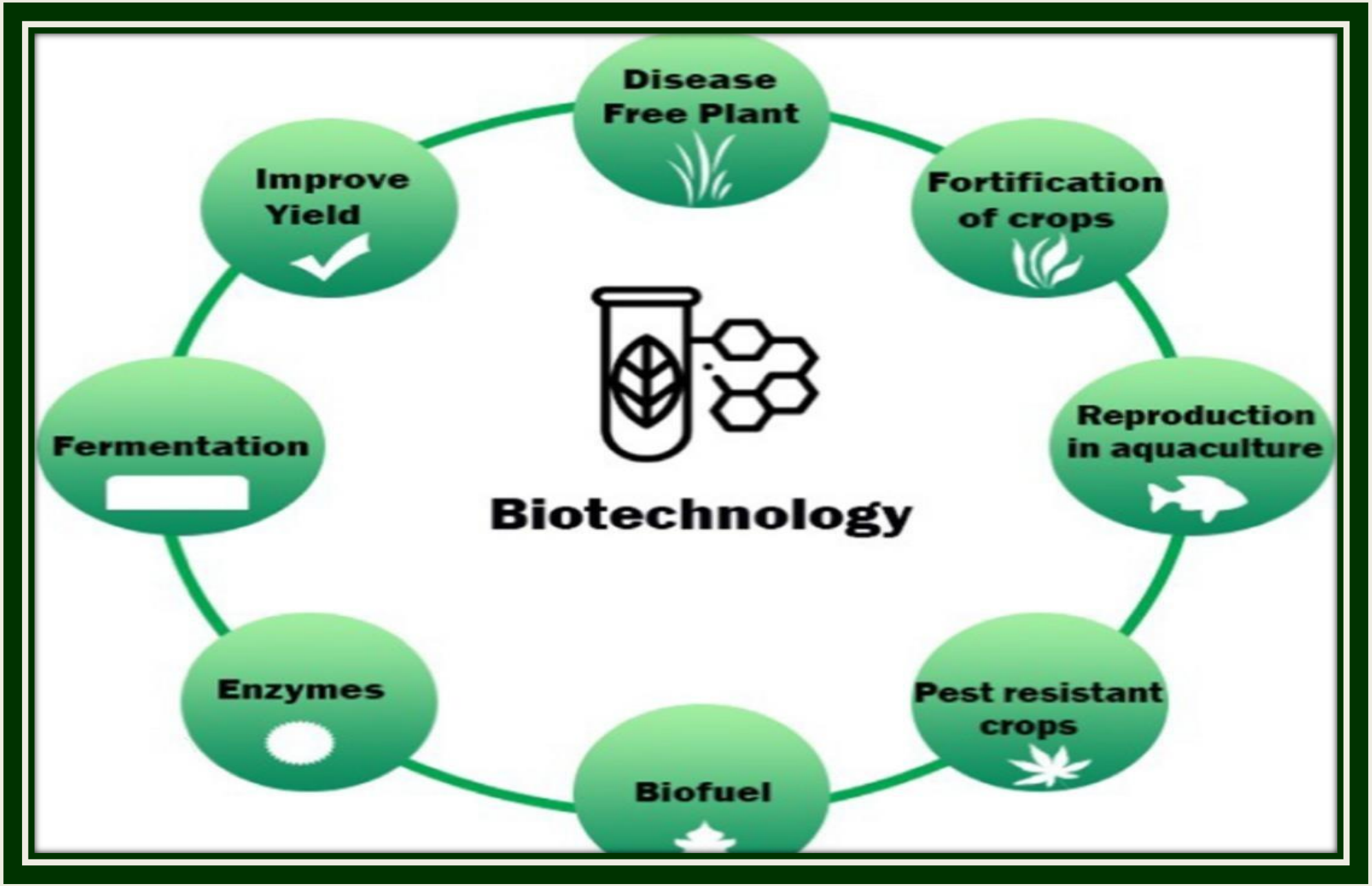
BIOTECHNOLOGY CENTURY AND ITS WORKFORCE

CHAPTER 1


Disease Free Plant
Fortification of crops
Reproduction in aquaculture
Pest resistant crops
Biofuel
Enzymes
Fermentation
Improve Yield
Biotechnology

The biotechnology century and its work force

- Biotechnology: using living organisms or the products of living organisms, for human benefits to make a product or solve a problem There two types of biotechnology

A -classical Biotechnology Practical

B -Modern Biotechnology

- Historical Examples of Biotechnology

1-Fermentation

2-Selective breeding

3-use of antibiotic

- These examples are Consider as ancient practices of biotechnology

- Of course, the ancient humans use These practices in their life, and at this moment These practices still be use.

1-Fermentation: the process respiration without oxygen. Use to make bread, cheese, yogurt, and alcoholic beverages such as beer and wine.

Some strains of Yeast they decompose sugars to derive energy, and in the process, they produce the ethanol as waste product.

2-selective breeding

Artificial mating between two organisms there have particular characteristics to produce offspring with more desired Characteristics.

- Example: if we have two strains of wheat, one is resistant cold and the second have the ability to give more abundant nutrients, we try to do mating between two strains to get the wheat plants that

have ability to resistant or stand the cold also give more nutrients.

- Another example: Casper fish

Casper fish: Zebrafish that was produce be artificial selective breeding mating between two types of mutant zebra fish, one has reflective pigment and the second lacked the black pigment.

- Casper fish has transparent body, this fish could be excellent model organism, to study the effect of drugs

in vivo and study the cancer cell migration (metastasis)

- **Example of Biotechnology – Selective Breeding**

(a)

Normal zebrafish

(b)

"Casper" zebrafish – made by selective breeding

3- using Antibiotics

Antibiotic: substance that produce by Microorganisms, Bactria, and fungi, and use to kill or inhabit the Growth the other Microorganisms.

