UNIT - IV

☆ Nucleic acid Metabolism and genetic information transfer :-

- Nucleic acid (DNA and RNA) are formed by the polymerisation of nucleotide subunits.
- Nucleotides are made up of a ribose sugar, a nitrogenous base, and phosphate group's.
- Deoxyribonucleic acid (DNA) and Ribonucleic acid (RNA) are the two types of nucleic acids that act as Source and Carrier of genetic information.

Structural Components of Nucleic Acids :-

Nucleic acids are polynucleotides (i.e polymers of nucleotides) bounded by 3' and 5' phosphate linkage. Thus nucleic acid consists of the monomeric units nucleotides.

- A nucleotide is made up of a nitrogenous base, a pentose Sugar, and a phosphate:

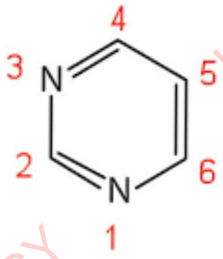
1. Pentose Sugar : It is the Sugar part of a nucleotide. In RNA pentose sugar is ribose, while in DNA deoxyribose Sugar.

2. phosphate Groups :-
They are found attached to the Sugar of a nucleotide The nucleotide is said to be a Monophosphate, diphosphate or triphosphate based on the presence of one, two, or three phosphate groups, respectively.

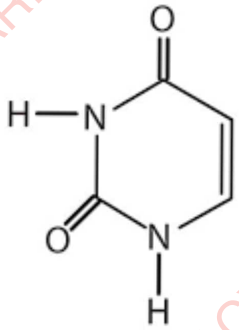
3. Nitrogenous Base:-

In DNA adenine, guanine, Cytosine and thymine nitrogenous agent are found: While in RNA thymine is replaced with Uracil.

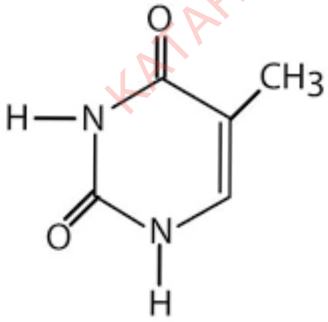
Structure of Nucleotide :-



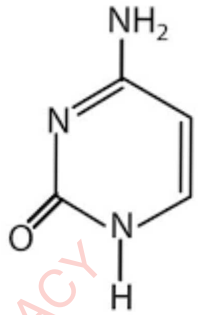
Pyrimidine



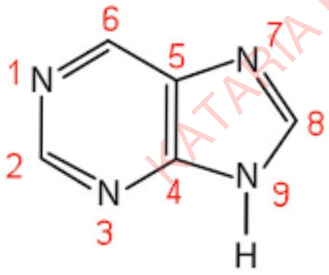
Uracil (U)
RNA only



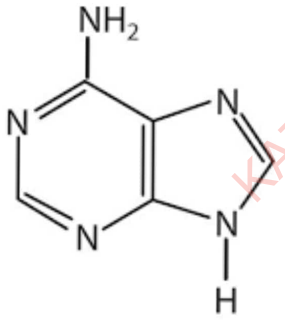
Thymine (T)
DNA only



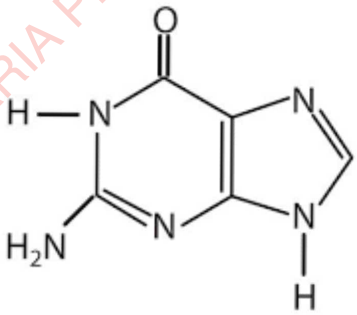
Cytosine (C)
both DNA and RNA



Purine



Adenine (A)



Guanine (G)

