Chapter 19

Health Care Applications

목 차

1 생명공학적 진단

2 생명공학적 치료

3 재생 의학

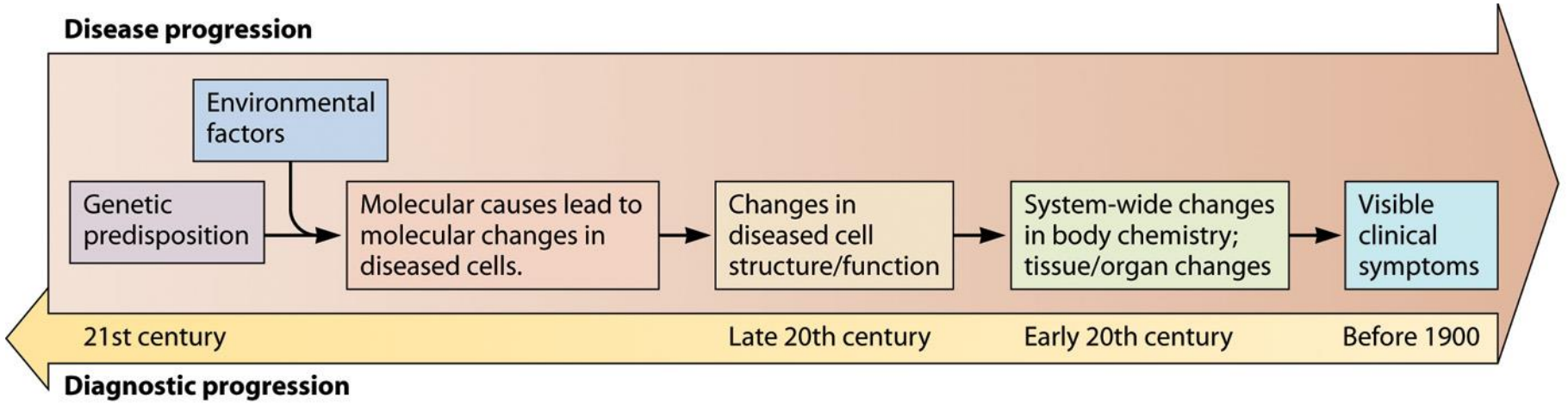
4 산업적 응용

5 대규모 생물공정

1. 생명공학적 진단
(Biotechnology-based Diagnostics)

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

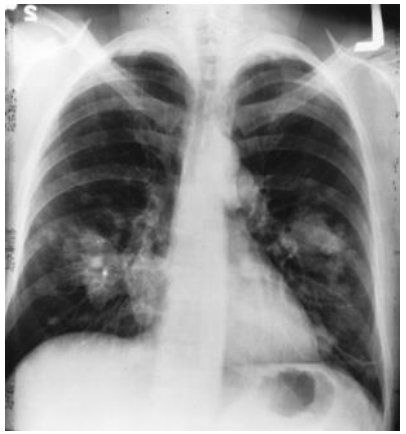


Disease Diagnostics

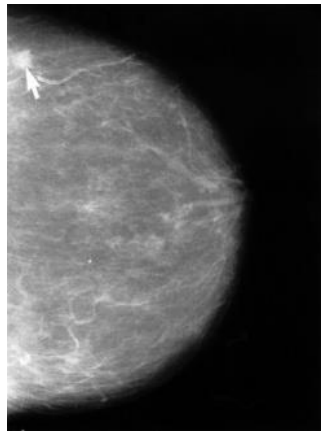
- Based on symptoms
  - Different disease with same symptoms
  - Maybe too late to cure

Disease Diagnostics

- 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



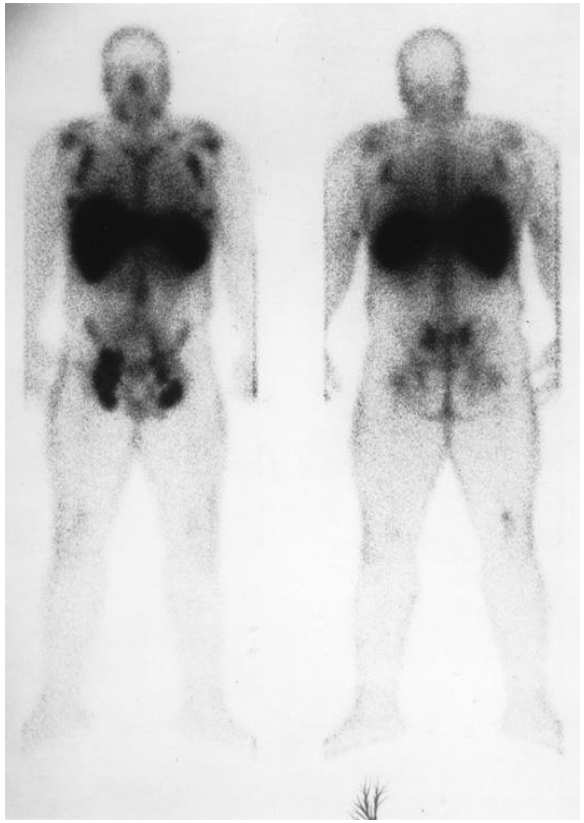
Lung cancer



Breast cancer

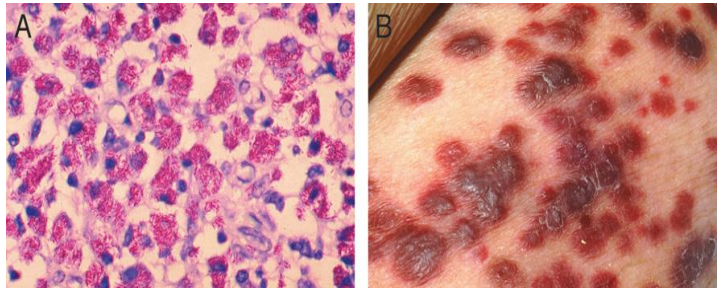
Monoclonal Antibodies in Cancer Detection

- A radioactive isotope attached to monoclonal antibodies



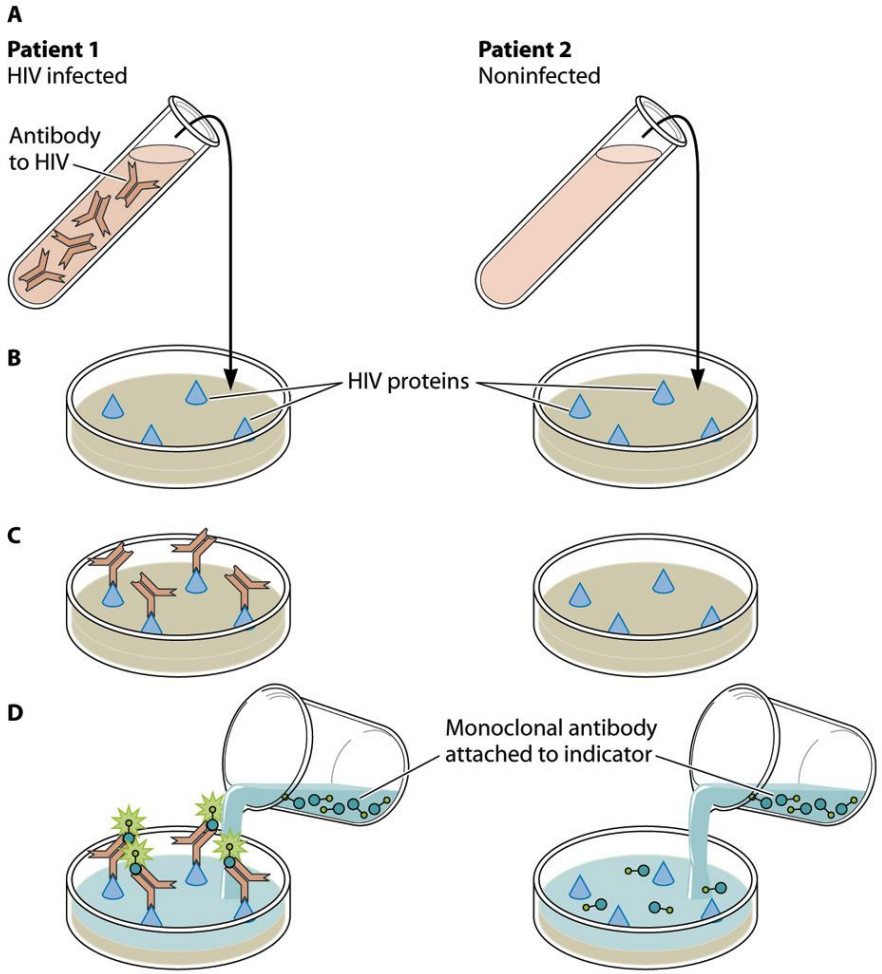
Early Diagnosis of Contagious Disease

- 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



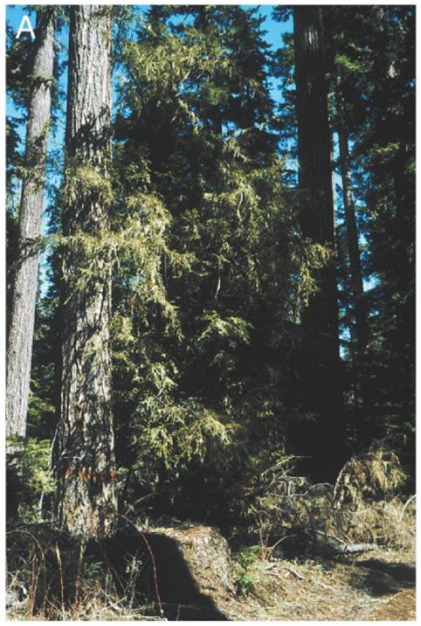
2. 생명공학적 치료
(Biotechnology-based Therapeutics)

