



Nucleic acid metabolism and Genetic information transfer

VIJAYA KUMAR MEHER



Genetic code

- The 3 nucleotide (triplet) base sequences in mRNA that act as code words for amino acids in protein constitute the genetic code or simply codons.
- The codons are composed of the four nucleotide bases, namely the purines-adenine (A) and guanine (C), and the pyrimidines-cytosine (C) and uracil (U).
- These 4 bases produce 64 different combinations of 3 base codons.
- The nucleotide sequence of the codon on mRNA is written from the 5'-end to 3' end.
- 61 codons code for the 20 amino acids found in protein.
- The 3 codons UAA, UAG and UCA do not code for amino acids. They act as stop signals in protein synthesis. These 3 codons are known as termination codons or non-sense codons

- The codons AUG and GUG are the chain initiating codons.
- **Universality** : The same codons are used to code for the same amino acids in all the living organisms.
- **Specificity** : A particular codon always codes for the same amino acid, hence the genetic code is highly specific or unambiguous.
- Eg: UGG is the codon for tryptophan.
- It is non-overlapping, commaless and without any punctuations
- The codes are consecutive and are read one after another in a continuous manner, e.g. AUG, CAU, GAU, GCA, etc.
- **Degenerate:** The codon is degenerate or redundant, since there are 61 codons available to code for only 20 amino acids (ie, one amino acid has more than one codon.)
- Eg: glycine has four codons.
- **Wobble hypothesis** explains the degeneracy of the genetic code, i.e. existence of multiple codons for a single amino acid.

