Nucleic acids

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Definition

- Any of a group of complex compounds found in all living cells and viruses, composed of purines, pyrimidines, carbohydrates, and phosphoric acid.

- Two forms of nucleic acids :-
- DNA (deoxyribonucleic acid)
- RNA (ribonucleic acid)

Functions

- Functions of DNA:-

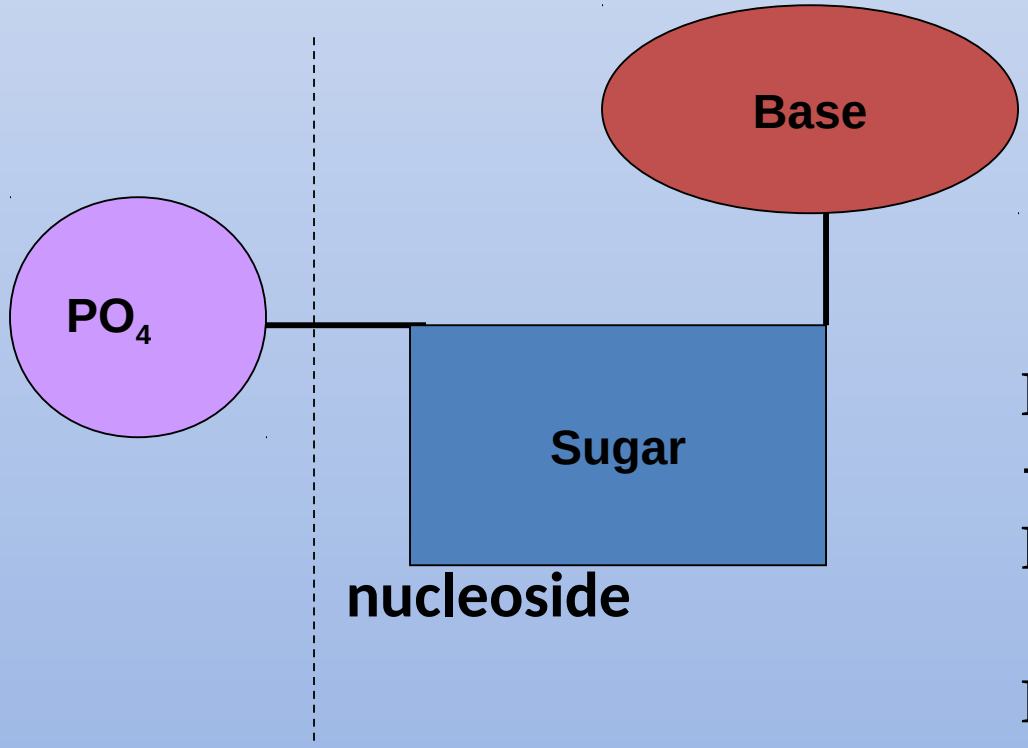
- A permanent storage place for genetic information.
- Controls the synthesis of RNA.
- Determines the protein development in new cells.

- Functions of RNA :-

- Messenger RNA (m RNA)
- Ribosomal (rRNA)
- Transfer (tRNA)
- In post transcription modify the other RNA’s
- Transfer genetic information

Component of nucleic acids

Nucleic acids are build up by the monomeric units -nucleotides that have a pentose sugar, nitrogen base, and phosphate



Nucleoside
+
Phosphate
=
Nucleotide

Function of nucleotides

- Build blocks or monomeric units
- Structural component of several coenzymes of B-complex vitamins.

  e.g. FAD. Coenzyme A
- Serve as intermediates in biosynthesis of carbohydrate, lipid & protins.

  e.g. S-adenosylmethionine
- Control several metabolic reaction.

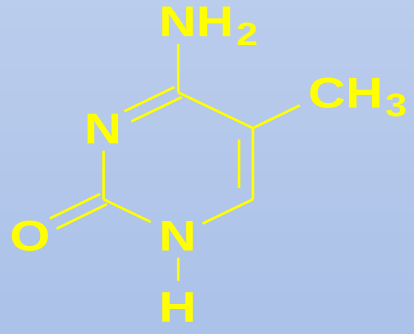
Structure of Nucleotides

- Nitrogen-Containing Bases (Purines &pyrimidines)

adenine (A)

thymine (T)

guanine (G)

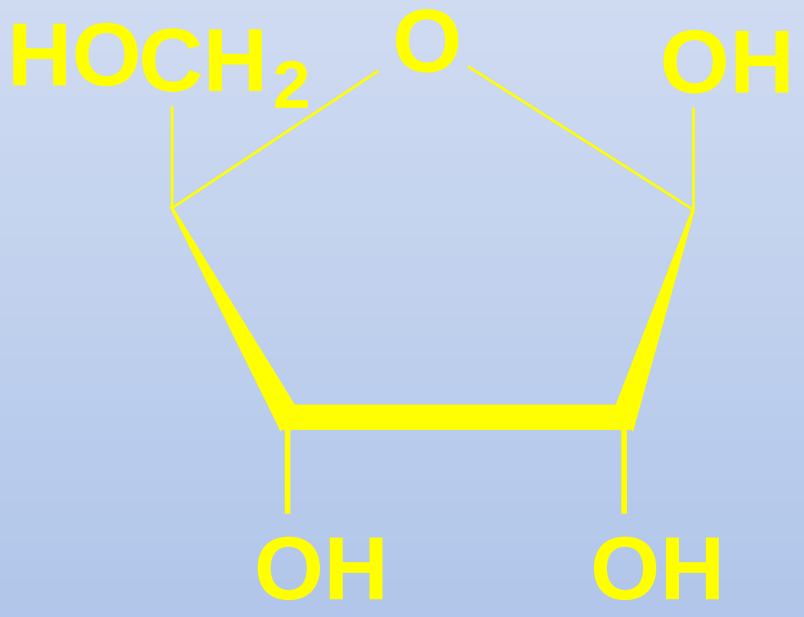


cytosine (C)

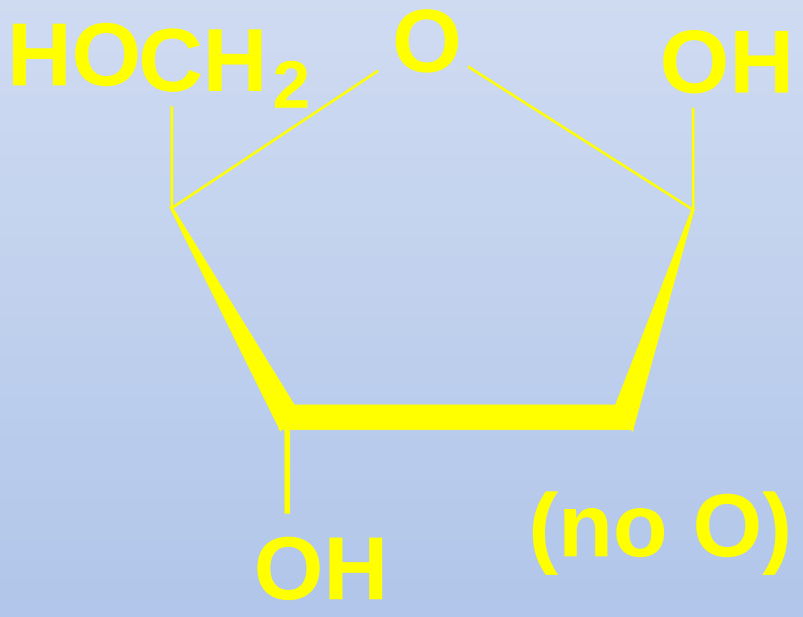
uracil (U)

Structure of purine (A,G) & pyrimidines (C, T, U)

- **Sugars**



ribose



deoxyribose

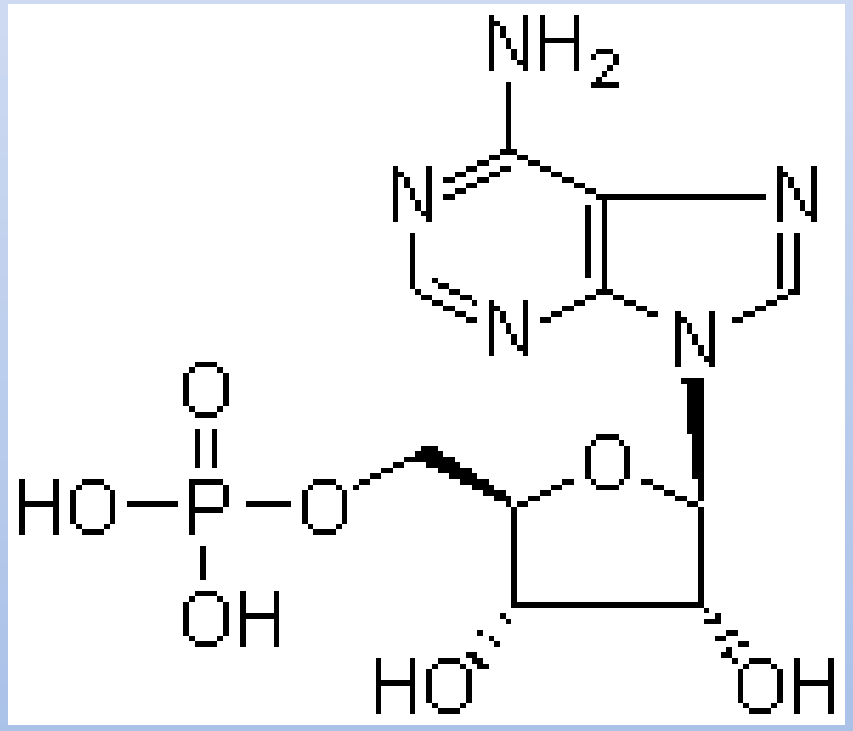
Nucleosides in DNA

Base	Sugar	Nucleoside
Adenine (A)	Deoxyribos	Adenosine
Guanine (G)	Deoxyribose	Guanosine
Cytosine (C)	Deoxyribose	Cytidine
Thymine (T)	Deoxyribose	Thymidine