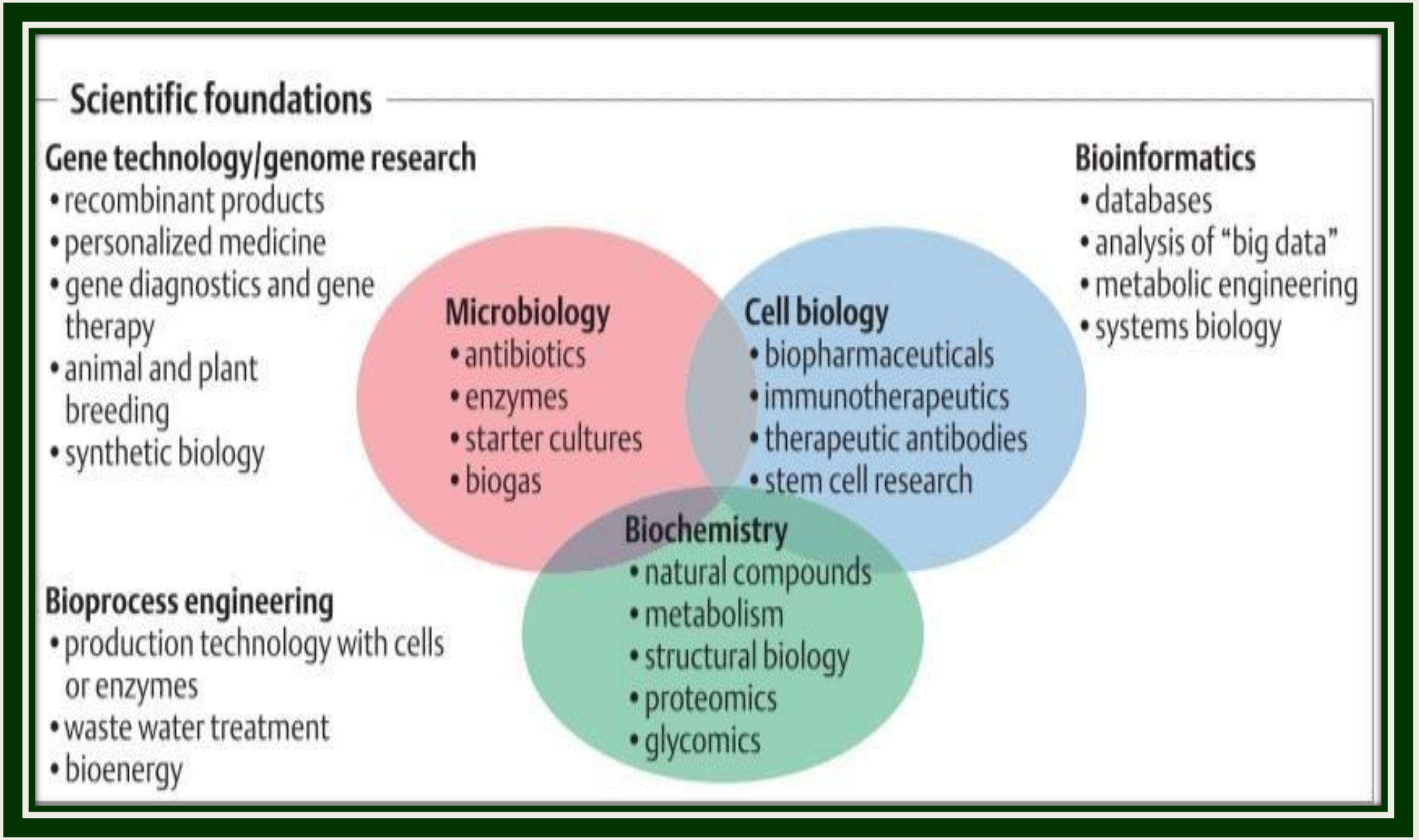
Examples: Penicillin ‹ampicillin, tetracycline……

- Antibiotic has important role in the medical fields.

- Super bugs: strains of Bacteria that are resistant to most Available antibiotics

- Modern Biotechnology

1- Gene cloning
2- Genetic Engineering
3- Recombinant DNA technology
4- Human genome project


Scientific foundations
Gene technology/genome research
• recombinant products
• personalized medicine
• gene diagnostics and gene therapy
• animal and plant breeding
• synthetic biology
Bioinformatics
• databases
• analysis of "big data"
• metabolic engineering
• systems biology
Microbiology
• antibiotics
• enzymes
• starter cultures
• biogas
Cell biology
• biopharmaceuticals
• immunotherapeutics
• therapeutic antibodies
• stem cell research
Biochemistry
• natural compounds
• metabolism
• structural biology
• proteomics
• glycomics
Bioprocess engineering
• production technology with cells or enzymes
• waste water treatment
• bioenergy

1-Gene cloning

Make more copies of gene by insert the gene into plasmid and then allow to make more plasmids.

The plasmid is extra chromosome which has ability to replicate independent from Bacteria chromosome, first we isolate the gene of interest from target organism, then insert the gene in plasmid, and introduce the plasmid in Bacteria, the plasmid start replicate and produce new copies, because the interest gene in plasmid, gene of interest also replicate, new copies of gene will produce.

2-genetic Engineering

modification into a sequence of DNA could be gene or just any piece of DNA.

Add or remove DNA/genes.

3-Recombinant DNA technology

combining DNA from two or more different sources.

Example: cloning

Yes, the cloning is the excellent example when we take about Recombinant DNA technology, when we need clone human gene for example in Bacteria, we need combine the gene and the plasmid and to gather, the plasmid come from Bacteria, the gene come from Human, so the gene and the plasmid come from different sources.

Example of “modern” biotechnology: - recombinant DNA technology started modern biotech as an industry.

