Molecular biology

GENE THERAPY

Proffesor

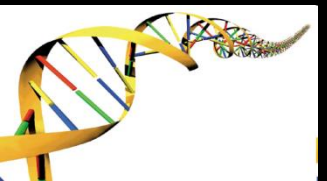
Dr. Mushtak T Salih

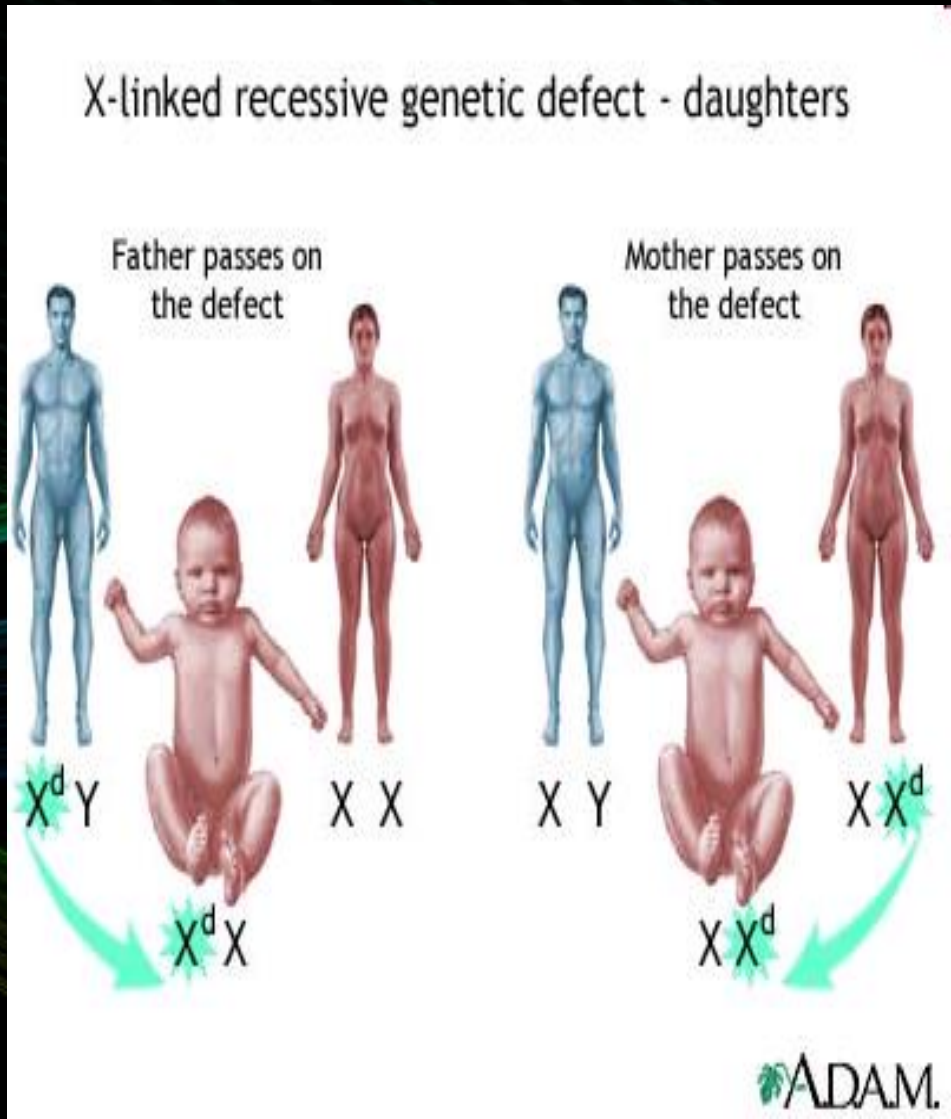
What Genes can do

- Genes, which are carried on chromosomes, are the basic physical and functional units of heredity. Genes are specific sequences of bases that encode instructions on how to make proteins. it's the proteins that perform most life functions and even make up the majority of cellular structures.

Why Genetic Disorders

- When genes are altered so that the encoded proteins are unable to carry out their normal functions, genetic disorders can result.



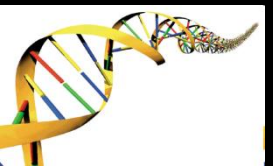


All of us carry some defective Genes, some are apparent and many in apparent

- Each of us carries about half a dozen defective genes. We remain blissfully unaware of this fact unless we, or one of our close relatives, are amongst the many millions who suffer from a genetic disease. About one in ten people has, or will develop at some later stage, an inherited genetic disorder, and approximately 2,800 specific conditions are known to be caused by defects (mutations) in just one of the patient's genes.

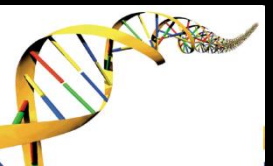
We Inherit from Parents

- Most of us do not suffer any harmful effects from our defective genes because we carry two copies of nearly all genes, one derived from our mother and the other from our father. The only exceptions to this rule are the genes found on the male sex chromosomes. Males have one X and one Y chromosome, the former from the mother and the latter from the father, so each cell has only one copy of the genes on these chromosomes



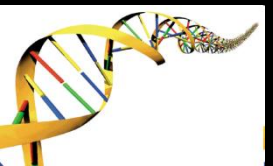
Law of Inheritance

- In the majority of cases, one normal gene is sufficient to avoid all the symptoms of disease. If the potentially harmful gene is recessive, then its normal counterpart will carry out all the tasks assigned to both. Only if we inherit from our parents two copies of the same recessive gene will a disease develop.



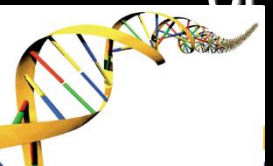
What is Gene Therapy

- **Gene therapy** is the insertion of genes into an individual's cells and tissues to treat a disease, such as a hereditary disease in which a deleterious mutant allele is replaced with a functional one. Although the technology is still in its infancy, it has been used with some success.



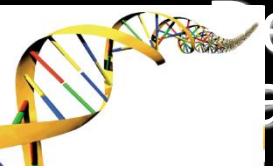
Goal of Gene therapy

- A normal gene may be inserted into a non-specific location within the genome to replace a non-functional gene. This approach is most common.
- An abnormal gene could be swapped for a normal gene through homologous recombination.
- The abnormal gene could be repaired through selective reverse mutation, which returns the gene to its normal function.
- The regulation (the degree to which a gene is turned on or off) of a particular gene could be altered.



