Gene therapy

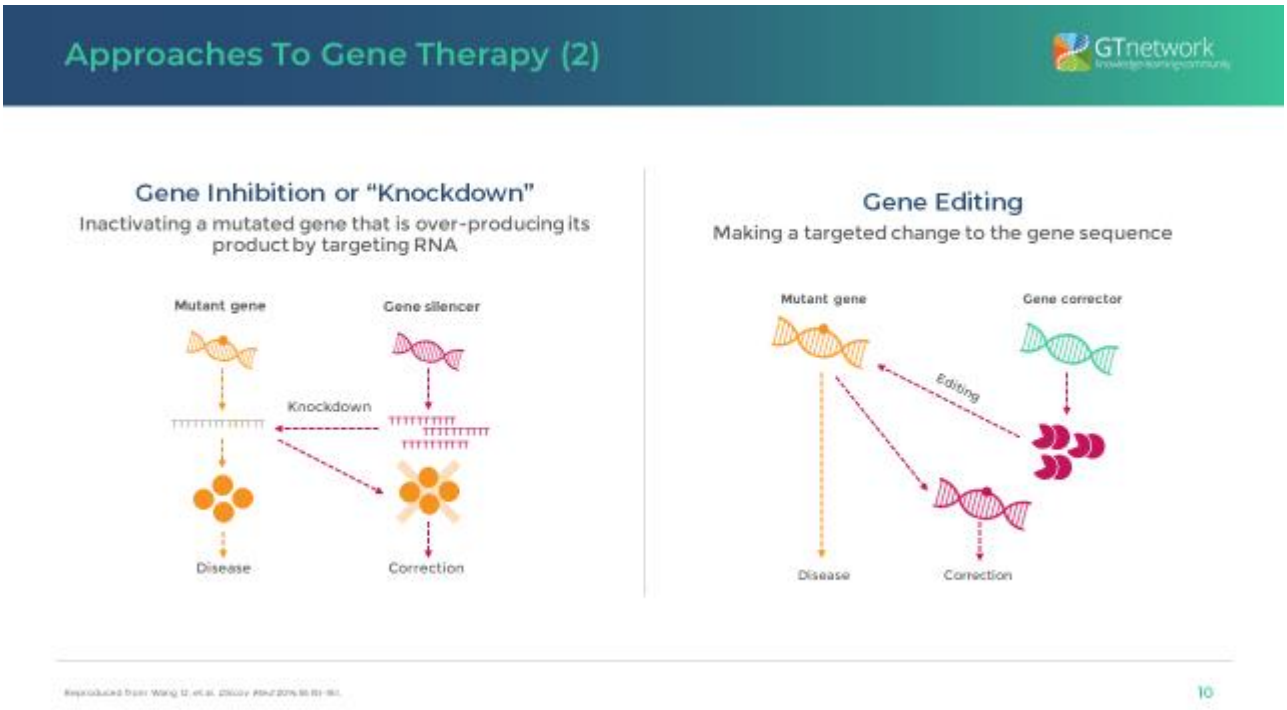
Gene therapy is an experimental technique that uses genes to treat or prevent disease. The most common approach for correcting faulty genes is to insert a “normal” gene into the genome to replace an “abnormal” disease-causing gene.