Examples of applications (for recombinant DNA technology)

-Development of disease-resistant plants

-food crops that produce greater yields (more food for us)

-“golden rice” engineered to be more nutritious (more vitamins)(golden rice: type of rice)

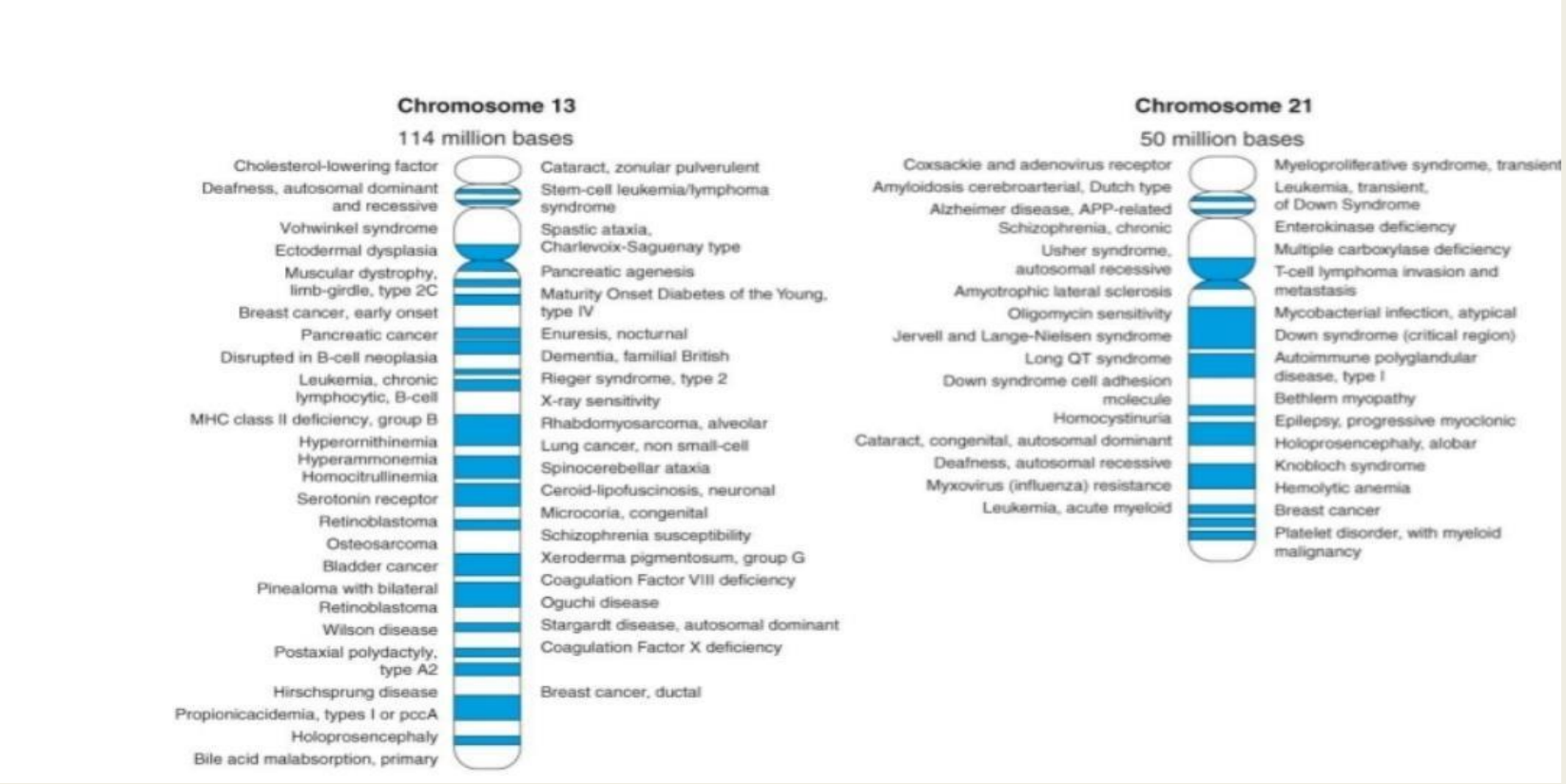
Genetically engineered bacteria that can degrade environmental pollutants (to clean environment from harmful chemicals)

We use Recombinant DNA technology to better understand and studying our genomes.

Scientist were able to map all Location of human genes in human genome and determine Location of genes on chromosomes.

4-human genome project

it was launch 1990 and finished 2003.



Scientists were determined which genes are involved Genetic Disease.

Human genome project relied on use gene cloning and Recombinant DNA technology.

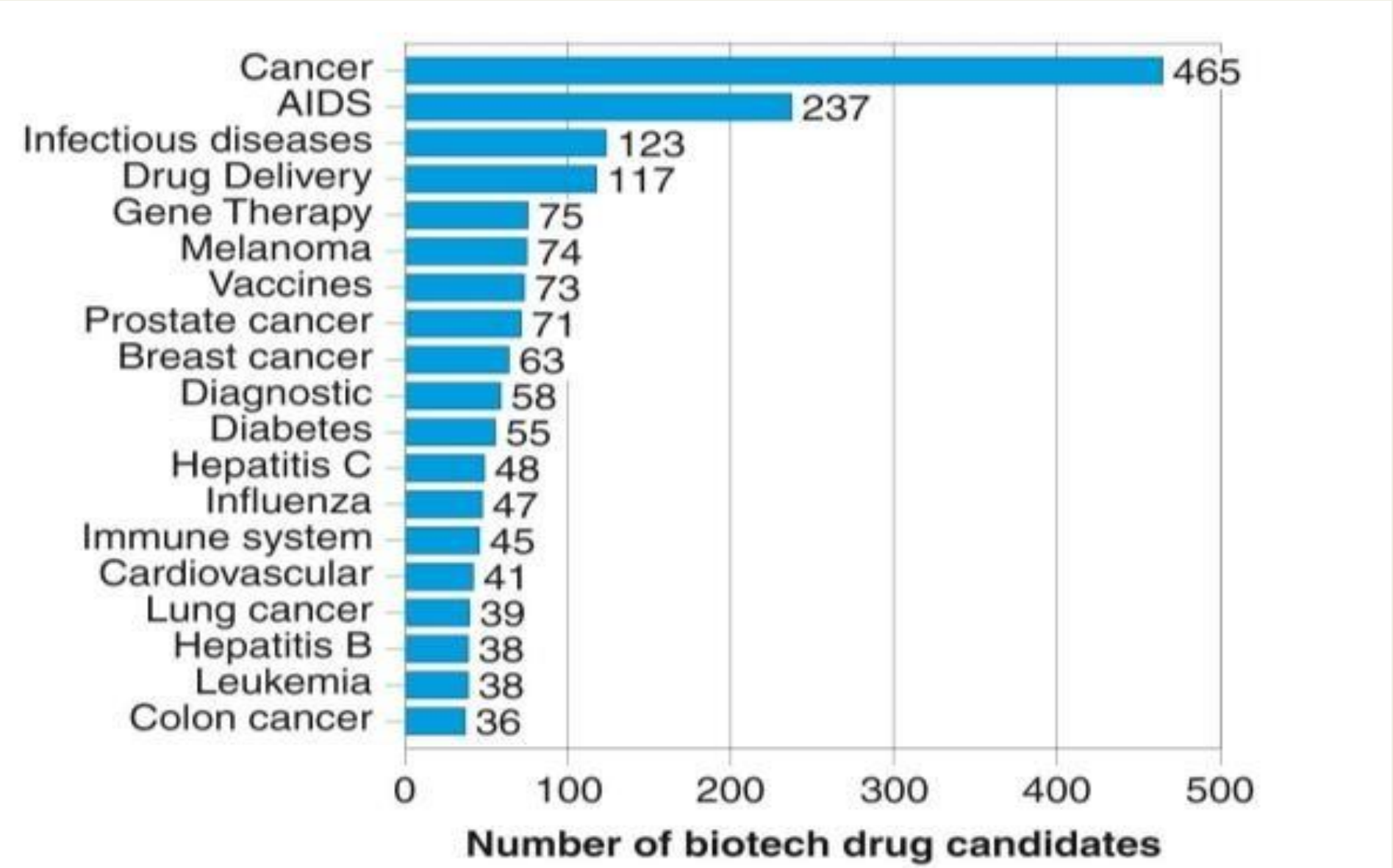
Currently many Scientists and Companies are using Recombinant DNA technology to come up with product that could be used to treat Diseases or prevent it.

