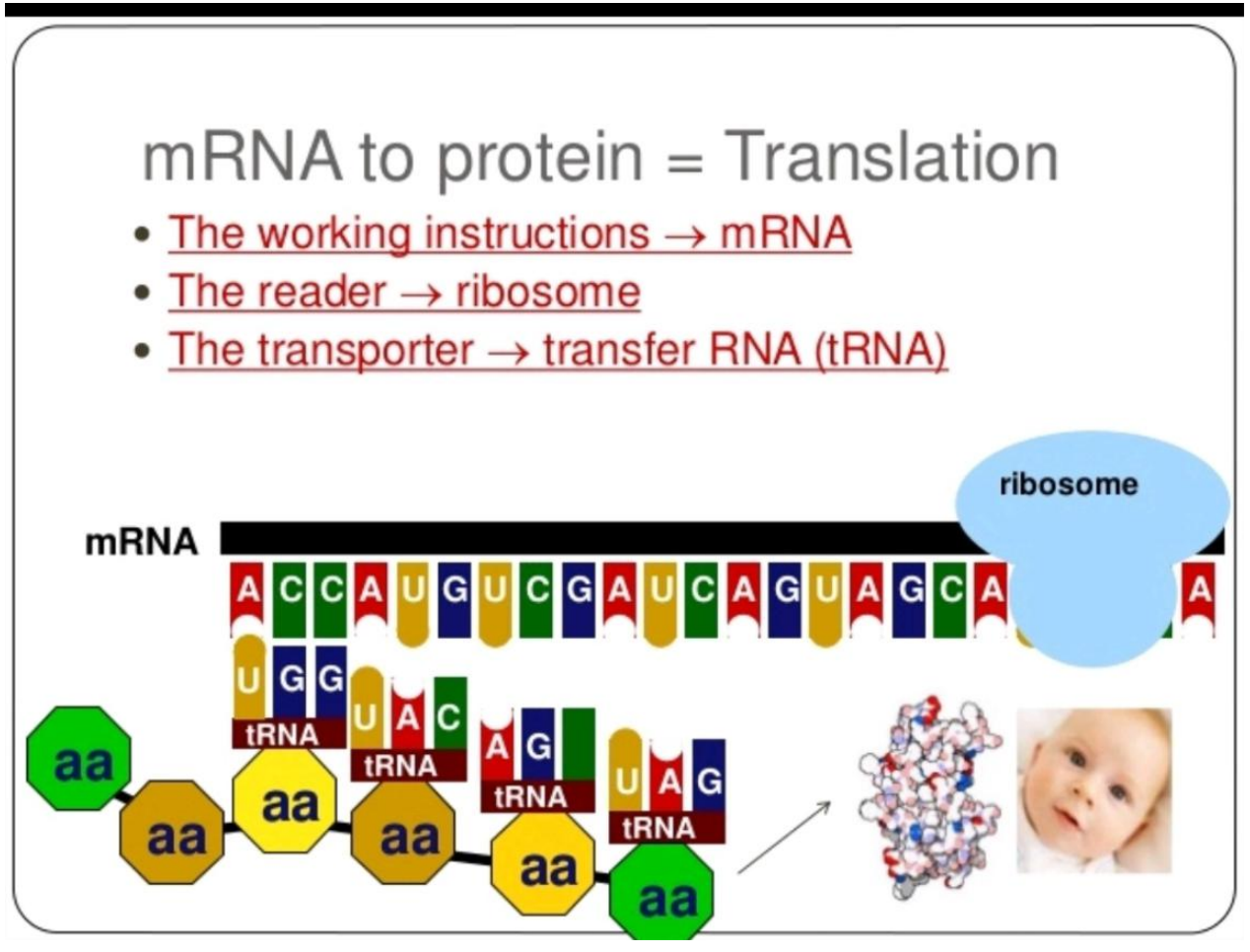