Types of gene therapy

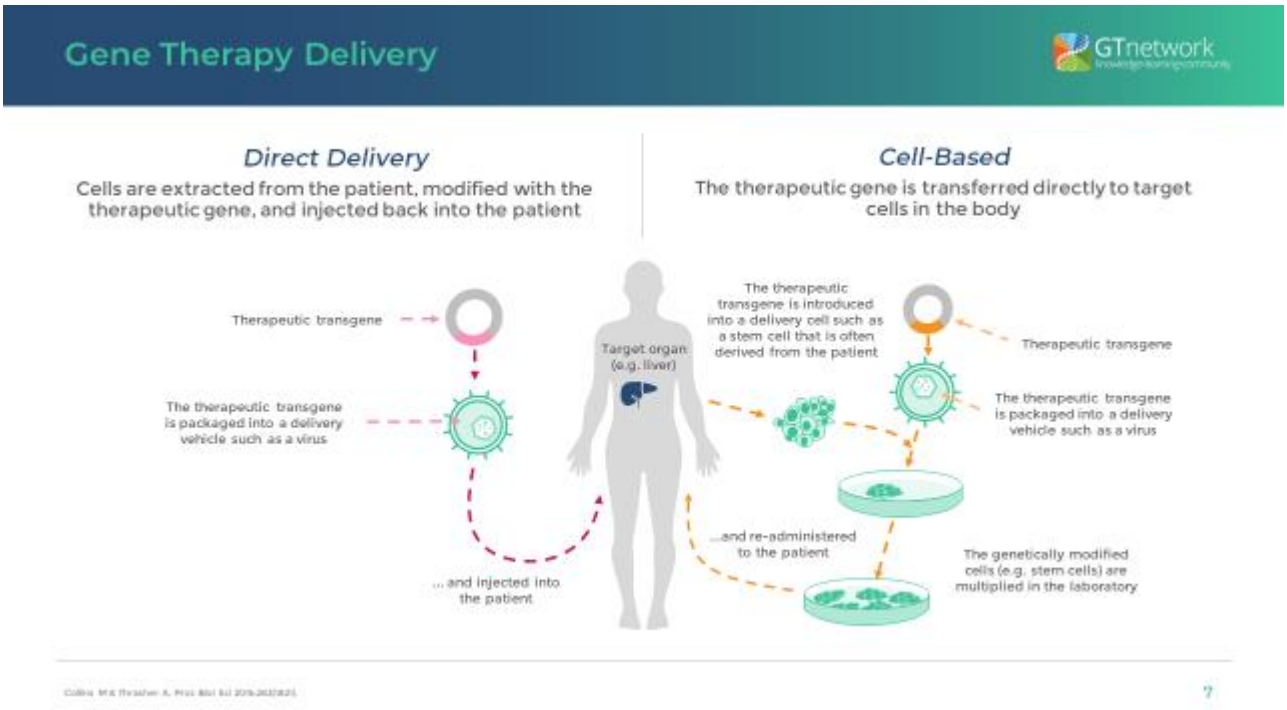
There are 2 types of gene therapy:

1- **Germ line gene therapy**: where germ cells (sperm or egg) are modified by the introduction of functional genes, which are integrated into their genome. Therefore, changes due to therapy would be heritable and would be passed on to later generation.

2- **Somatic gene therapy**: where therapeutic genes are transferred into the somatic cells of a patient. Any modifications and effects will be restricted to the individual patient only and will not be inherited by the patient's offspring or any later generation.



Gene delivery



Vectors used in gene therapy are:

1- Viral Vectors

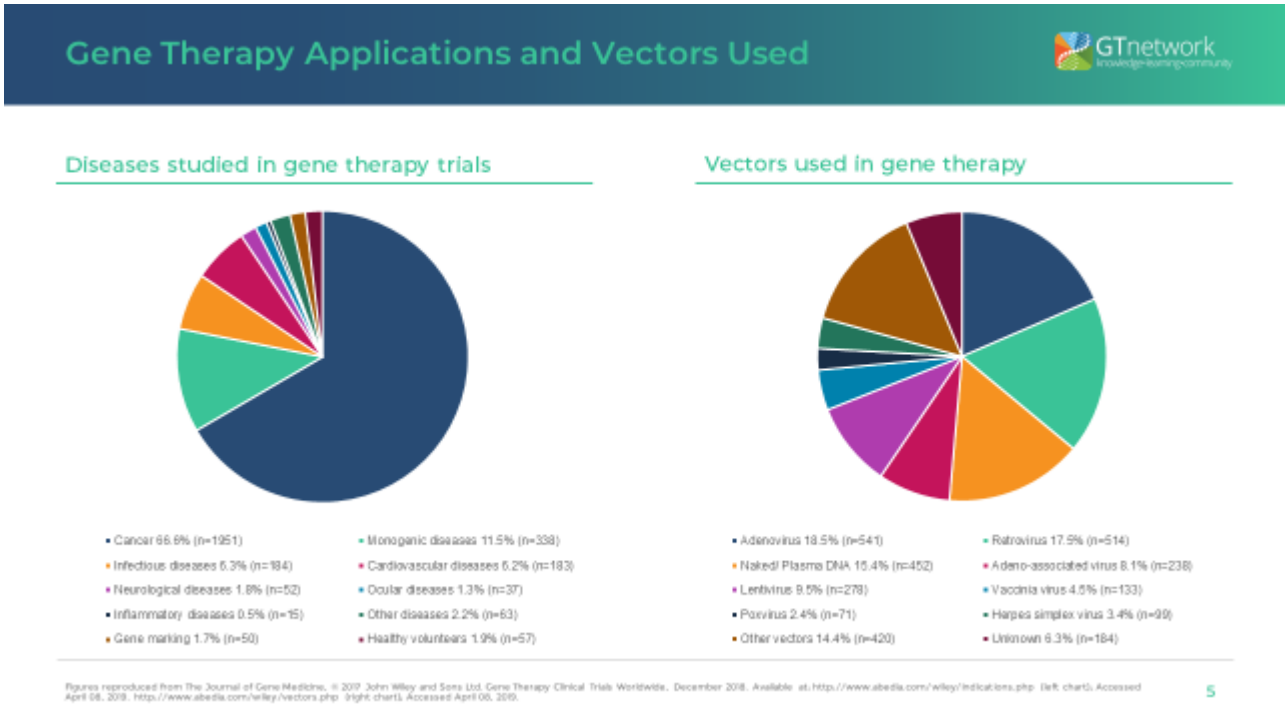
One of the most promising vectors currently being used is harmless viruses. Viruses have evolved a way of encapsulating and delivering their genes to human cells in a pathogenic manner. Some of the different types of viruses used as gene therapy vectors:

