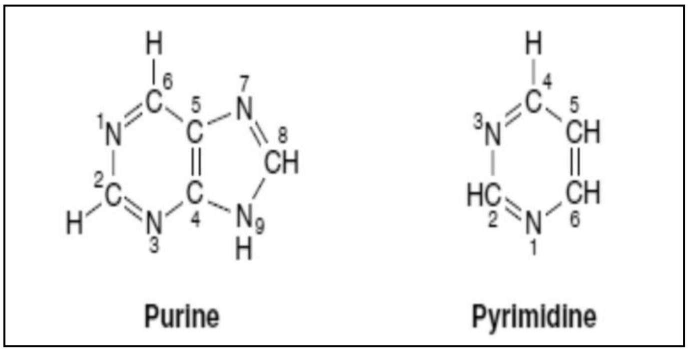
Nucleotides

Nucleic acids are macromolecules present in all living cells in combination with proteins to form nucleoproteins. The protein is usually protamines and histones. The nucleic acids are of two main types:
– Deoxyribonucleic acid or DNA
– Ribonucleic acid or RNA.
DNA is present in nucleolus and small amounts are also present in mitochondria, whereas 90% of the RNA is present in cell cytoplasm and 10% in the nucleolus. Genetic information is encoded in a nucleic acid molecule (DNA). RNA is very important role in protein synthesis.

Purine, Pyrimidine, Nucleoside & Nucleotide
Purines and pyrimidines are nitrogen-containing heterocycles:



Purine and pyrimidine.

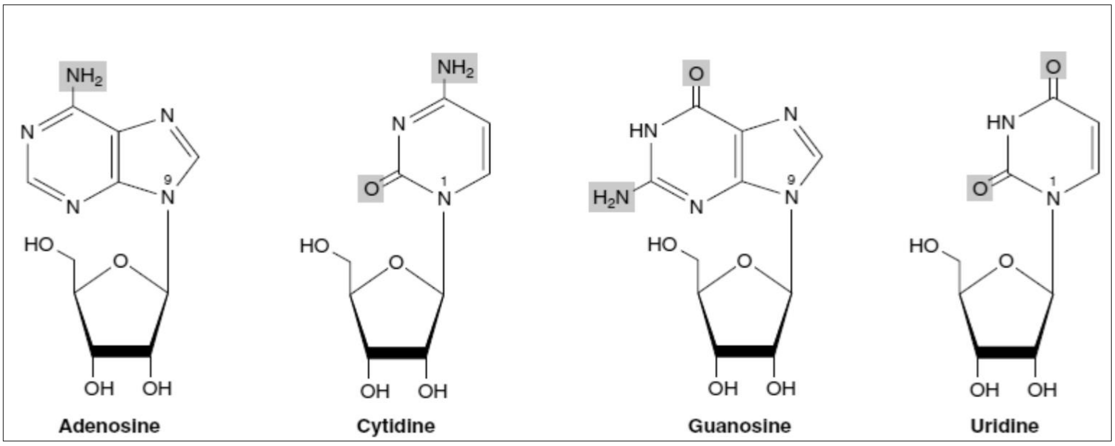
Two principal purine bases found in DNAs, as well as RNAs are: Adenine (A), Guanine (G), Three major pyrimidine bases are Cytosine (C), Uracil (U), Thymine (T). Nucleotides the monomer units or building blocks of nucleic acids serve multiple additional functions. They form a part of many coenzyme like (FAD, FMN, NAD, and $NADP^+$). In addition, nucleotides participate in cell signaling (cGMP and cAMP), and serve as donors of phosphoryl groups (eg, ATP or GTP). Nucleic acids are polymers of nucleotides, linked by phosphodiester bond, they are therefore called polynucleotides.

Each nucleotide consists of three components:
1. A nitrogenous base
2. A pentose sugar (ribose or deoxyribose)
3. A phosphate group.

Each Nucleoside consists of two components:
1. A nitrogenous base
2. A pentose sugar (ribose or deoxyribose)
In addition a nucleoside plus a phosphate group yields a nucleotide.

