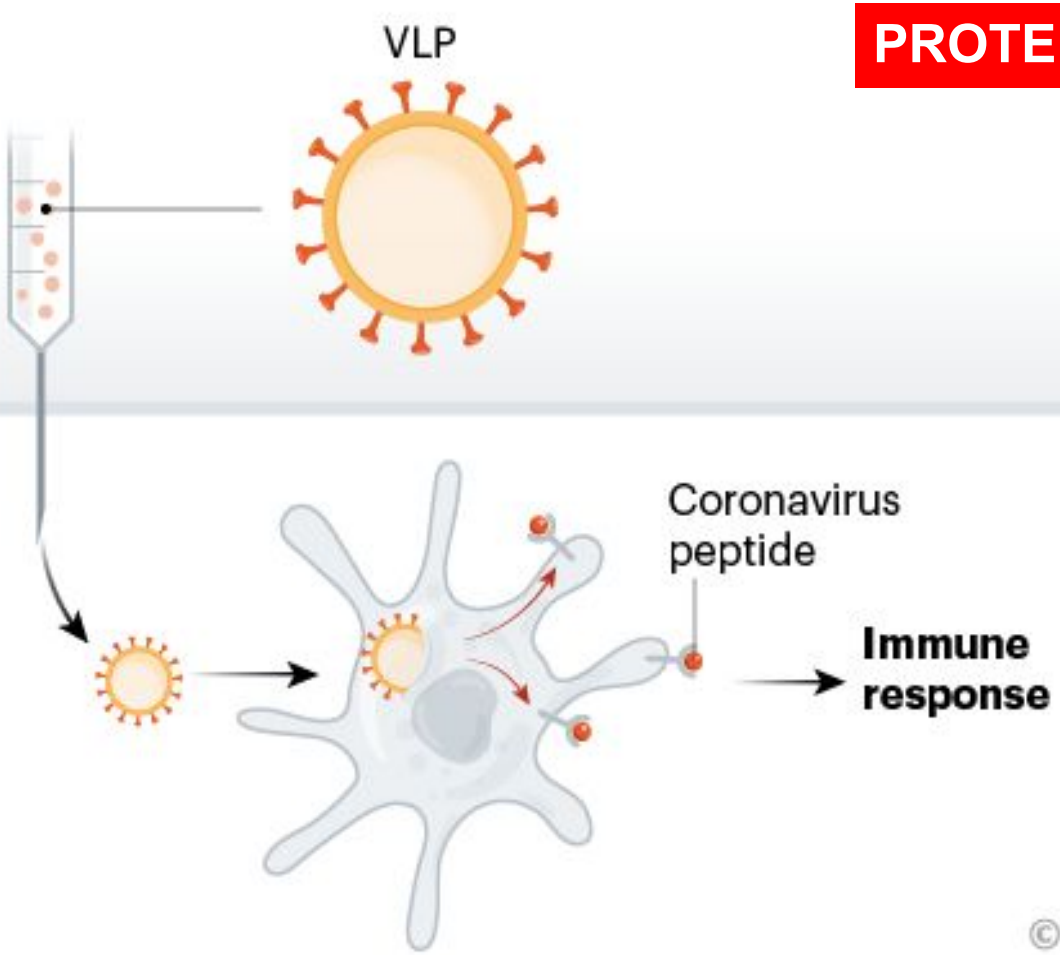


Virus-like particles

PROTEIN-BASED VACCINES

Virus-like particles

Empty virus shells mimic the coronavirus structure, but aren't infectious because they lack genetic material. Five teams are working on 'virus-like particle' (VLP) vaccines, which can trigger a strong immune response, but can be difficult to manufacture.



