# Lec4 \ Principles of Medical Biotechnology


قسم علوم التقنيات الاحيائية الطبية
المرحلة الاولى

اعداد

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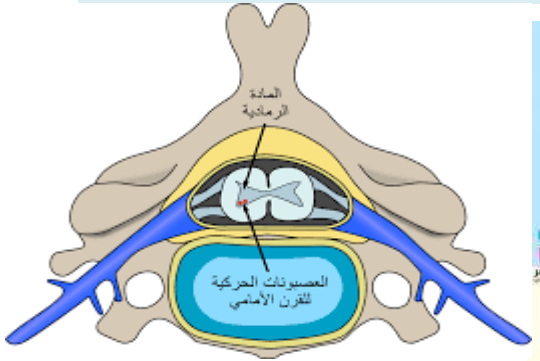
الايميل :

رمز الصف :

# قصة ( Spinal Muscular Atrophy (SMA) )





- في عام 2017، وُلد طفل يُدعى تشارلي وكان يعاني من مرض وراثي نادر يُعرف بـ Spinal Muscular Atrophy (SMA)، وهو مرض يؤدي إلى ضعف شديد في العضلات وغالبًا ما يكون مميتًا في سن مبكرة. الأطباء كانوا يعرفون المرض جيدًا...لكنهم لم يمتلكوا العلاج. في تلك الفترة، كان فريق من العلماء يعمل على تقنية جديدة تعتمد على البيوتكنولوجي، حيث تم تطوير علاج جيني يُدخل نسخة سليمة من الجين المفقود إلى خلايا الطفل باستخدام ناقل فيروسي معدل وراثيًا. العلاج كان تجريبيًا، مكلفًا، ومحفوفًا بالمخاطر.

- غم ذلك، تم إعطاء الطفل جرعة واحدة فقط من العلاج الجيني. بعد أشهر، حدث ما لم يكن متوقعًا: الطفل بدأ بتحريك أطرافه - قدر على الجلوس ثم الوقوف ثم المشي، يعيش تشارلي حياة طبيعية تقريبًا، بفضل العلاج الجيني ((Gene Therapy، وهو أحد أعظم تطبيقات البيوتكنولوجي في الطب الحديث.

# Introduction

Biotechnology use transgenic micro-organism, plants or animals as living "factories" to produce pharmaceuticals for the use in humans or animals. Other medical applications include gene therapy and stem cells

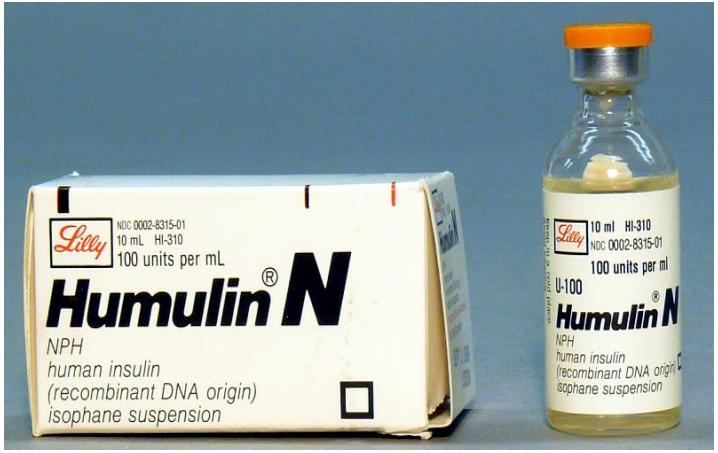
## Production of therapeutically proteins

