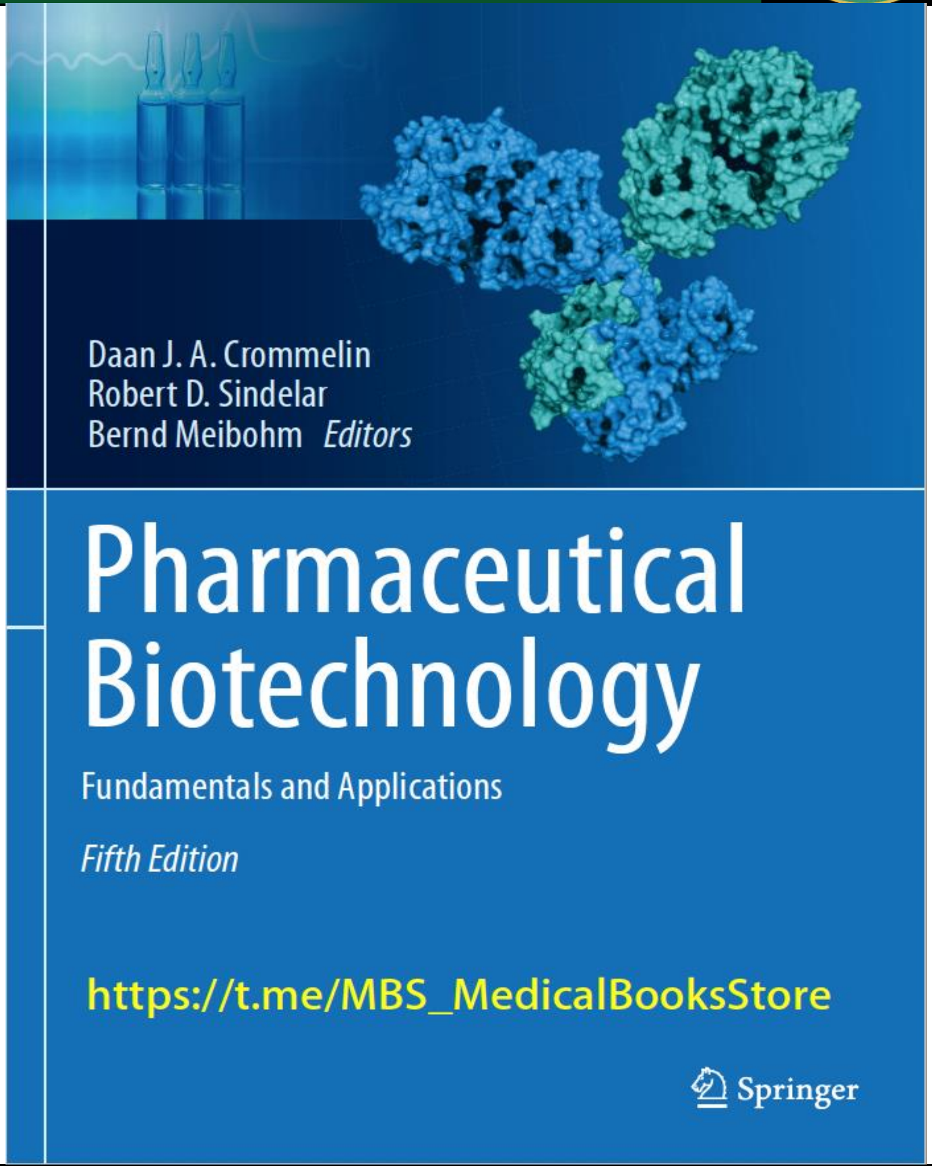
Introduction to Pharmaceutical Biotechnology

Syllabus

- **Required Textbook**
- **Course meet** Thursdays at 11:30-12:30 pm// room BC 01
- **Course evaluation**: Mid term 25%

  Atten. + Activities 5%

  Final exam 70%
- **Course Goals**:
- Students will learn the basics about biotechnology techniques.
- Students will learn pharmaceutical consideration in formulation of biopharmaceutical products.
- Student will learn basic processes required to manufacture safe and effective biopharmaceutical products.



