Chapter 8 Healthcare Biotechnology

Outline:

- 8.1 Introduction
- 8.2 Biopharming
- 8.3 Models of Human Disease
- 8.4 Detecting and Diagnosing Human Disease
- 8.5 Monoclonal Antibodies
- 8.6 Gene Therapy
- 8.7 Tissue engeneering
- 8.8 Stem Cell Technologies
- 8.9 Therapeutic cloning

Learning outcomes:

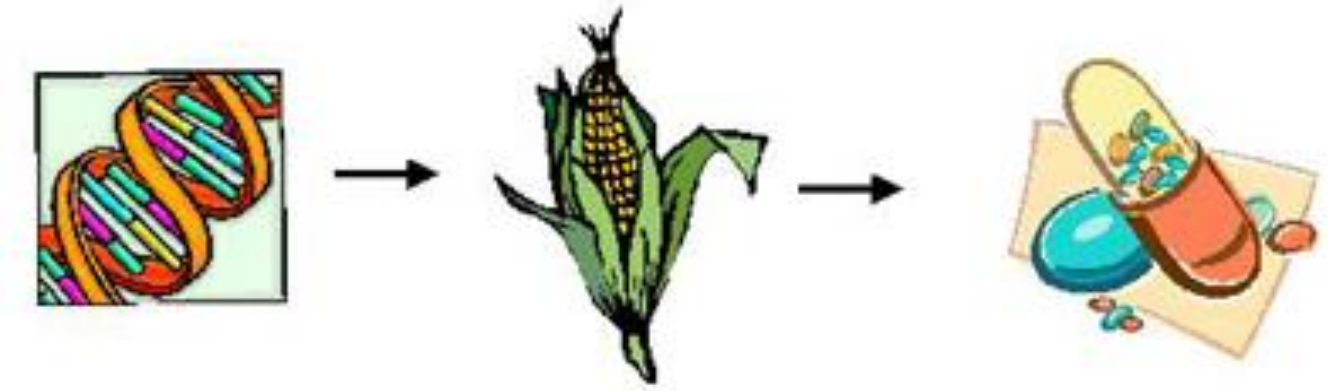
- **Describe the advantages of biopharming.**
- **Explain the applications models of human disease.**
- **List the methods for detecting and diagnosing human diseases.**
- **Describe the advantages of monoclonal antibody, gene therapy, tissue engineering, stem cell and therapeutic cloning.**
- **Apply biotechnology techniques in the treatment of disease.**

8.1 Introduction

- **Also term as Red Biotehnology**
- **refers to a medicinal or diagnostic product that consists of, or has been produced in, living organisms and may be manufactured via recombinant technology.**

8.2 Biopharming

- **Applications of GM plant or animals as bioreactor to produce pharmaceuticals**
- **More economical than producing desired proteins in cell culture**

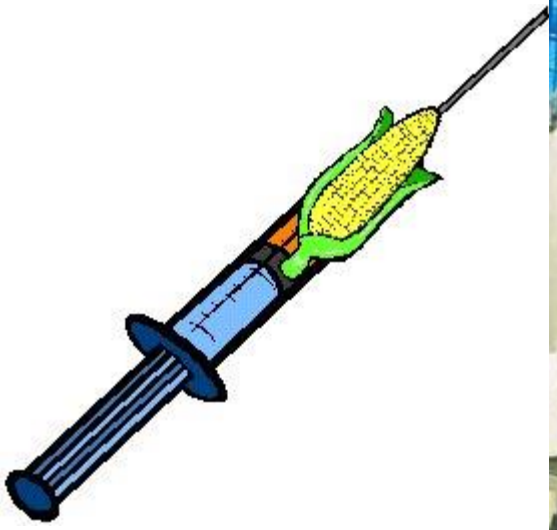


8.2 Biopharming

- **Examples**
  - Human lactoferrin in cows' milk
  - Alpha-1-antitrypsin in sheep
  - HGH in mouse urine (uroplakin promoters)
  - the production of "mammalian- like" glycans in plants.

Discussion

- **What are the advantages of biopharming?**



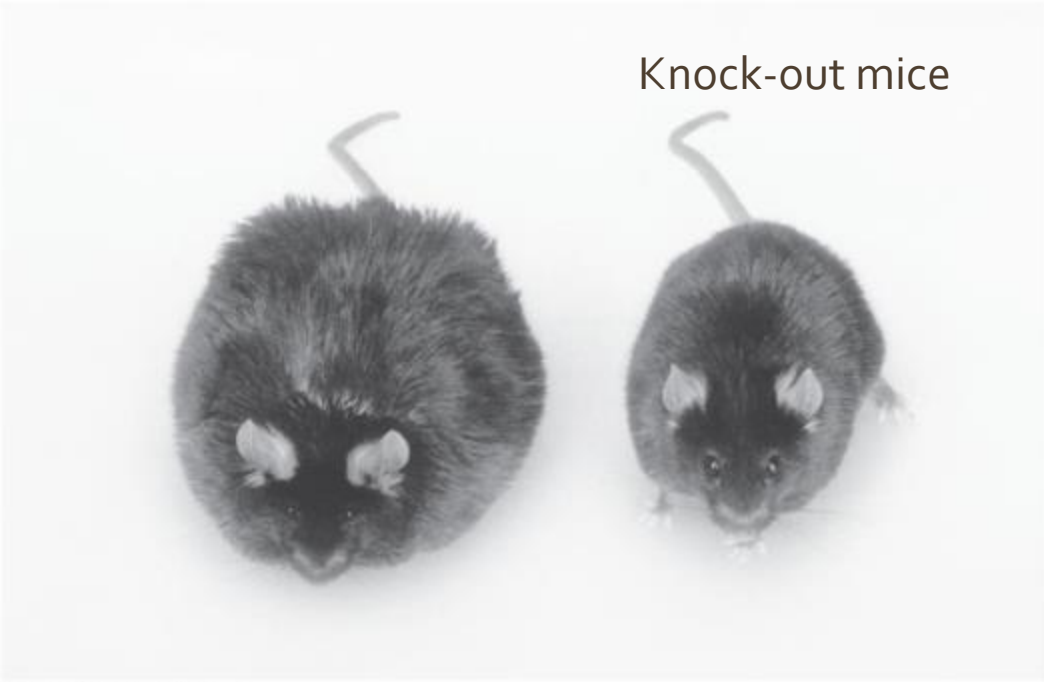
http://www.youtube.com/watch?v=XqphlQ_joNo

8.3 Models of Human Disease

- **Model organisms are nonhuman organisms that scientists use to study biological processes in experimental lab conditions.**
- **Examples include mice, rats, worms, fruit flies, & bacteria.**
- **Many human genetic disease occur in model organisms**

8.3 Models of Human Disease

- **Extremely important because we cannot manipulate human genetics for experimental purposes**



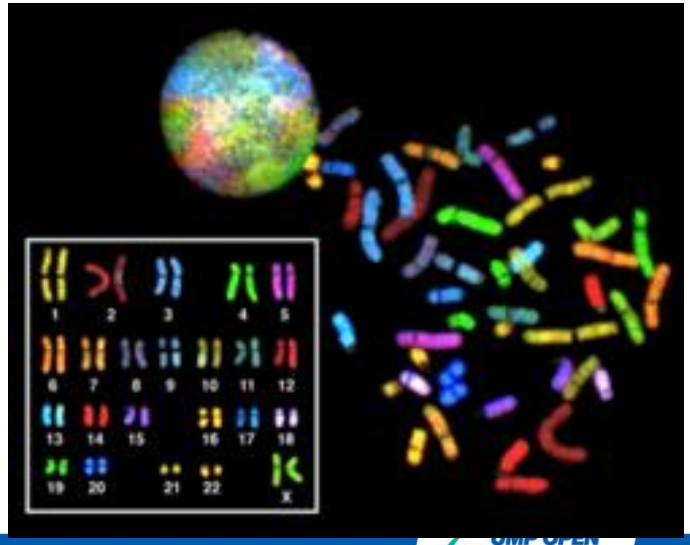
http://www.dnalc.org/resources/animations/model_organisms.html

8.4 Detecting and Diagnosing Human Disease

- **Biomarkers for Disease Detection**
  - **Early detection of disease is critical for providing the best treatment and improving the odds of survival**
  - **With the right diagnostic tools, may be possible to detect most every disease at an early stage**
  - **Biomarkers – typically proteins produced by diseased tissue or proteins whose production is increased when a tissue is diseased**
    - **PSA, prostate-specific antigen**

