Types of Vaccines (contd)

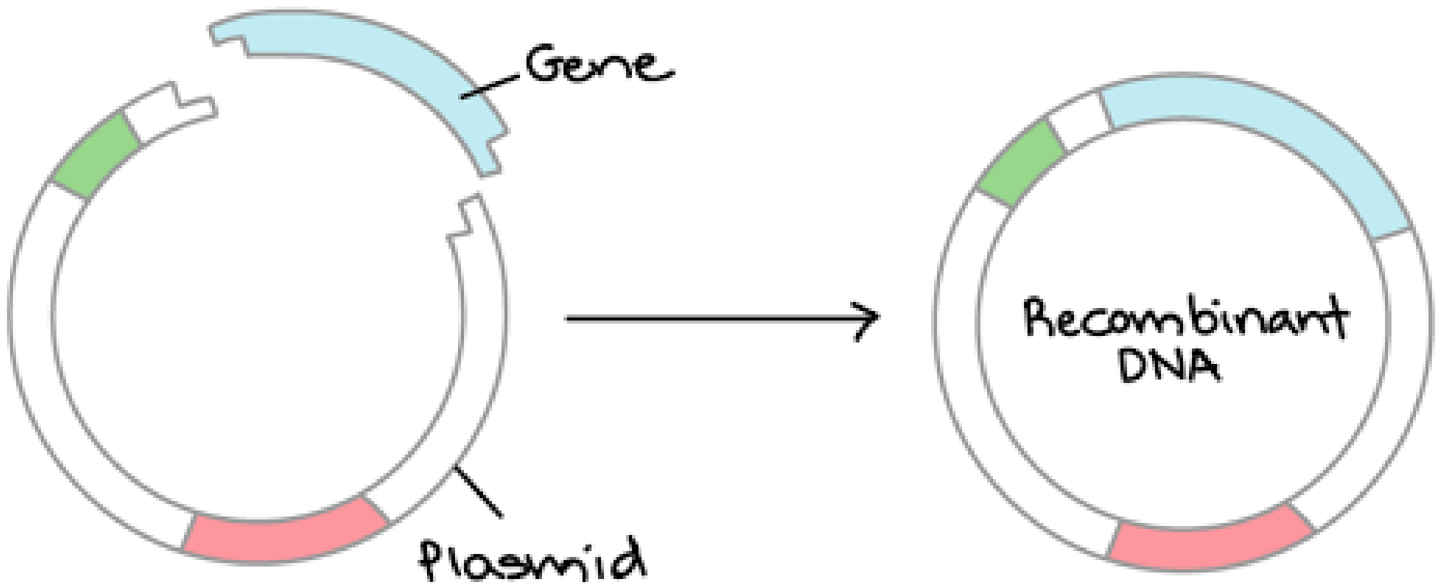
DNA VACCINES

-- DNA vaccines consist of **naked DNA**.

-- The DNA is introduced into a **plasmid**.

-- The altered plasmids carry only the genes **specifying** one or more antigenic proteins made by a selected pathogen.

-- In this way, the genes that would enable the pathogen to reconstitute itself and cause the disease are **excluded**.


Gene
Plasmid
Recombinant DNA

-- DNA vaccines for some **cancers** especially lymphomas, and prostate and colon cancers have also been tried.

-- Attachment of **cancer genes with bacterial or plant genes** enhance the immune response.

-- DNA vaccines for various infectious diseases are under preparation.

Generally speaking DNA vaccines for humans have not been as successful as expected due to some still unidentified reasons.

PREPARATION

-- A suitable vector (plasmid) capable of **expression in mammalian cells** is the basic tool.

-- It should also have the **capacity for introduction of multiple genes.**

-- Various vectors that have been used for preparation of DNA include pDX1, Tet C, pSC9 , pcDNA 3.1 , APL 400-003 1, 2.