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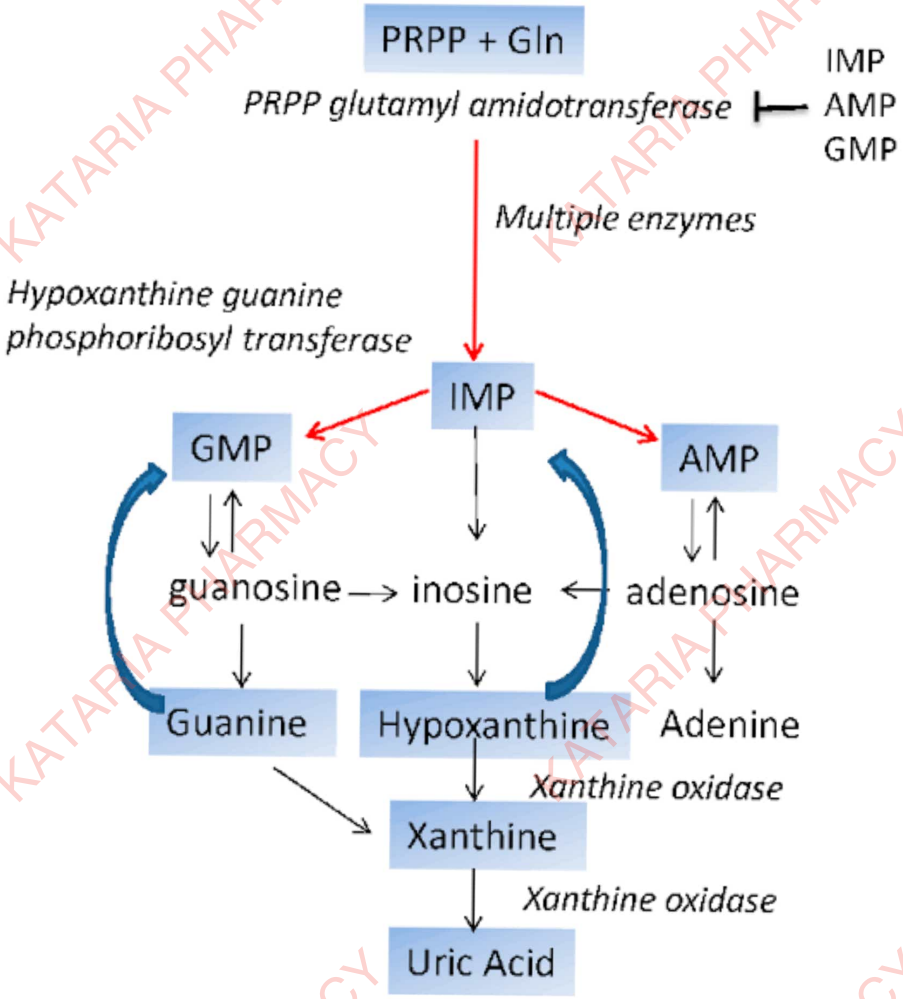
☆ Biosynthesis of purine :-

The two methods for the biosynthesis of purins are :

1. De Novo pathway : De novo means from the beginning.
2. Salvage pathway : In this pathway nucleotide are synthesised from the intermediate of the degradative pathway.

De Novo Synthesis of purine :-

The purine nucleotides of nucleic acids guansine-5-monophosphate (Gmp-guanylate) and adenosine-5-monophosphate (Amp-adenylate) have a purine base adenine and guanine respectively.