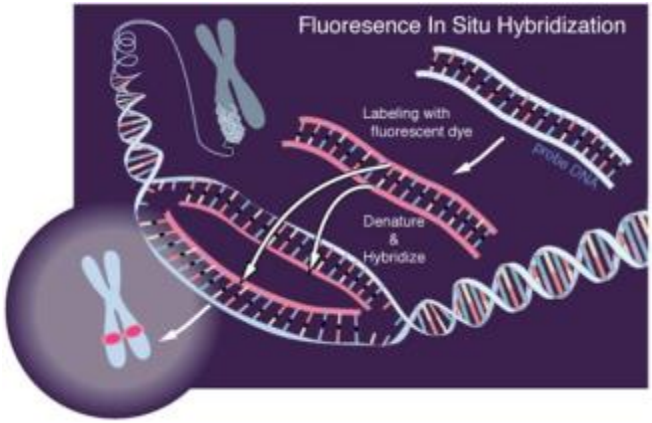
8.4 Detecting and Diagnosing Human Disease

- **Detecting Genetic Diseases**
  - **Testing for chromosome abnormalities**
  - **Remove a small portion of a layer of cells called the chronic villus that helps form the placenta**
  - **Create a karyotype**

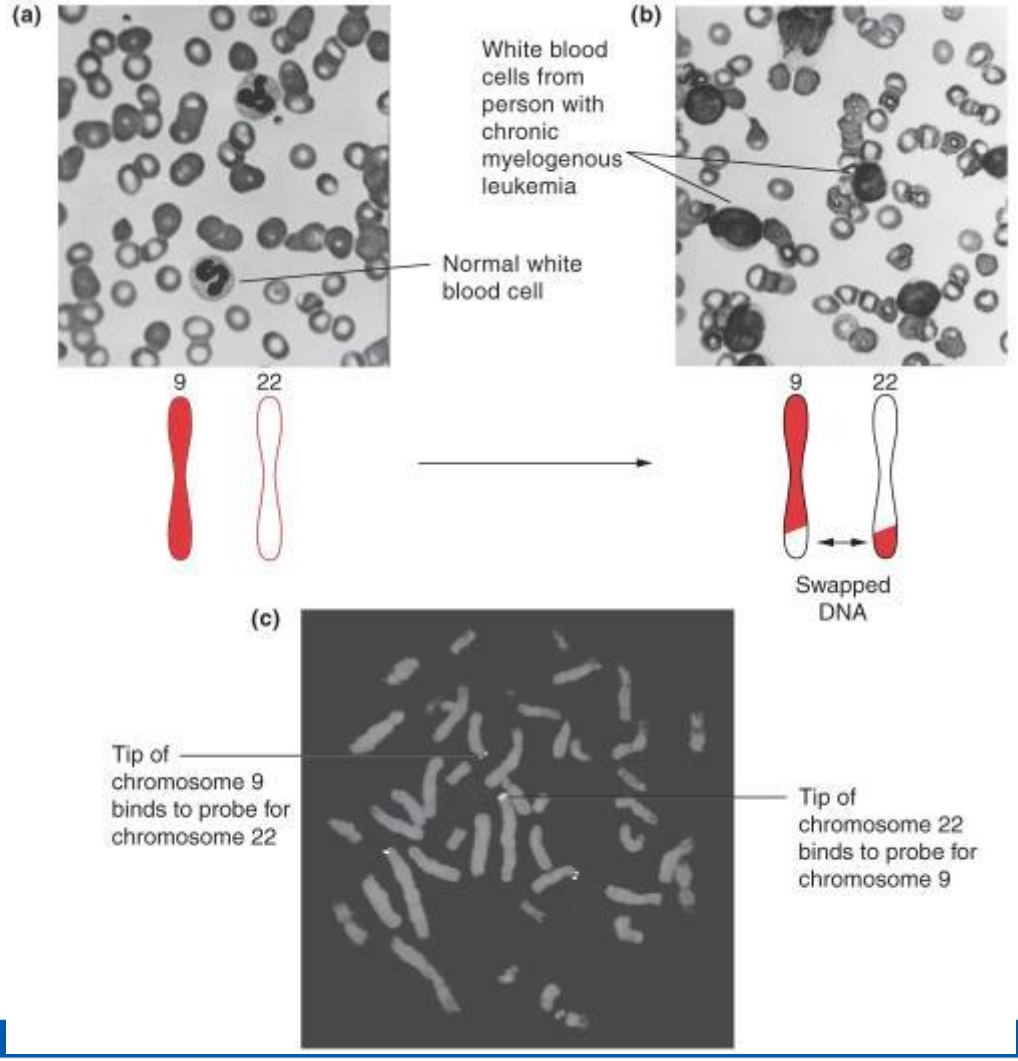


8.4 Detecting and Diagnosing Human Disease

- **Detecting Genetic Diseases**
- **Fluorescence *in situ* hybridization (FISH) – new technique for karyotyping**
  - **Useful for identifying extra chromosomes, missing parts of chromosomes Or DNA swapping across different chromosomes**
    - **Chronic myelogenous leukemia (DNA exchange between chromosome 9 and 22)**

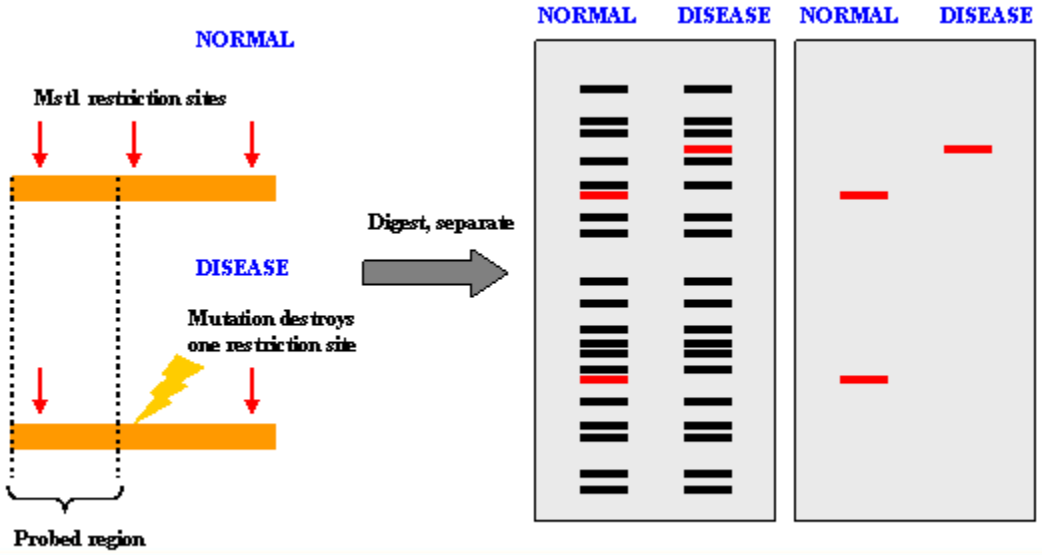


8.4 Detecting and Diagnosing Human Disease



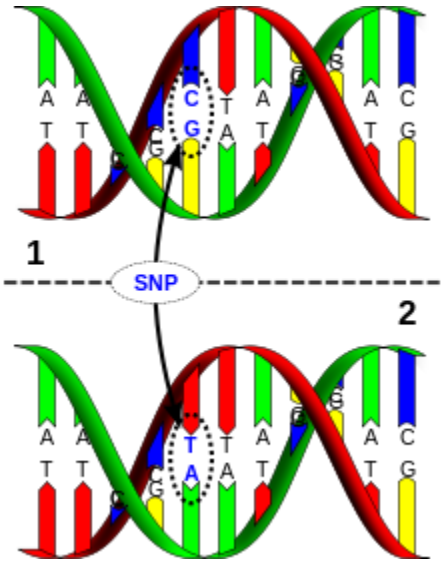
8.4 Detecting and Diagnosing Human Disease

- **Detecting Genetic Diseases**
- **Restriction fragment length polymorphism (RFLP)**
  - **a genetic variation that can be detected by enzymatic digestion.**



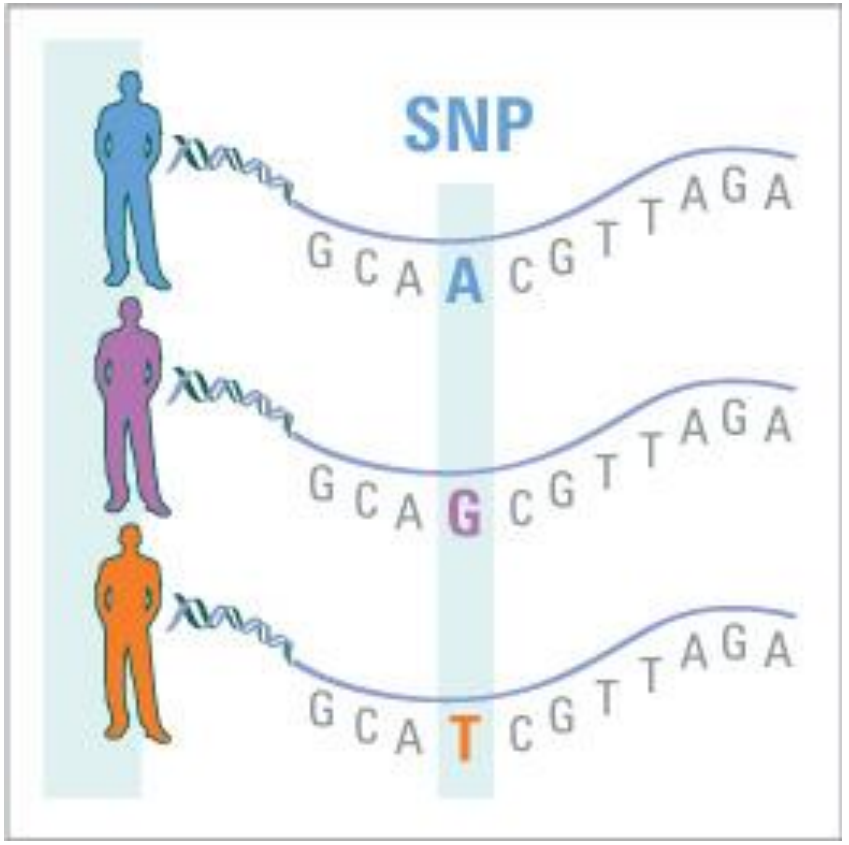
8.4 Detecting and Diagnosing Human Disease

