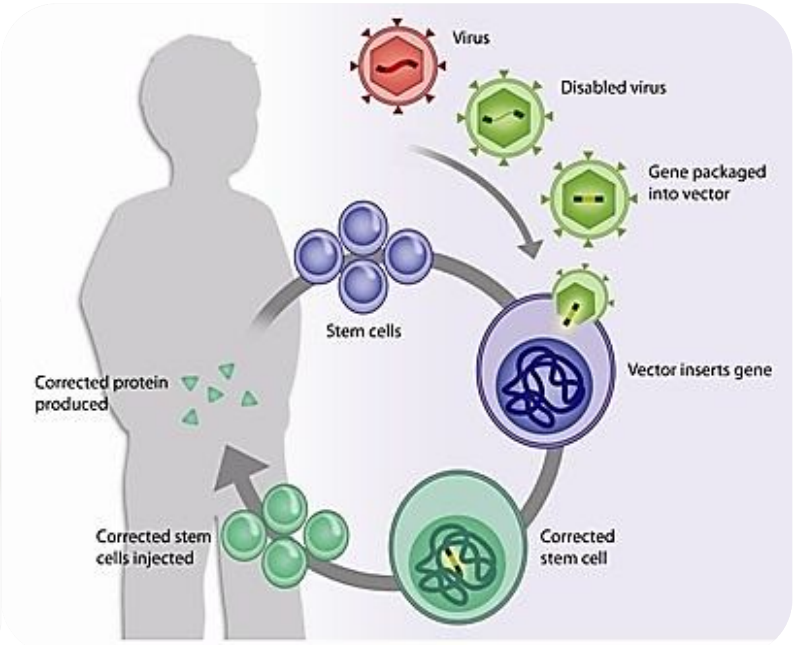
University of Duhok
College of Science
Department of Biology
4th Year Class
Biotechnology

Lecture9: Gene therapy

Lecture outlines:

- What is gene therapy?
- History and development.
- Types of gene therapy.
  - Germ line gene therapy.
  - Somatic gene therapy.
- How does gene therapy work?
- Advantages and disadvantages.



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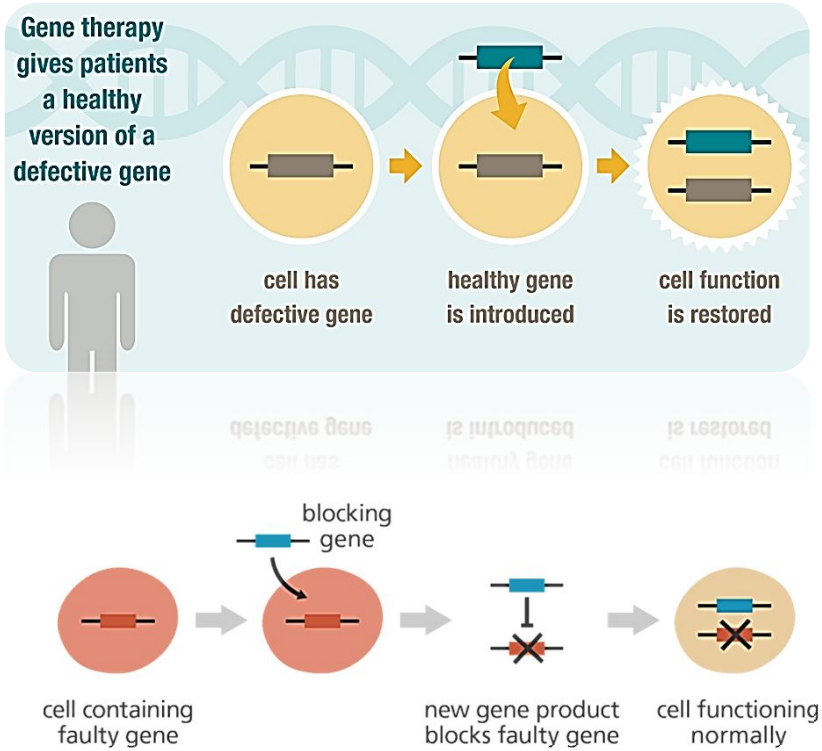
What is gene therapy?