✱ Biosynthesis of pyrimidine :-

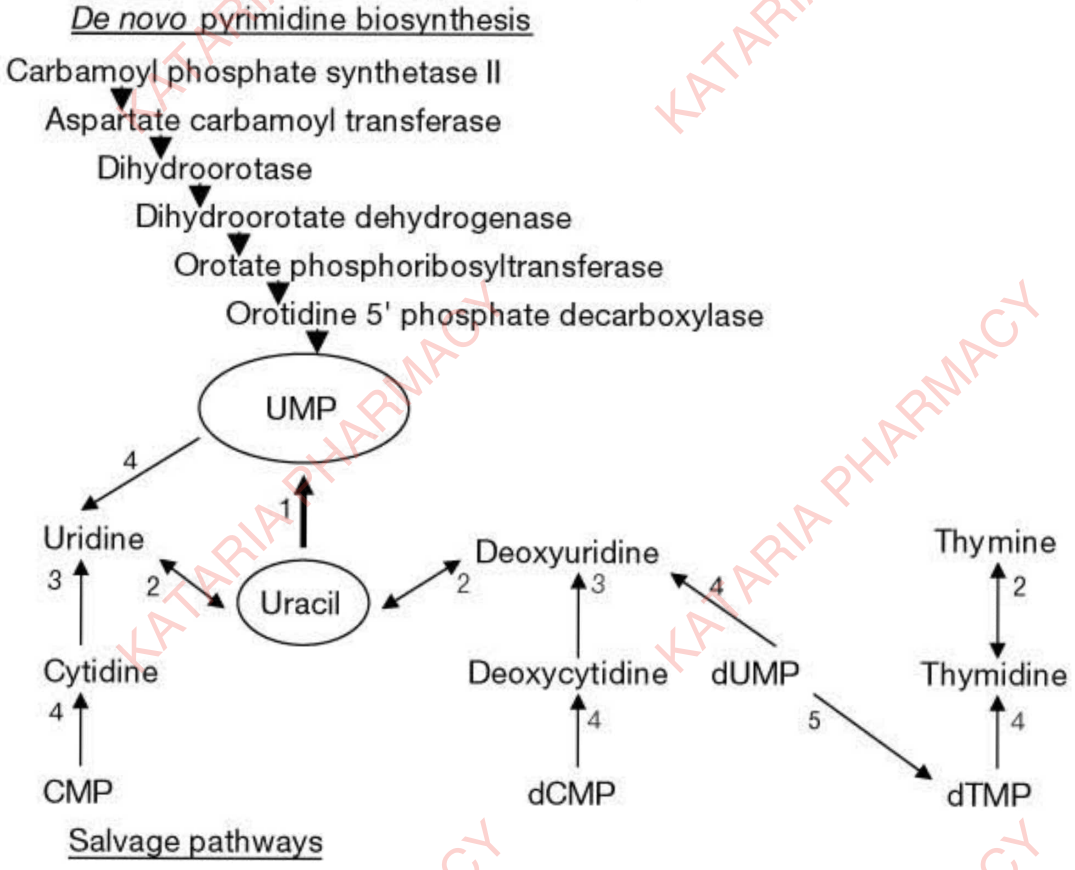
Biosynthesis of pyrimidine occur by -

1. De novo pathway : De novo means begining.
2. Salvage pathway : Describe nucleotide synthesis by degradative pathway intermediate.

De novo pathway of pyrimidine Synthesis :-

In de novo Synthesis of pyrimidine, a 6-membered pyrimidine ring is formed, which attaches itself to ribose phosphate to form PRPP. Given below are the pyrimidine nucleotide

1. Cytidine Monophosphate (CMP)
2. Uridine monophosphate (UMP)
3. Thymidine Monophosphate (TMP)



✱ Hyperuricemia :-

A Condition of excess uric acid in the blood is termed as hyperuricemia.

- Uric acid passes through the liver and reaches the blood stream.
- Maximum amount of uric acid is excreated in the form of urine (i.e removed from the body through Urinary System) or as Intestinal excreation.

Causes :-

- primary Hyperuricemia (Increase uric ~~acid~~ acid levels due to purine)
- Increas purine Consumption
- Renal insufficiency
- Malnutrition
- Hepatic failure (Reduction in uric acid biosynthesis.

Symptoms :-

- often asymptomatic
- Can lead to gout, characterized by Severe joint pain, redness, and swelling.
- Associated with kidney stones and Chronic kidney disease.

Diagnosis :-

- Blood test to measure serum uric acid levels
- Joint fluid analysis if gout is Suspected.
- kidney function test.

Treatment :-

- Lifestyle Changes : Low-purine diet, weight Management, reduced alcohol intake, and increased hydration.
- Medication :- Allopurinol, febuxostat (to reduce uric acid production), and probenecid (to increase uric acid excreation).

☆ Gout disease :-

- Gout is a type of arthritis characterized by sudden, severe attacks of pain, redness, and tenderness in joints often the joint at the base of the big toe.
- It occurs due to the accumulation of urate crystals in the joint, causing inflamation and intense pain.

Causes :

1. uric acid : Gout is caused by high level of uric acid in the blood.
2. Diet :- Foods rich in purines, such as red meat, seafood and alcohol, specially beer, can increase uric acid level.
3. Genetics : Family history of gout can ↑ the risk.
4. Medical Condition : Conditions like obesity, untreated high blood pressure, diabetes, & heart and kidney disease.
5. Medications :- Certain medications like diuretics and low dose aspirin, can ~~rise~~ raise uric acid levels

Symptoms:-

- Intense Joint pain: In Ankels, knees, elbows, wrists and fingers.
- Inflammation and Redness:-
- Limited Range of Motion

Diagnosis:-

- Joint Fluid test.
- Blood test: Level of uric acid in blood
- Imaging test: x-ray, ultrasound and CT scan

Treatment:-

- Medications: Nonsteroidal anti-inflammatory drug (NSAIDs) Colchicine and Corticosteroids to Manage pain and inflammation.
- Long-term medications like: Allopurinol and febuxostat reduce uric acid Levels.
- Lifestyle Change:-
  - Dietary adjustments to avoid high purine foods.
  - Reducing alcohol intake
  - Maintaining a healthy weight
  - Staying hydrated

☆ Organization of Mammalian genome:-

The organization of the mammalian genome is complex and highly structured, allowing for the regulation of gene expression, DNA replication and repair.

1. Chromosomes:-

Structure: The genome is divided into chromosomes, which are long, linear DNA molecules.

Number: Mammals typically have a diploid set of chromosomes, with each species having a specific number.
For Example, humans have 46 chromosomes (23 pair)

Types:- chromosomes are categorized into autosomes and sex chromosomes (X and Y).

