Name of Unit	Nucleic Acid Metabolism and Genetic Information Transfer
Subject /Course name	Biochemistry
Subject/Course ID	BP203T
Class: B.Pharm. Semester	II
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Learning Outcome of Module 04

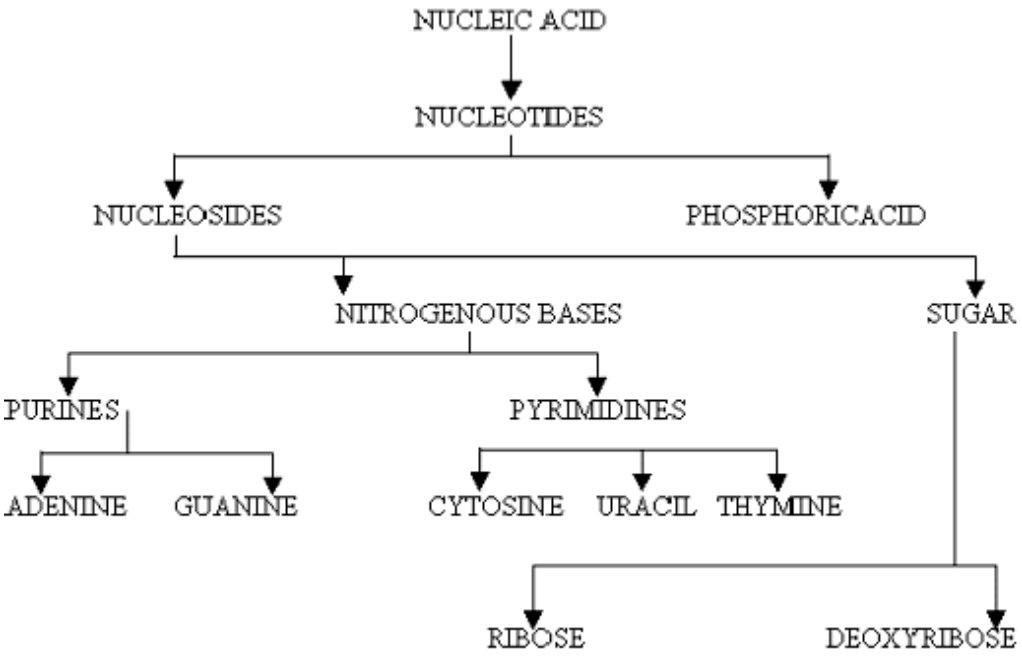
LO	Learning Outcome	Course Outcome Code
LO1	To learn about Properties of Nucleic Acid.	BP203.1
LO2	To gain knowledge about the biological roles of Nucleic Acid.	BP203.1
LO3	To Learn about metabolism of Nucleic Acid.	BP203.6
LO4	To gain knowledge about DNA replication, Translation and Transcription	BP203.4

Content Table

Topic
• Biosynthesis of Purine and Pyrimidine nucleotides • Catabolism of Purine nucleotides and Hyperuricemia and Gout disease. • Organization of mammalian genome • Structure of DNA and RNA and their functions DNA replication. • Transcription or RNA synthesis. • Genetic Code, Translation or Protein synthesis and inhibitors.

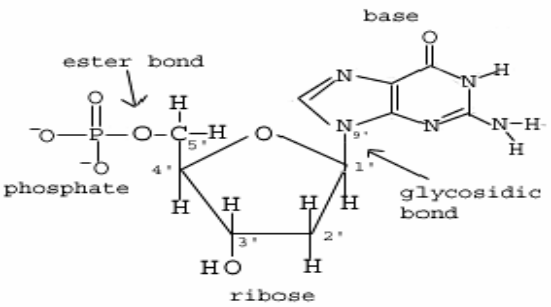
NUCLEIC ACID METABOLISM AND GENETIC INFORMATION TRANSFER

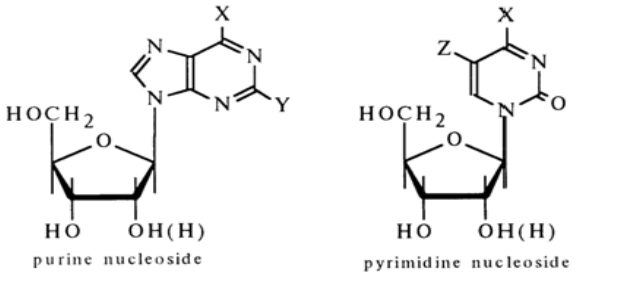
- Nucleic acids are large biomolecules and biopolymers which are essential for henetic information
- Nucleic acids are mainly of two types: DNA and RNA.
- Genes are the segment of DNA that carries the genetic information as a genetic code.
- Various components of DNA (nucleic acid) are as shown in flow chart.



Nucleotide: Phosphate + pentose sugar (ribose) + nitrogenous base

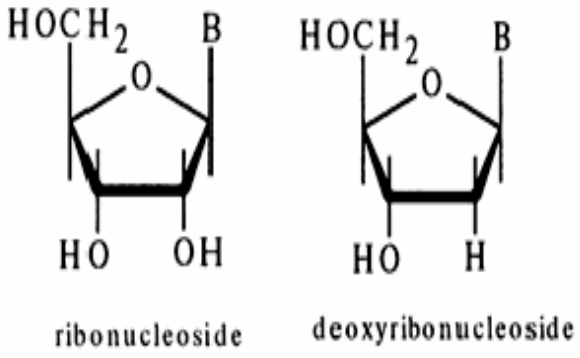
Nucleoside: pentose sugar (ribose) + nitrogenous base

