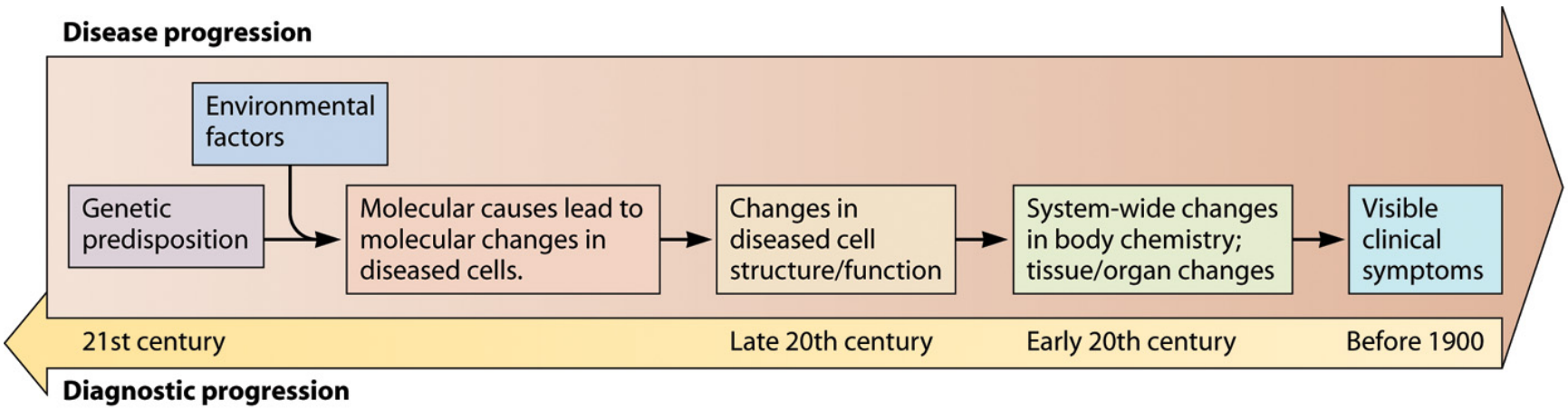
Chapter 19

Health Care Applications

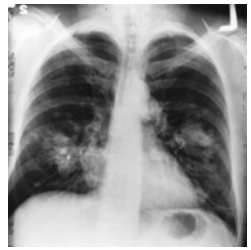
Better Medical Technology

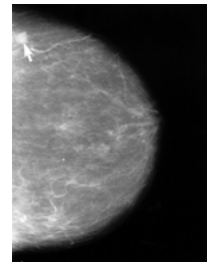
- More significant information for improving health
- Early and cheap diagnosis
- Identification of the cause, not a symptom
- Cure rather than management, disease prevention rather than treatment
- Fewer adverse side effects
- More efficacious and more affordable

