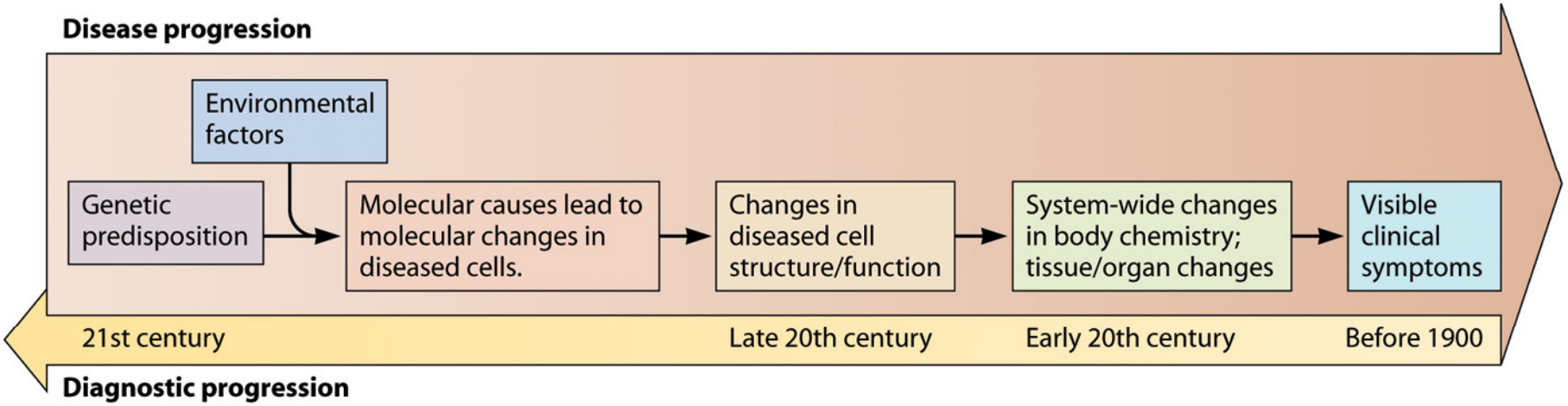
Chapter 19

Health Care Applications

Better Medical Technology

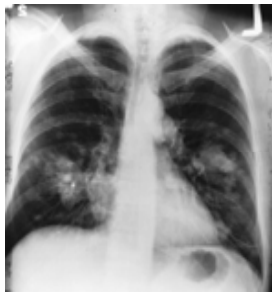
- More significant information for improving health
- Early and cheap diagnosis
- Identification of the cause, not a symptom
- Cure rather than management, disease prevention rather than treatment
- Fewer adverse side effects
- More efficacious and more affordable



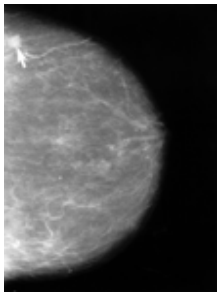
Molecular Diagnostics

- Diagnosis
  - Based on symptoms
    - Different disease with same symptoms
    - Maybe too late to cure
  - Visualization
    - X-ray
  - Chemical imbalance and blood disorders
  - Molecular diagnostics
    - Detection of a specific molecular event related to disease
    - Less invasive: use urine, blood, or saliva