Table 9.1: Different major bases with their corresponding nucleosides and nucleotides

Base	*Ribonucleoside*	*Ribonucleotide*
Adenine (A)	Adenosine	Adenosine monophosphate (AMP)
Guanine (G)	Guanosine	Guanosine monophosphate (GMP)
Uracil (U)	Uridine	Uridine monophosphate (UMP)
Cytosine (C)	Cytidine	Cytidine monophosphate (CMP)
Base	*Deoxyribonucleoside*	*Deoxyribonucleotide*
Adenine	Deoxyadenosine	Deoxyadenosine monophosphate (dAMP)
Guanine	Deoxyguanosine	Deoxyguanosine monophosphate (dGMP)
Uracil	Deoxyuridine	Deoxyuridine monophosphate (dUMP)
Cytosine	Deoxycytidine	Deoxycytidine monophosphate (dCMP)
Thymine	Deoxythymidine	Deoxythymidine monophosphate (dTMP)



Nucleosides

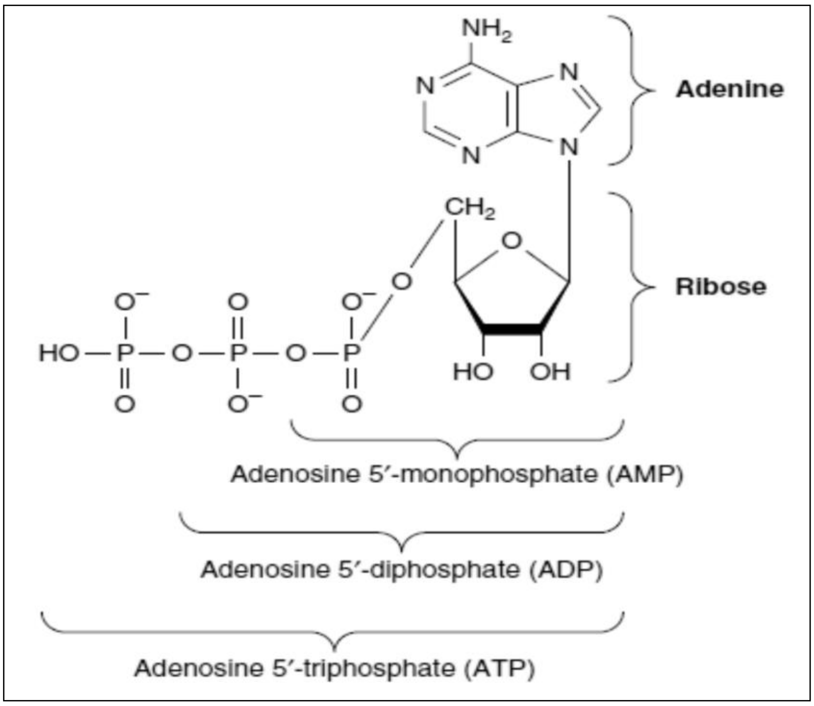


Figure: Nucleotide (ATP, ADP, AMP)