Pharmaceutical biotechnology

- **Biotechnology** is the technology based on biology.
- **Pharmaceutical biotechnology** can be defined as the **science** dealing with the **development, production** and **dispensing** of biological drugs.
- The United Nations Convention on Biological Diversity **defines** biotechnology as any technological application that uses biological systems, living organisms, or their derivatives, to make or modify products or processes for specific use.
- The **aim** of pharmaceutical biotechnology is to **design**, **produce** drugs that are **adapted** to each person's genetic build, which can give the maximum therapeutic effect.

Biopharmaceuticals

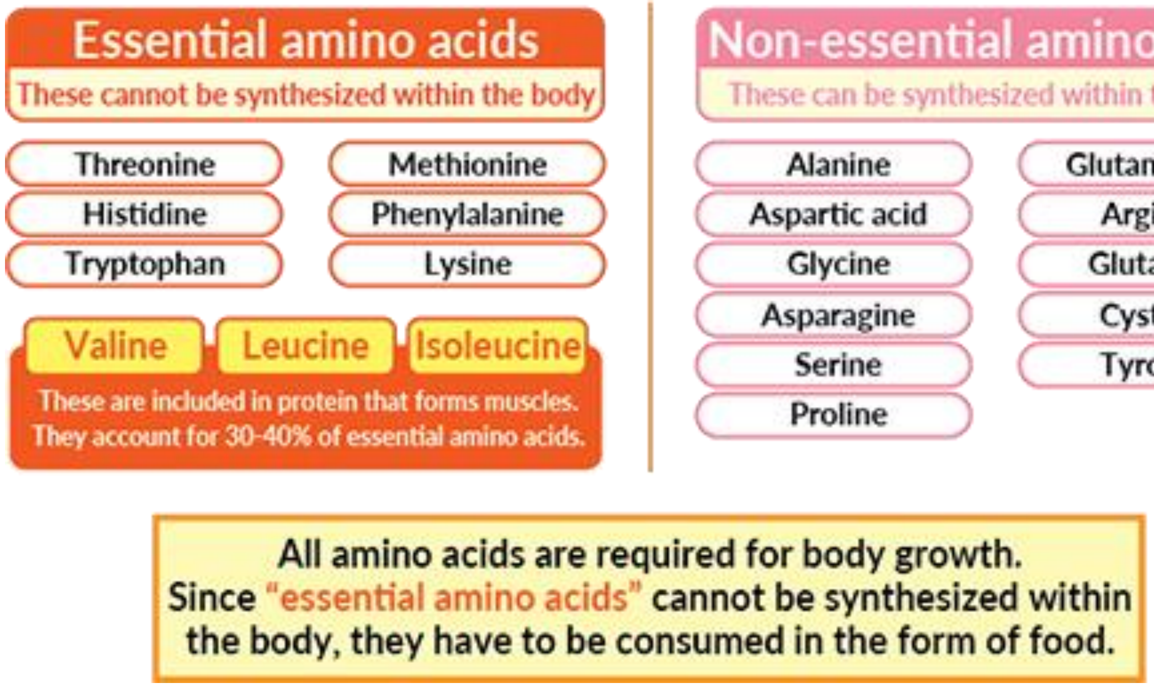
- Until now biopharmaceuticals are **primarily proteins**, but therapeutic DNA or RNA based molecules (think about gene therapy products, DNA vaccines, and RNA interference-based products) may soon become part of our therapeutic arsenal.
- One example is **mRNA vaccine** used against covid-19 which act by introducing a piece of virus RNA into human cells that will produce virus protein which will activate the human immune system to produce antibody against that virus.
- Other example is the Zolgensma® (onasemnogen abeparvovec) which replaced the missing gene (survival motor neuron 1(SMA1)) which responsible for production of a necessary protein the survival motor neuron protein which is needed for motor neuron cell survival.