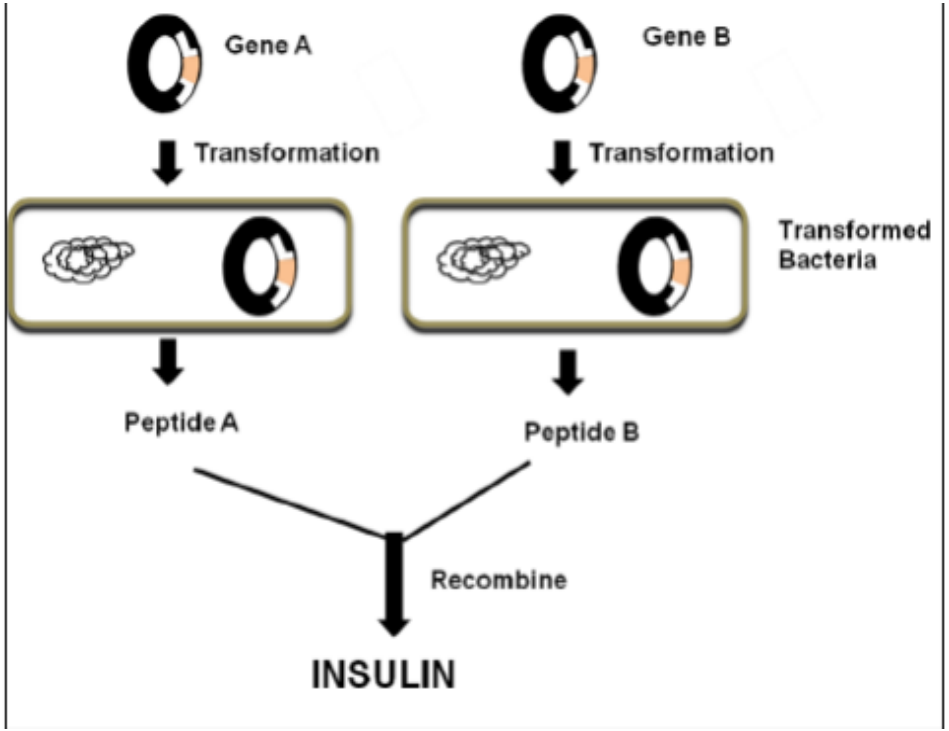
A large number of genetic or metabolic diseases can be corrected by the supplying proteins or factors. Following the advancement in the biotechnology, many other proteins or factor are produced in different bacterial expression systems In an approach, gene of the enzyme or proteins factor is cloned into the appropriate plasmid to produce recombinant clone, for example: production of human insulin.

**Insulin is** a dimer of an A chain and B-chain linked by disulphide bonds, composed of 51 amino acids with a molecular weight of 5808 Dalton.

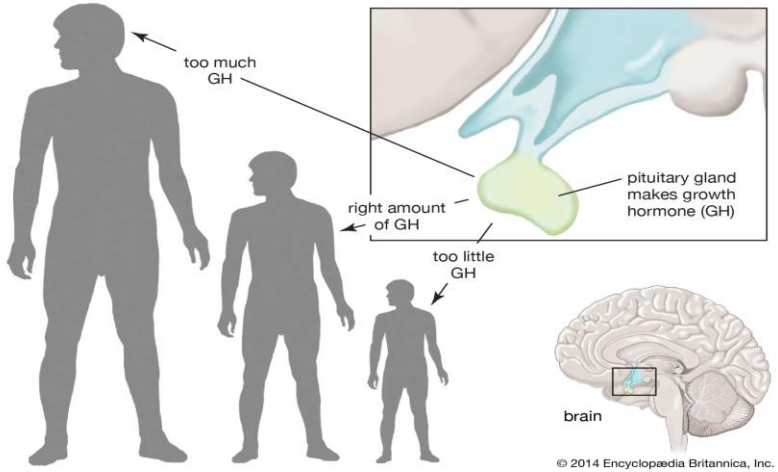
schematic presentation of steps in insulin production is given in Figure 1. In this process, gene A and B is cloned into the bacterial plasmid separately to produce two recombinant clones.

Peptide chain A and B is over-expressed in the *E.coli* and recombined together to produce functional insulin.

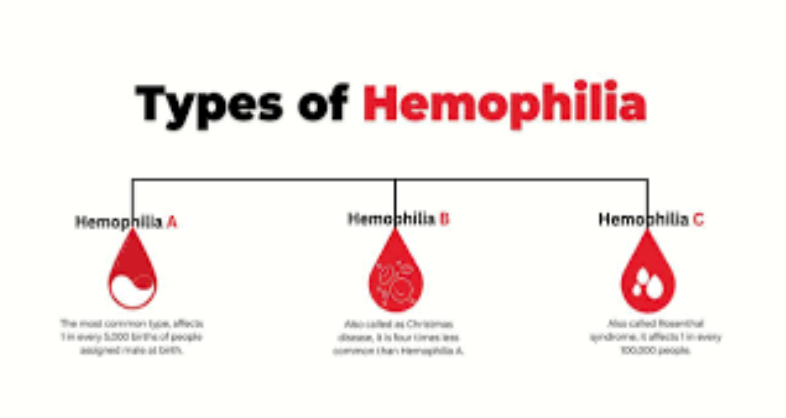

Lilly
NDC 0002-8315-01
10 mL HI-310
100 units per mL
Humulin® N
NPH
human insulin
(recombinant DNA origin)
isophane suspension
10 ml HI-310
NDC 0002-8315-01
100 units per ml
U-100
Humulin® N
NPH
human insulin
(recombinant DNA origin)
isophane suspension