Subunit vaccines for viruses

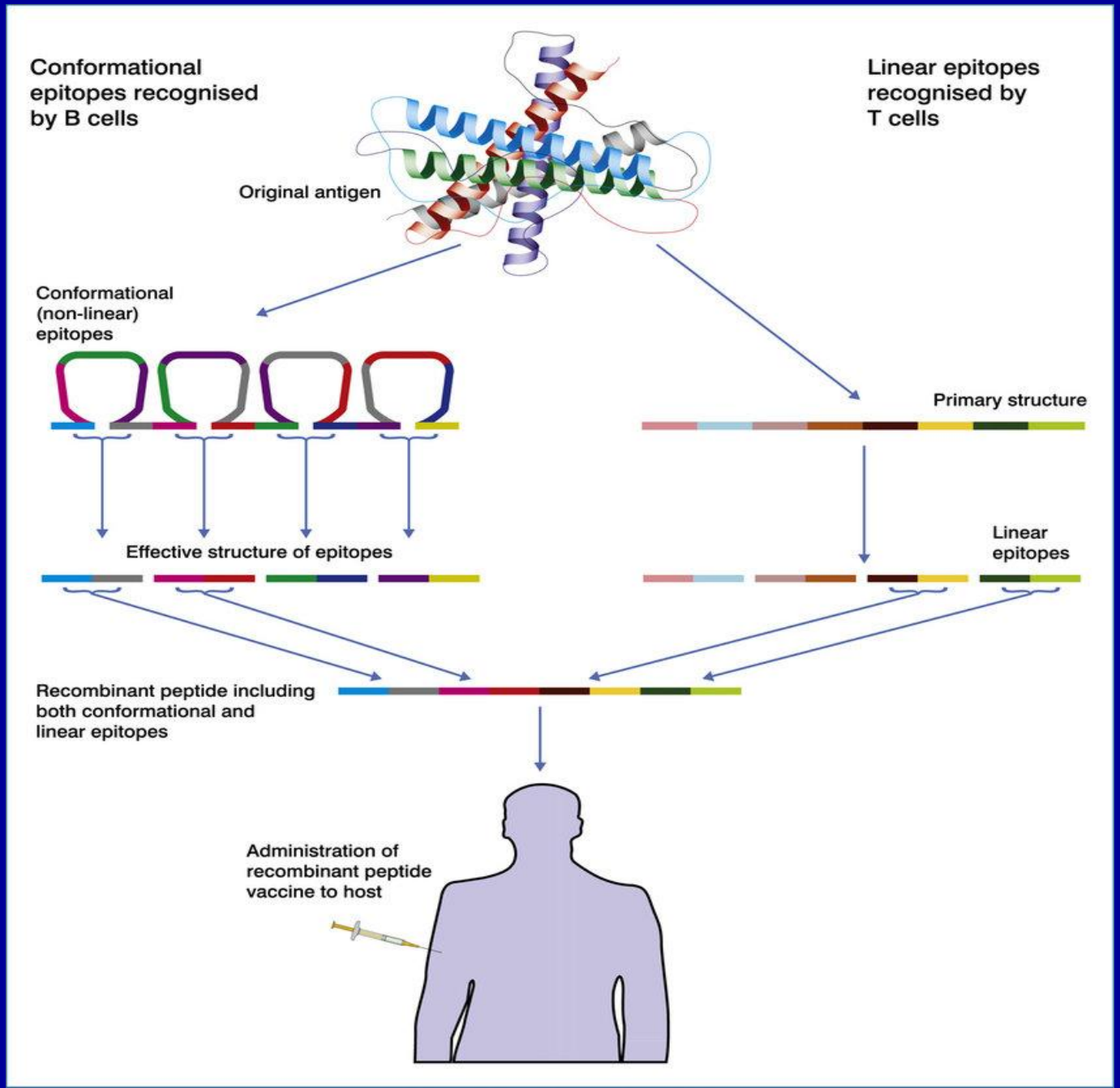
They can be developed after identification of the microbial components, that elicit a protec-tive immune response–protective antigens (S for SARS).

Immunogenic component may be isolated from viruses:

(1) by biochemical means (*chemical vaccines*) or

(2) by genetic engineering (*recombinant vaccines*) involving the expression of cloned viral genes in bacteria or eukariotic cell.

Subunit vaccines for viruses



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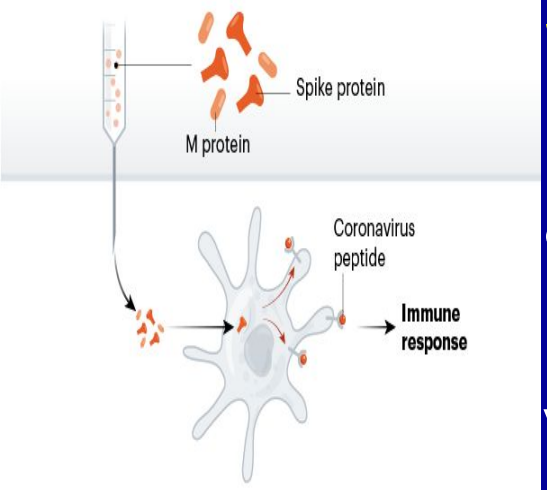