Disease diagnosis



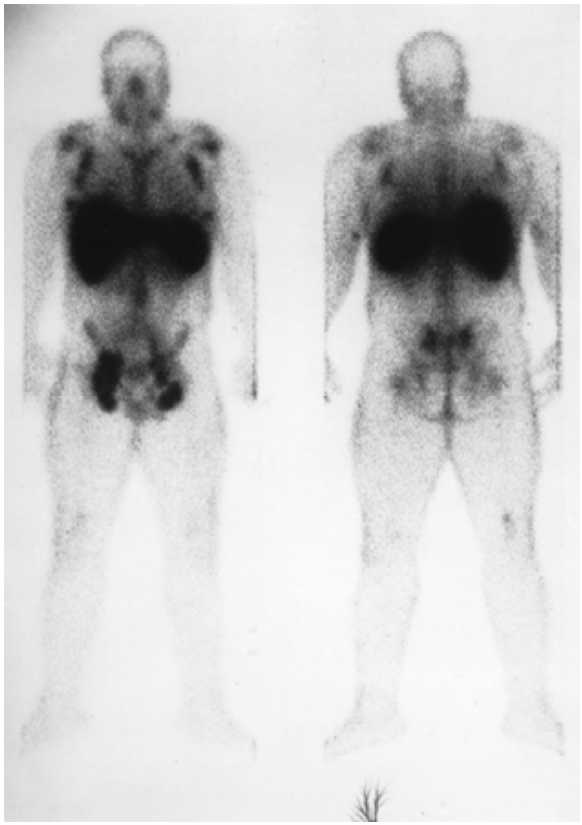
Lung cancer



Breast cancer

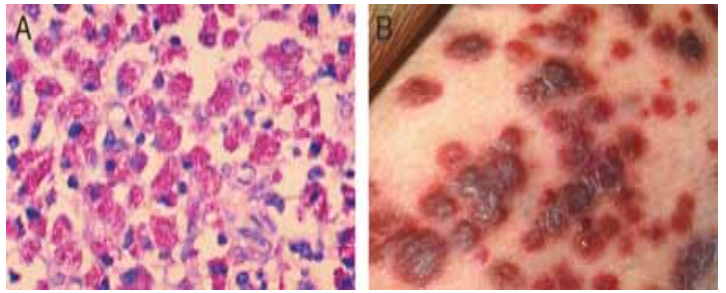
Monoclonal antibodies in cancer detection

- A radioactive isotope attached to monoclonal antibodies



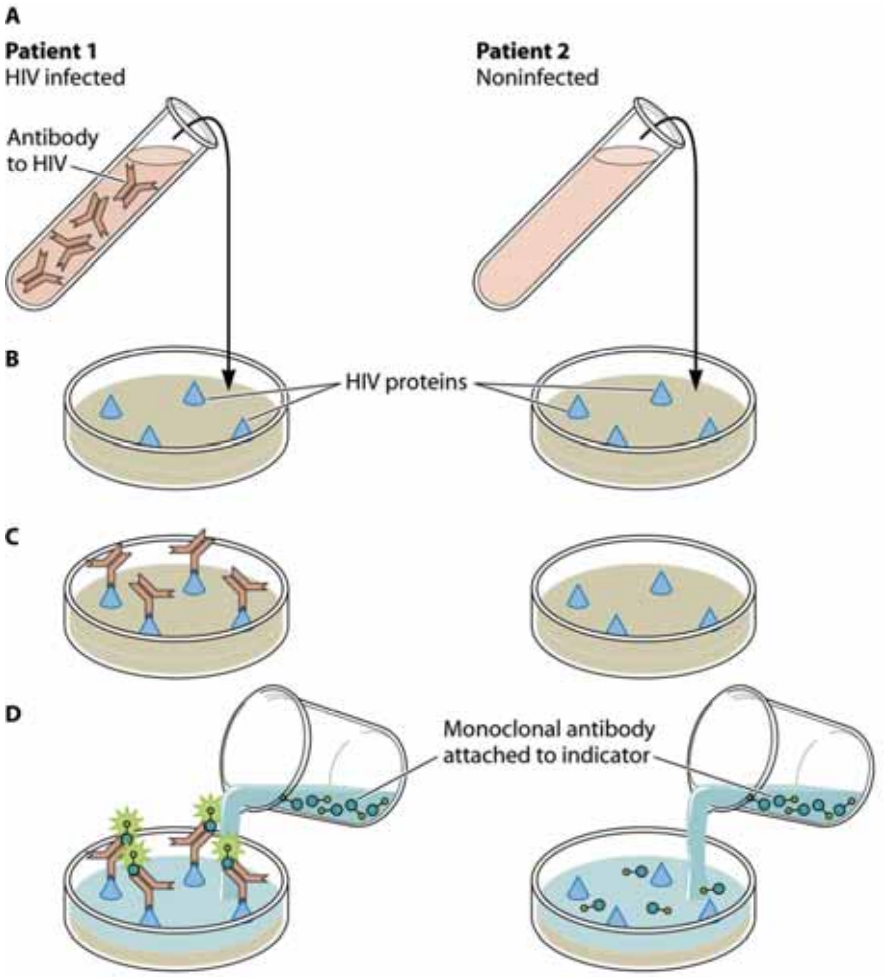
Early Diagnosis of Contagious Disease

- Monoclonal antibody-based diagnosis
  - Detection of pathogenic bacteria without culture
  - Diagnosis of HIV
    - AIDS-defining illnesses
      - – Rare infectious diseases and uncommon cancers
      - – Do not appear until 9 to 10 years after infection