Candidates' drugs: Therapeutic drugs still under development and research by biotechnology Companies.

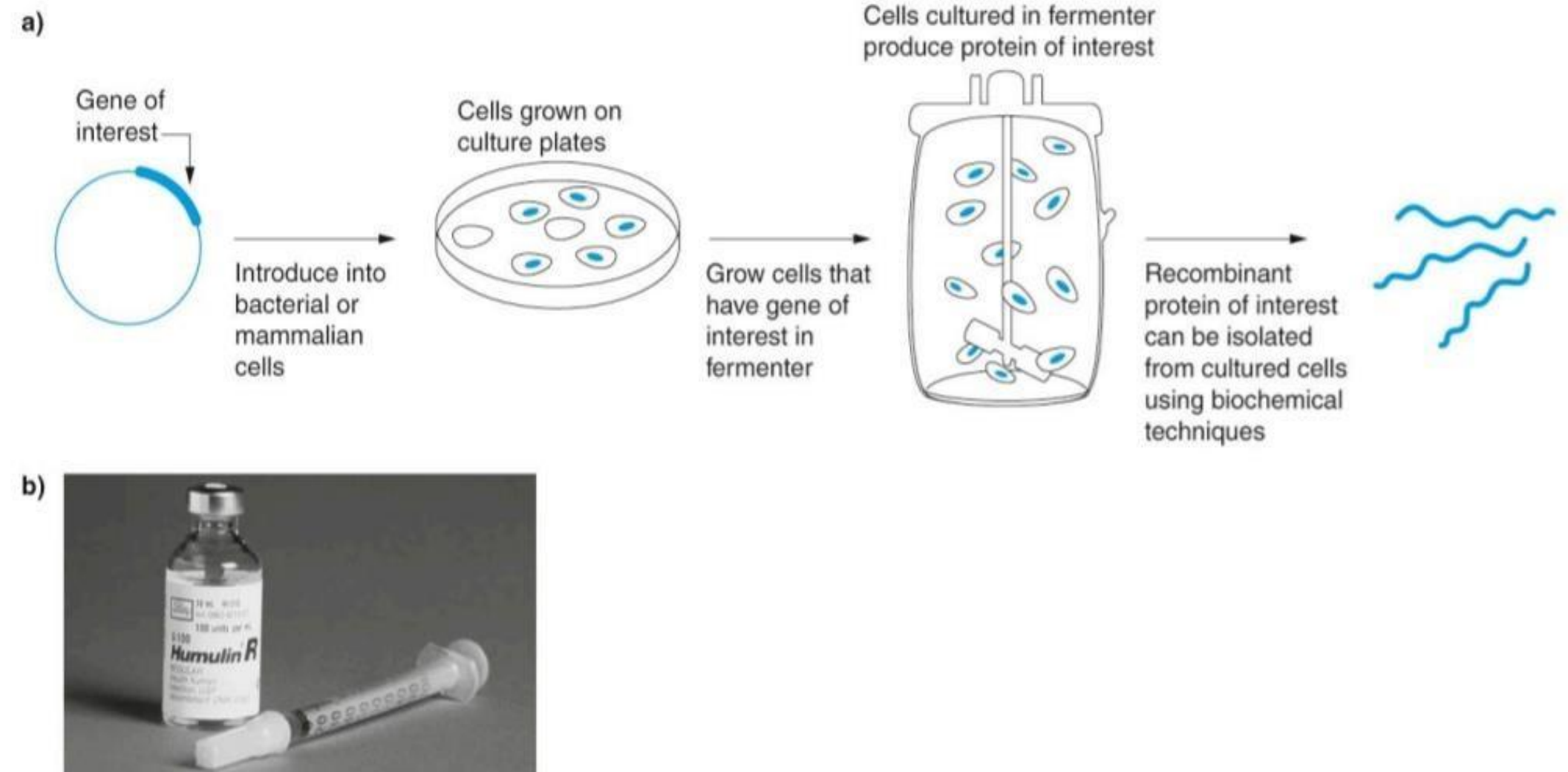
The large number of Candidates drugs being Develop to treat cancer but why?

Because cancer affected different Organs like skin, blood, lung, unlike other Diseases such as hepatitis C that affect only one Organ(liver).

- Candidates drugs are Develop to treat Diseases or environment conditions.