2. DNA Molecule:-

Nucleotides: The basic building blocks of DNA are nucleotides, which consists of a phosphate group, a sugar molecule (deoxyribose) and a nitrogenous base (adenine, thymine, cytosine, or guanine).

Double helix: Two complementary strands of DNA wind around each other to form a double helix. The strands are held together by hydrogen bonds between complementary bases (A-T and C-G)

3. Genomic Regions:-

Genes:- Segments of DNA that code for proteins or functional RNAs. They consist of exons (coding regions) and introns (non-coding regions)

Regulatory Elements:-
Include promoters, enhancers, silencers, and insulators that control gene expression.

Non-coding DNA: Includes various types of non-coding RNAs (e.g tRNA, rRNA, mRNA) and repetitive elements such as transposons and satellite DNA.

④ Replication and Repair:-

Origins of Replications: specific sequences where DNA replication begins.

Telomeres: protective end caps of chromosomes that prevent degradation and fusion.

DNA Repair Mechanism: system to fix DNA damage, including base excision repair, nucleotide excision repair, and double strand break repair.

✱ Structure of DNA and their functions :-

DNA, or deoxyribonucleic acid, is the Molecule that Carries the genetic instructions used in the growth, development functioning and reproduction of all known living organism, and Many viruses.

- DNA is made up of monomeric units called Nucleotides.
- A DNA Molecule has Four Types of nucleotides, each having different nitrogenous base.

1. Adenine (A) } purine base
2. Guanine (G) }
3. Cytosine (C) } pyrimidine
4. Thymine (T) }

Structure of DNA :-

- **Double Helix**: The two strands of DNA double helix Coil around each other forming a helical structure. The base sequences of both the strands are Complementary to each other due to the presence of A-T, G-C base pairing.
- **Antiparallel Strands**: Both the strands running in Antiparallel direction are linked via hydrogen bonds present between the bases.
  - The two DNA strands run in opposite directions, with one strand running 5' to 3' and the other running 3' to 5' which allows for Complementary base pairing.

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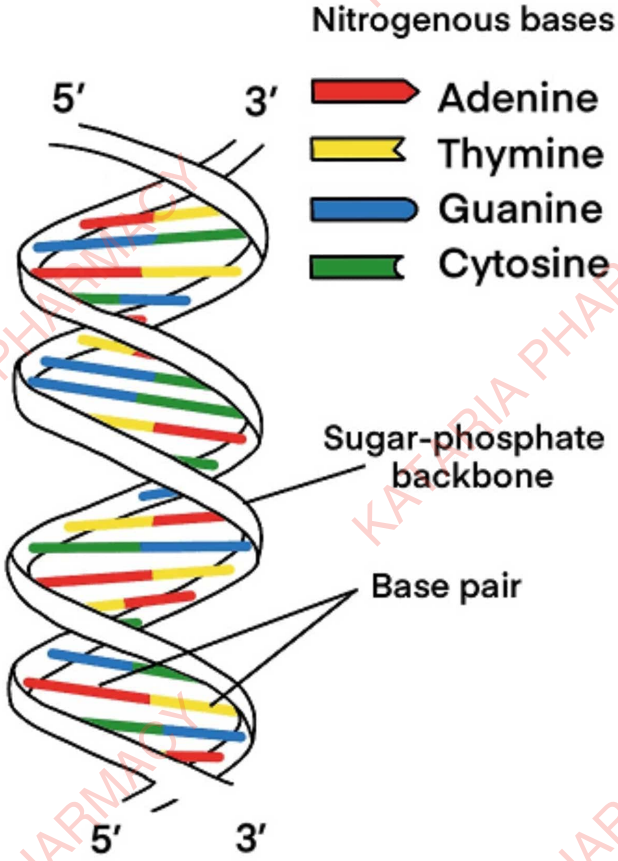


Functions of DNA :-

- DNA in living beings serves as a genetic material.
- DNA carry information specific to an individual.
- DNA molecule provide genetic information which implies to characteristic feature of living organism (e.g. Colour of the skin and eye, height, Intelligence etc.)
- Information on all cellular protein synthesis is carried by the DNA (by carrier 'Gene'.)
- DNA molecule has the capability of replication (i.e Can synthesize another copy of DNA) and transcription (i.e Can synthesise RNA molecule).