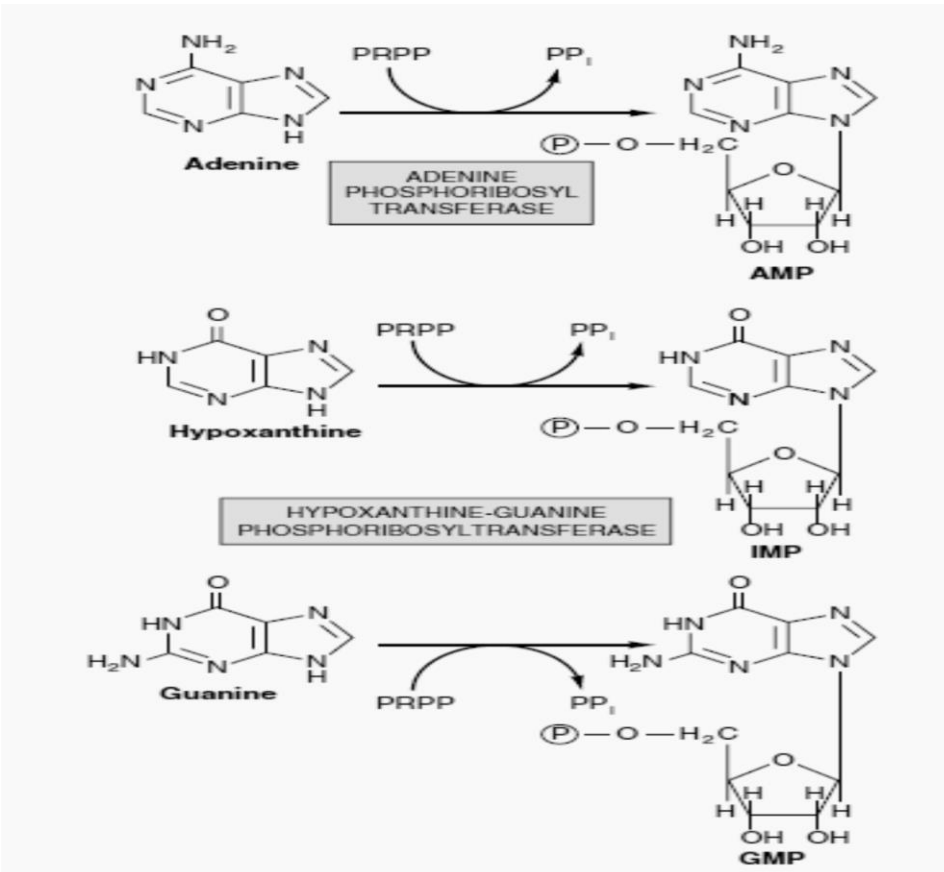


Figure: Phosphoribosylation of adenine, hypoxanthine, and guanine Physiologic Functions.

Nucleotides participate in reactions that fulfill physiologic functions as diverse as protein synthesis, nucleic acid synthesis, regulatory cascades, and signal transduction pathways. Genetic diseases of purine metabolism include gout, Lesch-Nyhan syndrome (the overproduction of uric acid. Uric acid is a waste product of normal chemical processes and is found in blood and urine. Excess uric acid can be released from the blood and build up under the skin and cause gouty arthritis caused by an accumulation of uric acid in the joints, also there are few clinically significant disorders of pyrimidine catabolism.

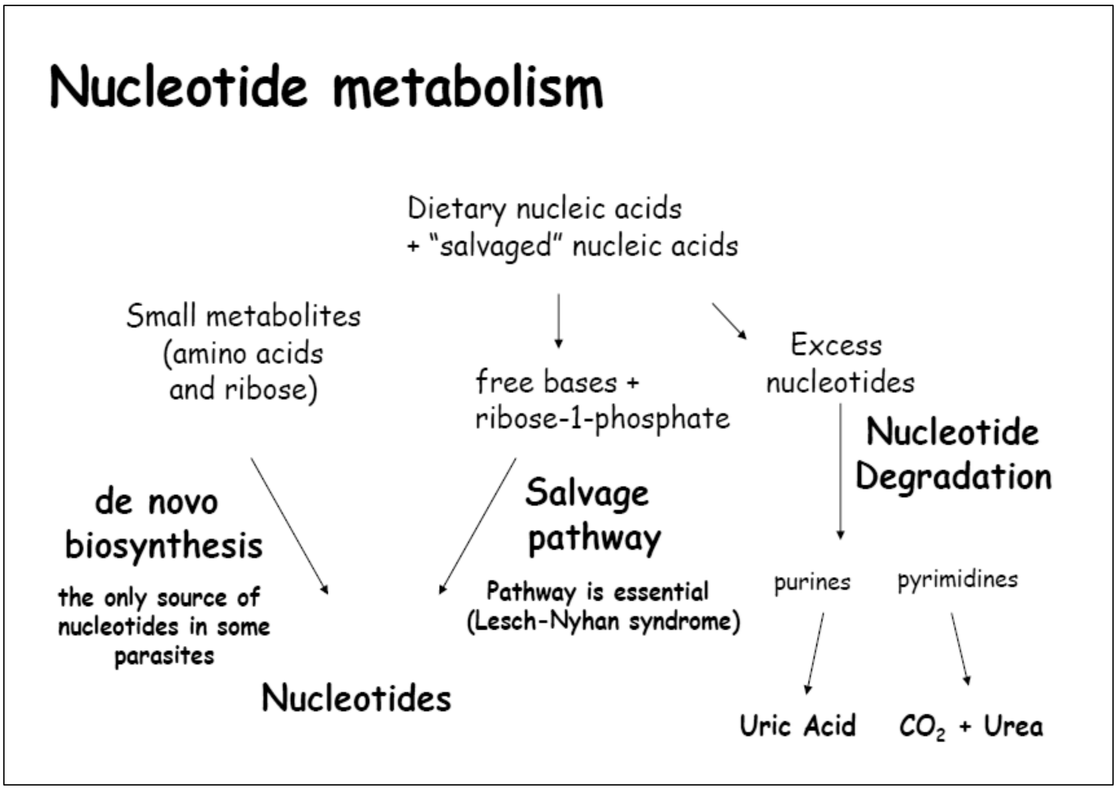
Biosynthesis Nucleotide

Ingested nucleic acids and nucleotides, which are degraded in the intestinal tract to mononucleotides, which may be absorbed or converted to purine and pyrimidine bases. The purine bases are then oxidized to uric acid, which may be absorbed and excreted in the urine. While little or no dietary purine or pyrimidine is incorporated into tissue nucleic acid.