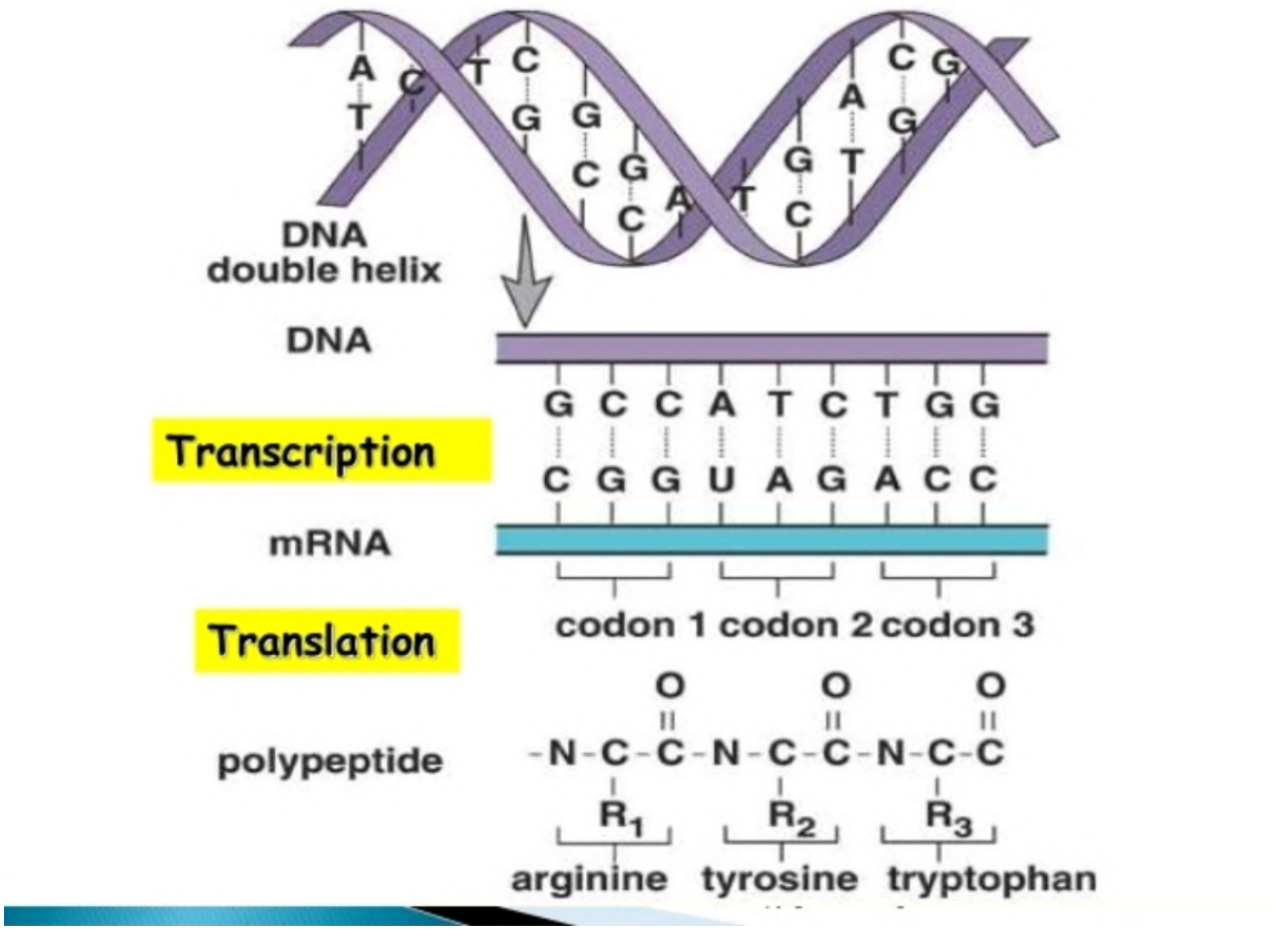
TRANSLATION



