NUCLEIC ACIDs

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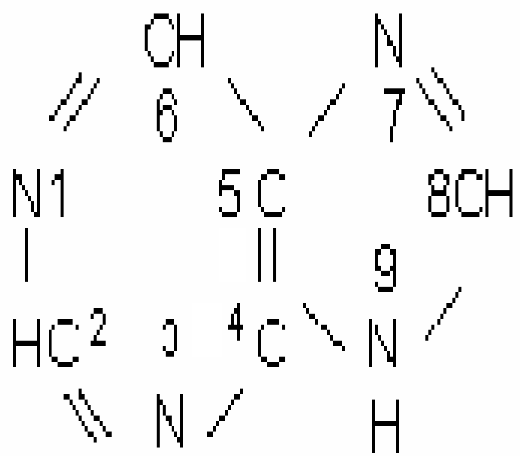
NUCLEIC ACIDs

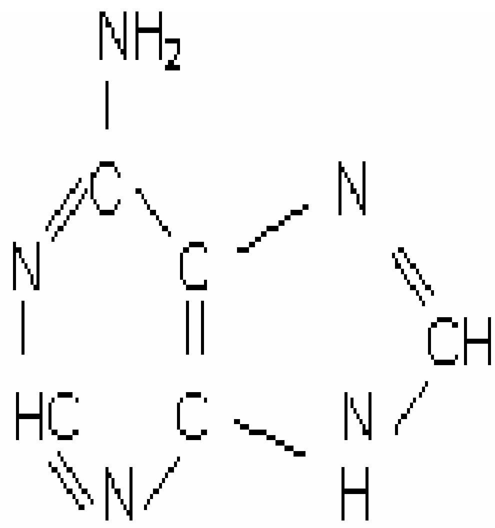
Nucleic acids are present in nucleus and Mitochondria They are found in two basic structural forms, deoxyribonucleic acid (DNA) and ribonucleic acid
(RNA).

THE STRUCTURE OF DNA

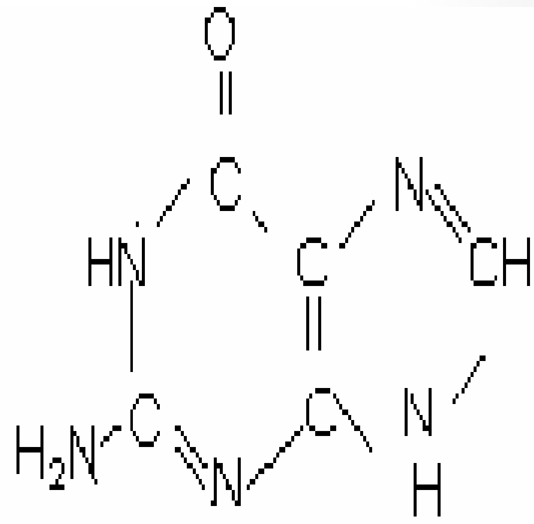
Deoxyribonucleic acid (DNA) is polymers of deoxyribonucleotides attached to each other by phosphodiester linkages. Each deoxyribonucleotide is composed of deoxyribonucleoside & inorganic phosphate group. Each deoxyribonucleoside is composed of nitrogen bases and a sugar deoxyribose. The nitrogenous bases are purines and pyrimidines.



The parental compound



Adenine

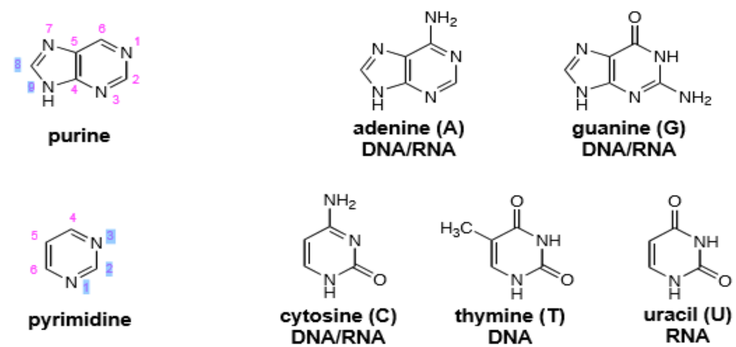


Guanine

Derivatives

The two purine bases are adenine and guanine. They are derived from their parental compound. The three pyrimidine bases are cytosine, thymine and uracil. It is important to know that thymine is found in DNA and uracil is found in RNA but the other above mentioned bases are found in both DNA and RNA.