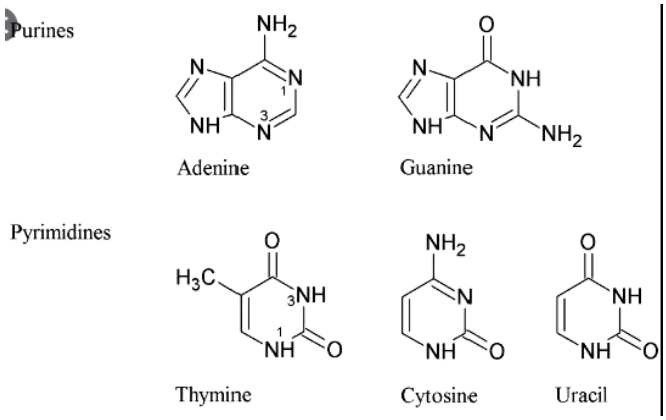


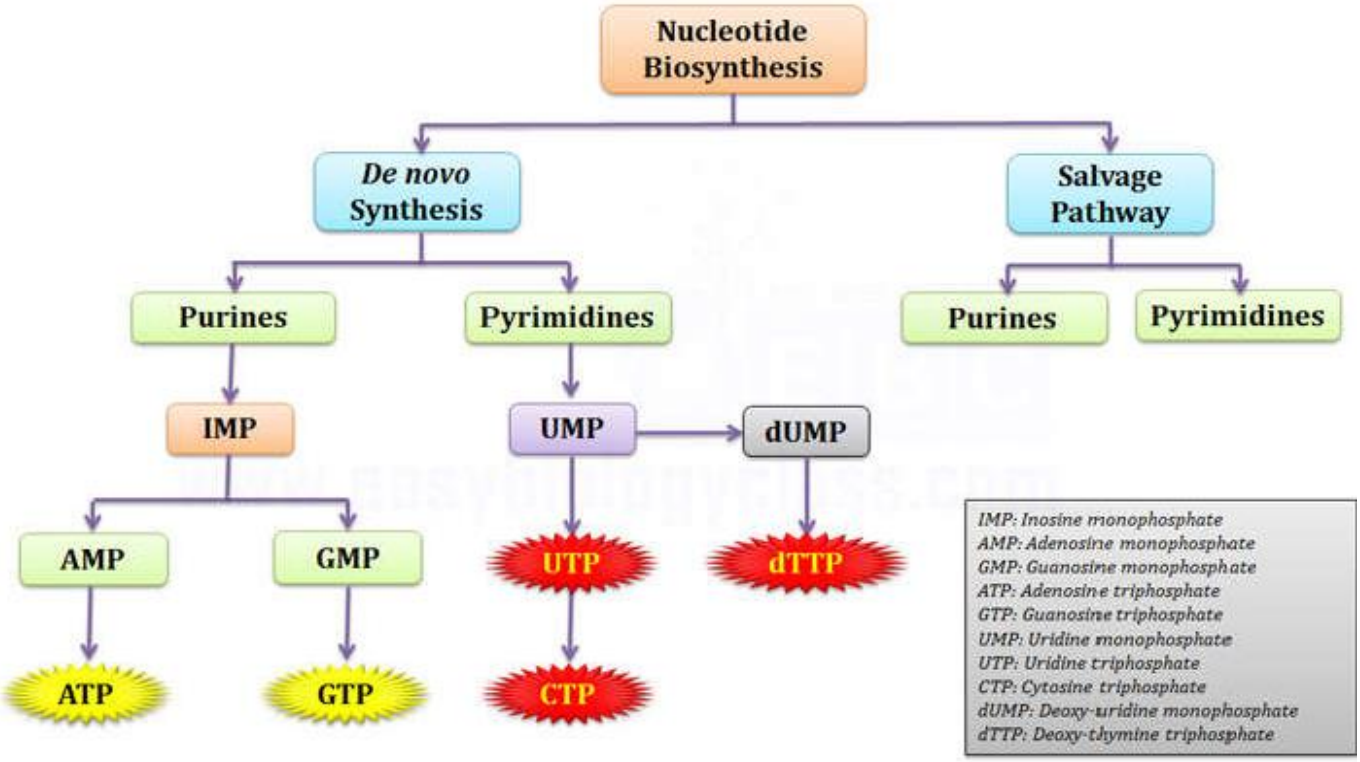


Type of sugar: a) Ribose, b) Deoxyribose

Type of nitrogenous base: a) Purines (Adenine, Guanine); b) Pyrimidines (Cytosine, Thymine, Uracil)

