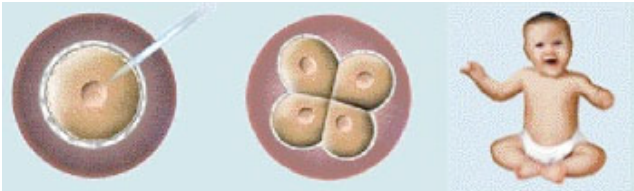


Germline Gene Therapy

US275 Scientific Ethics
John R. Hoffman
Arcadia University



Germline gene therapy is the placement of new DNA into a fertilized egg.

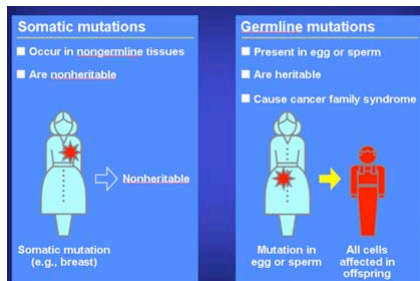


<http://genmed.yolasite.com/basics-of-gene-therapy.php>

- infant develops from the fertilized egg
 - cells divide
 - DNA in all cells of the body.
- DNA modification will be passed to future generations.

Germline therapy has many advantages over somatic therapy

- Germline:
 - Every cell will have the transplanted DNA
- Somatic
 - only small subset of cells
 - requires multiple treatments
 - does not stop transmission to future generations



National Cancer Institute

Approximately 2% of newborns in United States have a genetic disorder

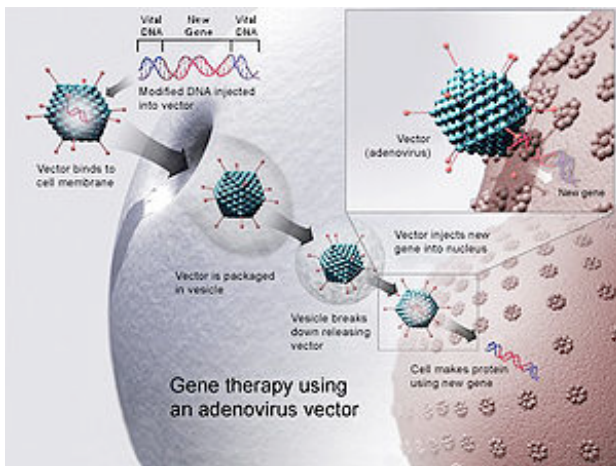
- 2,000 - 3,000 inherited diseases.
- range

- Cystic Fibrosis
 - 30,000 Americans
- Adenosine Deaminase Deficiency (ADA)
 - about 40 -50 people worldwide



Genetic Conditions
Source: <http://ghr.nlm.nih.gov/BrowseConditions>

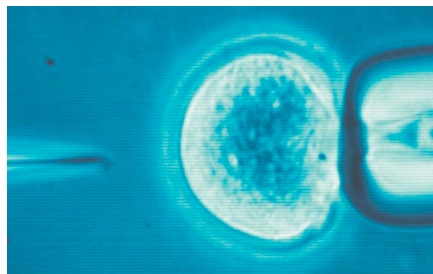
Somatic gene therapy uses viral vectors to insert DNA into “infected” cells.



<http://ghr.nlm.nih.gov/handbook/therapy/procedures>

Germline gene therapy uses a different approach.

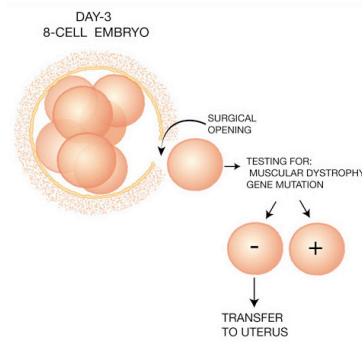
- New DNA inserted into the parents
 - egg cells
 - sperm cells
- In vitro fertilization



http://bio3400.nicerweb.com/Locked/media/ch22/22_05-nuclear_injection.jpg

This is different from the process of parents selecting zygotes.

