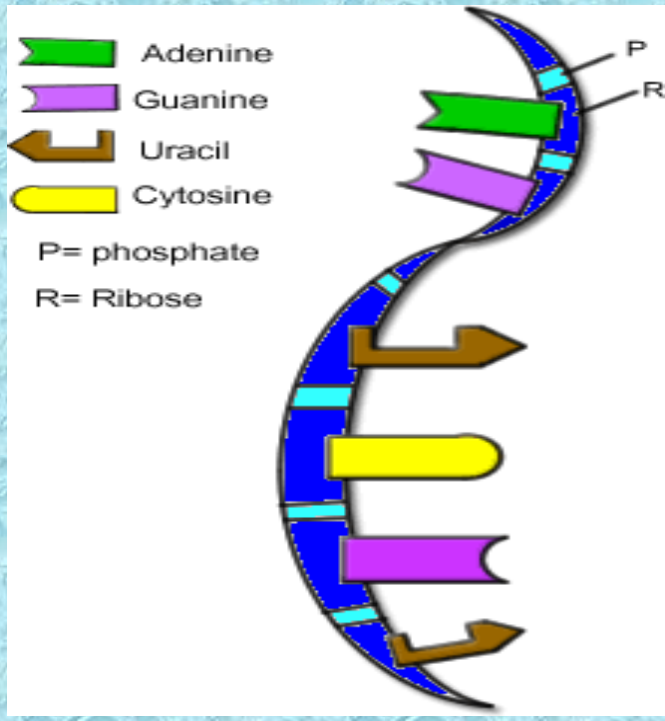

بسم الله الرحمن الرحيم

RIBONUCLEIC ACID



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Biochemistry


RIBONUCLEIC ACID

Objectives: (basic chemistry of genetic)

By the end of lecture we will able to know:

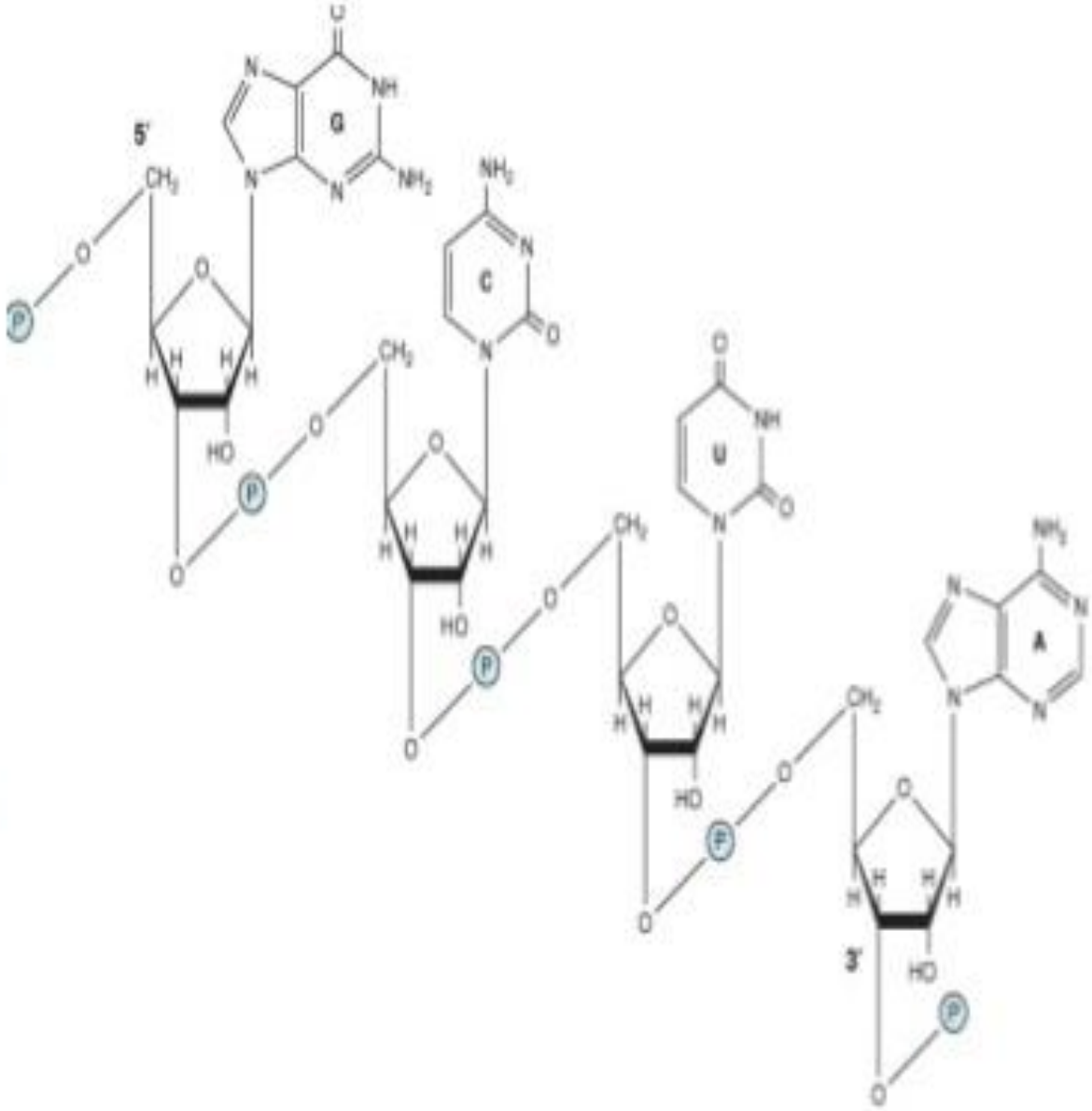
RNA

- (chemistry and structure)
- Types of RNA
- Chemical structure of different types of RNA
- Biochemical function


KEEP
CALM
AND
ACTIVATE PRIOR
KNOWLEDGE

RNA (Ribonucleic acid)

- RNA is a polymer of ribonucleotides linked together by 3’-5’ phosphodiester linkage



RIBONUCLEIC ACID

RNA a single stranded structure found in the nucleolus, ribosome, mitochondria and cytoplasm. The pentose sugar of the RNA is D-ribose.

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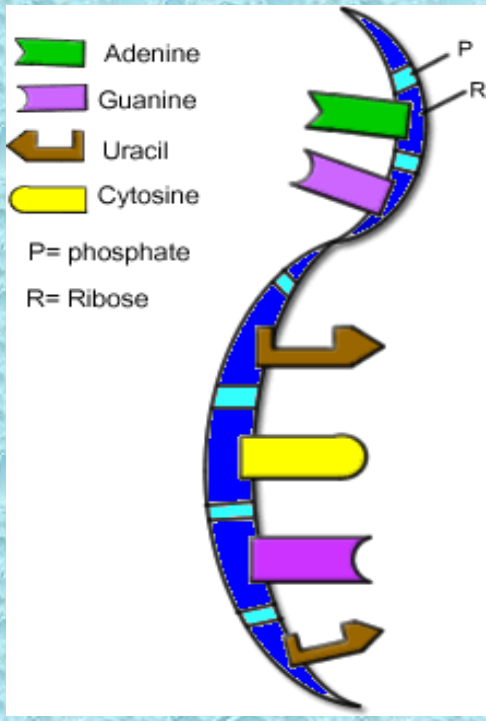
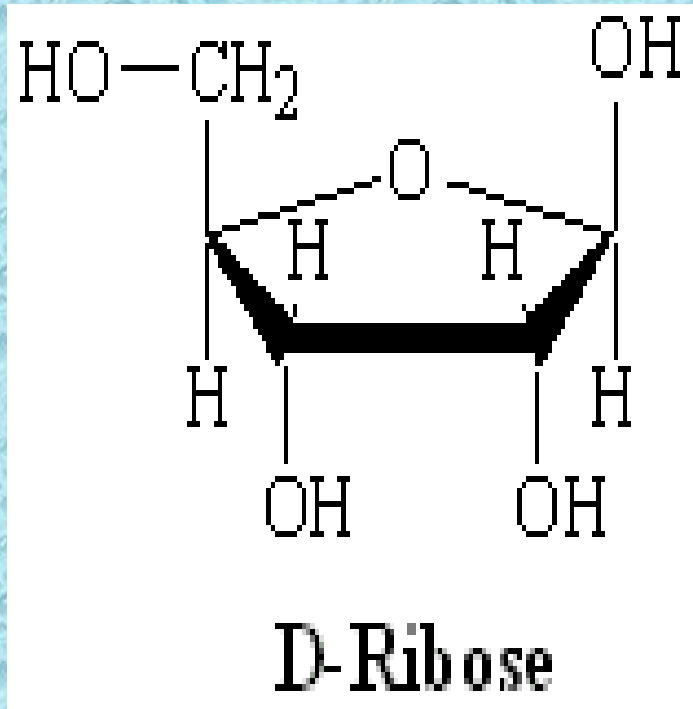


Sugars

These hydroxyl groups make RNA less stable than DNA because it is more prone to hydrolysis

D-Ribose



RNA perform multiple vital roles in the coding, decoding, regulation, and expression of genes.

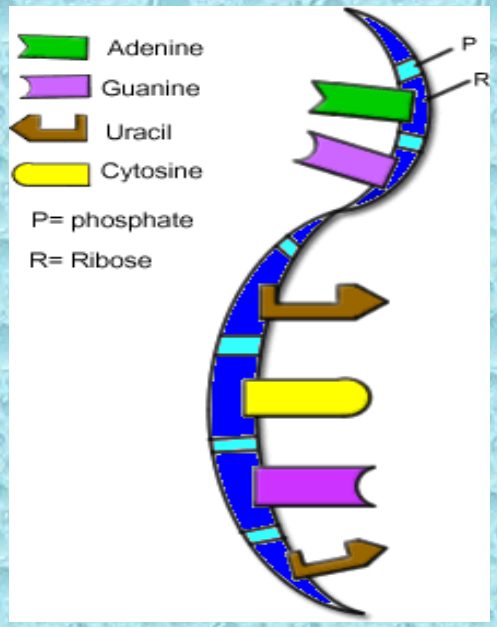
Together with DNA, RNA comprises the nucleic acids, which, along with proteins, constitute the macromolecules essential for all known forms of life.

RNA molecules play an active role within cells by catalysing biological reactions, controlling gene expression and active processes the protein synthesis.

MOLECULAR STRUCTURE OF RNA:

- Each nucleotide in RNA contains a ribose sugar, with carbons numbered 1' through 5'.
- A base is attached to the 1' position, generally adenine (A), cytosine (C), guanine (G) or uracil (U)
- Adenine and guanine are purine, cytosine and uracil are pyrimidine.
- A phosphate group is attached to the 5' position of one ribose and the 3' position of the next.