- Gene therapy is an experimental technique for correcting defective genes that are responsible for disease development.
- The most common form of gene therapy involves inserting a normal gene to replace an abnormal gene.
- Other approaches used:
  - Replacing a mutated gene that causes disease with a healthy copy of the gene.
  - Inactivating, or “knocking out,” a mutated gene that is functioning improperly.
  - Introducing a new gene into the body to help fight a disease.



- Researchers are studying gene therapy for a number of diseases, such as Severe combined immuno-deficiencies (SCID), Hemophilia, Parkinson's disease, Cancer and HIV.

History and development.

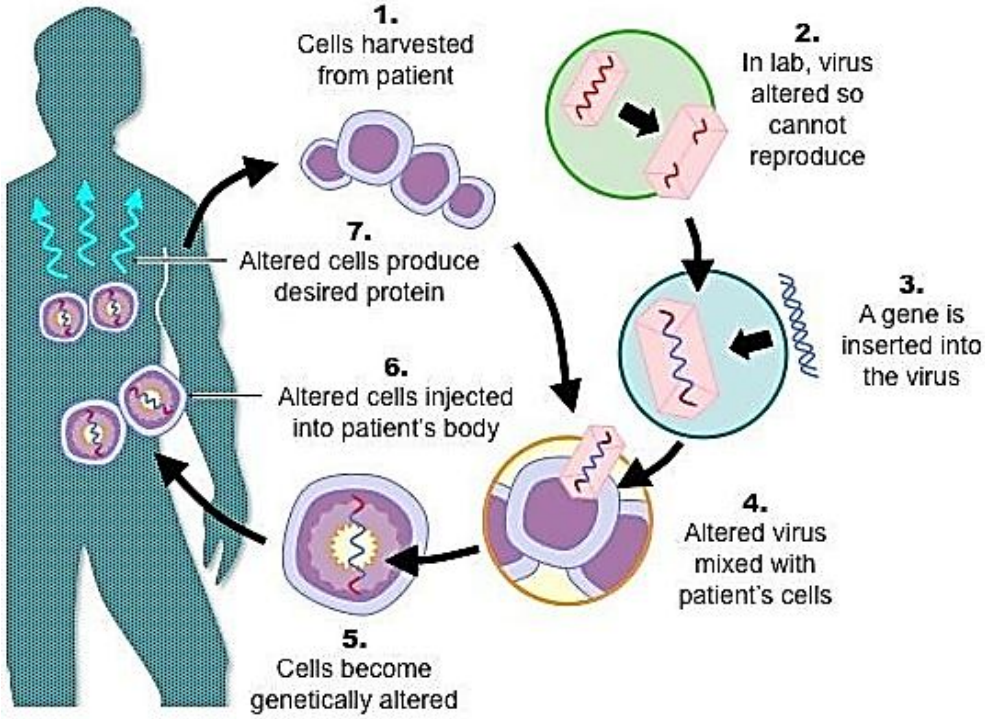
- The concepts of Gene Therapy was introduced in 1960.
- In 1970, Friedmann and Roblin published a paper in Science titled "Gene therapy for human genetic disease”
- The first approved gene therapy case was in 1990 at the National Institute of Health, U.K. It was performed on a four years old girl named Ashanti DeSilva. It was a treatment for a genetic defect that left her with an immune system deficiency.
- New gene therapy approach repairs errors in messenger RNA derived from defective genes. This technique has the potential to treat the blood disorders such as Thalassaemia, Cystic fibrosis, and some cancers.
- In 2006, scientists at the National Institutes of Health (Bethesda, Maryland) have successfully treated metastatic melanoma in two patients. This study constitutes one of the first demonstrations that gene therapy can be effective in treating cancer.
- Research is still ongoing and the number of diseases that has been treated successfully by gene therapy increases like Retinal disease, Colour blindness, and Adrenoleukodystrophy.