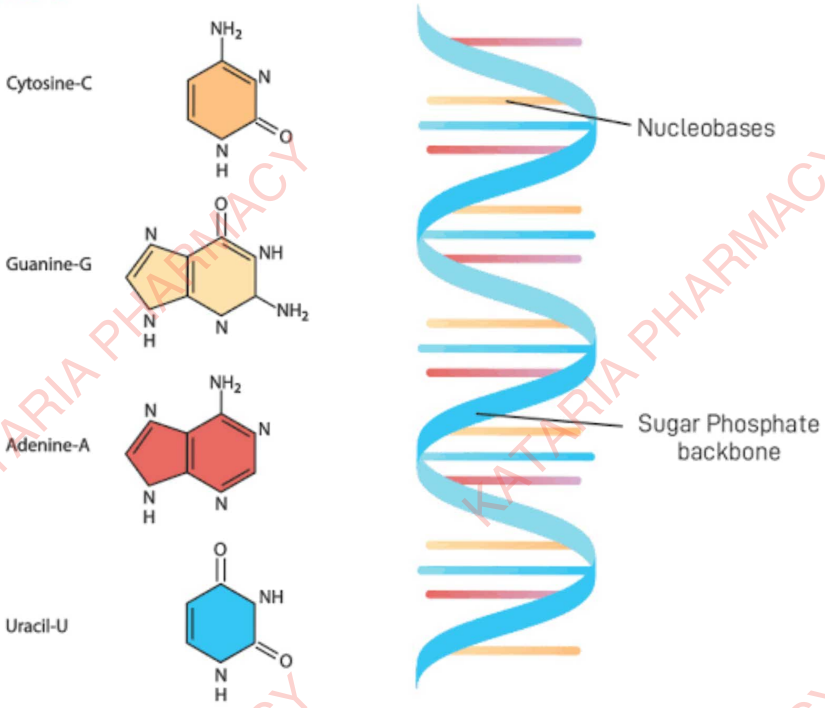
✯ Structure of RNA and its function :-

- Ribonucleic acid in a cell is present in amount 10 times more than that of DNA, because RNA performs a large number of cellular functions.
- RNA are three type - ① Ribosomal RNA (r-RNA)
  ② Transfer RNA (t-RNA)
  ③ Messenger RNA (m-RNA

- The structure of RNA is much similar to that of DNA. Both are chains of polynucleotides arranged linearly.

- However, RNA differs from DNA as in RNA the sugar present is ribose (instead of deoxyribose). The nitrogenous T-base of DNA is replaced with U (uracil), and some viruses have single-stranded RNA.

#Structure of RNA :-



Functions of RNA :-

- RNA is present in both prokaryotic and eukaryotic cells along with DNA.
- RNA molecule is less stable than DNA molecule.
- In some organism RNA molecules also carry the genetic information eg. RNA is the genetic material in certain viruses.
- The t-RNA transports specific amino acids to the ribosomes which decode the genetic information in the m-RNA in such a way that the proper amino acid is inserted in sequence of protein synthesised.
- The r-RNA provides the structural framework to the ribosome.
- The m-RNA carries genetic information from the nucleus to the ribosomes present in the cell cytoplasm.

★ DNA replication :-

- DNA replication means the mechnism of copying DNA molecules.
- This process is essential for cell division and is critical for growth, development, and ~~the~~ repair in living organisms.

process of DNA Replication :-

1. Initiation of Replication: DNA synthesis initiates ata site known as origin of replication or oric site.
   - A specific protein dnaA binds with oric site and replication is initiation by the separation of two complementary DNA strands.

2. Formation of Replication Bubbles:
   Separation of DNA strands occurs at the replication site to form a bubble.

3. RNA primer as platform for DNA Synthesis: A short fragment of RNA acts as a primer for DNA synthesis

4. Elongation :-
   DNA polymerase: DNA polymerases add nucleotides to the 3' end of the RNA primer, synthesizing a new strand of DNA complementary to the template strand.

   Leading and Lagging Strands
   DNA Synthesis is continuous on the leading strand, which runs in the 5' to 3' direction. On the Lagging strands, which runs in the opposite direction (3' to 5'), Synthesis occurs