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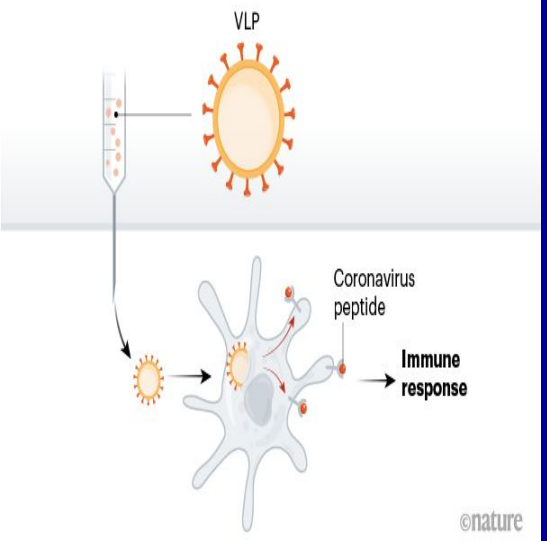
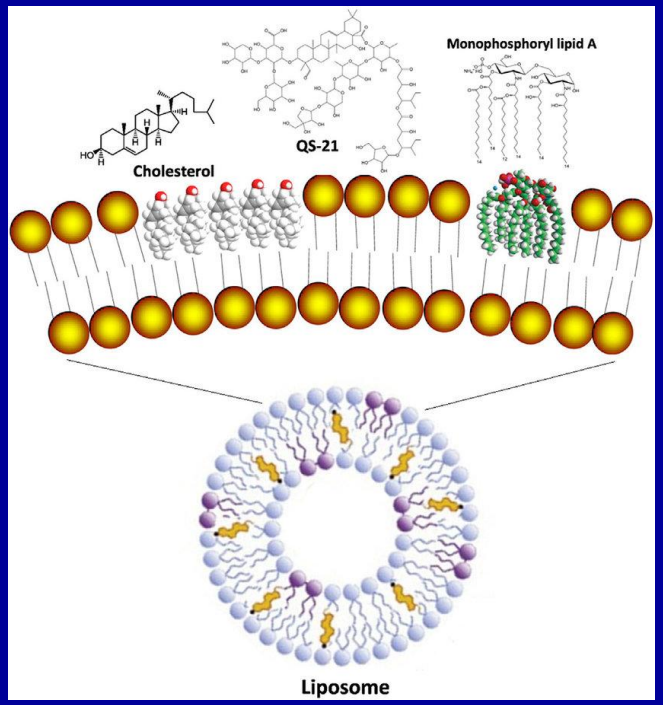


PROTEIN-BASED VACCINES disdvantages

Subunit VNs are poor immunogens and need to be administered with adjuvants or inside small lipid membrane vesicles - liposomes.