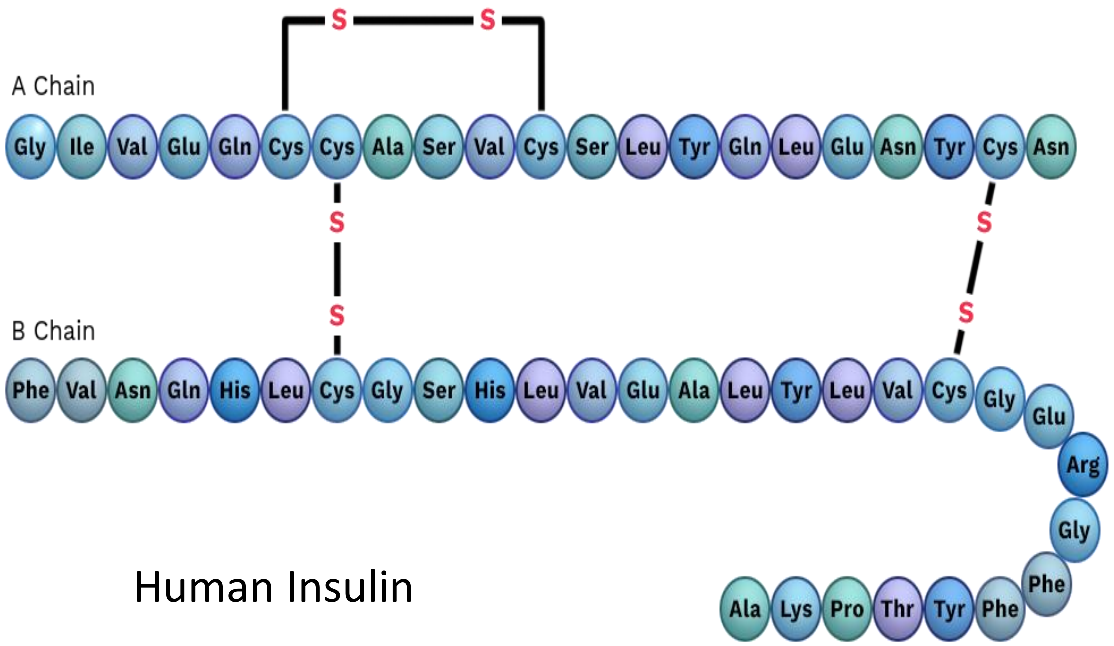
History

- **Proteins** are already used for more than 100 years to treat or prevent diseases in humans. It started in the early 1890s with "serum therapy" for the treatment of diphtheria and tetanus by Emile von Behring and others.
- A next big step in the development of therapeutic proteins was the use of purified **insulin isolated** from **pig or cow pancreas** for the treatment of diabetes type I in the early 1920s by Banting and Best.
- Thanks to advances in biotechnology (e.g., recombinant DNA technology, hybridoma technology), we have moved almost entirely away from animal-derived proteins to proteins with the complete human amino acid sequence.
- **Such therapeutic human proteins are less likely to cause side effects and to elicit immune responses.**
- In **1982, human insulin** became the first recombinant human protein approved for sale in the USA (produced by Eli Lilly)