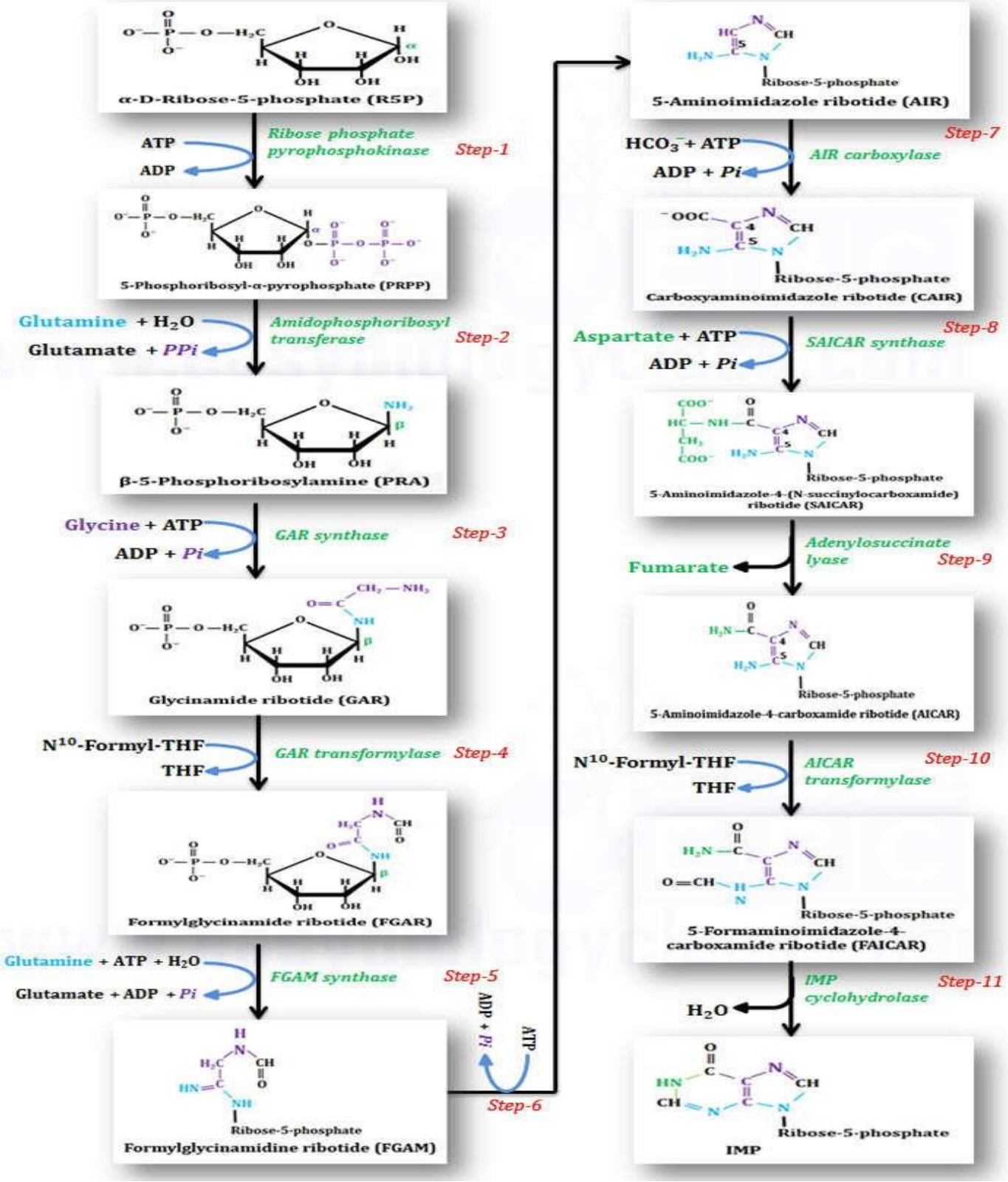




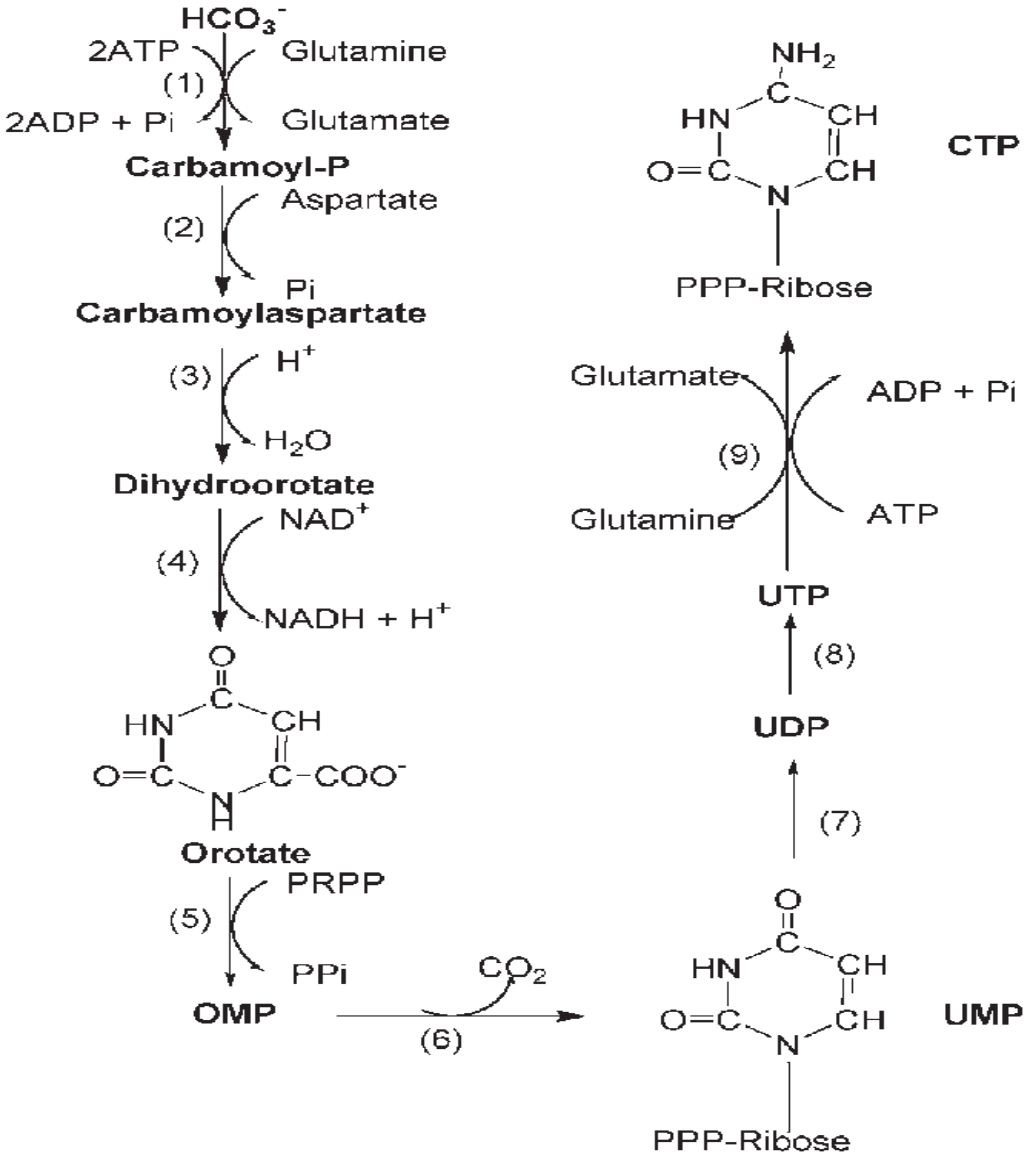


Biosynthesis of purine nucleotides:

1. It is the de novo synthesis by which a new purine ring is synthesized along with the nucleotide that attaches to the ribose sugar generated by HMP pathway.
2. D-ribose-5-phosphate serves as the starting material for stepwise synthesis of the purine ring.
3. The first biosynthesized purine product after 11 step is Inosine-5'-monophosphate (See figure on next page). IMP worked as precursor for various purine base. 4. It occurs in the liver. 5. In this whole reaction 6 ATP is utilized.