Uses of gene therapy

- Replace missing or defective genes;
- Deliver genes that speed the destruction of cancer cells;
- Supply genes that cause cancer cells to revert back to normal cells;
- Deliver bacterial or viral genes as a form of vaccination;
- Provide genes that promote or impede the growth of new tissue; and;
- Deliver genes that stimulate the healing of damaged tissue.

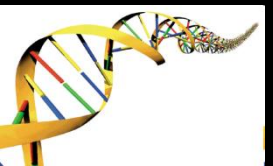


How It Works

- A vector delivers the therapeutic gene into a patient's target cell
- The target cells become infected with the viral vector
- The vector's genetic material is inserted into the target cell
- Functional proteins are created from the therapeutic gene causing the cell to return to a normal state

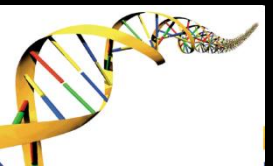
Gene Therapy is Experimental

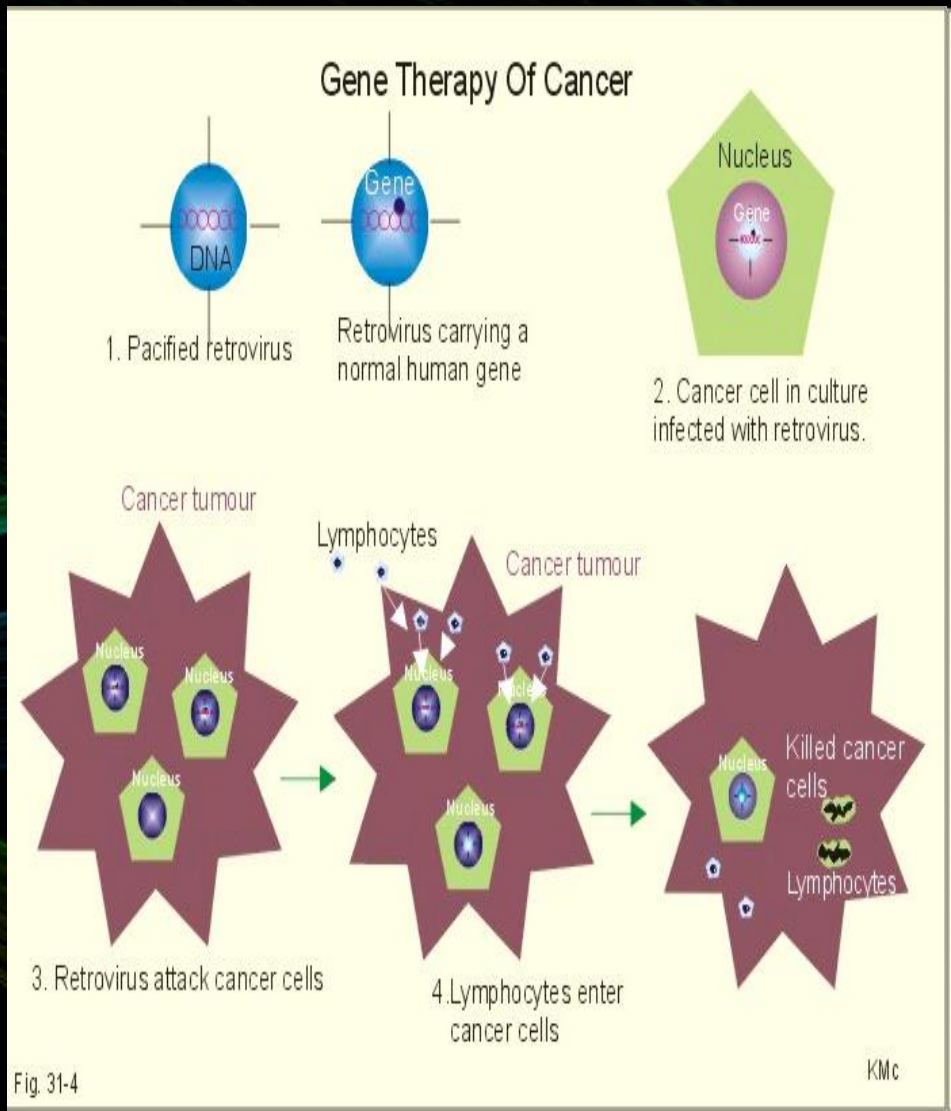
- Advances in understanding and manipulating genes have set the stage for scientists to alter a person's genetic material to fight or prevent disease. Gene therapy is an experimental treatment that involves introducing genetic material (DNA or RNA) into a person's cells to fight disease.