- **Detecting Genetic Diseases**
- **SNPs (single nucleotide polymorphisms)**
  - **One of the most common forms of genetic variation among humans**
  - **If an SNP occurs in a gene sequence, it may cause a change in protein structure that produces disease or influences traits in a variety of ways**



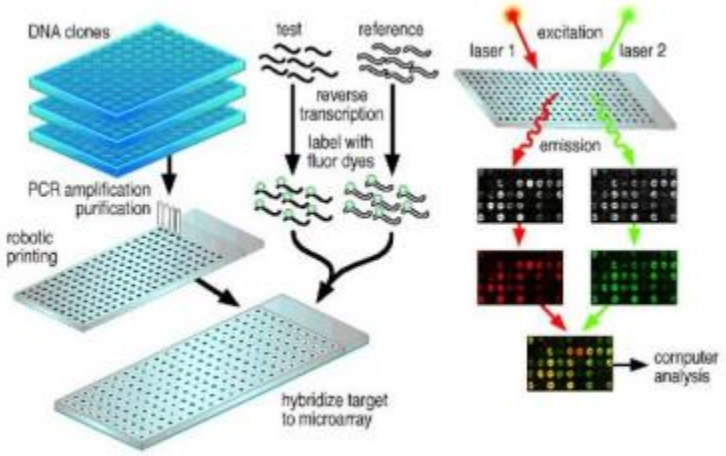
8.4 Detecting and Diagnosing Human Disease

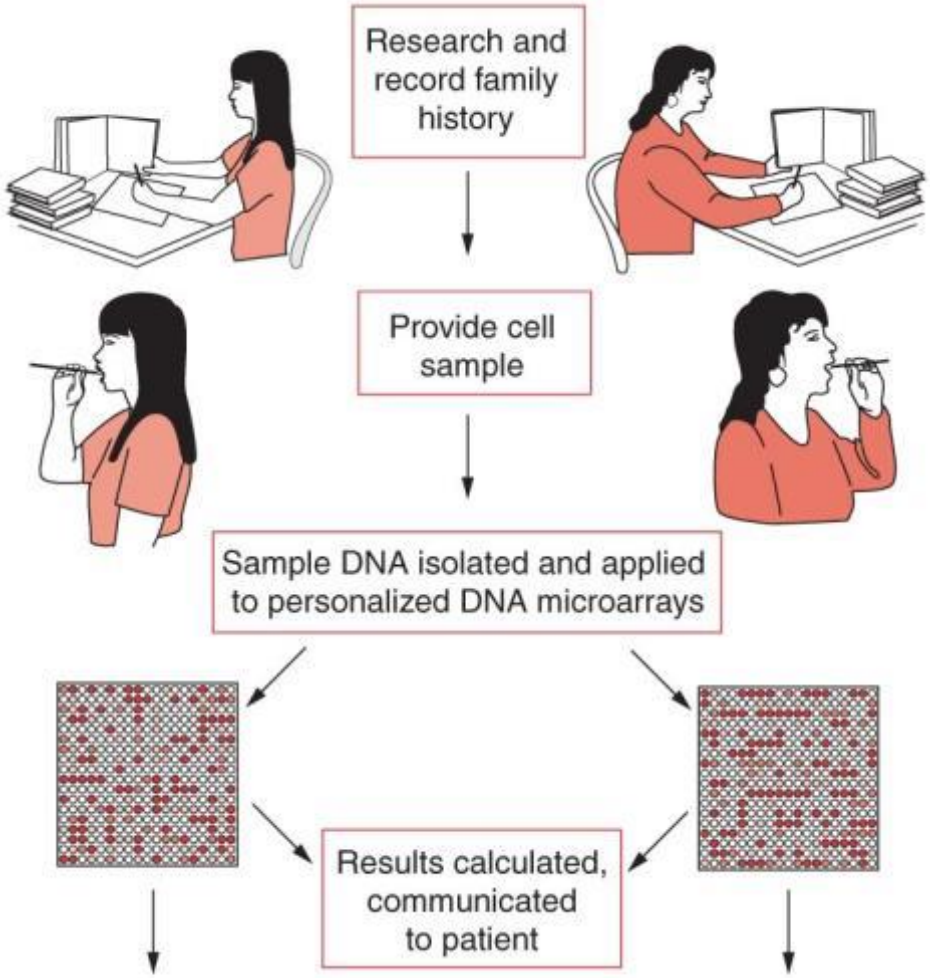
- **Might be used to predict susceptibilities to**
  - **Stroke, diabetes, cancer, heart disease, behavioral and emotional illnesses**



8.4 Detecting and Diagnosing Human Disease

- **Detecting Genetic Diseases**
- **DNA microarrays are glass microscope slides spotted with thousands of genes**
  - **Can be used to screen a patient for a pattern of genes that might be expressed in a particular disease condition**





Susan's Genetic Profile

Trait	Risk
Addictive behavior	: Greater than general population
Lung cancer	: Greater than general population
Colon cancer	: Less than general population
Alzheimer's disease	: Less than general population

Lisa's Genetic Profile

Trait	Risk
Cystic fibrosis	: 100% diagnosis
Type II diabetes mellitus	: Less than general population
Cardiovascular disease	: Greater than general population

8.4 Detecting and Diagnosing Human Disease

- **Pharmacogenomics – Customized Medicine**
  - **Designing the most effective drug therapy and treatment strategies based on the specific genetic profile of a patient**
  - **Individuals can react differently to the same drugs**
    - **Different degrees of effectiveness and side effects because of genetic polymorphisms**

8.4 Detecting and Diagnosing Human Disease

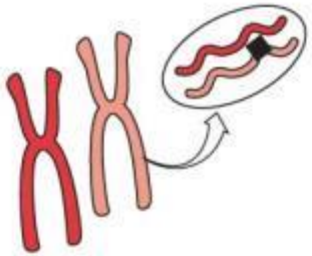
Individuals respond differently to the anti-leukemia drug 6-mercaptopurine.

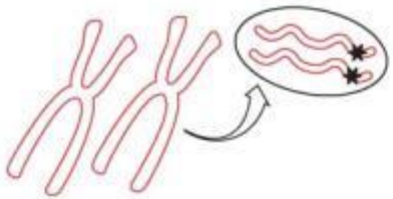
Most people metabolize the drug quickly. Doses need to be high enough to treat leukemia and prevent relapses.

Others metabolize the drug slowly and need lower doses to avoid toxic side effects of the drug.

A small portion of people metabollize the drug so poorly that its effects can be fatal.

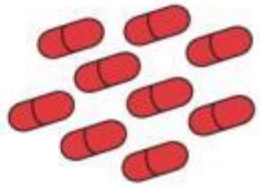
The diversity in responses is due to variations (mutations, ■ or ✱) in the gene for an enzyme called TPMT, or thiopurine methyltransferase.



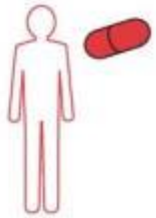


After a simple blood test, individuals can be given doses of medication that are tailored to their genetic profile.

