

BIOTECH II

- Biotechnology and Medicine
 - Bacterially expressed proteins
 - Pharm Animals
 - Gene Therapy
 - Genome Project

Therapeutic Proteins

- Human Growth Hormone
 - Promote bone and muscle growth
 - Treat individuals deficient in growth hormone
 - Symptom of deficit – short stature
 - Example Turners syndrome
- Tissue Plasminogen activator (tPA)
 - Breaks up blood clots
 - Treat stroke and heart attacks caused by blood clots
- Insulin
 - Allow tissues to absorb glucose
 - Treat individuals deficient in insulin (type 1 diabetes)

Diabetes

Diabetes, sugar stays in the bloodstream rather than entering cells because the body does not make or does not respond properly to insulin. The symptoms of diabetes are hyperglycemia (elevated sugar levels in the urine and blood), increased urination, thirst, hunger, weakness, weight loss, and possibly death.

Type 1 diabetes – insulin deficient **Type 2 diabetes** – insulin resistant

Type 1 diabetes often treated effectively by injection of insulin

Before 1984 medical insulin was purified from the pancreases of dead cows and pigs

Problems

1. not enough pancreas available to provide needed insulin
2. some people develop allergies to insulin from animals.

Humulin

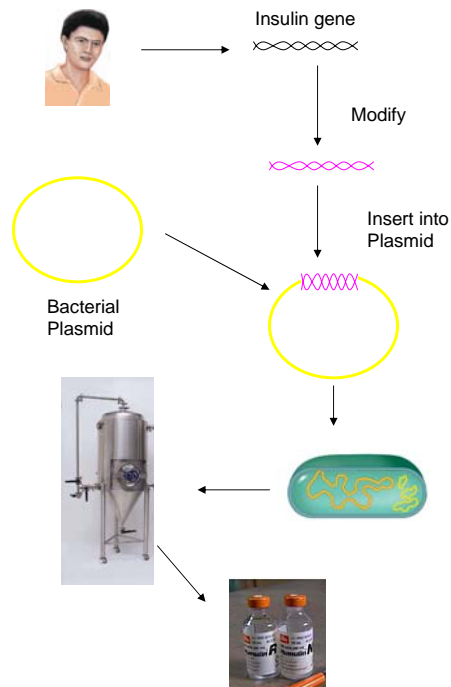
- **1982** Humulin, Genentech's human insulin drug produced by genetically engineered bacteria for the treatment of diabetes, is the first biotech drug to be approved by the Food and Drug Administration.



Humulin--synthetic insulin

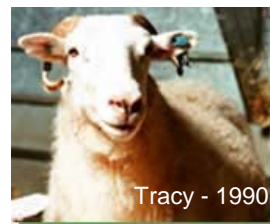
Cloning Insulin

1. Isolate human insulin gene
2. Modify gene to be expressed in bacteria
3. Insert human gene into bacterial plasmid
4. Transform plasmid into bacteria
5. Grow large amounts of bacteria
6. Purify "human" insulin produced by bacteria



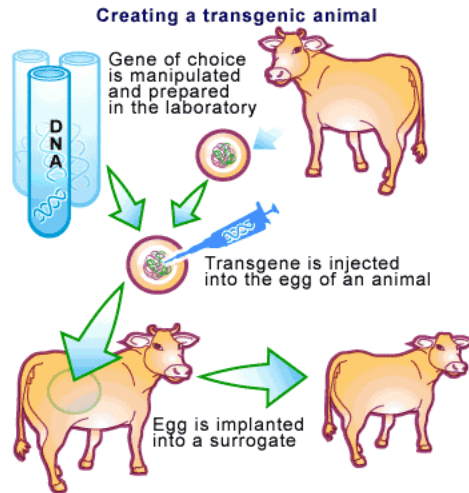
Pharm Animals

- Limits to bacterially expressed proteins
 - Bacteria may not fold or chemically modified proteins like animal cells
 - Therefore, unlike insulin, tPA or growth hormone, some therapeutic proteins cannot be produced in bacterial cells
 - Example human **Alpha-1-Antitrypsin** used to treat mucous in cystic fibrosis and emphysema patients.
- Pharm Animals
 - Transgenic animals engineered to express pharmaceutical (therapeutic) proteins in milk



Creating a Pharm Animal

- Isolate gene of interest - Alpha-1-Antitrypsin
- Modify gene to be expressed in mammary glands
- Inject gene into fertilized cow or goat egg.
- Implant egg in surrogate mother
- Offspring produces protein in milk