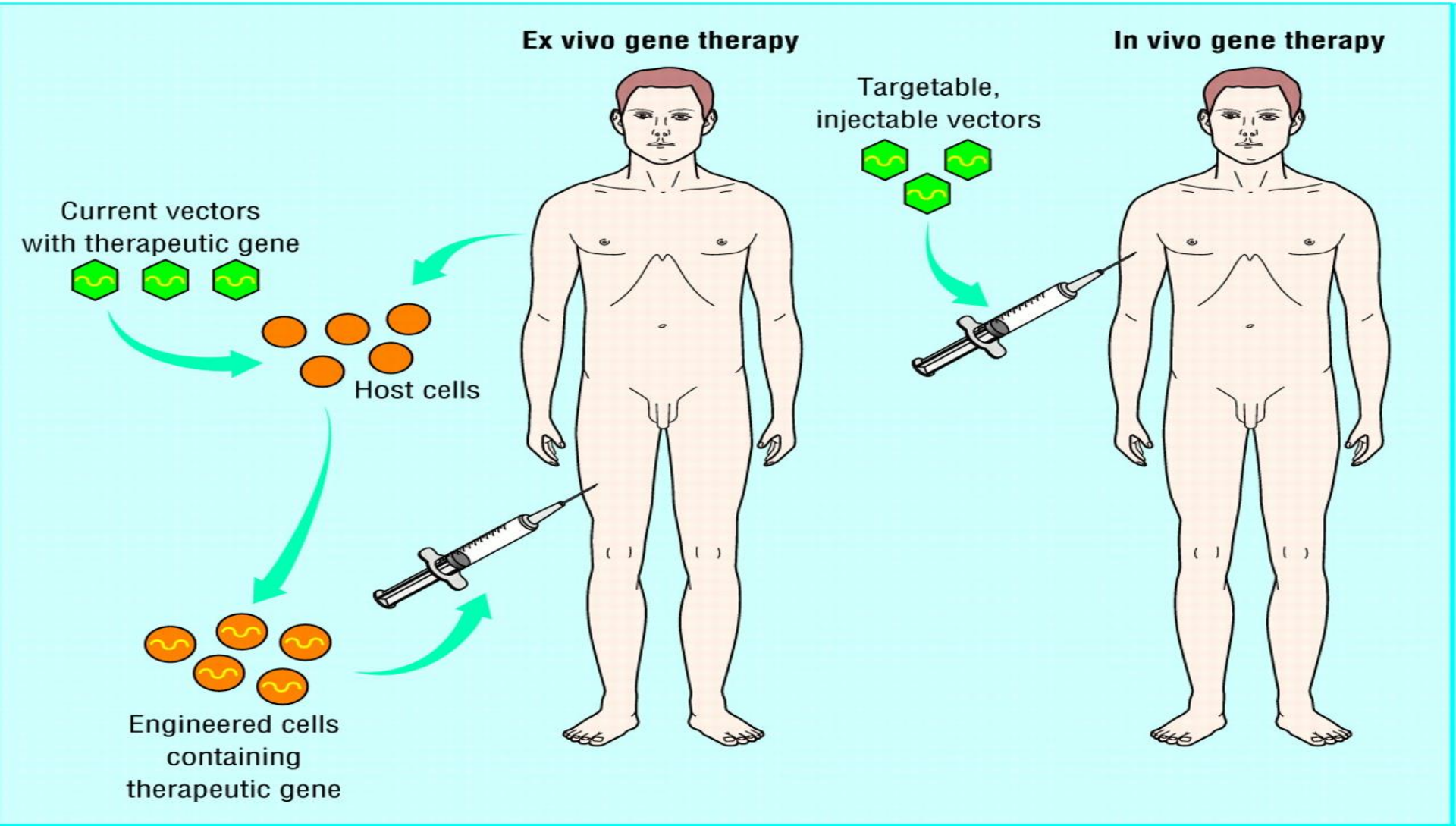
Majority are Trails

- Gene therapy is being studied in clinical trials (research studies with people) for many different types of cancer and for other diseases. It is not currently available outside a clinical trials



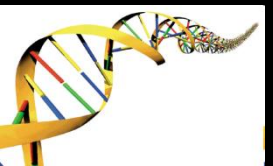


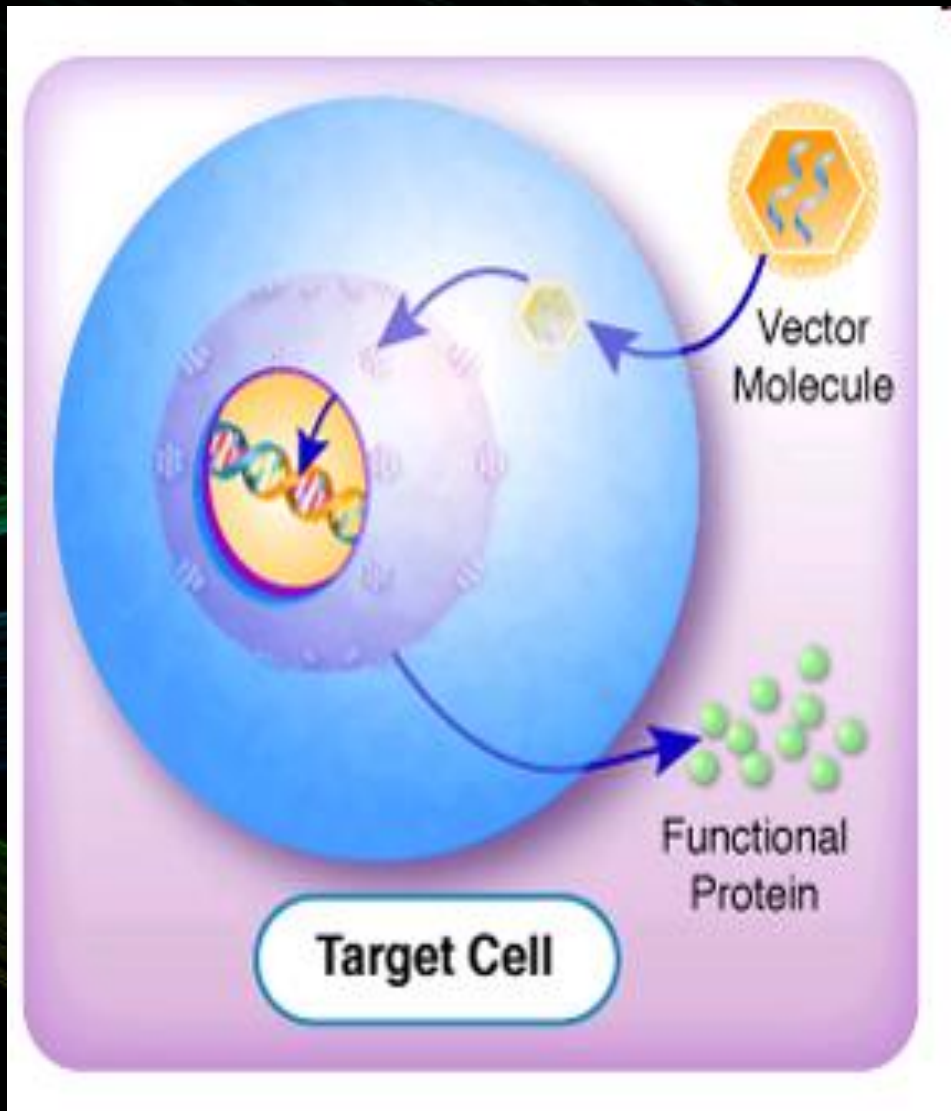
Vivo to Vitro



What Gene therapy can Achieve

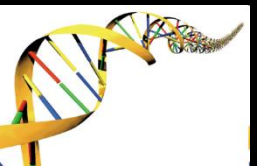
- Replacing a mutated gene that causes disease with a healthy copy of the gene.
- Inactivating, or “knocking out,” a mutated gene that is functioning improperly.
- Introducing a new gene into the body to help fight a disease.