- ***Translation—***
- is a process in which a polypeptide is synthesized according to the nucleotide sequence of m RNA.
- It is carried out by a translation complex comprising m RNA, tRNA, ribosomes.
- Occurs at the ribosome in the cytoplasm.
- Uses anticodon to the tRNA to bring an aminoacid to the ribosomes.

PROTEIN SYNTHESIS.



TRANSLATION.

Takes place in ribosomes.

tRNA brings aminoacid to ribosomes.

tRNA forms a complimentary message – anticodon.

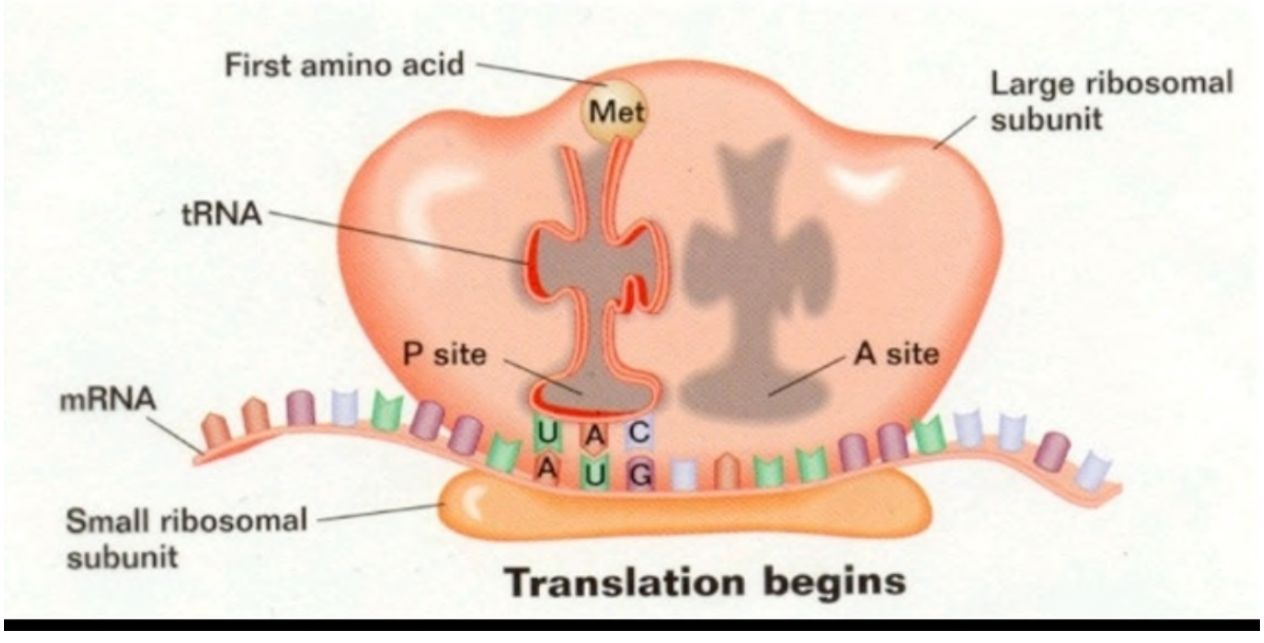
The aminoacid is read.

Aminoacid sequence continue until reaching a STOP codon.

PROTEIN SYNTHESIS.

rRNA:(ribosomal RNA)

- found in the cytoplasm and is the site of protein synthesis



STEPS FOR PROTEIN SYNTHESIS.

- *STARTS WITH DNA.*
- *Transcribe to mRNA.*
- *mRNA speccifies aminoacid sequence in polypeptide.*
- *Brought by tRNA to r RNA.*
- *Is translated into protein.*