28.1: Pyrimidines and Purines. The heterocyclic base; there are five common bases for nucleic acids (Table 28.1, p. 1166). Note that G, T and U exist in the keto form (and not the enol form found in phenols)

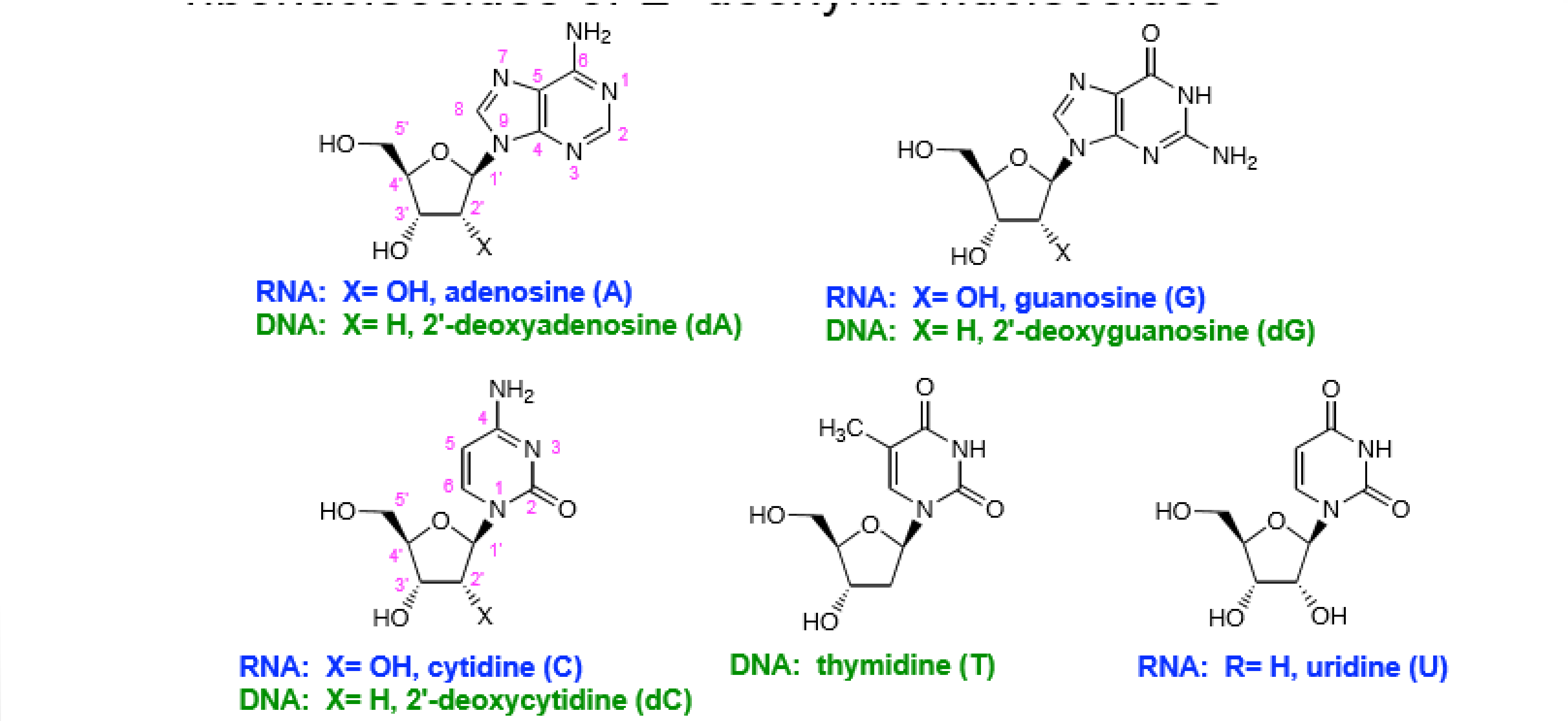


28.2: Nucleosides. N-Glycosides of a purine or pyrimidine heterocyclic base and a carbohydrate. The C-N bond involves the anomeric carbon of the carbohydrate. The carbohydrates for nucleic acids are D-ribose and 2-deoxy-D-ribose

Pyrimidine bases

The linkage in purine nucleotide is between 1 of sugar ribose and 9 of purine bases. The linkage in pyrimidine nucleotide is between 1 of sugar ribose and 1 of pyrimidine bases.