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

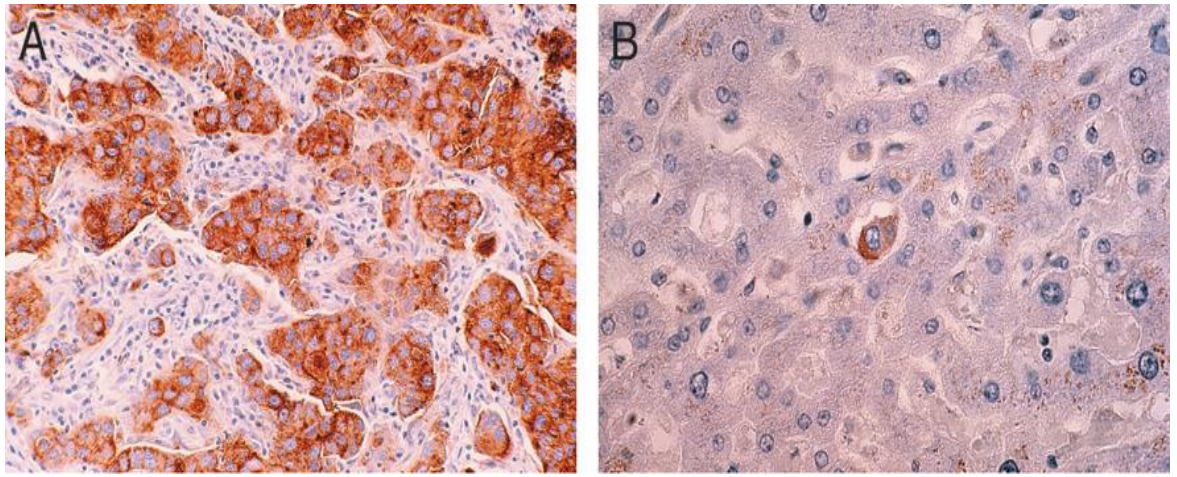
Taxol

- Anti-cancer drug
- Extracted from the bark of the Pacific yew tree
  - The slow-growing yew tree reaches 5 feet in a number of decades.
  - Between 2,000 and 4,000 trees had to be cut down to obtain 1kg of taxol.
- Development of plant cell culture process



Targeted Therapy with Monoclonal Antibodies

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



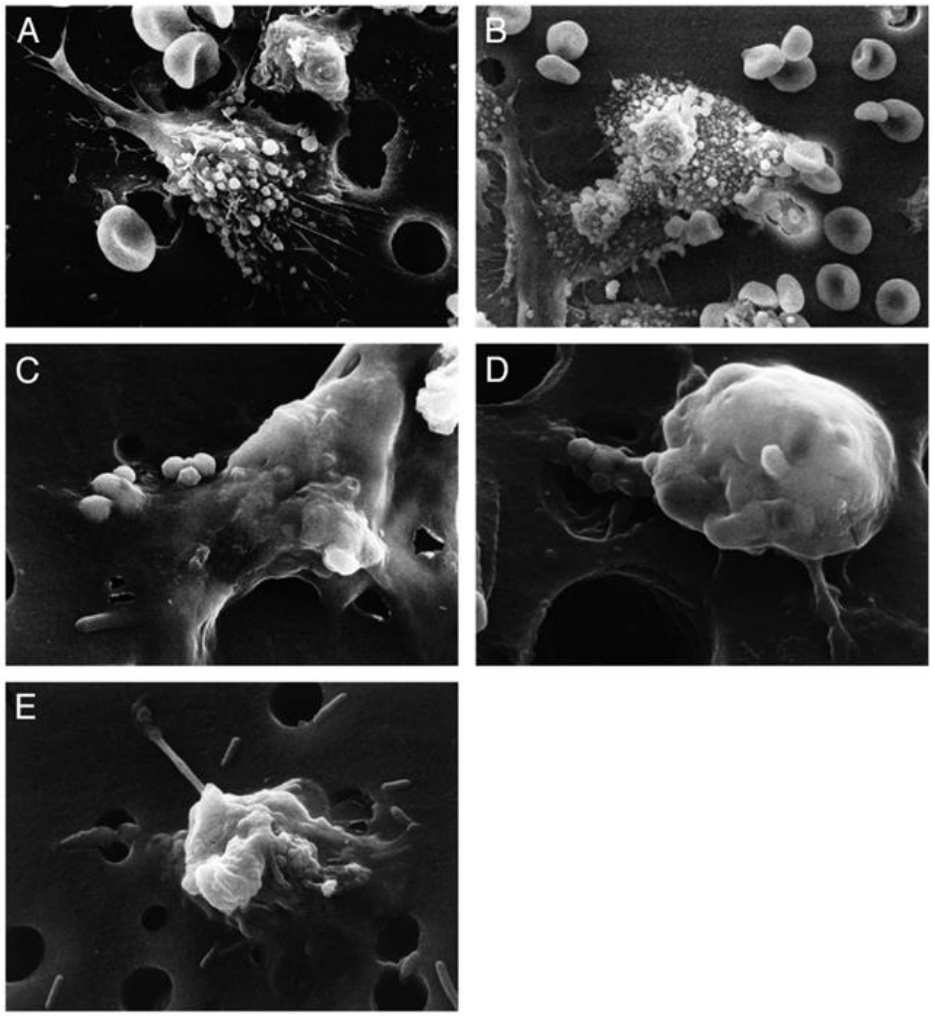
A. Cytoplasm of tumor cells in breast tissue is stained brown with a monoclonal antibody
B. The same monoclonal antibody is able to locate a single breast cancer cell that has metastasized to the patient's liver.

Use Immune Systems for Treatments

- Cytokines boosting immune response
  - Interleukin-2: cancer, AIDS
  - Interleukin-12: some infectious disease
- Cancer vaccines

Use Immune Systems for Treatments

- Cancer vaccines teach the immune system to recognize the tumor as foreign.



Replacement of Missing Proteins with Recombinant Proteins

- Insulin for diabetes
- Human growth hormone
- 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

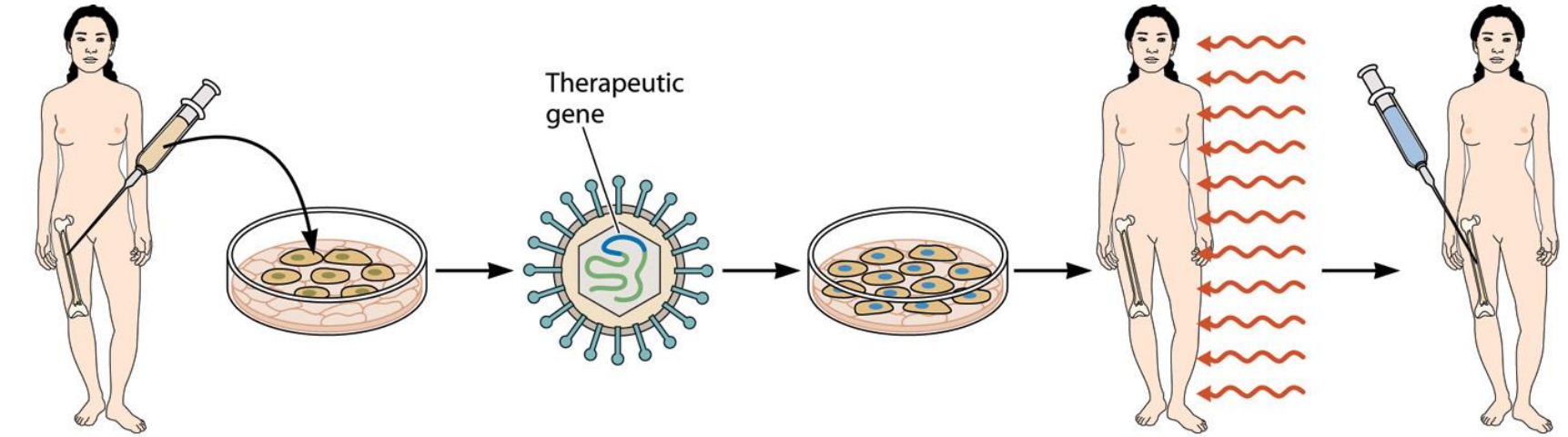
- Administration of correct gene
- Applicable to some hereditary monogenic diseases
  - Hemophilia
  - Severe combined immunodeficiency disease (SCID); bubble boy disease
- Trial to transient gene therapy for non-hereditary disorders like cancer, infectious disease
- Still many technical barriers to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

Gene Therapy

(A) Child with SCID
in germ-free chamber

(B) Two children with SCID
received gene therapy in 1991.