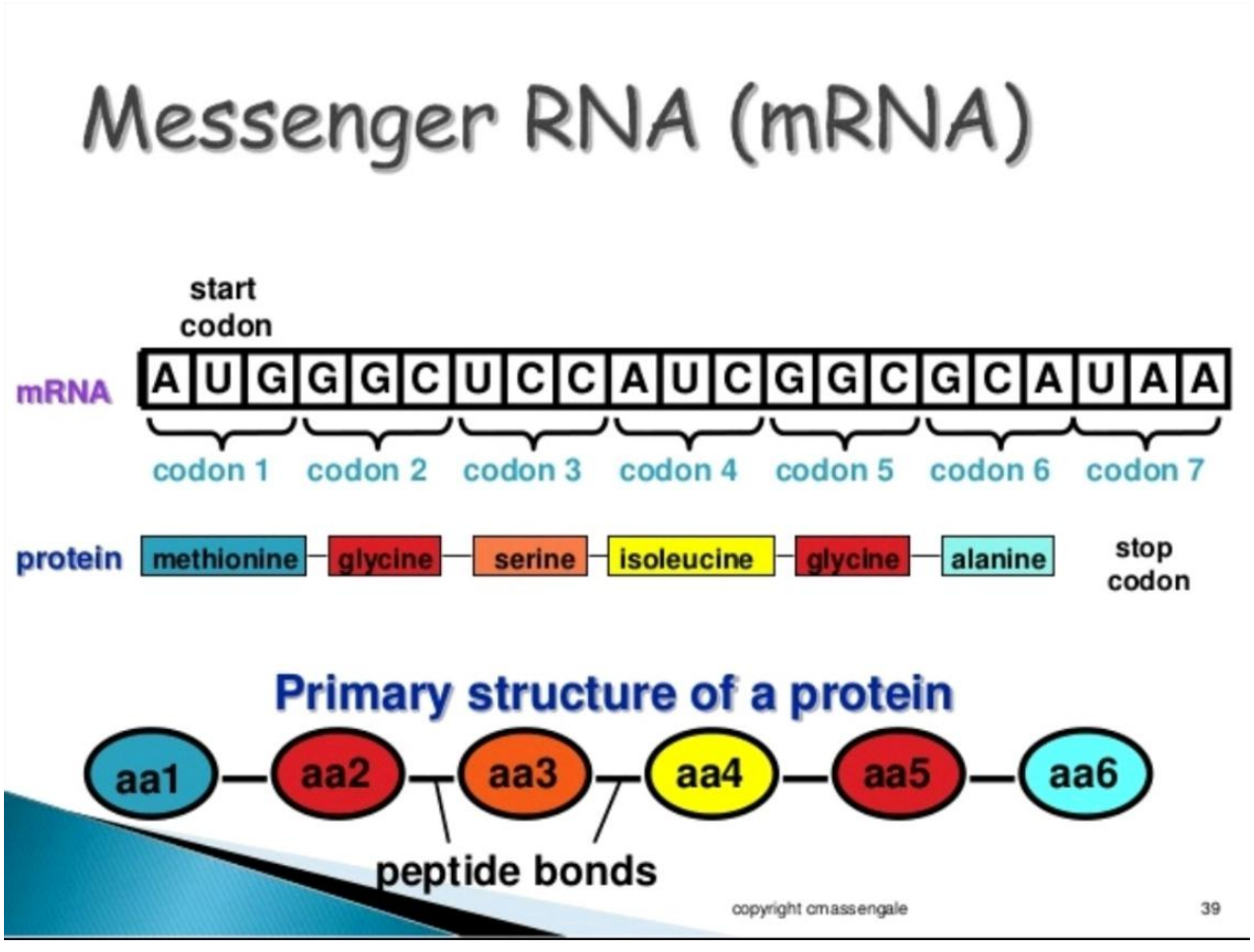
GENETIC CODE.

- GENETIC CODE-
- Genetic code is the language used to convert the sequence of nucleotides in mRNA into the sequence of amino acids of a protein.
- A codon is a combination of three consecutive nucleotides present on DNA or mRNA. Hence, it is commonly called a triplet i.e. a codon is a triplet of nucleotides.
- Three codons do not code for any amino acid and the signal the termination of protein synthesis. These are called termination codons or stop codons. These are UAA, UGA and UAG.

I

- AUG is used as the first or initiation codon in all the proteins synthesized from mRNA. It codes for methionine. Therefore, each newly synthesized polypeptide chain [nascent chain] has methionine as the first amino acid. However, it may not be present in final fully functional mature protein because this amino acid may be removed during processing and maturation of protein.
- Codons on mRNA or DNA(from which mRNA is transcribed) are read from 5` to 3` direction by the anti-codon loop of the tRNA.

TRANSLATION.