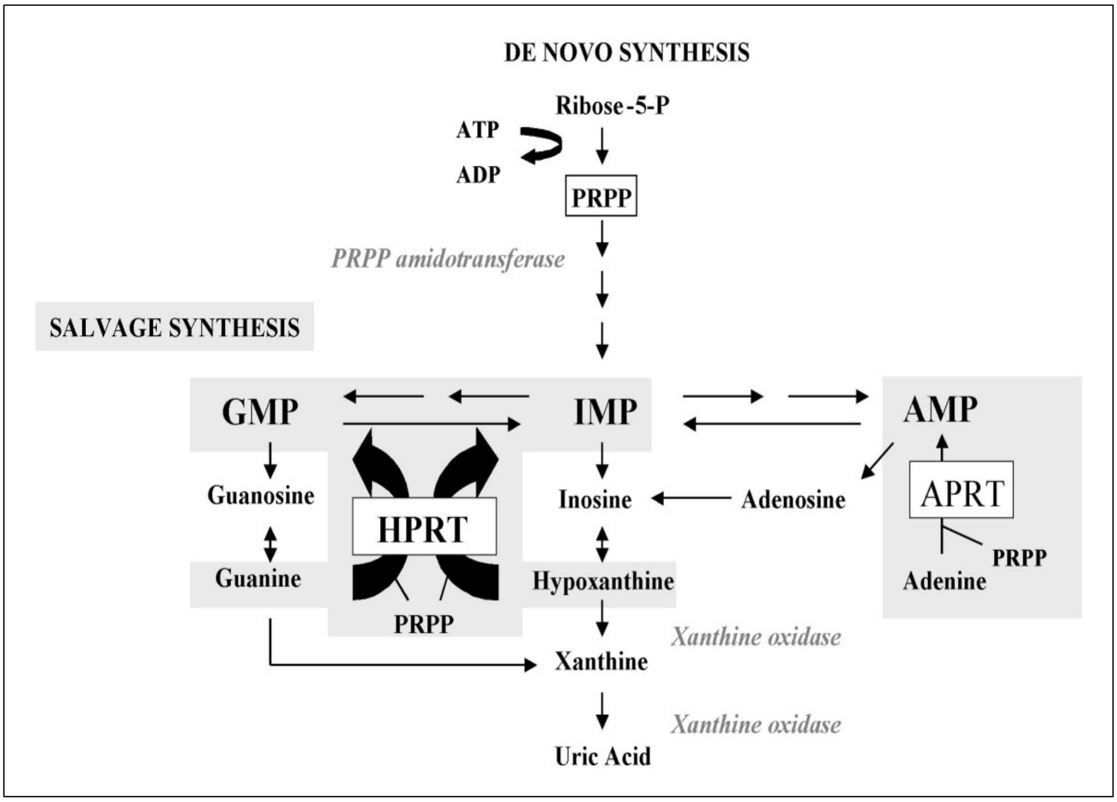
There are two principal routes for the synthesis of nucleotides:

1-de novo

2- Salvage pathways.