Normal dose



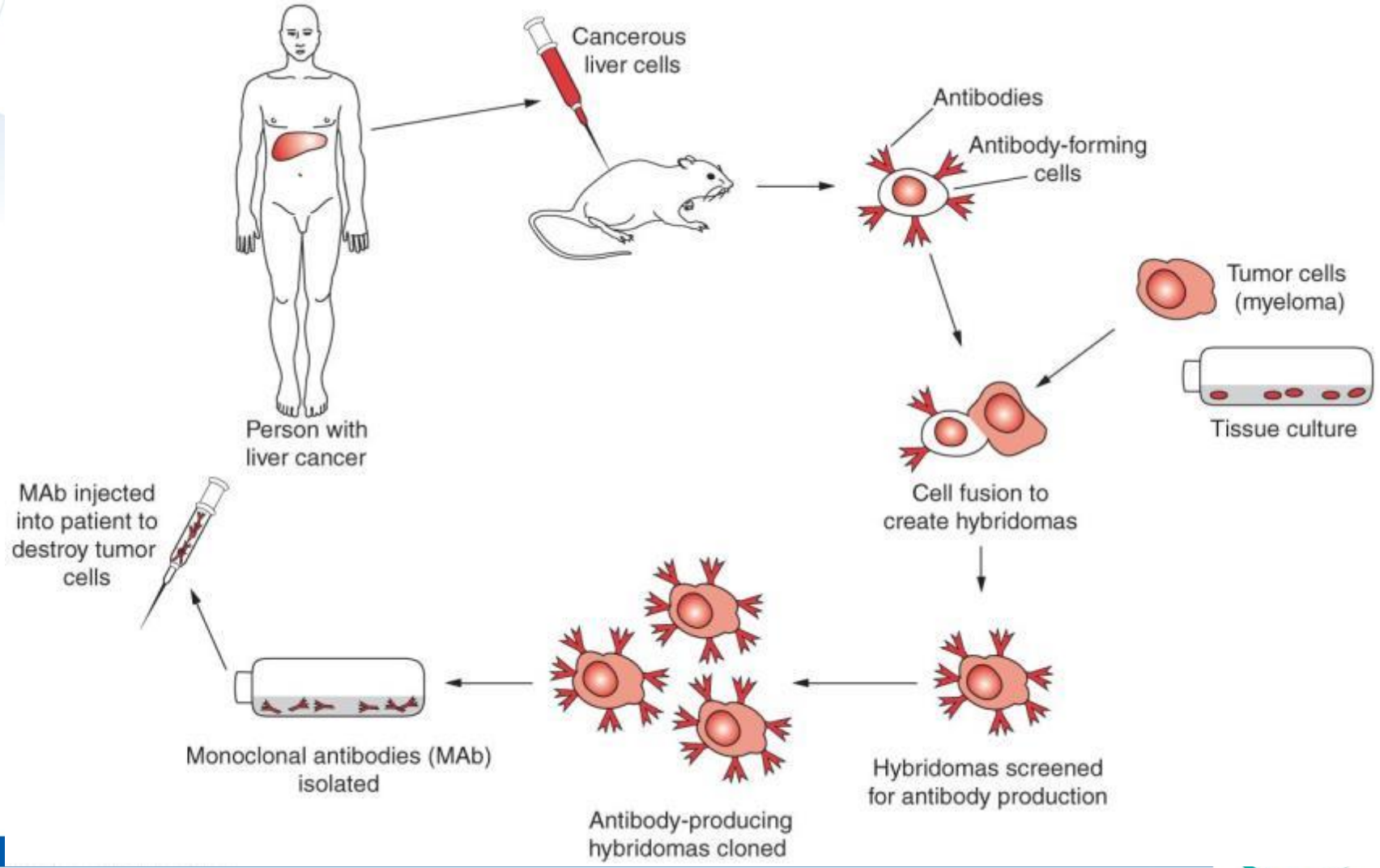
Dose for an extra slow metabolizer (TPMT deficient)



8.5 Monoclonal Antibodies

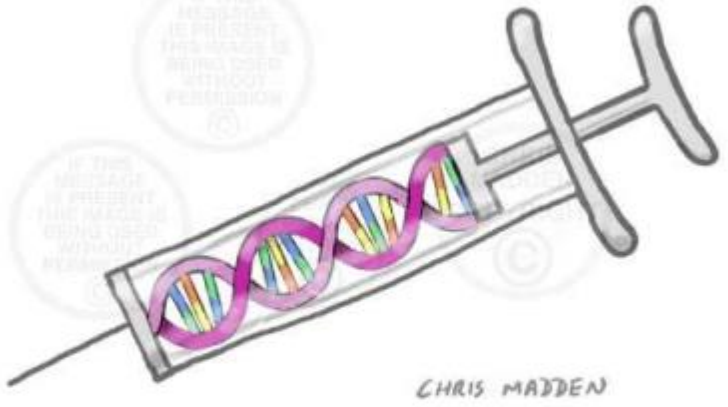
- **Monoclonal Antibodies – purified antibodies that are very specific for certain molecules**
  - **Cancer cells, arthritis, and Alzheimer's Disease**
  - **Treat addiction to harmful drugs**

8.5 Monoclonal Antibodies

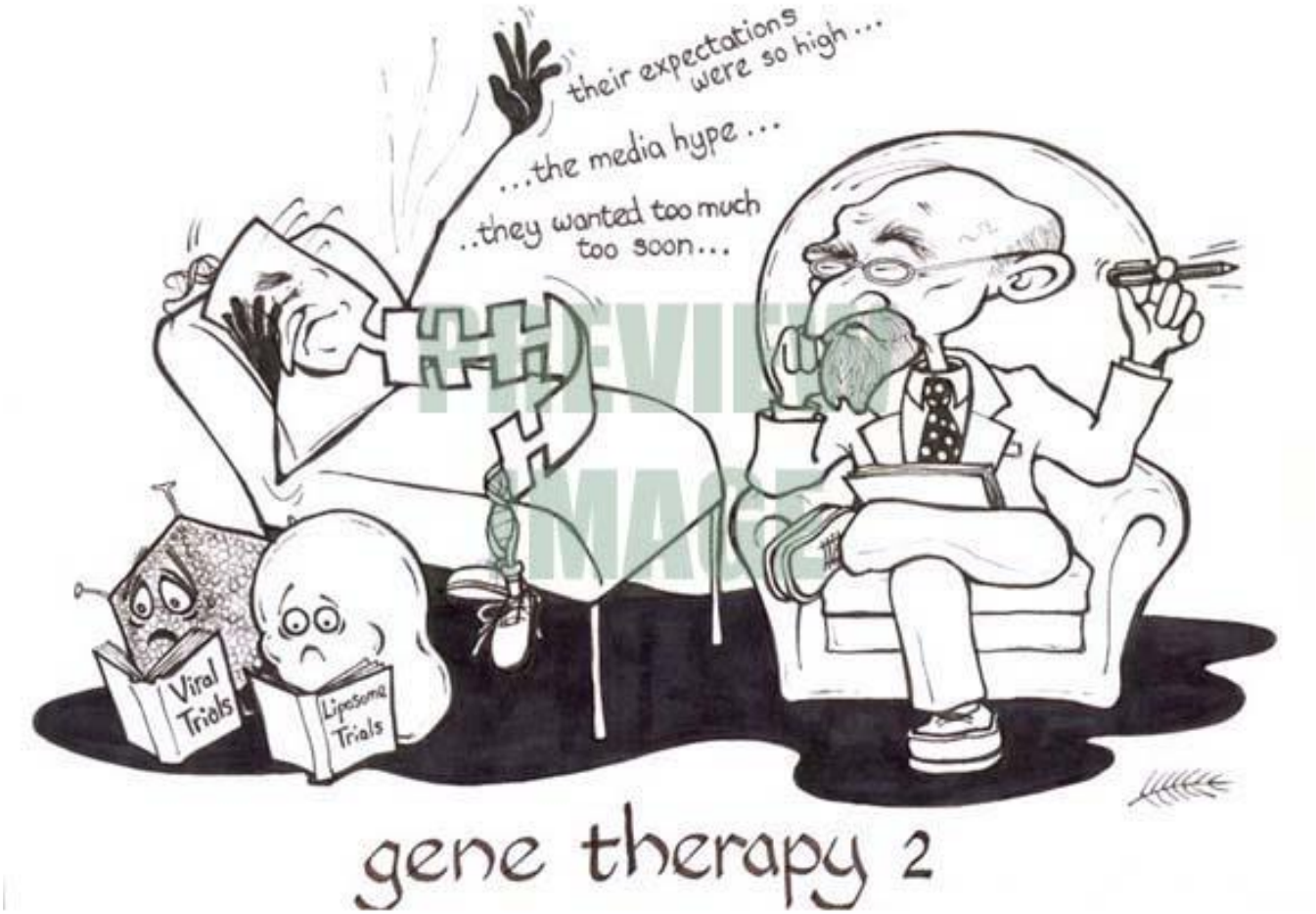


8.6 Gene Therapy

- **Gene therapy is the delivery of therapeutic genes into the human body to correct disease conditions created by a faulty gene**



8.6 Gene Therapy



University of Pennsylvania gene therapy shows promise in eradicating some blood cancers

December 10, 2012 | By Marie McCullough, Inquirer Staff Writer

A 7-year-old pixie named Emily Whitehead has erased any remaining doubts about the power of a University of Pennsylvania gene therapy to eradicate certain blood cancers.

The therapy is personalized using each patient's immune system "T cells." Three weeks after Emily's infusion in April, she was completely free of the leukemia that had been on the verge of killing her.