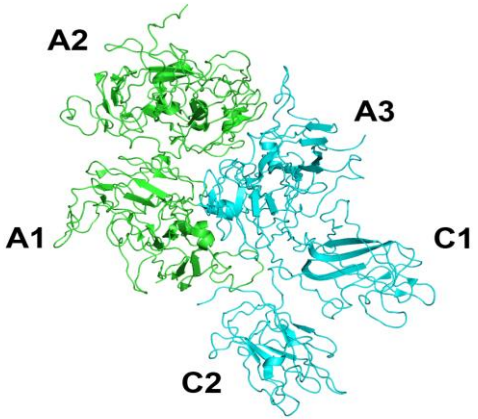

Gene A
Gene B
Transformation
Transformation
Transformed Bacteria
Peptide A
Peptide B
Recombine
INSULIN

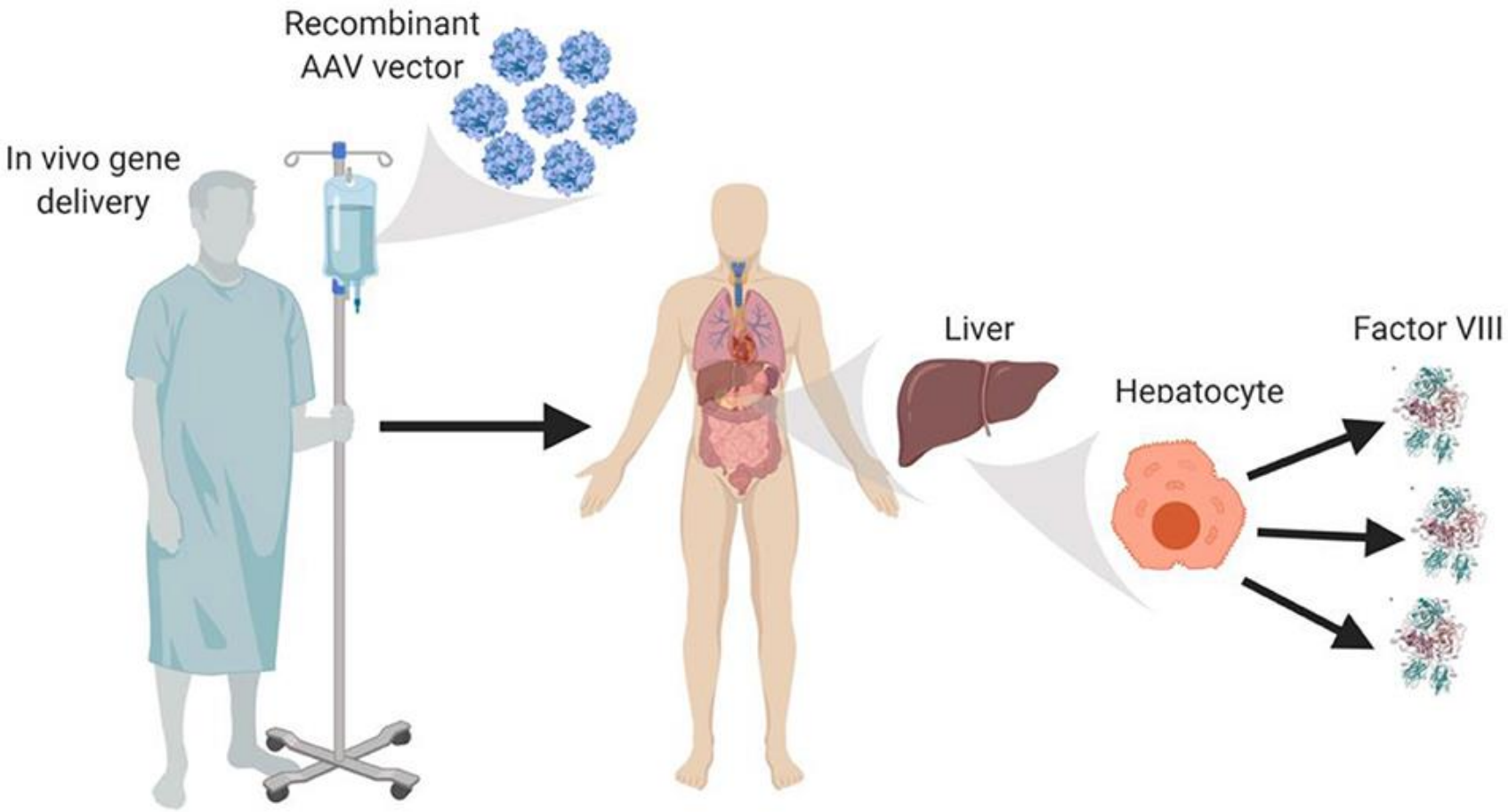
**The human growth hormones,** if this hormone from the pituitary gland الغدة النخامية, is present in reduced quantities in children that may suffer from dwarfism التقزم. Today, recombinant gene technology uses bacteria in order to produce it on a large scale; and technology seem to work so well that dwarfism may be overcome in few years' time.