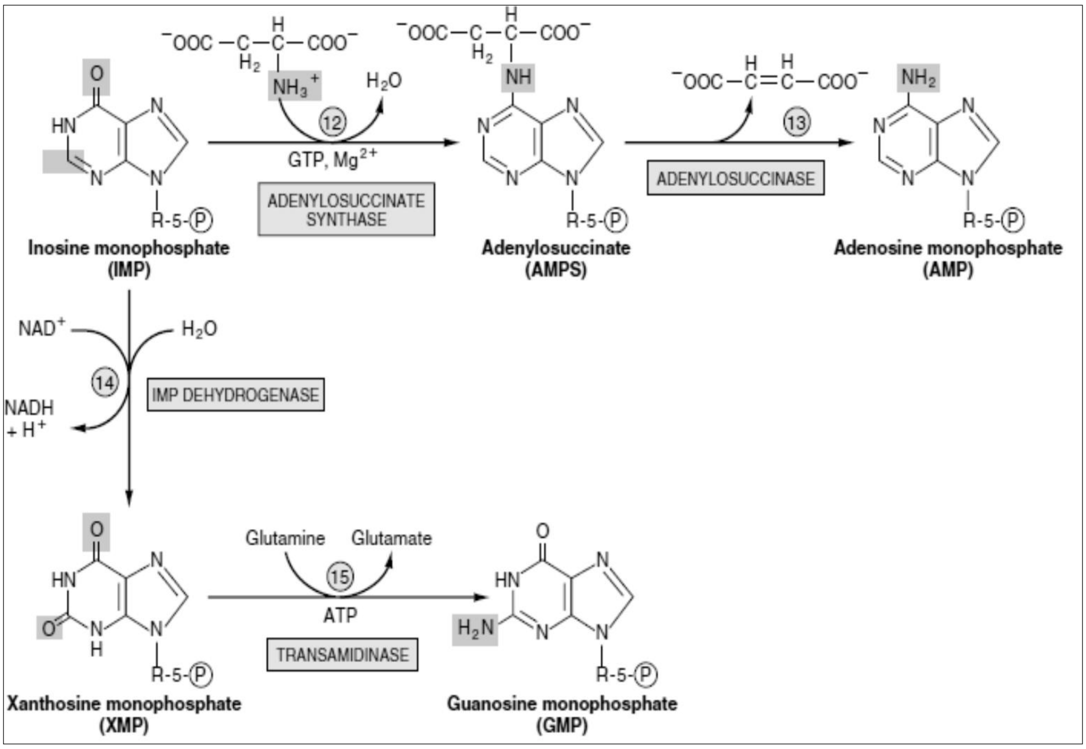


The salvage cycle interconverts purine bases, nucleosides and nucleotides released as by-products of cellular metabolism or from the catabolism of nucleic acids or nucleotide cofactors. This strategy for purine nucleotide synthesis is energetically favorable for a cell since only one salvage reaction requires ATP (phosphorylation of nucleosides to nucleotides).



De novo pathway

The de novo pathway using 5-phosphoribosyl-1-pyrophosphate (PRPP), with enzymes build purine and pyrimidine nucleotides from using simple molecules such as CO2, amino acids and tetrahydrofolate. This route of nucleotide synthesis has a high requirement for energy as compared that of the salvage pathway. For example, five of the 12 steps of de novo purine synthesis require hydrolysis of ATP or GTP but only one salvage cycle reaction uses ATP.