Amino Acids

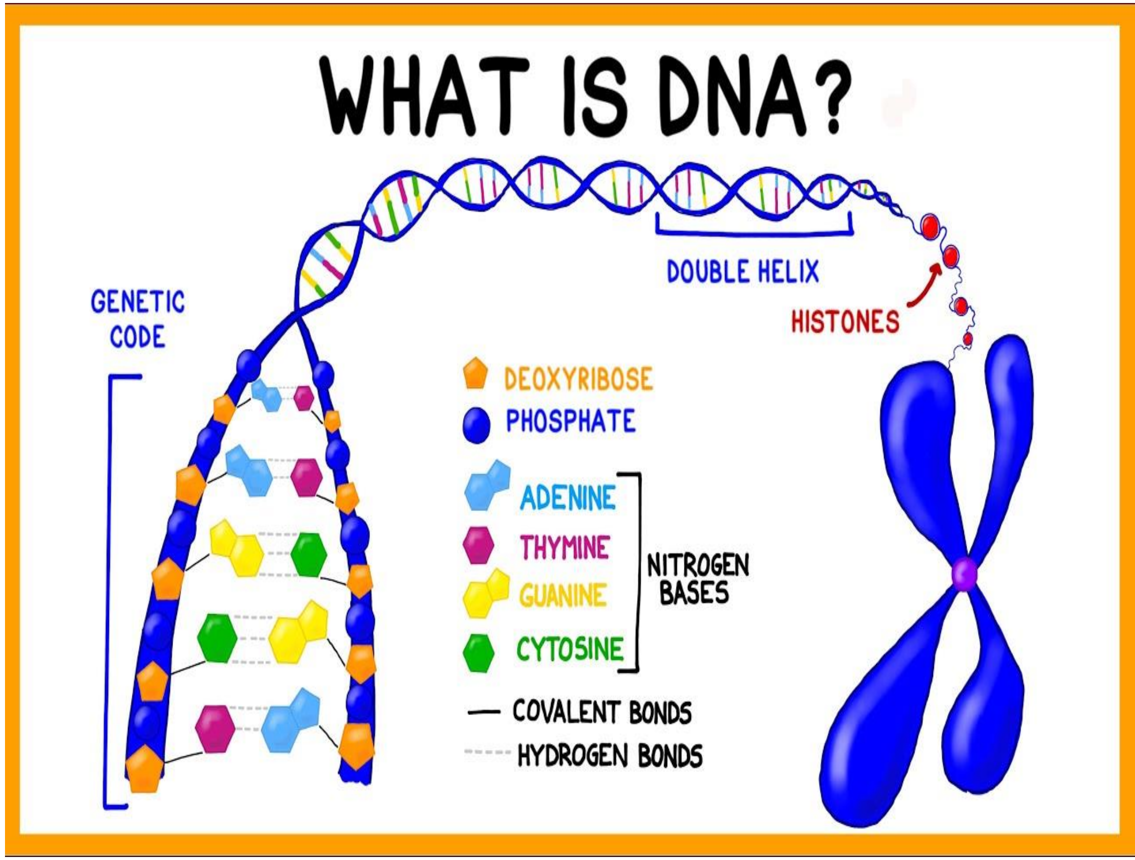
- **Amino Acid** : The building blocks of proteins.
- The unique sequence of amino acids in a chain defines the character of a protein molecule.





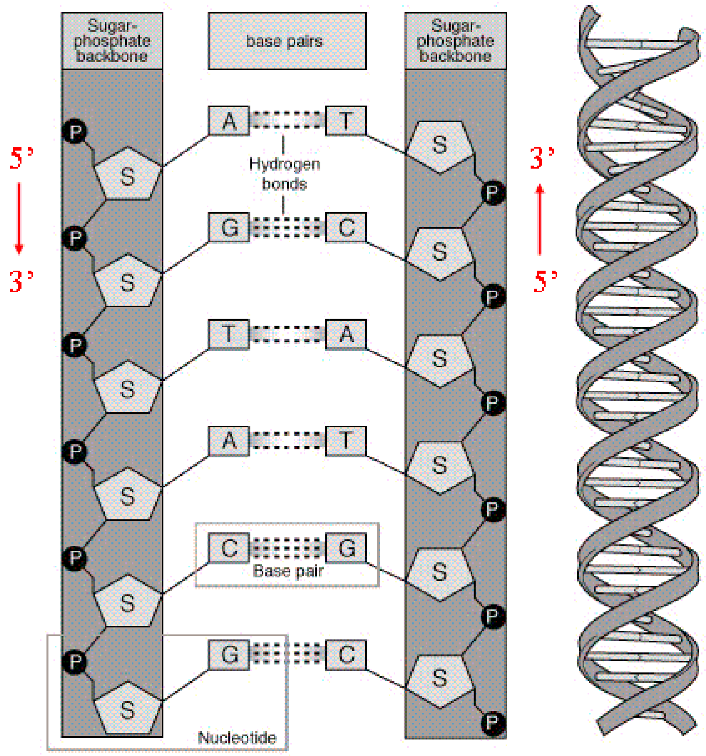
Basics of Biotechnology
DNA (Deoxyribonucleic acid)