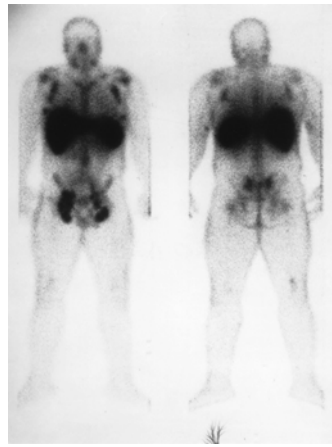


Molecular Diagnostics

- 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

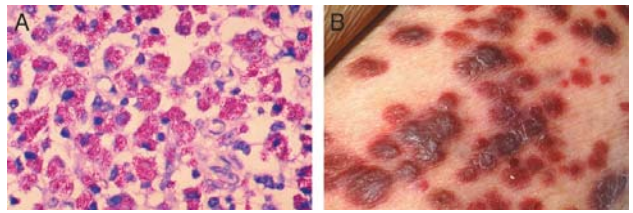




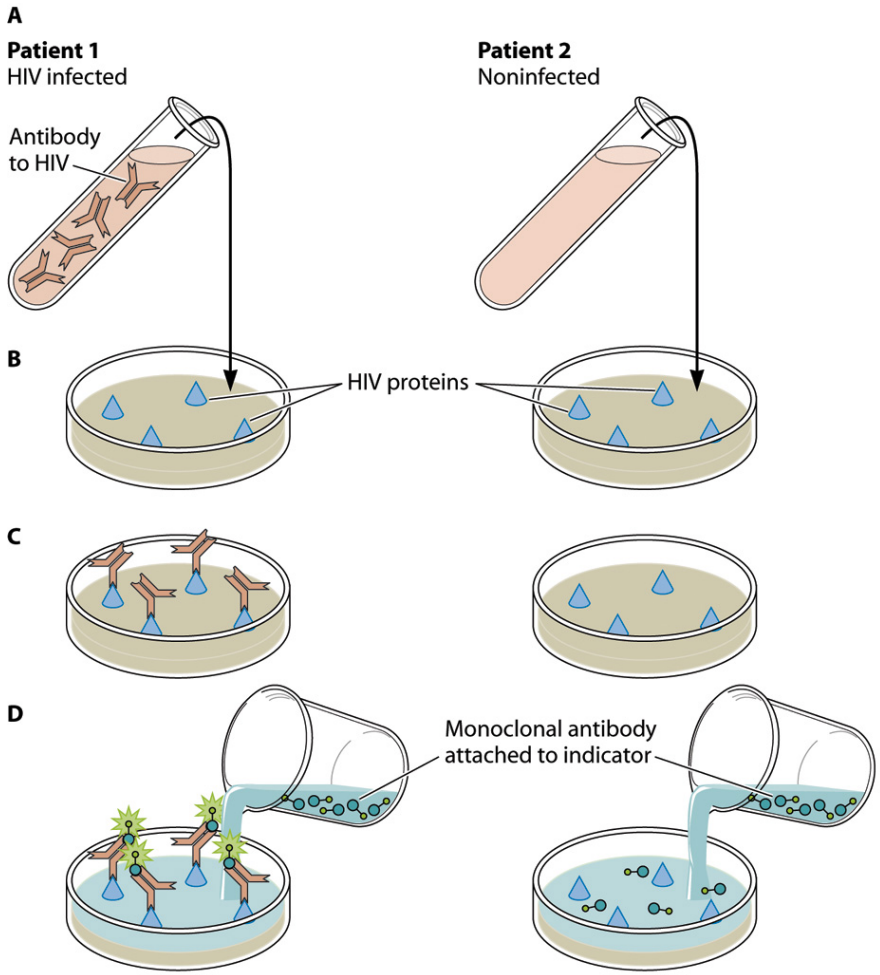


Early Diagnosis of Contagious Disease

- Monoclonal antibody-based diagnosis
  - Detection of pathogenic bacteria without culture: strep throat, chlamydia etc.
  - 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