N.B. Nitrogenous bases + Pentose = Nucleosides Nucleoside + Pi = Nuclotides. These are important biomolecules, central to maintenance & propagation of life.



1. ATP, GTP, CTP, UTP, NAD, FAD and CoA are important ribonucleotides which act as coenzymes.
2. Deoxyribonucleotides are required for DNA replication and repair. Ribonucleotides are required for RNA.
3. They are used in biosynthetic reactions like UDP-glucose, in glycogen synthesis and UDP galactose in lactose synthesis.
4. ATP acts as currency of free energy for all cellular contraction, biosynthesis of activities like muscle molecules and transfer reactions.
5. Some nucleotides act as intracellular messenger's .eg, c AMP, c GMP are involved in peptide hormone action 6. GTP is used in protein synthesis.
7.S-adenosyl methionine participates in transmethylation reactions

Primary Structure of DNA

The deoxyribonucleotides are linked together by phosphodiester bonds between the 3' –hydroxyl of the sugar of one nucleotide through a phosphate molecule to the 5' – hydroxyl on the sugar of another nucleotide. The sugar – phosphate linkages form the backbone of the polymer to which the variable bases are attached. The nucleotide polymer has a free phosphate group attached to 5' – position of sugar and a free 3' – hydroxyl group. The sequence of the polymer is written in the 5’ to 3’ direction with abbreviations to different bases e.g. GCAT bases.

Secondary Structure of DNA:

The secondary structure of DNA is performed when the two strands of DNA are paired together as it is illustrated in the figure below. In the secondary structure of DNA, the two strands are anti-parallel. That means, the 5’ ---- 3’ of one strand is in opposite direction to the other strand.

The bases are stacked in the inside of the two strands. The bases of one strand pairs with the bases of the other strand of the same plane such that adenine always pairs with thymine with two bonds. Guanine always pairs with cytosine with three bonds. The negatively charged phosphate group and the sugar units expose themselves to the outside of the chain. The two strands of DNA coil around a single axis forming right handed double helix.

A double helical model of DNA, having the following important characteristic features:

1. Two helical polynucleotide chains are coiled around a common axis. The chains run in opposite directions, (anti parallel)
2. The two antiparallel polynucleotide chains are not identical, but they are complimentary.
3. The purine, pyrimidine bases are on the inside of the helix, the phosphate and deoxyribose groups are on the outside. The planes of the sugars are at right angles to that of the bases.
4. The diameter of the helix is 20 A0,adjascent bases are separated by 3.4 A0
5. The helical structure repeats after 10 residues on each chain.

6. The two chains are held together by hydrogen bonds between pairs of bases. Adenine is always paired with thymine, Guanine always paired with cytosine. A to T is bonded by two hydrogen bonds (A= T), Guanine is bonded to cytosine by three hydrogen bonds

7. The double helix is stabilized by interaction between stacked bases of the same strand.

The mitochondrial DNA is circular and there can be formation of Z-DNA and C-DNA which canbe performed during either replication or transcription.