- **DNA** is a double stranded structure takes the shape of a **double helix** (like a ladder that has been twisted).
- It consists of a **deoxy ribose** sugar that attached to a **phosphate** backbone and a pairs of nitrogen bases of (Thymine and Adenine or uracil in RNA) and (Guanin and Cytosine).
- DNA is organized into chromosomes which are 22 pairs (44 autosomes) and one pair of sex chromosomes.
- **Genes** are pieces of DNA, and most genes contain the information for making a **specific** protein.



Basics of Biotechnology
DNA (Deoxyribonucleic acid)

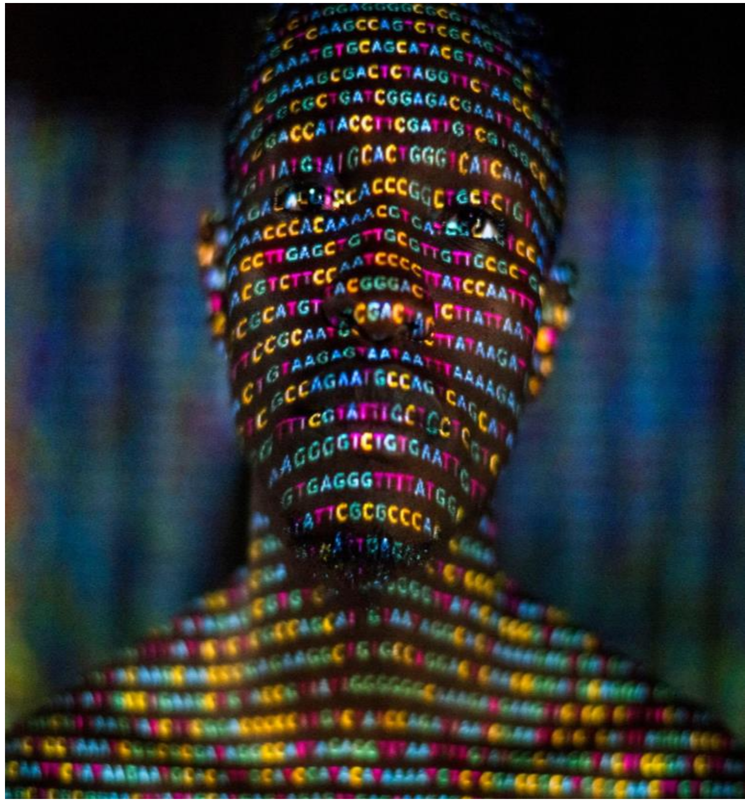
- The structure of the DNA is antiparallel in which the second strands is parallel to the first one but are **oriented is opposite directions**.
- Each strand of DNA is read in a specific direction from its 5′ (five prime) end to its 3′ (three prime) end.
- The 5' and 3' designations refer to the number of carbon atom in a deoxyribose sugar molecule to which a phosphate group bonds.
- DNA sequences in these databases are always given from the **5′ end to the 3**′ end.
- Protein sequences is given from the **amino- to the carboxy**-terminal end.