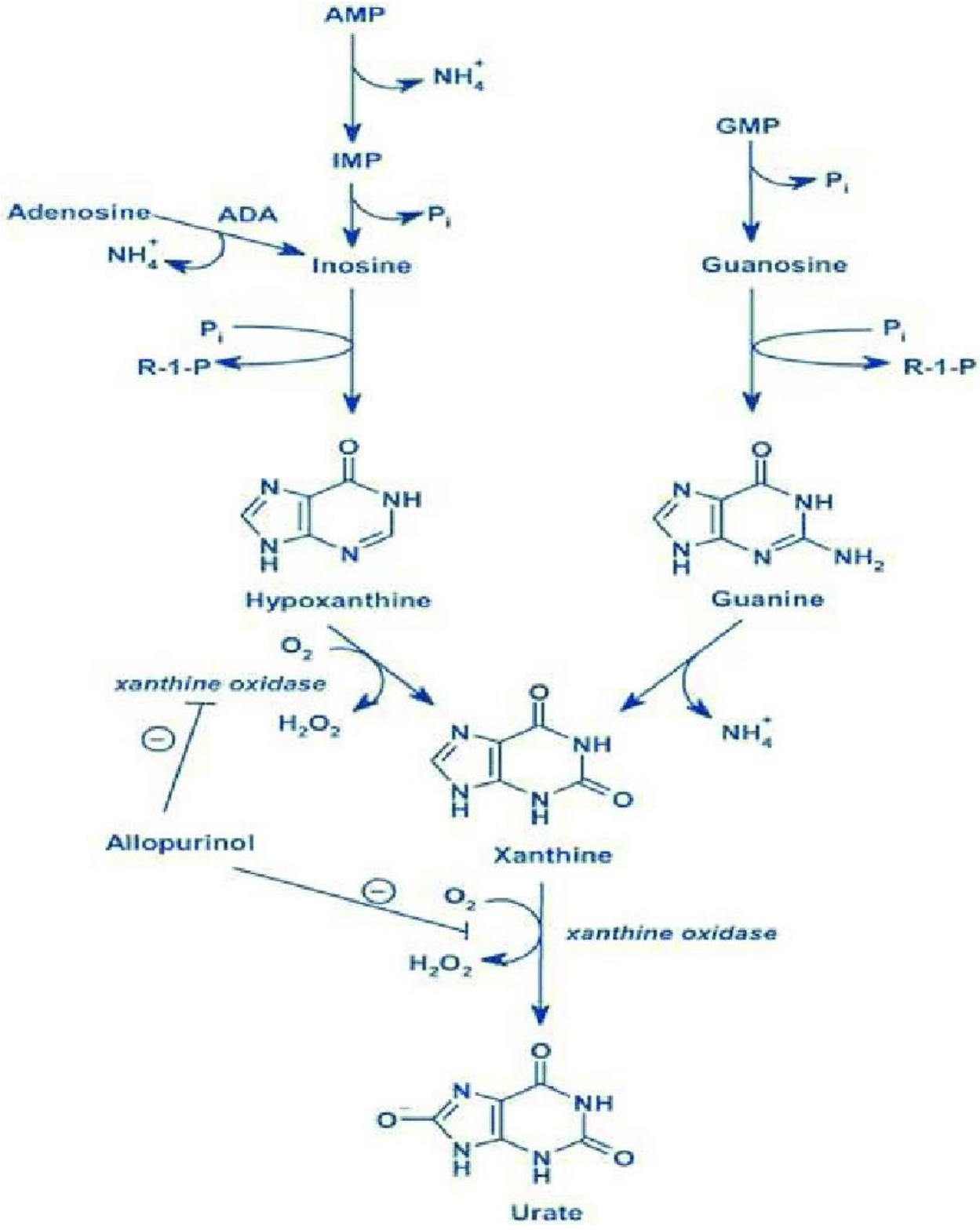

α-D-Ribose-5-phosphate (R5P)
ATP
ADP
Ribose phosphate pyrophosphokinase
Step-1
5-Phosphoribosyl-α-pyrophosphate (PRPP)
Glutamine + H2O
Glutamate + PPi
Amidophosphoribosyl transferase
Step-2
β-5-Phosphoribosylamine (PRA)
Glycine + ATP
ADP + Pi
GAR synthase
Step-3
Glycinamide ribotide (GAR)
N10-Formyl-THF
THF
GAR transformylase
Step-4
Formylglycinamide ribotide (FGAR)
Glutamine + ATP + H2O
Glutamate + ADP + Pi
FGAM synthase
Step-5
Ribose-5-phosphate
Formylglycinamidine ribotide (FGAM)
ADP + Pi
ATP
Step-6
Ribose-5-phosphate
5-Aminoimidazole ribotide (AIR)
HCO3− + ATP
ADP + Pi
AIR carboxylase
Step-7
Ribose-5-phosphate
Carboxyaminoimidazole ribotide (CAIR)
Aspartate + ATP
ADP + Pi
SAICAR synthase
Step-8
Ribose-5-phosphate
5-Aminoimidazole-4-(N-succinylocarboxamide) ribotide (SAICAR)
Fumarate
Adenylosuccinate lyase
Step-9
Ribose-5-phosphate
5-Aminoimidazole-4-carboxamide ribotide (AICAR)
N10-Formyl-THF
THF
AICAR transformylase
Step-10
Ribose-5-phosphate
5-Formaminoimidazole-4-carboxamide ribotide (FAICAR)
H2O
IMP cyclohydrolase
Step-11
Ribose-5-phosphate
IMP