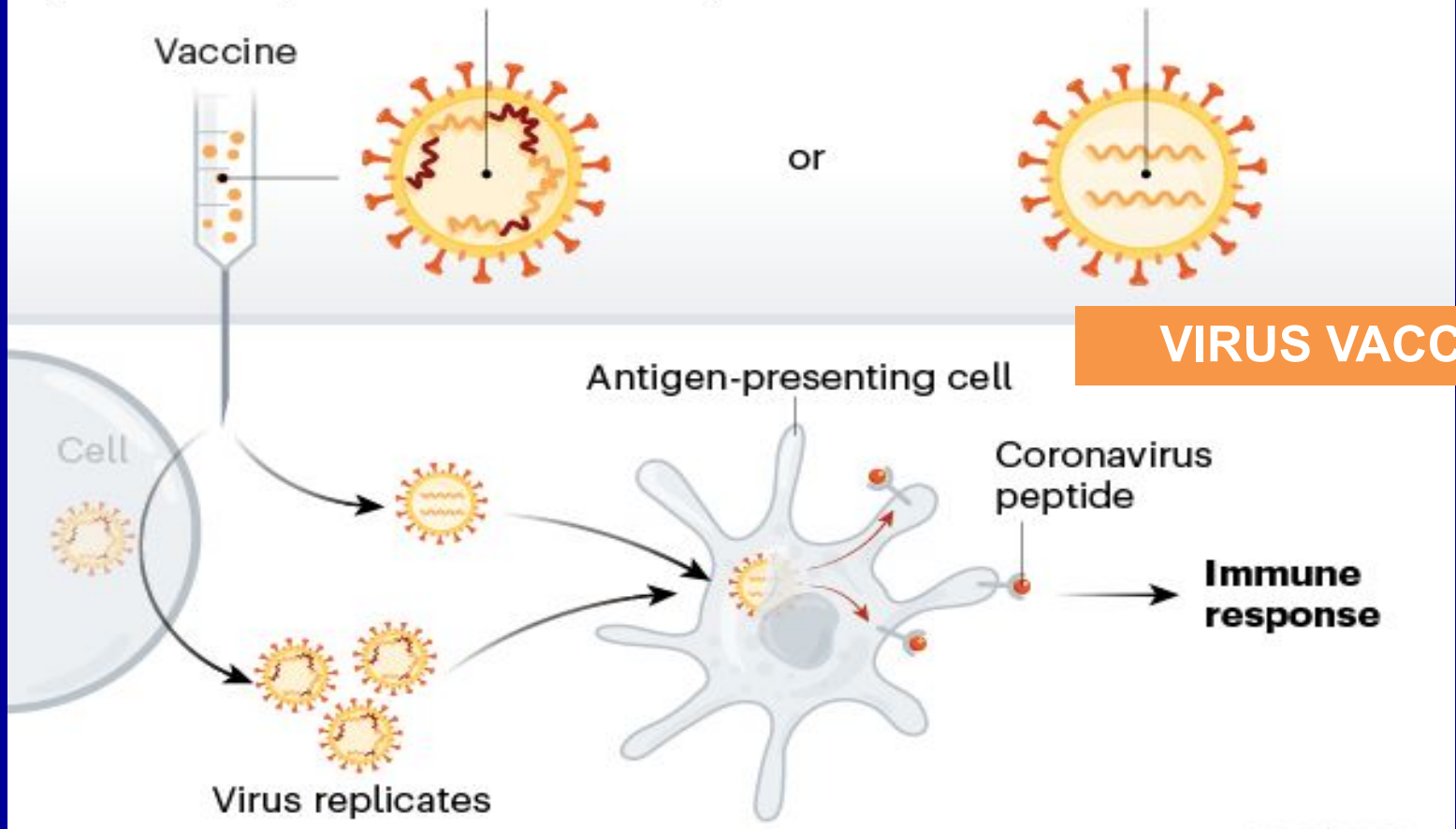


Weakened virus

A virus is conventionally weakened for a vaccine by being passed through animal or human cells until it picks up mutations that make it less able to cause disease. Codagenix in Farmingdale, New York, is working with the Serum Institute of India, a vaccine manufacturer in Pune, to weaken SARS-CoV-2 by altering its genetic code so that viral proteins are produced less efficiently.

Inactivated virus

In these vaccines, the virus is rendered uninfectious using chemicals, such as formaldehyde, or heat. Making them, however, requires starting with large quantities of infectious virus.



VIRUS VACCINES

Live vaccines: The advantages

(1) The **immunity is long live**, and mimics the normal immune responses.

(2) When vaccine is administrated orally, **SIgA** is secreted in the **gut** and **oropharynx** ***to protect*** **the mucous.**

This ***prevents*** the establishing of **carrier state** and ***facilitates*** the **eradication** of the **virus** from the community.

(3) Live vaccines are administrated in **low doses**. Basically **one single administration** is enough for protection because **organisms multiply** in a body.

Live vaccines: The disadvantages

(1) they may cause disease in immunosuppressed individuals;

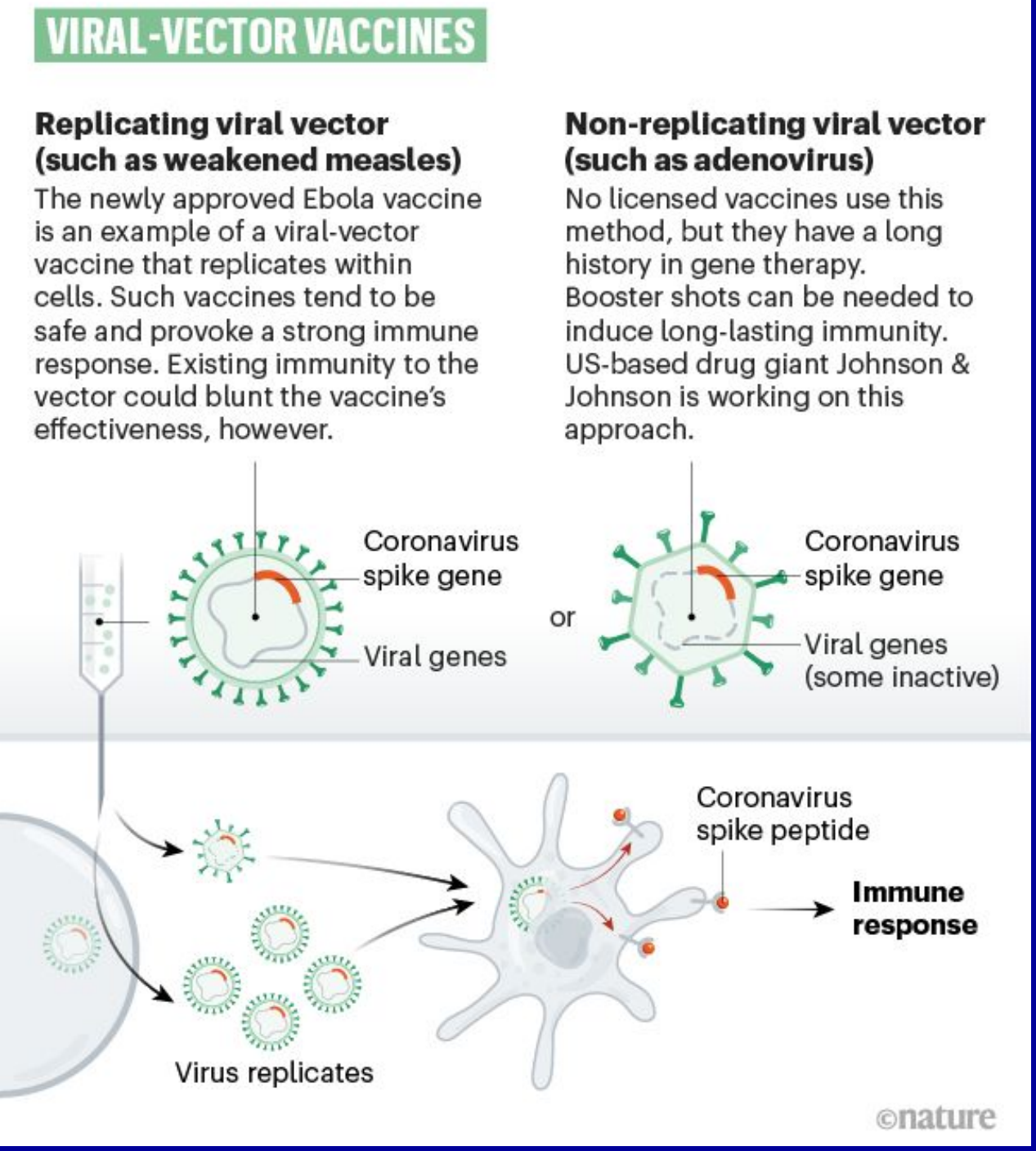
(2) the vaccine may revert to virulent form;