Types of gene therapy.

- Virtually all cells in the human body contain genes, making them potential targets for gene therapy. However, these cells can be divided into two major categories:
  1. **Somatic cells (most cells of the body).**
  2. **The germline cells (eggs or sperm).**

1. Somatic Cell Gene Therapy

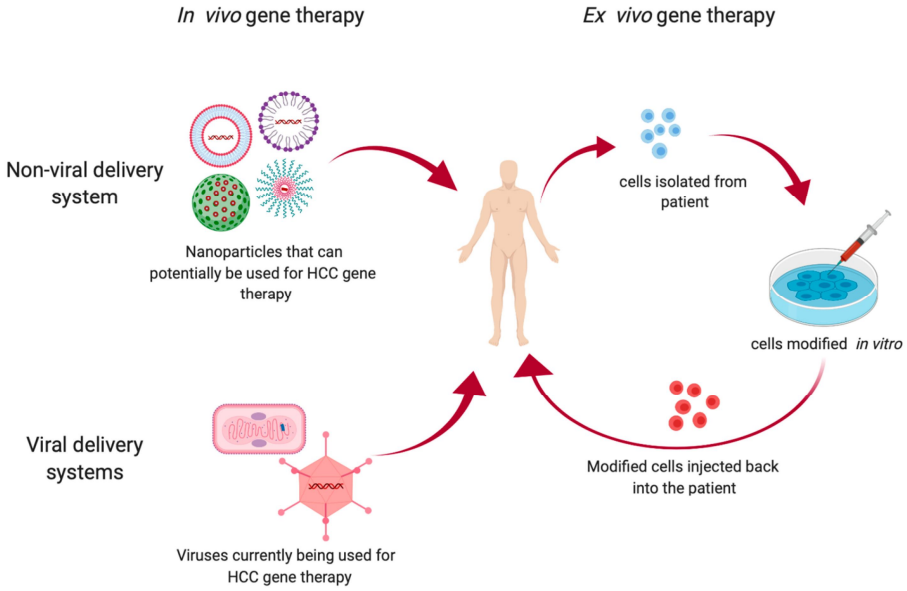
- Therapeutic genes transferred into the somatic cells.
- E.g. Introduction of genes into bone marrow cells, blood cells, skin cells etc.
- It will not be inherited by later generations.
- At present all researches directed to correct genetic defects in somatic cells.



Types of somatic gene therapy

1. **Ex vivo**: which means exterior (where cells are modified outside the body and then transplanted back in again).

- In some gene therapy clinical trials, cells from the patient's blood or bone marrow are removed and grown in the laboratory.
- The cells are exposed to the virus that is carrying the desired gene.
- The virus enters the cells and inserts the desired gene into the cells' DNA.