Antiparallel strands

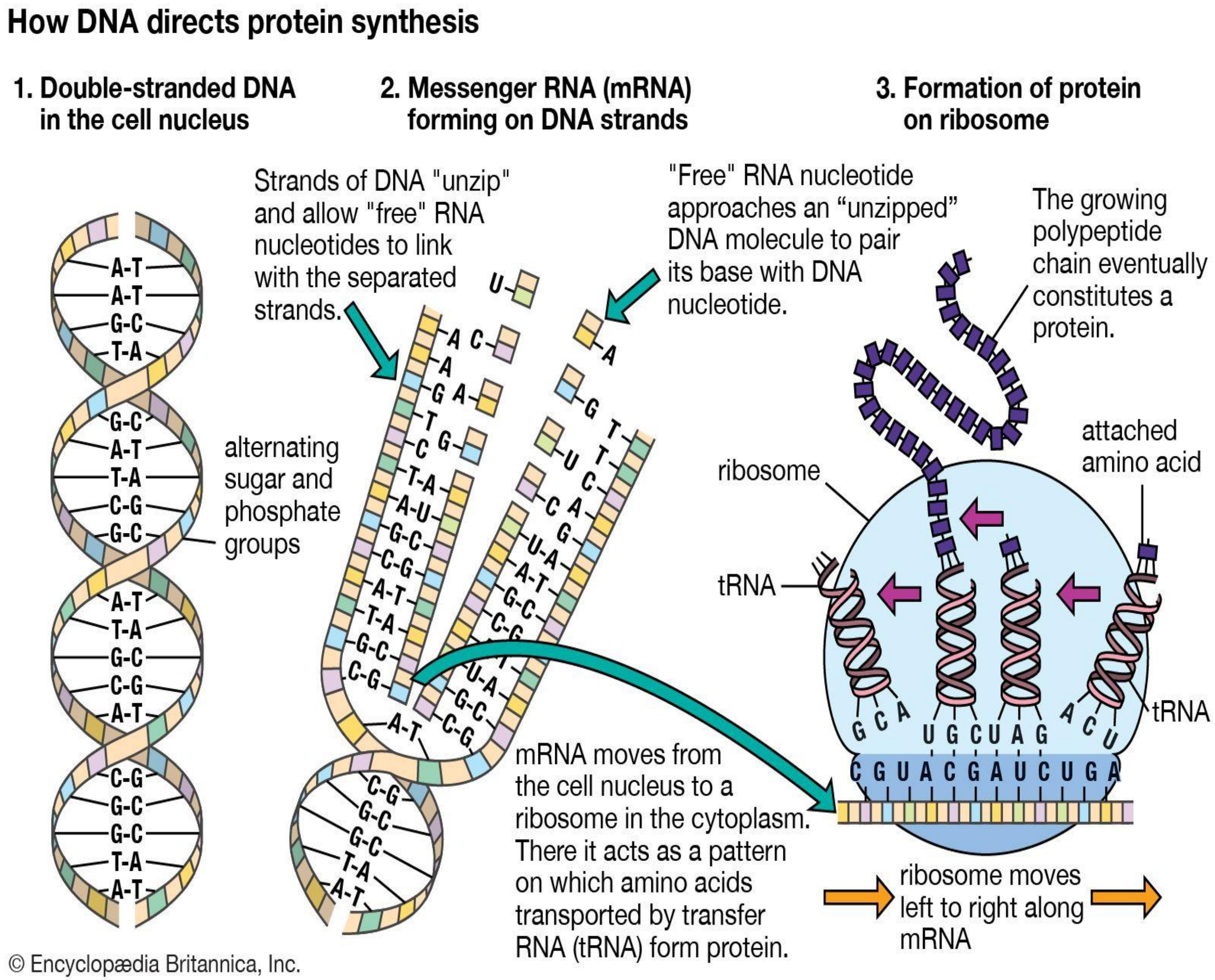
Basics of Biotechnology
What Does DNA Do?