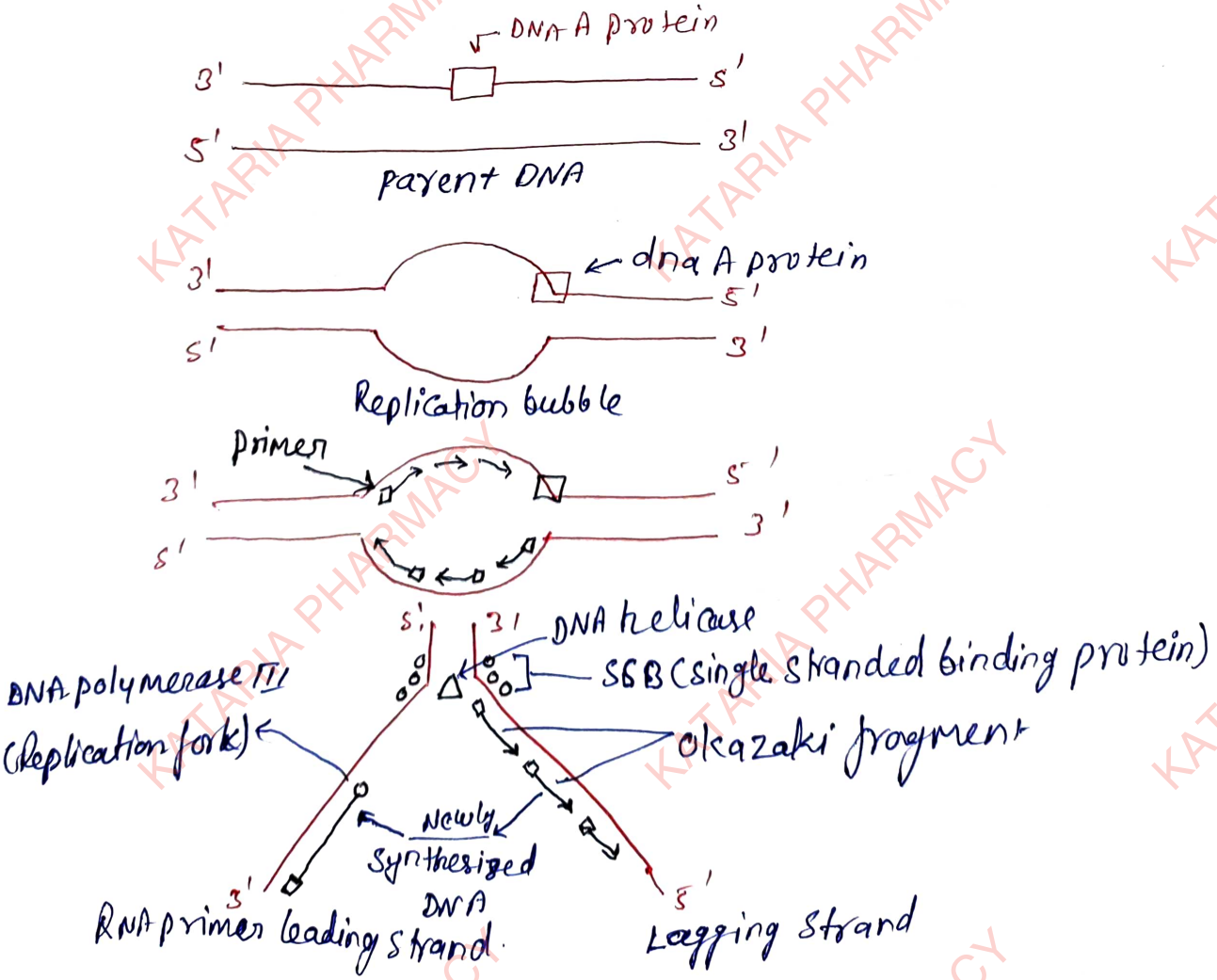
in short segments called okazaki fragments.

5. Ligation:-

- DNA ligase: The enzyme DNA ligase seals the nicks between the newly synthesised DNA fragments on the lagging, forming a continuous DNA molecule.