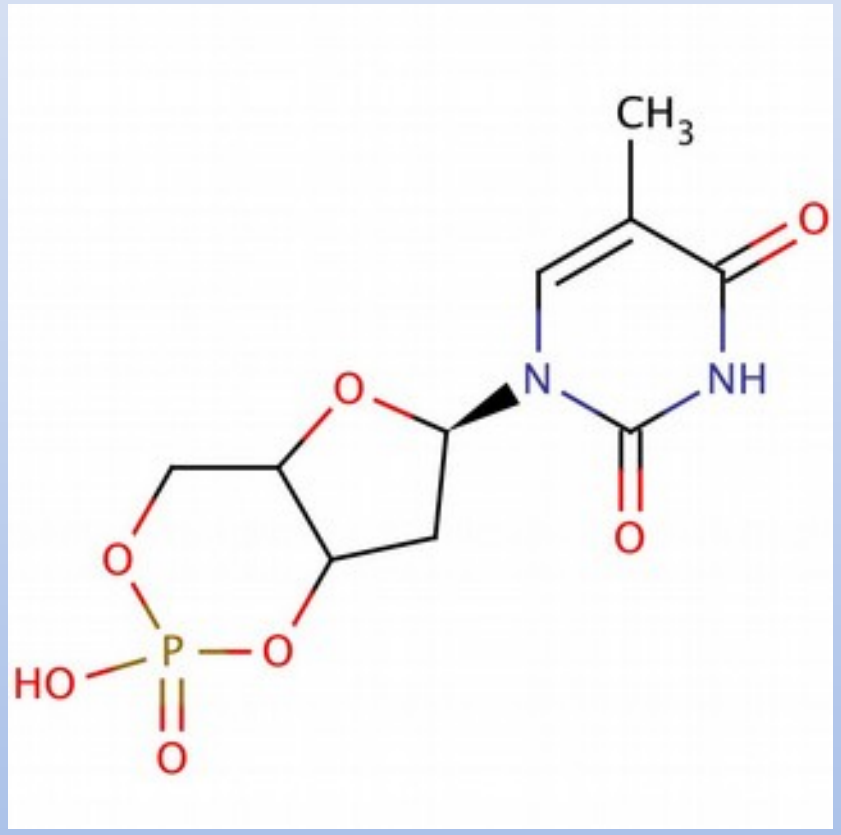
Nucleosides in RNA

Base	Sugar	Nucleoside
Adenine (A)	ribose	Adenosine
Guanine (G)	ribose	Guanosine
Cytosine (C)	ribose	Cytidine
Uracil (U)	ribose	Uridine

Nucleoside di and triphosphate



Adenosine 5’ monophosphate



Thymidine 5’ monophosphate

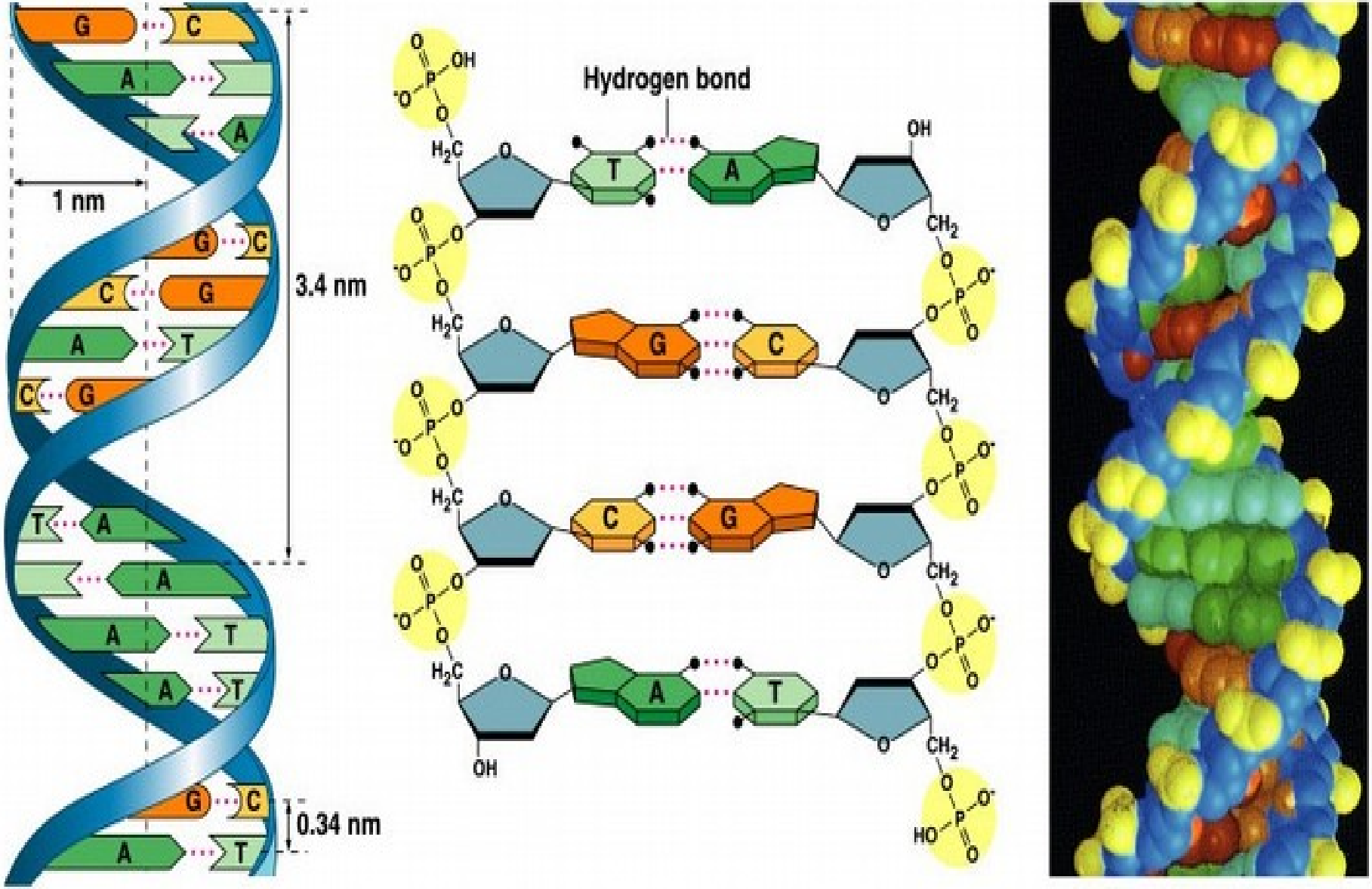
Different form of DNA double helix

- DNA exist in at least 6 different form-A to E and Z
- B-form of DNA double helix described by Watson ad crick.
- B-form has 10 base pairs spanning a distance of 3.4nm.ad width of double helix is 2nm.

The size of DNA

- DNA huge in size.
- B-DNA with a thickness of 0.34nm
- Molecular weight 660.
- The term kilo base paire [kb=1000 base paire] is commonly used in the DNA structure.

THE WASTON AND CRICK MODEL OF DNA



- James Watson (American biologist) and Frances Crick (English chemist) proposed Model of DNA to explain its structure in 1953

- DNA is right handed double helix . Consists of two polydeoxyriboncleotide chains
- Two strands are anti parallel

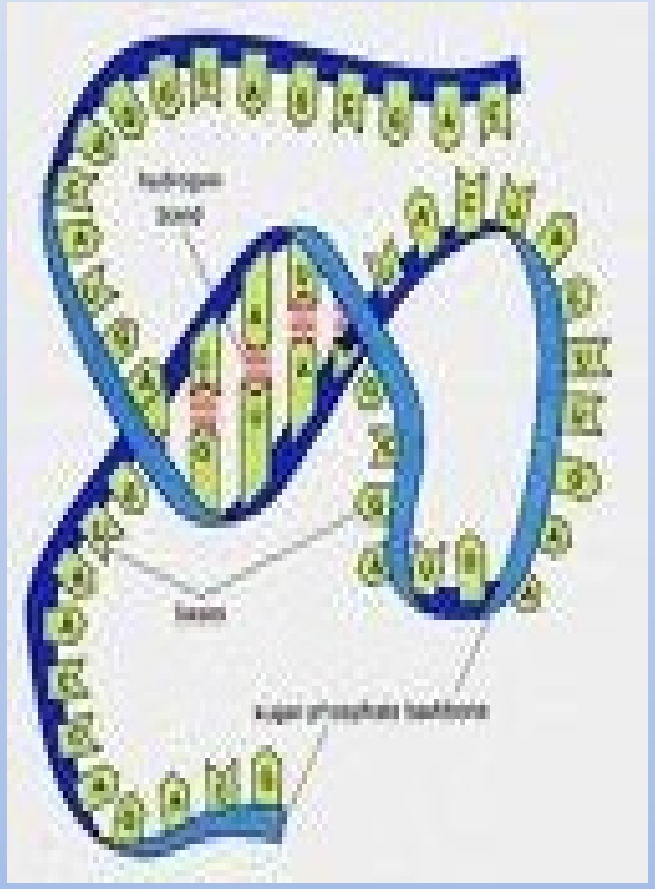
- Diameter of double helix is 2 nm

- Two polynucleotide chains complementary to each

- A – T pair has 2 hydrogen bonds while G – C pair has 3 hydrogen bonds

- Major grooves and minor grooves .

RNA



- The RNAs are synthesized by DNA,and are primarily involved in protein synthesis.
- It is the polymer of polynucleotide held together by 3,5-phosphodiester bridge.

How RNA different from DNA

- Pentose- The suger in RNA is ribose in DNA it is deoxyribose.
- Pyrimidine- RNA contain Uracil while in DNA it is thymine.
- Single strand- RNA is single stranded nucleotides and in DNA it may be folded or double stranded.