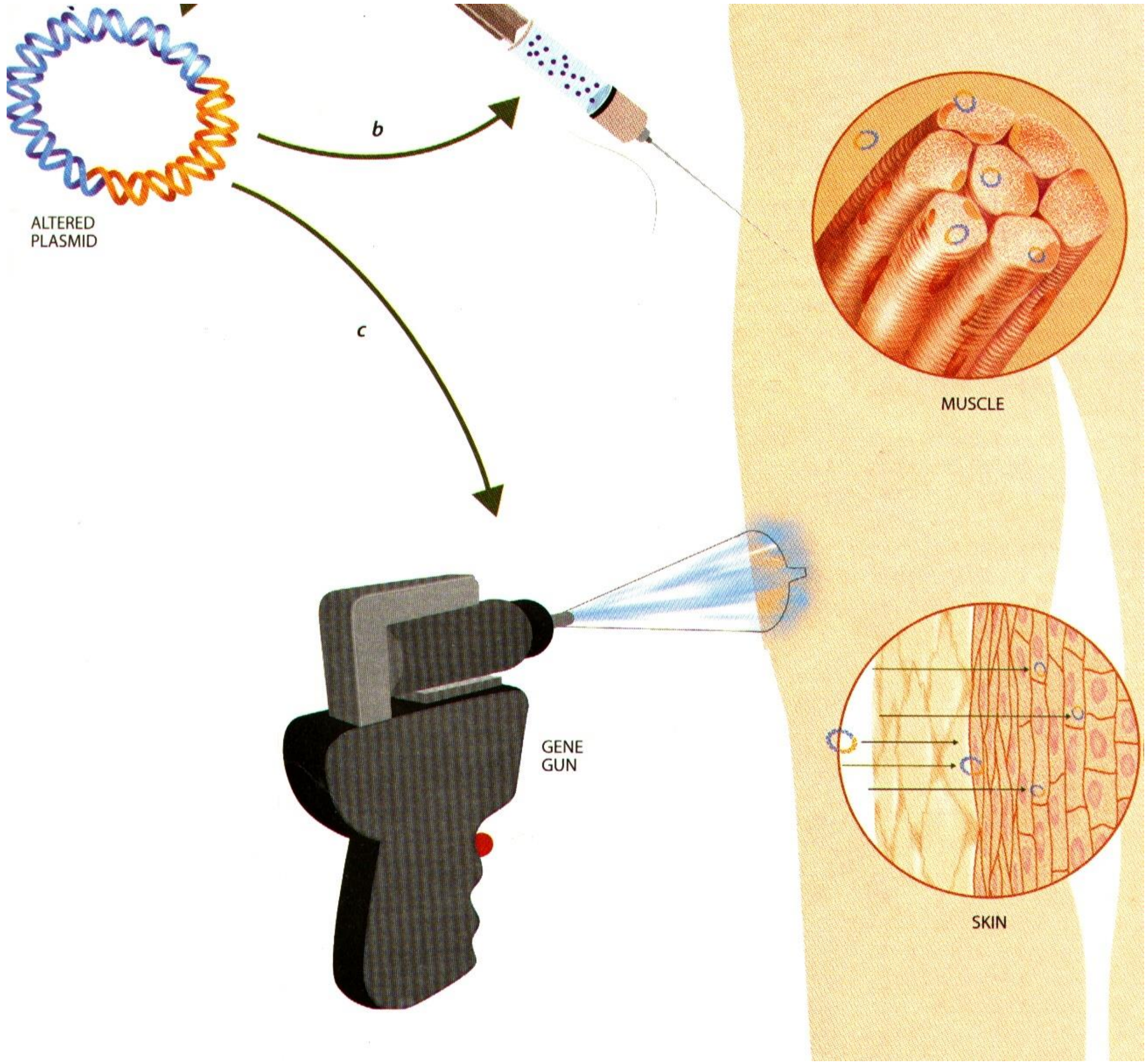
-- Genes of interest are inserted into these vectors by **conventional cloning methods**.

DELIVERY

-- The plasmids are usually delivered by **injection** or a device known as **gene gun**.