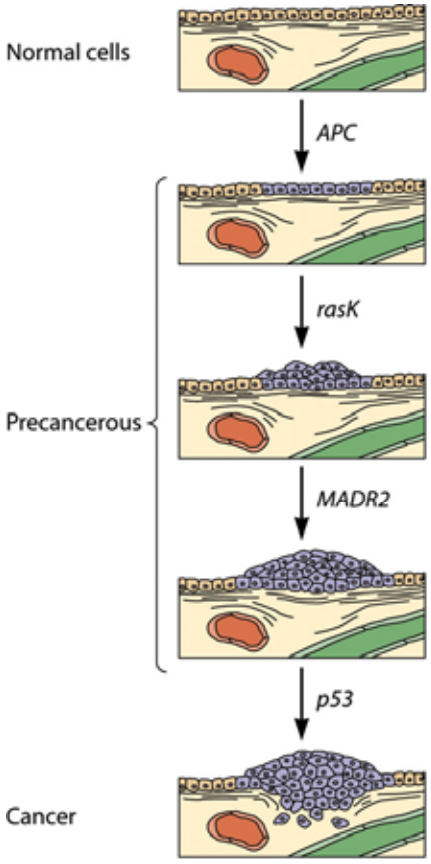
    - Detection of HIV using antibody
      - – HIV infection was identified as a cause of AIDS (1983)
      - – Detection of HIV antibody generated in the patient 6 to 12 months after infection
      - – Detection of HIV DNA by PCR

Detection of HIV



Other Diseases and Disorders

- Biomarkers
  - Molecular changes specific to the stages of disease progress
  - Provide targets for disease treatment
- For example, a number of mutations to become cancerous
- Identifying biomarkers and using them
  - Disease treatment
    → Disease prevention



Genetic Information for Familial Diseases

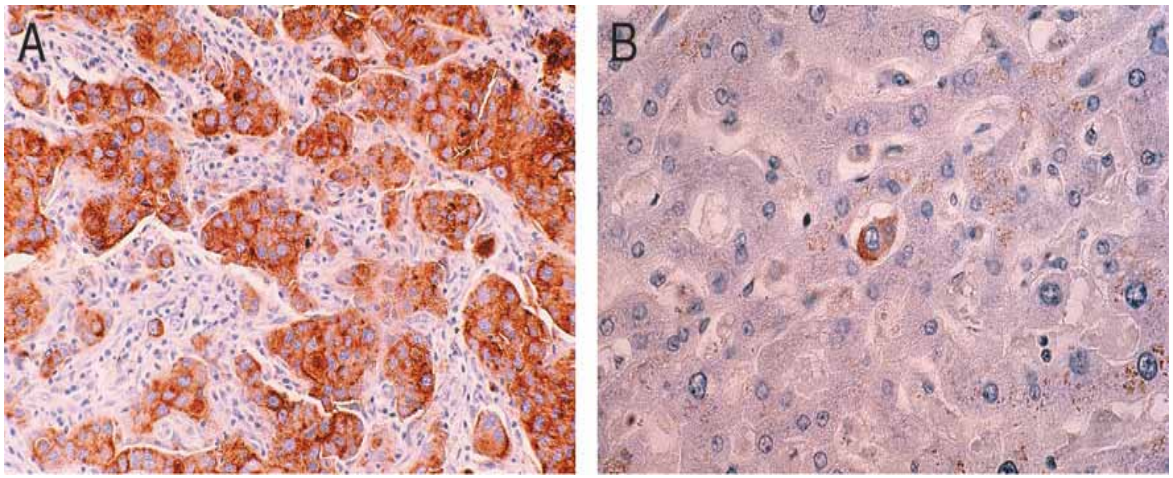
- Simple and complex genetic diseases
  - Simple genetic diseases
    - Caused by a single gene mutation
  - Multigenic disorder
    - Many genes contribute to the disorder
  - Multifactorial disorder
    - Genes and environmental factors interact and lead to the disorder
- Majority of mortal diseases are both multigenic and multifactorial.

Biotechnology Therapeutics

- Features of biotechnology-based therapeutics
  - Specificity
    - Specific inhibition of targets rather than general inhibition
      - Cancer-specific targeting
  - Biological therapeutics
    - Use natural products synthesized by plants, microbes, insects, and other animals
    - Search diverse ecosystems like sea
  - New production methods
    - Large-scale, economically feasible production
    - Recombinant DNA technology, cell culture, biomanufacturing technologies

Targeted Therapy with Monoclonal Antibodies

- Monoclonal antibodies can deliver chemo-therapeutic toxins specifically to cancer cells.



A. Cytoplasm of tumor cells in breast tissue is stained brown with a monoclonal antibody
B. The same monoclonal antibody is able to locate a single breast cancer cell that has metastasized to the patient's liver.