Advantages to Pharm Animals

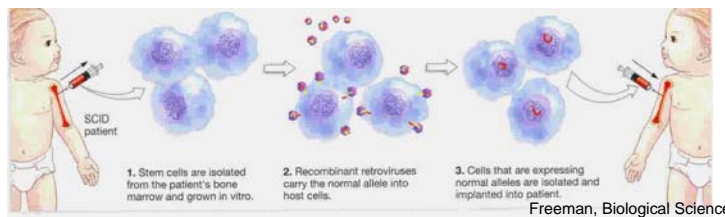
- Advantages
 - Protein modified and folded like in humans
 - Inexpensive to isolate protein from milk
 - No risk of infection due to blood
- Disadvantages
 - Very expensive to insert gene in pharm animal
 - More expensive to raise goat than bacteria
 - Animal Rights Concerns
 - Frankencow?

Gene Therapy (Transgenic Humans)



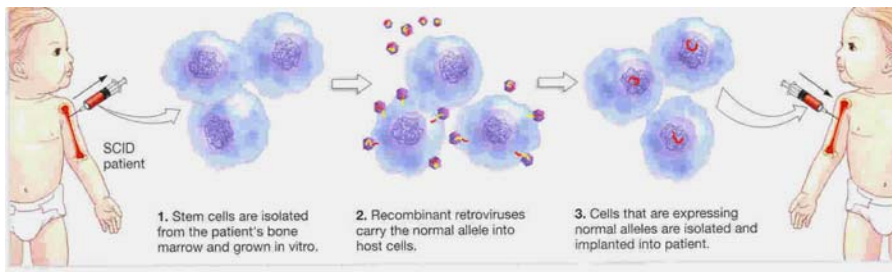
Freeman, Biological Science

- Severe Combined Immunodeficiency Syndrome (SCIDS)
 - X linked recessive trait
 - Mutation in allele encoding Adenine deaminase (ADA)
 - Bone marrow cells transformed with retrovirus containing functional human ADA gene.



Gene Therapy - SCIDS

- Healthy allele for ADA inserted into virus
- Adult stem cells are isolated from patients bone marrow.
- Stem cells infected with virus which inserts the gene into the chromosome
- Cells are implanted into patient
- Cells produce functional ADA and SCIDS is cured



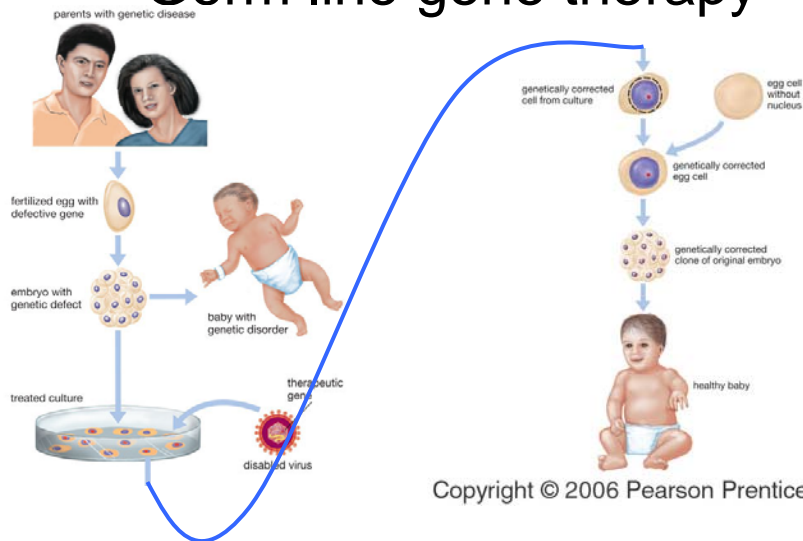
Problems with gene therapy

- In some early experiments, some patients had only temporary relief because stem cells did not permanently implant. (Better understanding of stem cells may reduce this.)
- Several patients developed leukemia when virus inserted near proto-oncogene. (Scientists are modifying gene delivery technique to limit this problem)

Concerns about gene therapy

- Ethical Issues
 - Eugenics Movement
 - New York to Nazi Germany
 - Assault on human dignity
 - Somatic vs Germ-line Transformation
- Safety Risk
 - Cancer side effect – insertion of virus next to oncogene.

Germ line gene therapy



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Human Genome Project

- Sequenced all the DNA on all the chromosomes.
- Identified 25000 human genes
- Importance of human genom project
 - Insight into the basic biology of humans.
 - Molecular Medicine
 - Genetic Testing
 - Pharmacogenomics
 - Complete genotyping