Gene Therapy



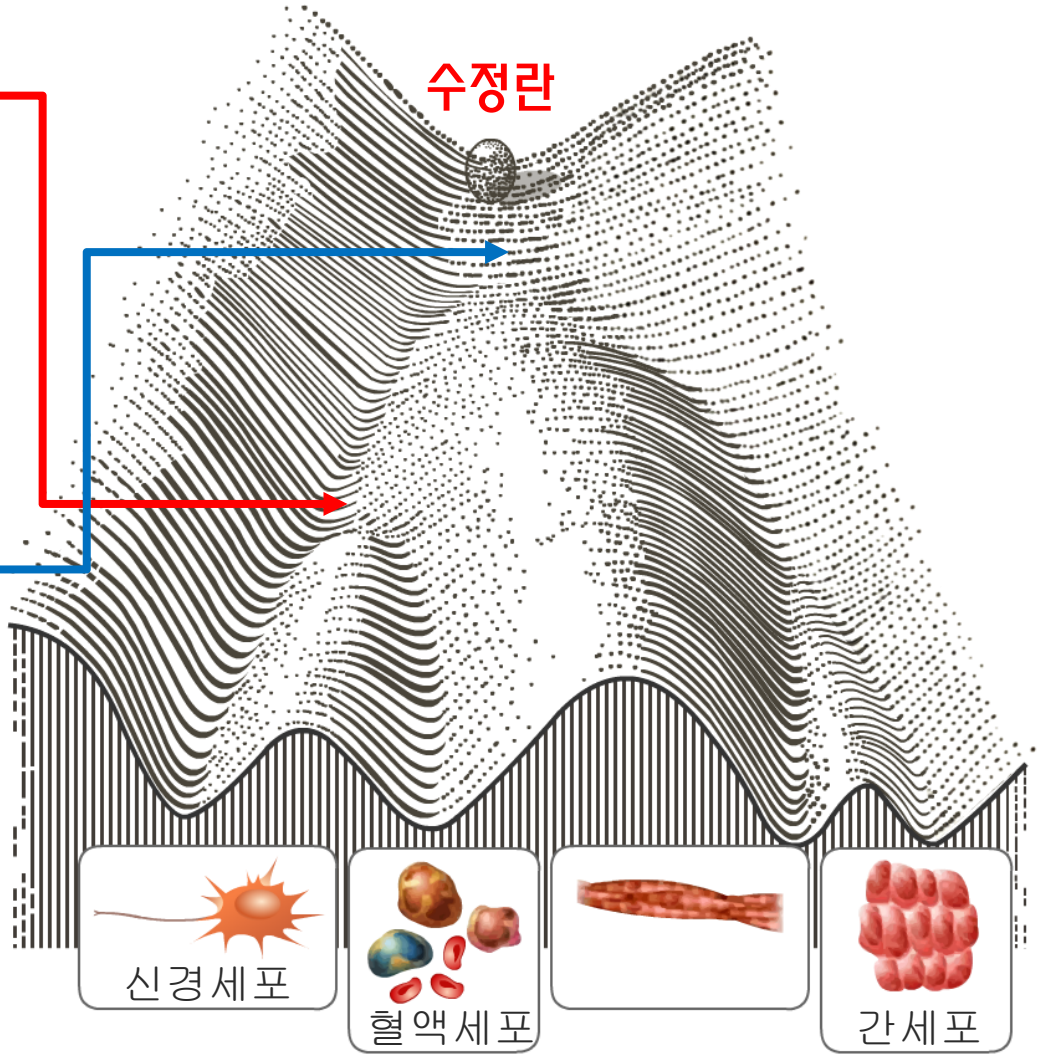
3. 재생 의학 (Regenerative Medicine)

Regenerative Medicine

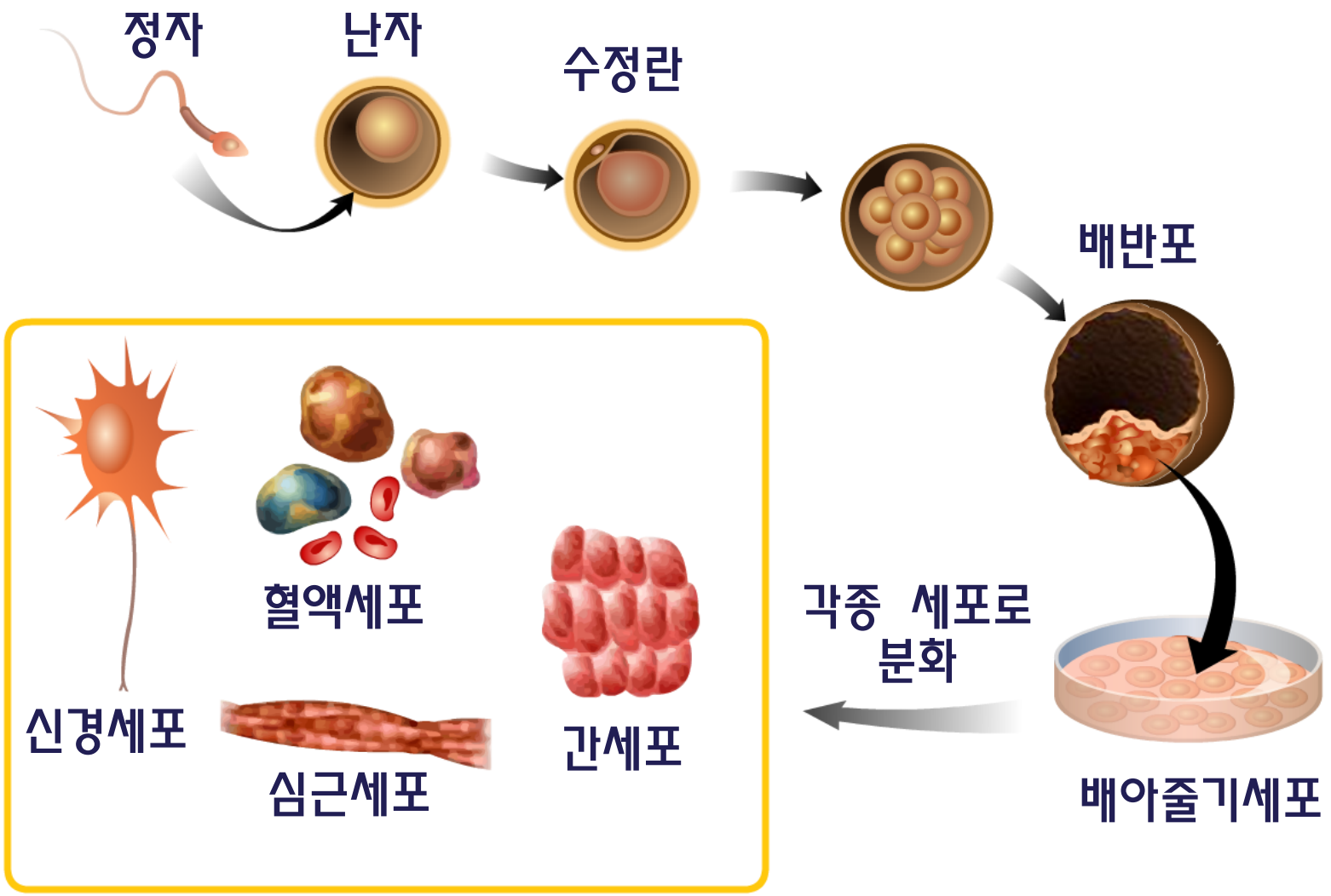
- Use the body's natural healing processes to cure diseases
- Endogenous proteins promoting cell division and differentiation
  - Epidermal growth factor: wound healing
  - Fibroblast growth factor: healing ulcers, broken bones, growing new blood vessels
  - Transforming growth factor β : promote cell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

줄기 세포

- **성체줄기세포**
  - 일부 분화된 전구세포
  - 예)
    - 골수 줄기세포 → 혈액 세포, 뼈 세포
    - 간 줄기세포
      → 간 세포: 담즙 분비 세포, 글리코겐 저장 세포
- **배아줄기세포**
  - 만능성(Pluripotent)
  - 배반포(blastocyst)의
    속세포덩이(inner cell mass)에서 채취