TRANSLATION IS COMPLETED IN 4 MAJOR STEPS.

- Charging of tRNA.
- Initiation.
- Elongation and translocation.
- Termination.
- Folding and processing.
- Transport.

ACTIVATION OF AMINOACID AND CHARGING OF TRNA.

- Components required.
- 20 aminoacid.
- 20 aminoacyl tRNA synthesis.
- ATP.
- Mg+

INITIATION.

- Component required.
- mRNA.
- fmet-Trna/met-tRNA
- 30s/50s – 70s
- 40s/60s—80s
- GTP
- Mg+
- Initiation factor.IF-1,IF-2,and IF-3.

ELONGATION AND TRANSLOCATION.

- Component required.
- *Initiation complex.*
- *Aminoacyl tRNA.*
- *Mg++*
- *Elongation factor.*
- *Peptidyl transferase.*

TERMINATION.

- Component required.
- ATP.
- Termination codon.
- Release factor, RF-1, RF-2,RF-3.

TRANSLATION.

- *INITIATION–*
- *several initiation factors , AMP, and GMP are required and occurs in the following stages.*
- *ACTIVATION OF AMINO ACID*
- *SPLITING OF RIBOSOMES*
- *PREINITIATION COMPLEX FORMATION*
- *FORMATION OF 48S PRE-INITIATION COMPLEX*
- *FORMATION OF FULLY ACTIVE 80S INITIATION COMPLEX.*
- *ELONGATION*
- *TERMINATION*

TRANSLATION IN PROKARYOTES.

- *INITIATION--*
- *The 70s ribosome dissociated to form 30s and 50s subunits. A set of three proteins called initiation factor (IF-1, IF-2, and IF-3) take part in initiation. Bacterial ribosome contain three specific sites that bind aminoacyl-t RNAs. They are the A site(aminoacyl site), the P site(peptidyl site) and the E site(exit site).*
- *Two initiation factor, IF-1 and IF-3, bind to the 30s ribosomal subunit .The m RNA now bind to the 30s subunit in such a fashion that the initiating codon (AUG) comes in to the P site on the ribosome. AUG is the codon for methionine which has two t RNAs.*

ELONGATION.

- ELONGATION–
- similar to initiation , a set of three elongation fact
  (EF-1, EF-2, EF-3) participate in the elongation .
- 1) Binding of an incoming aminiacyl –t RNA.
- 2) peptide bond formation.
- 3) Translocation.

TRANSLATION.

- **TERMINATION-**
- Elongation continues until last aminoacid is added as coded by the m RNA. One of the three stop codons –UAA, UAG,UGA occurs immediately after the codon for the last aminoacid .

TRANSLATION IN EUKARYOTES.

- *INITIATION-*

  DISSOCIATION OF RIBOSOME -- The 80s intact ribosome dissociate to its constituent subunits-40s and 60s. Two initiation factor (eIF-1 and eIF-2) bind to 40s subunit and delays its reassociation with the 60s subunit allowing the binding of other initiation factors to the 40s subunit.
- *FORMATION OF THE PREINITIATION COMPLEX-- The elongation factor -2 (eIF-2) binds GTP to form a binary complex which in turn associates with t RNA (carrying methionine) to form ternary complex.*
- *The ternary complex bind to the 40s ribosomal subunit to form 43s pre initiation complex.*

INITIATION.

- REQUIREMENT—
- Initiation factor.
- AMP, GMP.
- Occurs in following stages---
- ACTIVATION OF Amino acid—
- First amino acid combined to AMP to form aminoacyl adenylate which is then attached to the corresponding t RNA.
- SPLITING OF RIBOSOMES----
- Ribosomes split into a smaller 40-S subunits and 60-S subunit . eIF -3 and Eif -1a bind to 40S subunit and eLF-6 bind to 60s subunit to stabilize them and prevent their re association.
-

PRE INITIATION COMPLEX.