(3) the COVID – 19 vaccine may cause the effect of the virus (cytokine "storm")

Platforms for vector vaccines

Disadvantage:

Anti-vector immunity



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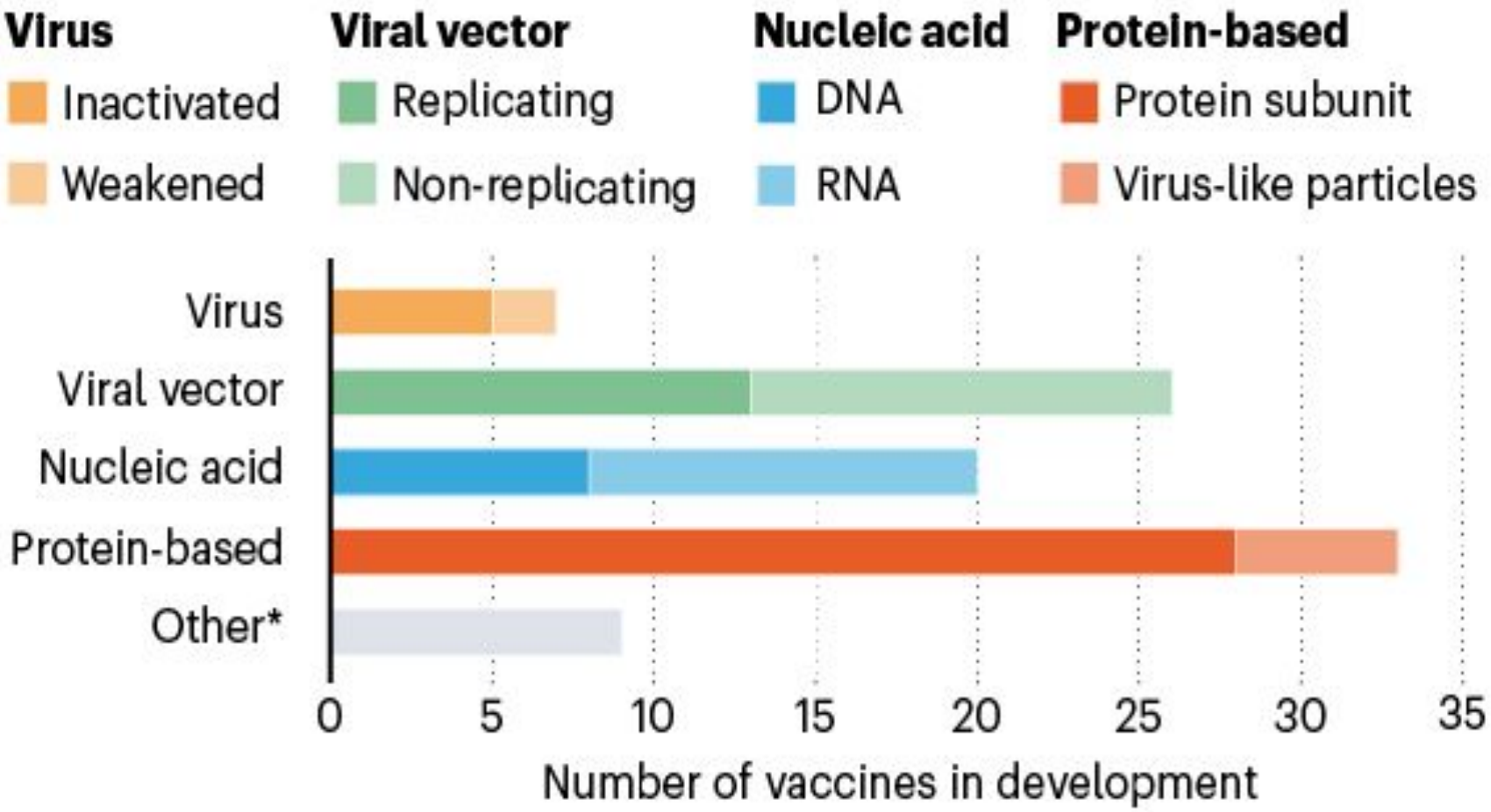