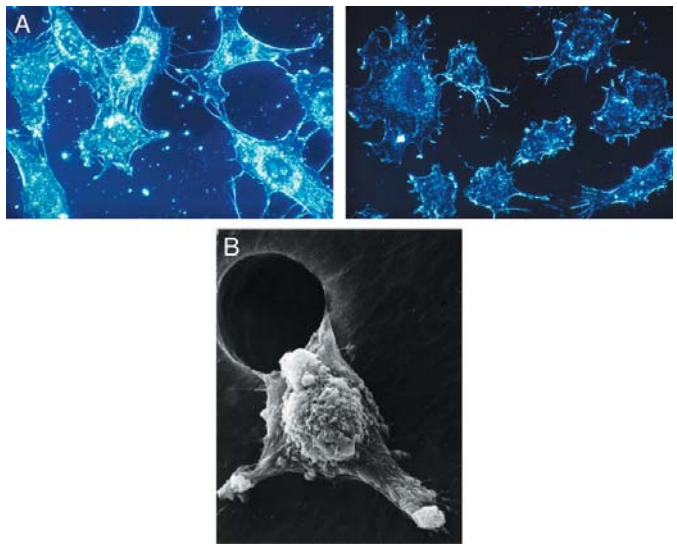
Detection of HIV Antibody

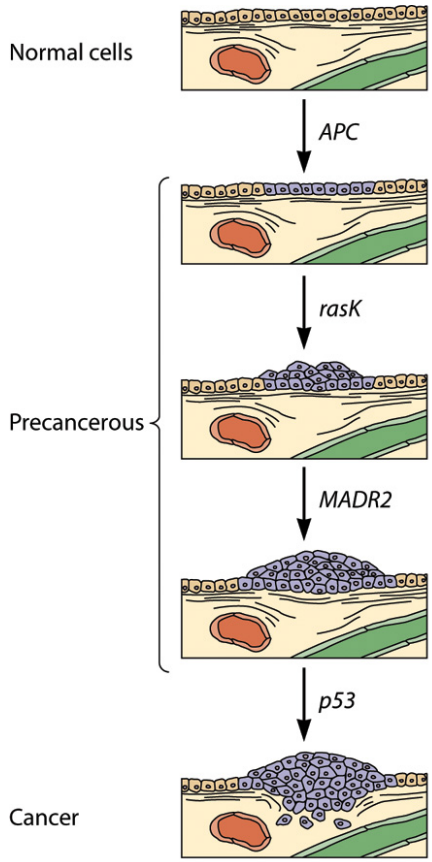


Fluorescence-labeled monoclonal antibody against HIV antibody

Other Diseases and Disorders

- Biomarkers
  - Molecular changes specific to the stages of disease progress
  - Provide targets for disease treatment





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
- Early detection of genetic disorder to prevent rather than treat disease
  - PKU, cystic fibrosis, early-onset Alzheimer's disease

Simple Genetic Diseases

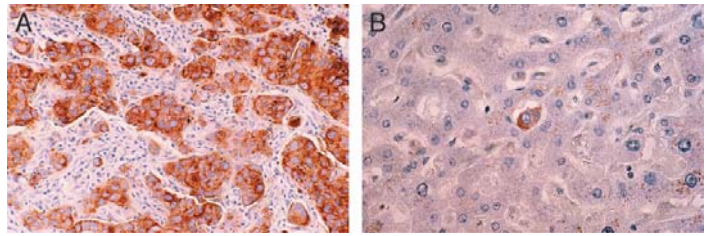
Table 19.2 Simple genetic diseases[a]

Disease (occurrence)	Protein function	Clinical symptoms
Autosomal dominant disorders		
Huntington's disease (1/10,000)	Cytoskeleton; vesicle transport	Degenerative nervous system function; dementia
Myotonic dystrophy (1/8,000)	Protein kinase enzyme	Muscle loss; defective heart contractions
Hypercholesterolemia (1/500)	Low-density lipoprotein receptor	Arterial blockage; severe coronary heart disease
Autosomal recessive disorders		
Cystic fibrosis (1/2,500)	Chloride channel protein	Respiratory disease; digestive disorders
Gaucher's disease type I (1/50,000)	Glucocerebrosidase enzyme	Enlarged spleen and liver; fragile bones
Beta-thalassemia (1/20,000)	Hemoglobin oxygen transport	Anemia; enlarged spleen; bone deformities
Alpha-antitrypsin deficiency (1/3,500)	Protective enzyme in lungs	Emphysema
PKU (1/10,000)	Phenylalanine degradation enzyme	Mental retardation
Sex-linked disorders		
Hemophilia A (1/5,000 males)	Blood clotting factor VIII	Excessive bleeding from small injuries
Duchenne muscular dystrophy (1/3,300 males)	Muscle contraction protein	Muscle degeneration
Color blindness (8/100 males)	Visual pigment molecule	Inability to detect red and green

[a]These are examples of disorders caused by mutations in a single gene. For decades, physicians have known that these diseases are inherited because they exhibit clear, predictable inheritance patterns and have obvious, definitive clinical symptoms. Using biotechnology-based research tools, scientists have now mapped, isolated, and sequenced mutant alleles responsible for these diseases and identified the defective proteins they encode. The proteins include enzymes, receptors, transporters, and structural proteins.