Cancer
AIDS
Infectious diseases
Drug Delivery
Gene Therapy
Melanoma
Vaccines
Prostate cancer
Breast cancer
Diagnostic
Diabetes
Hepatitis C
Influenza
Immune system
Cardiovascular
Lung cancer
Hepatitis B
Leukemia
Colon cancer
465
237
123
117
75
74
73
71
63
58
55
48
47
45
41
39
38
38
36
0
100
200
300
400
500
Number of biotech drug candidates

Scientists in company called GENENTECH successful produce the first Recombinant protein called "Humulin R"



They were cloning coding sequence of **human insulin** using plasmid,

1- Isolate human insulin gene
2- Isolate plasmids from Bacteria
3- Insert the gene of interest into Plasmid.
4- Introduce the Recombinant plasmid into Bacteria.
5- Allow Bacteria grow in large tanks.
6- Isolate the insulin from Bacteria.
7- Purify the insulin.
8- Ready for using.

- Humulin R was first biotechnology product that is used as a drug to treat a Human Diseases.

- Humulin R: Recombinant insulin that is used to treat diabetes.

- Humulin R produce by company called GENENTECH

- Insulin: is a hormone protein that is used to regulate Level of glucose in the body.

- Insulin is made of amino acids.

- **The procedure of clone human insulin**

- First isolate plasmid from Bacteria and human insulin gene from Human

- Insert the human insulin into the plasmid, now we have Recombinant plasmid Then return the Recombinant plasmid to Bacteria allow the Bacteria cells grow on culture plate, the grow cells that have gene interest will be transfer to large Tank “fermenter” to give large space for cells growing.

- The cells that carry gene of interest start produce protein of interest, Recombinant protein of gene interest will isolate and purify using biochemical techniques, the result is Recombinant protein ready to use to treat human Diseases.

- Recombinant proteins used to treat certain Diseases and medical conditions

These proteins produce by Recombinant DNA technology use gene cloning, some These proteins there were Genetically Engineered, which mean amino acids sequences different amino acid sequences of natural proteins used inside our bodies.

TABLE 1.2 EXAMPLES OF PROTEINS MANUFACTURED FROM CLONED GENES

Product	Application
Blood factor VIII (clotting factor)	Treat hemophilia
Epidermal growth factor	Stimulate antibody production in patients with immune system disorders
Growth hormone	Correct pituitary deficiencies and short stature in humans; other forms are used in cows to increase milk production
Insulin	Treat diabetes
Interferons	Treat cancer and viral infections
Interleukins	Treat cancer and stimulate antibody production
Monoclonal antibodies	Diagnose and treat a variety of diseases including arthritis and cancer
Tissue plasminogen activator	Treat heart attacks and stroke

TABLE 1.1 *2016—Top 10 Biotechnology Drugs (Each with Worldwide Sales over $5 Billion)

Drug Name	Developer	Drug Type	Function (Treatment of Human Disease Conditions)
Humira	AbbVie	Antibody (monoclonal)	Rheumatoid arthritis, Crohn's disease, Ulcerative colitis
Harvoni	Gilead Sciences	Small molecule	Hepatitis C
Rituxan	Roche	Antibody (monoclonal)	Non-Hodgkin's lymphoma
Revlimid	Celgene	Small molecule	Multiple myeloma
Avastin	Roche	Antibody (monoclonal)	Colorectal cancer; breast cancer; non–small cell lung cancer; ovarian, brain, and cervical cancer
Herceptin	Roche	Antibody (monoclonal)	Breast cancer, gastric cancer
Enbrel	Amgen	Recombinant protein	Rheumatoid arthritis, psoriasis
Prevnar 13	Pfizer	Vaccine	Pneumococcal (*Streptococcus Pneumoniae*) antibacterial vaccine
Lantus	Sanofi	Peptide	Diabetes mellitus types I and II
Neulasta	Amgen	Recombinant protein	Anemia (neutropenia/leukopenia)

*Data based on the most recent source available at the time of publication: Morrison C, Lähteenmäki R. Public biotech in 2016—the numbers. *Nat Biotechnol.* 2017;35:623–629.

Single Nucleotide polymorphisms (SNPs)

- Single Nucleotide change in DNA sequences that vary from individuals cause of some genetic Diseases (sickle cell anemia).
- SNPs also contribute to genetic Diversity observed among individuals.

- if change greater than 1% it considers SNPs if not it considers Mutation

- If this change is less than 1% of certain population it Consider a Mutation.
- In General, any change in DNA sequence we call it Mutation, the change could be one or two or many Nucleotides or could be a huge change at the Level of chromosome.

- The SNPs just change in one Nucleotide.

- SNPs will help identify genes involved in medical conditions include arthritis, stroke, cancer, heart disease, diabetes, and behavioral and emotional illnesses.