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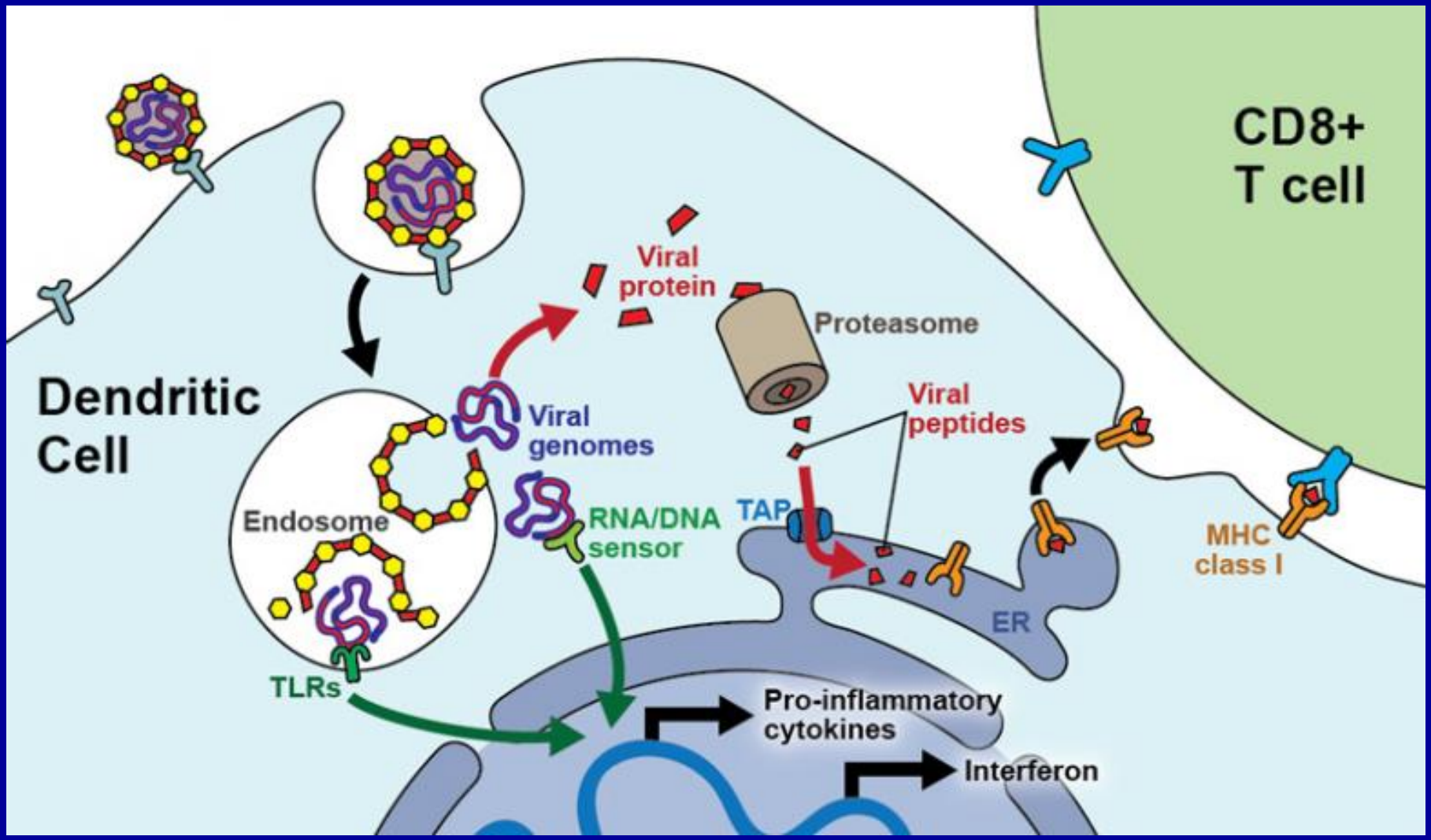
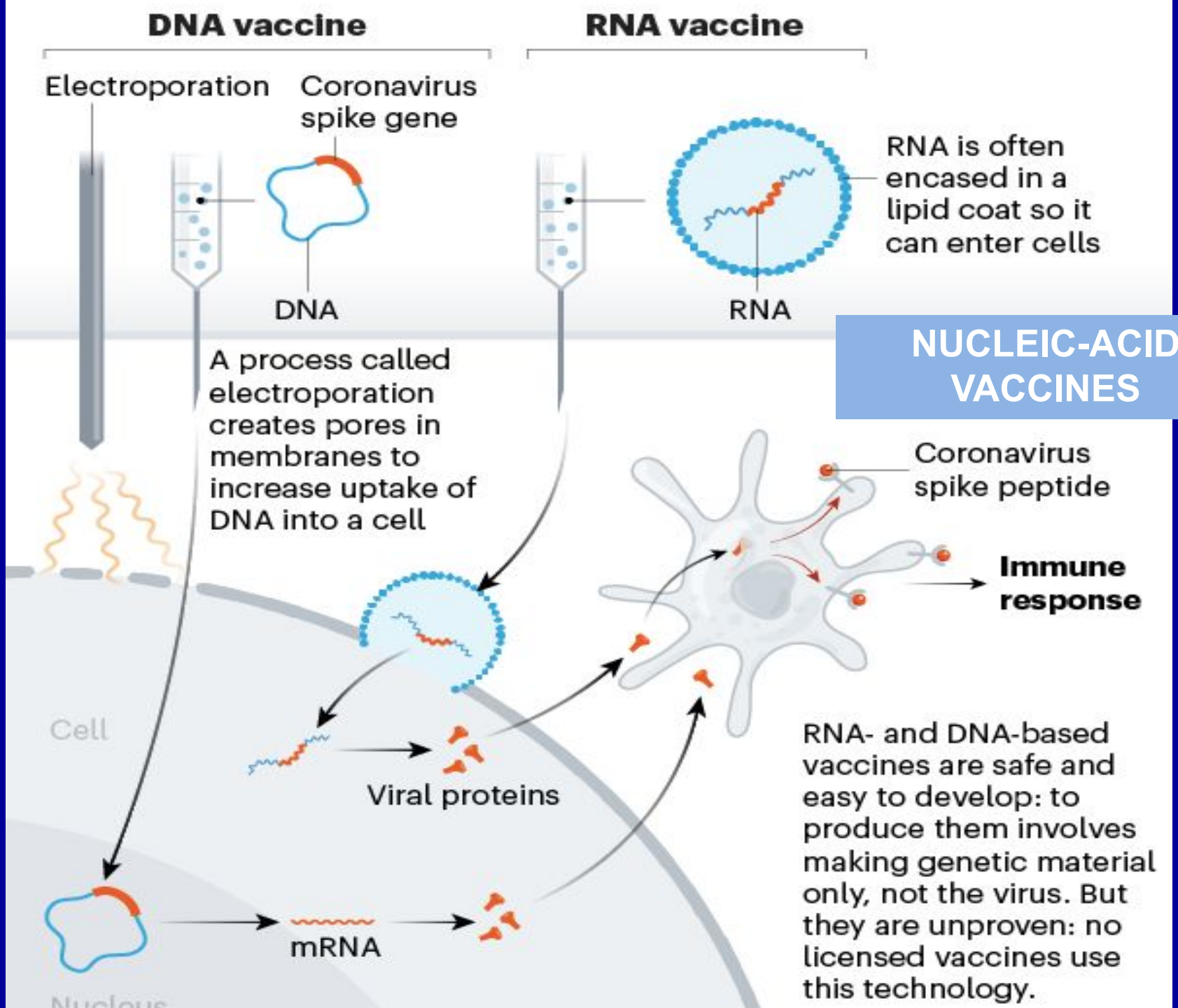
Mechanisms of immune activation by vaccine vector particles (VVP) through two pathways (Advantage)