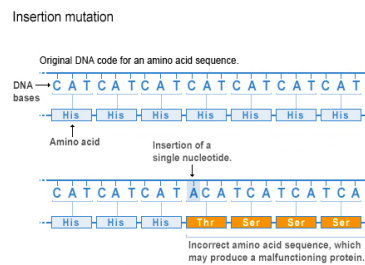
- In vitro fertilization
 - genetic testing of zygote prior to implantation
 - test for presence of
 - genetic condition
 - gender



http://4.bp.blogspot.com/_VRHubD07bg0/TFf_nfZBevl/AAAAAAAAAAc/oAvLH4wMIEs/s1600/pgd.jpg

Germline gene therapy can create a new problem while repairing the gene.

- placement of the new DNA
 - could insert into an existing gene
 - making it dysfunctional
 - could be lethal
 - but may not appear until much later

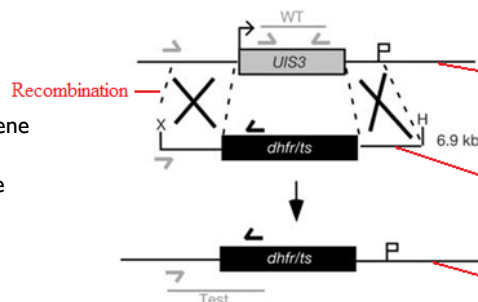


<http://ghr.nlm.nih.gov/handbook/illustrations/insertion>

8

Developing technology is the process of targeted replacement of a gene.

- removal of defective gene
- proper insertion of the replacement DNA



<http://www.cambridgemedicine.org/sites/default/files/55-191-1-sp.png>

Germline technology has not been used on humans but has been used to create transgenic animals.

- new breeds of animals
 - expressing specific genes
- inefficient process
 - many unsuccessful DNA transfers
 - very rare successful ones are used to establish new breeding lines.



10 Mouse on the left expresses rat growth-hormone.

Genetic modification of human beings sits on a slippery slope.

- treat lethal diseases
- treat genetic conditions
- genetic enhancement?



11

What genetic conditions should be treated?

- Sickle cell anemia
 - damaged gene for hemoglobin
 - impairs ability of blood cells to carry oxygen
 - one copy of allele
 - resistance to malaria

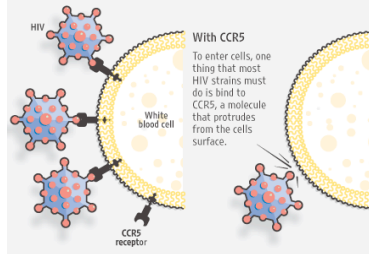


12

Should we fix “mutations” we don’t understand?

- CCR5-Δ32

- deletion mutation
- about 10% of people from Northern European descent
 - protects against the bubonic plague
 - protects against small pox and HIV



<http://eemb40.blogspot.com/2011/01/black-death-and-hiv-resistance.html>

Assignment

Assignment

Germline Therapy: autonomy or predestination?

One of the arguments used against the use of germline gene therapy is that it violates the principle of autonomy. Under normal circumstances an individual is given the opportunity to provide informed consent to receive a medical procedure or enroll in a clinical study. However, parents often make decisions in the best interests of their children.

In your discussion group:

Discuss under what situations parents should be allowed to make decisions to alter the genome of their unborn child.

14

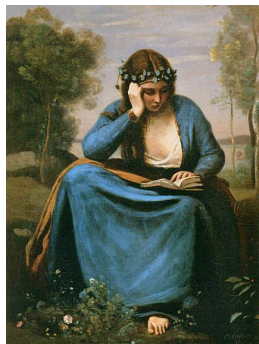
Readings

Nielsen (1997) Human Germline Gene Therapy. *MJM* 3:126-132.

<http://www.medicine.mcgill.ca/mjm/v03n02/v03p126/v03p126.pdf>

Locke (2004) Choosing Hope: The Reality of Germline Engineering. from *A Companion to Genethics*, 2004.

<http://www.bama.ua.edu/~joshua/archive/may04/Cody%20Locke.pdf>



The Reader Wreathed with Flowers (Virgil's Muse)

15 Jean Baptiste Camille Corot, 1845

Any Questions?

Email me at:
hoffmanj@arcadia.edu



<http://www.vippitbullkennels.com/images/animated-question-mark.gif>