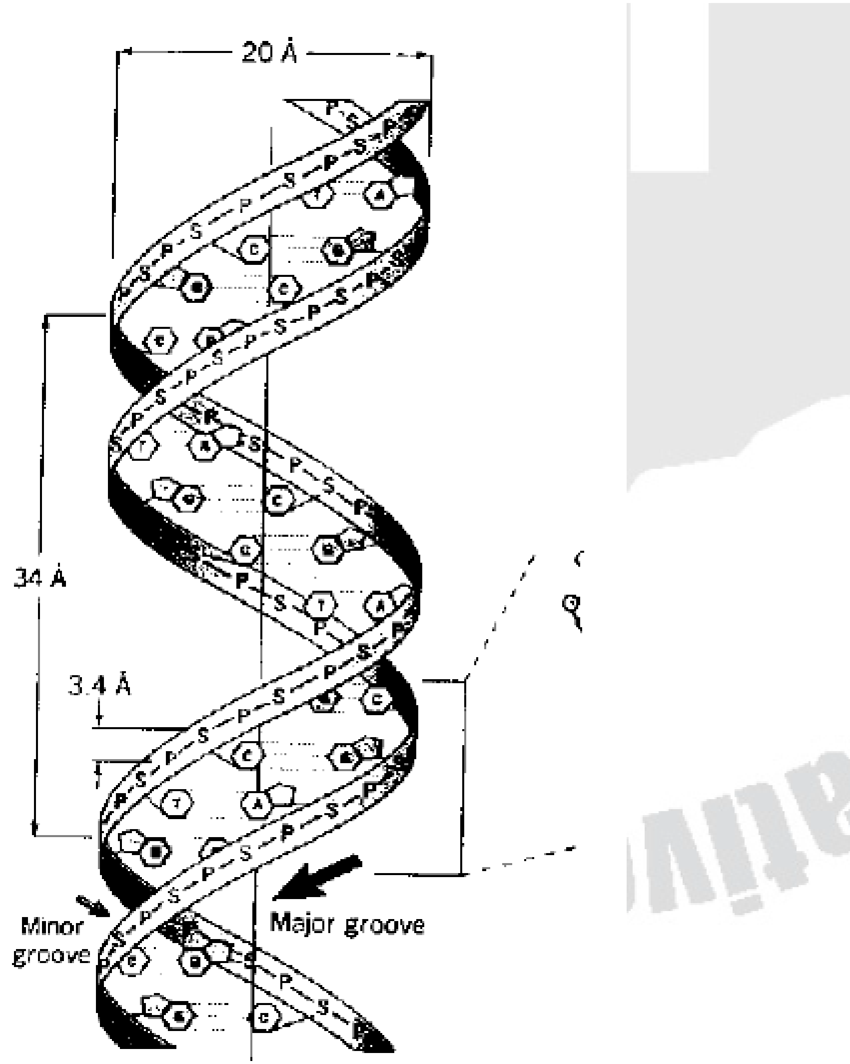


Fig 8.6 secondary structure of DNA

The Structure of RNA

The building unit of RNA is ribonucleotide. Ribonucleotide differs from deoxyribonucleotide in that ribonucleotide contains “O” in the carbon 2’ sugar ribose.

Uracil is found in RNA while Thymine is found in DNA. The nuclear DNA is in secondary structure, but RNA is the primary structure. Only t-RNA after post transcriptional process can be changed to tertiary structure.