Just as important, she showed that the T cell therapy can have catastrophic side effects, and pointed the way for her doctors to find an antidote.

Without that antidote, she, and probably several later patients, would be dead. And a novel therapy that has tamed terminal leukemia in seven of the first 10 patients might be deemed too risky for further testing.

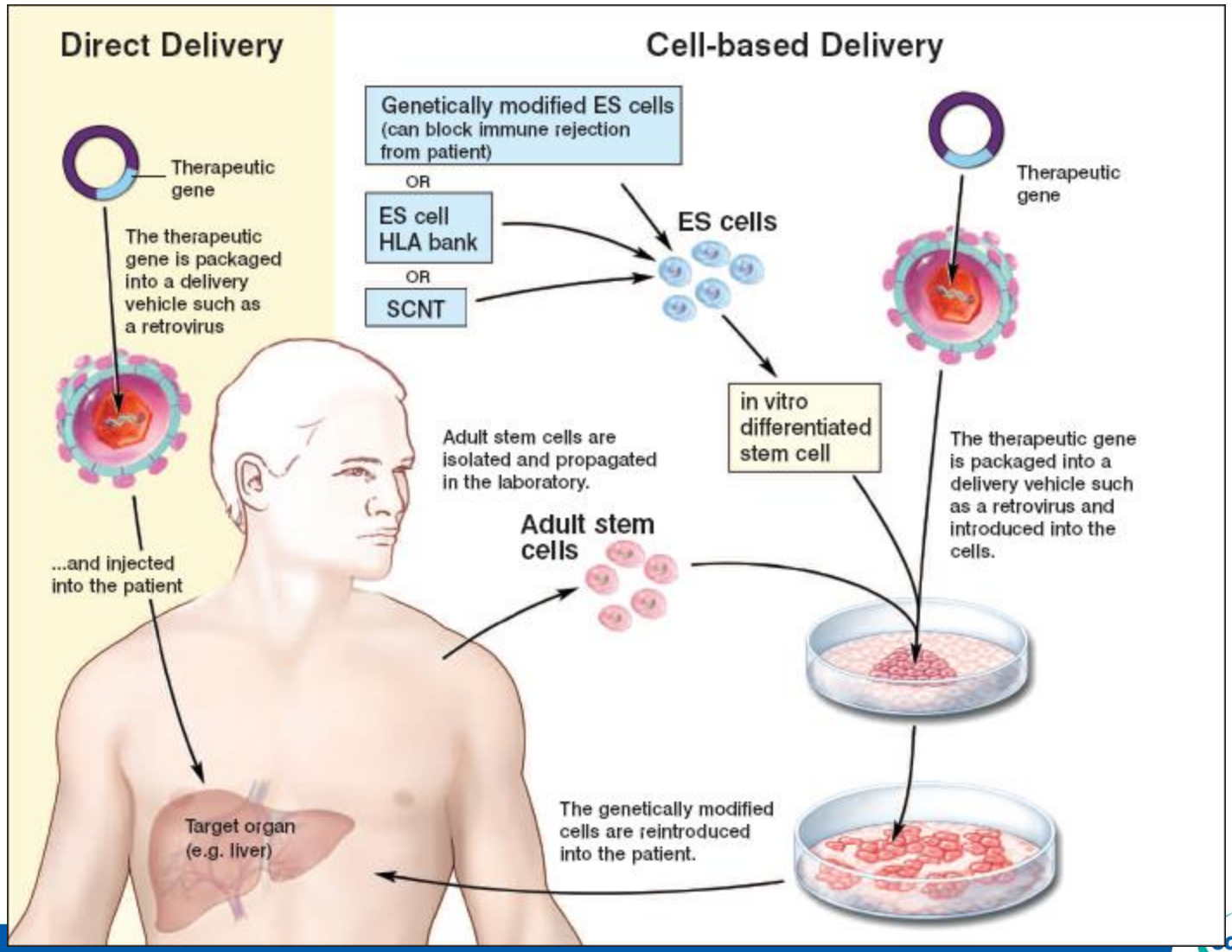
Image 1 of 2 View Gallery

Emily Whitehead, 7, gets the gene therapy from nurse Colleen Wallace. Emily's...

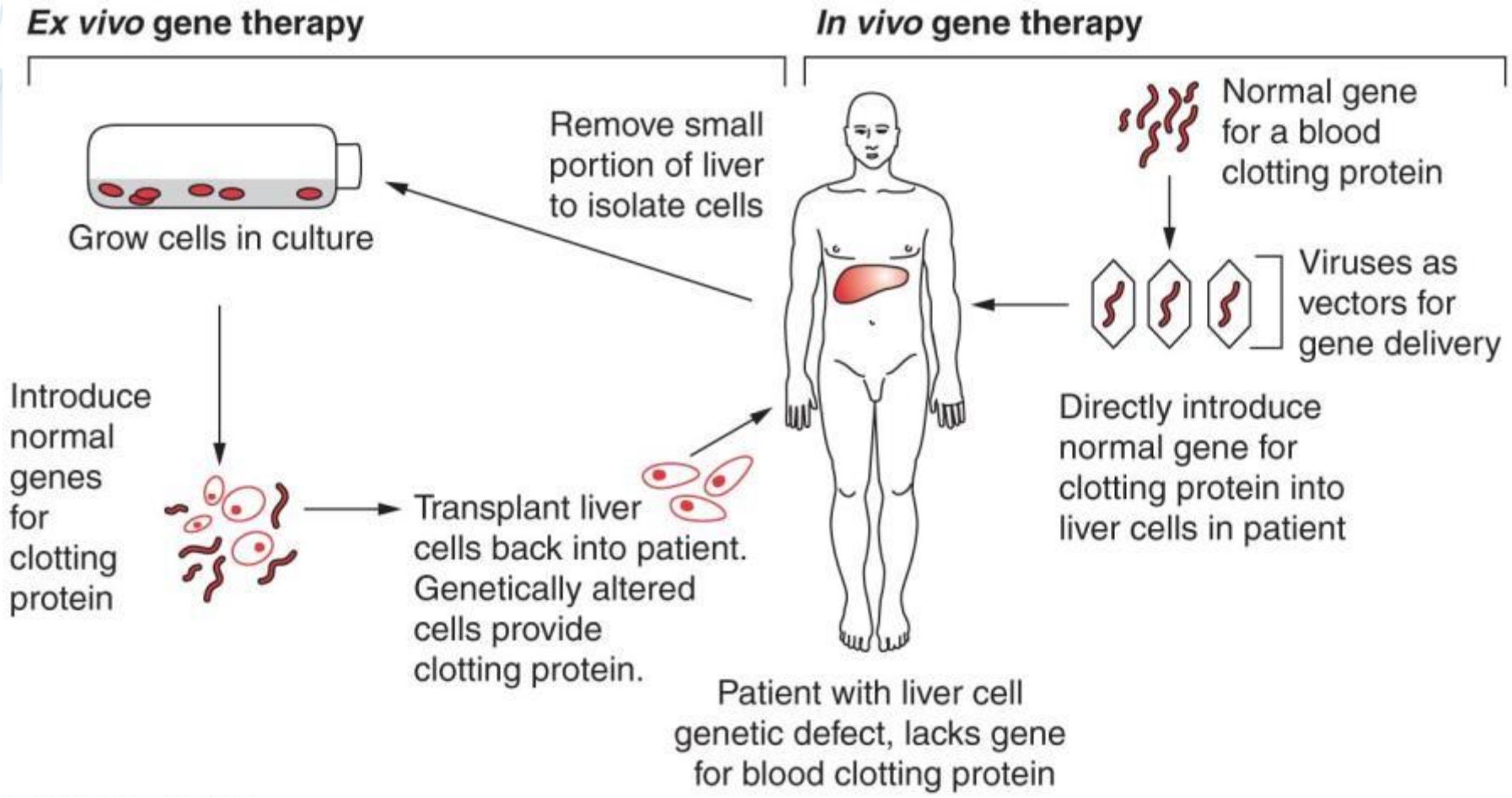

8.6 Gene Therapy

- **Two primary strategies:**
  - ***Ex vivo* gene therapy**
    - **Cells are removed from the patient, treated with techniques similar to transformation, and then reintroduced to the person**
  - ***In vivo* gene therapy**
    - **Introducing genes directly into tissues and organs in the body**
    - **Challenge is delivering genes only to intended tissues and not tissues throughout the body**