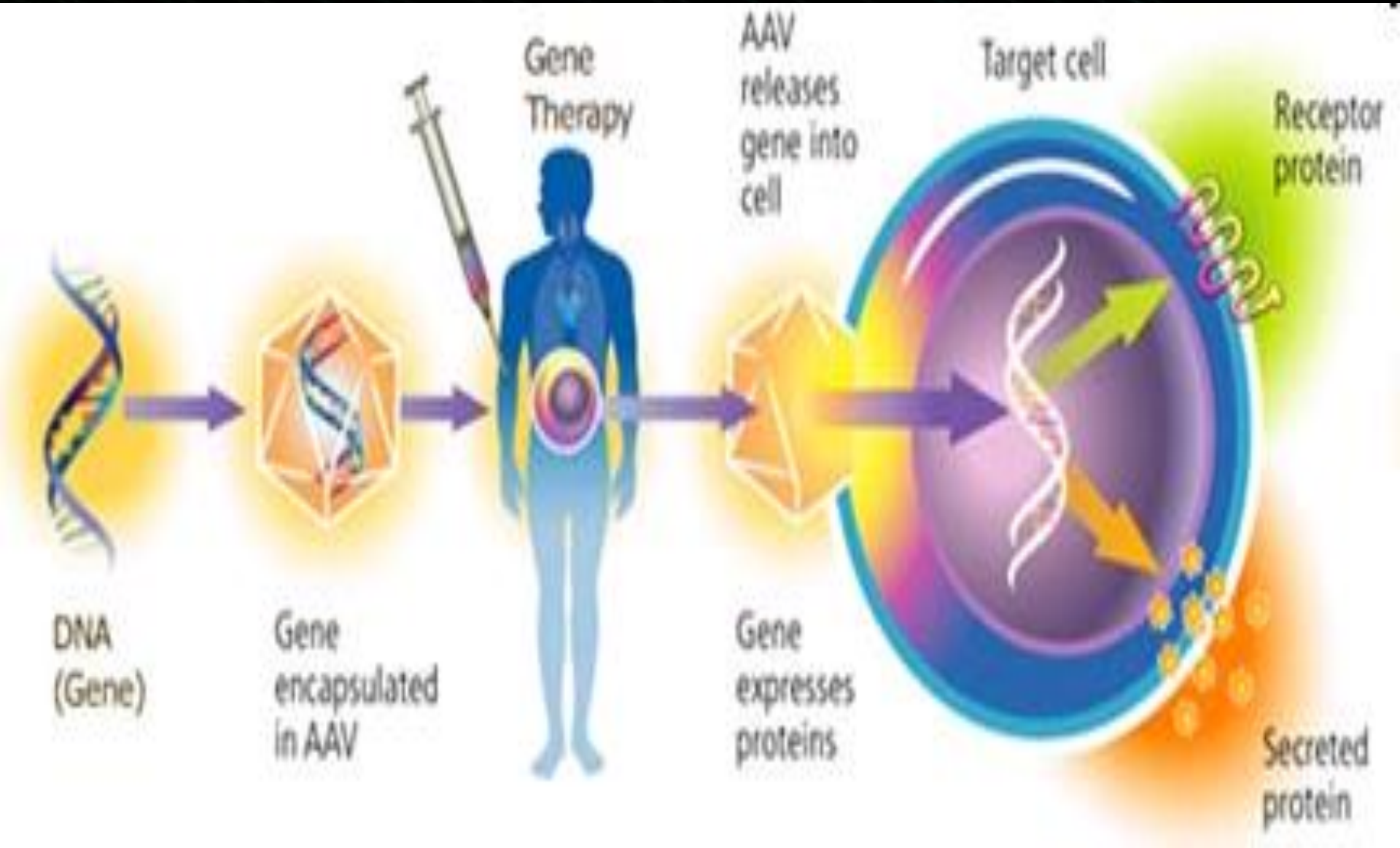


Genes are Medicine ?

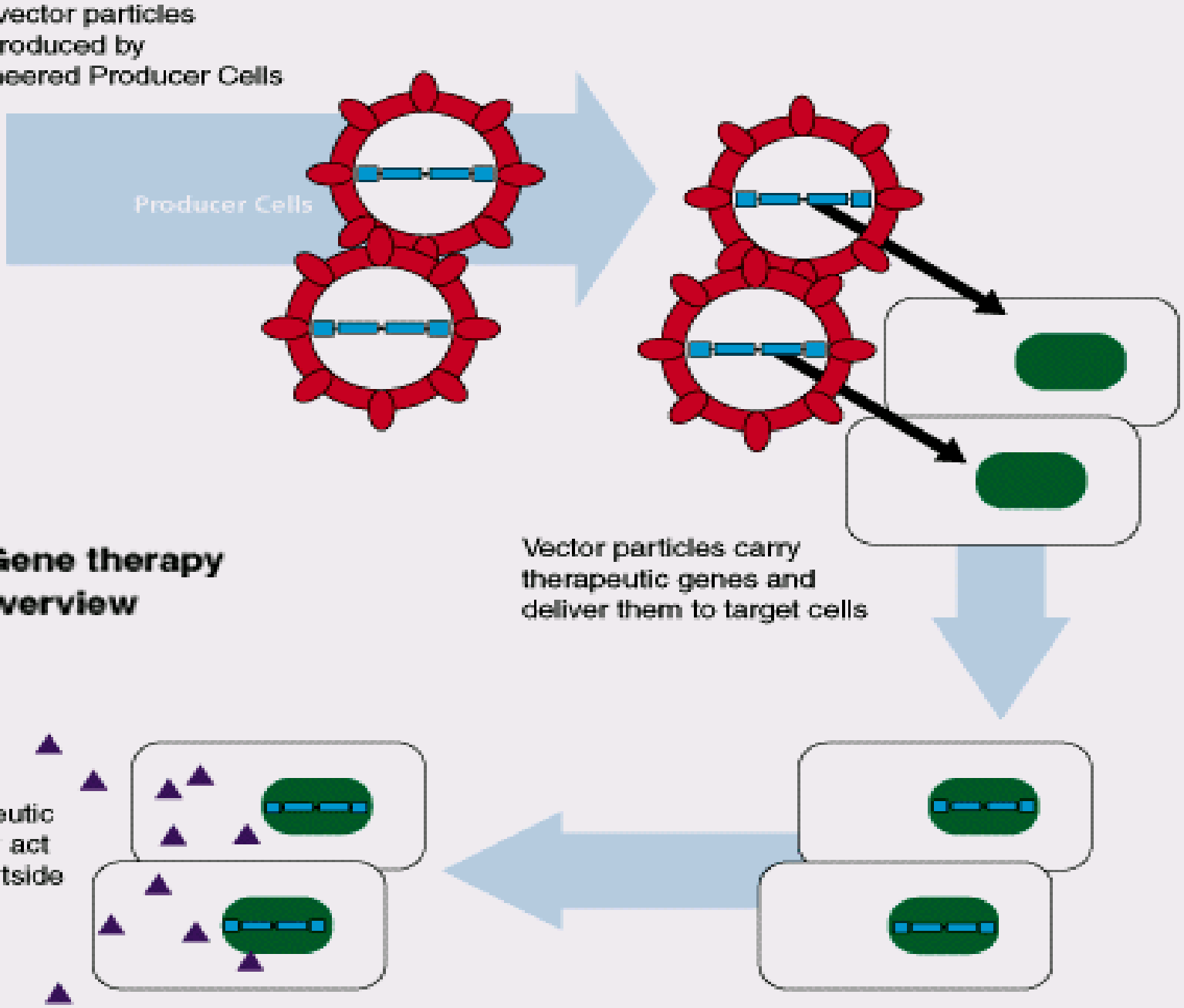
- Gene therapy is ‘the use of genes as medicine’. It involves the transfer of a therapeutic or working gene copy into specific cells of an individual in order to repair a faulty gene copy. Thus it maybe used to replace a faulty gene, or to introduce a new gene whose function is to cure or to favourably modify the clinical course of a condition.