⑥ Termination:-

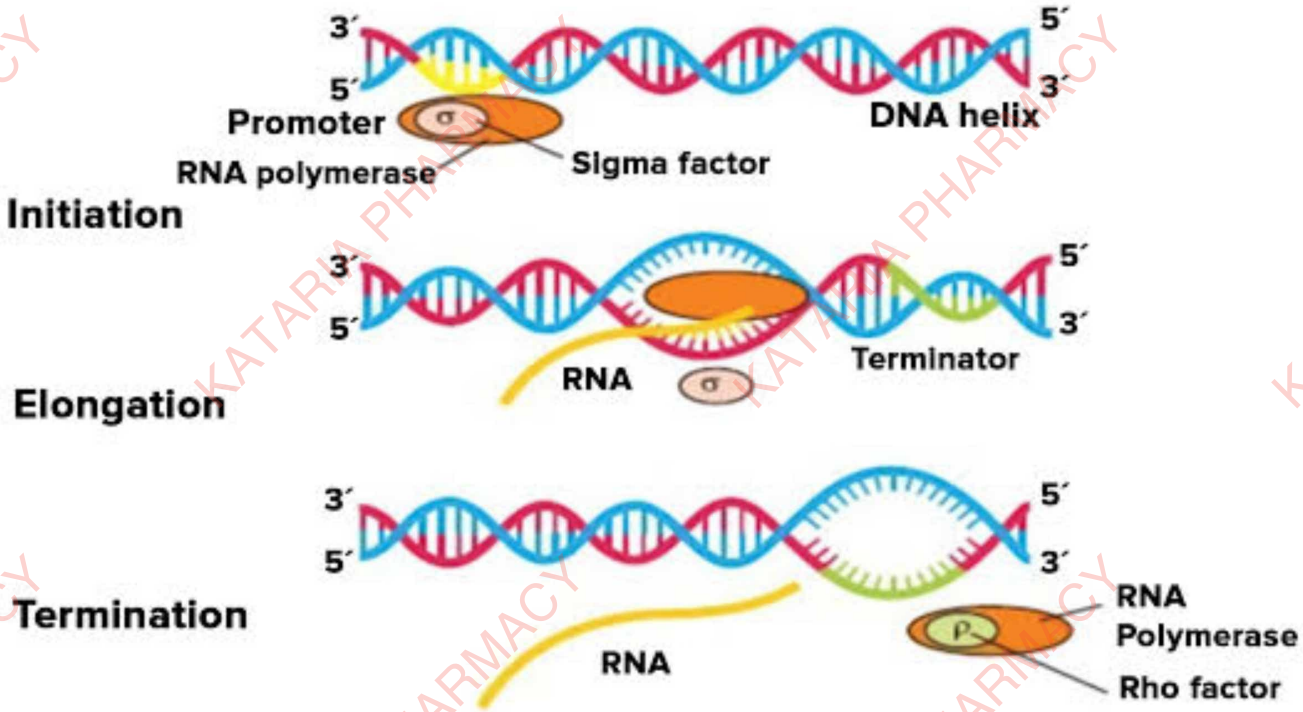
- Replication forks meet: In prokaryotes, replication ends when two replication forks meet. In eukaryotes replication termination is more complex and involves specific termination sequences and proteins.



★ Transcription (RNA Synthesis) :-

- The very first step in gene expression is transcription which utilises genetic information to form a functional product like proteins.
- Thus transcription involves the formation of a RNA copy of a gene's DNA sequence.

process of transcription :-



① Initiation :-

RNA polymerase binds with a sequence of DNA known as the promoter, present near the begining of a gene.

- The DNA double helix is unwound by RNA polymerase to expose the template strand. This creates a transcription bubble where the DNA is accessible for transcription.

② Elongation :-

- RNA Synthesis: RNA polymerase moves along the template strand of the DNA, synthesizing a complementary strand of RNA
- Direction of Synthesis: RNA polymerase synthesizes the mRNA in the 5' to 3' direction, reading the DNA template strand from 3' to 5'.
- Formation of mRNA: As the RNA polymerase progresses, the newly formed RNA strand peels away from the DNA template, allowing the DNA to re-anneal.

③ Termination :-

- Termination Signal: Transcription continues until RNA polymerase encounters a termination signal in the DNA sequences.
- Release of mRNA: The mRNA molecule is released from the RNA polymerase and the DNA template. In eukaryotes, this primary transcript (pre-mRNA) undergoes further processing.

★ Genetic Code :-

Genetic Code is the information possessed by the m-RNA and this information is used for protein synthesis.

1. **Codons:**
   - A codon is a sequence of three nucleotides in mRNA. Each codon specifies a particular amino acid or a termination signal during protein synthesis.

2. **Redundancy:-**
   The genetic code is redundant, meaning that multiple codons can encode the same amino acid. For instance, the amino acid Leucine is encoded by six different codons (UUA, UUG, CUU, CUC, CUA, CUG).