STRUCTURE OF RNA

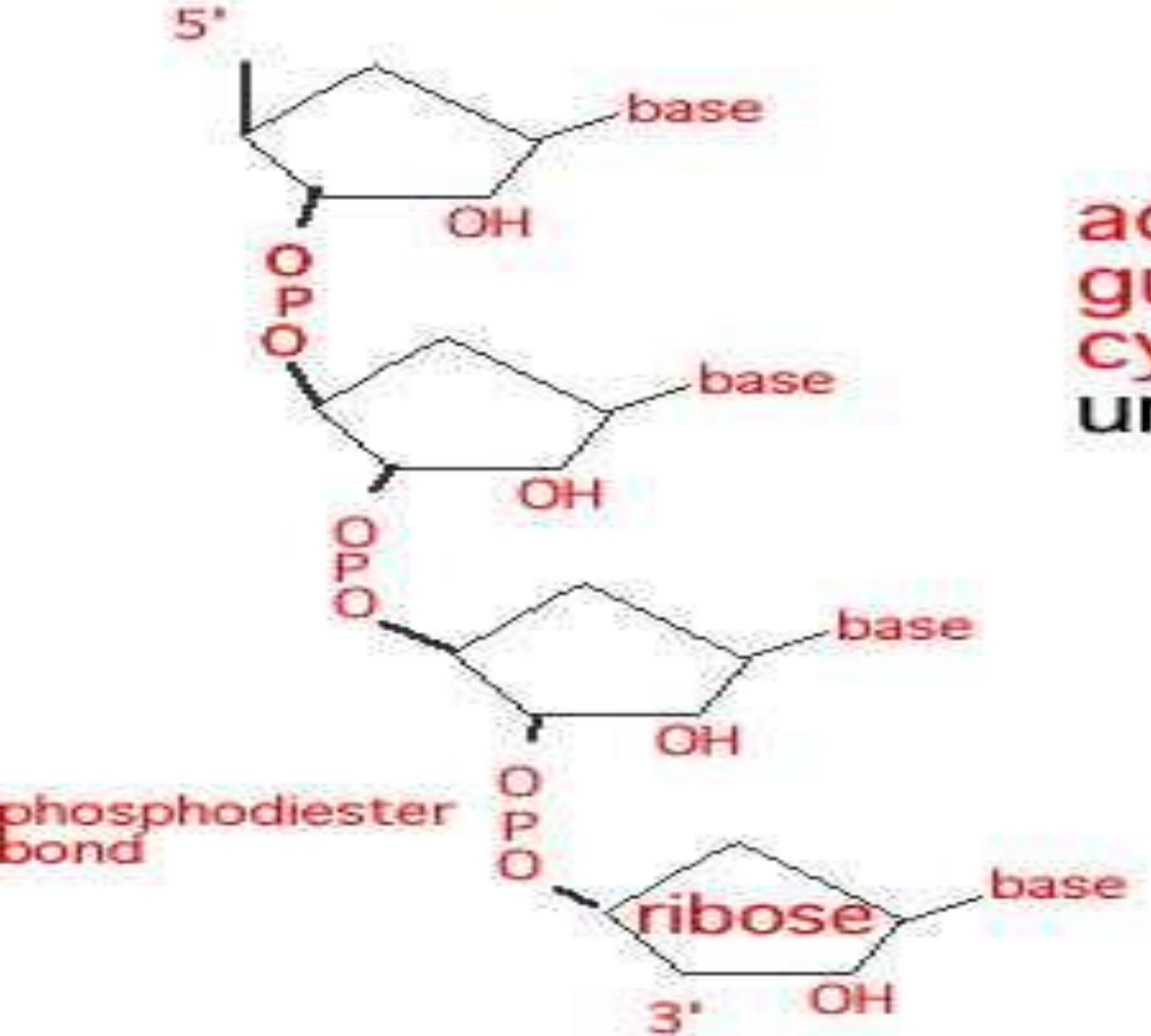


PRIMARY STRUCTURE OF RNA:

It is the number and sequence of ribonucleotides in the straight chain.

Like DNA, RNA is assembled as a chain of nucleotides, but is usually single-stranded.

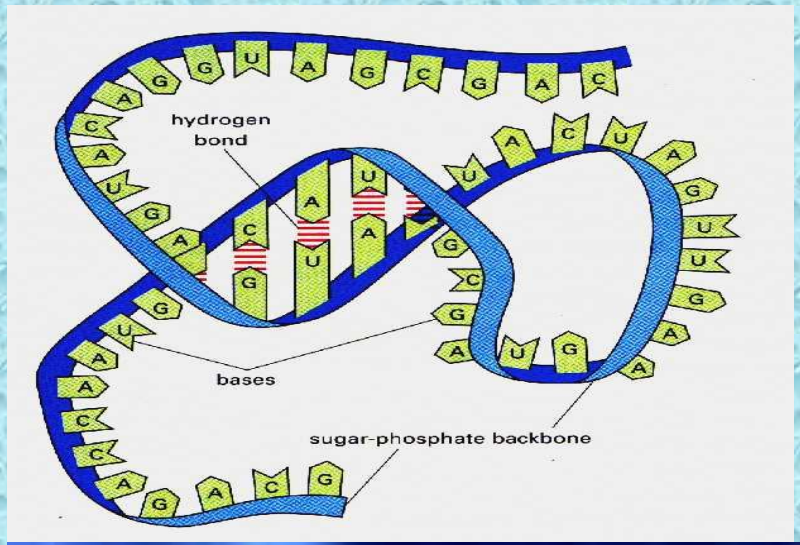
Ribonucleic acid



adenine
guanine
cytosine
uracil

SECONDRY STRUCTURE OF RNA:

- It is a coil formation by various polyribonucleotide.
- This coiled structure is stabilized by hydrophobic interaction between purine and pyrimidine bases.
- There are intra-chain H.bonds between G ≡C and A = U.



TERTIARY STRUCTURE OF RNA:

It is the folding of RNA molecule into 3D (three dimensional) structure.

The cross-linking also occurs at various sites stabilized by H.bounds producing a compact coiled globular structure.

Types of RNA

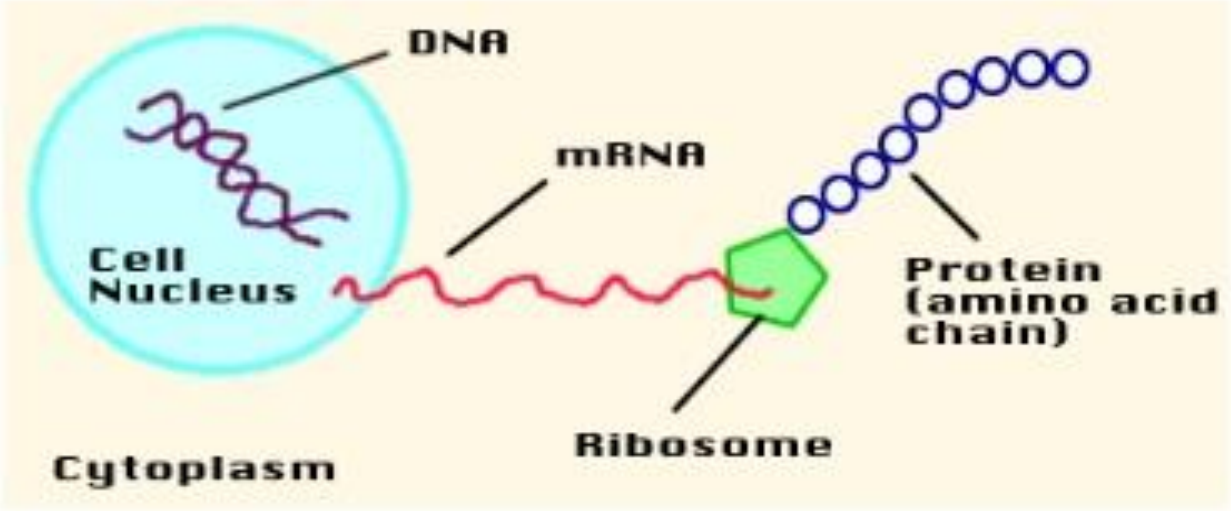
In all prokaryotic and eukaryotic organisms, three main classes of RNA molecules exist-

1) Messenger RNA(m RNA)
2) Transfer RNA (t RNA)
3) Ribosomal RNA (r RNA)

The other are –

- small nuclear RNA (SnRNA),
- micro RNA(mi RNA) and
- small interfering RNA(Si RNA) and
- heterogeneous nuclear RNA (hnRNA).

Messenger RNA (m-RNA)

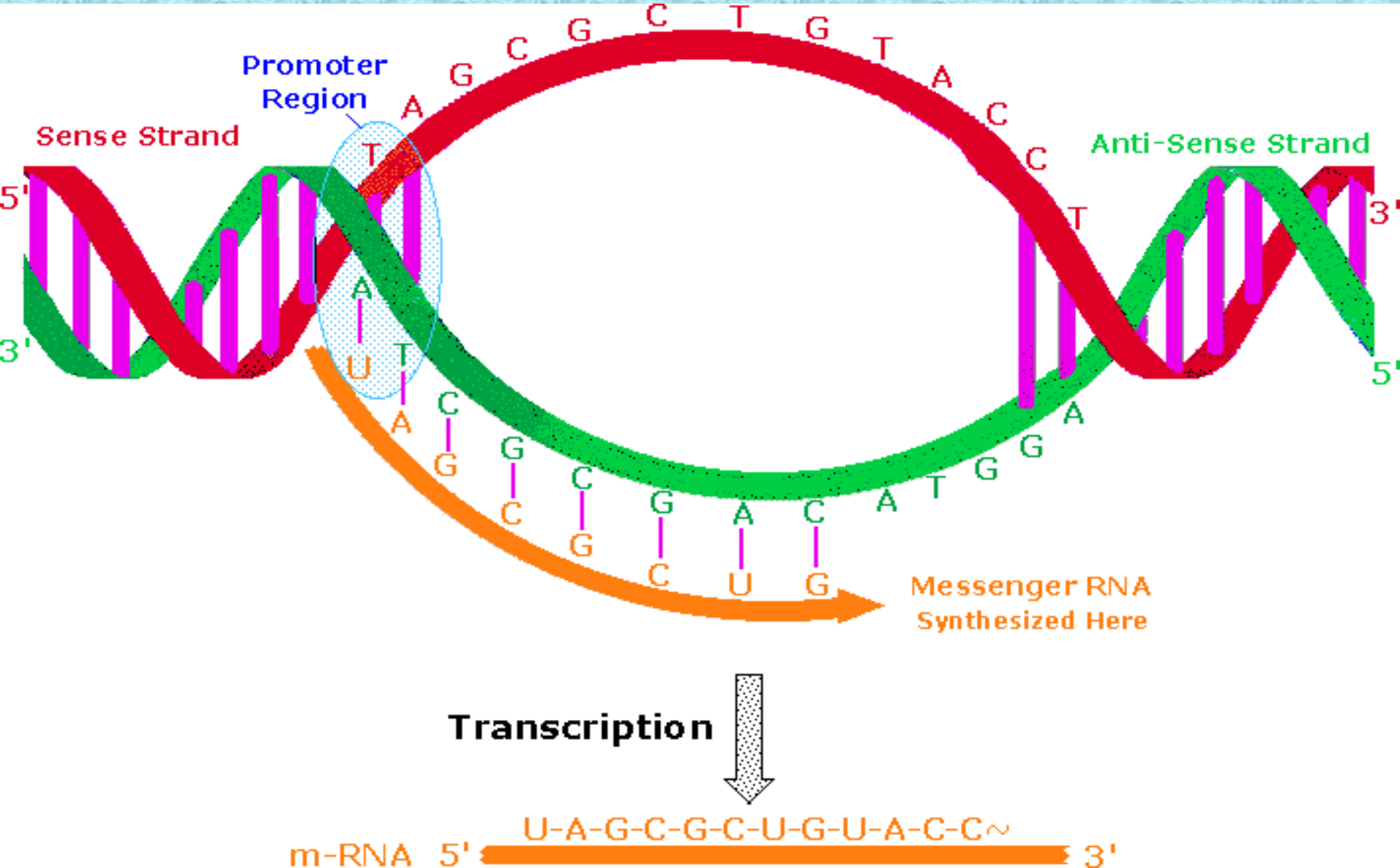


- Comprises only 5% of the RNA in the cell
- Most heterogeneous in size and base sequence
- All members of the class function as messengers carrying the information in a gene to the protein synthesizing machinery

Messenger RNA[mRNA]:

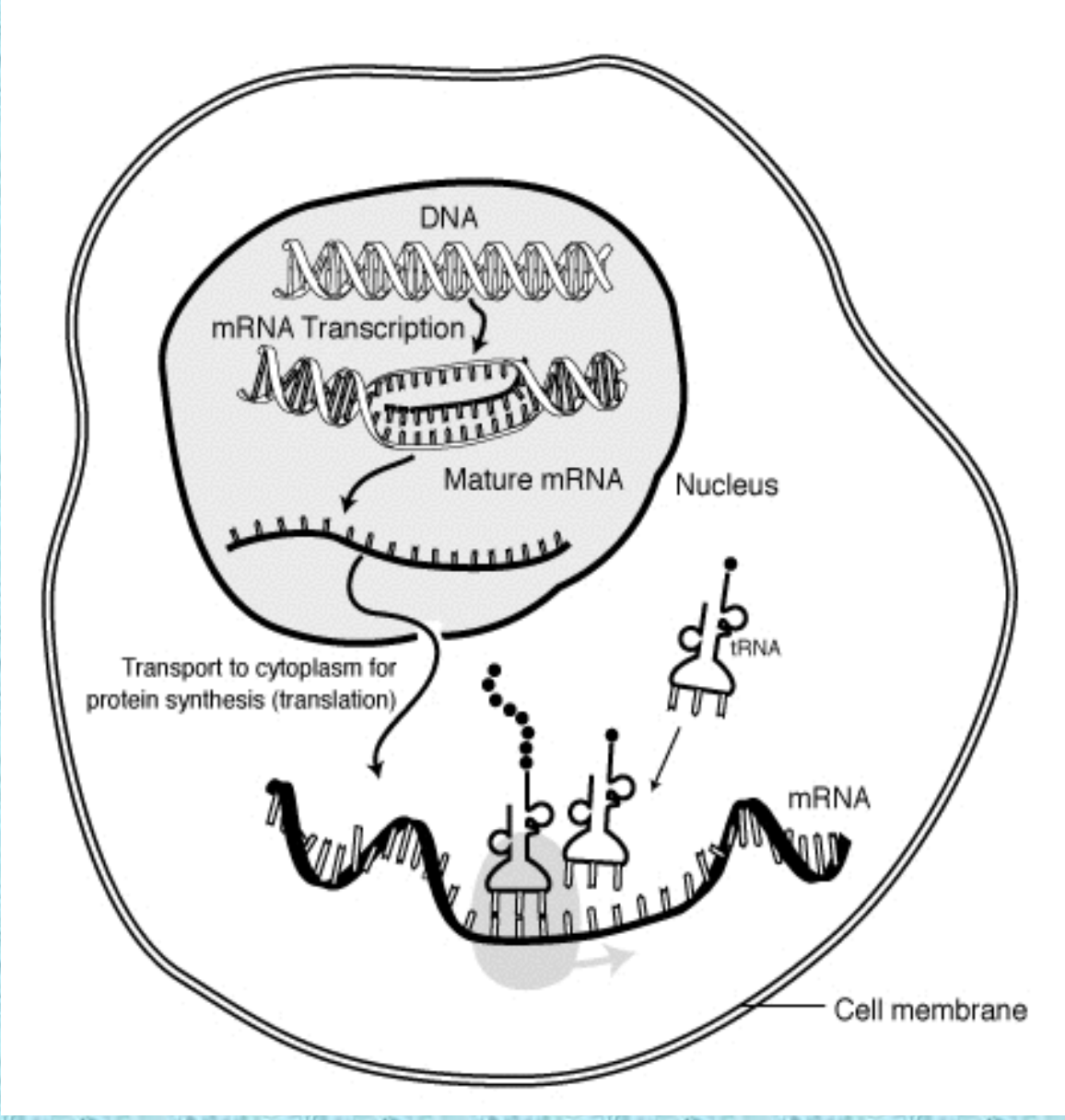
- Main bases present in m RNA are adenine, guanine, cytosine and uracil.
- m RNA is formed from DNA template strand [3`- 5`] during the process of transcription.
- m RNA carries the specific nucleotide sequences in(triplets) called codon responsible for the synthesis of a specific protein.
- It has 70 ⟶ 20000 nucleotides.
- The mol . wt varies 2×10^6 to 3×10^4.
- 3 ` - OH end called poly A tail.
- 5 ` - OH end carries a cup structure involved in protein synthesis and RNA protection.

MESSENGER RNA



mRNA:

- A molecule of RNA that serves as a template for protein synthesis. The mRNA is transcribed from a gene and then translated by ribosome in order to manufacture a protein.



Structural Characteristics of m-RNA(Contd.)

- The m- RNA molecules are formed with the help of DNA template during the process of transcription.
- The sequence of nucleotides in m RNA is complementary to the sequence of nucleotides on template DNA.
- The sequence carried on m -RNA is read in the form of codons.
- A codon is made up of 3 nucleotides
- The m-RNA is formed after processing of heterogeneous nuclear RNA

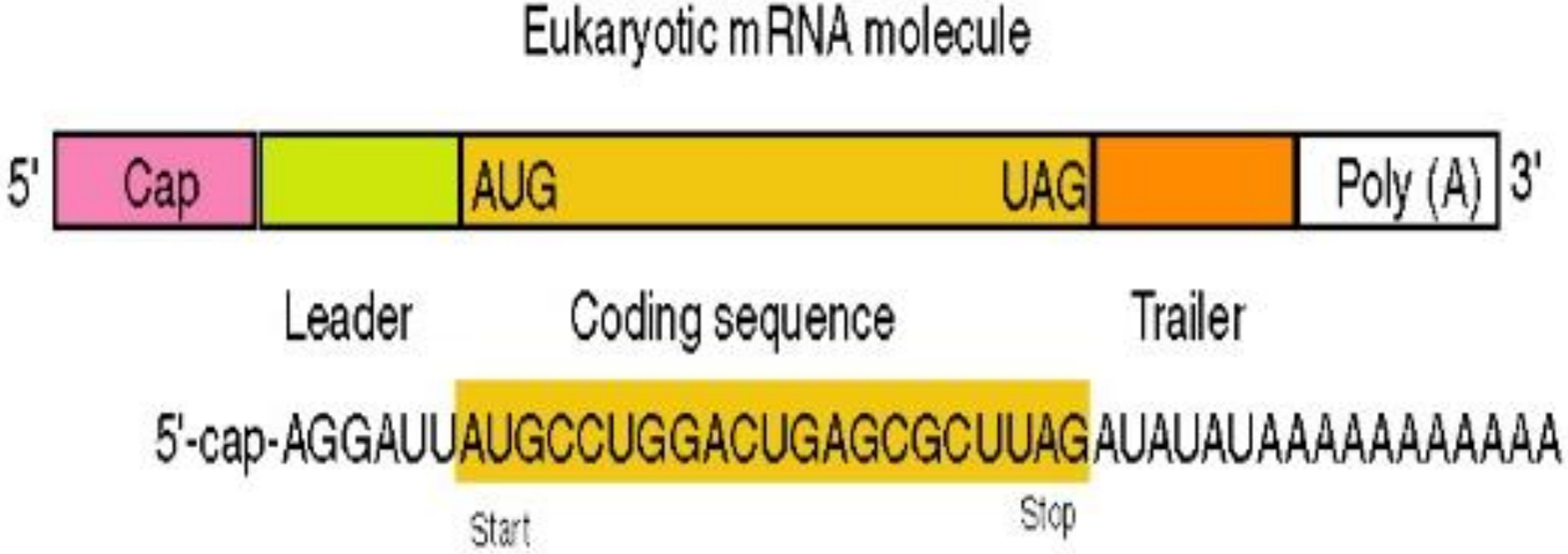
Structural Characteristics of m-RNA

- The 5’ terminal end is capped by 7-methyl guanosine triphosphate cap.
- The cap is involved in the recognition of mRNA by the translating machinery
- It stabilizes m RNA by protecting it from 5’ exonuclease

Structural Characteristics of m-RNA(contd.)

- The 3'end of most m-RNAs have a polymer of Adenylate residues(20-250)
- The tail prevents the attack by 3' exonucleases
- Histones and interferons do not contain poly A tails
- On both 5' and 3' end there are non coding sequences which are not translated (NCS)
- The intervening region between non coding sequences present between 5' and 3' end is called coding region. This region encodes for the synthesis of a protein.

Structural Characteristics of m-RNA



5’ cap and 3’ tail impart stability to m RNA by protecting from specific exo nucleases.

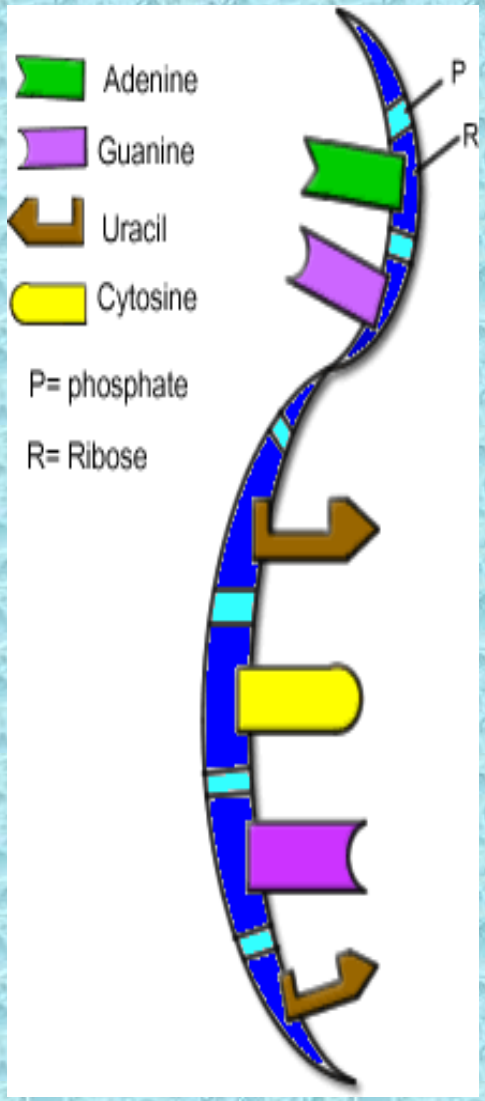
Transfer RNA (t- RNA)

- Transfer RNA are the smallest of three major species of RNA molecules
- They have 74-95 nucleotide residues
- They are synthesized by the nuclear processing of a precursor molecule
- They transfer the amino acids from cytoplasm to the protein synthesizing machinery, hence the name t RNA.
- They are easily soluble , hence called "Soluble RNA or s RNA
- They are also called Adapter molecules, since they act as adapters for the translation of the sequence of nucleotides of the m RNA in to specific amino acids
- There are at least 20 species of t RNA one corresponding to each of the 20 amino acids required for protein synthesis.