-- **Injection (muscle)** puts genes **directly** into some cells and also leads to uptake by cells in the **vicinity** of the inserted needles.

-- The **gene gun** propels plasmids into cells near the **surface** of the body (usually skin).


ALTERED
PLASMID
b
c
MUSCLE
GENE
GUN
SKIN

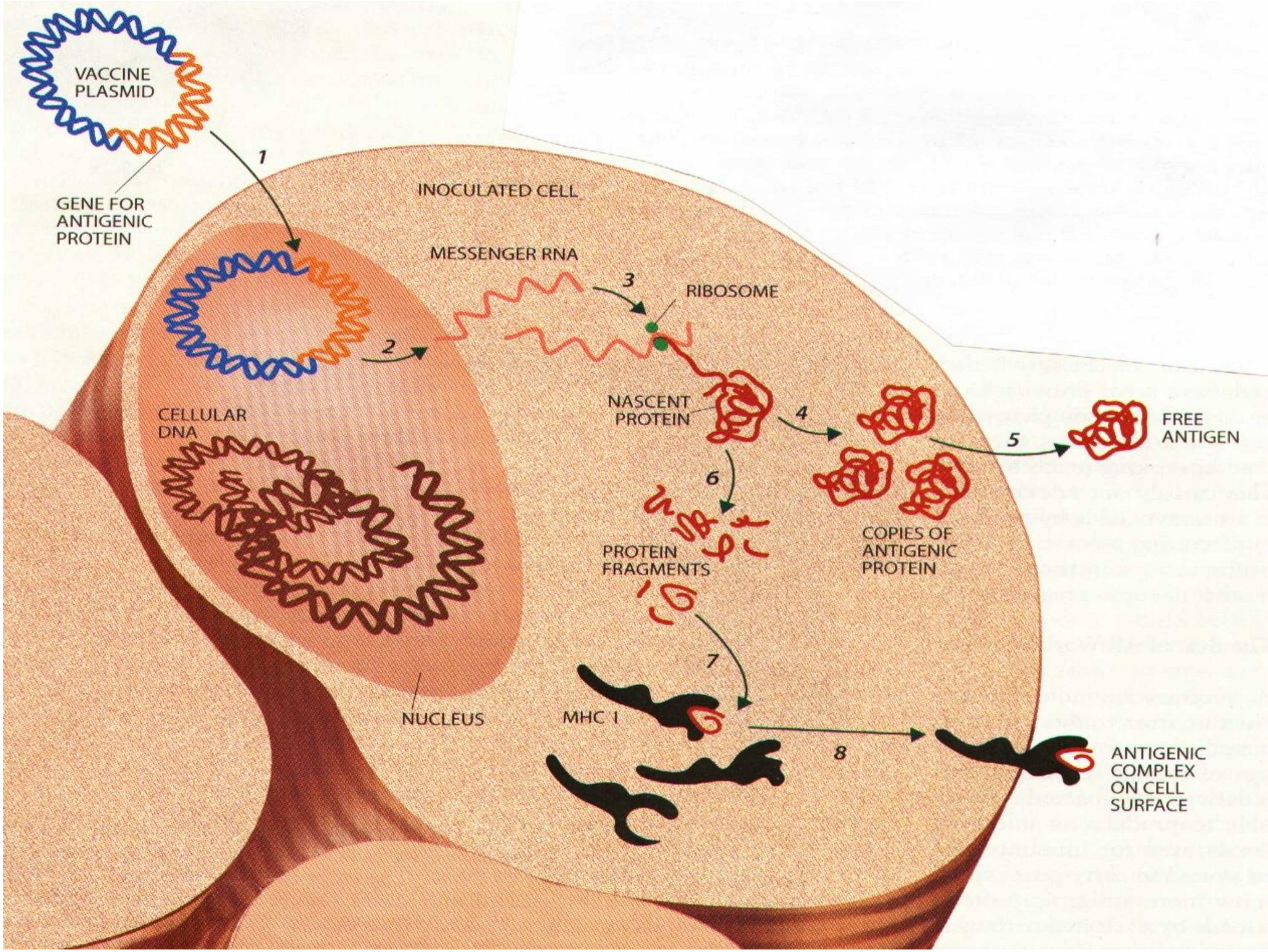
IMMUNE RESPONSE

-- DNA vaccines evoke **both humoral and cellular** responses by classical pathways.