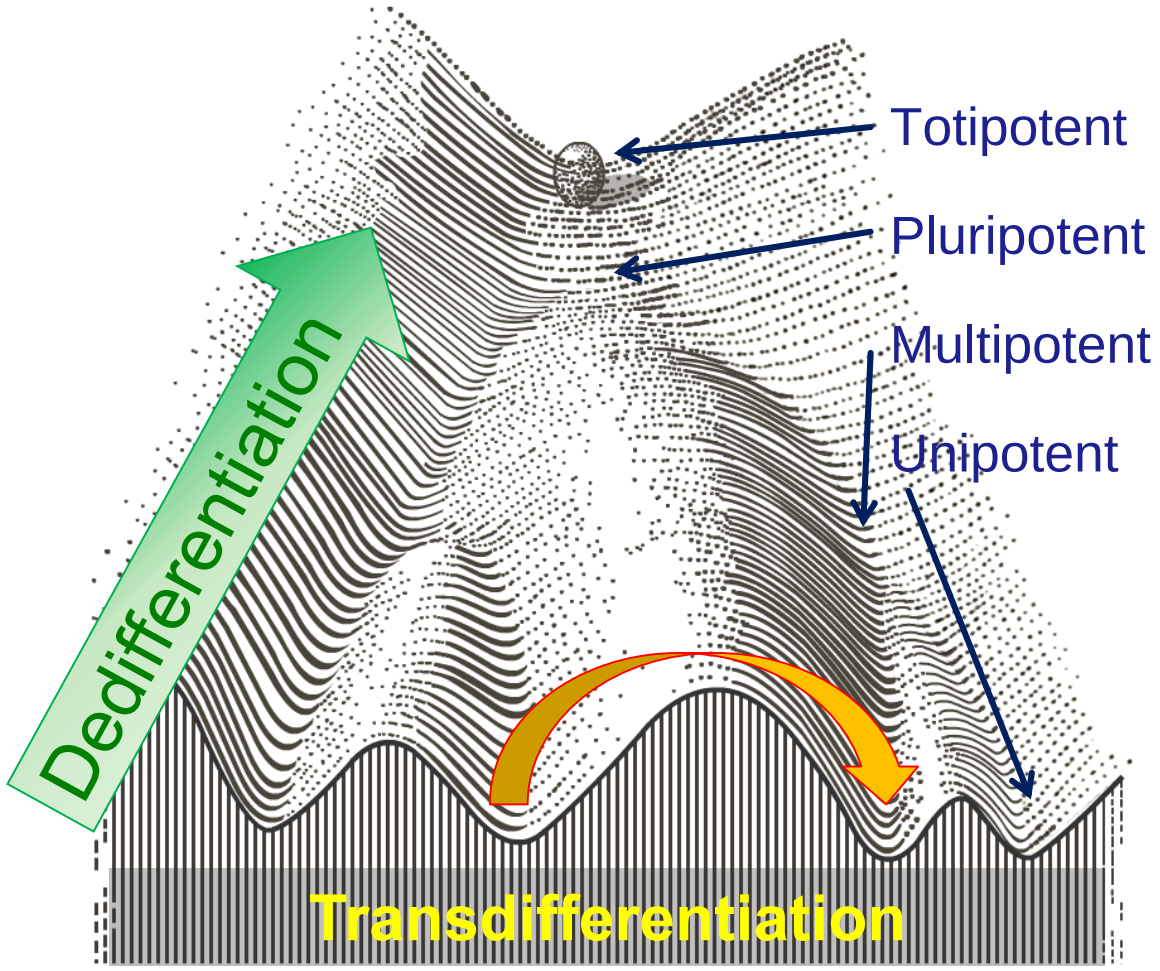


배아줄기세포 (Embryonic Stem Cell)

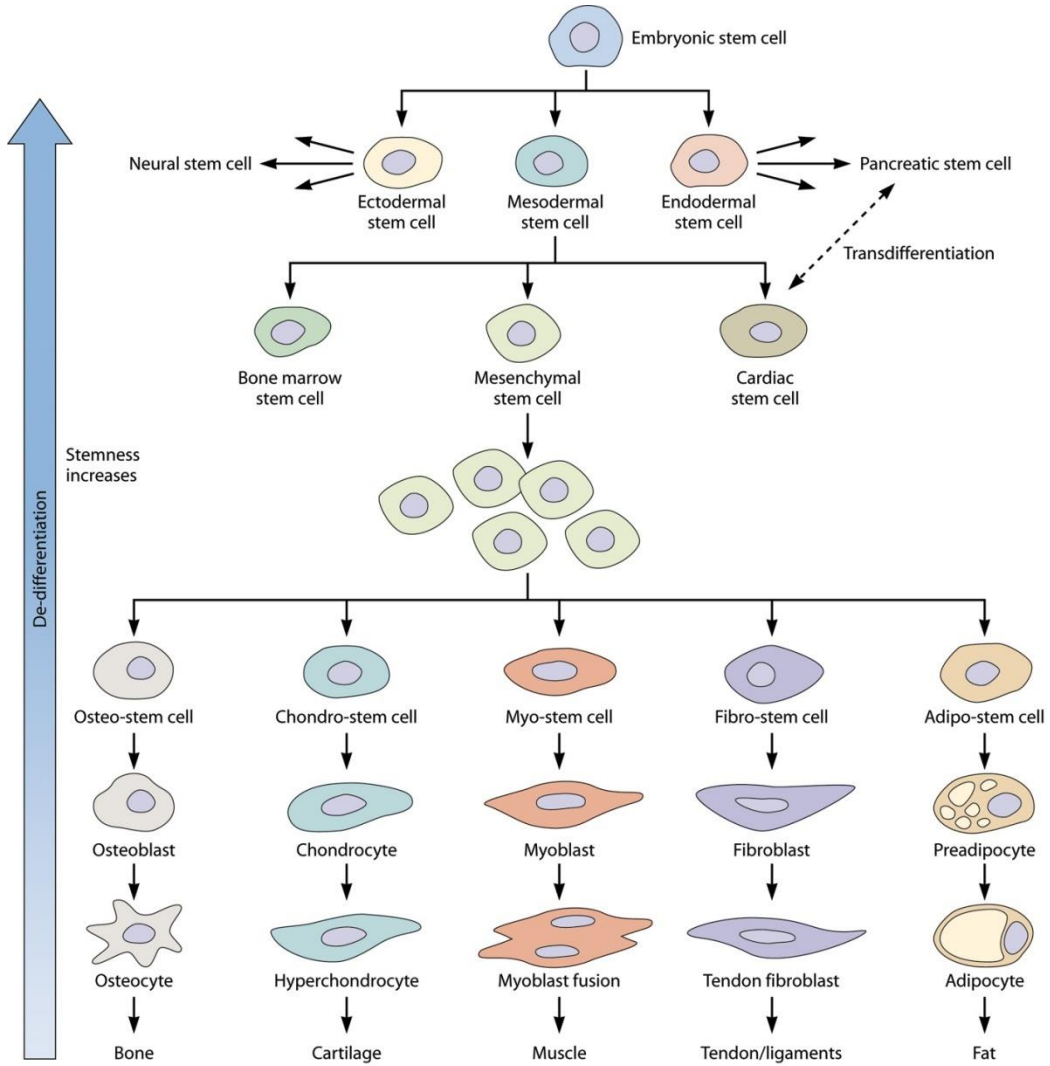


Therapeutic Potential of Stem Cells

- Replacement of damaged cells with AS or ES cells
- Research on differentiation
  - Identification of proper growth factors, nutrients, and environmental factors for specific differentiation
- Research on dedifferentiation and transdifferentiation
  - Factors that reverse differentiation