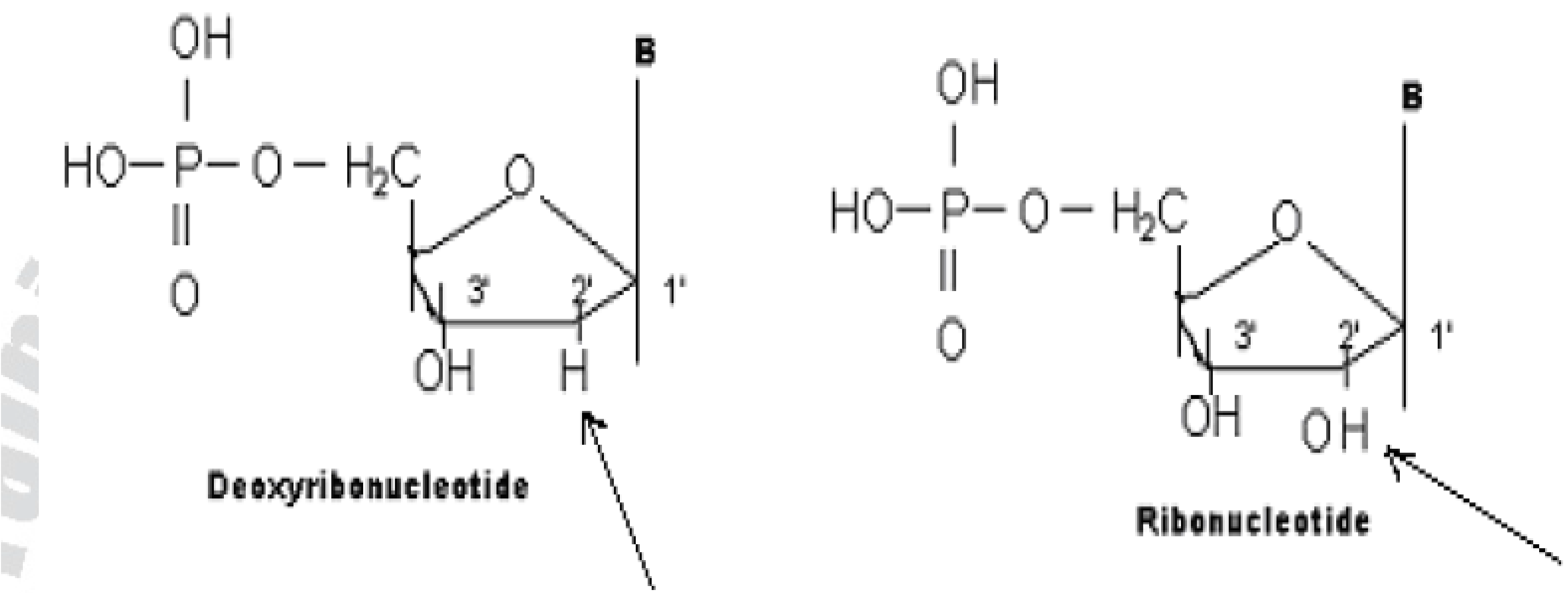


Fig 8.7 structure of Ribose and Deoxy-ribose in nucleotides

Differences between DNA and RNA

	properties	DNA	RNA
1	Uracil	absent	Present
2	Sugar	Deoxyribose Ribose	Ribose
3	Site	Nucleus, mitochondria Nucleus, ribosome, but never in cytosol	Nucleus, ribosome, cytosol, Nucleolus, mitochondria
4	Strands	Strands Two helical	Single strand
5	Types	Types Major forms are A,B &Z .	t-RNA ,m-RNA, r- RNA, hn RNA,& sn RNA. hn RNA, sn RNA .
6	Carries genetic information -	non	Only m-RNA carries genetic information

7	synthesize	DNA can synthesize RNA by transcription	Usually RNA can't form DNA, except by reverse transcriptase
8	Number of Bases	equal	Not equal
9	Thymine	Present	Absent

RNA: The three RNAs that have important role in protein synthesis are:

1. Messenger RNA (mRNA)
2. Transfer RNA (tRNA)
3. Ribosomal RNA (rRNA)

Messenger RNA (mRNA)

mRNA in all eukaryotic cells contain cap at the 5' end of the chain. Cap characterizes 7- methylated guanosine tri phosphate. These mRNAs contain poly-A at 3'- end of the chain. Poly- A characterizes about 200 successive adenylate residues. It is illustrated on the given diagram.

Poly-A also serves to protect the mRNA form exonuclease attack and Serves for the transport of the mRNA form nucleus to cytosol. Cap is for the protection of DNA from exonuclease attack. It is also used for the recognition during protein synthesis