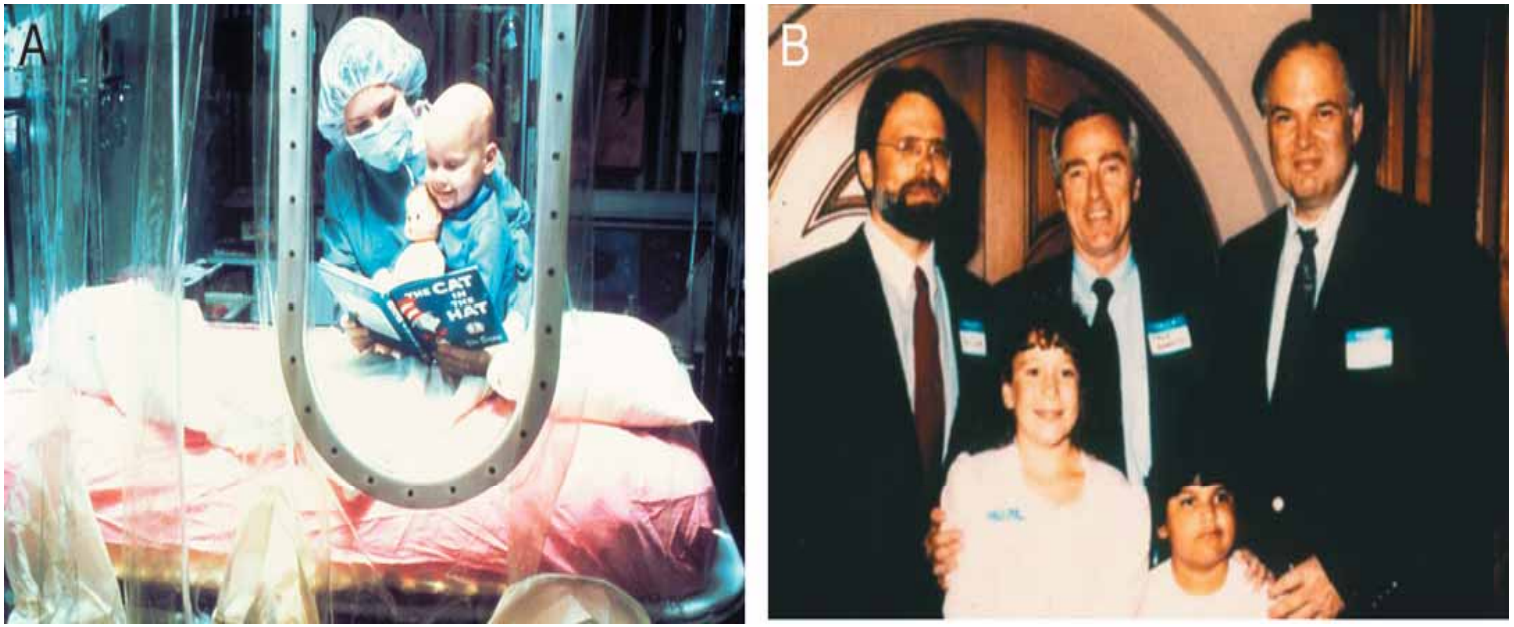
Biotechnology Therapeutics

- Use immune systems for treatments
  - Cytokines boosting immune response
    - Interleukin-2: cancer, AIDS
    - Interleukin-12: some infectious disease
  - Cancer vaccines
- Replacement of missing proteins with recombinant proteins
  - Insulin for diabetes
  - Glucocerebrosidase for Gaucher's disease
  - Hemophiliacs: missing components in the formation of a blood clot
    - Treatment of recombinant factor VIII (for hemophilia A) or factor IX (for hemophilia B)

Gene Therapy

- Administration of correct gene
- Applicable to some hereditary monogenic diseases
  - Hemophilia
  - Severe combined immunodeficiency disease (SCID); bubble boy disease
- Trial to transient gene therapy for non-hereditary disorders like cancer, infectious disease
- Still many technical barriers to overcome
  - e.g. gene delivery

