Somatic Gene Therapy

US275 Scientific Ethics
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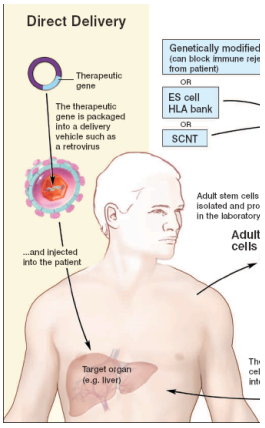
Arcadia University

Gene therapy uses recombinant DNA technology to treat diseases in humans.

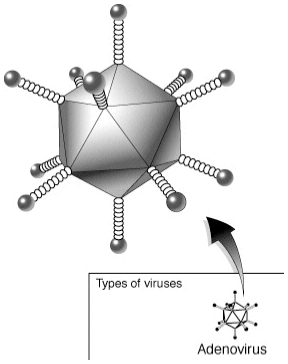
- fix defective gene
- normally place the replacement gene into an individual's cells
- very rarely will swap replacement gene for the damaged gene



http://stemcells.nih.gov/info/2006report/2006Chapter4.htm

The most common way of delivering the replacement gene to human cells using a viral vector

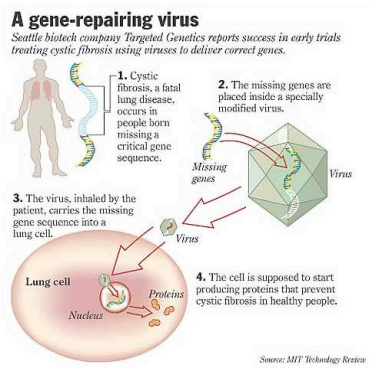
- Retroviruses
  - RNA virus (ex. HIV)
- Adenoviruses
  - common cold virus
- Herpes simplex virus
  - cold sore virus



Adenovirus structure
National Human Genome Research Institute

Currently patients must undergo multiple rounds of gene therapy.

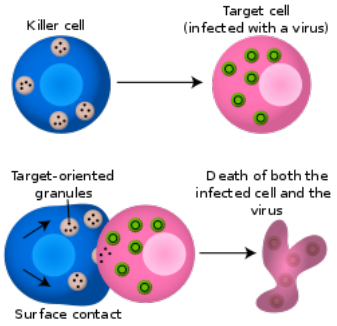
- DNA must be integrated into the cells.
- DNA must continue to be expressed
- Rapidly dividing adult cells gradually stop expressing DNA



http://www.biology.ewu.edu/aHerr/Genetics/Bio310/Media/ch3jpegs/GeneTherapy-Targeted.jpg

The immune system will often attack the cells expressing the "new" DNA.

- continued exposure to new protein immunizes body for stronger immune response
- immune system will often attack DNA-treated cells



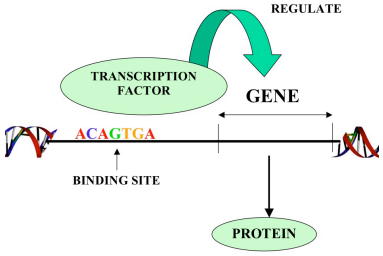
Immune system cells attack other cells carrying foreign or abnormal antigens on their surfaces.
Wikimedia commons

Viral vectors are not perfect

- virus could trigger immune and inflammatory responses
- inability to target specific cells

Viral vectors are not perfect (cont.)

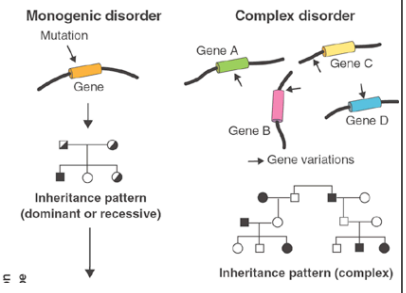
- varied control of the replacement gene
- could recover its ability to cause disease



http://howardhughes.trinity.duke.edu/blogs/2011/06/24/zinc-fingers-plasmids-and-my-battle-with-e-coli

Currently, gene therapy is only effective in treating single gene disorders.

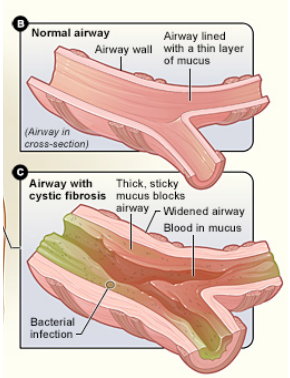
- Most conditions are multigene and multifactoral disorders
  - heart disease
  - high blood pressure
  - Alzheimer's disease



http://www.si.mahidol.ac.th/simi/genome/disease_postgenomics_files/1224-3-med.gif

Cystic fibrosis is associated with a single gene defect.

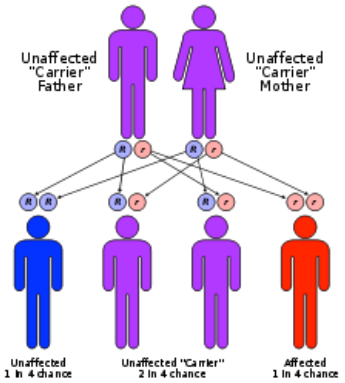
- Cystic Fibrosis Transmembrane Regulator gene discovered in 1989
  - more than 900 identified mutations
- allows cells to release chloride
  - water accumulates
  - dilutes mucus



http://www.nhlbi.nih.gov/health/health-topics/topics/cf/signs.html

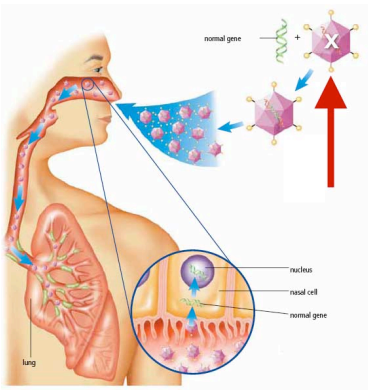
Cystic fibrosis is a common, fatal disease affecting 30,000 people in the United States.

- Cystic Fibrosis common among Caucasians
  - 1 out of 31 Americans is a carrier (10 million carriers)
  - 1 in 2,500 - 3,000 caucasian newborns
- mucus accumulates in lungs
  - difficulty breathing
  - lung infections



In 1993, gene therapy was used in a clinical trial to treat cystic fibrosis.

- used common cold virus as vector
- now trying different delivery methods



http://nametsomathiba.blogspot.com/

TO BE CONTINUED

in the next lecture:

Somatic Gene Therapy: History of Gene Therapy