AS Cell De-differentiation



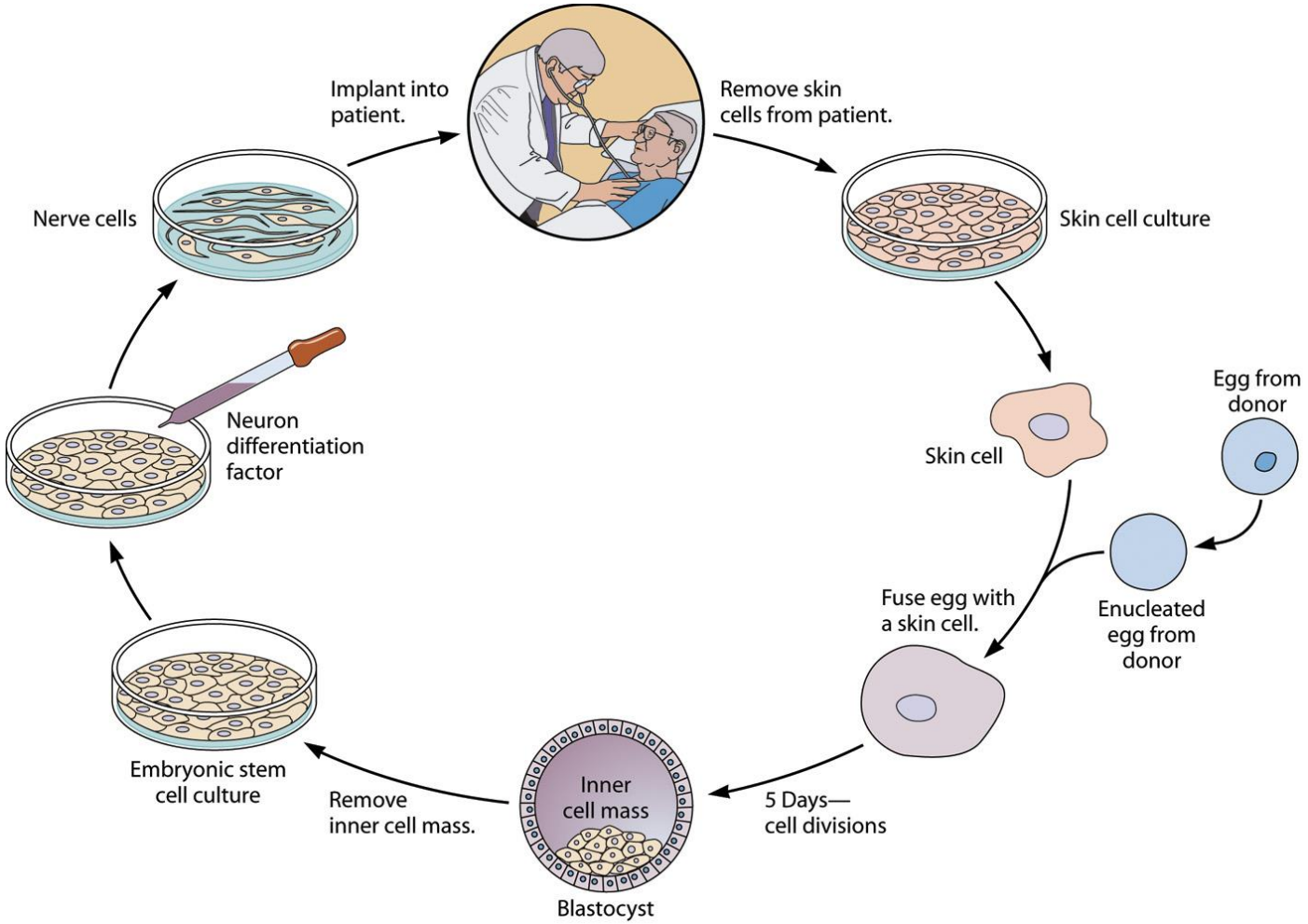
Tissue Engineering

- 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

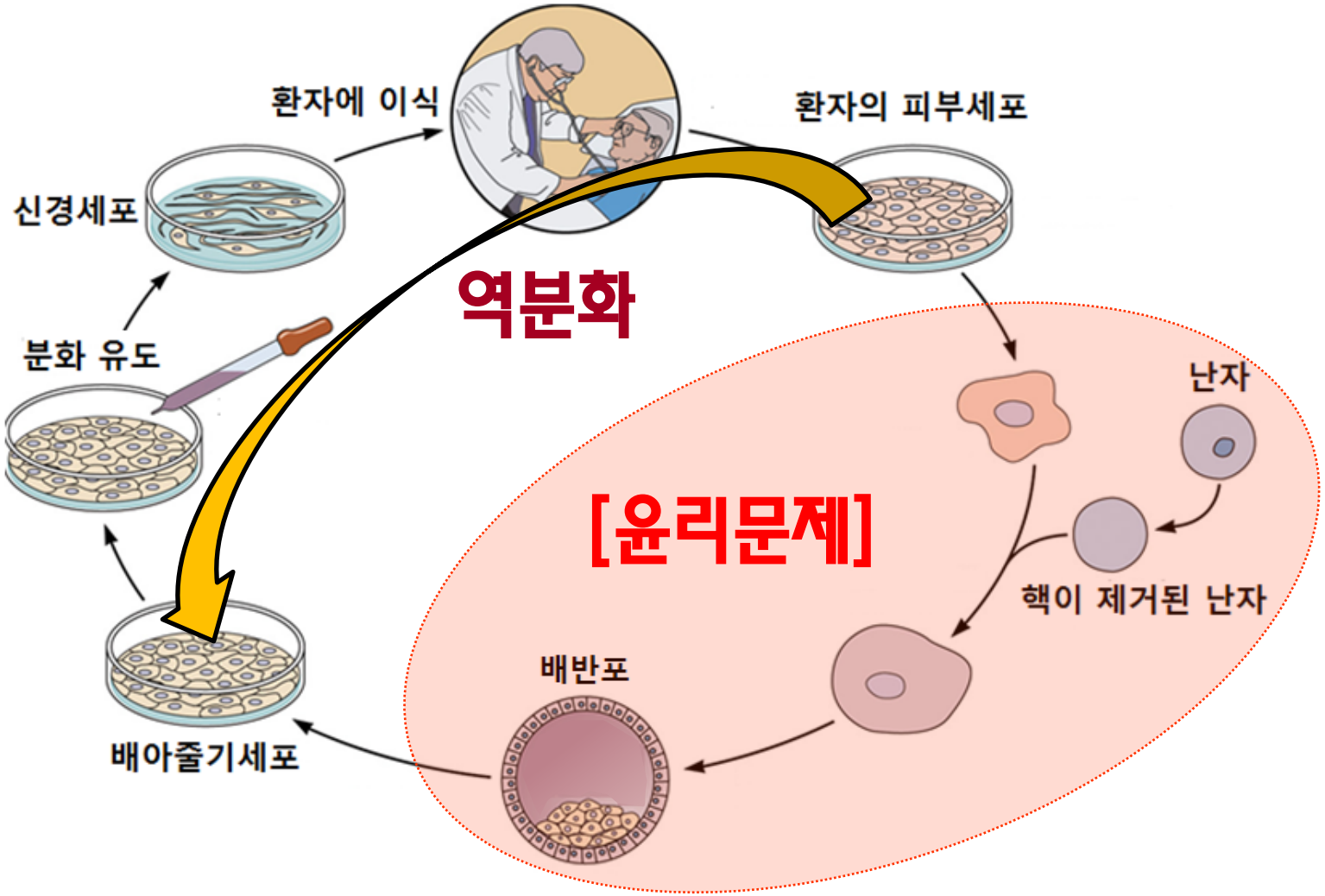
거부 반응 문제 해결

- 환자 자신의 성체 줄기세포 사용
- 미래 사용에 대비한 제대혈 보관
- 면역 적합성 줄기세포
  - 체세포 핵 치환
- 유도만능 줄기세포 (iPS cell)

Immune-Compatible Stem Cells

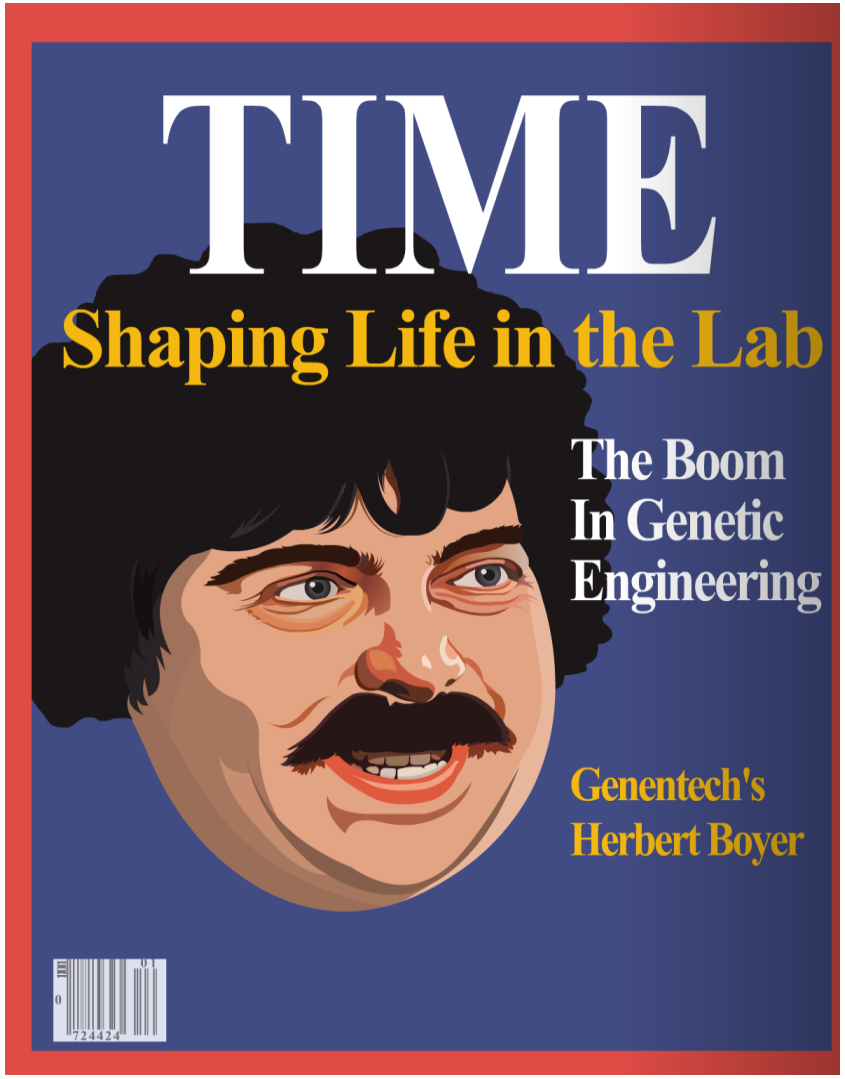


유도만능 줄기세포 (iPS Cell)



4. 산업적 응용 (Industrial Applications)

재조합 DNA 기술의 산업화

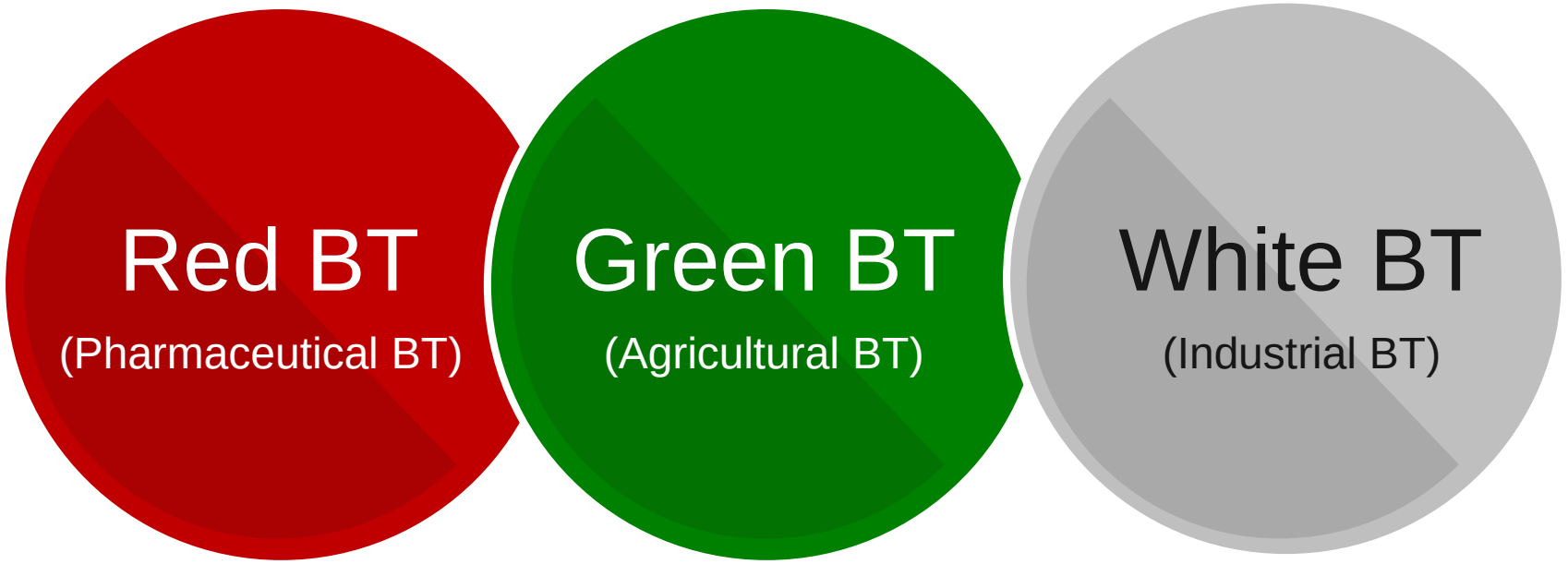


제넨텍(Genentech)