STRUCTURE OF tRNA:

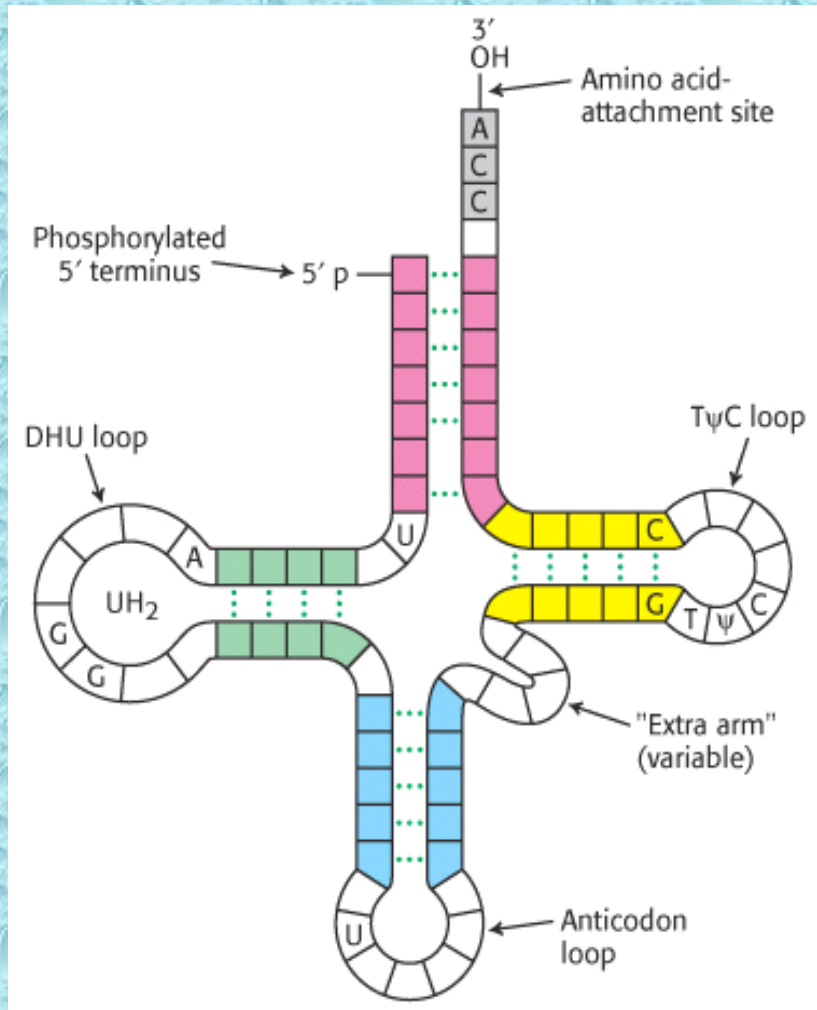
1. PRIMARY STRUCTURE:

- Single strand of tRNA molecule held by phosphodiester bonds.
- There are about 75 ribonucleotides in tRNA molecules.



SECONDARY STRUCTURE:

- It is a clover leave structure, formed by folding of the single strand of tRNA molecule.
- The secondary structural folds are stabilized by hydrogen bonds.
- The double stranded helical structure are called as stem.
- It has five arms or loops.



Structural characteristics of t- RNA

1) Primary structure- The nucleotide sequence of all the t RNA molecules allows extensive intrastand complimentarity that generates a secondary structure.

2) Secondary structure- Each single t- RNA shows extensive internal base pairing and acquires a clover leaf like structure. The structure is stabilized by hydrogen bonding between the bases and is a consistent feature.

Structural characteristics of t-RNA

Secondary structure (Clover leaf structure)

All t-RNA contain 5 main arms or loops which are as follows-

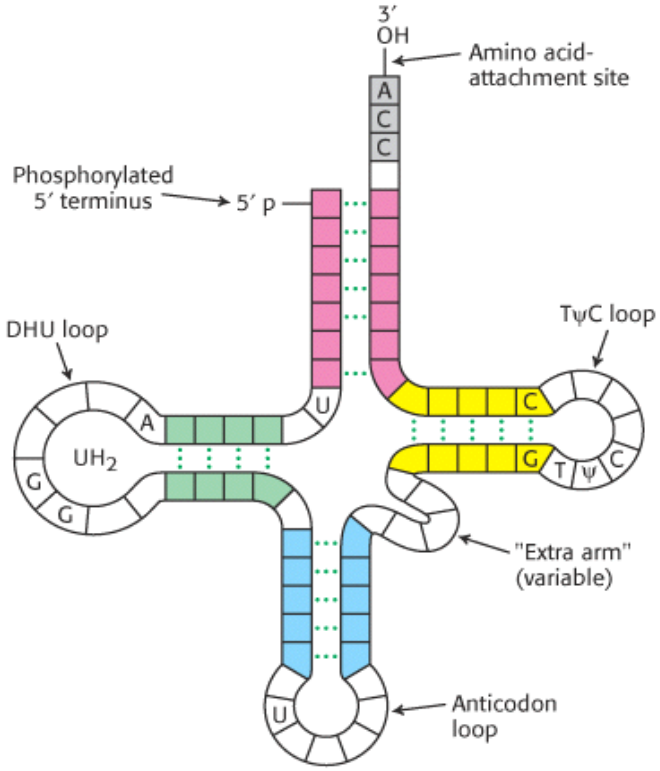
a) Acceptor arm

b) Anticodon arm

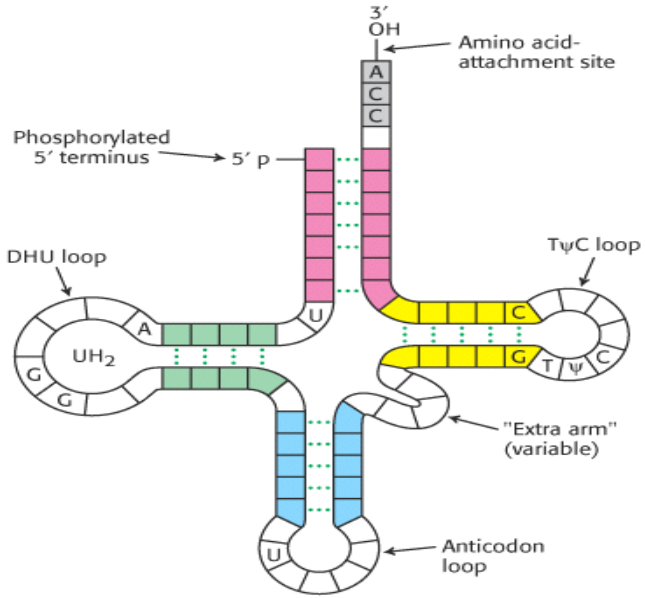
c) D HU arm

d) TΨ C arm

e) Extra arm



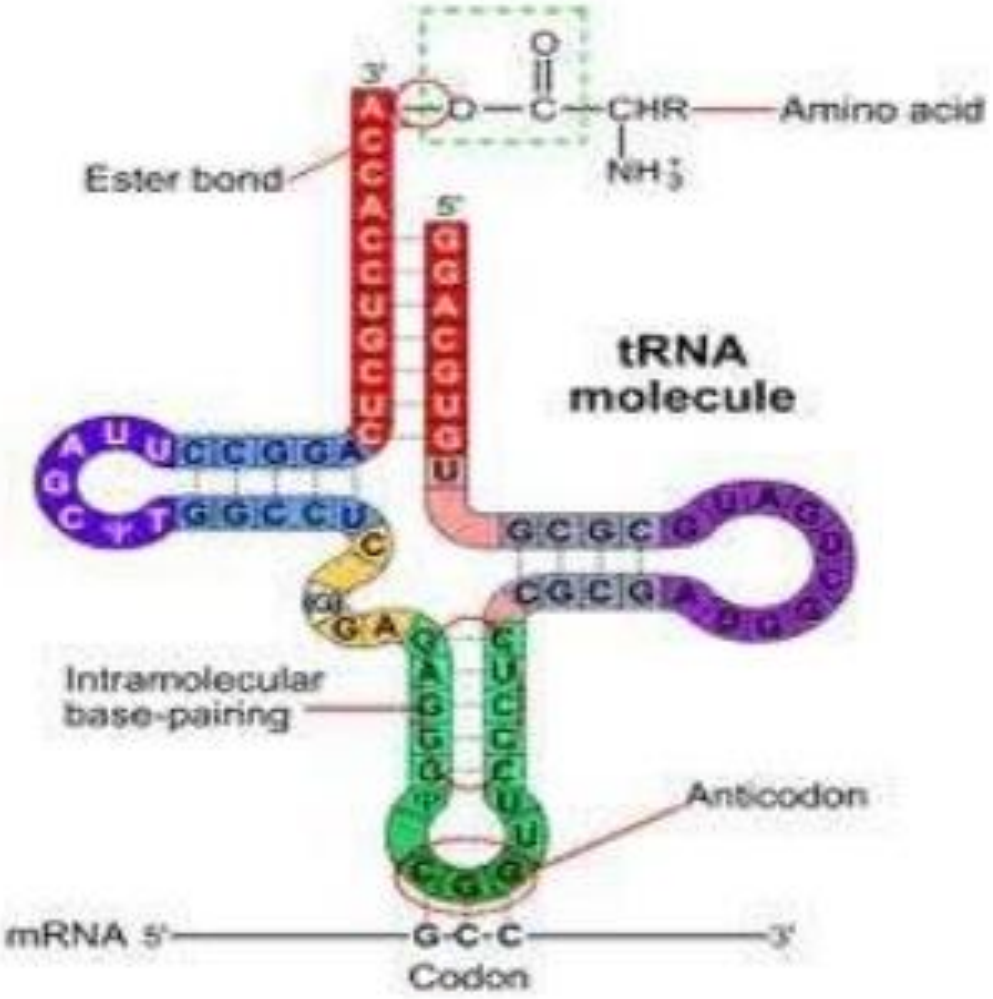
Secondary structure of t- RNA



a) Acceptor arm

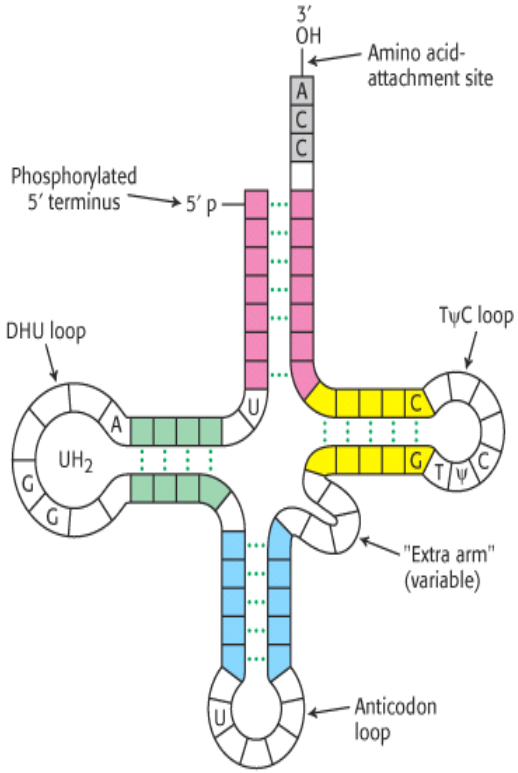
- The acceptor arm is at 3’ end
- It has 7 base pairs
- The end sequence is unpaired Cytosine, Cytosine-Adenine at the 3’ end
- The 3’ OH group terminal of Adenine binds with carboxyl group of amino acids
- The t RNA bound with amino acid is called Amino acyl t RNA

Secondary structure of t- RNA



The carboxyl group of amino acid is attached to 3'OH group of Adenine nucleotide of the acceptor arm. The anticodon arm base pairs with the codon present on the m- RNA

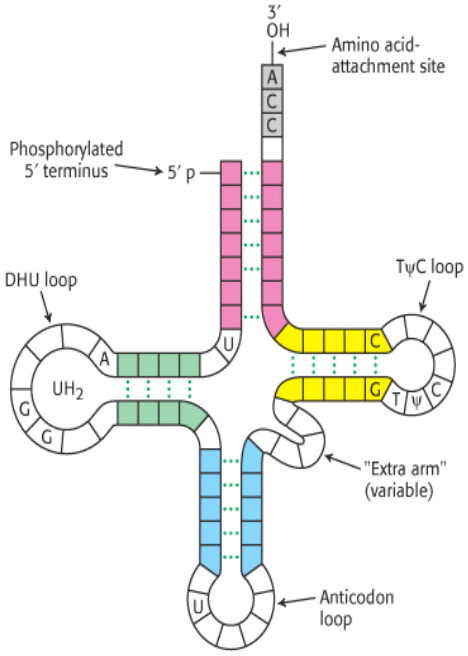
Secondary structure of t-RNA(contd.)



b) Anticodon arm

- Lies at the opposite end of acceptor arm
- 5 base pairs long
- Recognizes the triplet codon present in the m RNA
- Base sequence of anticodon arm is complementary to the base sequence of m RNA codon.
- Due to complimentarity it can bind specifically with m RNA by hydrogen bonds.