Types of RNA

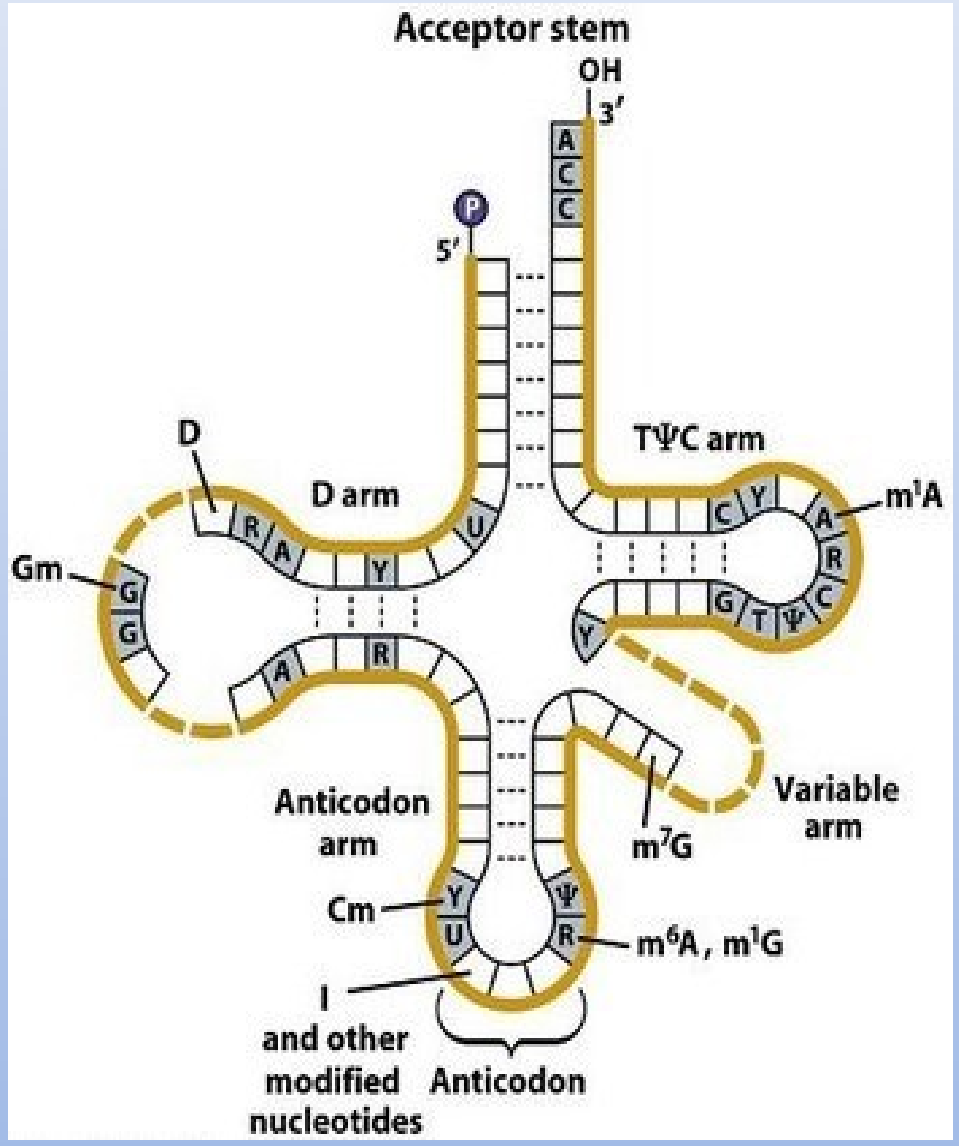
- Messenger RNA (mRNA)
- Transfer RNA (tRNA)
- Ribosomal RNA (rRNA)

Messenger RNA (mRNA)

- It synthesized in nucleus as heterogeneous nuclear RNA and on processing it liberates functional mRNA.
- It has high molecular weight with short half life.
- It carries the information from DNA to the Ribosome i.e. the site of protein synthesis.
- coding sequence of mRNA determines the amino acid sequence in proteins.(4-5%)

Transfer RNA (tRNA)

- tRNA contains 71-80 nucleotides (mostly75)
- 20 species of tRNAs as 20 amino acids present the protein structure.
- Structure -- clover leaf



- Accepter arm
- Anticodon arm
- D arm
- TΨC arm
- The variable arm

Ribosomal RNA （ rRNA)

- Protein synthesis takes place.
- It is the catalytic component of the ribosomes.

RNAs and their functions

Types of RNA	Abbreviation	Function
Messenger RNA	mRNA	Trancfer of genetic information from genes to ribosomes to synthesis proteins
Transfer RNA	tRNA	Transfer amino acid to mRNA for protein synthesis
Ribosomal RNA	rRNA	Provide structural framework for ribosomes.
Small nuclear RNA	snRNA	Involved in mRNA processing
Small cytoplasmic RNA	scRNA	Involved in selection of protein for export

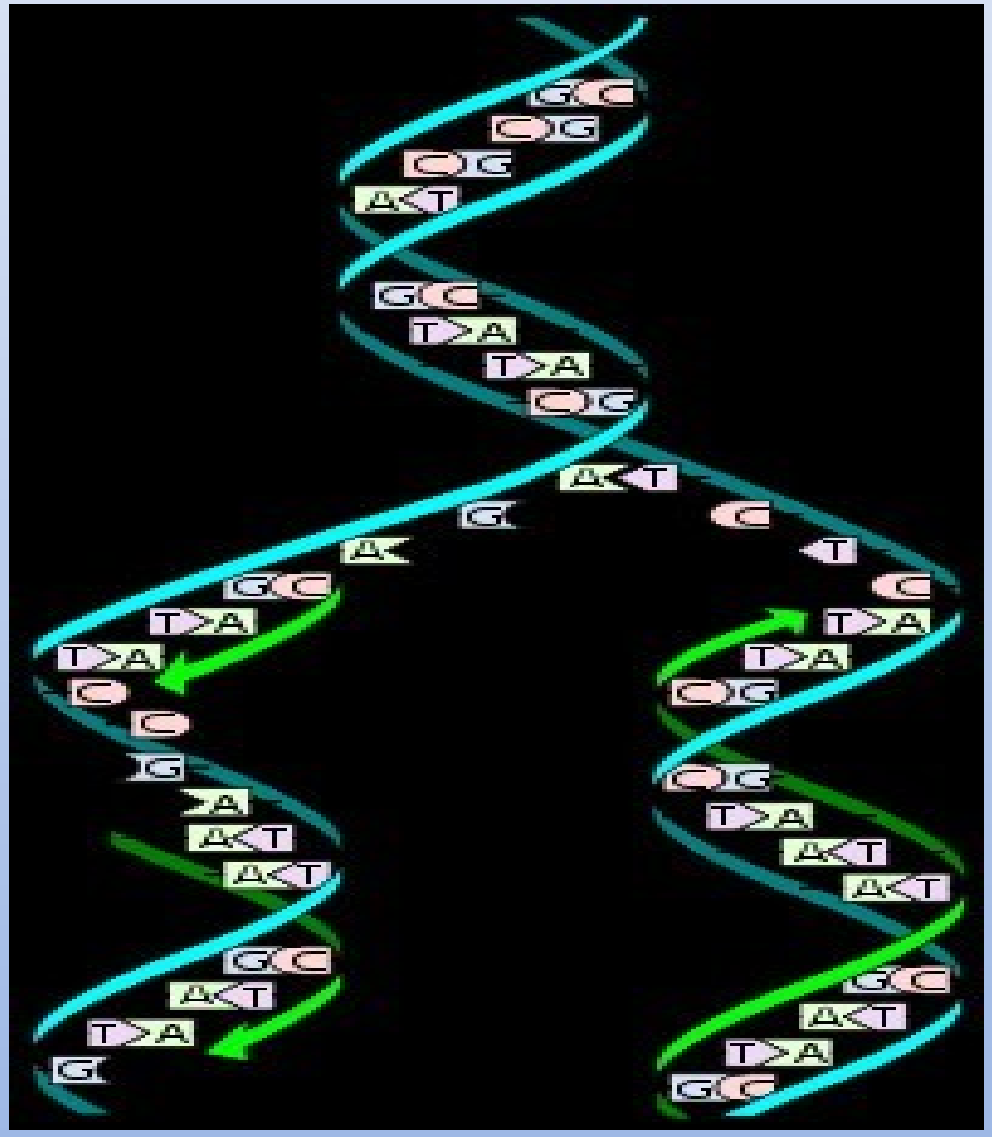
Important features of DNA replication

- DNA replication is Semiconservative.