Retrovirus, Adenovirus, Adeno-associated viruses [AAVs], Herpes simplex virus [HSV]. Alpha viruses, and Vaccinia or pox viruses.

2- Non-Viral Vectors

Simplest method of non-viral transfection is direct DNA injection. several non-viral methods gene transfer such as: Electroporation, sonoporation, magnetofection and gene guns.

However, these processes are still inefficient, are limited to ex-vivo gene transfer and have undefined cytotoxic effects.



The ideal gene delivery vector should be:

1- Very specific

2- Capable of efficiently delivering one or more genes of the size needed for clinical application

3- Unrecognized by the immune system

4- Purified in large quantities at high concentration

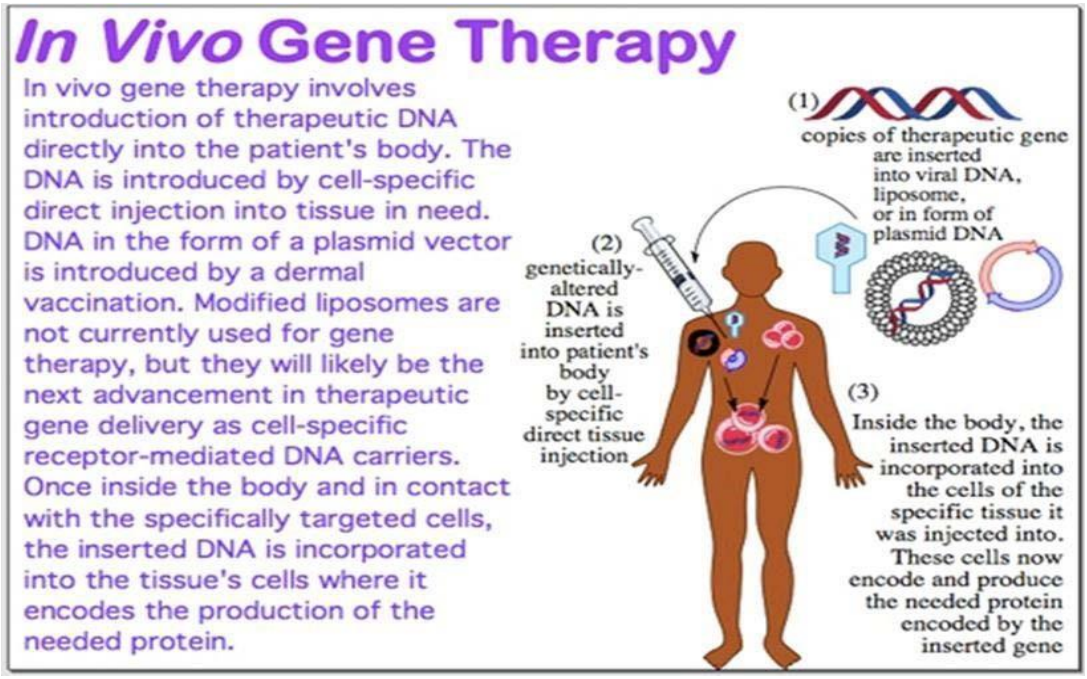
5- Not induce an allergic reaction or inflammation