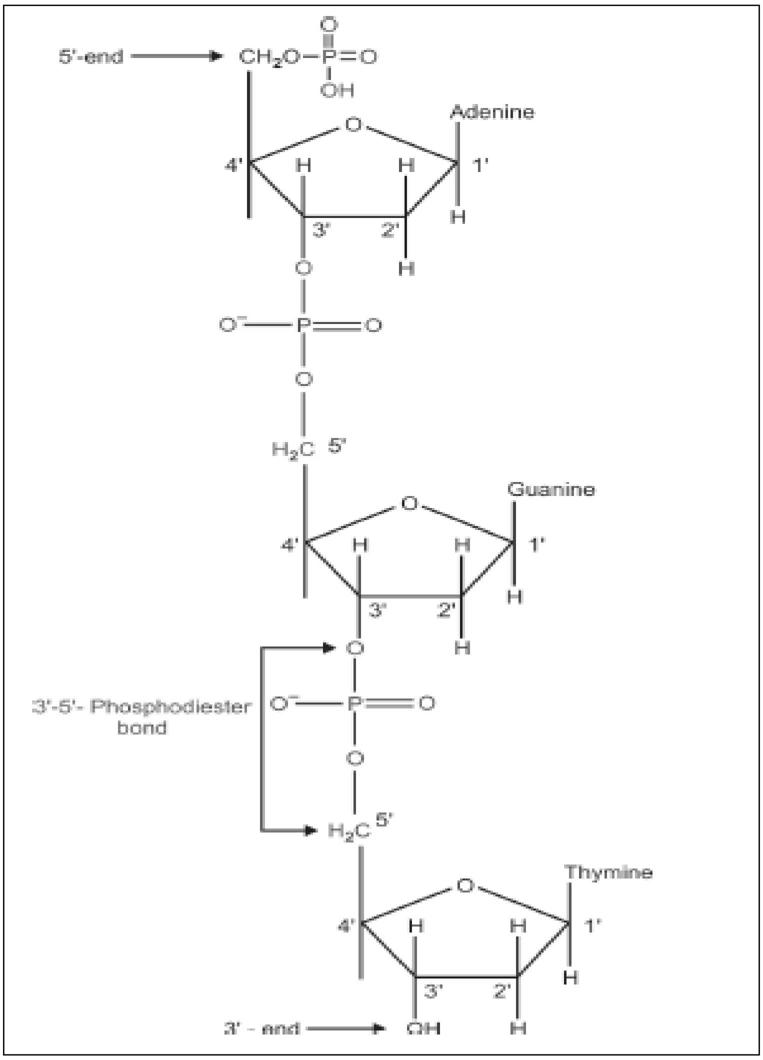


Conversion of IMP to AMP and GMP

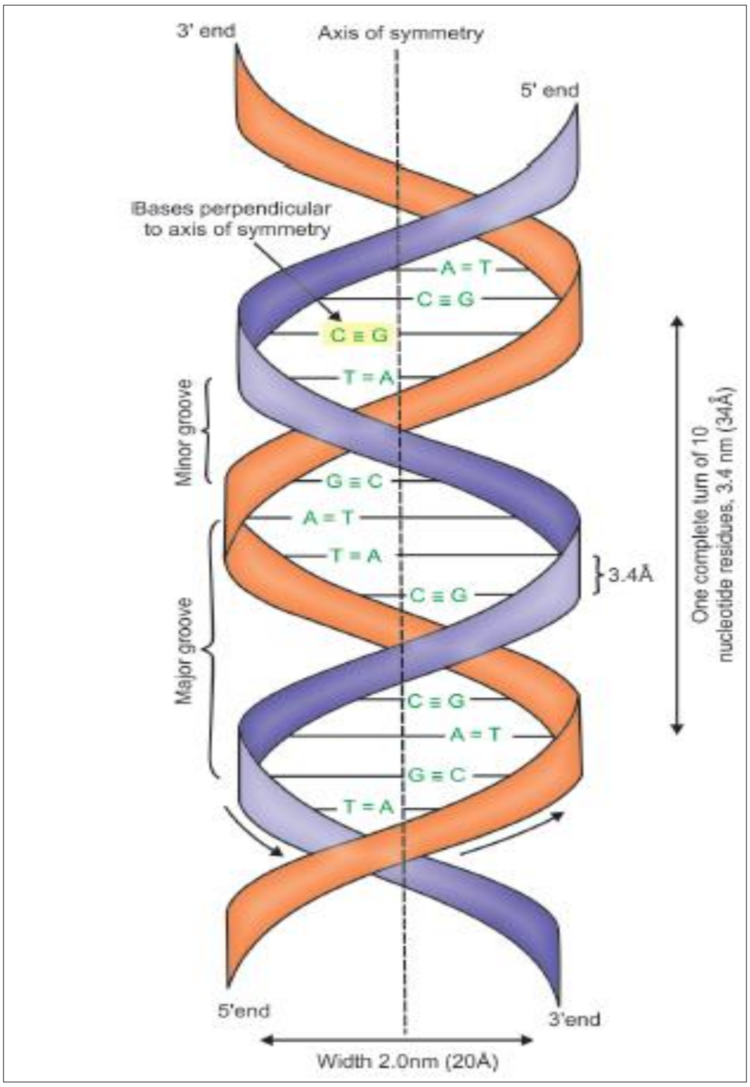
Salvage reactions that require far less energy than de novo synthesis. The more important mechanism involves phosphoribosylation by PRPP of a free purine (Pu) to form a purine 5′-mononucleotide. Purine deficiency states, which are rare in humans, generally reflect a deficiency of folic acid. Compounds that inhibit formation of tetrahydrofolates and therefore block purine synthesis have been used in cancer chemotherapy.

DNA Structure

Deoxyribonucleotide is composed of a nitrogenous base, a sugar and phosphate group. Since the genetic information resides in the order of the monomeric units within the polymers, there must exist a mechanism of reproducing or replicating this specific information with a high degree of fidelity (A = T), (G = C) The complementary base pairing proves the **Chargaff's Rule**. The 5'-hydroxyl group of the sugar moiety of one deoxyribonucleotide is joined to the 3'-hydroxyl group of the adjacent sugar moiety of deoxyribonucleotides by a phosphodiester linkage DNA is a very long, thread like macromolecule made up of a large number of deoxyribonucleotides.