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
    - Use biological effects for treatment (e.g. growth inhibition or activation)
  - New production methods
    - Large-scale, economically feasible production
    - Recombinant DNA technology, cell culture, biomanufacturing technologies

Biotechnology Therapeutics

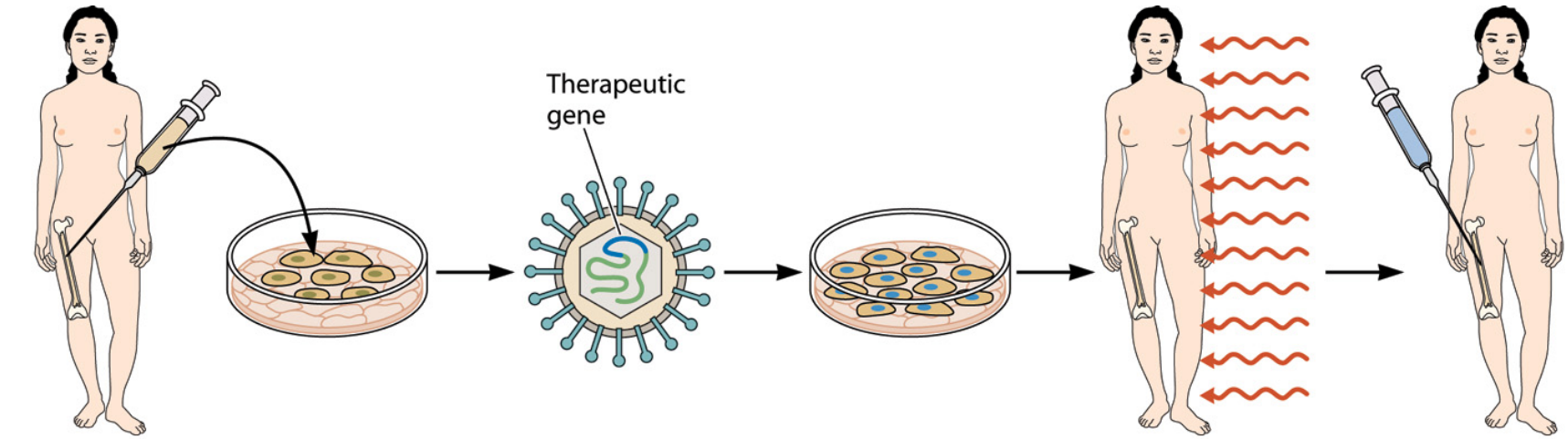
- Use immune systems for treatments
  - Cytokines boosting immune response
    - Interleukin-2: cancer, AIDS
    - Interleukin-12: some infectious disease
  - Cancer vaccines
- Replacement of missing proteins with recombinant proteins
  - Insulin for diabetes
  - Glucocerebrosidase for Gaucher's disease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

Treatment of Gaucher's disease by enzyme replacement therapy

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



Remove bone marrow stem cells from patient.

Grow stem cells in culture.

Infect stem cells with altered RNA virus containing "healthy" human gene.

Propagate genetically altered stem cells.

Whole-body radiation to destroy patient's "diseased" bone marrow cells.

Introduce altered cells to patient. Repaired cells populate bone marrow cavities and give rise to normal RBCs.