Secondary structure of t-RNA(contd.)



c) DHU arm

- It has 3-4 base pairs
- Serves as the recognition site for the enzyme (amino acyl t RNA synthetase) that adds the amino acid to the acceptor arm.

d) TΨC arm

- This arm is opposite to DHU arm
- Since it contains pseudo uridine that is why it is so named
- It is involved in the binding of t RNA to the ribosomes

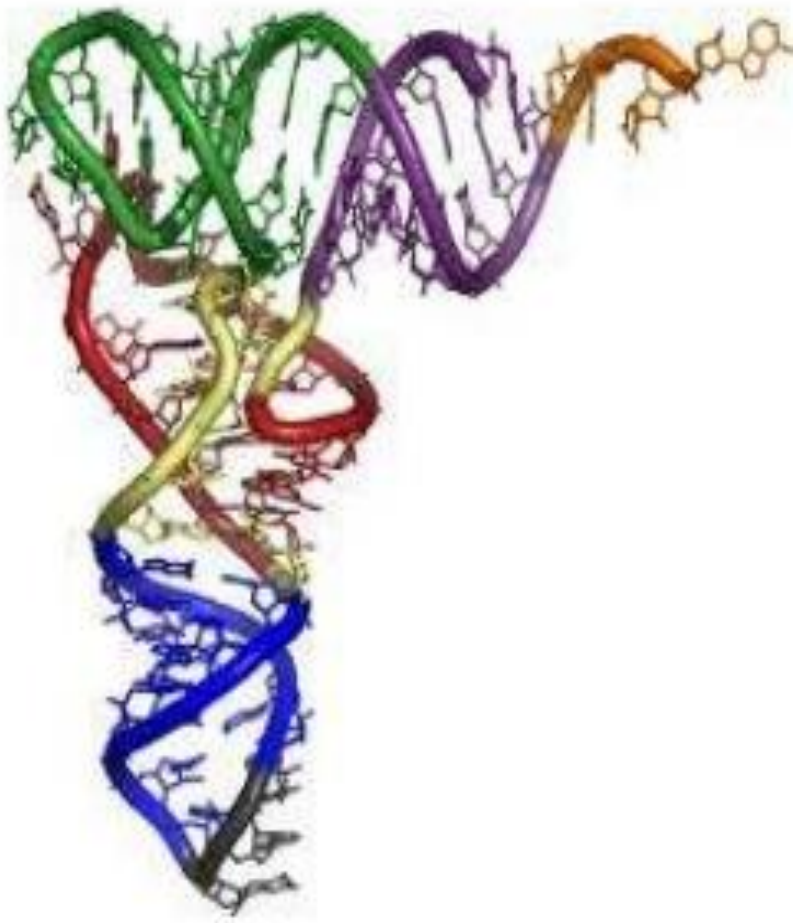
Secondary structure of t-RNA(contd.)

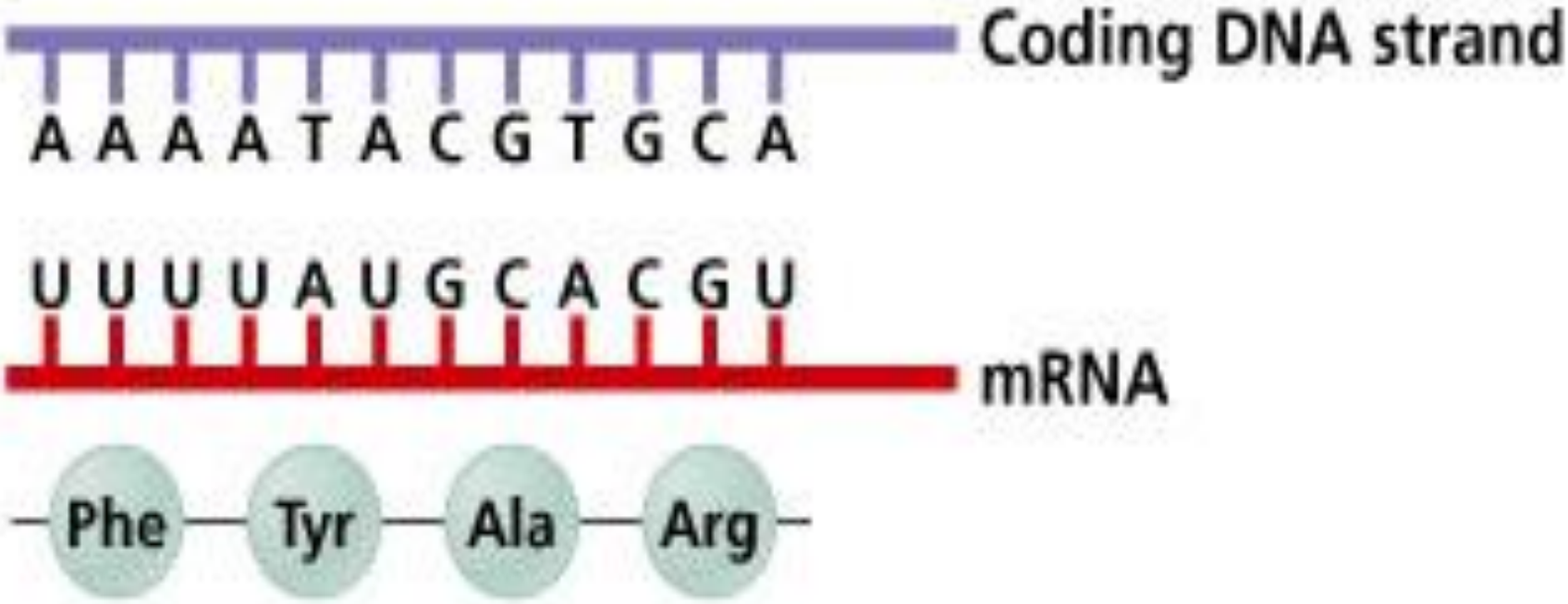
e) Extra arm or Variable arm

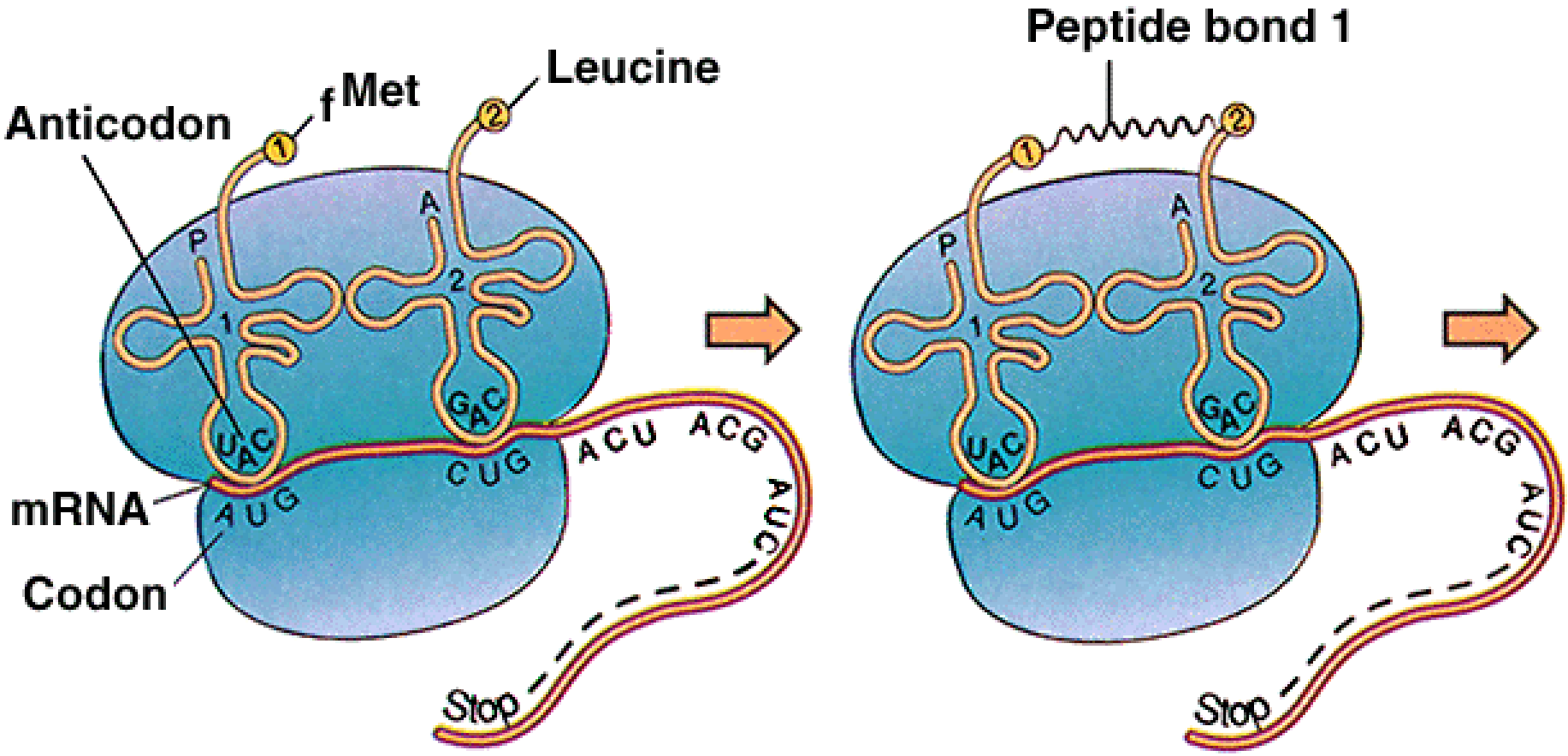
- About 75 % of t RNA molecules possess a short extra arm
- If about 3-5 base pairs are present the t-RNA is said to be belonging to class 1. Majority t -RNA belong to class 1.
- The t –RNA belonging to class 2 have long extra arm, 13-21 base pairs in length.