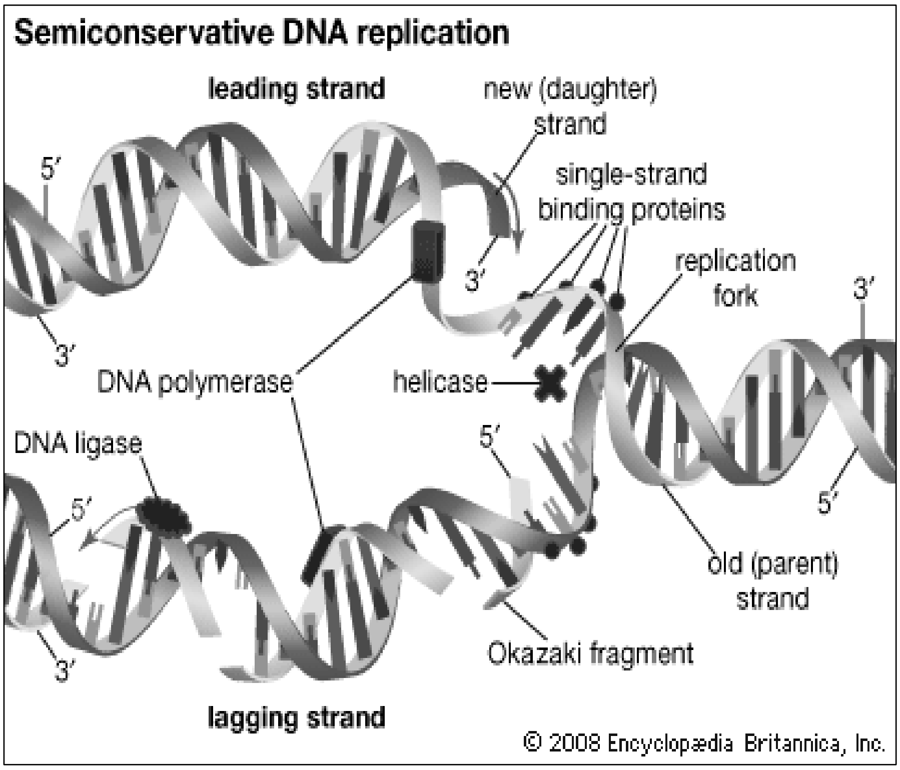


In 1950s a model of a double- stranded DNA molecule. The two strands of this double-stranded helix are held in register by hydrogen bonds between the purine and pyrimidine bases. The pairings between the purine and pyrimidine nucleotides on the opposite strands are very specific and are dependent upon hydrogen bonding of A with T and G with C. This common form of DNA is said to be one strand runs in the 5′to 3′direction and the other in the 3′ to 5′direction.