8.6 Gene Therapy

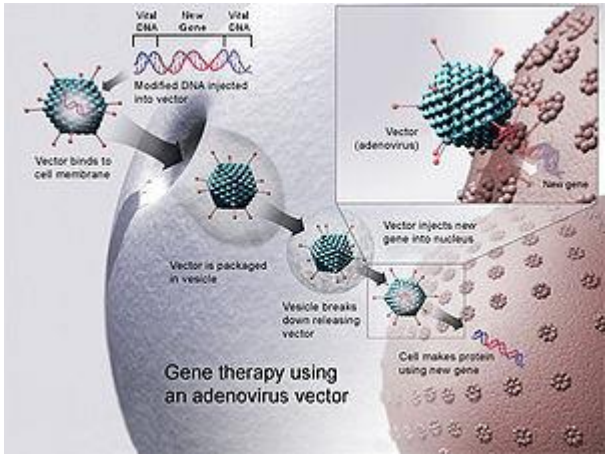


8.6 Gene Therapy



8.6 Gene Therapy

- **Vectors for Gene Delivery**
  - **viruses**
  - **Naked DNA – DNA by itself that is injected directly into body tissues**
  - **Liposomes – small, hollow particles made of lipid molecules**



8.7 Tissue engeneering

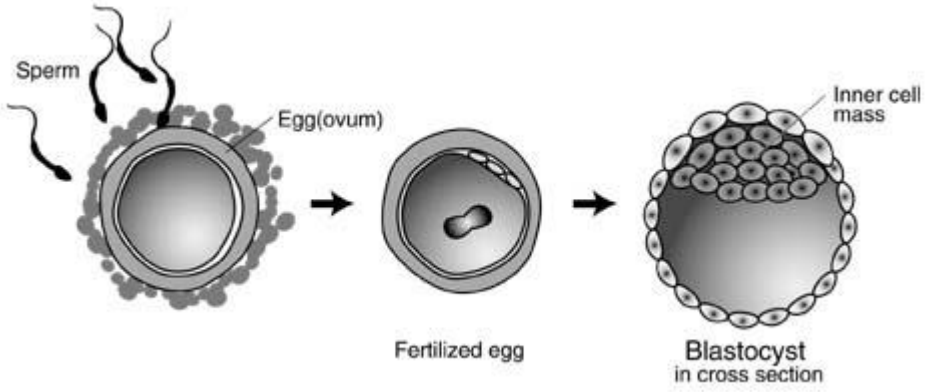
- **Tissue Engineering**
  - **May provide tissues and organs that can be used to replace damaged or diseased tissues**
  - **Process**
    - **Design a framework or scaffold**
    - **Seed the scaffold with human cells**
    - **Bathe in nutrient-rich media**
    - **Cells will build layers and assume the shape of the scaffold**

8.7 Tissue engeneering

- **Sheets of skin grafts**
- **Human bladders, rudimentary kidney**
- **ear on mouse**

8.8 Stem Cell Technologies

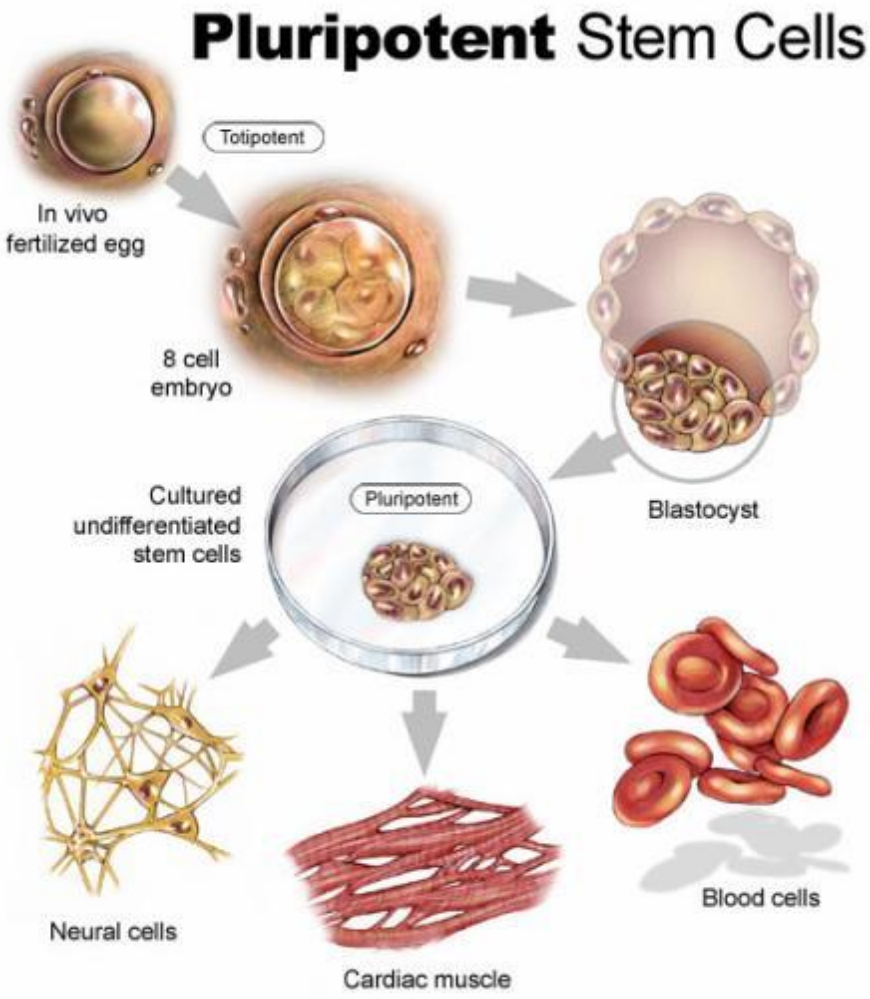
- **What are stem cells?**
  - **Fertilization of egg by sperm results in a zygote**
  - **Zygote divides rapidly to form a compact ball of cells called a morula**
  - **Morula develops into embyro consisting of a small hollow cluster of cells called a blastocyst**



8.8 Stem Cell Technologies

- Two layers to the blastocyst
  - Outer layer forms the placenta
  - Inner cell mass is the source of human embryonic stem cells (hESCs)
- hESCs have the ability to undergo differentiation
  - Maturation process in which cells develop specialized functions
  - Eventually can differentiate to form all of the more than 200 cell types in the human body (pluripotent)

8.8 Stem Cell Technologies



8.8 Stem Cell Technologies

- Other source of stem cell

Bone marrow

Peripheral blood stem cells

Umbilical cord blood

Storage of Hematopoietic Stem Cell

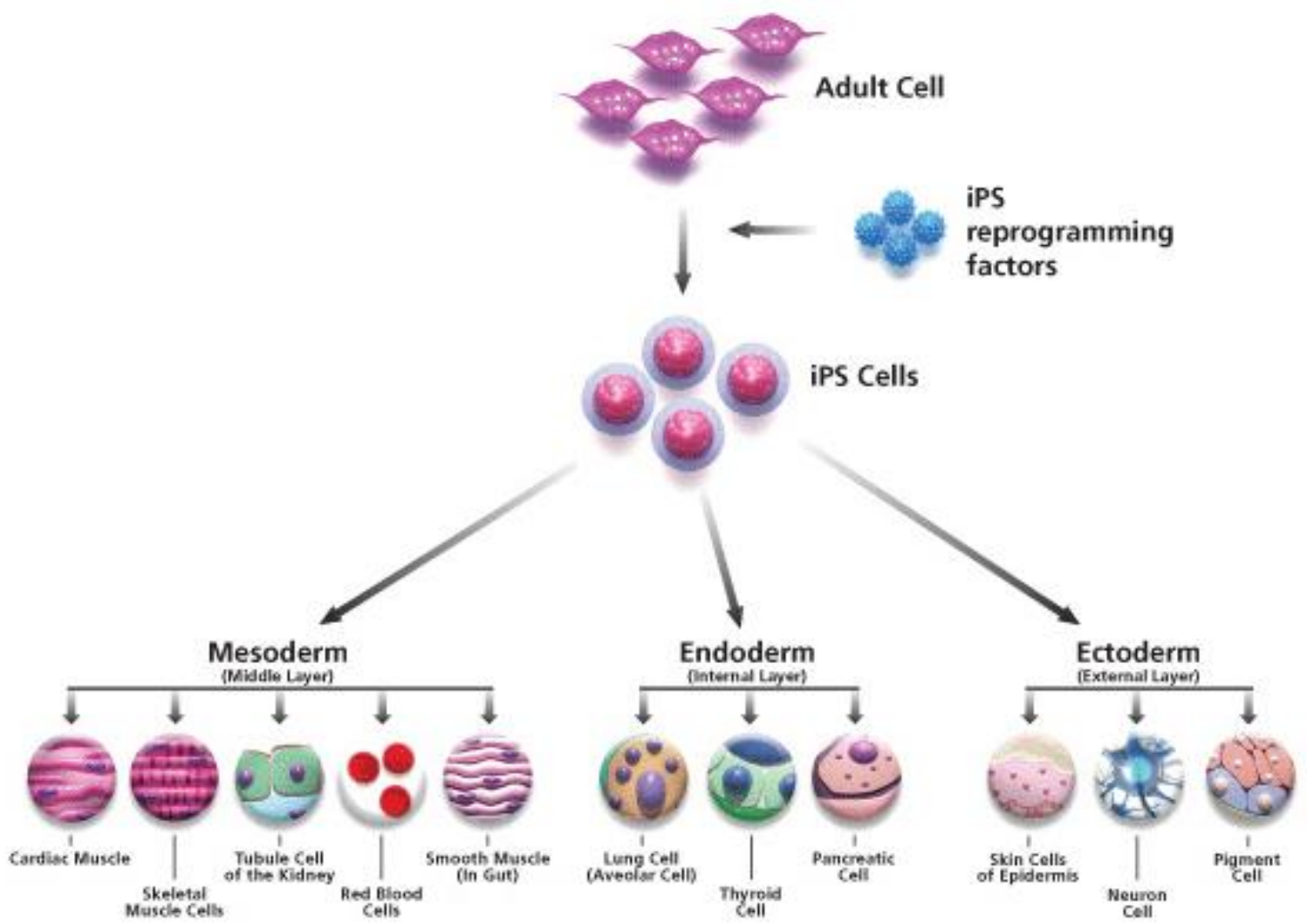
8.8 Stem Cell Technologies

- **Adult stem cells**
  - **Cells that reside in mature adult tissue and could be cultured and differentiated to produce other cell types**
  - **Small in number and not yet discovered in all adult tissues**
  - **Can differentiate into another different specialized cell type, but may not be as pluripotent as hESCs**