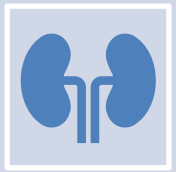


**Factor VIII** **is** very familiar to those people who suffer from hemophiliaA ; again with the help of biotechnology, this factor is produced by bacteria; it has greatly reduced the likelihood of hemophiliacs to contract AIDS, as previously applied substances originating from blood-plasma donors.




Recombinant
AAV vector
In vivo gene
delivery
Liver
Hepatocyte
Factor VIII



**Erythropoitin** الإريثروبويتين is a hormone produced by the kidneys; it stimulates the production of red blood cells (erythrocytes). Patients with kidney failure do not produce this hormone anymore; therefore, they often suffer from anemia, are always tired, and apart from dialysis, the need a constant supply of fresh blood transfusions. Today, this hormone is made by a transgenic

Today, this hormone is made by a transgenic معدل وراثي mammal, of the **Chinese hamster.** Extracting plasma from the animal, isolating the hormone, is a safer way to obtain this hormone, rather than relying again on human donors .

## Table1 \ some recombinant proteins that are used therapeutically
## البروتينات المستخدمة علاجيا

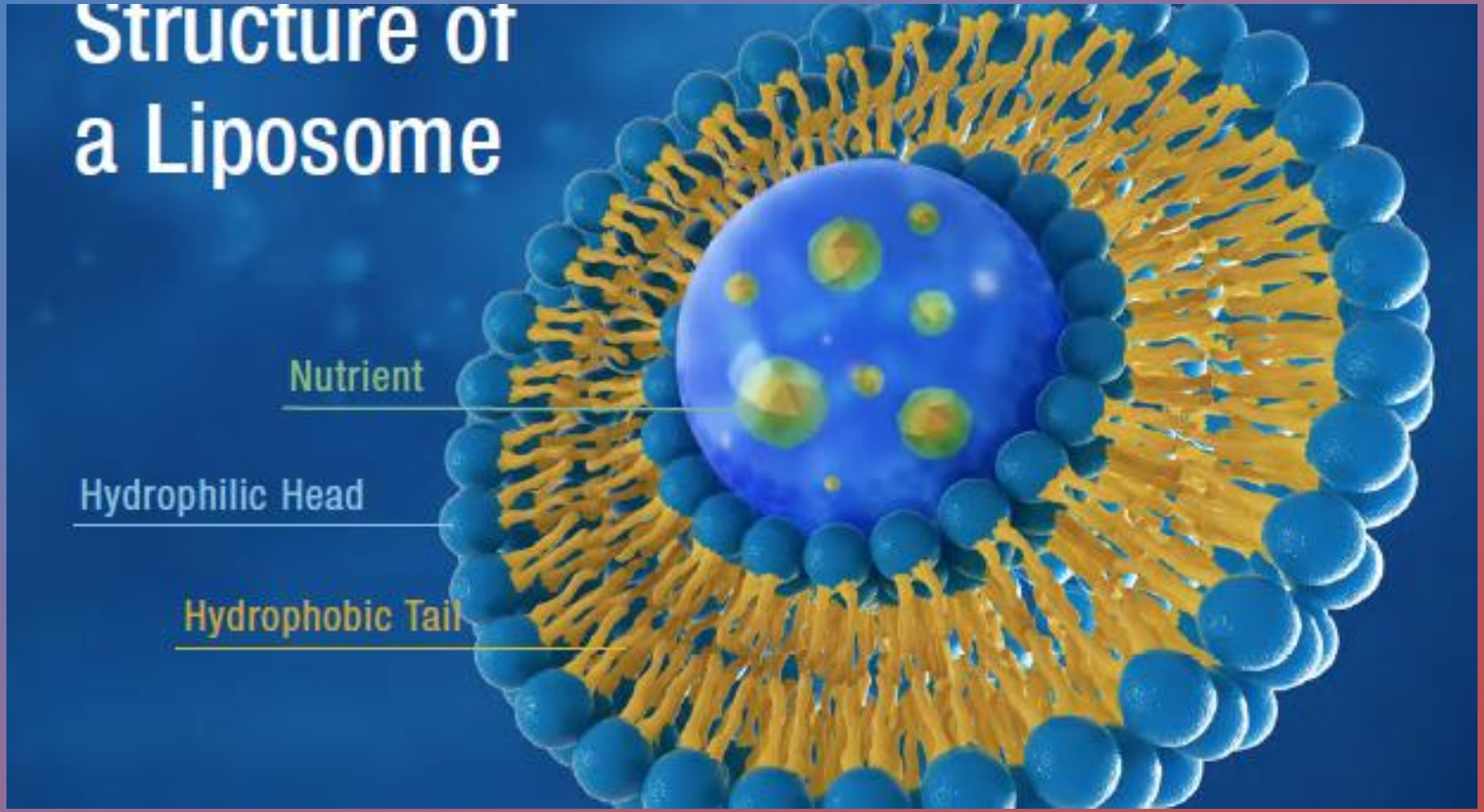
| Protein | Clinical indication |
|---|---|
| Hepatitis B vaccine | Prevention of hepatitis B infection |
| Interferon$\alpha_{2a}$ | Leukemia |
| Human DNase | Cystic fibrosis |
| Fibrinogen | Wound healing |
| Pro542 | HIV infection |
| Collagen I | Tissue repair |

# Gene therapy

As discussed before, production and supply of recombinant proteins is a temporarily solution for the treatment of a disease condition. In another approach, human expression system is used to produce the proteinous factor after inserting the recombinant clone into the human cells or inside the human body. Recombinant DNA is packed into the appropriate DNA delivery system (either a virus or liposome mediated) to deliver the gene into the human cells to correct the mutated genes or encode a therapeutic protein drug to provide treatment

# Liposomes الليبوسومات

Liposomes Artificially formed single-layer or multilayer spherical lipid bilayer structures. Made from solutions of lipids, etc. in organic solvents dispersed in aqueous media. Under appropriate conditions, liposomes form spontaneously. Often used as models of the plasma membrane. May also be **used experimentally and therapeutically for delivering drugs** etc. To cells, since liposomes can fuse with a plasma membrane and deliver their contents to the interior of the cell vary in size from submicron diameters to centimeters.