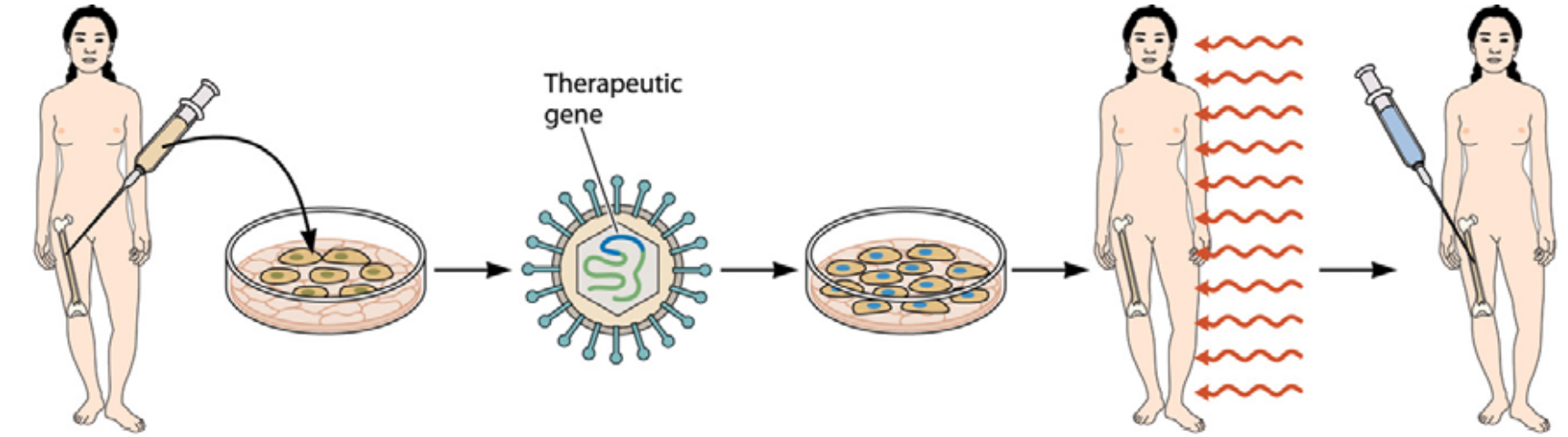
Gene Therapy



A. Child with SCID in germ-free environments

B. In 1991, two children with SCID received gene therapy to correct the genetic defect.

Gene Therapy



Cell or Organ Transplantation

- Not enough supply of organ donations
  - In U.S. 60,000 people are on organ recipient list
  - 12 death/day while waiting
- Xenotransplantation
  - Organs from other animals like pig
  - Problems
    - Self protection mechanism of body
    - Risk of infectious viruses or retroviruses
  - Solutions
    - Genetic modification of the donor animals
      - Deletion of pig genes triggering the rejection
      - Adds genes of human membrane proteins
- Cell transplant therapy

Cell Transplant Therapy

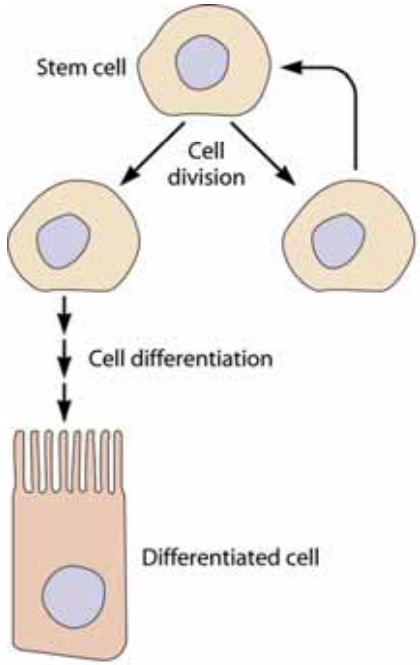
- Bone marrow transfer
  - In some cases, the patient's own bone marrow cells are removed, grown in culture, and reimplanted after chemotherapy
  - In the case of leukemia or other blood cell cancer, the transplanted bone marrow must come from a healthy donor who is genetically similar to the patient.
- Implantation of insulin-producing cells for diabetes
- Prevention of immune response
  - Monoclonal antibodies to various receptors on T cells, that recognize and reject foreign cells.
  - Cell encapsulation: prevent recognition by the immune system

Regenerative Medicine

- Use the body's natural healing processes to cure diseases
- Endogenous proteins promoting cell division and differentiation
  - Epidermal growth factor: wound healing
  - Fibroblast growth factor: healing ulcers, broken bones, growing new blood vessels
  - Transforming growth factor β : promote cell differentiation
  - Nerve growth factor: repair damage resulting from head and spinal cord injuries, degenerative neural diseases

Stem Cells for Regenerative Medicine

- Adult stem cells
  - Partially differentiated progenitor cells
  - Types of AS cells
    - Bone marrow AS cells → cells in blood and bone
    - Liver AS cells → liver cells: bile-secreting cells, glycogen storage cells
- ES cells
  - Pluripotent
  - Isolation of human ES cells (1998)
    - From blastocysts or progenitor germ cells from aborted fetuses