8.8 Stem Cell Technologies

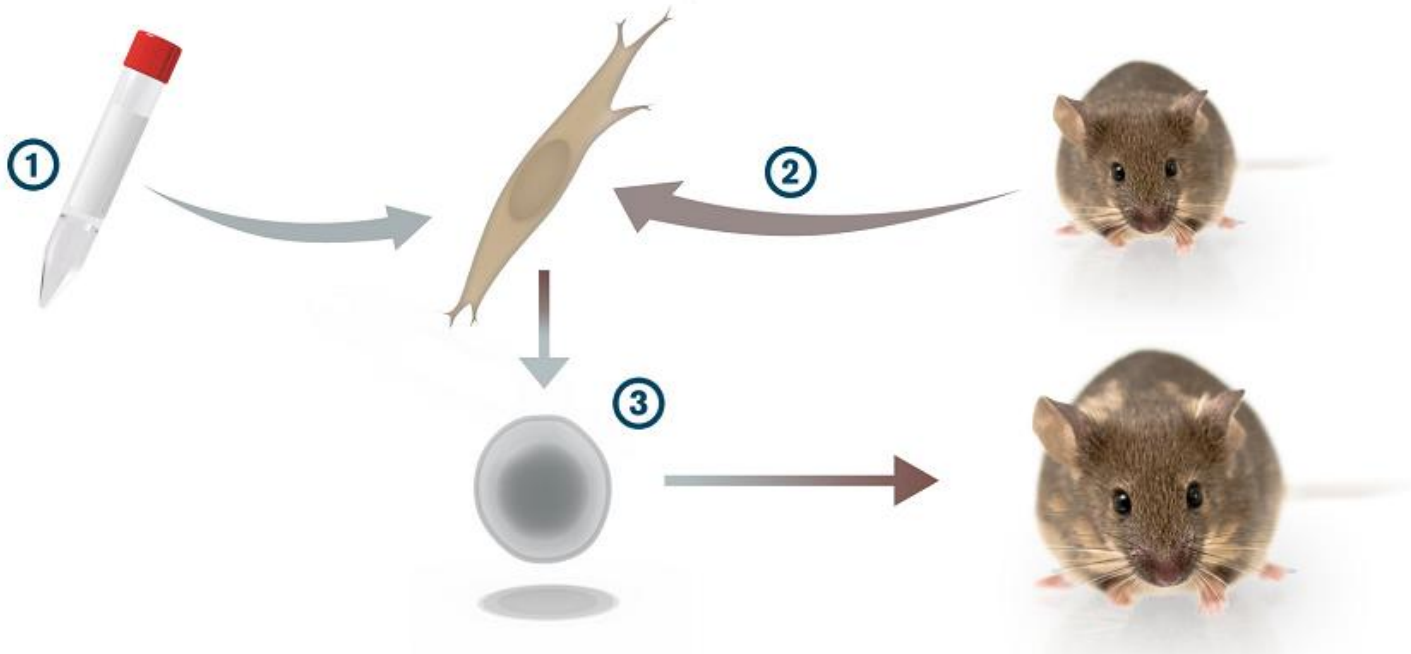
- **Induced pluripotent stem cell**
- **a type of pluripotent stem cell artificially derived from a non-pluripotent cell - typically an adult somatic cell - by inducing a "forced" expression of specific genes.**

8.8 Stem Cell Technologies



8.8 Stem Cell Technologies

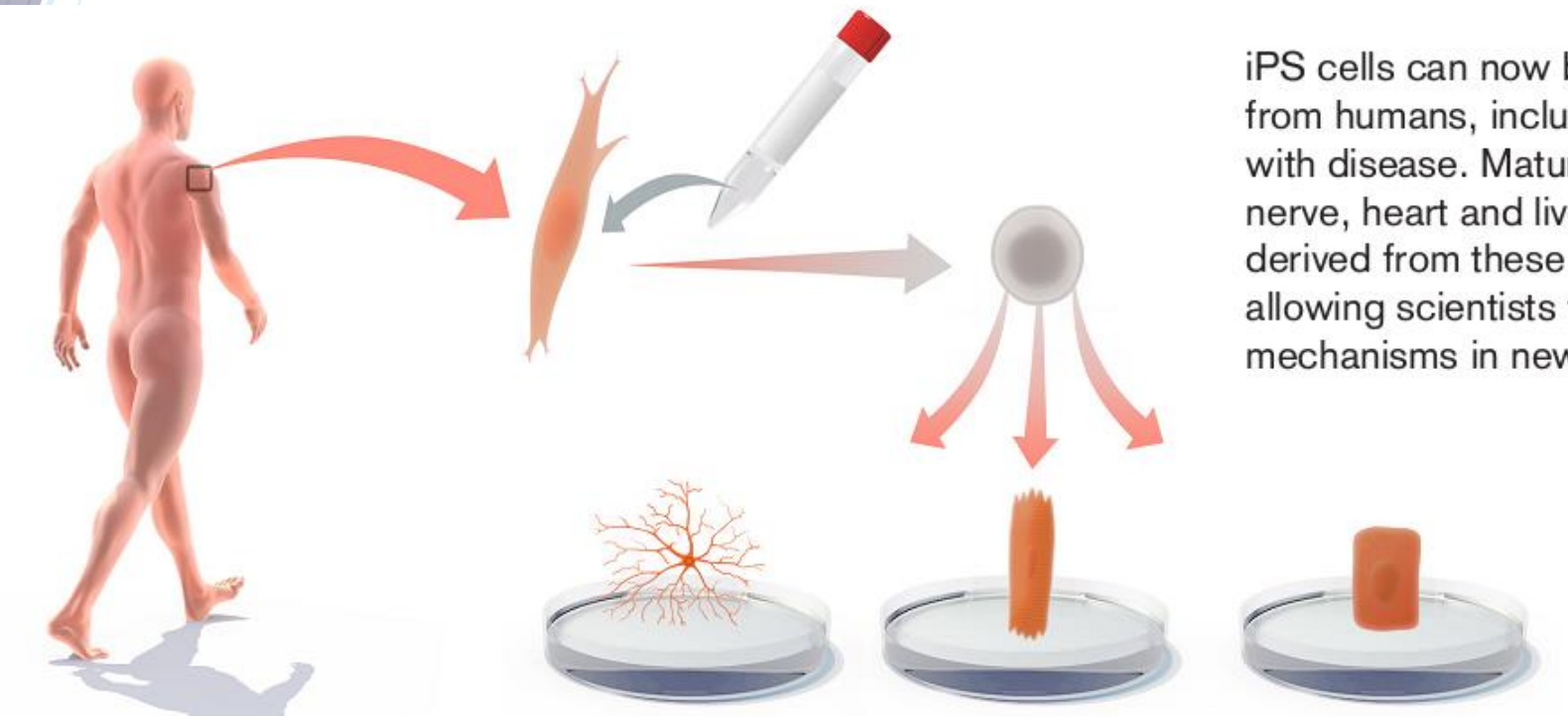
The Nobel Prize in Physiology or Medicine 2012



Shinya Yamanaka

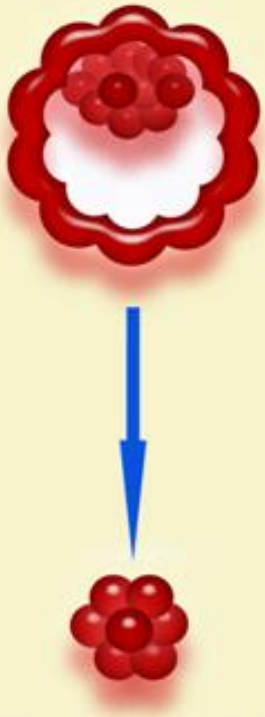
Shinya Yamanaka studied genes that are important for stem cell function. When he transferred four such genes (1) into cells taken from the skin (2), they were reprogrammed into pluripotent stem cells (3) that could develop into all cell types of an adult mouse. He named these cells induced pluripotent stem (iPS) cells.