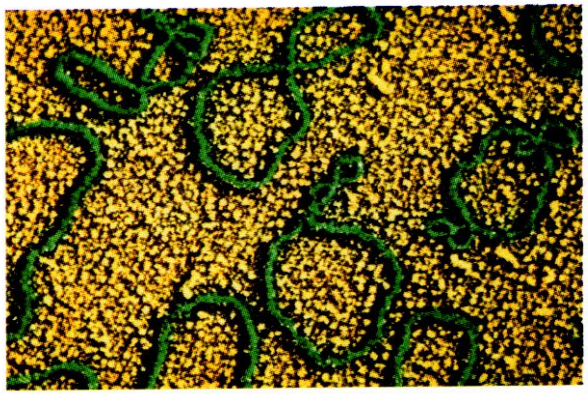
- VVP infect DCs of a vaccinee, taken up by receptor-mediated endocytosis and release their genome into the cytoplasm of the DC. TLRs sense it in endosome or/and by cytoplasmic sensors of viral nucleic acids (“RNA/DNA sensor”). Both pathways signal through common pathways such as the NFκB and MAPK pathways, resulting in the transcriptional activation of pro-inflammatory cytokines but also in type I interferon production. These events lead to functional activation of the DCs dendritic cell as APCs. Simultaneously, the viral genomic information will be expressed, leading to synthesis of viral proteins and endosomal processing. Viral peptides are loaded onto MHC class I molecules, which are then exported to the cell surface for presentation to virus-specific CD8+ T