Tertiary structure of t- RNA

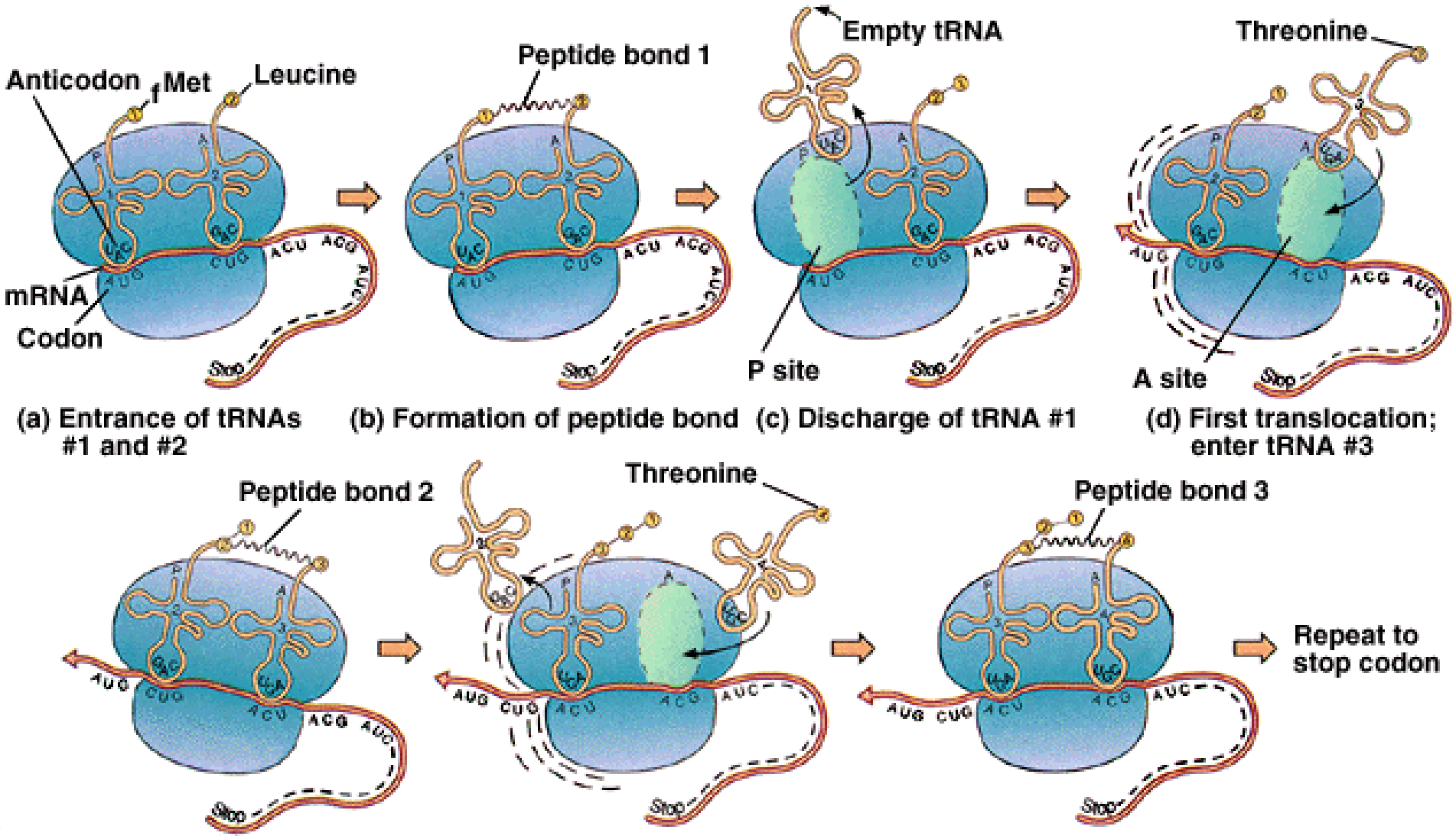
- The L shaped tertiary structure is formed by further folding of the clover leaf due to hydrogen bonds between T and D arms.
- The base paired double helical stems get arranged in to two double helical columns, continuous and perpendicular to one another.




Coding DNA strand
A A A A T A C G T G C A
U U U U A U G C A C G U
mRNA
Phe
Tyr
Ala
Arg


Anticodon
f Met
Leucine
Peptide bond 1
P
A
1
2
UAC
GAC
CUG
ACU
ACG
AUC
mRNA
AUG
Codon
Stop
(a) Entrance of tRNAs #1 and #2
(b) Formation of peptide bond

The Events in Protein Synthesis.



(a) Entrance of tRNAs #1 and #2

(b) Formation of peptide bond

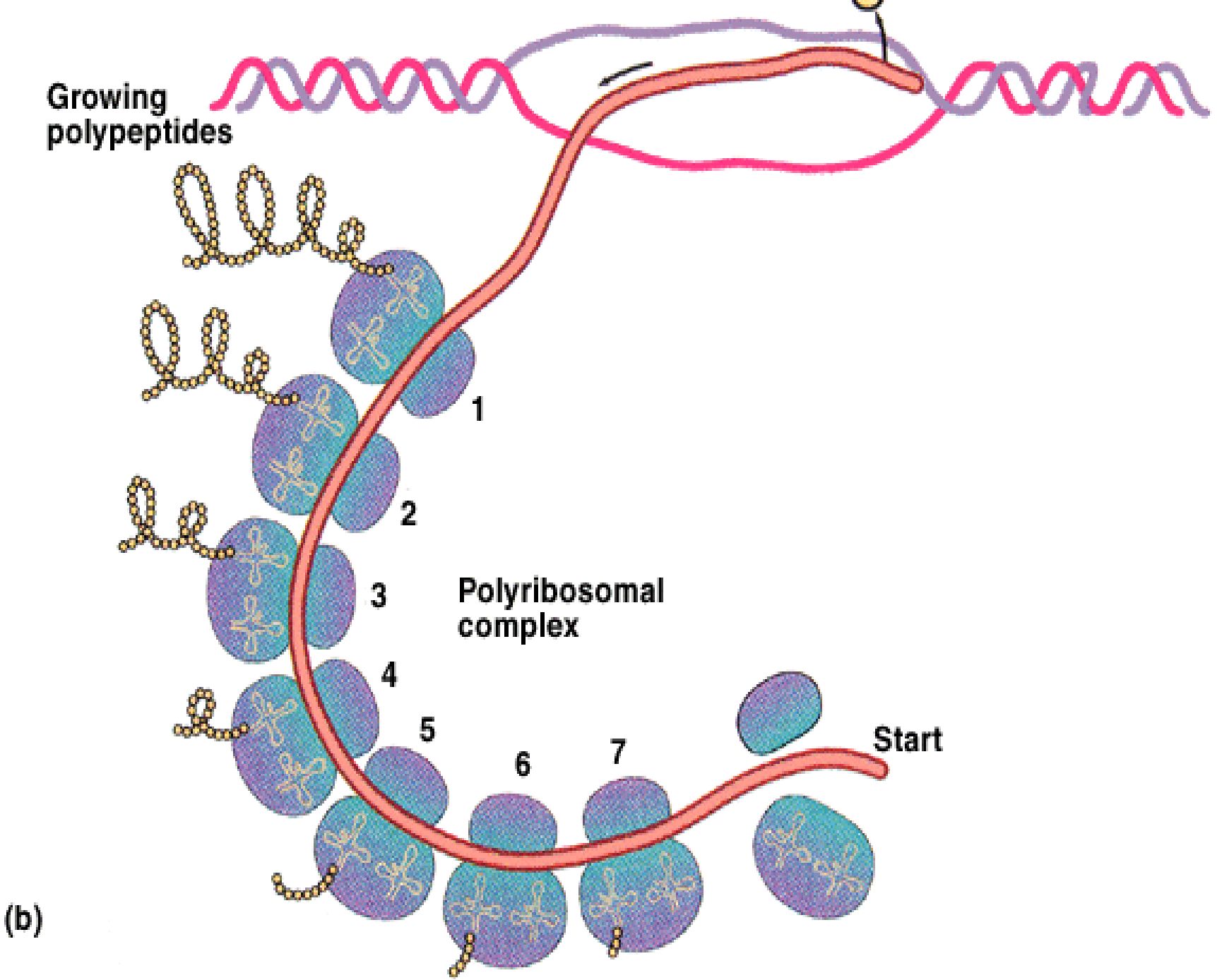
(c) Discharge of tRNA #1

(d) First translocation; enter tRNA #3

(e) Formation of peptide bond

(f) Discharge of tRNA #2; second translocation; enter tRNA #4

(g) Formation of peptide bond


Growing polypeptides
1
2
3
4
5
6
7
Polyribosomal complex
Start
(b)

Distinction between m RNA & t RNA:

m RNA :

1. High mol,wt.
2. Most hetrogenous molecule
3. Has condons
4. Acts as a templates for protein synthesis
5. Varies in shape & size

t RNA :

1. Low mol.wt.
2. 20 different t RNA molecules [one for each aminoacid
3. Has anticondons
4. Acts as a carrier of aminoacids
5. Shape & size is constant for all t RNA

6. 3-OH` end has a poly A tail	6. [colver leaf]3`-OH end has C.C.A sequence where specific amino acid is bound
7. Cap structure is found on 5` -OH end	7. No such structure
8. Precursor is hn-RNA	8. No such precursor
9. Unusual bases are not found	9. Unusual bases e.g pseudouridine , and thymine are found
10. Stem and loop structure is not present	10. Stem and loop structure is always present

RIBOSOMAL RNA

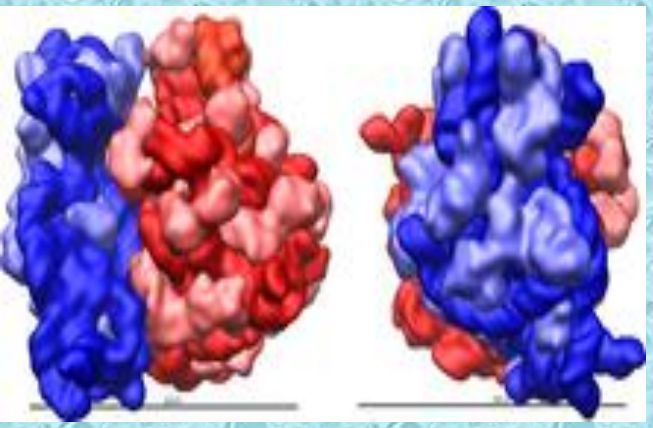
It is a nucleoprotein present in cytoplasm.

The r RNA forms 80% of the total cellular RNA and are metabolically stable.

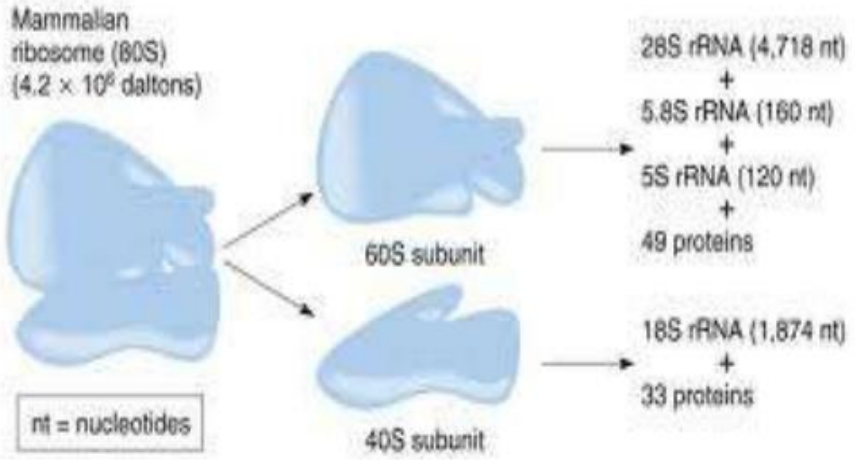
It is an important constituent of ribosomes and provides a structural frame work for ribosomes and a part of protein synthesis apparatus.

Ribosomal RNA (rRNA)

The mammalian ribosome contains two major nucleoprotein subunits—a larger one with a molecular weight of 2.8×10^6 (60S) and a smaller subunit with a molecular weight of 1.4×10^6 (40S).



Ribosomal RNA (rRNA)



Ribosomal RNA (rRNA)

- The functions of the ribosomal RNA molecules in the ribosomal particle are not fully understood, but they are necessary for ribosomal assembly and seem to play key roles in the binding of mRNA to ribosomes and its translation
- Recent studies suggest that an rRNA component performs the peptidyl transferase activity and thus is an enzyme (a ribozyme).