8.8 Stem Cell Technologies



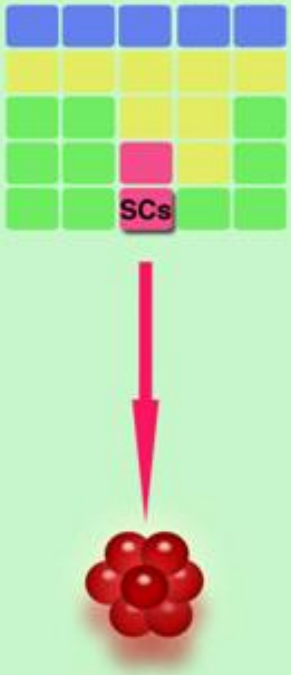
iPS cells can now be generated from humans, including patients with disease. Mature cells including nerve, heart and liver cells can be derived from these iPS cells, thereby allowing scientists to study disease mechanisms in new ways.

Embryonic Stem Cells



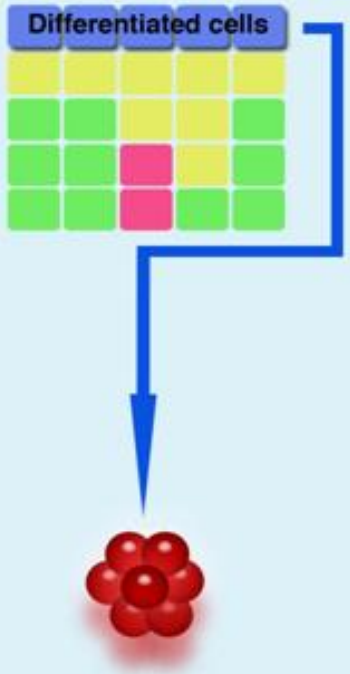
- ESCs originate from the inner cell mass of the blastocyst
- Self-renewal
- Pluripotent
- Generation of mouse chimeras
- Generation of 254 cell types originating adult tissues

Adult Stem Cells



- ASCs are created during ontogeny and persist within the niche in most adult animal tissues/organs
- Self-renewal
- Multipotent
- Maintenance of tissue homeostasis in physiological and pathological conditions

Induced Pluripotent Stem Cells



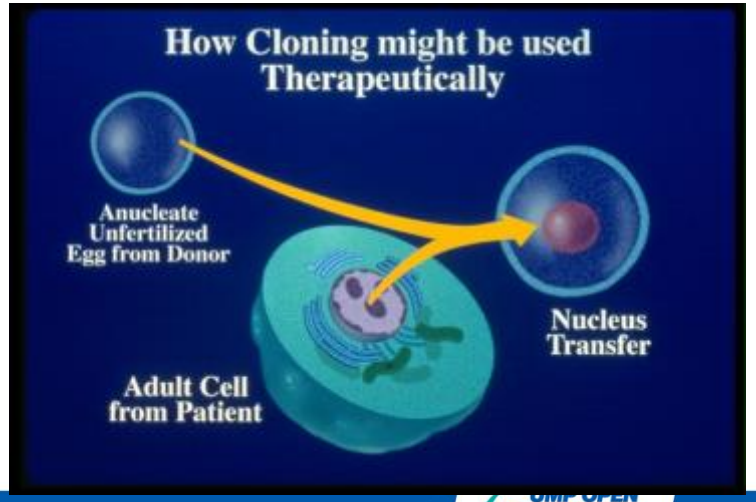
- iPS originate from somatic differentiated cells after transduction with cMic, Klf-4, Oct-3/4 and Sox-3
- Self-renewal
- Pluripotent
- Generation of mouse chimeras
- Patient-specific stem cells

8.8 Stem Cell Technologies

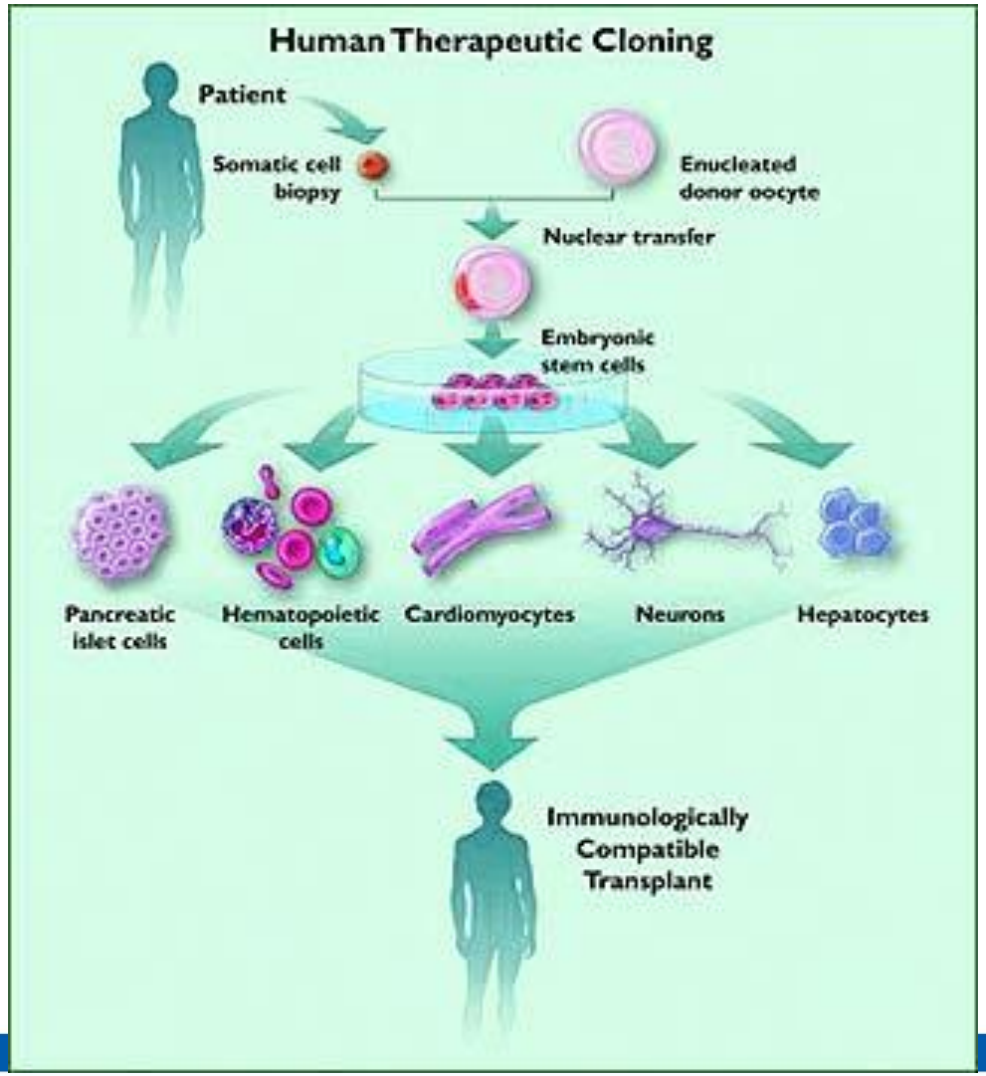
- **Potential Applications of Stem Cells**
  - **Using stem cells to make white blood cells is becoming an effective way to treat leukemia**
  - **Stem cells from umbilical cord blood used to treat sickle cell anemia and other blood deficiencies**
  - **Stem cells from fat have been used to form bone tissue in the human skull**
  - **Repair of heart cells**
  - **Adult stem cells isolated from brain and used to make neurons in culture**

8.9 Therapeutic cloning

- **Therapeutic cloning-**
  - **Also called somatic-cell nuclear transfer**
  - **provides stem cells that are a genetic match to a patient who requires a transplant**
    - No fear of immune rejection



8.9 Therapeutic cloning



Group Discussion

By utilizing natural elements/biodiversity in Malaysia, propose potential healthcare biotechnology products that can be commercialized. One group one product.

Format:

1.Name of product:

2.Function:

3.Problem statement:

4.Novelty:

5.Overall methodology:

Extra reading

- http://www.nih.gov/science/models/mouse/knockout/
- http://www.dnalc.org/view/897-Gene-knockout-in-mice.html
- http://www.creative-biolabs.com/fish/tissuearray5.htm
- http://www.broadinstitute.org/education/glossary/snp
- http://learn.genetics.utah.edu/content/health/pharma/snips/

Extra reading

- http://www.bbc.co.uk/news/health-16107411
- http://www.youtube.com/watch?v=11maHFwC35s
- http://learn.genetics.utah.edu/content/tech/genetherapy/
- **http://www.youtube.com/watch?v=QyoZuxHhvvE**

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