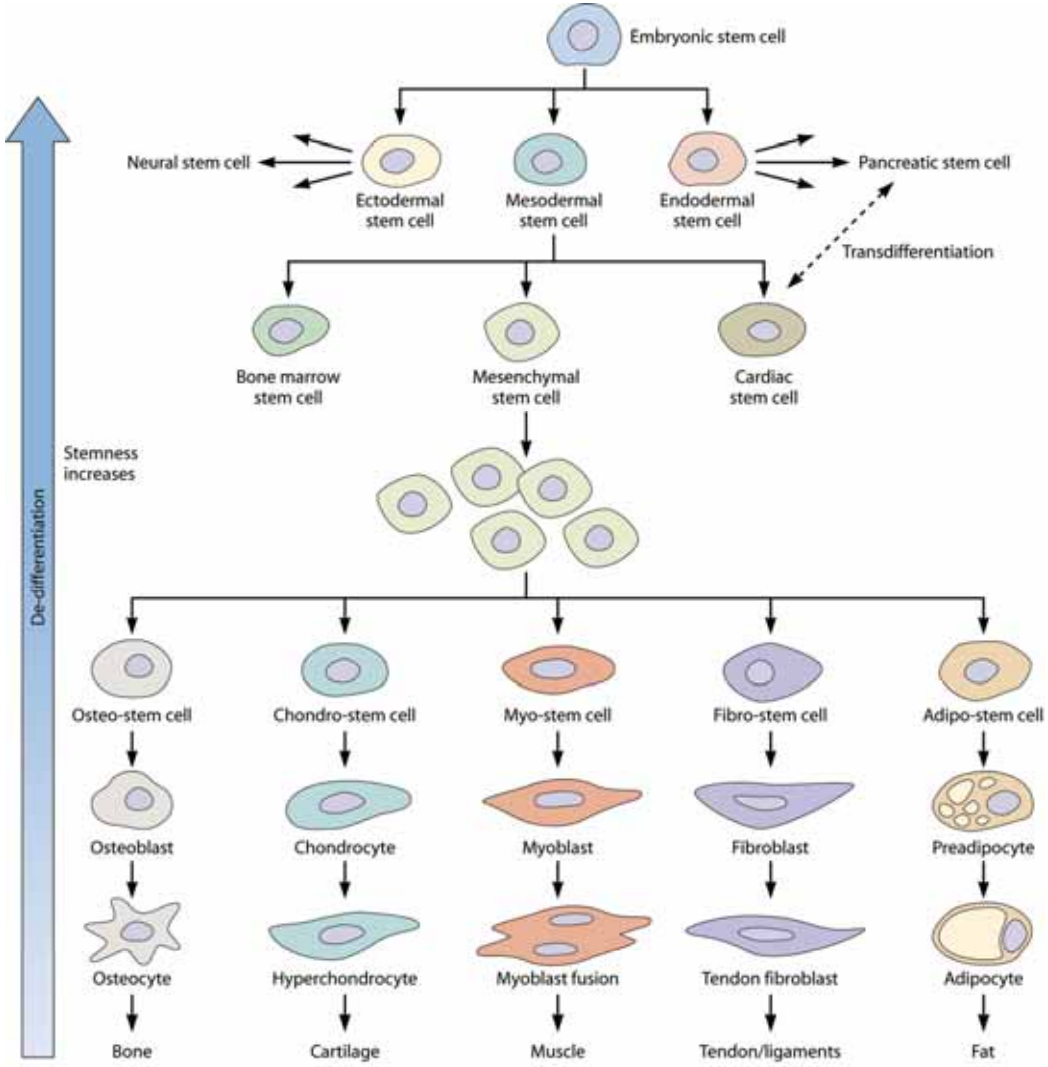


One stem cell and one differentiated cell after cell division to maintain a constant supply

Therapeutic Potential of Stem Cells

- Replacement of damaged cells with AS or ES cells
- Research on differentiation
  - Identification of proper growth factors, nutrients, and environmental factors for specific differentiation
  - Transdifferentiation
    - From one AS cell to another type of AS cell
- Research on dedifferentiation
  - Factors that reverse differentiation
  - Dolly: cloning from the fully differentiated somatic cell
  - Dedifferentiation can provide ES cells without using embryo, BUT… it is hard to study dedifferentiation without using ES cells