Biosynthesis of Pyrimidine nucleotides



1. Pyrimidine nucleotide biosynthesis takes place with six membered pyrimidine ring synthesis followed by attachement to ribose phosphate in 8 step.
2. The synthesis begins with combined CO_2 and NH_3 and Pyrimidine ring is formed first.
3. Formation of cytosolic carbamoyl phosphate is a regulatory step.
4. This biosynthesis occurs in cytoplasm.
5. Carbamoyl phosphate is used in urea synthesis which is made in the mitochondrion.

Catabolism of purine nucleotides: It is an important pathway of the nucleic acid metabolism. Nucleic acids are degraded in the digestive tract to nucleotides by various enzymes.



Hyperuricemia:

Hyperuricemia is an excess of uric acid in the blood. Uric acid passes through the liver, and enters your bloodstream. Most of it is excreted (removed from your body) in your urine, or passes through your intestines to regulate "normal" levels.

Normal uric acid level: 2.4-6.0 mg/dl (Female) and 3.4-7.0 mg/dl (male).

Causes: alcohol consumption, high levels of meat ingestion or high levels of seafood ingestion.

Risk factor: Hypertension, Kidney diseases, gouty arthritis.

Treatment: uricosuric drug (e.g. probenecid, allopurinol) and NSAID drugs.

Gout:

A form of arthritis characterised by severe pain, redness and tenderness in joints.

Pain and inflammation occur when too much uric acid crystallises and deposits in the joints.

Type: a) acute gout which is also known as gout attack.

b) Chronic gout attacks are caused by the deposition of urate in various joints in body.

Symptoms of gout include severe pain, redness and swelling in joints, often the big toe. Attacks can come suddenly, often at night.

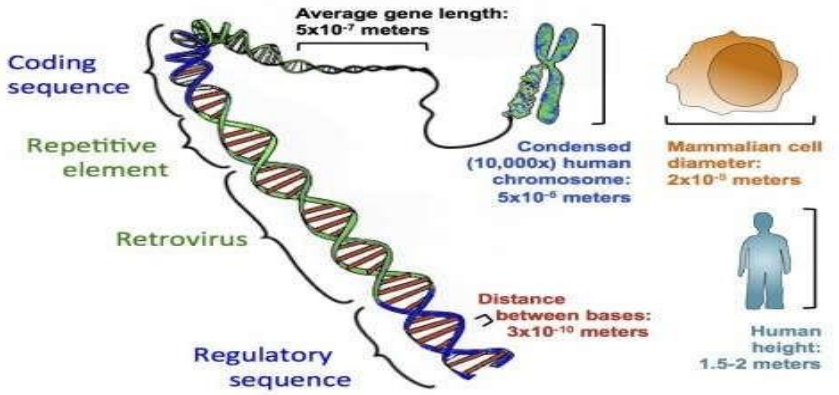
Treatment: During an acute attack, anti-inflammatory medication (NSAIDs) can help to relieve pain and shorten the duration of the attack. Patients with chronic gout can use behavioural modification such as diet, exercise and decreased intake of alcohol to help minimise the frequency of attacks. Additionally, patients with chronic gout are often put on medication to reduce uric acid levels.

ORGANIZATION OF MAMMALIAN GENOME:

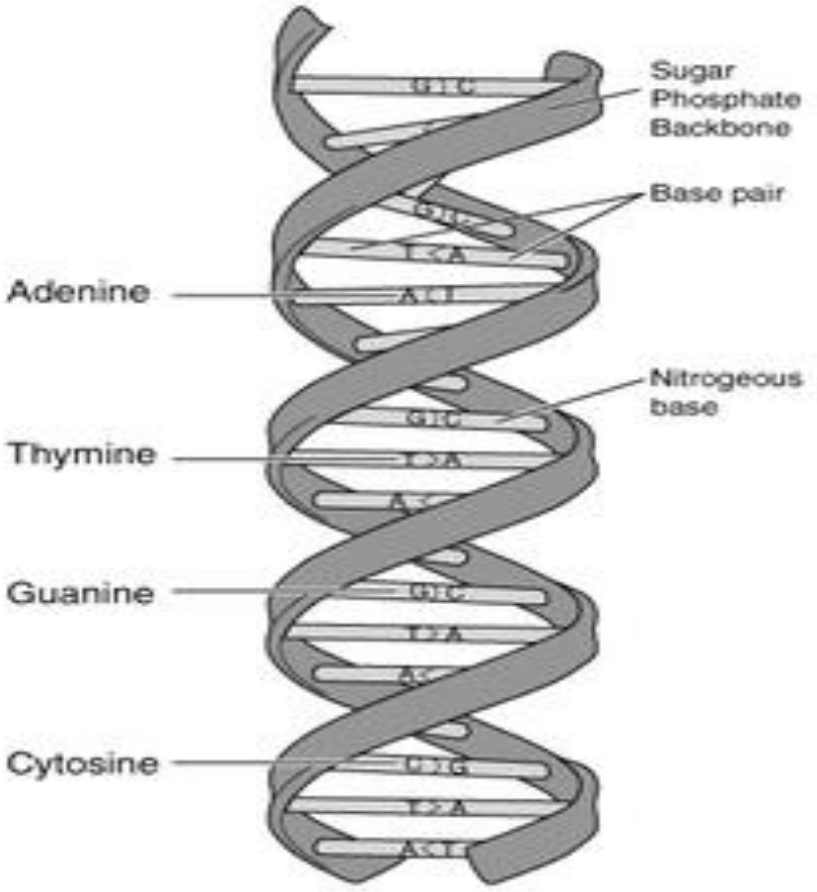
The **genome** of an organism is the whole of its hereditary information encoded in its DNA (or, for some viruses, RNA). This includes both the genes and the non-coding sequences of the DNA. The **human genome** is stored on 23 chromosome pairs in the cell nucleus and in the small mitochondrial DNA. Chromosomes are storage unit of genes.