- 재조합 DNA 기술로
  인간 인슐린을
  대장균에서 생산

바이오산업의 트렌드

- 부가가치가 높은 의약품 분야에서 가장 먼저 산업화 진행
- 다음으로 농산물 산업, 에너지/화학소재 산업 등으로 확산

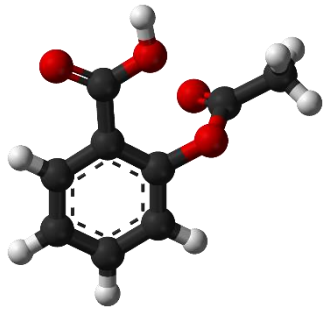
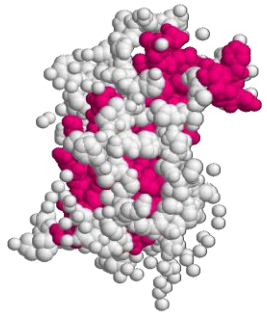
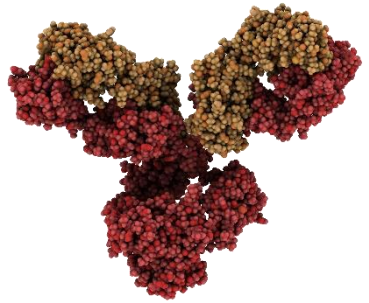


바이오 의약품

바이오 의약품

- 인슐린 (당뇨병 치료)
- t-PA (막힌 혈관 뚫음)
- 인간 성장 호르몬 (왜소증)
- EPO (빈혈 치료제)

바이오 의약품

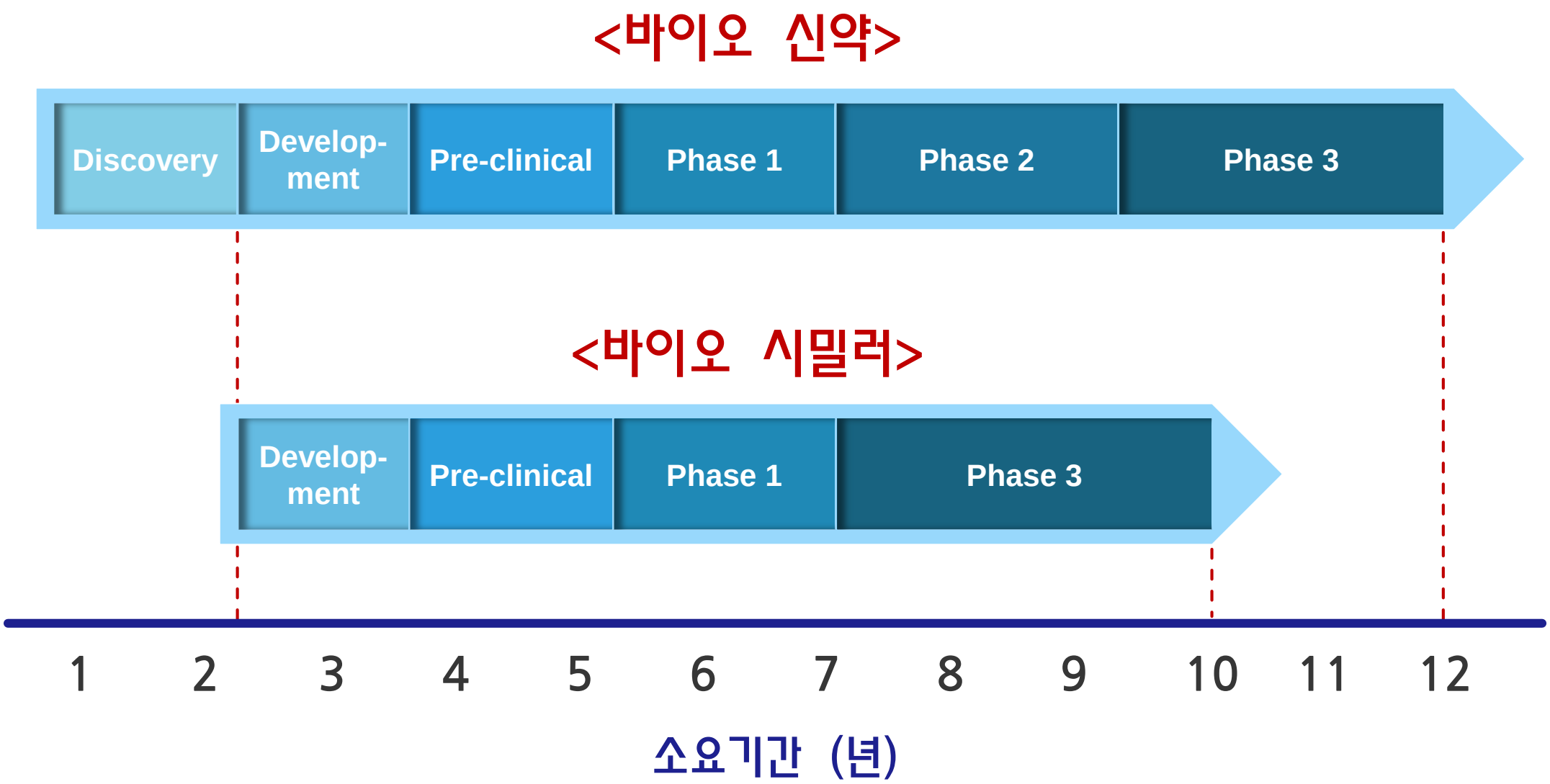
	소분자 의약품 (Small Molecule Drug)	바이오 의약품 (Biopharmaceutical)	
크기	아스피린 21원자 	성장 호르몬 3,000원자 	항체 25,000원자 
복잡도	자전거 21파운드 	자동차 3,000파운드 	비즈니스 제트 30,000파운드 

※ 출처 : 아스피린, 성장호르몬, https://ko.wikipedia.org
자전거, 자동차, 비행기, https://pixabay.com

바이오 의약품 개발 과정

- 바이오 신약
  - 평균 기간: 12년
    (디스커버리 기간(2~6년)에 따라 더 길어질 수도 있음)
  - 평균 비용: 10~20억불
- 바이오 시밀러
  - 평균 기간: 7~8년 (디스커버리, 임상 2상 없음)
  - 평균 비용: 1~2억불

바이오 의약품 개발 과정


<바이오 신약>
Discovery
Develop-ment
Pre-clinical
Phase 1
Phase 2
Phase 3
<바이오 시밀러>
Develop-ment
Pre-clinical
Phase 1
Phase 3
1 2 3 4 5 6 7 8 9 10 11 12
소요기간 (년)

농산물

제초제 내성 작물

- HT(Herbicide-tolerant) Crop
- Monsanto, ‘Roundup Ready’
  - Roundup
    - 거의 모든 식물을 죽이는 범용성 제초제
  - Roundup Ready
    - 라운드업에 내성이 있는 종자