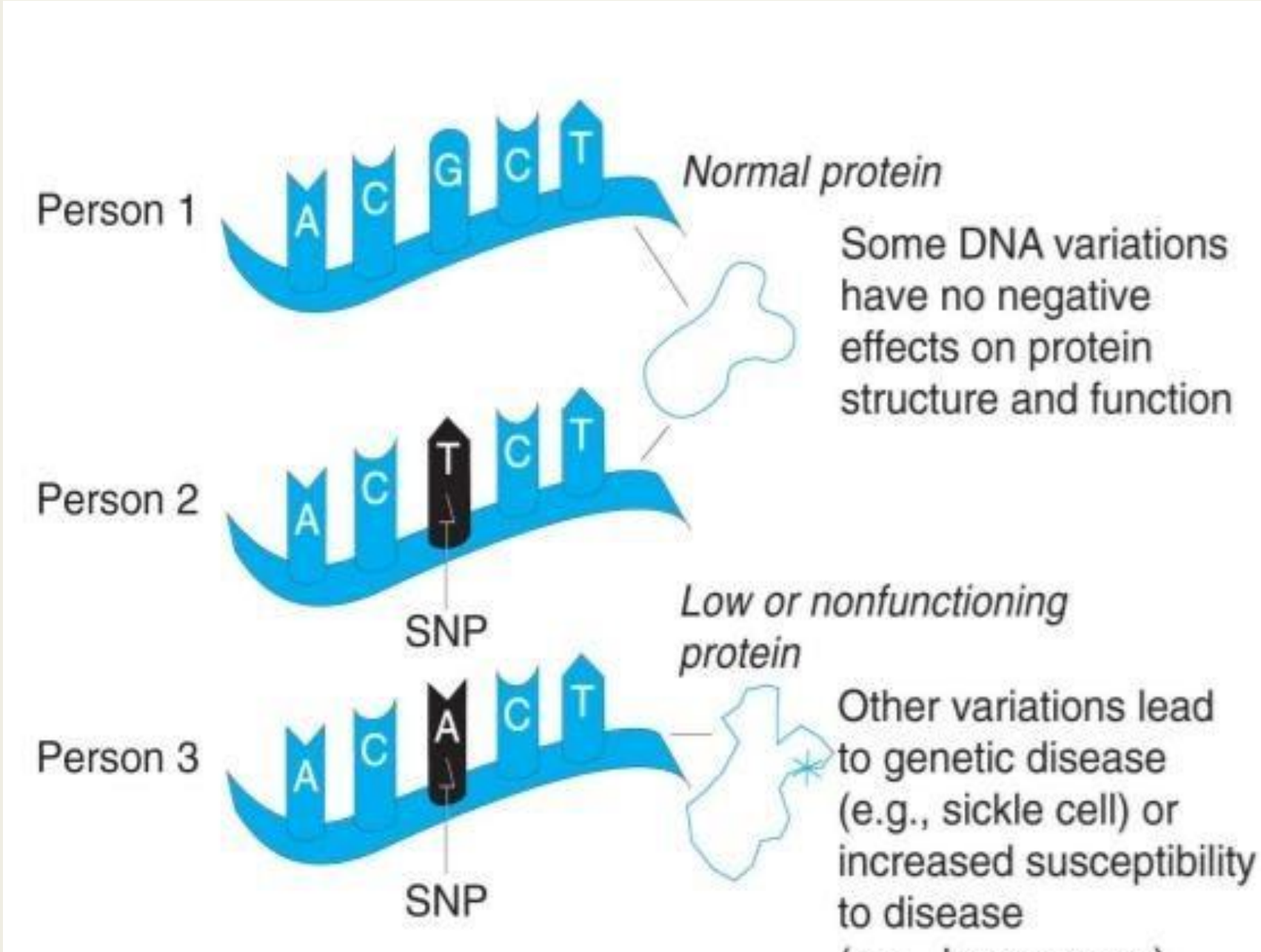
- Also, some of SNPs a being found to alter or determine how our bodies can respond to drug or food, or how our bodies interact with environment.

So how Scientists found certain SNPs are linked to certain types of Diseases or medical conditions?

Part of Diagnosis of breast cancer and part of pregnant of breast cancer and many types of cancer is to determine mutations and types of SNPs found in certain types of proto-oncogenes or tumor suppresser.

Because it tends out that certain SNPs or identifying certain SNPs is important for designing a specific type of treat.

A certain females have high risk of developing breast cancer because they have certain SNPs in BRCA1 and BRCA2 genes that are involved in promoting breast cancer in female.


Person 1
A
C
G
C
T
Normal protein
Some DNA variations have no negative effects on protein structure and function
Person 2
A
C
T
C
T
SNP
Low or nonfunctioning protein
Person 3
A
C
A
C
T
SNP
Other variations lead to genetic disease (e.g., sickle cell) or increased susceptibility to disease

How can you test one person’s DNA for many different SNPs?

Microarray (gene chip)

-Isolate DNA from patient

-Apply this sample to a microarray which contains many DNA sequences

-Compare patterns of DNA binding between patients’

-DNA and DNA on microarray to reveal patient’s SNP Patterns

Customized medicine

- Mean if we have two individuals suffer the same Disease, each of them might receive different treatment or different doses base on type of SNPs.

- Customized medicine is being now practices in determining the treatment for different Diseases for example certain types of cancer.

- SNPs are found to be important when we take drugs.

Some drugs work on some people but it might not work for other this because the maybe present certain SNPs.

- Also, some people take the drugs and suffer side effect, that also because present certain SNPs

- SNPs become important in the Case in the situation where is the Diseases, and when we need take a drug in order to treat Disease.

- Most the SNPs Location at noncoding regions, actually they do not contribute direct to genetic Diseases, but they become important whenever Disease happen or whenever need to treat Disease with drugs.
- Some SNPs have no negative effects on protein structure and function

- Other SNPs have negative effect on protein, the protein might be non-function or the Active of this protein is low, or maybe indirect increase the chance that the individual will have Disease.

From multiple population Scientists found more than 300 million SNPs in all humans in all populations.

- If we compare the genome of individuals, we will find that between 4-5 Million sites of variation between individuals.

There are some techniques could be used to determine all the SNPs within genome.

- Microarray (genes ship)

Is used for determining all the different types of SNPs might found in specific Genome.

- For some diseases before describing for example drugs for treatment Disease the patient must test their genome for certain SNPs and based on these SNPs doctor will determine which type of drugs give to patient and the dose of the drug.

- Pharmacogenomics is customized medicine Tailor-designing drug therapy and t treatment strategies based on genetic profile of patient.

- Designing drugs based on the Genetic profile of a patient, by doing micro array analysis and then design drugs against genes that are mutated for an Individual patient.

- Metabolomics: involves determining all types of small molecules inside the body and these small molecules are of the metabolic reaction that are happening inside our cells.

For example, we could look at the concentration hundreds of molecules in blood sample at same time and based on concentration of These molecules, Glucose, ATP, cholesterol, and other molecules that found in tissue sample we could determine individual healthy or maybe he or she might have specific type of Disease.

Protein, lipids, carbohydrates, and nucleic acid large molecules not small molecules.

Genomics: is study whole DNA collection in certain organism

Proteomics: is study all Characteristics of proteins in an organism

Transcriptomics: studying all collections of m-RNA in all cells.