Structure of DNA:

DNA (Deoxyribonucleic acid) is a molecule composed of two chains that coil around each other to form a double helix carrying genetic instructions for the development.



DNA is **made** up of molecules called nucleotides. Each nucleotide contains a phosphate group, a sugar group and a nitrogen base. The four types of nitrogen bases are adenine (A), thymine (T), guanine (G) and cytosine (C). The order of these bases is determines **DNA's** instructions, or genetic code.



The Biological function of DNA

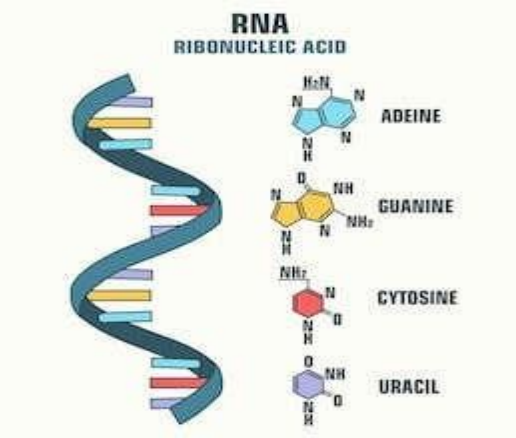
DNA is the genetic material which carries all the hereditary information. Genes are the small segments of DNA, consisting mostly of 250 – 2 million base pairs. A gene code for a polypeptide molecule, where three nitrogenous bases sequence stands for one amino acid.

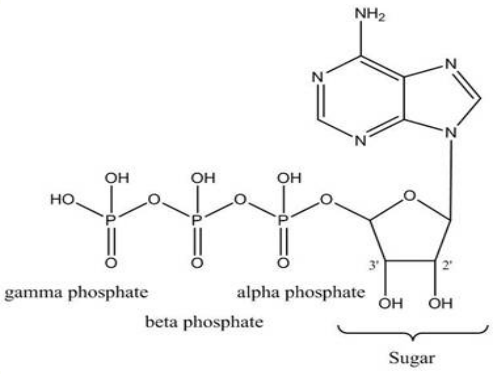
Polypeptide chains are further folded in secondary, tertiary and quaternary structures to form different proteins. As every organism contains many genes in its DNA, different types of proteins can be formed. **Proteins** are the main functional and structural molecules in most organisms. Apart from storing genetic information, DNA is involved in:

- Replication process: Transferring the genetic information from one cell to its daughters and from one generation to the next and equal distribution of DNA during the cell division
- Mutations: The changes which occur in the DNA sequences
- Transcription
- Cellular Metabolism
- DNA Fingerprinting
- Gene Therapy

Structure of RNA:

RNA's are single standard. RNA consist of ribose nucleotides (nitrogenous bases appended to a ribose sugar) attached by phosphodiester bonds, forming strands of varying lengths. The nitrogenous bases in RNA are adenine, guanine, cytosine, and uracil, which replace thymine in DNA.





Function and Type of RNA:

There are main function of RNA is the transfer of genetic information from the nucleus to the cells. They make up ribosome and help to assemble proteins. There are 3 main types of RNA, each encoded by its own type of gene:

mRNA - Messenger RNA: Encodes amino acid sequence of a polypeptide.

tRNA - Transfer RNA: Brings amino acids to ribosomes during translation.

rRNA - Ribosomal RNA: With ribosomal proteins, makes up the ribosomes, the organelles that translate the mRNA.

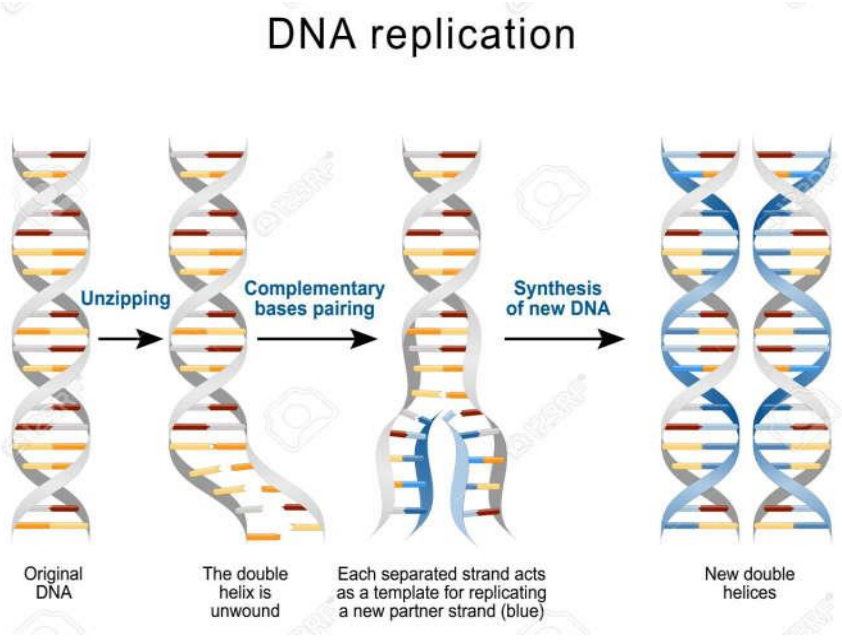
DNA Replication (Semi-conservative model):

Semi-conservative replication was discovered by Watson and Crick. Semi- conservative replication means that during DNA replication, the two strands of nucleotides separate. Both strands then form the template for free nucleotides to bind to create the two identical daughter strands. Hence each daughter strand has half of the DNA from the original strand and half newly-formed DNA.