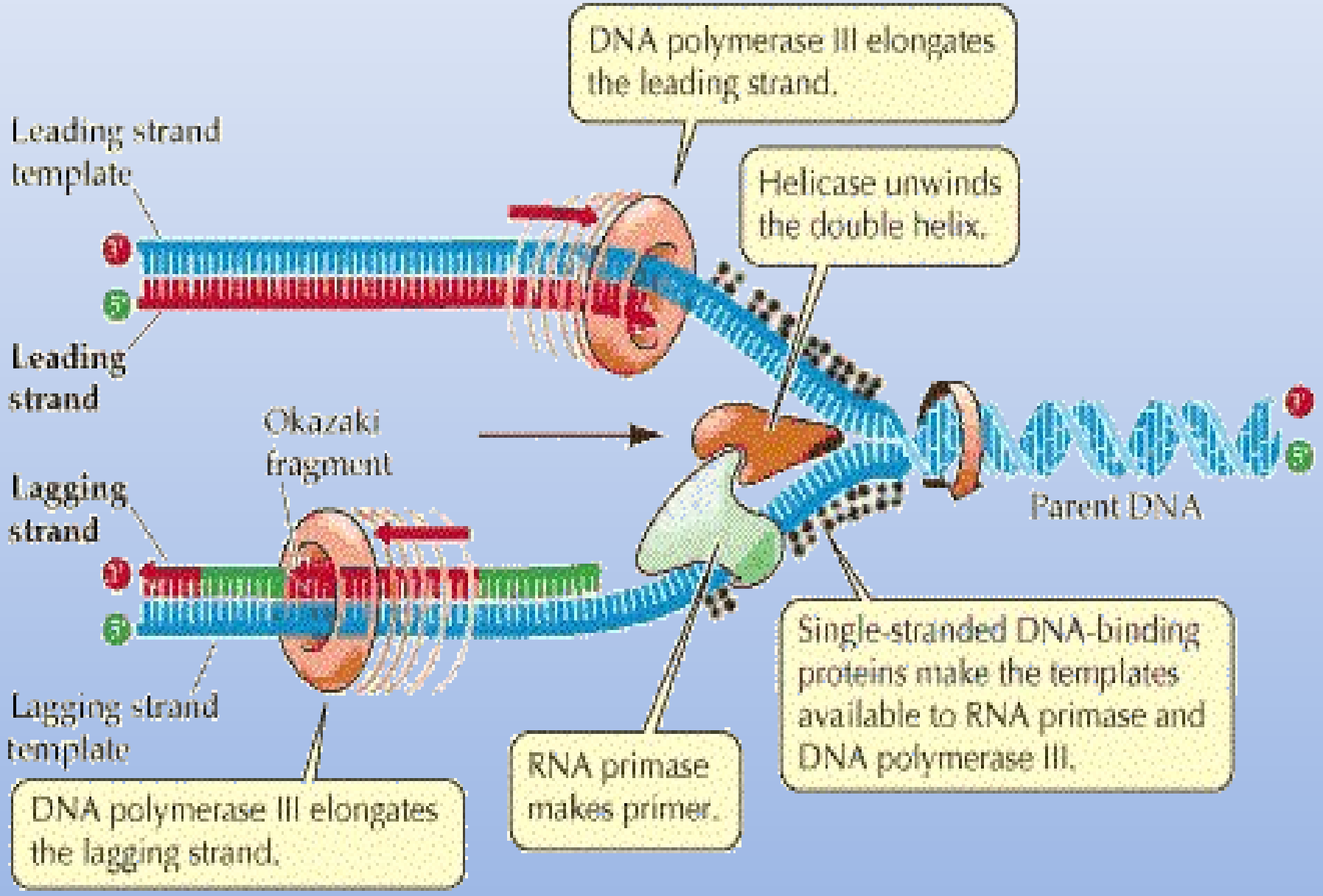
  (First experiment evidence was provided by Mathew Meselson and Franklin Stahl in 1958.)
- Replication begins at the origin and usually proceeds bidirectionally.
- DNA synthesis proceeds in 5’ to 3’ direction.
- DNA synthesis is semidiscontinous.

- Replication fork:
- Single stranded DNA binding (SSB) proteins:
- Lagging strand:
- Leading strand:
- Okazaki pieces:
- RNA primer:
- Enzymes:
  Helicase
  polymerase

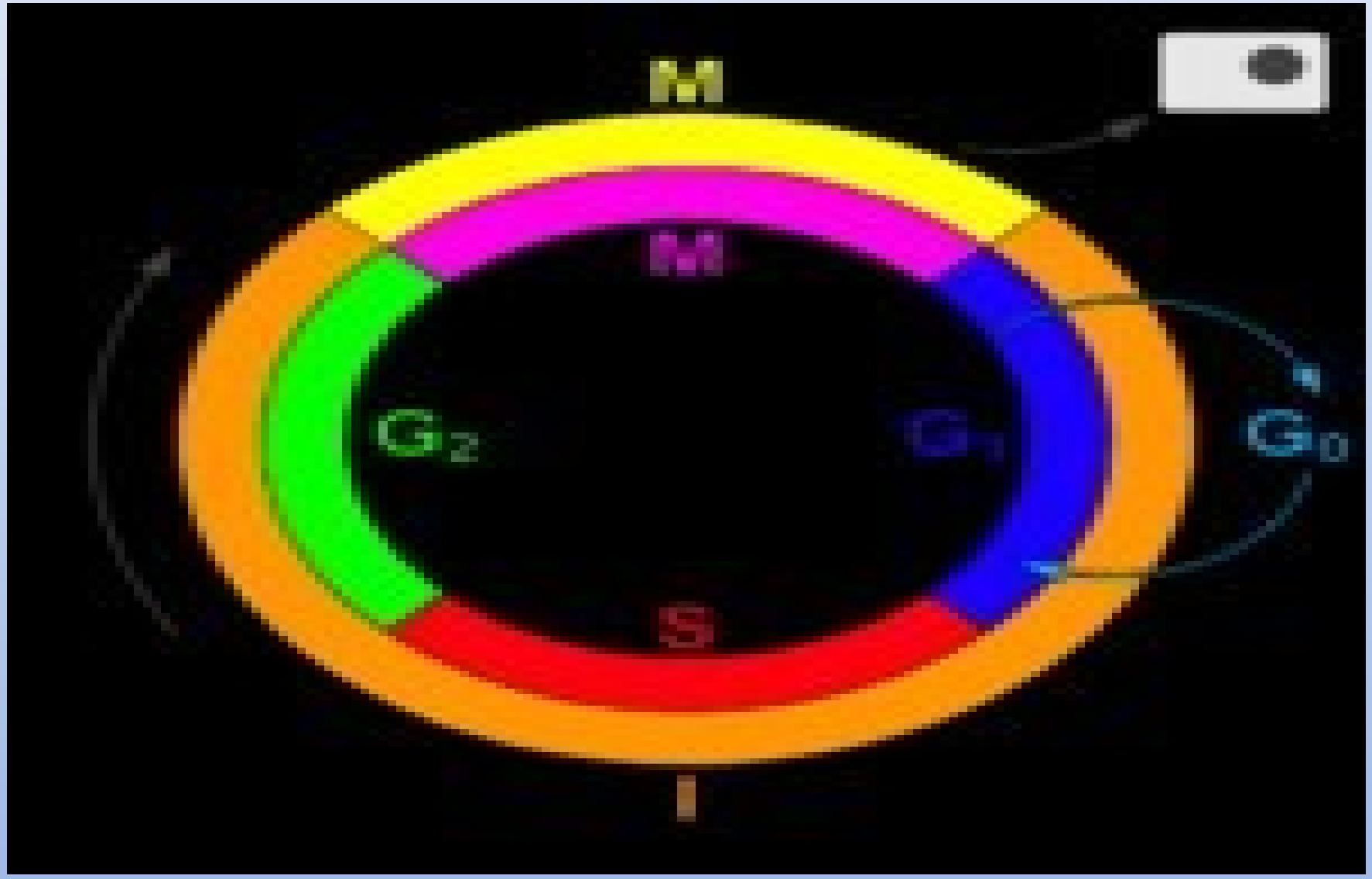
DNA replication:



Process:


DNA polymerase III elongates the leading strand.
Helicase unwinds the double helix.
Leading strand template
3'
5'
Leading strand
Okazaki fragment
Lagging strand
3'
5'
Parent DNA
Single-stranded DNA-binding proteins make the templates available to RNA primase and DNA polymerase III.
Lagging strand template
DNA polymerase III elongates the lagging strand.
RNA primase makes primer.

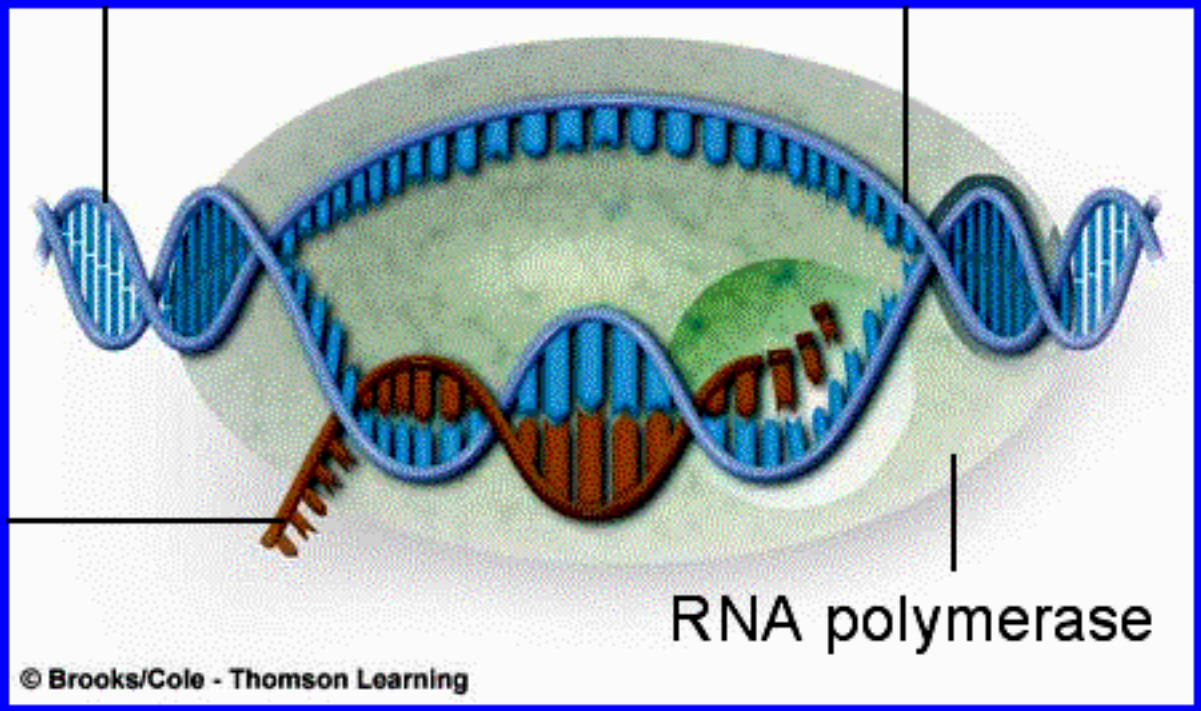
Life cycle:



Transcription: overview

- In prokaryotes transcription and translation are coupled.
- In eukaryotes transcription and translation are separated. Transcription occurs in the nucleus, and translation occurs in the cytoplasm on ribosomes.