- Chemotherapy: is used to kill cancer cells but this chemical that cant distinguishes between normal cells and cancer cells.

- the patients who undergo Chemotherapy suffer many side effects.

- The chemotherapy is powerful effect in kill cancer cells, but also kill normal cells by using nanotechnology, we can solve this problem

- Nano-biotechnology intersection between Nano technology and biotechnology.

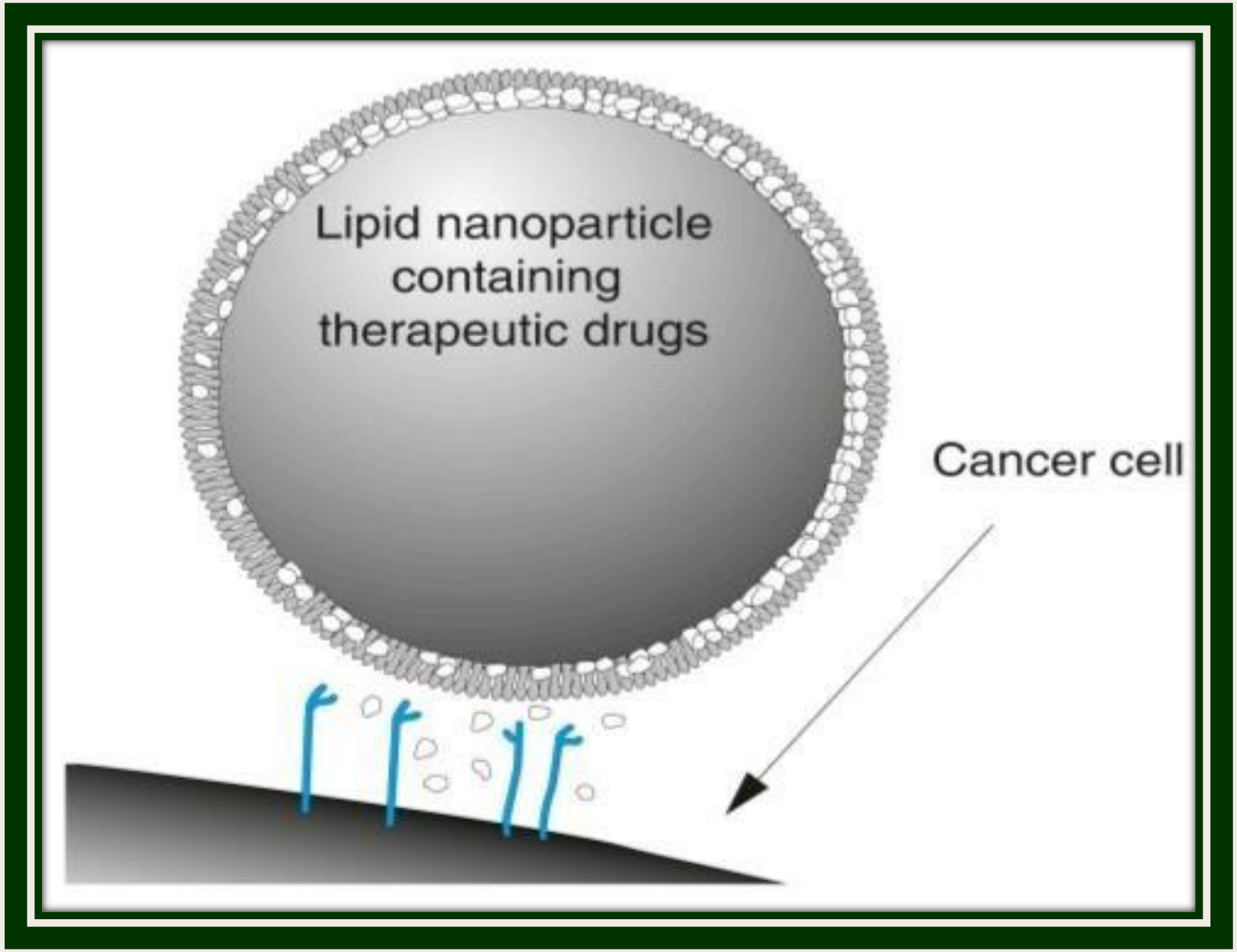
- Nano: we talk about molecules in scale Nano meter, there have scale or size very small.

- One application of Nano-biotechnology is used very small lipid Nano particles to derive Chemotherapy drugs.

- These Nano particles might have receptors or proteins at surfaces that can recognize only receptors on surface of cancer cells.

- This allow more target delivery of drugs, normal cell will be intact, because the drugs only present inside the Nano particles.

- Cancer cells affect by drugs, normal cells not affected.


Lipid nanoparticle
containing
therapeutic drugs
Cancer cell

Gene therapy

- Replacing or adding normal copy of the gene inside the cell to replace or add the normal gene Instead of the Defective gene we need a something that can carry the gene and deliver to inside the cell, we call it “vector” or we can use Another technique not based on vector to do gene editing or gene therapy the most popular example is” Crisper Cas 9”.

Small interfering RNA (SIRNA)

New technology currently use to treat some diseases, by gene silencing, Silence the genes that involved in Diseases progression the first RNAI drugs was approved 2018 drug called onpattro (patisiran), and this drug approve treatment type of medical conditions In 2019 was developed Another siRNA called givlaari (givosiran) siRNA--- small RNA molecules they can bind Complementary sequence to certain mRNA molecule sirna can do

Silencing

1-blokage of translation

2-mRNA degradation

- **Stem cell technology**

-Stem cells are immature cells that grow and divide to produce different cell types