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
      - Addition of genes of human membrane proteins
- Cell transplant therapy

Cell Transplant Therapy

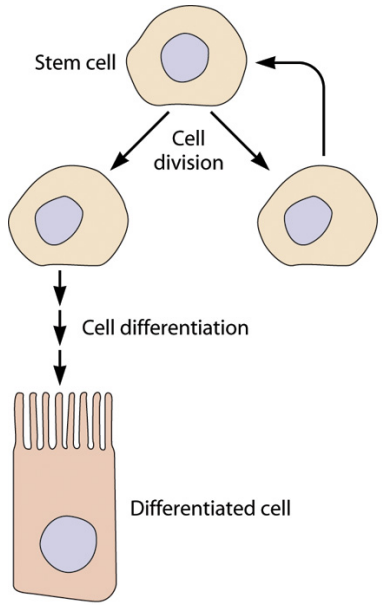
- Bone marrow transfer
  - Transfer own bone marrow for cancer patients under chemotherapy
  - Bone marrow transfer from a donor for leukemia treatment
- Implantation of insulin-producing cells for diabetes
- Prevention of immune response
  - Monoclonal antibodies to various T cell receptor
  - Cell 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

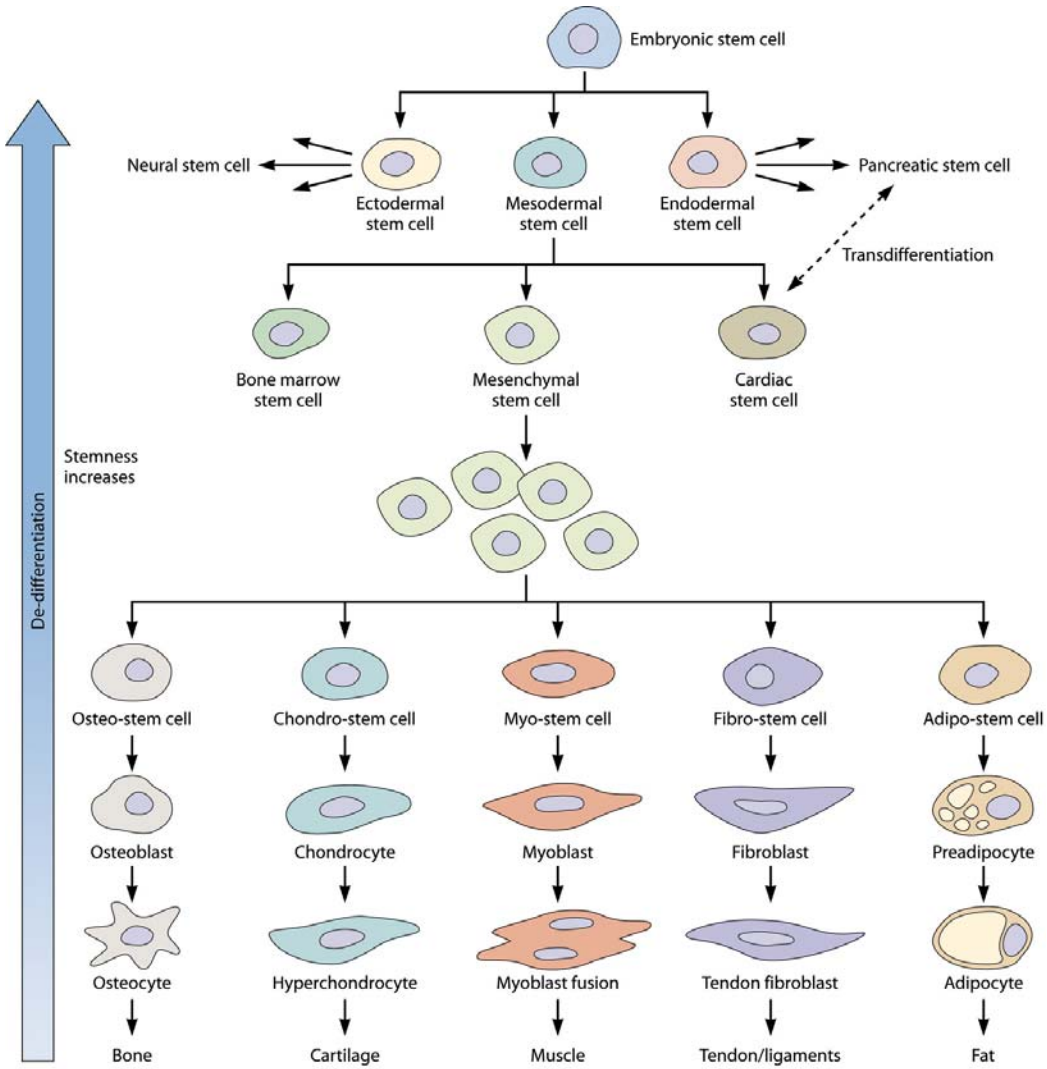
- Adult stem cells
  - Partially differentiated progenitor cells
  - One stem cell and one differentiated cell after cell division
  - Types of AS cells
    - Bone marrow AS cells → cells in blood and bone
    - Liver AS cells → liver cells: bile-secreting cells, glycogen storage cells
- ES cells
  -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