The step are as follow:

Replication fork formation: Double helix of DNA unzipped in single stand in the presence of enzyme DNA helicase.

Primer Binding: A primer (RNA piece) binds in the presence of enzyme DNA primase



Elongation: Enzyme DNA polymerases are responsible for creating the new strand by elongation process.

Termination: An Enzyme exonuclease removes all RNA primers from the original strands when the continuous and discontinuous strands are formed and there after primers are replaced with appropriate bases.

Telomerase enzyme catalyzes the synth sis of telomere sequences at the end of the DNA

Finally two DNA molecules formed by replication half part of parent and half part as new stand.

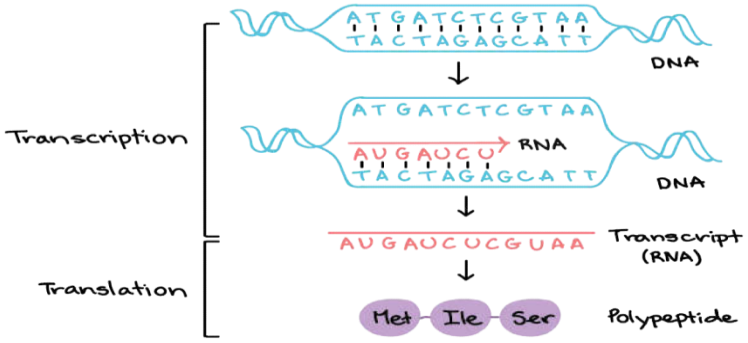
Transcription or RNA synthesis:

Transcription is the first step in gene expression, in which information from a gene is used to Construct a functional product such as a protein.

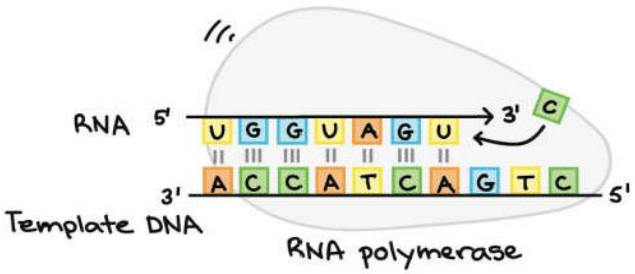
The goal of transcription is to make a RNA copy of a gene's DNA sequence.

For a protein-coding gene, the RNA copy, or transcript, carries the information needed to build a polypeptide (protein or protein subunit).

Eukaryotic transcripts need to go thr ugh some processing steps before translation into proteins.

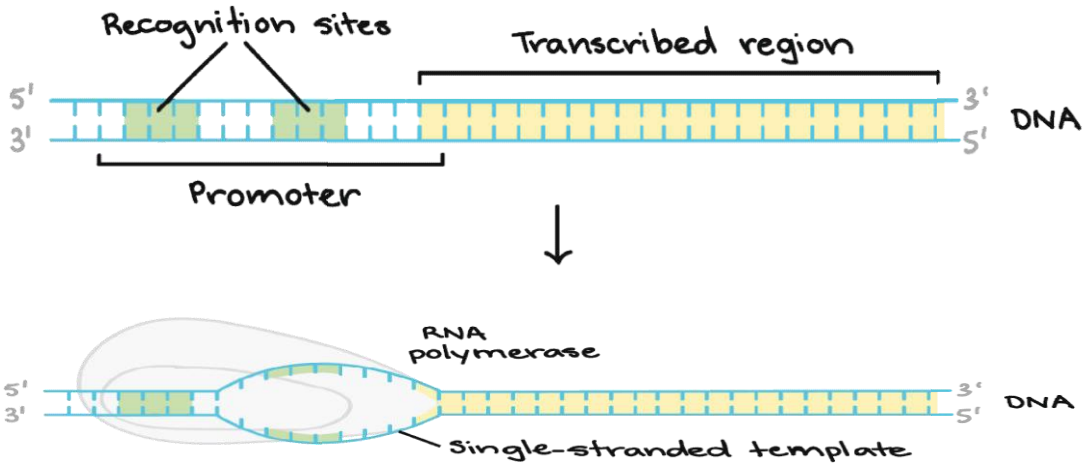


RNA polymerase is the main transcription enzyme. Using a DNA template, RNA olymerase builds a new RNA molecule through base pairing. For instance, if there is a G in the DNA template, RNA polymerase will add a C to the new, growing RNA strand.

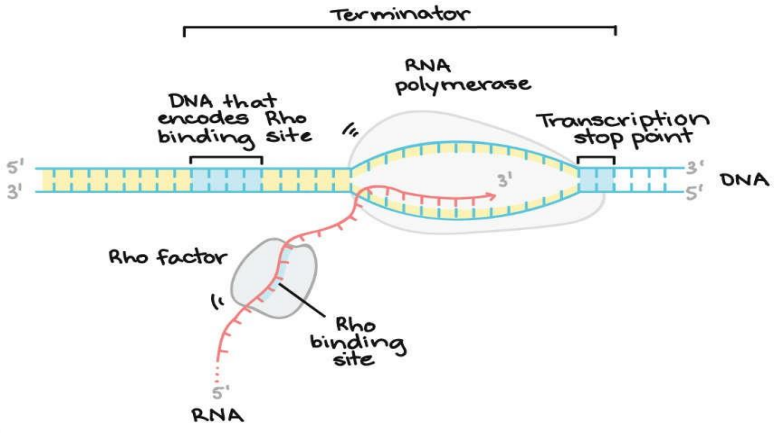


Steps:

- **Transcription initiation:** To begin transcribing a gene, RNA polymerase binds to the DNA of the gene at a region called the **promoter.**
- **Elongation:** Once RNA polymerase is in position at the promoter, the next step of transcription—elongation—can begin. Basically, elongation is the stage w en the RNA strand gets longer.



