GENE THERAPY

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The administration of genetic material to treat a disease, or at least to improve the patient's health. The introduction of genes to cure a defect or the progression of a disease and enhance the quality of life [1, 2].

The Human Genome Project have opened new ways to cure genetic disease.

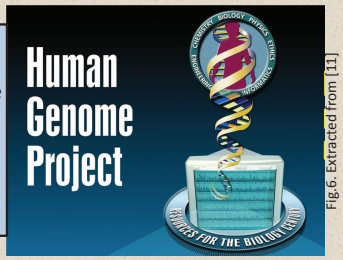

Fig.6. Extracted from [11]

Through the successes and failures of gene therapy experimental trials, scientists are closer to find a proper cure for genetic disorders, providing hope for those with the disorders. Although not all diseases can be cured by gene therapy, the chart below (Table 1) lists diseases that are common, and that in most cases can be treated by gene therapy [3].

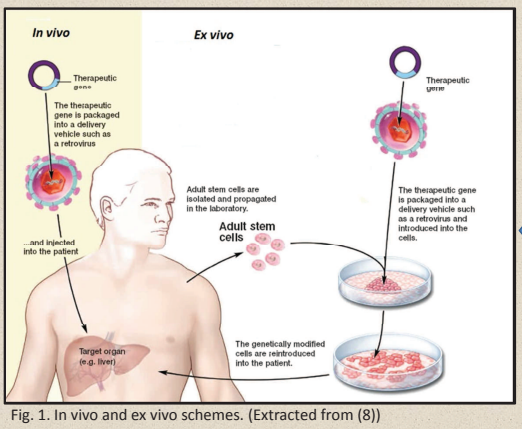

Fig. 1. In vivo and ex vivo schemes. (Extracted from (8))

In vivo: Techniques to introduce genetic material into the target cells directly to the patient, without an *in vitro* phase [1, 4].

Ex vivo: Cells from the target tissue are removed from the patient, and then this cells are mixed with the virus that carries the therapeutic gene. Patient's cells are returned to their place [1, 4].

Disease	Defect	Incidence	Target Cells
Severe combined immunodeficiency (SCID)	Adenosine deaminase (ADA) in 25% of SCID patients	Rare	Bone-marrow cells or T lymphocytes
Hemophilia A	Factor VII deficiency	1:10,000 males	Liver, muscle, fibroblasts or bone marrow cells
Hemophilia B	Factor IX deficiency	1:30,000 males	
Familial hypercholesterolemia	Deficiency of low-density lipoprotein (LDL) raeceptor	1:1 million	Liver
Cystic fibrosis	Faulty transport of salt in lung epithelium	1:3000 Caucasians	Airways in the lungs
Hemoglobinopathies thalassemias	(Structural) defects in the α or β globin gene	1:600 in certain ethnic groups	

Table 1. List of some disease with their characteristics. (Extracted from (3)).

Different vectors:

-Nonviral vectors: Synthetic gene delivery systems. Available categories:

- Inorganic particles
- Synthetic or biodegradable particles
- Physical methods (electroporation)

-Viral vectors: Based on viral strategy to infect cells. Integrating vectors or non integrating vectors [4, 5].

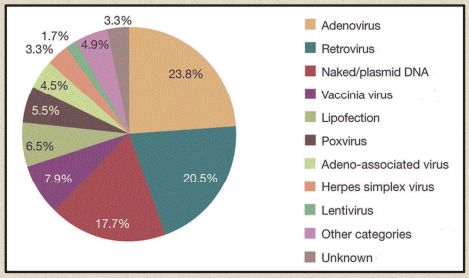

Fig. 3. Breakdown of vectors used in gene therapy. (Extracted from 5)

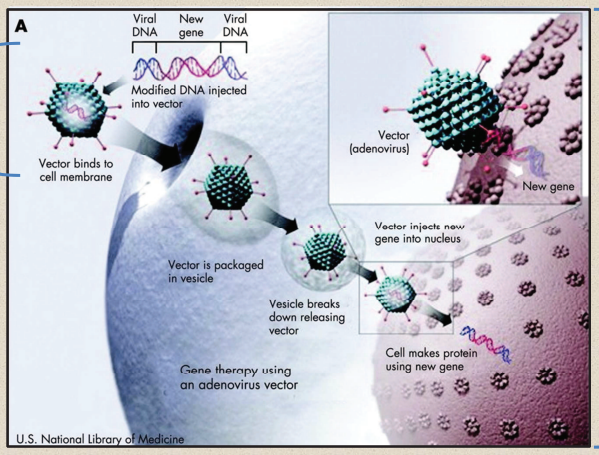

Fig. 2.general gene therapy scheme (extracted from (7))

Target cells :

-Germ cells: Modify cells involved in the formation of the reproductive cells. Transmitted to the progeny. Definitive way to correct congenital diseases[4,6].