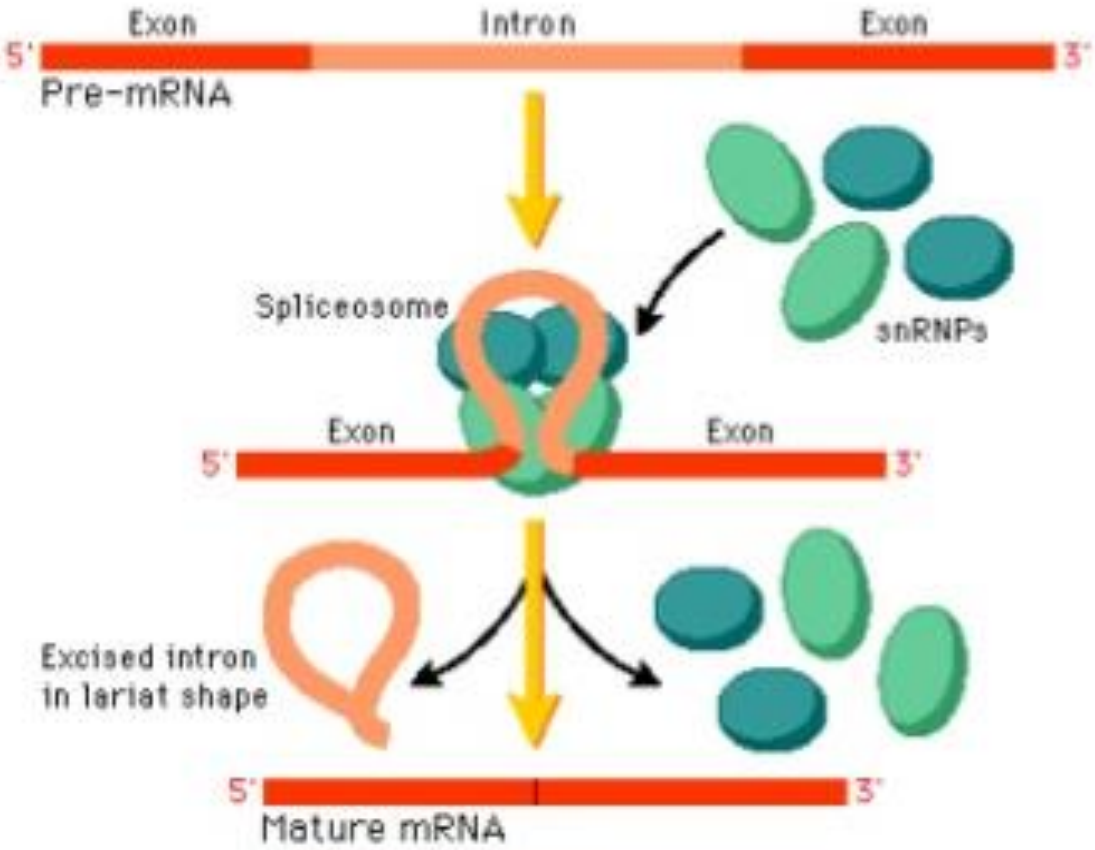
Small RNA

- Most of these molecules are complexed with proteins to form ribonucleoproteins and are distributed in the nucleus, in the cytoplasm, or in both.
- They range in size from 20 to 300 nucleotides and are present in 100,000–1,000,000 copies per cell.

Small Nuclear RNAs (snRNAs)

- snRNAs, a subset of the small RNAs, are significantly involved in mRNA processing and gene regulation
- Of the several snRNAs, U1, U2, U4, U5, and U6 are involved in intron removal and the processing of hnRNA into mRNA
- The U7 snRNA is involved in production of the correct 3' ends of histone mRNA—which lacks a poly(A) tail.

Small Nuclear RNAs (snRNAs).



Sn RNA s are involved in the process of splicing (intron removal) of primary transcript to form mature m RNA. The Sn RNA s form complexes with proteins to form Ribonucleoprotein particles called snRNPs

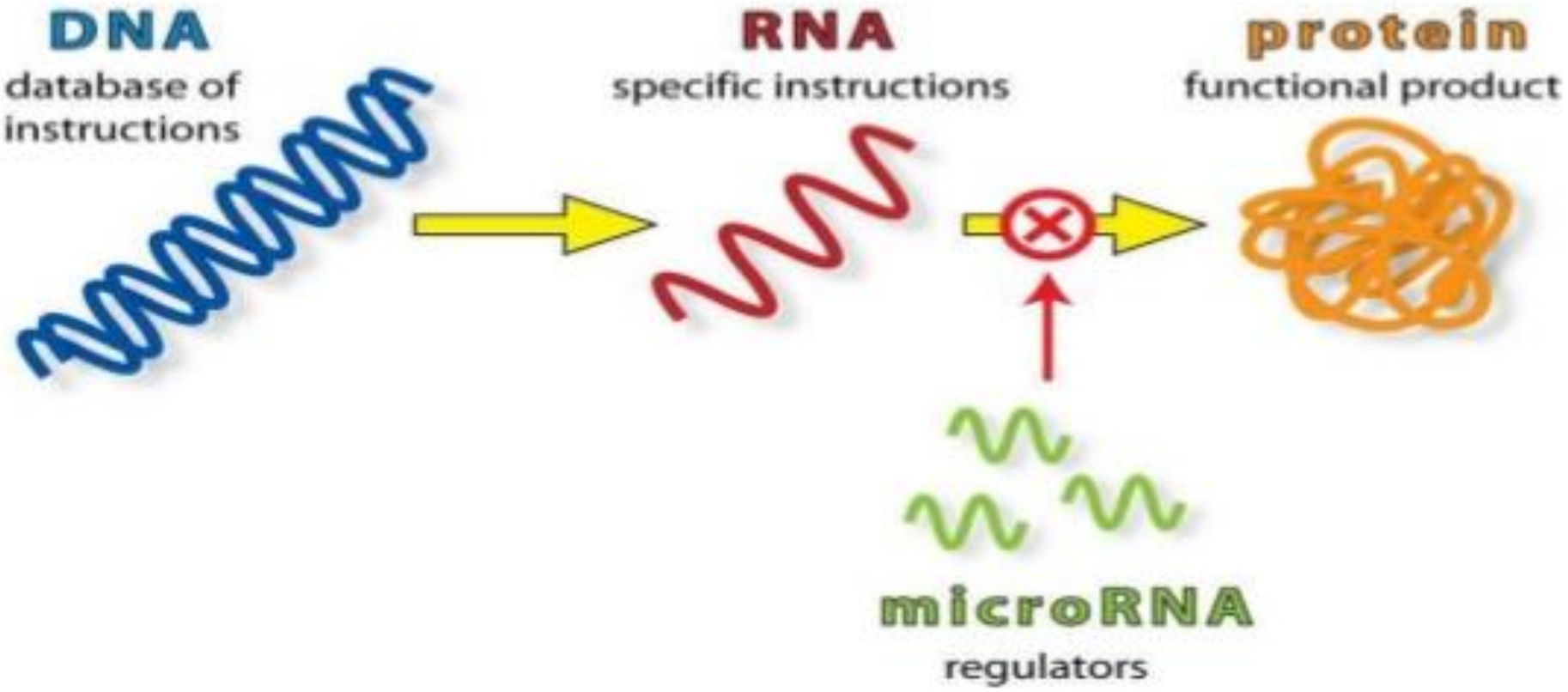
Micro RNAs, miRNAs, and Small Interfering RNAs, siRNAs

- These two classes of RNAs represent a subset of small RNAs; both play important roles in gene regulation.
- **miRNAs and siRNAs cause inhibition of gene expression** by decreasing specific protein production

Micro RNAs (miRNAs)

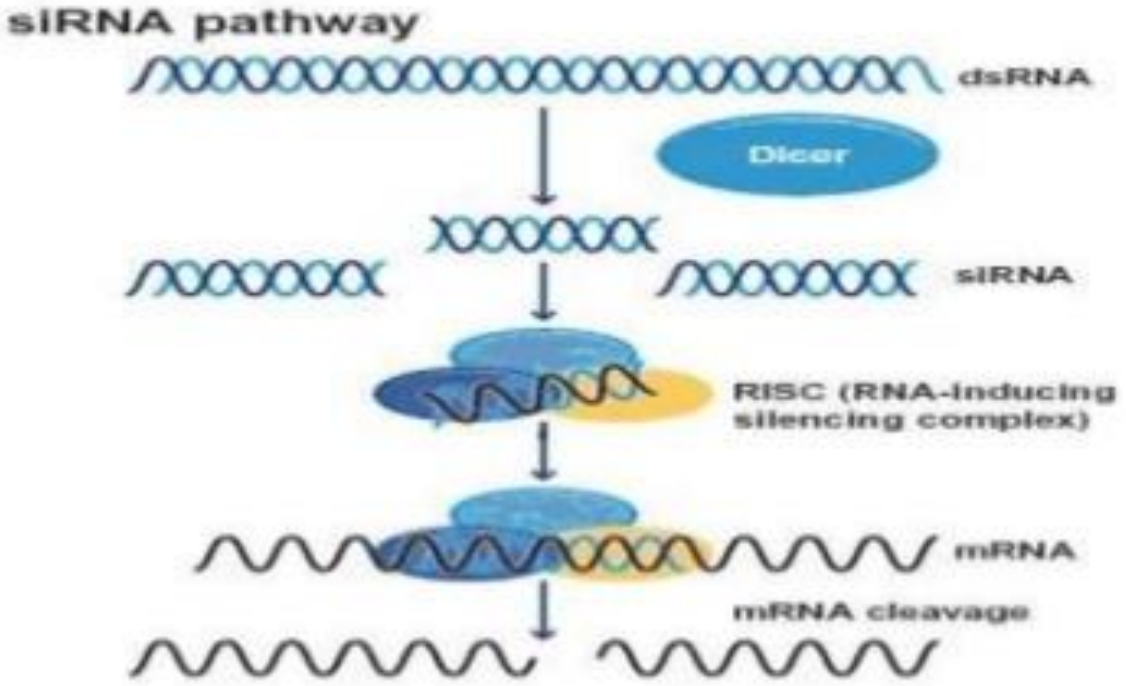
- miRNAs are typically 21–25 nucleotides in length and are generated by nucleolytic processing of the products of distinct genes/transcription units

Micro RNAs (miRNAs)



microRNAs, short non-coding RNAs present in all living organisms, have been shown to regulate the expression of at least half of all human genes. These single-stranded RNAs exert their regulatory action by binding messenger RNAs and preventing their translation into proteins.

Small Interfering RNAs (siRNAs)



Small interfering RNA (siRNA) are 20-25 nucleotide-long double-stranded RNA molecules that have a variety of roles in the cell. They are involved in the RNA interference (RNAi) pathway, where it interferes with the expression of a specific gene by hybridizing to its corresponding RNA sequence in the target mRNA. This then activates the degrading mRNA. Once the target mRNA is degraded, the mRNA cannot be translated into protein.

Significance of mi RNAs and si RNAs

- Both miRNAs and siRNAs represent exciting new **potential targets for therapeutic drug development in humans.**
- In addition, siRNAs are frequently used to decrease or "knock-down" specific protein levels in experimental procedures in the laboratory, an extremely useful and powerful alternative to gene-knockout technology.

RNA

- The major role of RNA is to participate in protein synthesis, which requires three classes of RNA:

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

Messenger RNA

- mRNA is transcribed from DNA, carrying information for protein synthesis.
- the mRNA carries the genetic information from the nucleus to the site of protein synthesis (ribosome) in the cytoplasm to be translated.

Transfer RNA

- Short-chain RNA molecules present in the cell that attach the correct amino acid to the protein chain that is being synthesized at the ribosome of the cell.
- The major role of tRNA is to **translate** mRNA sequence into amino acid sequence.