Therapeutic Potential of Stem Cells

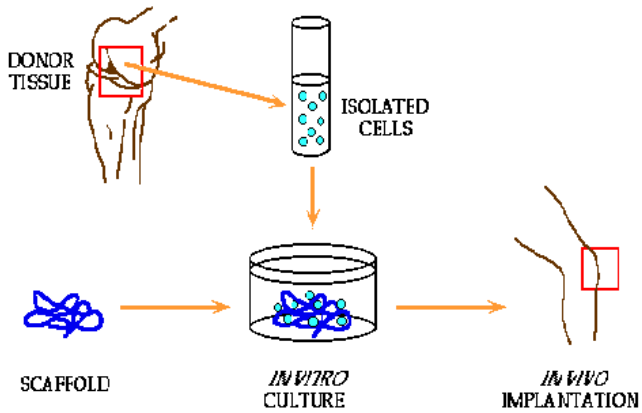
- Replacement of damaged cells with AS or ES cells
- Research on differentiation
  - Identification of proper growth factors, nutrients, and environmental factors for specific differentiation
  - Transdifferentiation
    - From one AS cell to another type of AS cell
- Research on dedifferentiation
  - 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

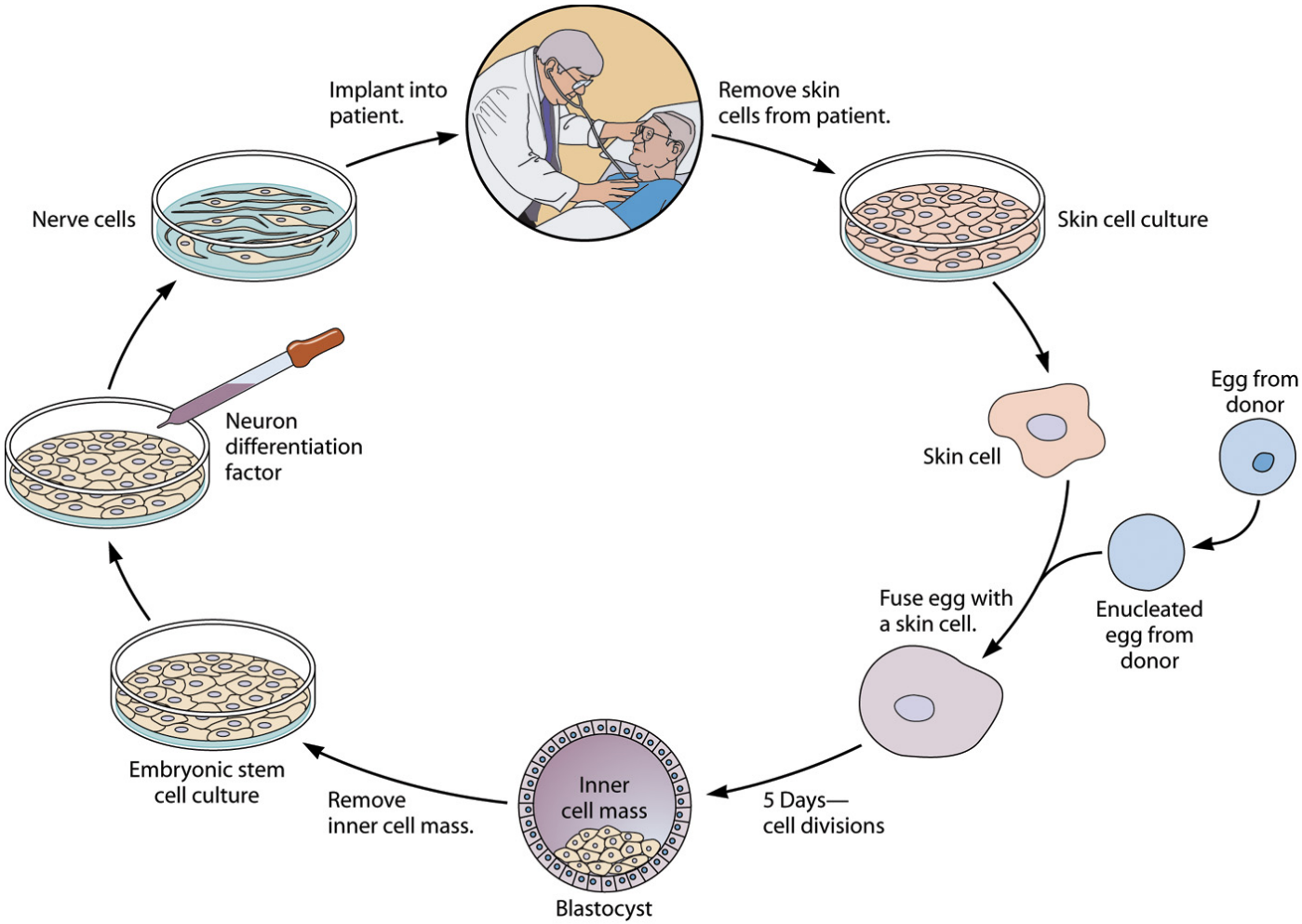


- From simple tissues and organs (skin, cartilage, urinary bladders) to whole organs using stem cells
  - Hybrid kidney
    - Hollow tubes seeded with kidney stem cells
    - Release aldosterone, filtration, respond to hormonal signals from other organs and tissue

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

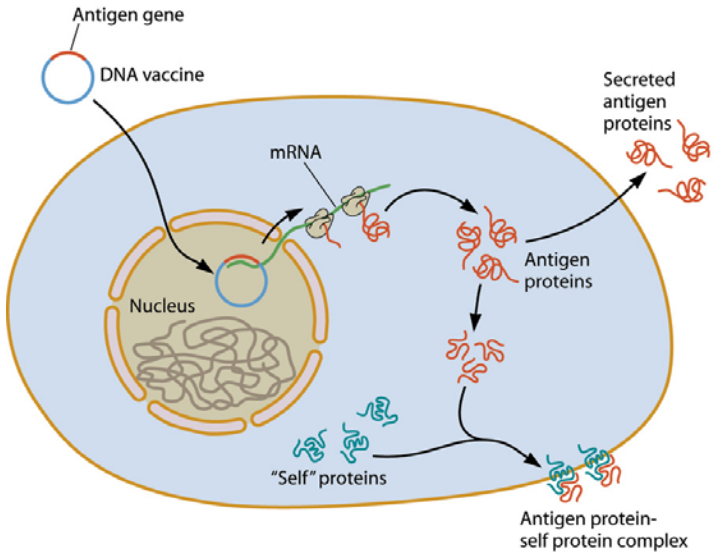


Vaccines

- 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