- The discovery of the DNA double-helical structure in **1953** and genome sequencing has advanced the accumulation of biological insights.
- The genomic DNA of any organisms is constantly under the influence of **various intrinsic and extrinsic agents**.
- These agents sometimes lead to the generation of thousands of **genetic mutations**, resulting in nonfunctional protein production leading to genetic disorders.
- DNA in nucleus control protein synthesis by process of **transcription and translation**.



Protein Synthesis

- DNA in nucleus control protein synthesis by process of transcription and translation.
- DNA double helix unwind and allow encoding of messenger RNA (mRNA) which transfer the information to ribosome in the cytoplasm.
- The ribosomal RNA (rRNA) in the ribosome translates (read) the codes in mRNA and transfer RNA (tRNA) help in transferring amino acids corresponding the code and amino acid chain starts growing which will them form a protein.



How Are Biotechnology Medicines Made?

- The manufacturing process consists of the following four main steps:

1. Producing the **master cell** line containing the **gene that makes** the desired protein.
2. **Growing** large numbers of cells that produce the protein.
3. **Isolating** and purifying the protein.
4. **Preparing** the biologic for use by patients.

- Some biologics can be made using common **bacteria**, such as E coli.
- Others require **cell lines** taken from mammals, such as hamsters. This is **because** many proteins have structural features that only mammalian cells can create.
- For example, certain proteins have sugar molecules attached to them, and they don't function properly if those sugar molecules are not present in the correct pattern.

Genetic Engineering

- **Genetic engineering** is the cornerstone of modern biotechnology. It is based on scientific **tools**, developed in recent decades, that enable researchers to:

1. **Identify** the gene that produces the protein of interest.
2. **Cut the DNA** sequence that contains the gene from a sample of DNA.
3. Place the gene **into a vector**, such as a **plasmid** or bacteriophage.
4. Use the vector to **carry the gene** into the DNA of the host cells, such as Escherichia coli (E coli) or mammalian cells grown in culture.
5. **Induce** the cells to activate the gene and produce the desired protein.
6. **Extract** and purify the protein for therapeutic use.

Genetic Engineering

- When segments of DNA are cut and pasted together to form new sequences, the result is known as **recombinant DNA**.
- When recombinant DNA is inserted into cells, the **cells use** this modified blueprint and **their own** cellular machinery to make the **protein encoded** by the recombinant DNA.
- Cells that have recombinant DNA are known as **genetically modified or transgenic cells**.
- Genetic engineering allows scientists to manufacture molecules that are too complex to make with chemistry.
- This has resulted in important new types of therapies, such as therapeutic proteins.
- Therapeutic proteins are used to replace or augment a patient's naturally occurring proteins, especially when levels of the natural protein are low or absent due to disease.

Genetic Engineering

- **Monoclonal antibodies** are a specific **class of therapeutic proteins** designed to target foreign invaders (or cancer cells) by the immune system.
- Therapeutic antibodies can target and inhibit proteins and other molecules in the body that contribute to disease.

- **Vaccines** stimulate the immune system to provide protection, mainly against viruses. Traditional vaccines use weakened or killed viruses to prime the body to attack the real virus. Biotechnology can create recombinant vaccines based on viral genes.

Most common Biopharmaceuticals

- **Hormones** (insulin, glucagon, growth hormone, gonadotrophins).
- **Monoclonal** antibodies (mAbs) (**Humira**® (adalimumab) , **Ritoxan**® (Rituximab), **Avastin**® (bevacizumab), **Actemra**® (tocilizumab).
- **Blood factors** (Factor VIII and Factor IX).
- **Thrombolytic** agents (tissue plasminogen activator) (Activase® Alteplase)
- **Hematopoietic** growth factors (Erythropoietin, colony stimulating factors)
- **Interferons** (Interferons-α, -β, -γ)
- **Interleukin**-based products (Interleukin-2)
- **Vaccines** (Hepatitis B surface antigen)
- Additional products (tumor necrosis factor)