-- Immune responses **vary**.

-- **Plasmid DNA** surrounding the antigenic genes has its **own immunogenic effect.**

-- This is because **GC groups are non-methylated** (due to bacterial origin) in contrast to GC sequences of vertebrates which are methylated.


VACCINE PLASMID
1
GENE FOR ANTIGENIC PROTEIN
INOCULATED CELL
MESSENGER RNA
3
RIBOSOME
2
NASCENT PROTEIN
4
FREE ANTIGEN
5
CELLULAR DNA
6
COPIES OF ANTIGENIC PROTEIN
PROTEIN FRAGMENTS
7
NUCLEUS
MHC I
8
ANTIGENIC COMPLEX ON CELL SURFACE

ADVANTAGES

1. Viral and parasitic antigens are presented to the host immune system in **native form**.

2. DNA vaccines are **more thermostable** than other vaccines.

3. Double stranded DNA itself is **poorly immunogenic**.

4. Immune response can be **boosted** substantially by repeat immunization.

5. Utilizing **identical** or **similar** vector backbones a **wide range** of infectious disease and cancer targets can be addressed.

SAFETY CONCERNS

1. Hypothetically, production of **anti-DNA antibodies** or other **autoimmune diseases** is possible.

2. In very rare cases, **malignant transformation** of cells that have taken up injected nucleic acids may occur.

3. Foreign DNA may become **chromosomally integrated** and the integration event may result in **tumor suppressor gene (e.g., p53) inactivation**.

CONJUGATE VACCINES

CONJUGATE VACCINES

*Conjugate vaccines are so-called because their production involves the **conjugation of the polysaccharide antigen with a protein.***