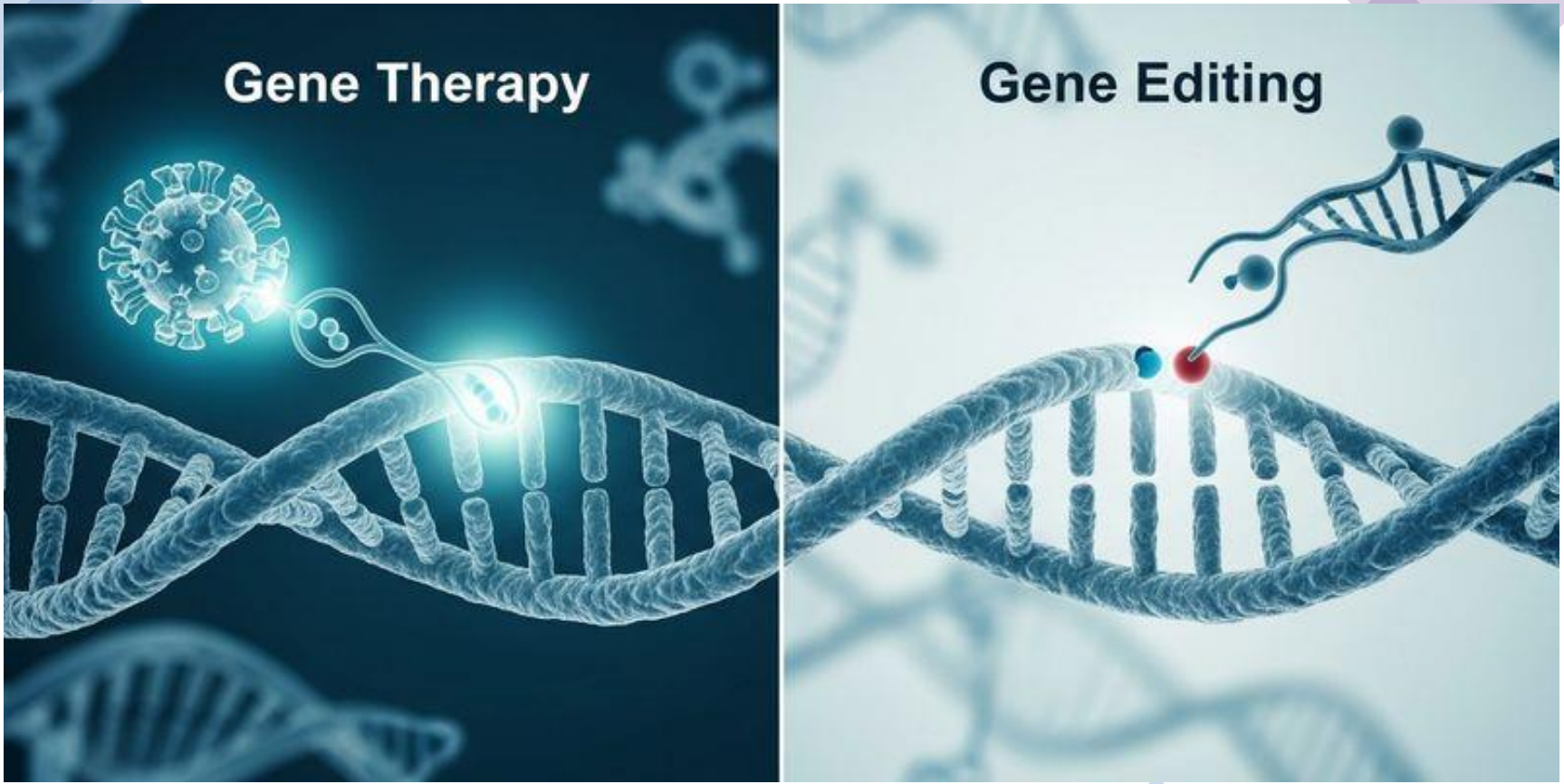

Structure of
a Liposome
Nutrient
Hydrophilic Head
Hydrophobic Tail

# Types of gene therapy

There are two different types of gene therapy

**Somatic Gene therapy العلاج الجيني الجسدي:** In this therapeutic approach, the therapeutic genes are transferred into the somatic cells as per the requirement of individual to treat the functional defects. This treatment does not move to the patient's offspring or next generations.

**Germ line gene therapy العلاج الجيني للخلايا التناسلية** : In this therapeutic approach, germ cells (sperm or egg cells) are transformed by the introduction of the required gene to produce the protein or correct the mutated gene.


Gene Therapy
Gene Editing

## The technical problems associated with the gene therapy are as follows

1. Short lived: Therapeutic gene delivery into the cells gives short term effects, either by rejection of recombinant DNA or suppression of the gene expression. Due to this problem , patient needs to go for several rounds of gene therapy.

2. Immune reaction: virus containing gene is treated as the foreign object, and immune system is stimulated to attack the invader. It is the main reason of reduced effectiveness of gene therapy.

## The technical problems associated with the gene therapy are as follows

3. Viral vector used as a vector to deliver the gene causes much adverse immune reactions and toxicity in patients.

4. Disturbance of host physiology: if the genes integrate to a wrong place in the genome, it may cause functional defects. In few cases, it may disrupt the function of the tumor suppression genes results into the development of the tumor.

# سؤال جماعي للمناقشة

**ما هي التحديات بالعلاج الجيني؟**


إنما الأمم الأخلاق ما بقيت
فإن هم ذهبت أخلاقهم ذهبوا