NUCLEIC-ACID VACCINES

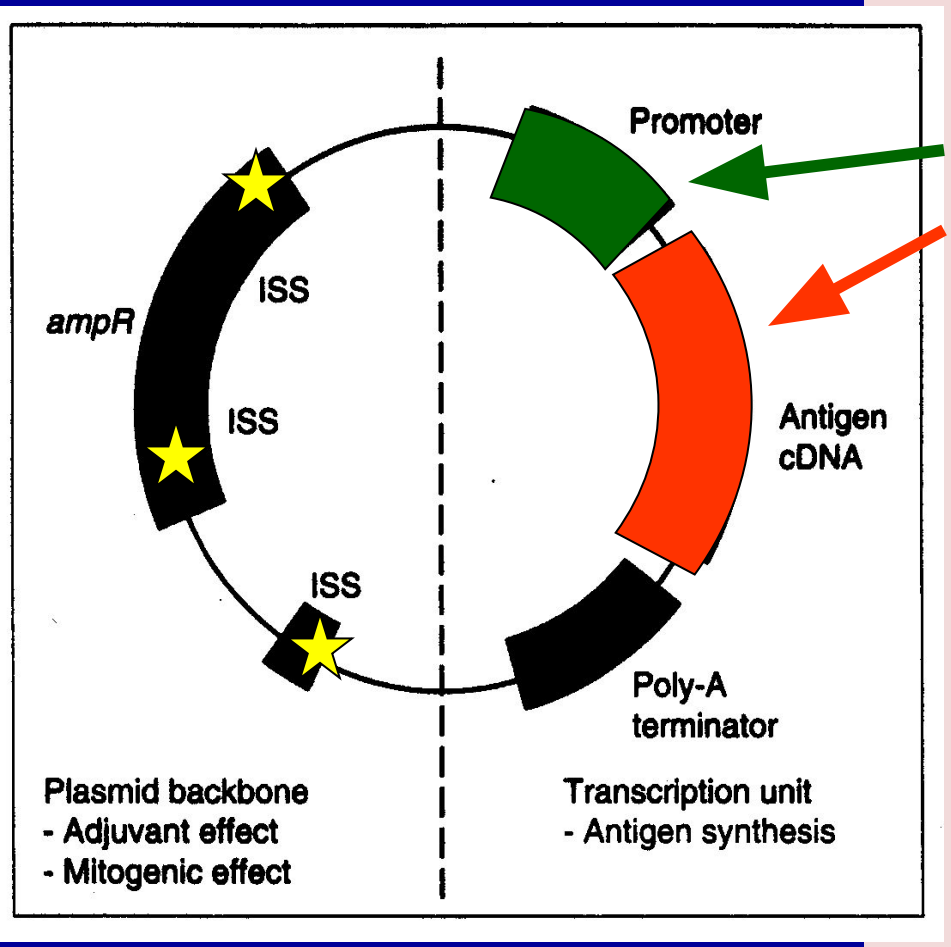
DNA vaccines

- DNA vaccines consist of naked DNA code for a gene for vaccinal protective antigen. This construct is produced by cloning gene, code for protective antigen, into a bacterial plasmid.



- The use of DNA vaccines makes possible developing vaccines against infectious agents such as HIV, herpes virus, malaria, and others, which require not only *humoral* but also *cellular* immune responses for protection.

Plasmid DNA for gene vaccination



has two major units:

(1) A transcription unit comprising promoter, an antigen cDNA, and poly-adenylation (A) addition sequence, which together direct protein synthesis.

(2) A plasmid backbone deli-vers adjuvant and mitoge-nic activity via immuno-stimulatory sequences (ISS). ISS are located within the ampicillin antibiotic resistance gene (ampR). ISS are the noncoding region of the plasmid.

Immune responses elicited by DNA vaccines

The DNA plasmid is injected into the muscle cell or skin of the vaccine recipient.

The plasmid can be uptaken by both muscle cell and antigen-presenting cell (APC).

The *gene for the antigen* (Ag) will be *expressed in muscle cell* and this antigen will be produced by the recipient muscle cells in large amounts.

(1) When uptaken by APC, the Ag can be presented on the APC together with class MHC-II to activate T helper cells to mediate humoral immunity.

(2) When the Ag is produced and presented as endogenous Ag together with class MHC-I on the surface of the muscle cell, it can elicit TH1 cell-mediated immune response.

DNA vaccines: Disadvantages

Vaccines	Advantages	Disadvantages
Viral vectored vaccines	Stimulation of innate immune response; induction of T and B cell immune response.	induction of anti-vector immunity: cell based manufacturing
DNA vaccines	Non-infectious; stimulation of innate immune response; egg and cell free; stable, rapid and scalable production; induction of T and B cell immune response.	Potential integration int human genome; poor immunogenicity in humans.