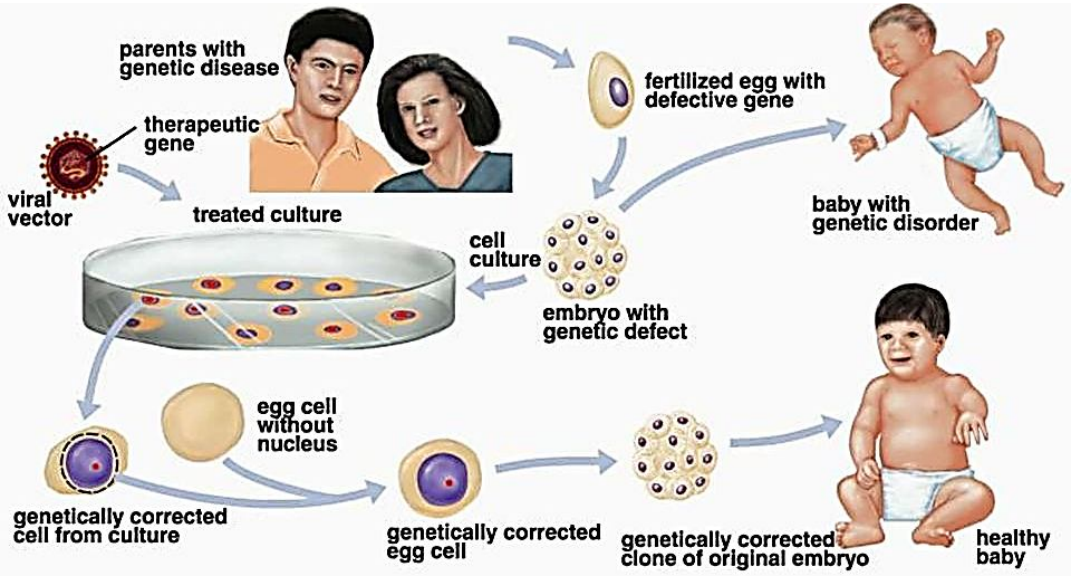


- The cells grow in the laboratory and are then returned to the patient by injection into a vein. This type of gene therapy is called ex vivo because the cells are treated outside the body.

2. **In vivo**: which means interior (where genes are changed in cells still in the body). *In vivo* gene therapy refers to direct delivery of genetic material either intravenously (through an IV) or locally to a specific organ (eg, directly into the eye, brain, liver, or muscle)

2. Germ Line Gene Therapy

- Therapeutic genes transferred into the germ cells.
- E.g. Genes introduced into eggs and sperms.
- Gene therapy using germ line cells results in permanent changes that are passed down to subsequent generations. It is heritable and passed on to later generations.



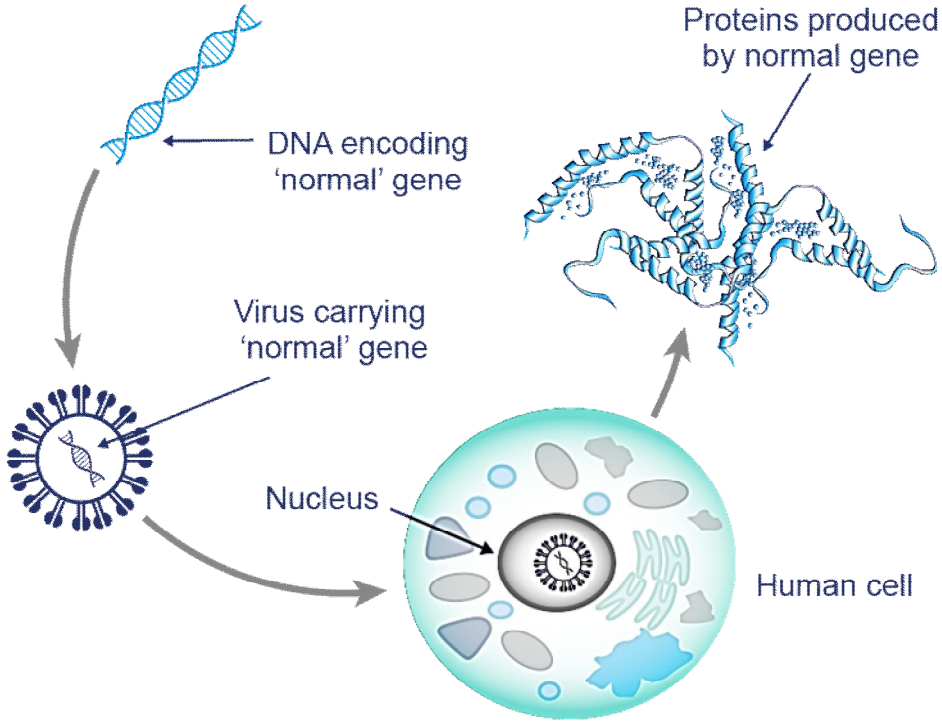
- If done early in embryologic development, such as during preimplantation diagnosis and in vitro fertilization, the gene transfer could also occur in all cells of the developing embryo.
- For safety, ethical and technical reasons, it is not being attempted at present, for example:
  - Some people view this type of therapy as unnatural, and liken it to "playing God".
  - Others have concerns about the technical aspects.