6- Safe for the patient and environment

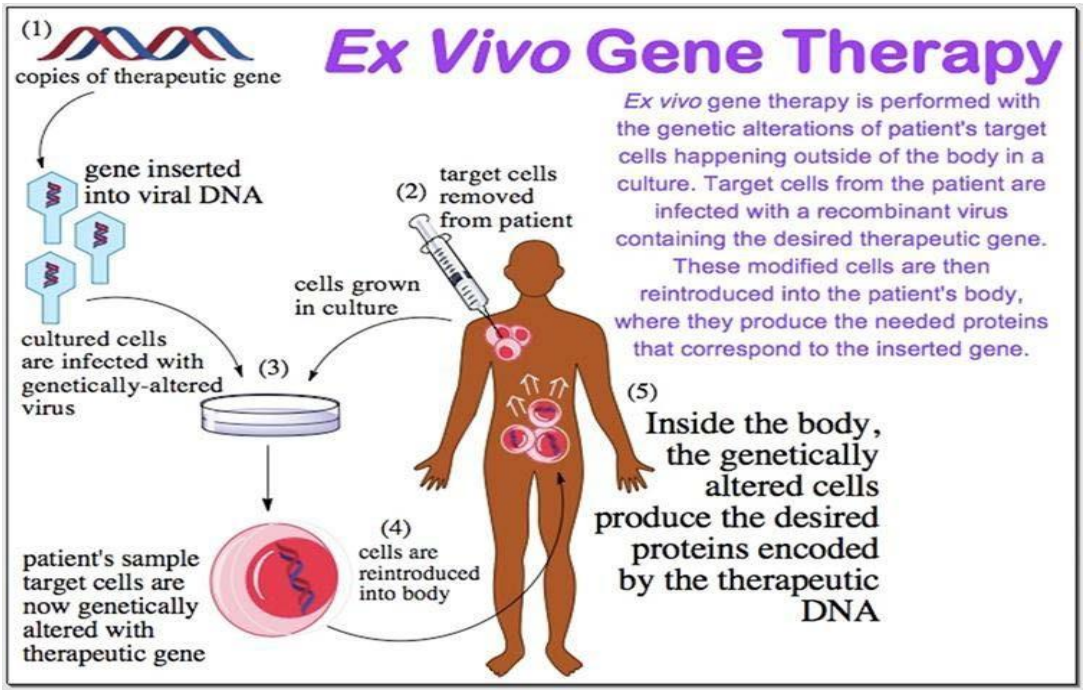
7- Able to express the gene for as long as is required, generally the life of the patient

Two techniques have been used to deliver vectors;

1- In vivo gene therapy; the vector can be injected or given intravenously (by IV) directly into a specific tissue in the body, where it is taken up by individual cells.



2- Ex vivo gene therapy; a sample of the patient's cells can be removed and exposed to the vector in a laboratory setting. The cells containing the vector are then returned to the patient. If the treatment is successful, the new gene delivered by the vector will make a functioning protein.



Approved Gene Therapies

FDA-approved therapy	Indication (approval date)	Delivery	Viral vector
Imlygic (talimogene laherparepvec)[1]	Melanoma (2015)	In vivo	HSV-1
Kymriah (tisagenlecleucel)[2]	B-cell precursor acute lymphoblastic leukemia (2017); diffuse large B-cell lymphoma (2018)	Ex vivo	Lentivirus
Yescarta (axicabtagene ciloleucel)[3]	Large B-cell lymphoma (2017)	Ex vivo	Retrovirus
Luxturna (voretigene neparvovec-rzyl)[4]	Biallelic RPE65 mutation-associated retinal dystrophy (2017)	In vivo	AAV
EMA-approved therapy	**Indication (approval date)**		
Imlygic[5]	Melanoma (2015)	In vivo	HSV-1
Strimvelis[6]	ADA-SCID (2016)	Ex vivo	Retrovirus
Zalmoxis[7]	Adjunctive treatment in HSCT in high-risk blood cancer (2016)	Ex vivo	Retrovirus

AAV, adeno-associated virus; ADA-SCID, severe combined immunodeficiency due to adenosine deaminase deficiency; EMA, European Medicines Agency; FDA, US Food and Drug Administration; HSCT, hematopoietic stem cell transplantation; HSV-1, Herpes simplex virus type 1.
1. Imlygic Prescribing Information. 2. Kymriah Prescribing Information. 3. Yescarta Prescribing Information. 4. Luxturna Prescribing Information. 5. Imlygic SmPC. 6. Strimvelis SmPC. 7. Zalmoxis SmPC. Hyperlinks last accessed September 2018.