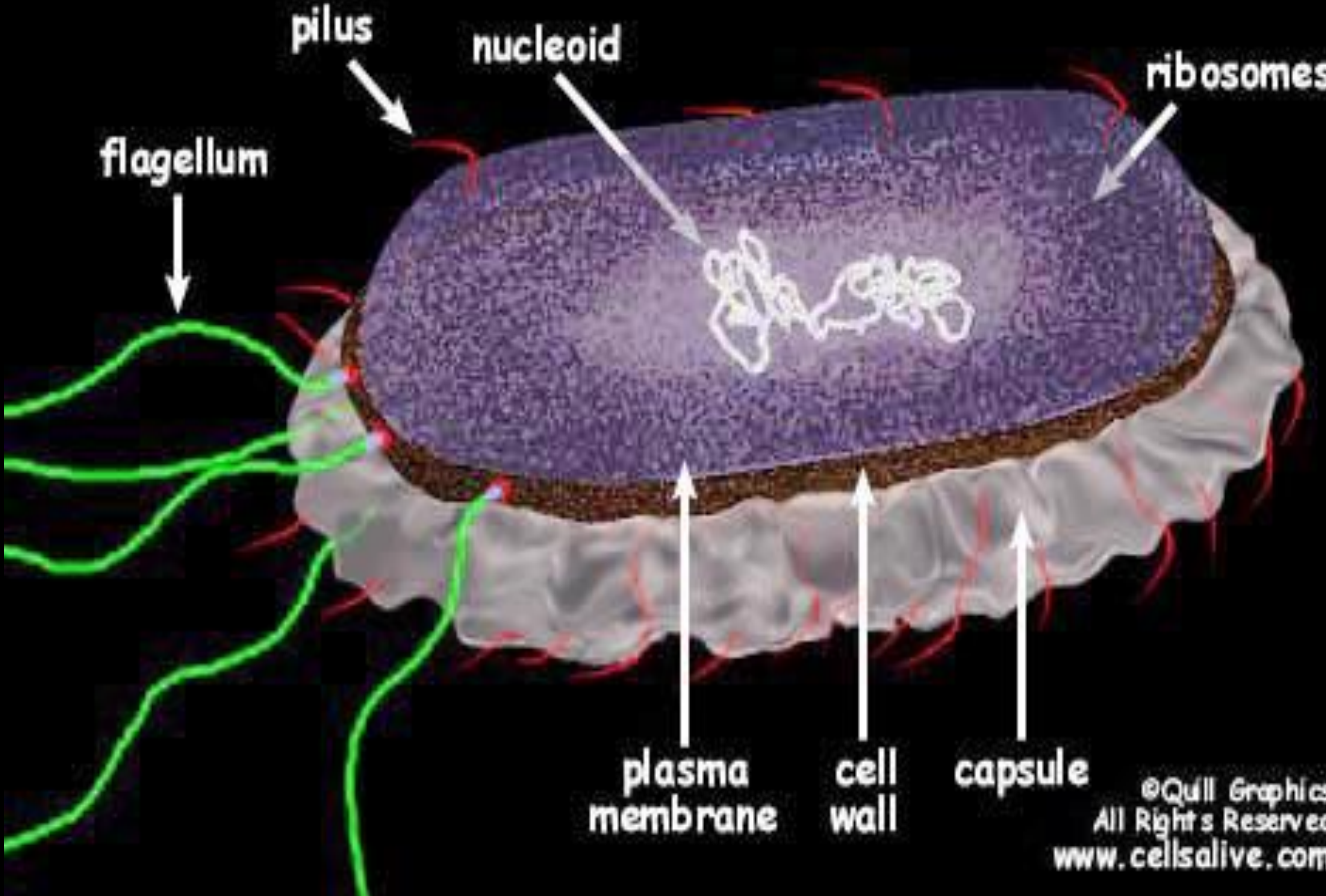
*This conjugation **converts** the **T- cell independent carbohydrate antigen into a T-cell dependent antigen**, with all the associated benefits in terms of immunological response.*

CONJUGATE VACCINES

- Most of the bacteria for which conjugated vaccines are designed have an important **structural feature in common**.

- They are all surrounded by **a thick and slippery capsule** which determines their virulence to an extent. It is polysaccharide in nature.

- Most of bacterial pathogens that cause **childhood diseases** belong to this class.