How Does Gene Therapy Work?

- Inserting a new gene directly into the body, as naked DNA, usually does not work. That is why researchers need to use a delivery system, also called a vector.
- The vector carries the healthy gene (known as therapeutic gene or transgene) to the target cells, tissues or organs.
- Choosing the right vector is critical as it effects how the patient has the gene therapy applied to them, how often the therapy needs to be applied and an easy-to-use efficient vector will allow researchers to potentially expand the use of a gene therapy within diagnostics, biotechnology, and basic science research.
- There are two ways of delivering a vector: it can either be transferred directly into cells while they are still in the patient (in vivo); or a sample of the target cells is taken from the patient, exposed to the vector in the laboratory, and then returned into the patient (ex vivo).
- Broadly speaking there two types of vectors;
  - **A. Viral vectors.**
  - **B. Non-viral (or 'engineered') vectors**.

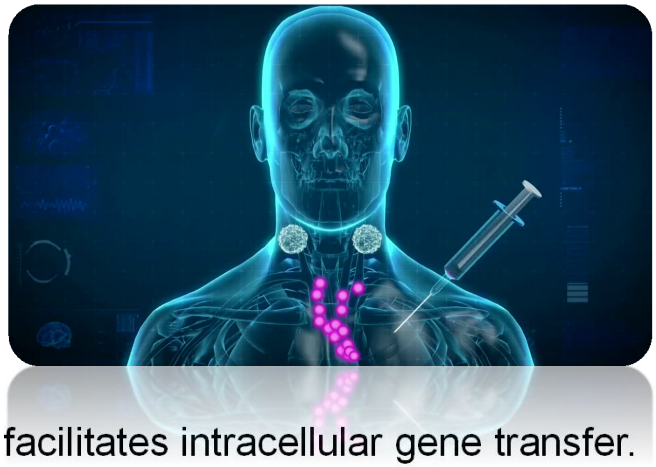
A. Viral vectors

- Researchers can take every day viruses but modify them so that when they are used to ‘infect’ cells with the new genes, this can happen without making the person ill. Once administered into the body, the virus’ genetic material, which now includes the healthy gene, is integrated into the cell DNA and corrects the defective or mutated gene.
- Despite the viruses being specifically ‘programmed’ to become vectors, the body’s immune response remains one of the main hurdles to this approach, as it tries to tackle the virus.