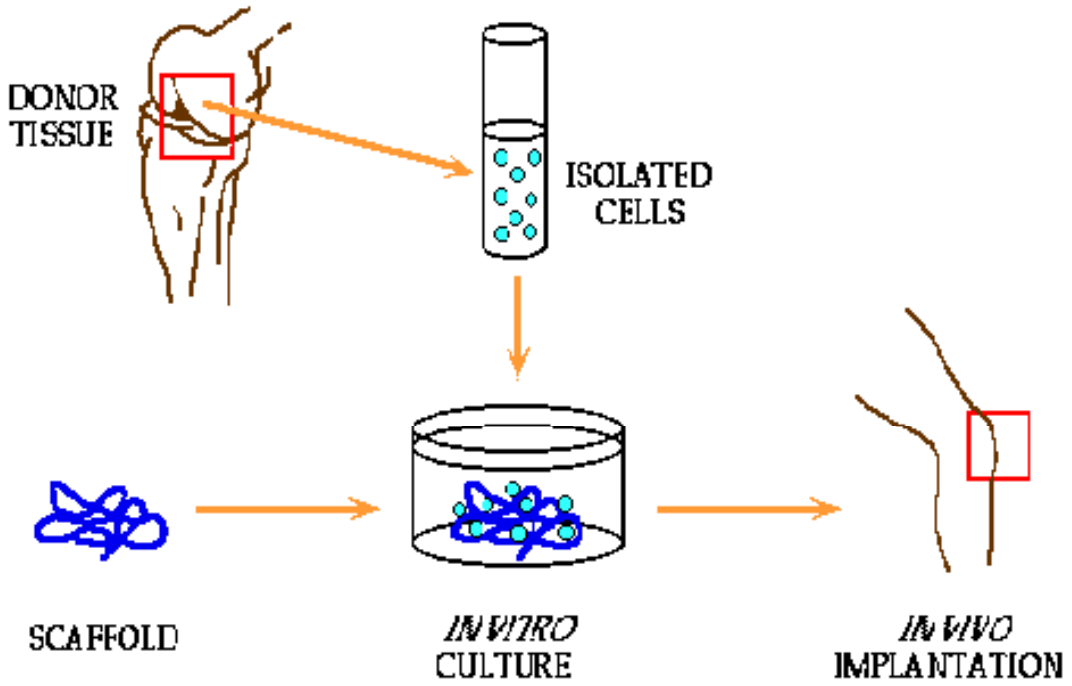
AS Cell De differentiation



Tissue Engineering

- Generation of semisynthetic tissues and organs
  - Biocompatible scaffolding materials
    - Synthetic polymer or natural material (e.g. collagen)
  - Living cells grown in culture
    - Fully differentiated cells
- From simple tissues and organs (skin, cartilage, urinary bladders) to whole organs using stem cells