Gene Transcription



Stages of Transcription

- Chain Initiation
- Chain Elongation
- Chain Termination

TRANSLATION

- ***genetic code*** : composed of 4 nucleotide bases.
- Produce 64 different combination of codon.
- Termination codons - UAA,UAG and UGA.
- Initiating codon – AUG (Met) , GUG (Val).

Protein Synthesis

- It occurs in three stages-

1. Requirement of the components

- Amino acids
- Ribosome
- m RNA
- t RNA
- Energy sources

2. Activation of amino acids –
- Aminoacyl-tRNA synthetase
- Corresponding t-RNA

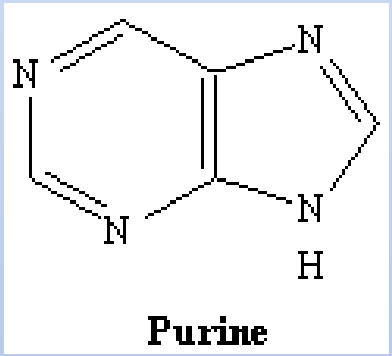
3. Protein synthesis proper

- Initiation :
- Elongation :
- Termination :

Nucleic Acid Bases

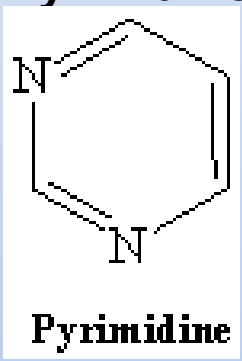
- **Derived from purine or pyrimidine**

Purines

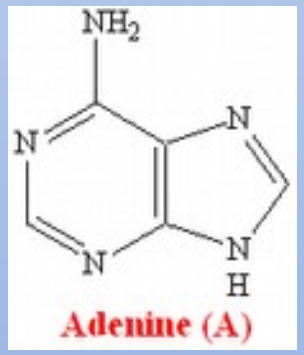


Purine

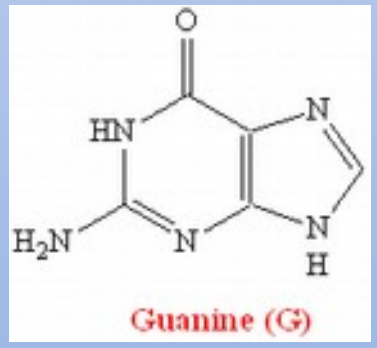
Pyrimidines



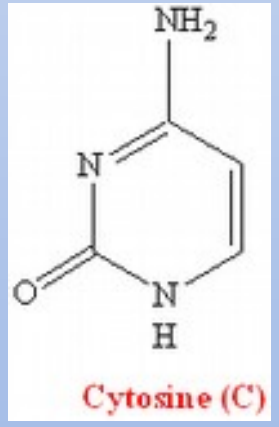
Pyrimidine



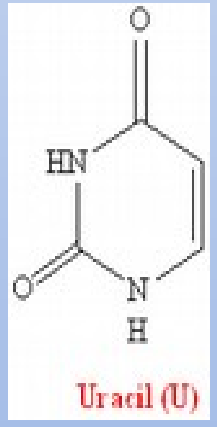
Adenine (A)



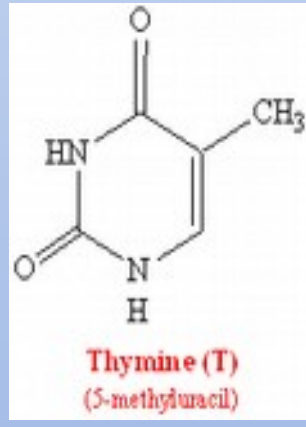
Guanine (G)



Cytosine (C)



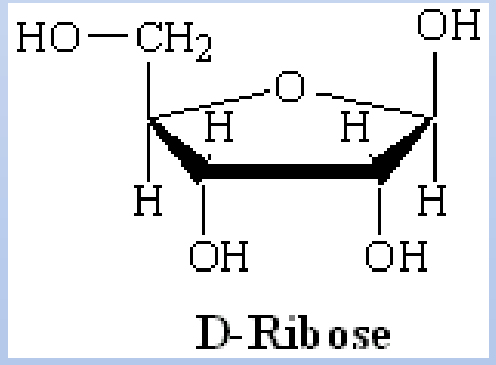
Uracil (U)

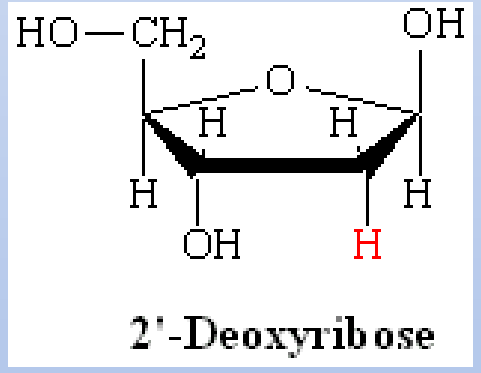


Thymine (T)
(5-methyluracil)

Sugars

D-Ribose and 2’-Deoxyribose



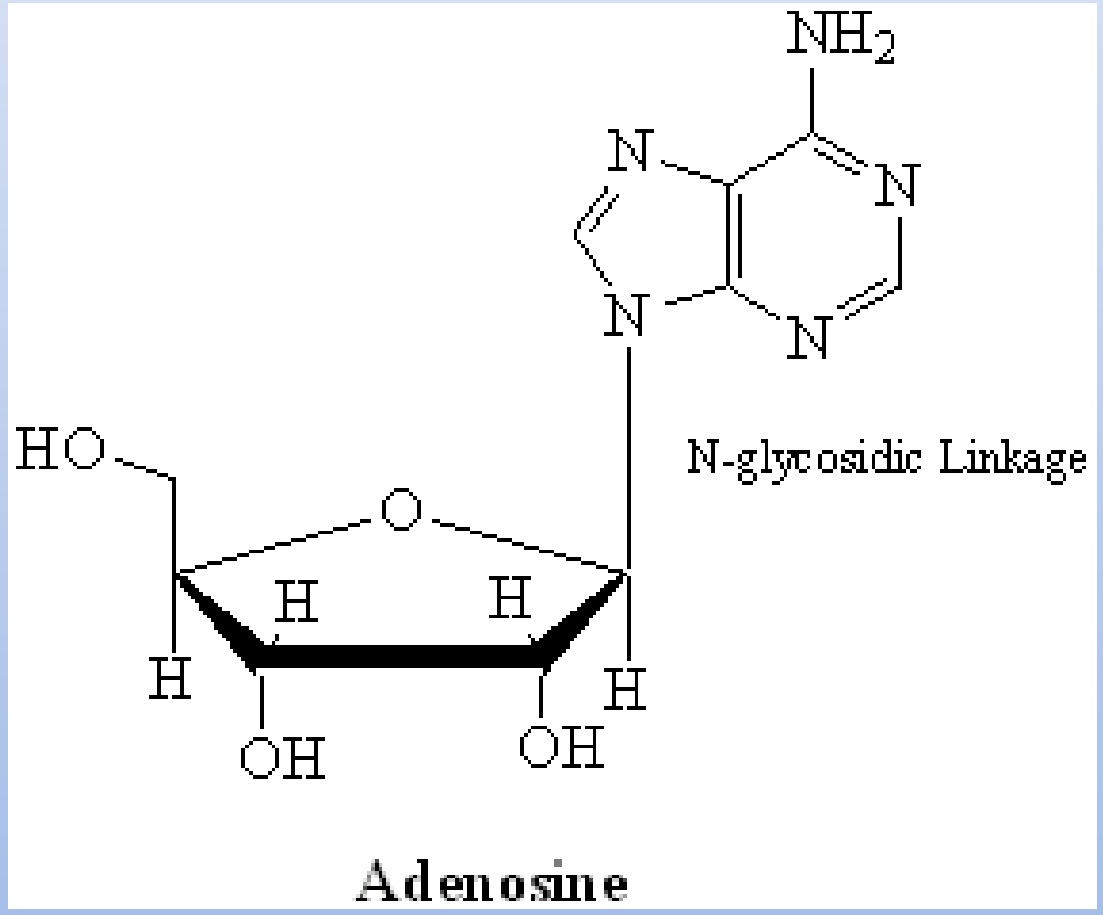


*Lacks a 2’-OH group

Nucleosides

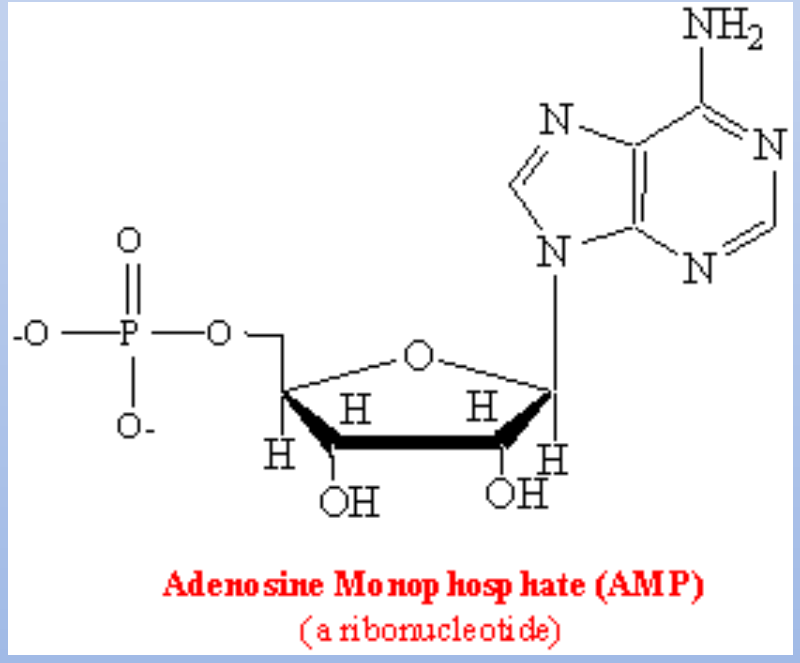
- Result from linking one of the sugars with a purine or pyrimidine base through an N-glycosidic linkage