- Somatic cells: No transmitted to the progeny. The main (only) way to make gene therapy, based on safety and ethic reasons [4, 6].

Integrating : long expression of the new gene. For dividing cells.
Non integrating: Remain in extrachromosomal way (episome). For nondividing cells [6].

Ideal vector :

1. Easy production
2. Safe
3. Proper gene expression
4. Good targeting
5. Good transduction to dividing/non-dividing cells.
6. Site-specific integration

REPRESENTATIVE EXAMPLES

Severe combined immunodeficiency

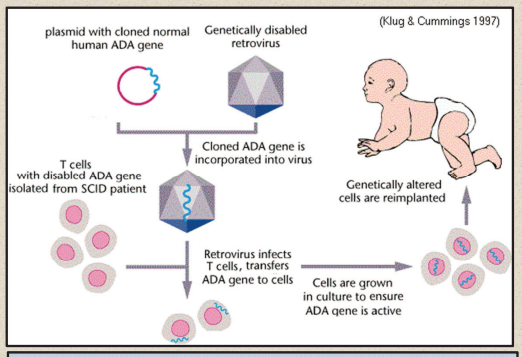

Fig. 4. Extracted from (10).

Retrovirus used for ADA gene delivery: tropism for dividing cells, integrating with cell genome and long lasting transgene expression.

Cancer

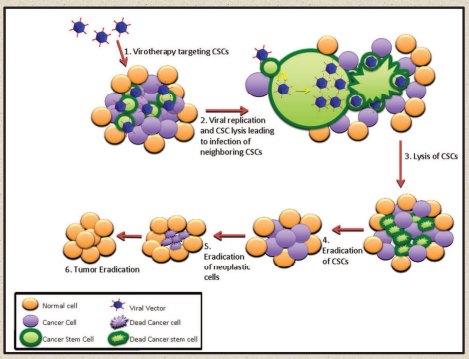

Fig. 5. Extracted from (9).

Adenovirus with anti-tumor gene which causes tumor cell death: tropism for dividing and non-dividing cells, non-integrating with the host genome, and transient transgene expression (9)

(1) C.L. Ronchera-Oms, J.Mª. González, "Terapia Génica". (2) Lazo PA. "Terapia Génica humana tendencias y problemas." Med Clín (Barc) 1996; 106:469-476. (3) "Gene therapy: your genes, your cure" 2013. *http://gene-therapy.yolasite.com/* (4) Cormac Sheridan, 2011. "Gene therapy finds its niche", Nature America, Inc. (5) Ana del Pozo-Rodríguez and María Ángeles Solinís ,. 2013, "Gene therapy- Tools and Potential applications: Chapter 1: non-viral Delivery Systems in gene therapy", edited by Francisco Martin Molina, ISBN. (6) Alexander Pfeifer, Inder M. Verma, 2001. "Gene therapy: Promises and Problems", Annu. Rev. Genomics Hum Genet. (7) http://www.news-medical.net/health/What-is-Gene-Therapy.aspx (8) http://smallbrightstones.blogspot.com.es/2013/04/gene-therapy.html (9) Mahua Dey, Ilya V. Ulasov. 2010. "Virotherapy against malignant glioma stem cells". Cancer Lett. 2010 march 1; 289(1): 1-10. (10) http://www.mun.ca/biology/scarr/Somatic_Therapy_for_SCID.htm (11) M. Cavazzana-Calvo, Frank Yates, et al. 2001. "Gene therapy of severe combines immunodeficiencies", The Journal of Gene Medicine, 3:201-206. (11) http://www.bioinformaticonline.com/human-genome-project.php