- PRE INITIATION COMPLEX--
- Methionine is the starting amino acid , so activated methionine , that is t RNA met first binds eLF -2 and GTP to form the ternary complex. Then ternary complex then bind to stablized 40S subunit to form the 43s pre initiation complex.
- FORMATION OF 48S pre-initiation complex –
- Binding of mRNA to 43s pre-initiation complex leads to the formation of 48s pre-initiation complex. This is mediated by eLF-3, eLF-4F.
- The 48s-pre-initiation complex then scans the mRNA in 5'-3' direction for the initiation codon.

INITIATION COMPLEX.

- FORMATION OF FULLY ACTIVE 80S INITIATION COMPLEX-
- eIF-5 fascilitate the binding of 60S ribosomal subunit to pre-initiation complex to form 80S initiation complex. At this point ,met-t-RNA(initiator tRNA) is on the P site of ribosome to start the elongation.

INITIATION COMPLEX.

- *FORMATION OF INITIATION COMLEX--*
- *Activated m RNA is then transferred to the 43s pre initiation complex to form 48s initiation complex. The 48s initiation complex bind to the 60s ribosomal subunit to form the 80s initiation complex.*

ELONGATION.

- ELONGATION—
- once the process of translation is initiated, the polypeptide chain is expanded in length by the sequential addition of aminoacids.
- Elongation is a cyclic process occurs in three steps.
- 1.Binding of amino acyl –t RNA to the A site.
- 2.Peptide bond formation.
- 3.Translocation.

TRANSLATION

- *TERMINATION-----*
- *After several cycles of elongation incorporating the required number of aminiacids one of the three stop codons (UAA, UAG, UGA) appears in the A site. The stop codon is not recognised by any specific t RNA but a releasing factor (RF) recognises and binds to the stop codon.*

INHIBITORS OF PROTEIN SYNTHESIS

- Several antibiotics selectively act on bacterial ribosomes and other ribosomes and other translation components to inhibit protein synthesis and kill them.

MECHANISM OF ACTION OF ANTIBIOTICS.

TETRACYCLIN	INHIBIT BINDING AMINOACYL tRNA to A site.
STREPTOMYCIN	Bind to 30s ribosome.
chloremphenicol	Inhibit peptidyl transferase.
Erythromycin	Binds to 50s ribosomes.
tetracycline	Blocking the a site on the ribosome.

CONTROL OF PROTEIN SYNTHESIS.

- ***CONTROL OF PROTEIN SYNTHESIS-***
- Control of protein synthesis occurs at the stage of initiation at two levels.
- By eIF-2, preventing 43S PIC formation and
- BY eIF-4F complex and preventing 48S PIC formation.

REGULATION.

- REGULATION BY eIF-2 -
- eIF-2 is a trimeric protein having *a, B and y* subunits. It is activated by phosphorylation of *a*- subunits by several kinases.
- Phosphorylated a-subunits binds to eLF2B and inctivates it. This prevents 43S PIC formation and stops translation.

REGULATION.

REGULATION BY eIF-4F

- eIF-4F is inactive when bound by a protein (4E-BP).
- On phosphorylation of 4EBP 4E becomes free and takes part in 4F complex formation.
- 4F then binds to mRNA cap and ultimately leads to the formation of 48S PLC.

PROTEIN FOLDING

- Nascent protein undergoes folding with the help of chapreons to acquire an appropriate three dimensional structure to become active.
- Protein that do not fold properly and become non functional, are degraded . Some may aggregate to produce Prion disease.

POST – TRANSLATIONAL MODIFICATION.

most of the newly synthesised proteins are not functional. After attaining a three – dimensional structure by folding mechanism, these proteins undergo several structural and chemical alteration to become fully functional.

COVALENT MODIFICATION.

- PHOSPHORYLATION.—
- Phosphorylation – Dephosphorylation depending on cellular needs.This process is under the control of hormones and is the major mechanism of enzyme regulation.
- HYDROXYLATION.—
- collagen synthesised as procollagen undergoes extensive post translational modification to form mature collagen.
- GLYCOSYLATION.—
- many proteins contain extensive carbohydrate side chain.
- CARBOXYLATION...
- ACETYLATION....
- Most of the translational processing occurs in the endoplasmic reticulam and Golgi complex.