pilus
nucleoid
ribosomes
flagellum
plasma membrane
cell wall
capsule
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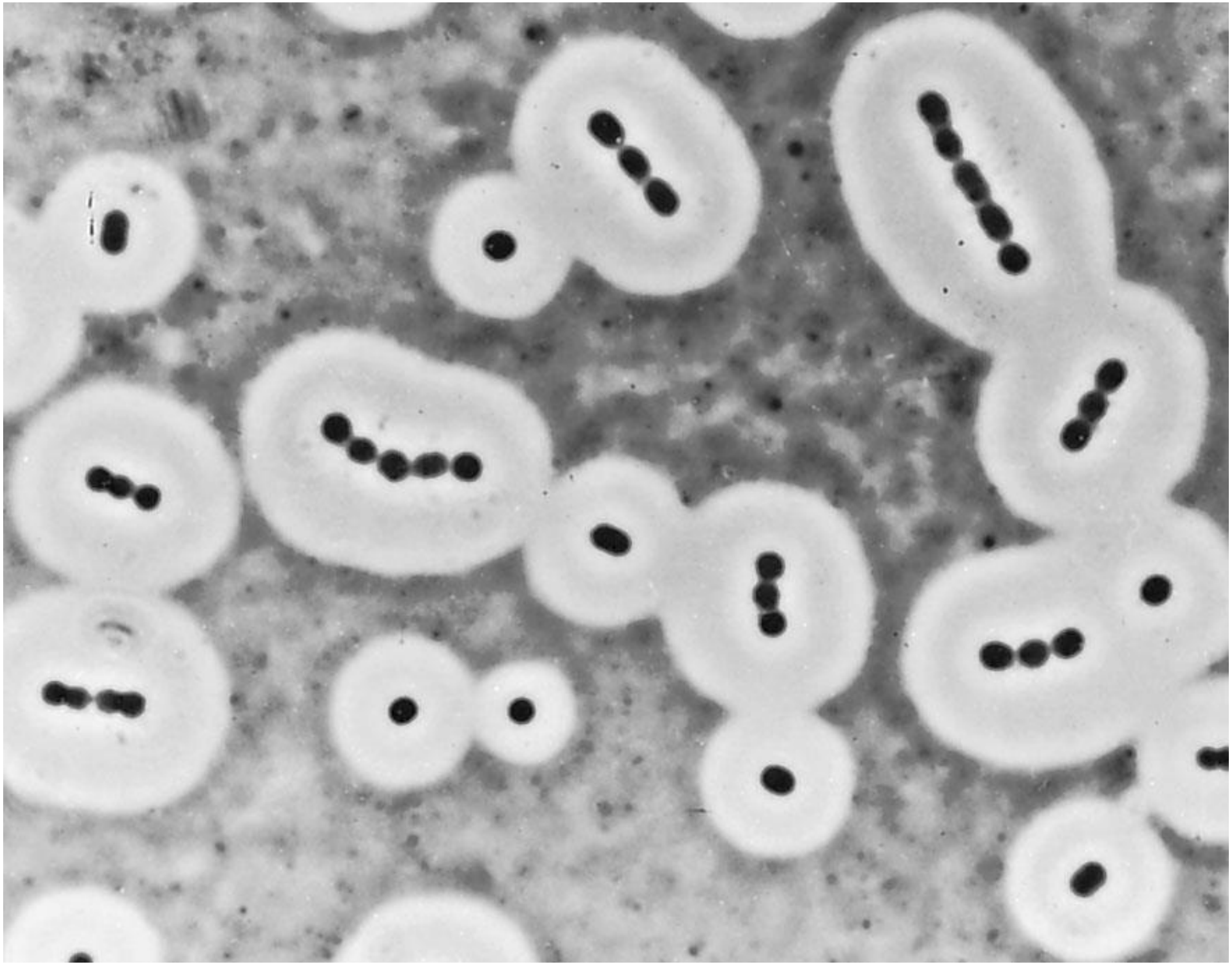
www.cellsalive.com



IMMUNE RESPONSE TO POLYSACCHARIDES

-- The immune system of **children under two years of age does not respond to carbohydrate antigens**, so pure polysaccharides are of no use.

-- Even in older children and adults, these vaccines induce only **short-term immunity** because memory cells are not formed.

-- Protection decreases rapidly and is generally gone by around **two years from vaccination.**

IMMUNE RESPONSE TO POLYSACCHARIDES- PROTEIN CONJUGATES

After conjugation with a protein, following benefits are gained:

-- Because of protein presence, **cellular immune system** is evoked leading to **higher production of antibodies**.

-- **Memory cells** are formed.

-- **Affinity maturation** takes place, whereby B cells refine and improve the antibodies they produce with time.

THERAPEUTIC VACCINES

-- **Traditional vaccines** are **prophylactic** and are used to protect **healthy persons**.