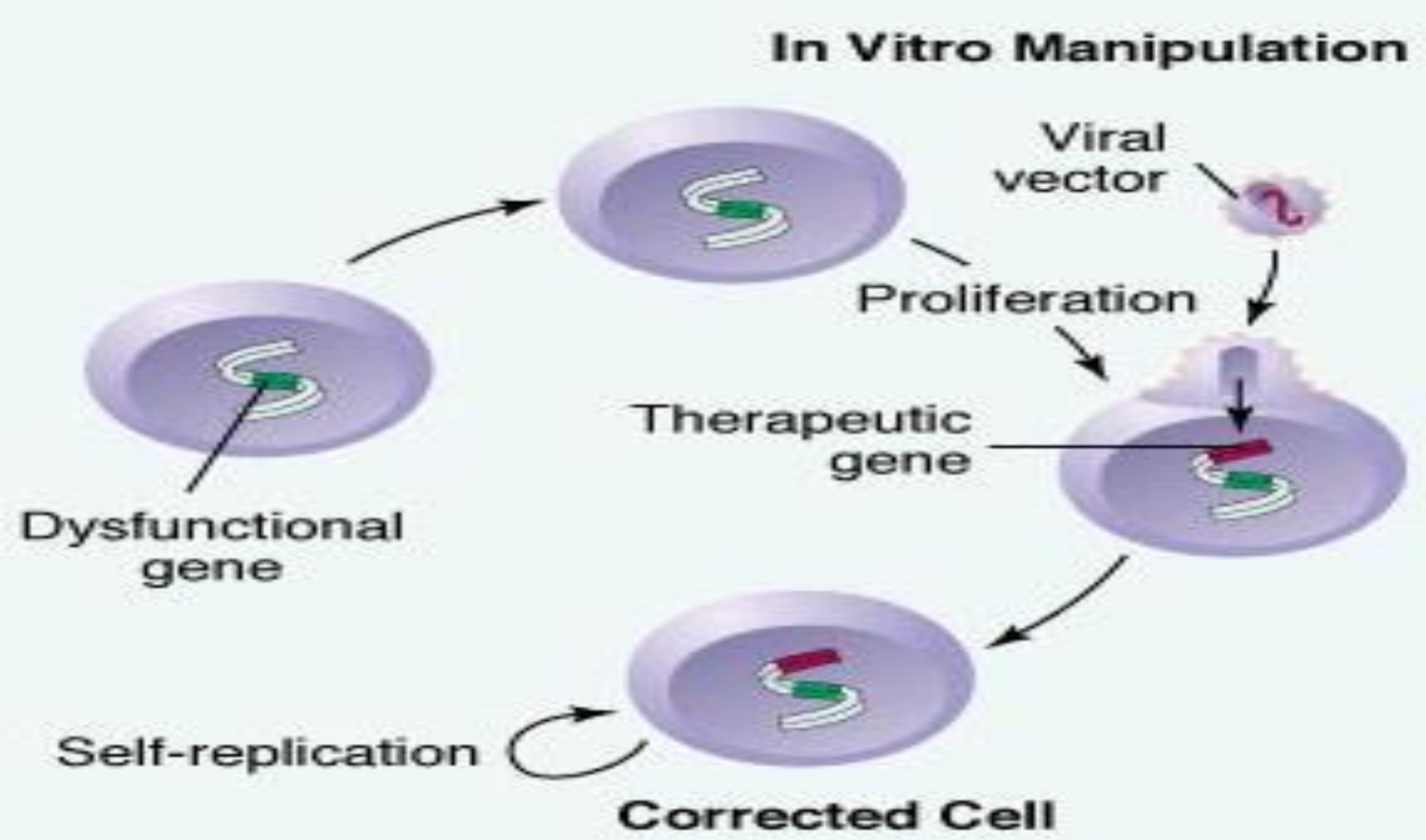
Steps in Gene Therapy



Viral Gene therapy
- an overview

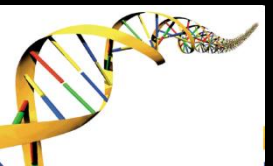


Manipulation corrects the Defective Genes



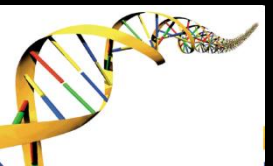
Antisense therapy

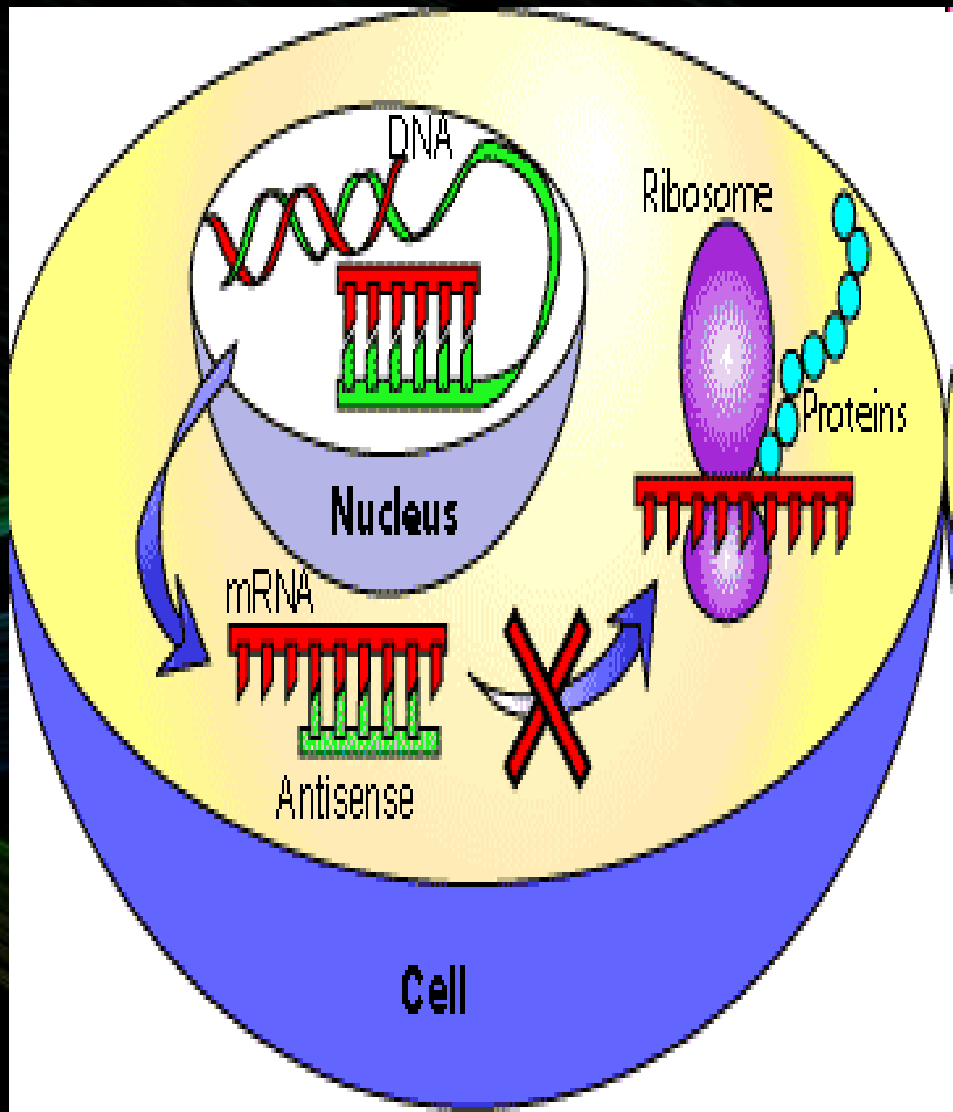
- **Antisense therapy** is a form of treatment for genetic disorders or infections. When the genetic sequence of a particular gene is known to be causative of a particular disease, it is possible to synthesize a strand of nucleic acid (DNA, RNA or a chemical analogue) that will bind to the messenger RNA (mRNA) produced by that gene and inactivate it, effectively turning that gene "off".