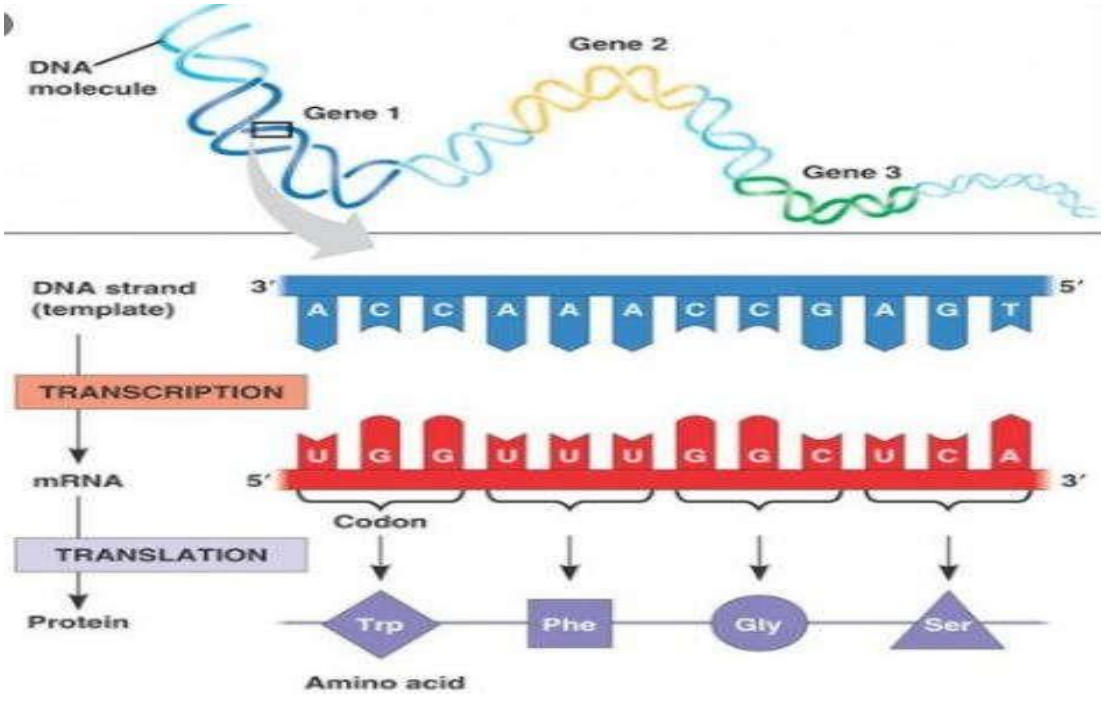
- **Transcription termination:** RNA polymerase will keep transcribing until it gets signals to stop. The process of ending transcription is called termination. There are two major termination strategies found in bacteria: Rho-dependent and Rho-independent. In **Rho-dependent termination**, the RNA contains a binding site for a protein called Rho factor. Rho factor binds to this sequence and starts "climbing" up the transcript towards RNA polymerase.



Genetic Code:

- The genetic code is the set of rules by which information encoded in genetic material (DNA or RNA sequences) is translated into proteins (amino acid sequences) by living cells.
- The genetic code consists of 64 triplets of nucleotides.
- Each of these triplets is defined as **codones**. Eg. AAA, AUG etc
- Each unit of triplets represents a nucleotide (A, G, C, **T, U**) such as A stand for adenosine nucleotide.
- There are two specific types of genetic codes called as RNA codons (read on MRNA) and DNA codons (read on DNA).
- The codones are of two types, viz:
- **Sense codons**: They code for amino acids. There are 61 sense codones in the genetic code which code for 20 amino acids e.g. AAA etc
- **Signal codons**: They code for signals during protein synthesis. There are four codons namely AUG, UAA, UAG, and UGA.
- **Properties**: a) triplet, b) Universal, c) Coma-less, d) Non-overlapping, e) polar in nature, f) Non-ambiguous, g) Redundant.
- **Application**: 1) ATG is used as start codon, 2) TAG, TGA, and TAA are used as stop codon, 3) Start codon inform to ribosome to start translation., 4) Stop codon stops translation of specific amino acid chain.

Translation or Protein synthesis



1. Protein synthesis is accomplished through a process called **translation**.
2. After DNA is transcribed into a messenger RNA (mRNA) molecule during transcription, the mRNA must be translated to produce a protein.
3. In translation, mRNA along with transfer RNA (tRNA) and ribosomes work together to produce proteins.
4. There are three important steps namely initiation, elongation, and termination.

Inhibitors of Translation or Protein synthesis

1. Protein synthesis inhibitors are a substance that stops or slows the growth of prokaryotic and eukaryotic cells at ribosomal level.
2. Inhibitors of both prokaryotic and eukaryotic protein synthesis: Edeine, Fusidic acid, Tetracycline
3. Inhibitors specific for prokaryotes (only in bacterial cell): Chloramphenicol, Colicin E3, Erythromycin, Streptomycin.
4. Inhibitors specific for eukaryotes: anisomysin, Pactamicin,

Very Short Answer Questions (2marks)

1. What is Genetic code?
2. Write inhibitors of Protein synthesis.
3. Define Translation.
4. What is Hyperuricemia?
5. Define Nucleic Acid.
6. What do you mean by Elongation?

Short Answer Questions (5marks)

1. Write Salvage pathways for Purine and Pyrimidine synthesis.
2. Write a short note on Synthesis of Purine nucleotides.
3. What are functions of DNA?
4. Write short note on De-novo Synthesis of Purine nucleotides.
5. Write a short note on Gout.

Long answer questions (10marks)

1. Explain denovo synthesis of pyrimidine nucleotides along with its regulation.
2. Explain purine catabolism and its disorders.
3. Describe pyrimidine catabolism and its disorders.