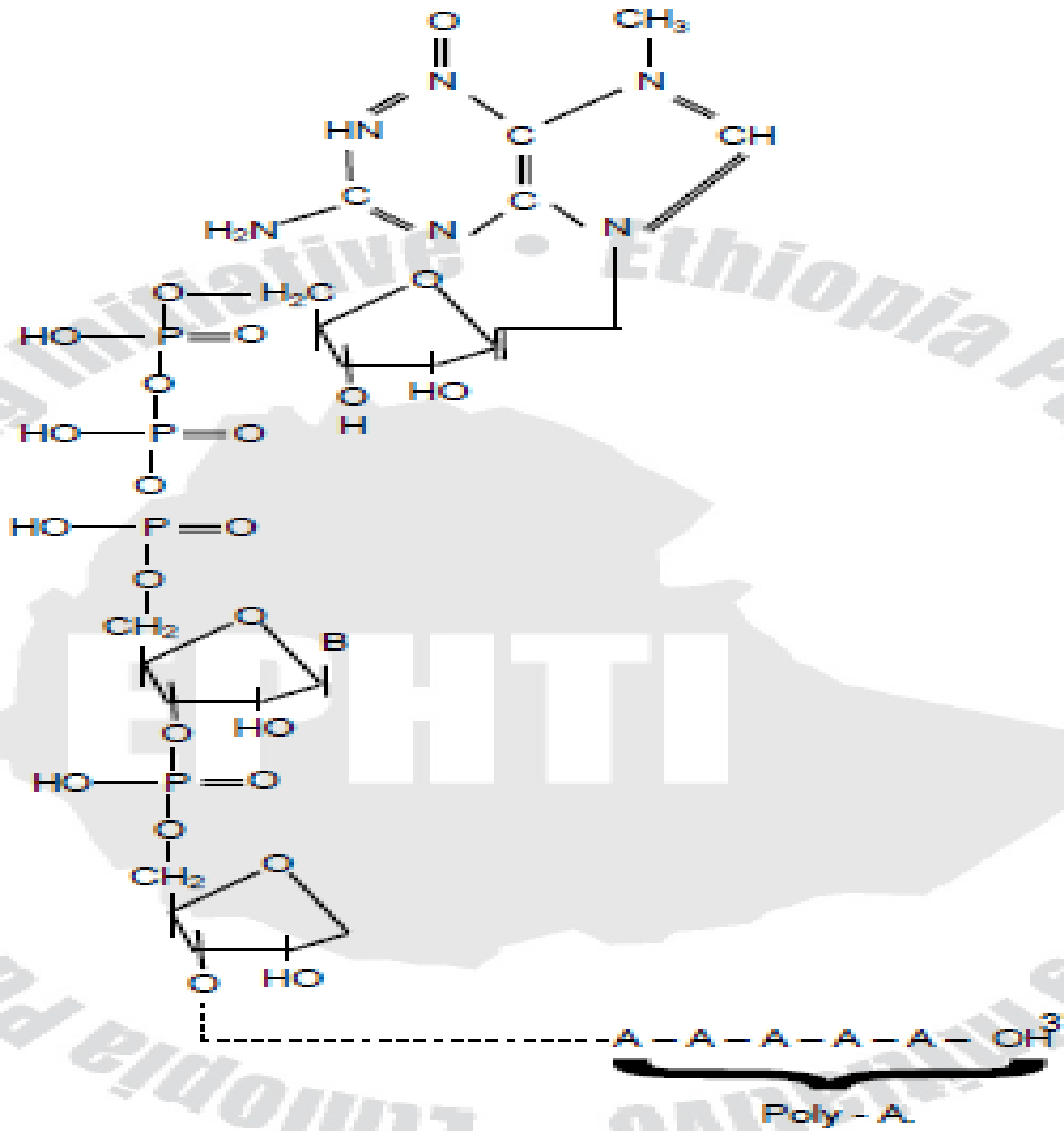


Fig.8.8 Messenger RNA (mRNA)

Ribosomal RNA (rRNA)

rRNA is highly methylated as compared to the other RNAs. rRNA participates in the structure of ribosome. rRNA, ribosomal proteins and Mg++ constitute ribosome. The ribosome is made of two subunits big and small. Ribosomes are ribonucleotide-protein particles, serve as work benches for protein synthesis .About 2/3 of the mass is RNA and rest is protein. In prokaryotes, they float freely in cytoplasm or attach to plasma membrane. Each ribosome consists of a large subunit and a small subunit .They is held together by non-covalent interactions. Ribosomes are not only found in cytosol but also in mitochondria.

Transfer RNA (tRNA)

All tRNA have 4 arms.

1. Amino acid arm: the one that carries amino acid
2. DHU arm: the one that binds with active center of the enzyme aminoacyl tRNA synthetase.
3. TψC arm: the one that binds to ribosome during protein synthesis.
4. Anticodon arm: which pairs with the codon of mRNA during protein synthesis