- We have two major type of stem cells

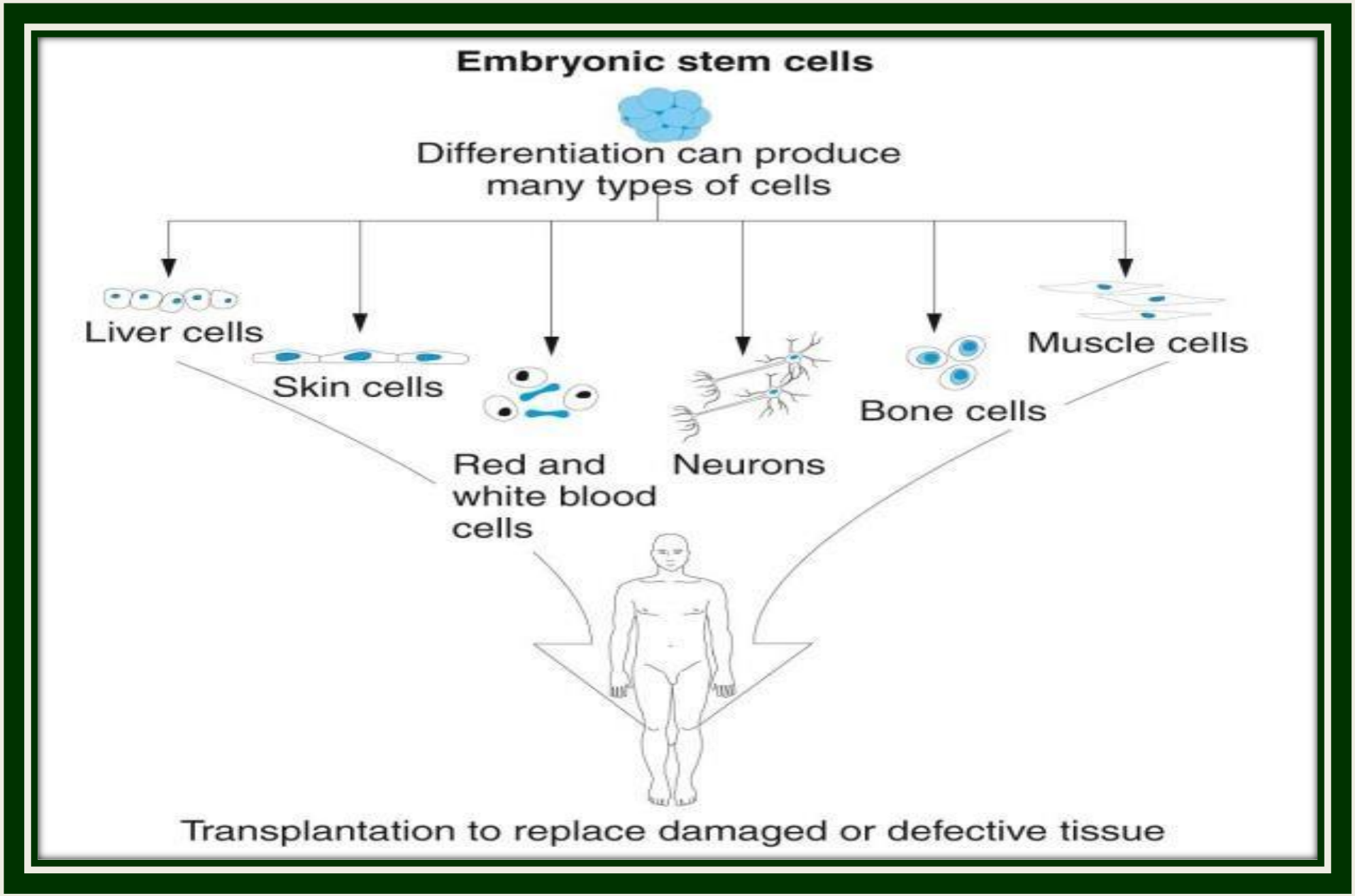
1. adult stem cell
2. embryonic stem cell.
3.

- could be used to grow organ replace

–Most stem cells are from embryos called embryonic stem cells (ESCs) but they are controversial since the process involves death of an embryo

-Some stem cells are from adult cells (ASCs)

- Either type of stem cell can be coaxed to grow into cells of interest to replace damaged tissue or failing organs (liver, pancreas, retina)


Embryonic stem cells
Differentiation can produce many types of cells
Liver cells
Skin cells
Red and white blood cells
Neurons
Bone cells
Muscle cells
Transplantation to replace damaged or defective tissue

- How will medical biotechnology change our lives in the years ahead? Regenerative medicine.

- Genetically modifying stem cells of patients to treat genetic disease conditions.

- In future scientists will be able to…

1. Isolate adult stem cells from a patient with a genetic disorder

2. Genetically manipulate these cells by gene therapy approaches

3. Reinsert the cells into the same patient to help treat their genetic disease.
   Regenerative medicine (Using stem cell to treat a genetic disease).

   The idea in the previous slide is if someone is suffering genetic disease because mutant gene, we could Obtend stem cells from patient and introduce.

   normal gene to these stem cells and back these stem cells into the body

   of patient in order for these stem cells will make new cells and these new cells have normal gene.

TABLE 1.3 **Top Five Biotechnology Companies and Top Five Pharmaceutical Companies by Revenue in 2017**

Biotech Companies	Revenue (Billions)
Amgen	$129
Gilead Sciences	$103
Novo Nordisk	$ 96
Celgene	$ 77
Biogen	$ 66
Pharma Companies	**Revenue (Billions)**
Johnson & Johnson	$379
Novartis	$216
Pfizer	$208
Roche	$199
AbbVie	$153

Biotechnology companies: - only produce biotechnology drugs.

pharma companies: -produce traditional drugs also they developed biotechnology drugs.

new Consider as biotechnology companies because they produce. traditional drugs but also produce biotechnology drugs.

1- for example, pifzer produce COVID-19 vaccine.

2- jhonson and jhonson produce many vaccines.

The Biotechnology Workforce

- How does a biotech company start?

Generally created as a startup company with few employees backed by venture capital investments (derived from financial institutions and private donors called angel investors)

Why invest as an angel donor? To ultimately have

company ownership in exchange for donating funds – get rich if company is successful! Takes 10 years to get a product to market at a big cost!

- Eventually startups are bought out by bigger established companies

Bringing drug close to market = value to the company – File for initial public offering (IPO) stock

- The first biotechnology company is Genenetic.

- This company is American company was found in 1976 by scientist called Herbort Boyer

- the first biotechnology product produce by this company was Humulin(recombinant insulin) .