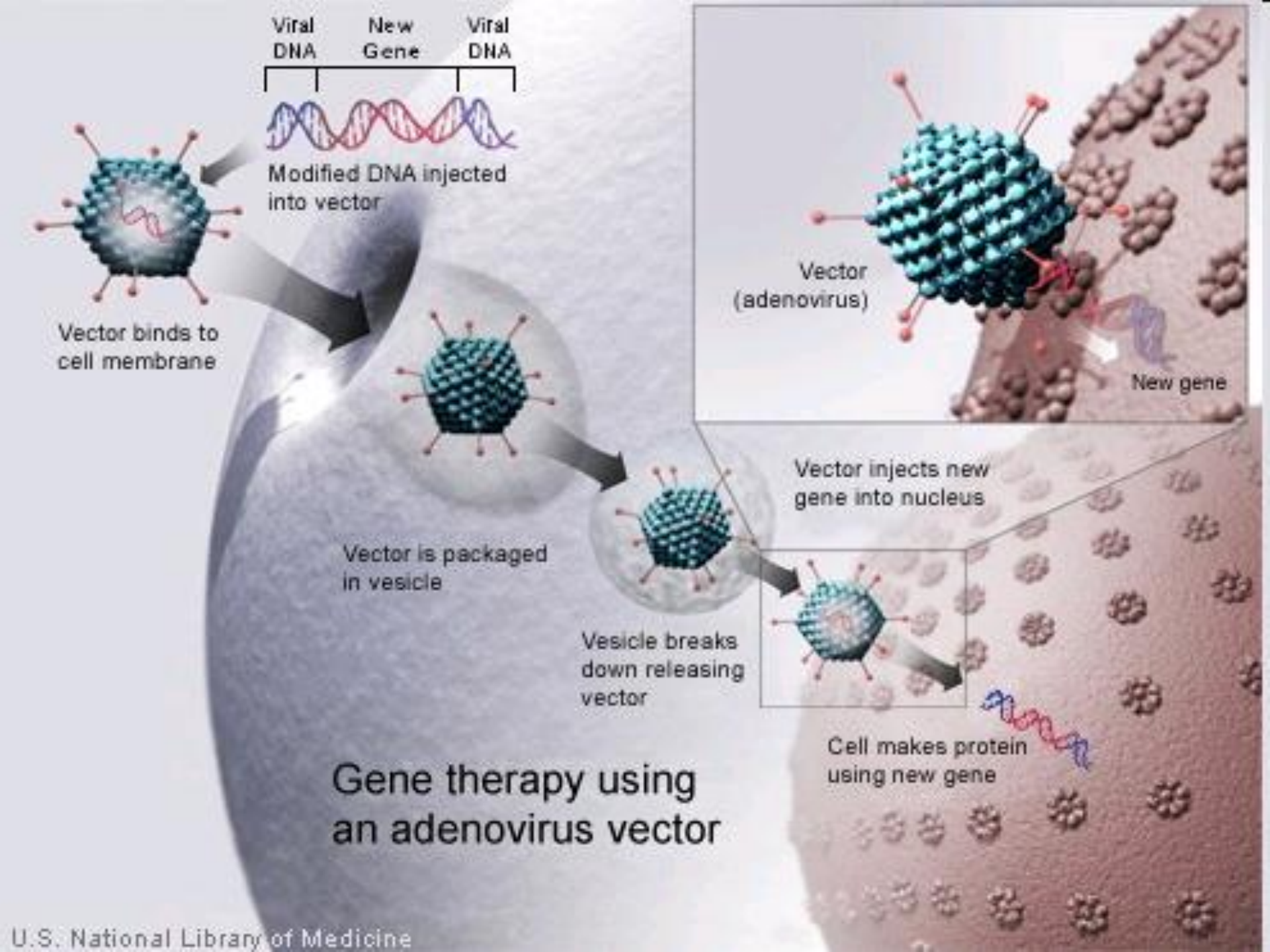


Antisense Therapy

- Antisense therapy is not strictly a form of gene therapy, but is a genetically-mediated therapy and is often considered together with other methods

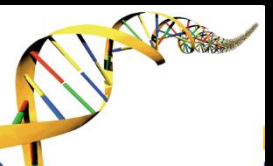





Viral DNA
New Gene
Viral DNA
Modified DNA injected into vector
Vector binds to cell membrane
Vector is packaged in vesicle
Vesicle breaks down releasing vector
Vector injects new gene into nucleus
Vector (adenovirus)
New gene
Cell makes protein using new gene
Gene therapy using an adenovirus vector
U.S. National Library of Medicine

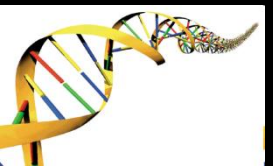
Gene Therapy Depends on Delivery of Corrective Genes

- **Viral vectors** are a tool commonly used by molecular biologists to deliver genetic material into cells. This process can be performed inside a living organism (*in vivo*) or in cell culture (*in vitro*). Viruses have evolved specialized molecular mechanisms to efficiently transport their genomes inside the cells they infect.



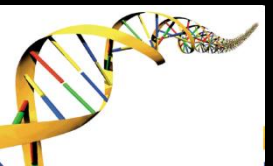
Viruses are used as Delivery Tolls

- Viruses are used as vectors to introduce the genetic material inside the bodies.
- These viruses are inactivated, they are not able to reproduce
- Adenoviruses
- Herpes viruses — DNA tumor viruses
- Retroviruses — RNA tumor viruses



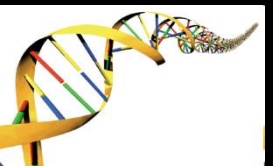
Somatic and Germ Line Gene Therapy

- Gene therapy can target somatic (body) or germ (egg and sperm) cells. In somatic gene therapy the recipient's genome is changed, but the change is not passed on to the next generation; whereas with germ line gene therapy the newly introduced gene is passed on to the offspring.



Creating New Chromosome

- Researchers are also experimenting with introducing a **47th artificial chromosome** to the body.
- It would exist autonomously along side of the other 46, not affecting their workings or causing any mutations.
- It would be a large vector capable of carrying substantial amounts of genetic information and the body's immune system would not attack it.



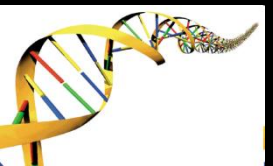
Law interferes in Gene Therapy

What are the ethical issues surrounding gene therapy?

- How can “good” and “bad” uses of gene therapy be distinguished?
- Who decides which traits are normal and which constitute a disability or disorder?
- Will the high costs of gene therapy make it available only to the wealthy?
- Could the widespread use of gene therapy make society less accepting of people who are different?
- Should people be allowed to use gene therapy to enhance basic human traits such as height, intelligence, or athletic ability?

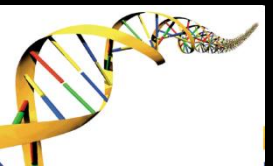
Creating 47th Chromosome

- Researchers are also experimenting with introducing a **47th artificial chromosome** to the body.
- It would exist autonomously along side of the other 46, not affecting their workings or causing any mutations.
- It would be a large vector capable of carrying substantial amounts of genetic information and the body's immune system would not attack it.