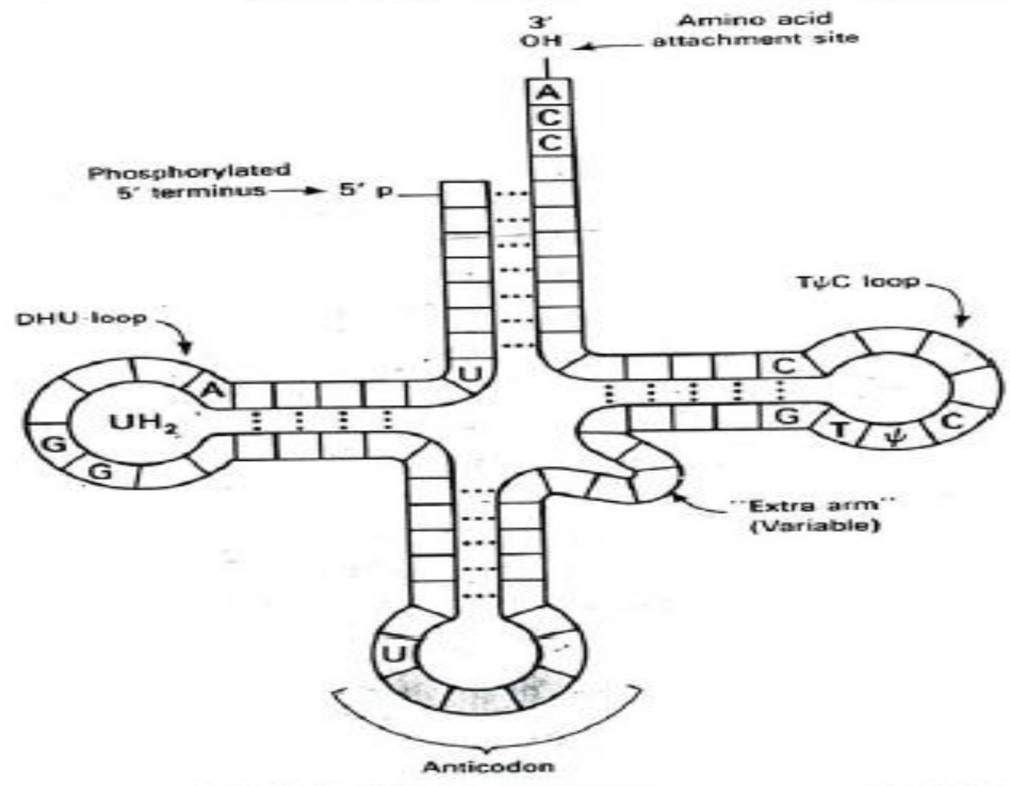


Fig 8.9 Transfer RNA (tRNA)

RNA Synthesis (transcription):

Transcription is the process of RNA Synthesis directed by a DNA template. It occurs in three phases:-

1. Initiation

2. Elongation

3. Termination

1. Initiation

Initiation includes promoter. Promoter is a specific sequence in DNA template which is responsible for directing RNA polymerase to initiate transcription at particular point. The left side of that particular point is called upstream. The promoter is found at this ,upstream. The promotes exceeds about 200 base pairs. Here is found TATA box which is close to the initiation or starting point. It is within -10 base pairs. About -35 base pairs away is found the consensus base sequences. In between the consensus and TATA box the base sequences are highly variable and subunit 2 α-and 2β-subunits.

it is this sequence that 234 can be recognized by σ (sigma) subunit or RNA polymerase in prokaryotic cell and by transcription factor in eukaryotic cell. The RNA polymerase is made up of σ- (sigma) subunit 2 α-and 2β-subunits.

To initiate transcription the sigma subunit of RNA polymerase recognizes the promoter site on DNA and separates the two strands of DNA. After the two strands of DNA are separated the RNA Polymerase with the sigma subunit starts the pairing of purine nucleotide i.e. ATP or GTP to the template of DNA.

2. Elongation

Once RNA – synthesis is started, there occurs the step by step addition of ribonucleotides i.e. ATP, GTP, CTP and UTP at 3' – OH end of RNA. The phosphodiester linkage takes place after P – Pi is removed. The template or the DNA base sequences determine the RNA base sequences. The forward movement of RNA – polymerase continuous until it reaches the termination site. The area of DNA transcribed by polymerase rewinds back to the double helix.

3. Termination:

After the RNA is synthesized adequately the termination process is carried out by two ways a. By hair pin like structure of the new synthesized RNA itself. This hair-pin like structure disturbes the RNA – polymerase not to continue its synthesis. This is called rho. Independent termination. b. A special protein called ρ-(rho-protein) prevents the RNA - polymerase from synthesizing RNA. These two termination mechanisms are carried out in prokaryotic cells. But in eukaryotic cells termination may occur by transcription factors themselves.