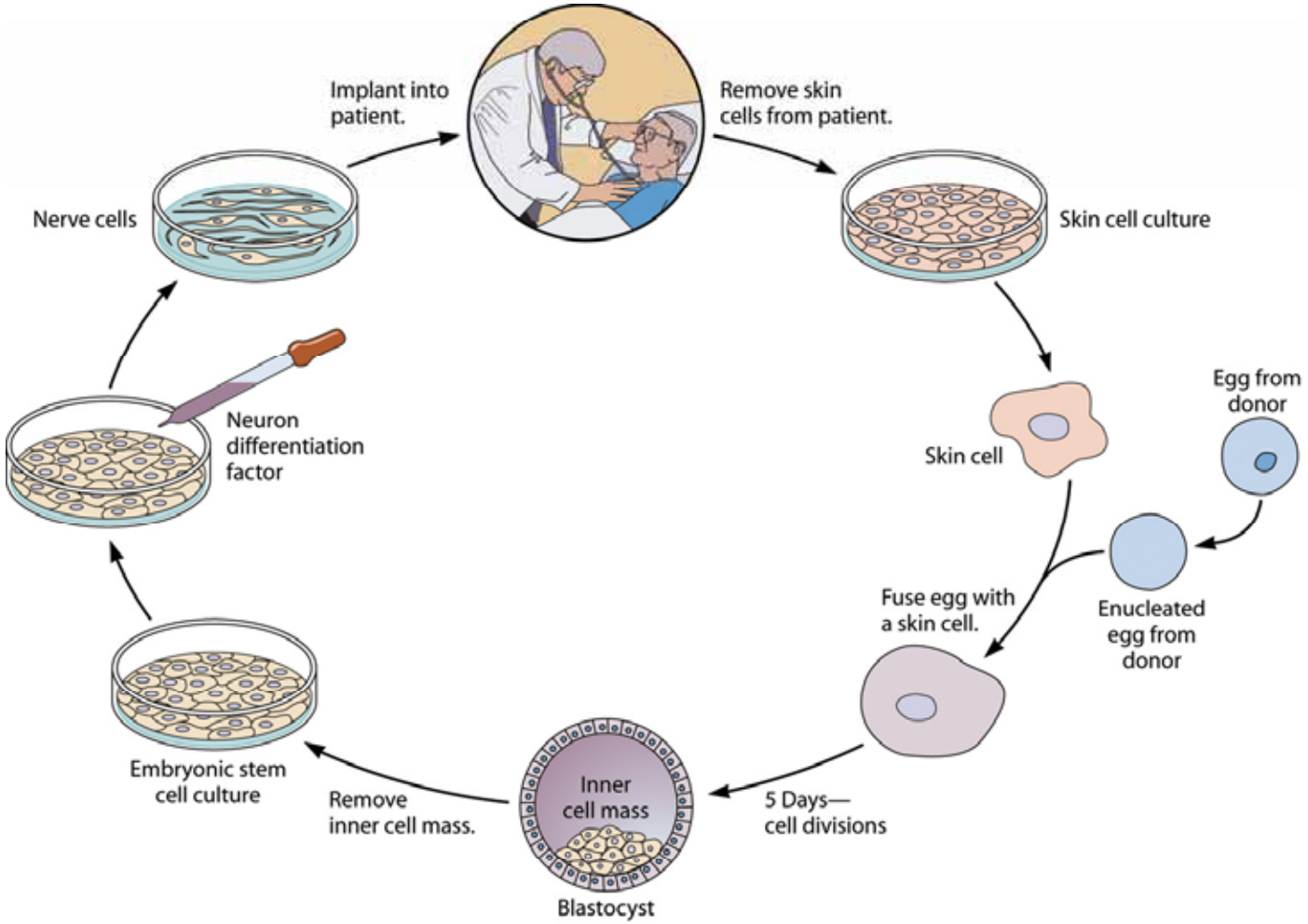
Tissue Engineering



Solving the Problem of Tissue Rejection

- Use AS cells from the patient
- Freeze umbilical cord blood with plasticity for the future use
- Somatic cell nuclear transfer
  - Therapeutic cloning
  - Generate differentiated cells from ES cells

Immune-Compatible Stem Cells

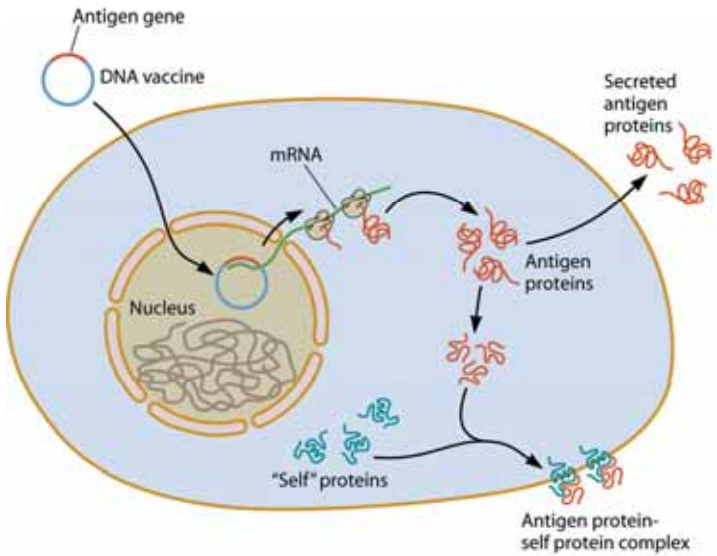


Vaccines

- Vaccines
  - harmless agents that elicit an immune response, thereby providing protective immunity against a potential pathogen
- Types of vaccines
  - Killed vaccines, attenuated vaccine
    - Potential problems
      - Side effects: allergic reactions, cause disease
      - Difficulty in mass production outside of the human body
      - Potential risk during human testing
  - Subunit vaccines
    - Surface proteins of pathogen inducing immune response
    - Production using recombinant DNA technology
    - Vaccines for infectious virus (Hepatitis B), diabetes, cancer, chronic inflammatory disease etc.

DNA or Edible Vaccines

- DNA vaccines
  - Delivery of vector containing antigen gene



- Edible vaccines
  - Genetically modified animals or plants producing vaccines
    - Vaccines in milk
    - Vaccines in bananas or potatoes