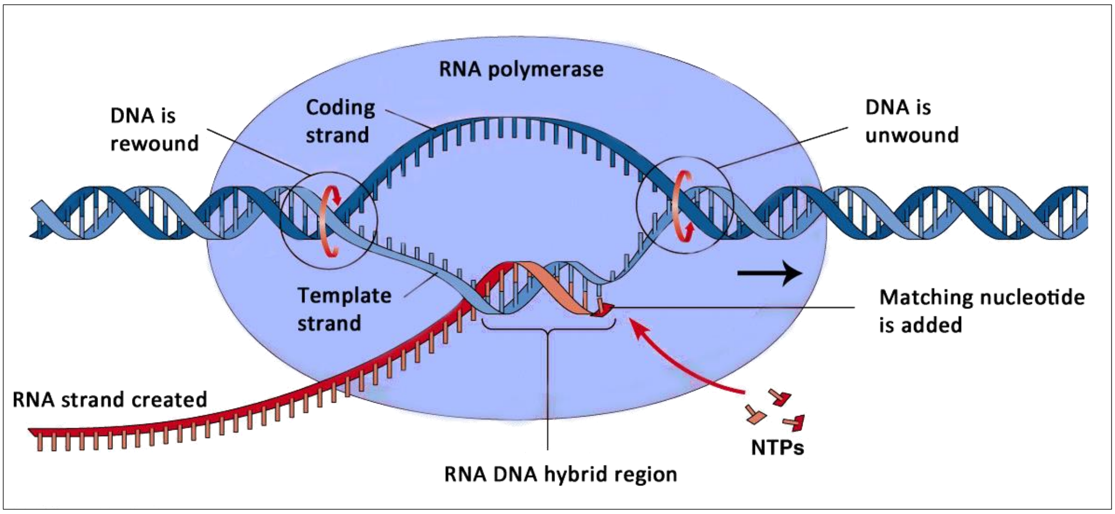


DNA provides Template for Replication & Transcription

The genetic information stored in the nucleotide sequence of DNA serves two purposes. It is the source of information for the synthesis of all protein molecules of the cell and organism, and it provides the information inherited by daughter cells. Both of these functions require that the DNA molecule serve as a template in the first case for the **Transcription** of the information into RNA and in the second case for the **Replication** of the information into daughter DNA molecules. The complementarity of the Watson and Crick double- stranded model of DNA strongly suggests that molecule occurs in a semiconservative manner. Thus, when each strand of the double- stranded parental DNA molecule separates from its complement during replication, each serves as a template on which a new complementary strand is synthesized. The two newly formed doublestranded daughter DNA molecules, each containing one strand (but complementary rather than identical).



Replication process



Transcription process

The difference between RNA and DNA

Ribonucleic acid (RNA) is a polymer of purine and pyrimidine ribonucleotides linked together by 3′,5′-phosphodiester bridges analogous to those in DNA. Although sharing many features with DNA, RNA possesses several specific differences:

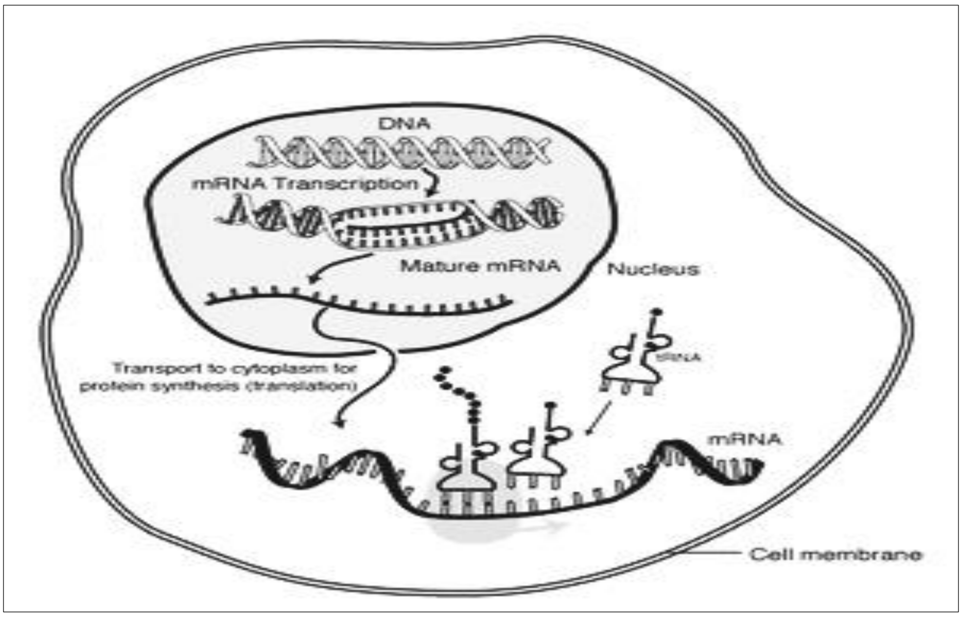
1-In RNA, the sugar moiety to which the phosphates and purine and pyrimidine bases are attached is ribose rather than the 2′-deoxyribose of DNA.

2- Although RNA contains the ribonucleotides of adenine, guanine, and cytosine, it does not possess thymine that found in DNA. Instead of thymine, RNA contains the ribonucleotides of uracil.

3- RNA exists as a single strand, whereas DNA exists as a double-stranded helical molecule.

Translation and RNA Types

Ribonucleic acid (RNA) is a family of large biological molecules that perform multiple vital roles in the coding, decoding, regulation, and expression of genes. RNA including tRNA , rRNA , mRNAs. **Messenger RNA (mRNA)** is carries the genetic information in the form of codons and convey genetic information from DNA to the ribosome, which are arranged into codons consisting of three bases each. Each codon encodes for a specific amino acid, except the stop codons, which terminate protein synthesis (translation). This process of translation of codons into amino acids requires two other types of RNA was **Transfer RNA (tRNA)** is a small RNA chain of about 80 nucleotides that transfers a specific amino acid to a growing polypeptide chain at the ribosomal site of protein synthesis during translation. **Ribosomal RNA (rRNA)** that is the central component of the ribosome's protein-manufacturing machinery.



Translation process