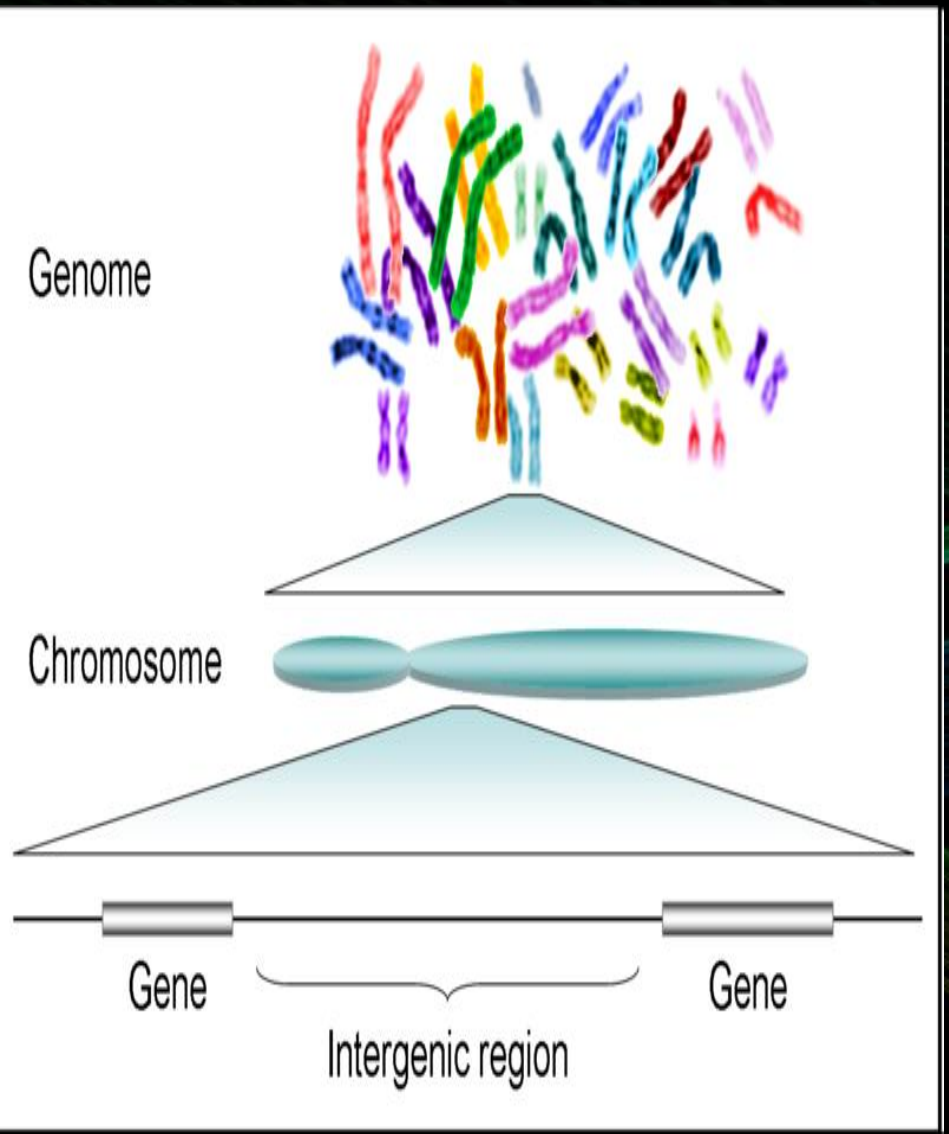


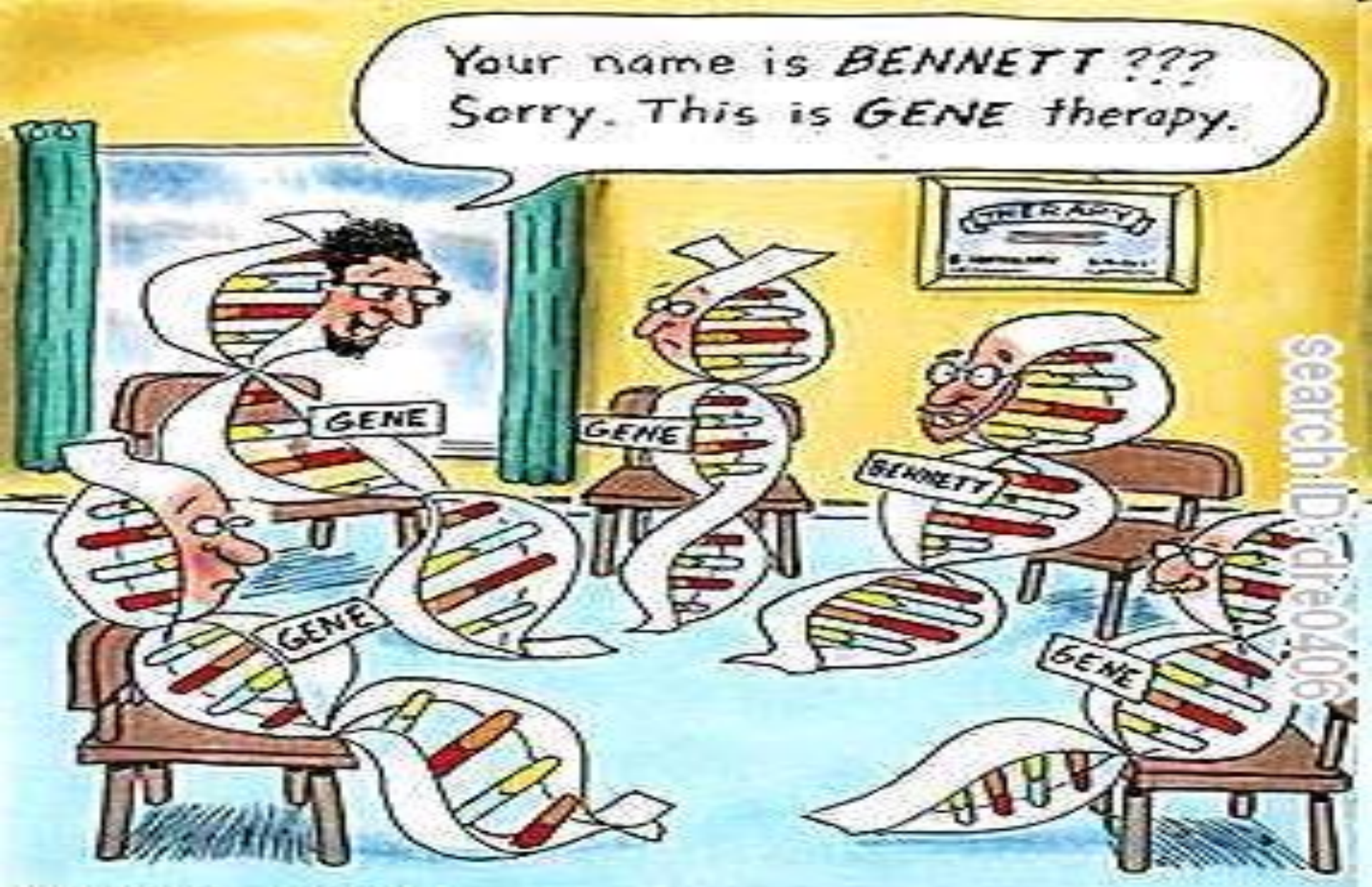
Last two decades made rapid progress

- Over the last 20 years, the initial thoughts of gene therapy have been transformed into reality with more than 175 clinical trials and 2,000 patients already treated . Yet with all the trials, there is still no conclusive evidence for efficacy.



Understanding Genome and Human Genome Project is a boost to Gene Therapy





Do not forget Genes can be Unpredictable ?