Ribosomal RNA

- rRNA molecules are produced in the nucleus, they are transported to the cytoplasm, where they combine with tens of specific proteins to form a ribosome.

Small RNA molecules

- Major types of small RNA molecules:
- Small nuclear RNA (snRNA) – involved in mRNA splicing.
- Small nucleolar RNA (snoRNA) – directs the modification of ribosomal RNAs.
- Micro RNA (miRNA) and short interfering RNA (siRNA) – regulate gene expression.

Summary

- RNA exists in several different single-stranded structures, most of which are directly or indirectly involved in protein synthesis or its regulation.
- The linear array of nucleotides in RNA consists of A, G, C, and U, and the sugar moiety is ribose.
- The major forms of RNA include messenger RNA (mRNA), ribosomal RNA (rRNA), transfer RNA (tRNA), and small nuclear RNAs (snRNAs; miRNAs).
- Certain RNA molecules act as catalysts (ribozymes).
- miRNAs and siRNAs represent exciting new **potential targets for therapeutic drug development in humans.**

Distinction between DNA & RNA:

DNA :

Similarities:

1. Both have A,G and C
2. Bonds between nucleoitides is phosphodiester.
3. Bonding is form 3`→ 5` direction
4. Main function is in protein biosynthesis.

RNA:

Differences between RNA and DNA

S.No.	RNA	DNA
1)	Single stranded mainly except when self complementary sequences are there it forms a double stranded structure (Hair pin structure)	Double stranded (Except for certain viral DNA s which are single stranded)
2)	Ribose is the main sugar	The sugar moiety is deoxy ribose
3)	Pyrimidine components differ. Thymine is never found(Except tRNA)	Thymine is always there but uracil is never found
4)	Being single stranded structure- It does not follow Chargaff's rule	It does follow Chargaff's rule. The total purine content in a double stranded DNA is always equal to pyrimidine content.

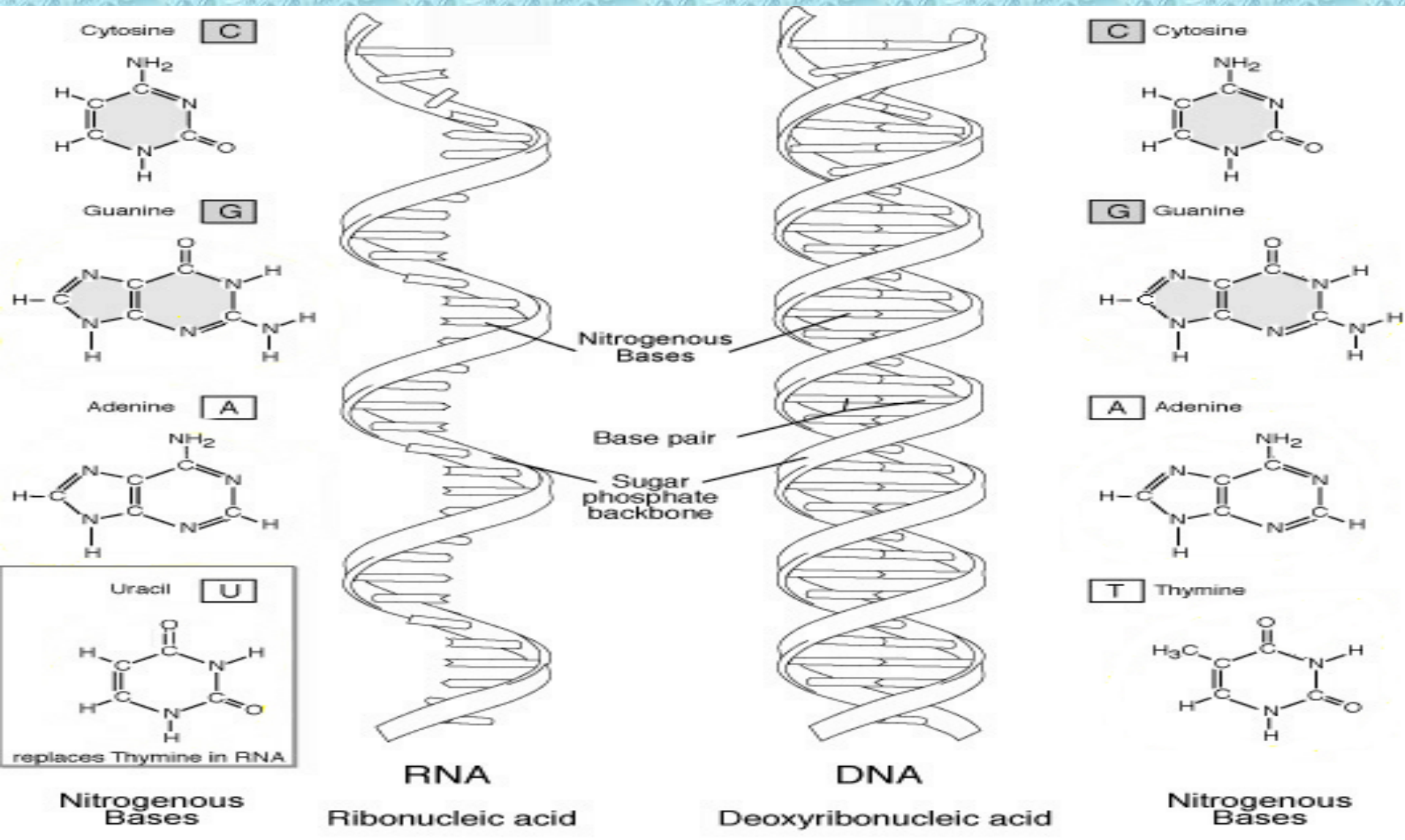
Differences between RNA and DNA

S.No.	RNA	DNA
5)	RNA can be easily destroyed by alkalies to cyclic diesters of mono nucleotides.	DNA resists alkali action due to the absence of OH group at 2' position
6)	RNA is a relatively a labile molecule, undergoes easy and spontaneous degradation	DNA is a stable molecule. The spontaneous degradation is very 2 slow. The genetic information can be stored for years together without any change.
7)	Mainly cytoplasmic, but also present in nucleus (primary transcript and small nuclear RNA)	Mainly found in nucleus, extra nuclear DNA is found in mitochondria, and plasmids etc
8)	The base content varies from 100- 5000. The size is variable.	Millions of base pairs are there depending upon the organism

Differences between RNA and DNA

S.No.	RNA	DNA
9)	There are various types of RNA – mRNA, r RNA, t RNA, Sn RNA, Si RNA, mi RNA and hn RNA. These RNAs perform different and specific functions.	DNA is always of one type and performs the function of storage and transfer of genetic information.
10)	No variable physiological forms of RNA are found. The different types of RNA do not change their forms	There are variable forms of DNA (A to E and Z)
11)	RNA is synthesized from DNA, it can not form DNA(except by the action of reverse transcriptase). It can not duplicate (except in certain viruses where it is a genomic material)	DNA can form DNA by replication, it can also form RNA by transcription.
12)	Many copies of RNA are present per cell	Single copy of DNA is present per cell.

RNA vs DNA


Cytosine C
Guanine G
Adenine A
Uracil U
replaces Thymine in RNA
Nitrogenous Bases
Base pair
Sugar phosphate backbone
RNA
Ribonucleic acid
DNA
Deoxyribonucleic acid
C Cytosine
G Guanine
A Adenine
T Thymine
Nitrogenous Bases

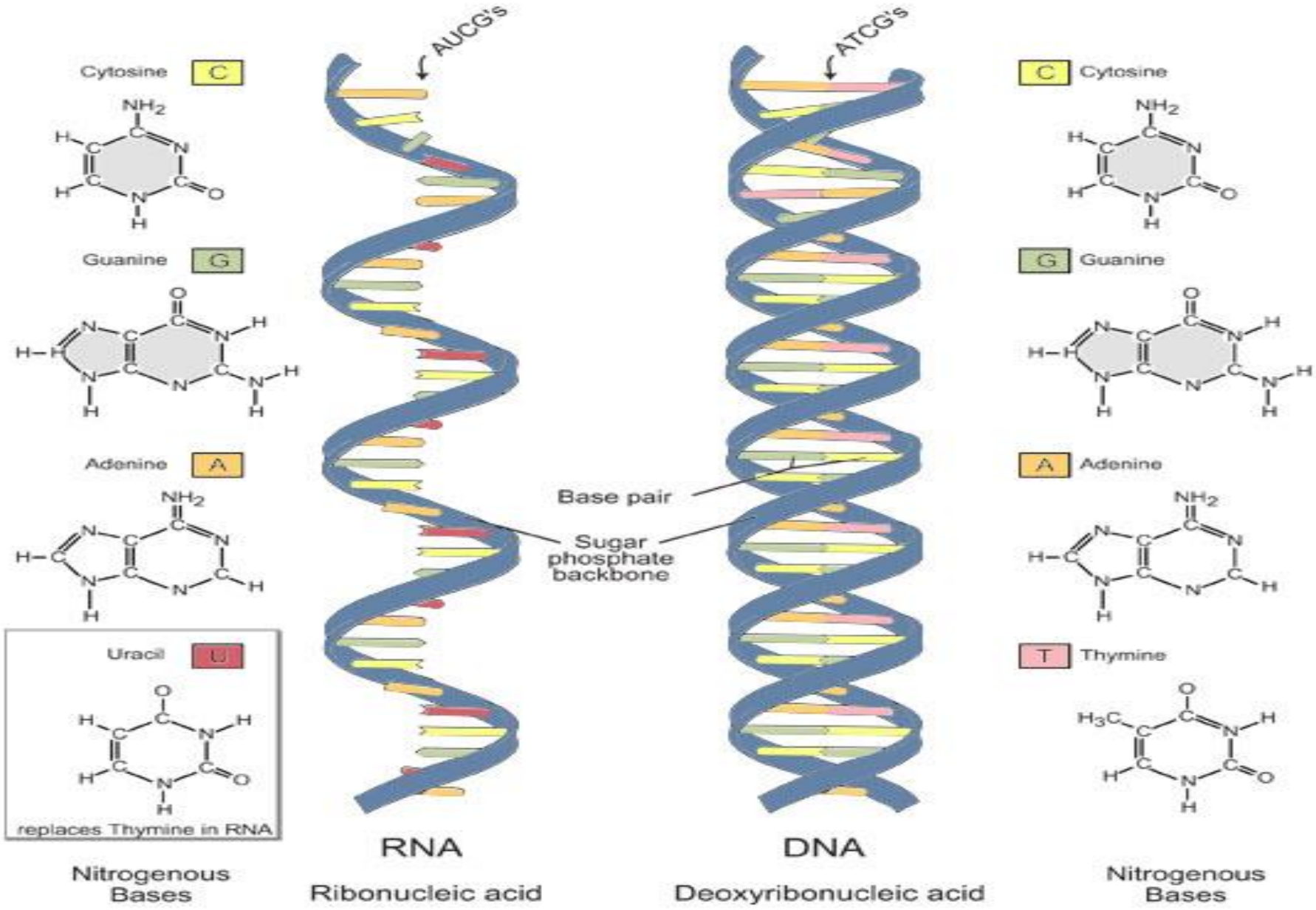


Image adapted from: National Human Genome Research Institute. Talking Glossary of Genetic Terms. Available at: www.genome.gov/Pages/Hyperion//DIR/VIP/Glossary/Illustration/rna.shtml.


This is LIFE

ANY QUESTION

- CHATTERJEA BIOCHEMISTRY
- LIPPINCOTT BIOCHEMISTRY
- HARPERS BIOCHEMISTRY
- SATYANARAYANA BIOCHEMISTRY
- INTERNET

Thank you