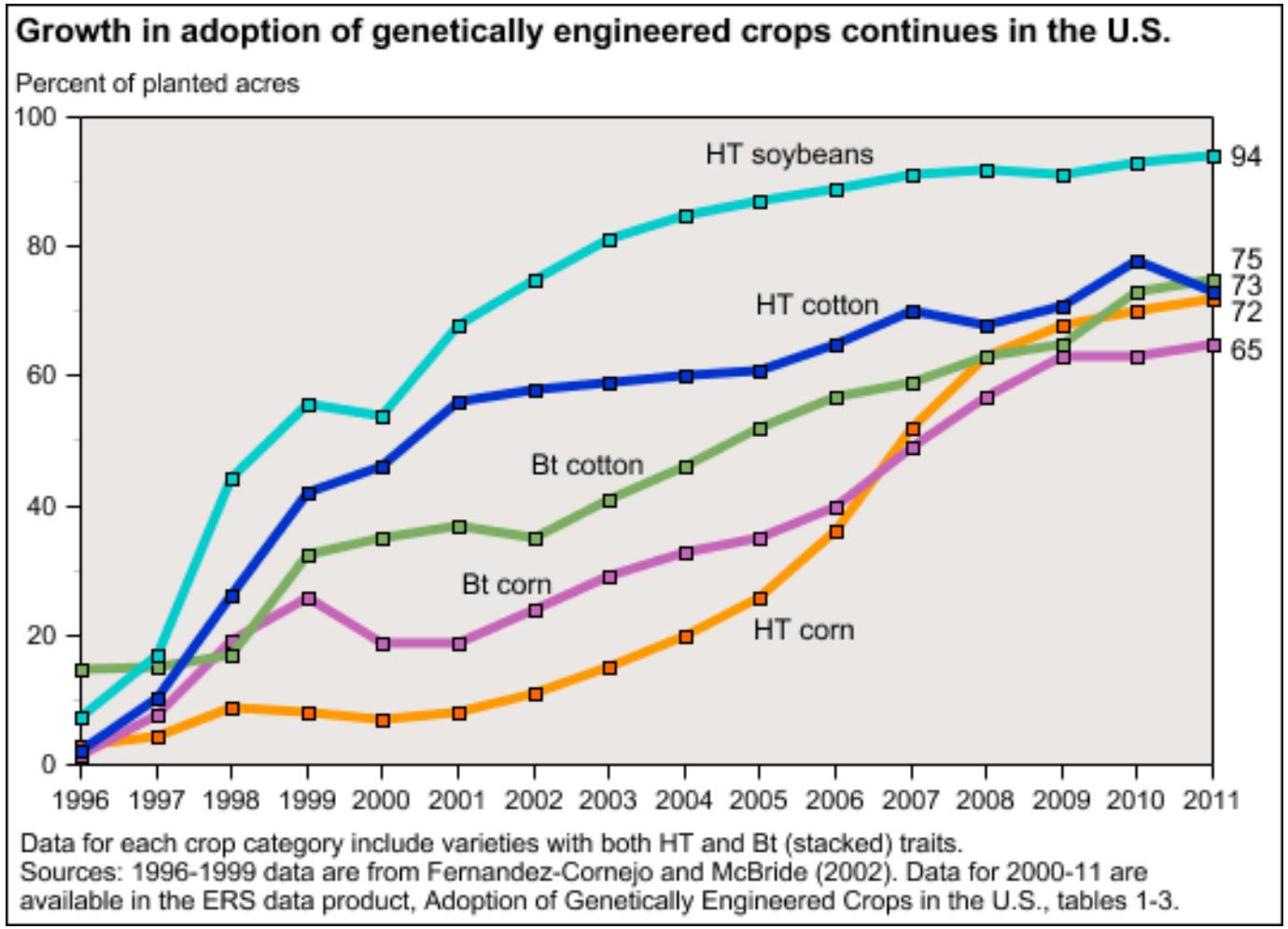
바이오 살충제

- Bt toxin (바이오 살충제)
  - *Bacillus thuringiensis toxin*
  - pH가 높은 곤충 유충의 위장에서는 활성이 있으나,
    pH가 낮은 대다수 동물의 위장에서는 활성이 없음

- Bt toxin 유전자를 작물의 유전체 속으로 도입
  - 그 작물을 먹는 곤충에게만 작용
  - 해당 식물의 모든 세포가 그 독소를 가짐

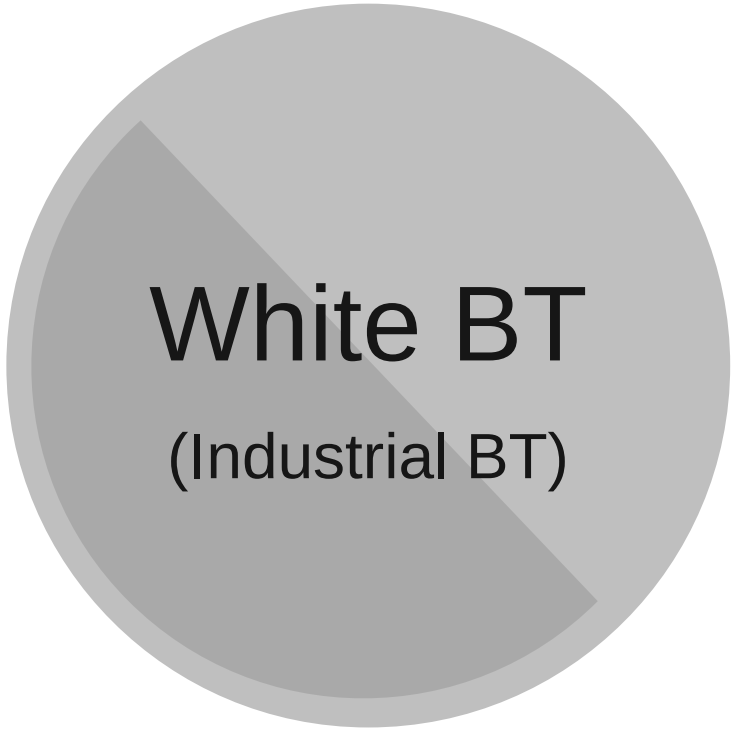
Bt 작물

- Bt 옥수수
- Bt 감자
- Bt 목화
- Bt 콩



※ 출처 : https://commons.wikimedia.org

산업 바이오



<에너지/화학물질>

바이오 자원

- 바이오 에너지, 바이오 화학물질 생산에 이용되는 바이오매스 자원
  - 자연계의 식물 자원
  - 인공적으로 배양한 식물자원 (작물, 나무)
  - 바이오 폐자원
    (예, 폐기 목재 등의 셀룰레이스)

셀룰로우스 성분의
바이오매스

바이오 자원

- 바이오 에너지
  - 바이오 에탄올
  - 바이오 디젤
  - 바이오 가스
- 바이오 리파이너리 (Bio-refinery)
  - 바이오 플라스틱
  - 바이오 정밀화학제품
  - 바이오 신소재

바이오 디젤 버스

생분해성 플라스틱 용기

5. 대규모 생물공정 (Large-Scale Bioprocess)

Chapter 24

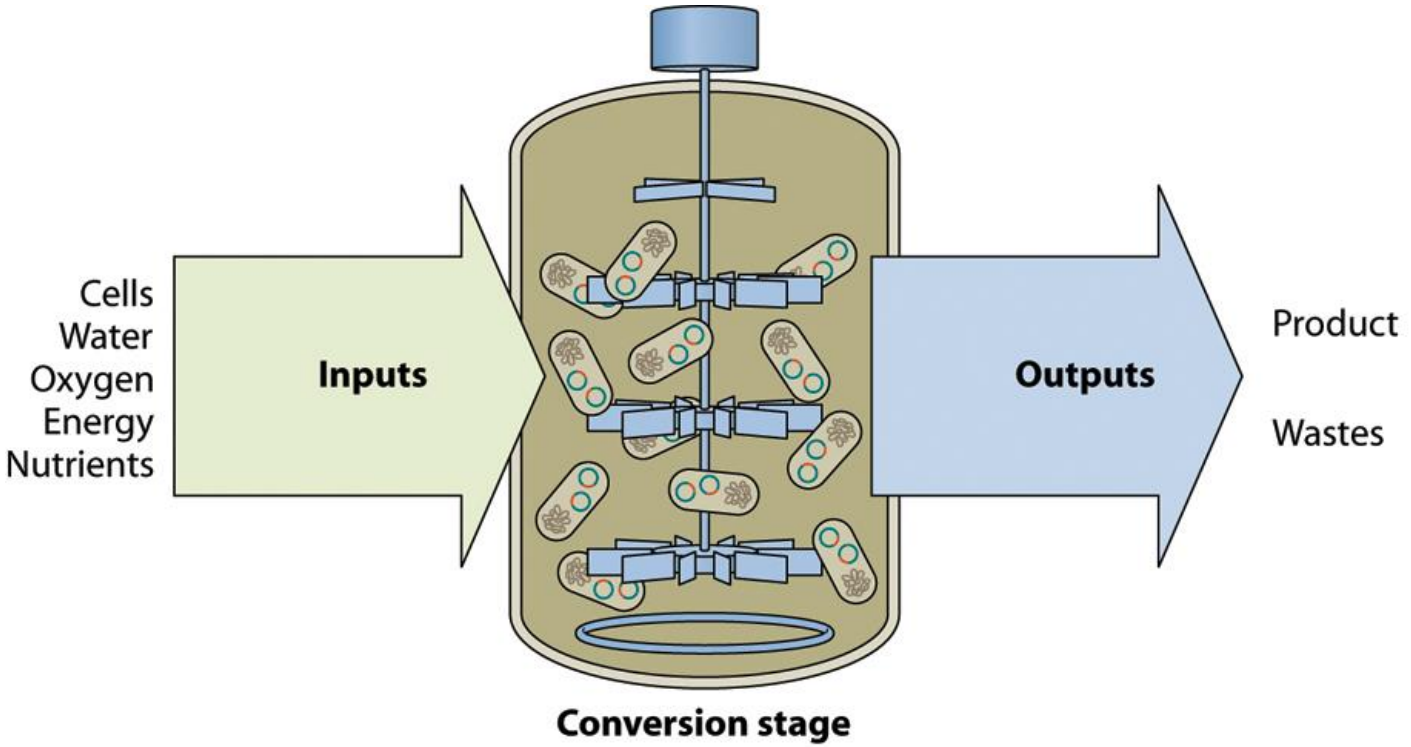
Environmental Sustainability and Biotechnology