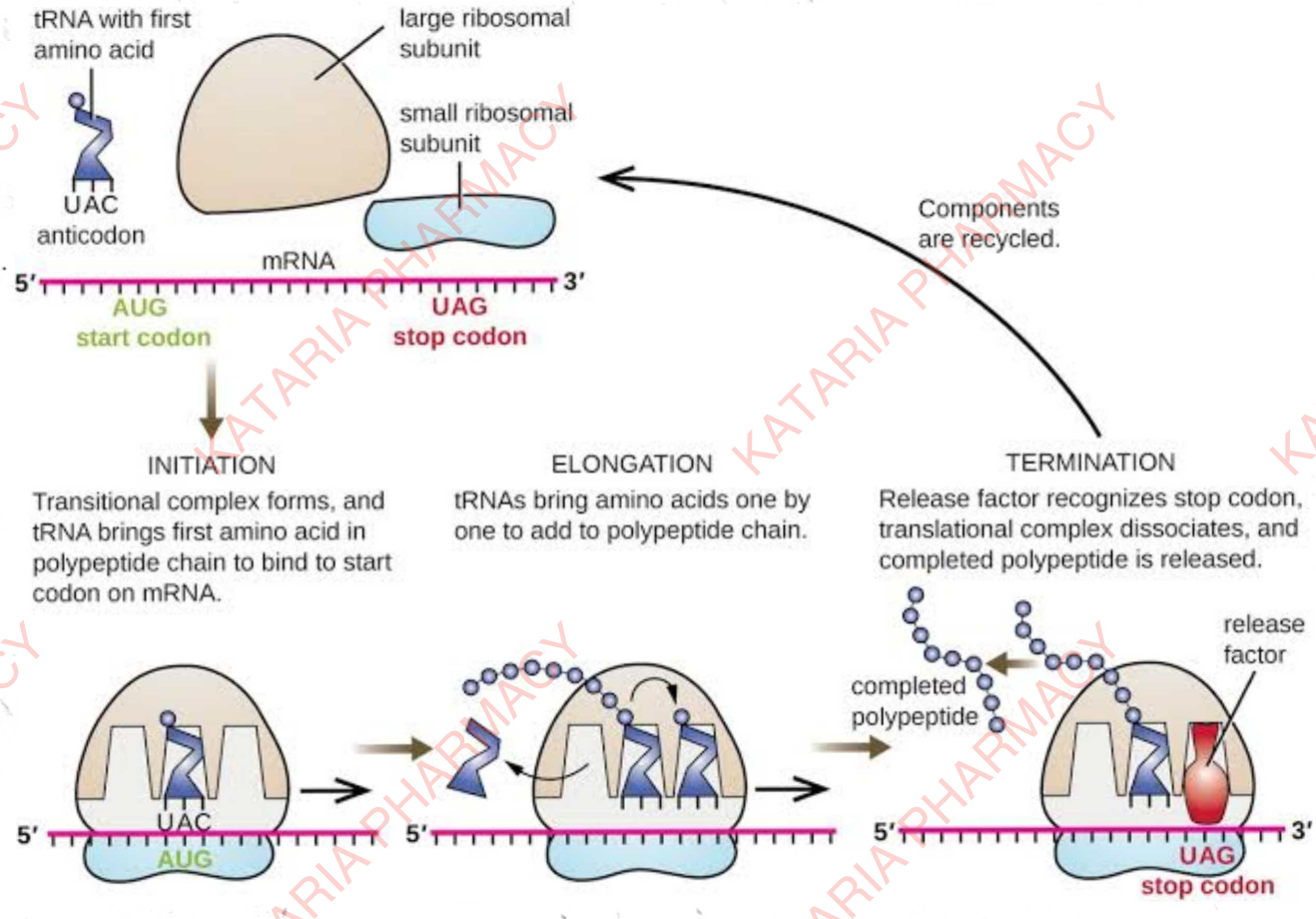
3. **Start and Stop Codons :-**
   - The start codon (AUG) signals the beginning of translation
   - Stop codons (UAA, UAG, UGA) signal the end of translation, instructing the ribosome to release the newly synthesized polypeptide.

✯ Translation or protein Synthesis :-

Translation is a process of protein Synthesis. In the transcription process DNA is transcribed into an m-RNA molecule, which is translated to produce protein.

- In translation m-RNA, t-RNA and ribosomes work together to synthesise protein.

process of translation :-



① Initiation :-

- mRNA Binding : The mRNA molecule, transcribed from DNA attaches to the Small Subunit of a ribosome at the mRNA binding site.
- Start Codon : The ribosome scans the mRNA for the Start Codon (AUG), which Signals the begining of the protein Coding Sequence.
- Initiator tRNA :- A special Initiator tRNA Molecule Carrying methionine (met) binds to the start Codon on the mRNA. This tRNA has An anticodon Sequence (UAC) Complementy to the AUG Codon.
- Ribosome Assembly : The large ribosomal Subunit joins the Small Subunit, forming a Complete ribosome. This Complex is now ready to start translation.

② Elongation :-

- Codon Recognition : The ribosome has three sites : the A (Aminoacyl), P (peptidyl) and E (exit) Sites.
  - The Initiator tRNA Starts in the p site.. The next Codon on the mRNA is positioned in the A site,
- peptide bond formation : The ribosome Catalyze the formation of a peptide bond between the amino acid attached to the tRNA in the p site and the amino acid attached to the A site.

- Translocation: The ribosome moves one codon down the mRNA. The tRNA in the P site moves to the E site and is released.

③ Termination :-

- Stop Codon Recognition : Elongation continues until the ribosome encounters a stop codon (UAA, UAG, or UGA) on the mRNA.
- These codons do not code for an amino acid and signal the end of translation.