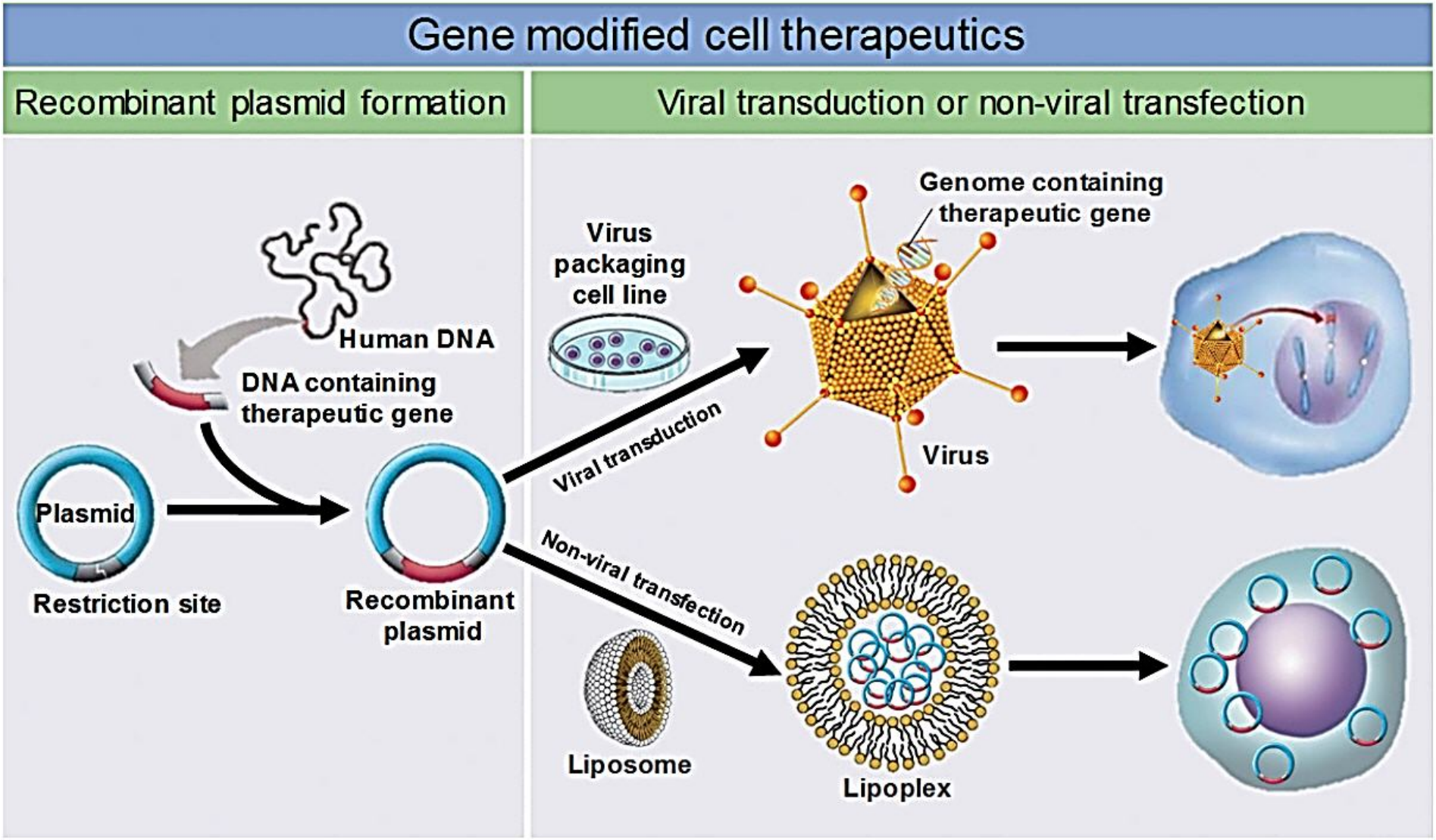
B. Non-viral or engineered vectors

- Methods of non-viral gene delivery have also been explored using physical (carrier-free gene delivery) and chemical approaches (synthetic vector-based gene delivery).
- **Physical approaches,** including:
  - ✓ Needle injection.
  - ✓ Electroporation.
  - ✓ Gene gun.
  - ✓ Ultrasound.
  - ✓ Hydrodynamic delivery.



- Employ a physical force that permeates the cell membrane and facilitates intracellular gene transfer.

- **Chemical methods,** that enhance the delivery of gene therapy includes:
  - Lipoplexes: plasmid DNA can be covered with lipids in an organized structure like a liposome. Polyplexes: consist of cationic polymers that enclose the DNA. Complexes of polymers with DNA are called Polyplexes.


Gene modified cell therapeutics
Recombinant plasmid formation
Viral transduction or non-viral transfection
Human DNA
DNA containing therapeutic gene
Plasmid
Restriction site
Recombinant plasmid
Virus packaging cell line
Viral transduction
Genome containing therapeutic gene
Virus
Non-viral transfection
Liposome
Lipoplex

Advantages

- Give a chance of a normal life to baby born with genetic disease.
- Give hope of healthy life to cancer patient.
- For certain disease that do not have any cure except gene therapy, it could save many lives.

Disadvantages

- The genetic testing, screening and research in finding the availability of certain gene is very controversy.
- May increase rate of abortion if prenatal test regarding baby with genetic disease is done.
- The cost is very high and the patient might need an insurance to cover the treatment.
- Cosmetic industry may monopolized this gene therapy if it is used in enhancing beauty and in vanishing the aging effect, rather than used for treatment of a disease.


TIME FOR QUESTIONS
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