Cell Culture Process

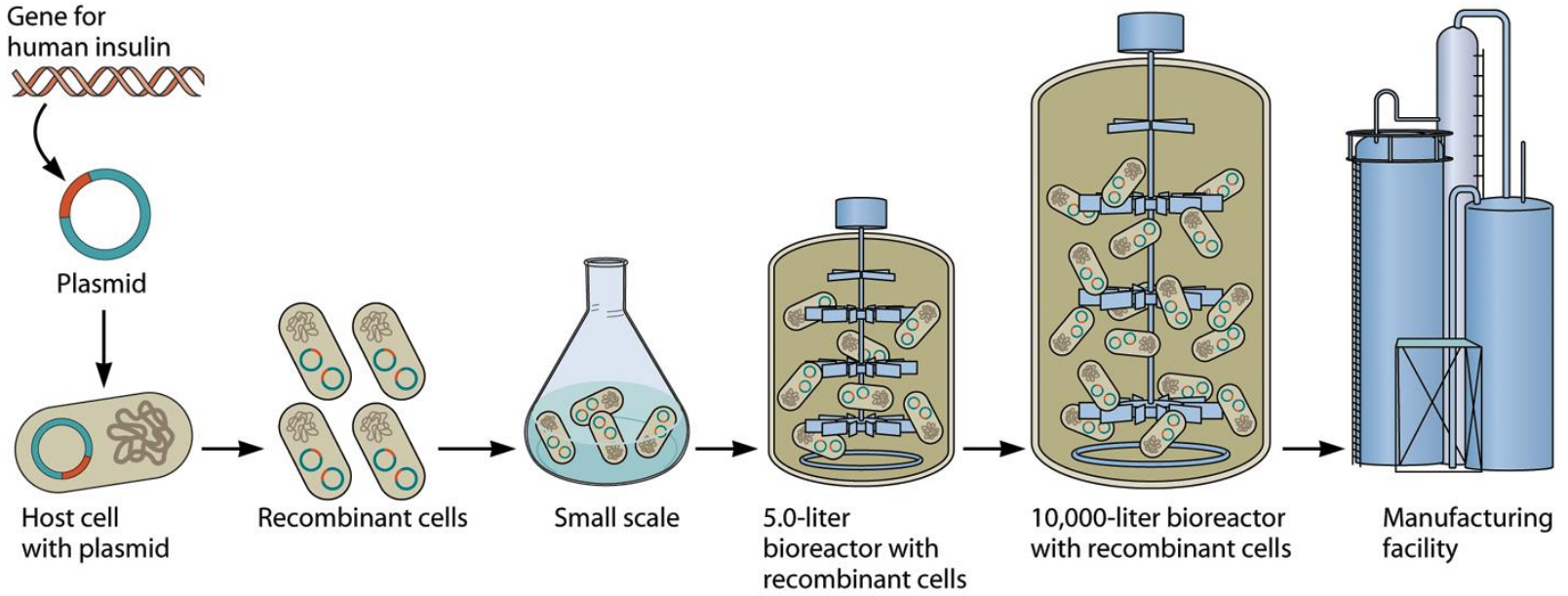
- **미생물 배양** (Microbial fermentation)
  - **천연 미생물**
    - 다양한 발효 제품
  - **재조합 미생물**
    - 대장균*(E.coli)*, 효모*(Saccharomyces cerevisiae)*
    - 바이오 의약품, 바이오 에너지, 바이오 화학물질
- **포유동물세포 배양** (Mammalian cell culture)
  - CHO (Chinese Hamster Ovary) cell
    - 바이오 의약품 (예, 치료용 항체)

Cell Culture Process

- Bioreactor, Fermentor
  - Medium supply
  - Optimal conditions
    - Temperature
    - pH
    - O2 concentration

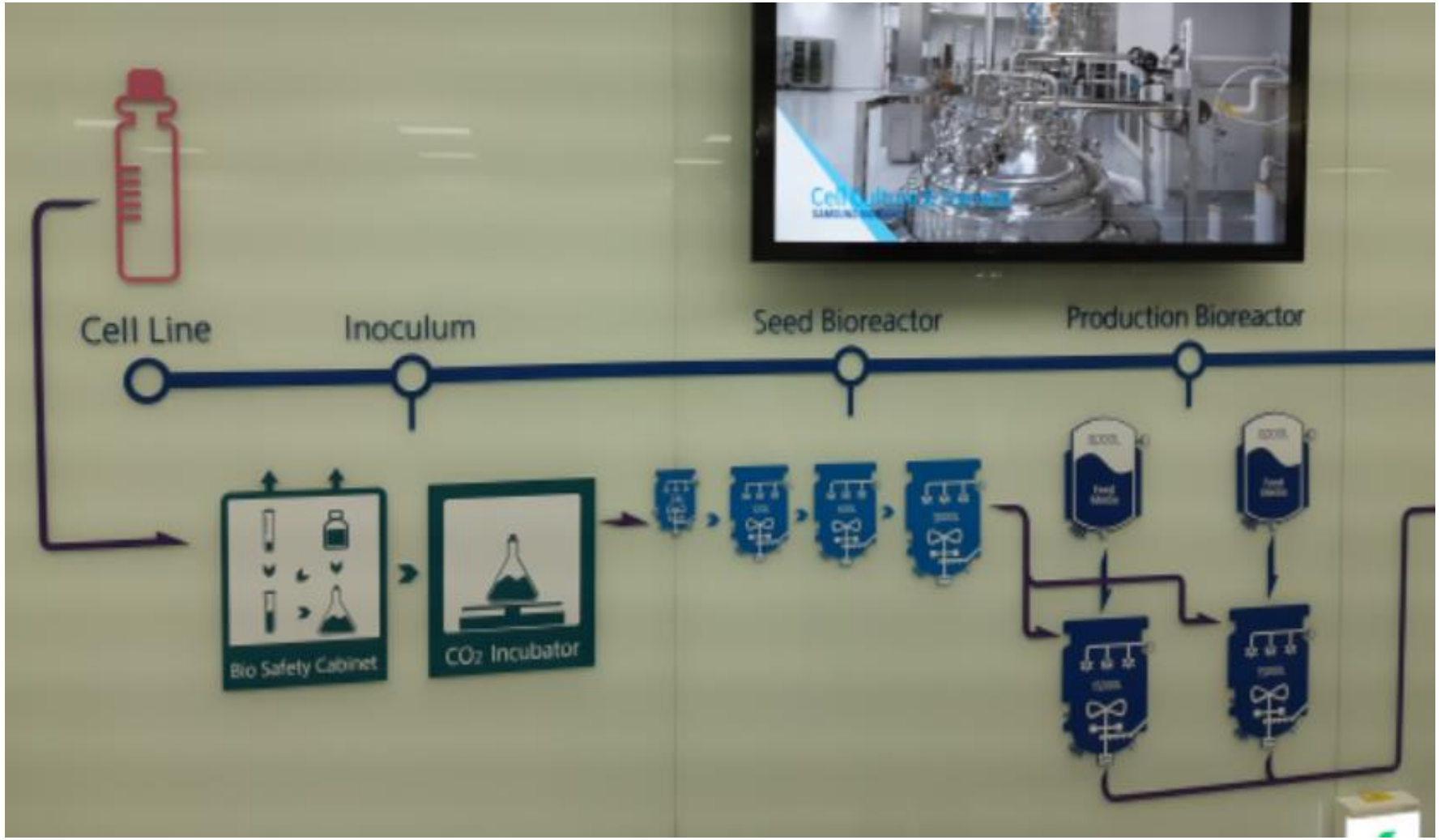


Large-Scale Biomanufacturing (Microbial Cells)



Large-Scale Biomanufacturing (Microbial Cells)

Large-Scale Biomanufacturing (Mammalian Cells)



Large-Scale Biomanufacturing (Mammalian Cells)

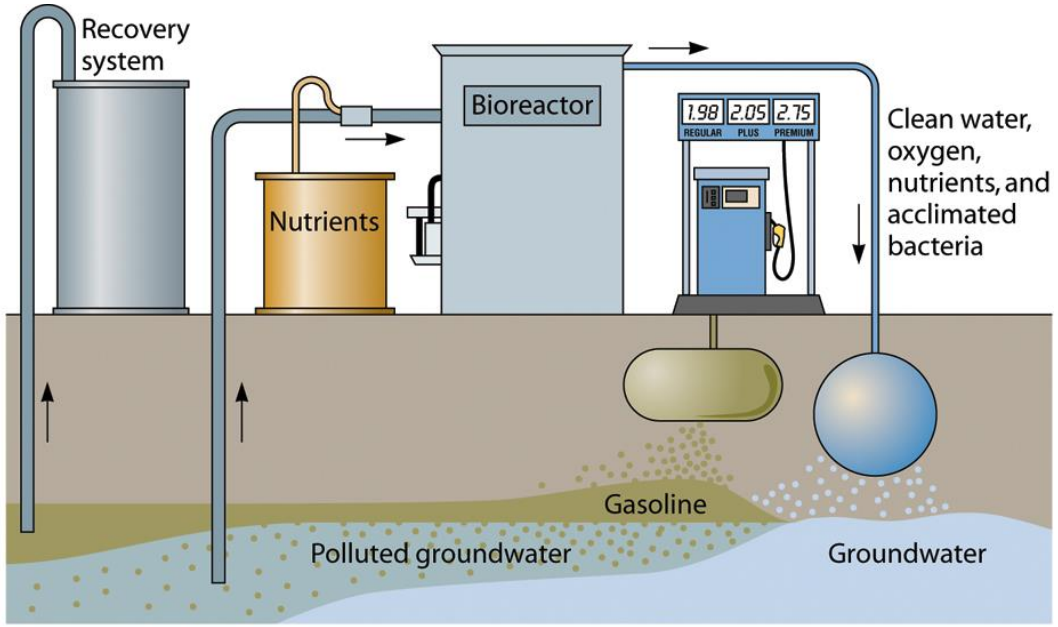
Remediation of Environmental Problems

- Treatment of sewage and waste water
- Remediation of oil spills
- Treatment of hazardous wastes

A sewage treatment plant in Hawaii

Bioremediation

- Bioremediation
  - Use microbes to remove pollutants
    - (oil, toxic waste sites)



Bioremediation of a gasoline spill

생명공학 응용

- 의학적 응용
  - 분자 진단
  - 의약품 개발, 유전자 치료, 줄기세포/조직공학 치료
- 산업적 응용
  - 바이오 의약품 (Red BT)
  - 농산물 (Green BT)
  - 산업 바이오 (White BT)
    - 바이오 에너지, 바이오 화학물질 (Bio-refinery)
- 서비스 창출 및 사회문제 해결
  - 범죄 수사, 친자 확인, 전사자 신원 확인 등
  - 환경 처리, 생물 복원 등