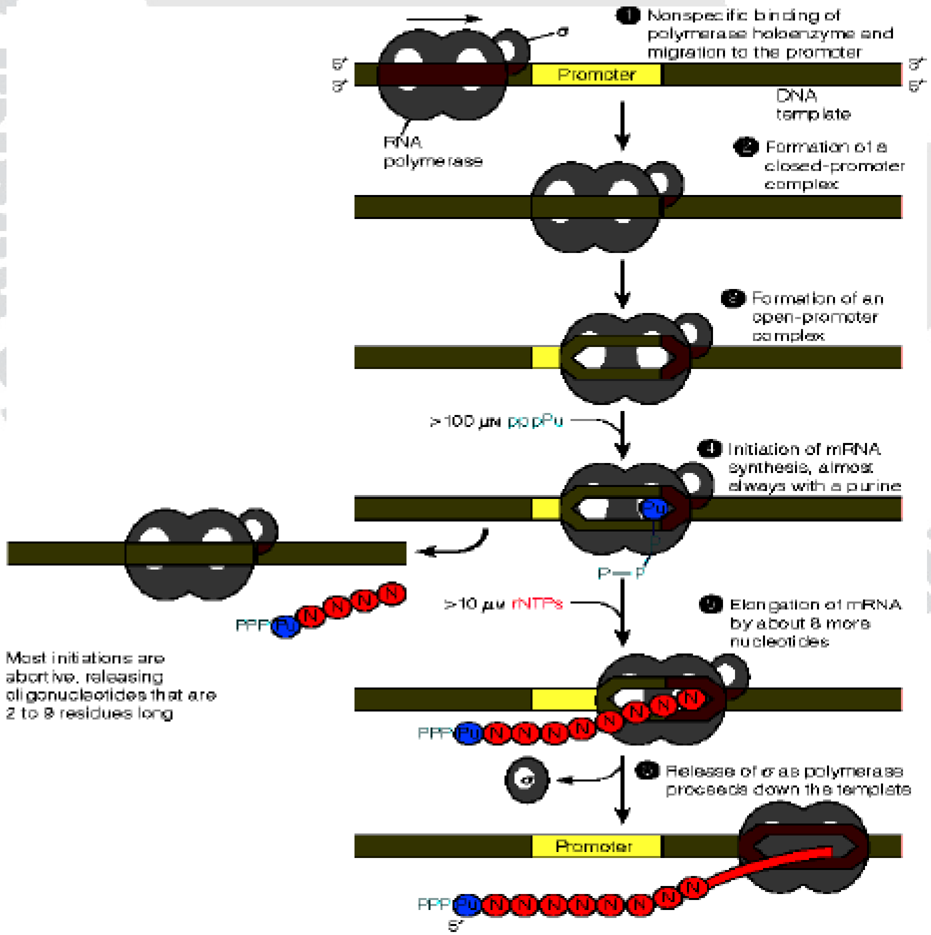


Fig 8.14. Transcription mechanism

DNA REPLICATION

Synthesis of DNA is called replication. DNA replication starts at the early stage of cell division. It is the way in which the genetic information can pass from parental cell to daughter cell. As stated before, the double helical structure of DNA depends on the base complementarity. Also this complementarity represents the fundamental basis for the formation of new DNA strands from the parent DNA strand in a semi conservative manner. In this process, two daughter DNA's are produced, each has one parent strand (conserved) and newly synthesized strand.

Steps of Replication

Origin of DNA - Replication starts at particular DNA sequence called origin. Origin is rich in TA- T sequence. In prokaryotic cells origin is at one site.In eukaryotic cells origin is at many sites. To start DNA replication origin is recognized by special protein called DNA a. Gyrase is a protein which recognizes DNA - origin with the help of DNA b protein. The main function of gyrase is to put the negative super twist on double helix of DNA. But the two strands of DNA can be separated by special protein Helicase. Helicase melts the hydrogen bond of the two strands of DNA. To prevent the recoiling back to the double helix single strand binding protein (SSB) plays the role. SSB binds to the single stranded DNA and thus protects the single strand from rejoining.

Primer synthesis: After the two strands of DNA are separated at origin, short complementary RNA to the single strand parental DNA is synthesized. This RNA is called a primer. In prokaryotic cell the primer length is about 10 - ribonucleotides, but in Eukaryotic cell it is about 30. This primer is synthesized by the enzyme called primase. The primer grows in the 5’ → 3’ direction which is anti-parallel to the parental DNA. Primer is needed to provide 3’- OH group for building of new DNA by DNA polymerase.


Thank You