Nucleosides

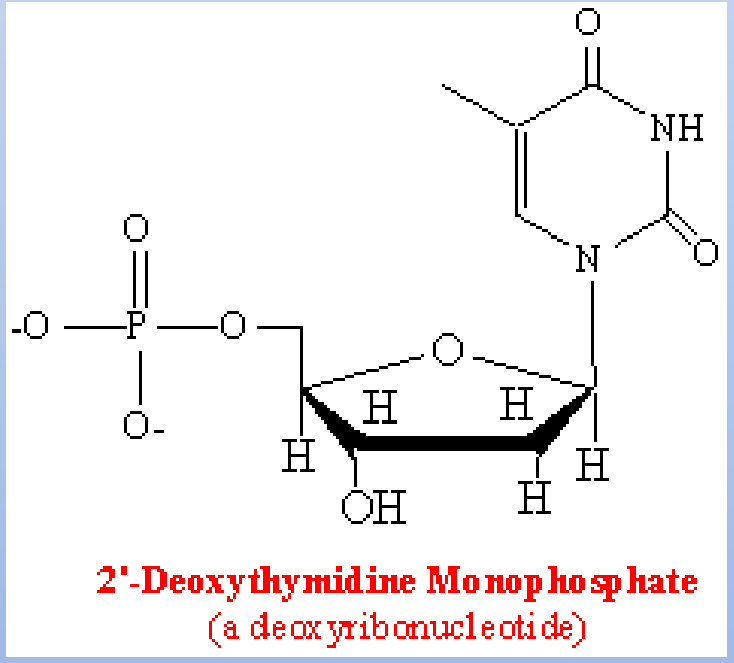


Nucleotides

- Result from linking one or more phosphates with a nucleoside onto the 5’ end of the molecule through esterification



Adenosine Monophosphate (AMP)
(a ribonucleotide)



2'-Deoxythymidine Monophosphate
(a deoxyribonucleotide)

Nucleotides

- RNA (ribonucleic acid) is a polymer of ribonucleotides
- DNA (deoxyribonucleic acid) is a polymer of deoxyribonucleotides
- Both deoxy- and ribonucleotides contain Adenine, Guanine and Cytosine
  - Ribonucleotides contain Uracil
  - Deoxyribonucleotides contain Thymine

Nucleotides

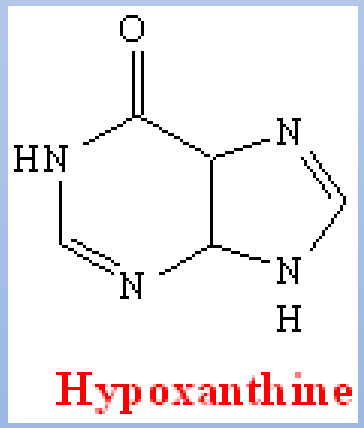
- Monomers for nucleic acid polymers
- Nucleoside Triphosphates are important energy carriers (ATP, GTP)
- Important components of coenzymes
  - FAD, NAD^+ and Coenzyme A

Naming Conventions

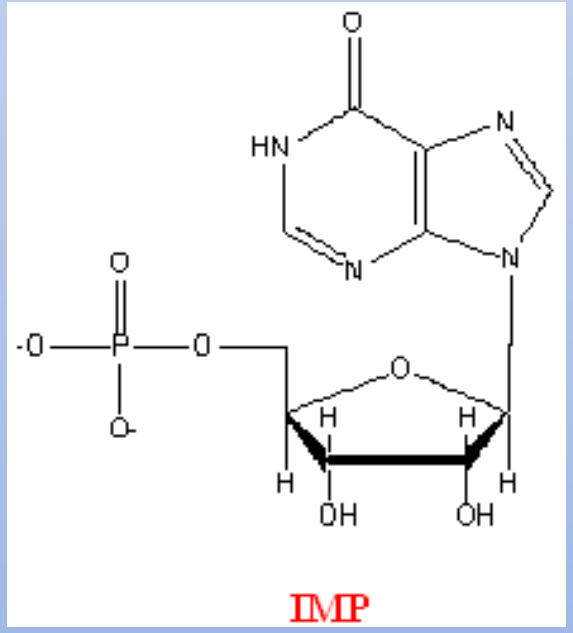
- Nucleosides:
  - Purine nucleosides end in “-sine”
    - Adenosine, Guanosine
  - Pyrimidine nucleosides end in “-dine”
    - Thymidine, Cytidine, Uridine
- Nucleotides:
  - Start with the nucleoside name from above and add “mono-”, “di-”, or “triphosphate”
    - Adenosine Monophosphate, Cytidine Triphosphate, Deoxythymidine Diphosphate

Nucleotide Metabolism

- PURINE RIBONUCLEOTIDES: formed *de novo*
  - i.e., purines are not initially synthesized as free bases
  - First purine derivative formed is Inosine Mono-phosphate (IMP)
    - The purine base is hypoxanthine
    - AMP and GMP are formed from IMP



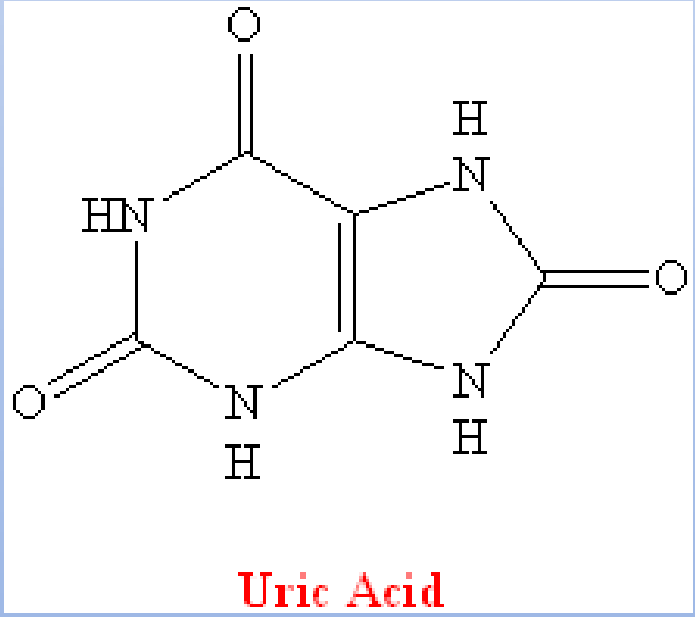
Hypoxanthine



IMP

Purine Nucleotides

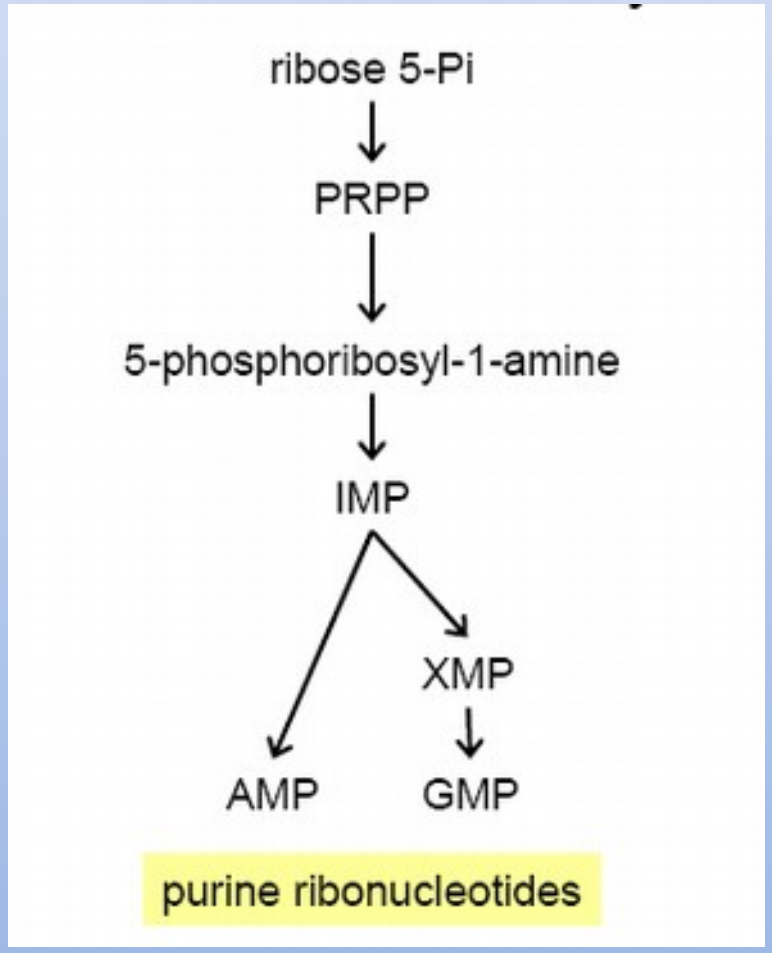
- Get broken down into Uric Acid (a purine)