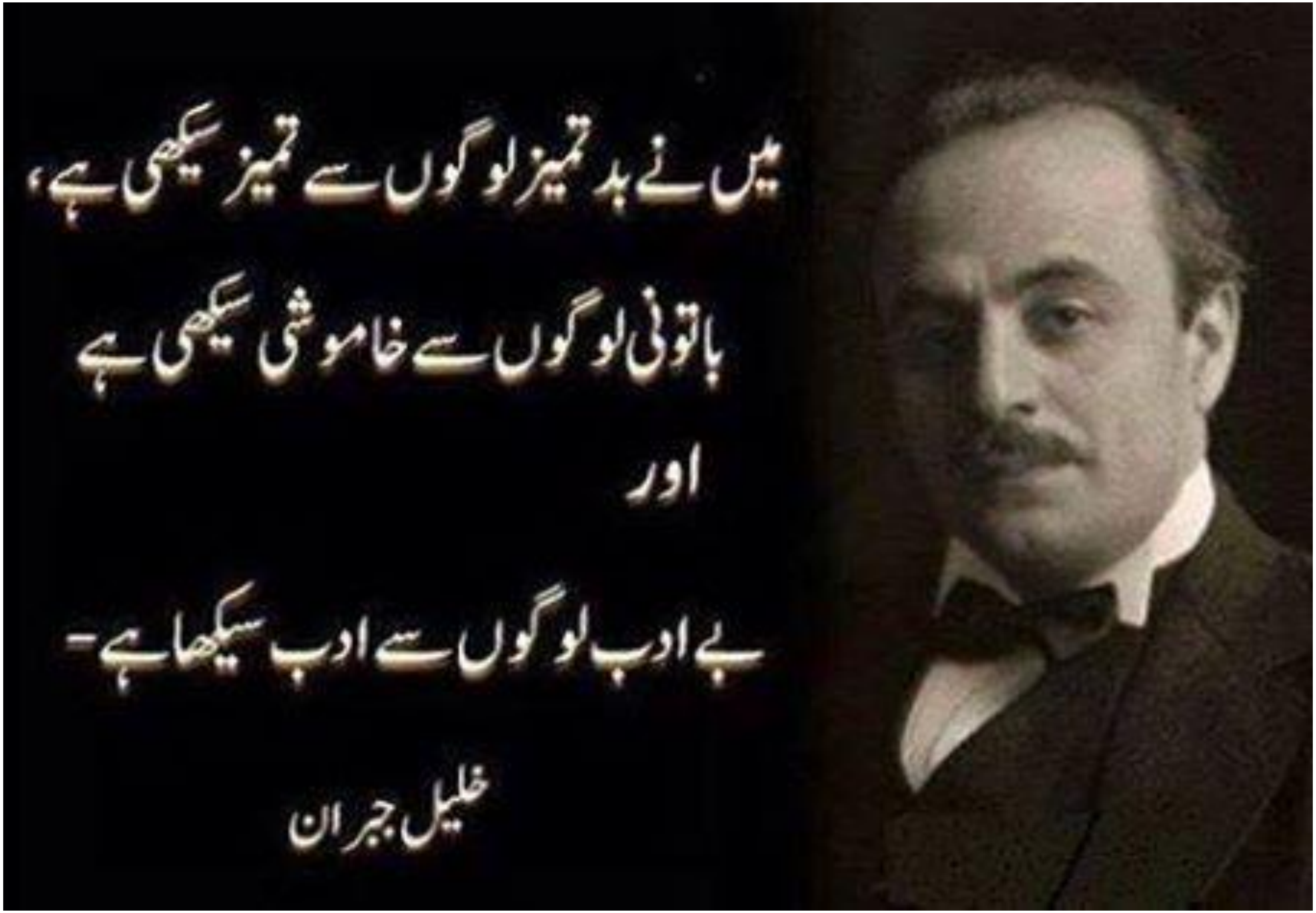
-- **Therapeutic vaccines** are used for **patients** to **stimulate** natural mechanisms of the immune system to overpower the infection or disease.

-- These have been used for **cancer treatment** and **viral diseases.**

- In therapeutic vaccination against **cancer** there is a requirement to **overcome tolerance** and to **activate a weakened immune repertoire.**

- Induction of **CD4+ T helper cells** is critical for both antibody and T cell effector responses for **cancer**.

- Evidence from human and animal studies point to an instrumental role for **CD8+CTL** in controlling **HIV-1 infection.**


میں نے بد تمیز لوگوں سے تمیز سیکھی ہے،
باتونی لوگوں سے خاموشی سیکھی ہے
اور
بے ادب لوگوں سے ادب سیکھا ہے۔
خلیل جبران

Daisugi technique used by Japanese for last 700 years


Thank You!