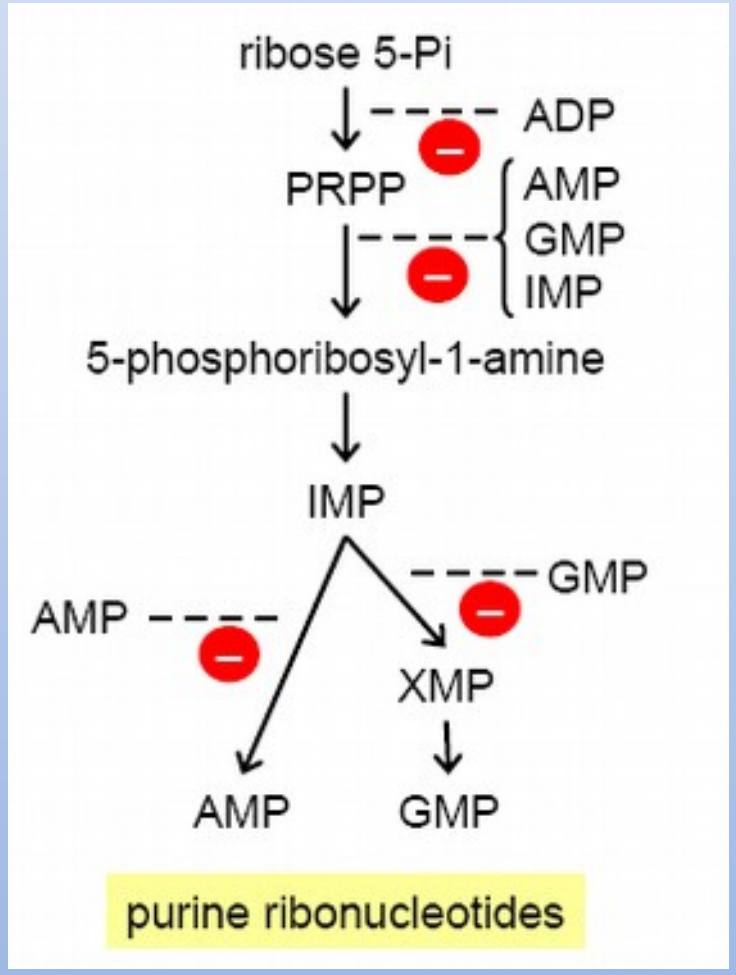


Uric Acid

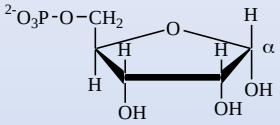
N_1: Aspartate Amine
C_2, C_8: Formate
N_3, N_9: Glutamine
C_4, C_5, N_7: Glycine
C_6: Bicarbonate Ion

Purine nucleotide Synthesis- overview



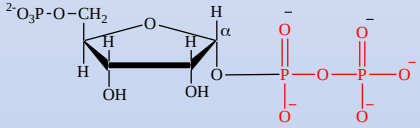


Purine Nucleotide Synthesis



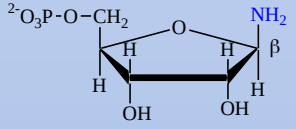
α-D-Ribose-5-Phosphate (R5P)

ATP → AMP: Ribose Phosphate Pyrophosphokinase



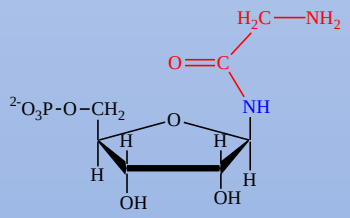
5-Phosphoribosyl-α-pyrophosphate (PRPP)

Glutamine + H_2O → Glutamate + PP_i: Amidophosphoribosyl Transferase



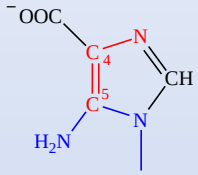
β-5-Phosphoribosylamine (PRA)

Glycine + ATP → ADP + P_i: GAR Synthetase



Glycinamide Ribotide (GAR)

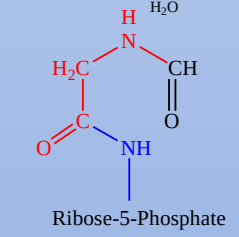
N^{10}-Formyl-THF → THF: GAR Transformylase



Ribose-5-Phosphate

Formylglycinamide ribotide (FGAR)

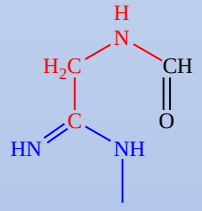
FGAM Synthetase: ADP + Glutamate + P_i ; ATP + Glutamine + H_2O



Ribose-5-Phosphate

Formylglycinamidine ribotide (FGAM)

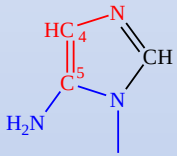
AIR Synthetase: ADP + P_i ; ATP



Ribose-5-Phosphate

5-Aminoimidazole Ribotide (AIR)

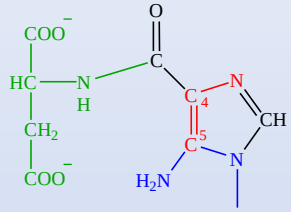
AIR Car boxylase: ADP + P_i ; ATP + HCO_3^-



Ribose-5-Phosphate

Carboxyamidoimidazole Ribotide (CAIR)

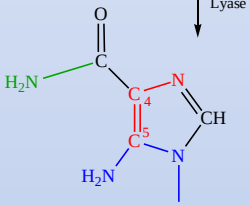
Aspartate + ATP → ADP + P_i: SAICAR Synthetase



Ribose-5-Phosphate

5-Aminoimidazole-4-(N-succinylocarboxamide) ribotide (SAICAR)

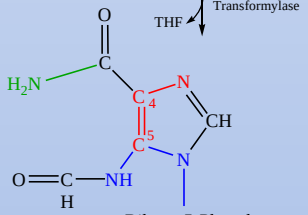
Fumarate ← Adenylosuccinate Lyase



Ribose-5-Phosphate

5-Aminoimidazole-4-carboxamide ribotide (AICAR)

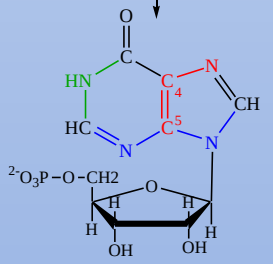
N^{10}-Formyl-THF → THF: AICAR Transformylase



Ribose-5-Phosphate

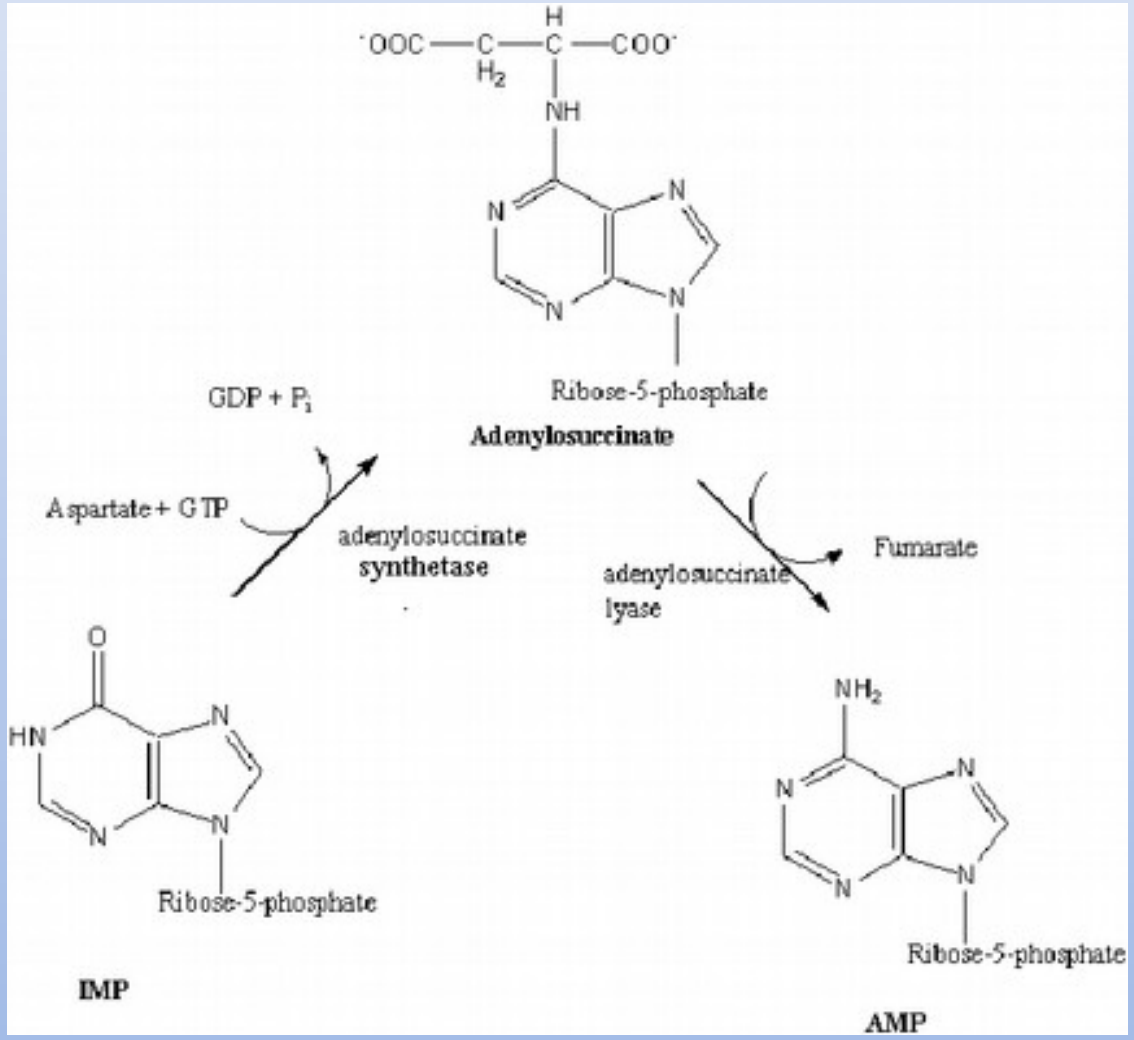
5-Formaminoimidazole-4-carboxamide ribotide (FAICAR)

H_2O ← IMP Cyclohydrolase

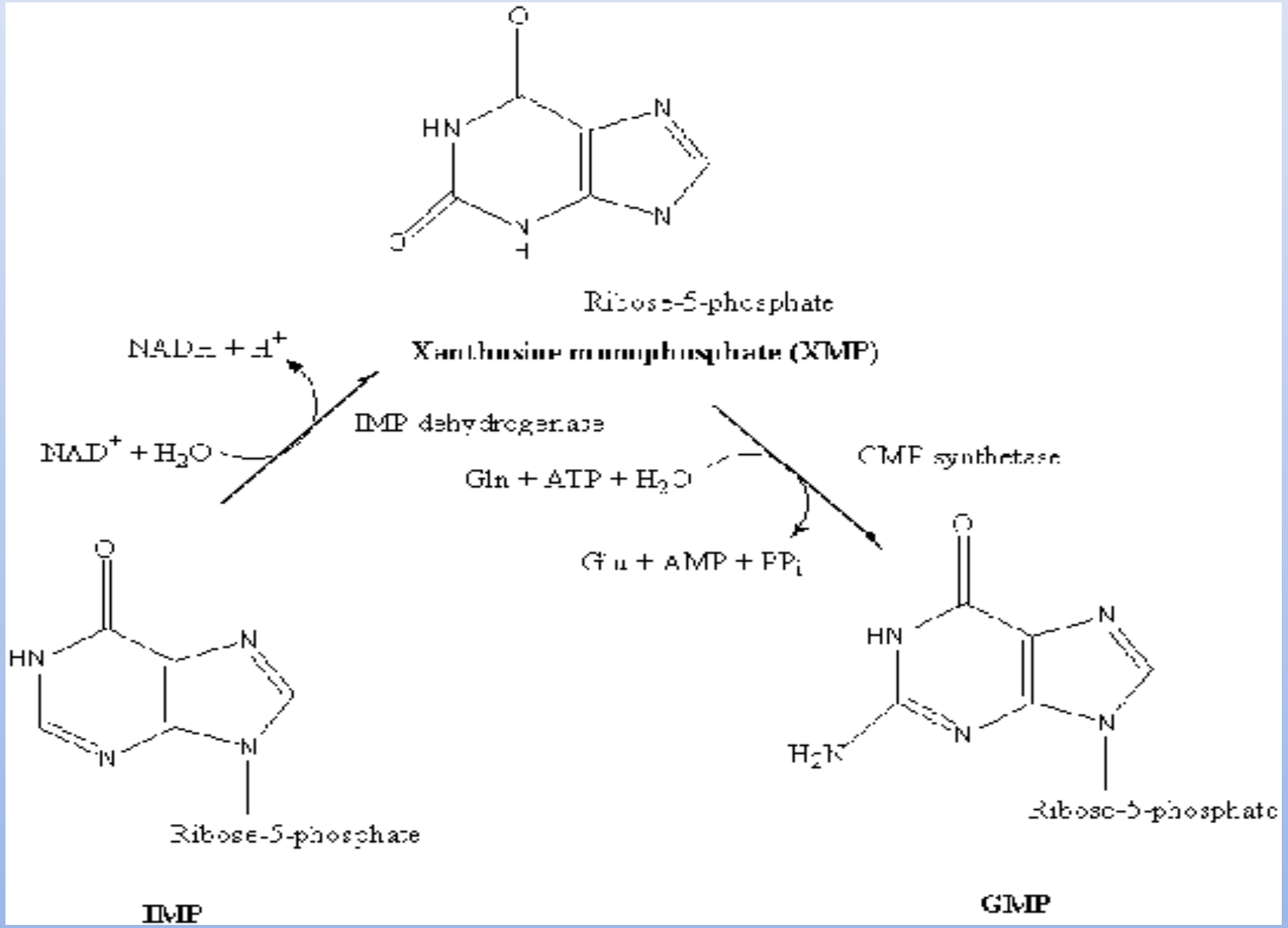


Inosine Monophosphate (IMP)

IMP Conversion to AMP



IMP Conversion to GMP



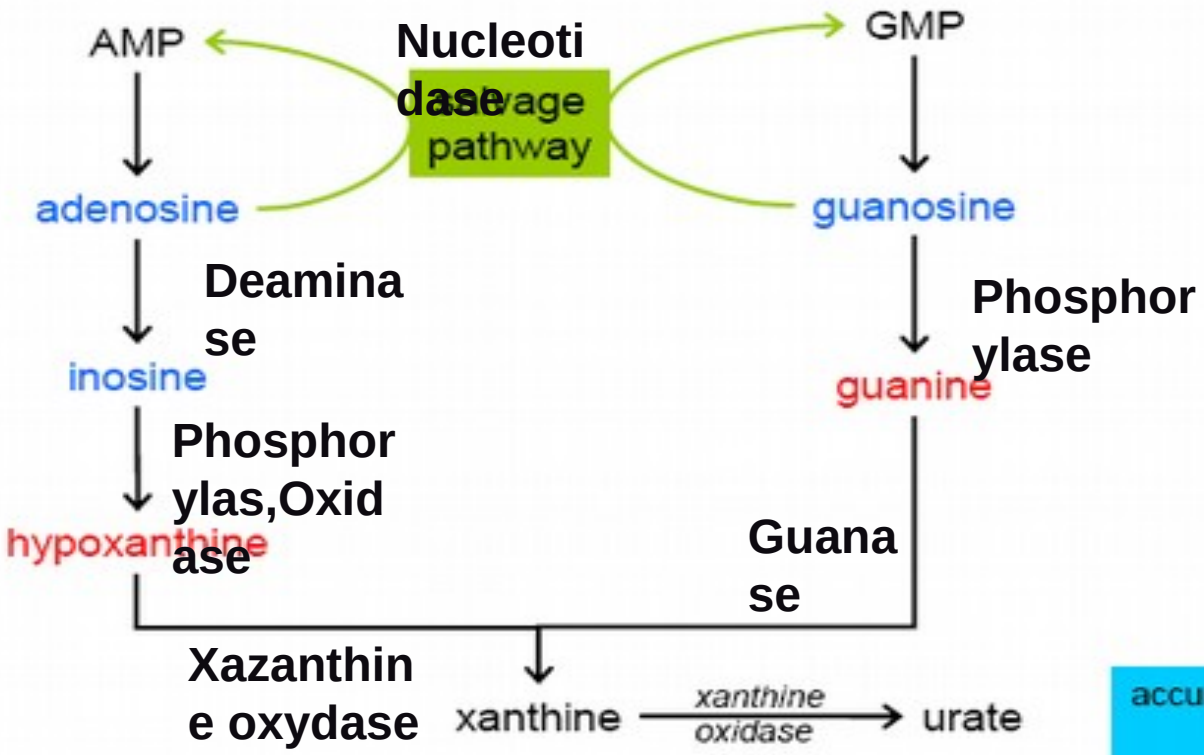
IMP

GMP

Purine Catabolism and Salvage

Nucleotide degradation

- Degradation and salvage



What Happened to the toe? Why is it swollen?

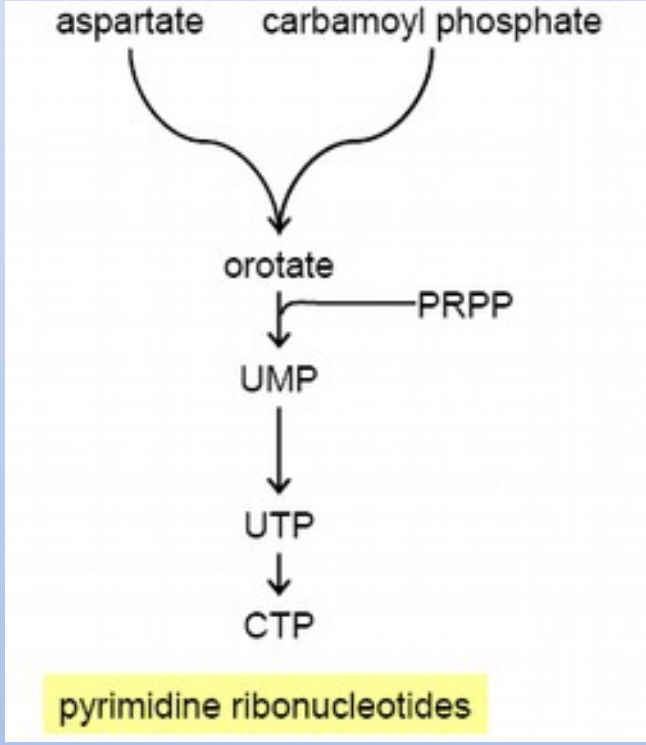
Uric Acid Excretion

- Humans – excreted into urine as insoluble crystals
- Birds, terrestrial reptiles, some insects – excrete insoluble crystals in paste form
  - Excess amino N converted to uric acid
    - (conserves water)
- Others – further modification :

Uric Acid Allantoin Allantoic Acid Urea Ammonia

Gout

- Impaired excretion or overproduction of uric acid
- Uric acid crystals precipitate into joints (Gouty Arthritis), kidneys, ureters (stones)
- Lead impairs uric acid excretion – lead poisoning from pewter drinking goblets
  - Fall of Roman Empire?
- Xanthine oxidase inhibitors inhibit production of uric acid, and treat gout
- Allopurinol treatment – hypoxanthine analog that binds to Xanthine Oxidase to decrease uric acid production



pyrimidine ribonucleotides

Pyrimidine Synthesis