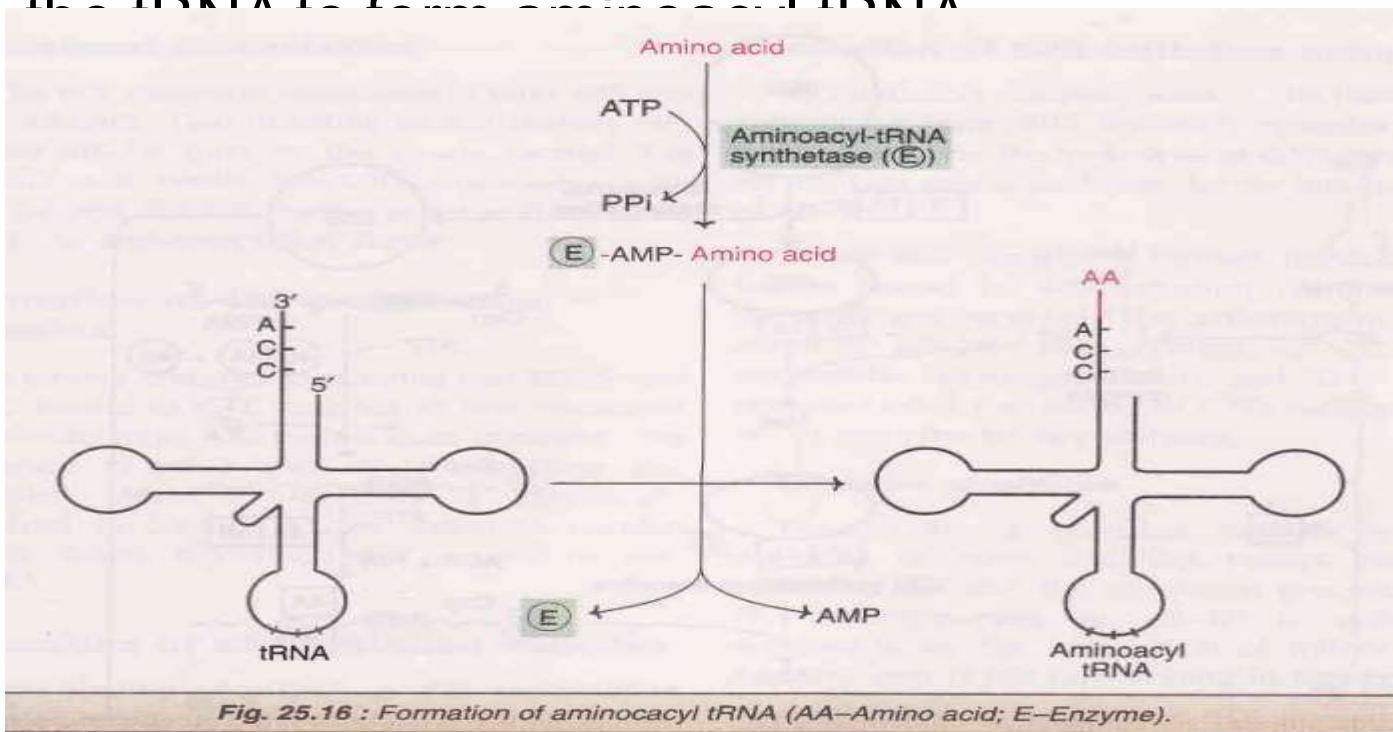


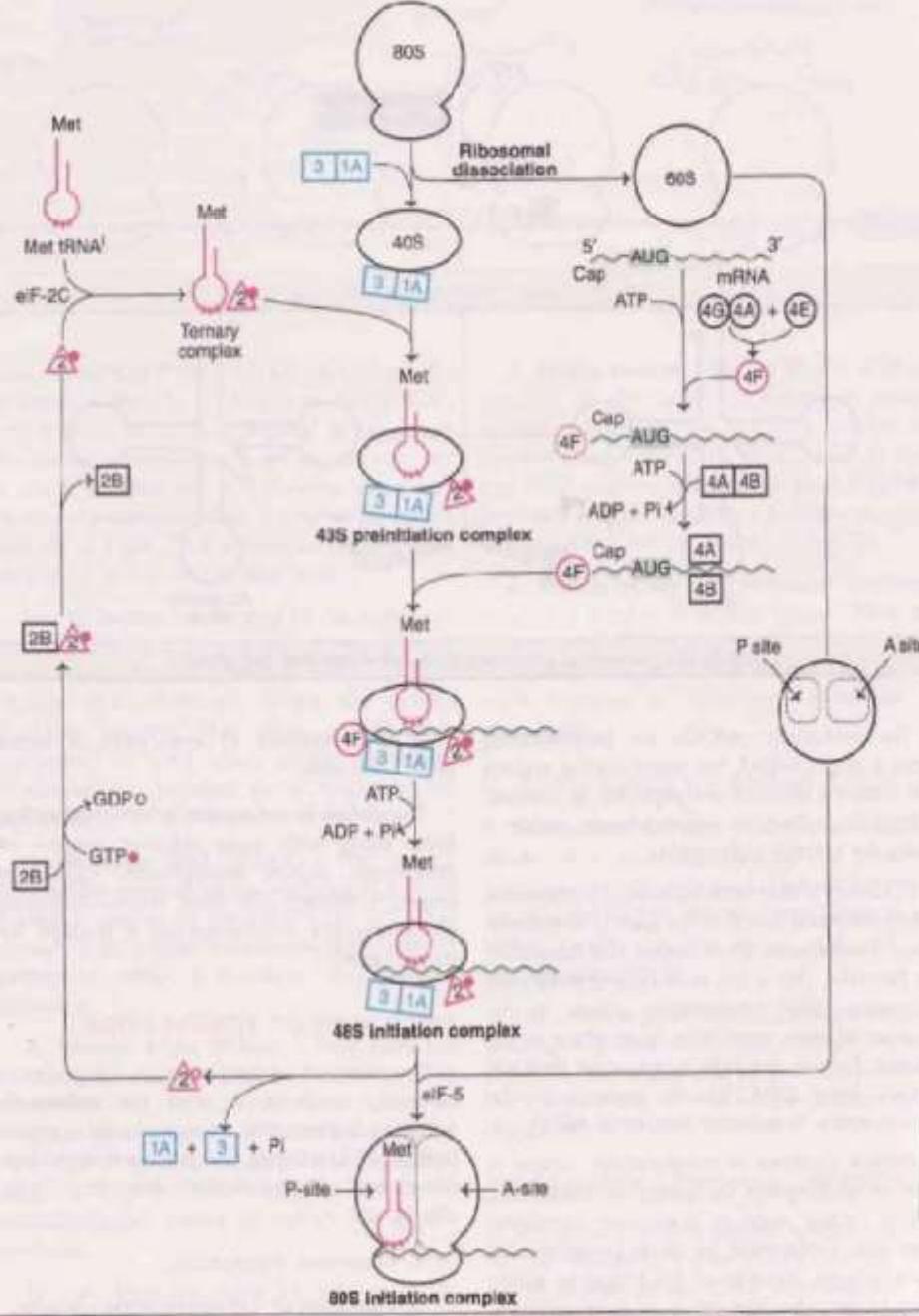
Translation or protein synthesis

- The biosynthesis of a protein or a polypeptide in a living cell.
- The protein synthesis occurs on the ribosomes .
- The mRNA is read in the 5' to 3' direction and the protein synthesis proceeds from N-terminal end to C-terminal end.
- Steps involved in translation:
 1. Activation of amino acid
 2. Initiation
 3. Elongation
 4. Termination
 5. Post-translational processing.

Activation of amino acid:

- The enzymes aminoacyl tRNA synthetase activate the amino acids.
- The amino acid is first attached to the enzyme utilizing ATP to form enzyme-AMP-amino acid complex.
- The amino acid is then transferred to the 3' end of the tRNA to form aminoacyl tRNA.





Initiation of translation :

- It involves use of **initiation factors (eIF)**
- The process of translation initiation can be divided into **4 steps**
 1. **Ribosomal dissociation.**
 2. **Formation of 43S preinitiation complex.**
 3. **Formation of 48S initiation complex.**
 4. **Formation of 80S initiation complex.**
- The 80S ribosome dissociates to form 40S and 60 S subunits
- A ternary complex containing met-tRNA and eIF-2 bound to GTP attaches to 40S ribosomal subunit to form 43S preinitiation complex.
- The binding of mRNA to 43S preinitiation complex results in the formation of 48S initiation complex through the intermediate 43S initiation complex.
- 48S initiation complex binds to 60 S ribosomal subunit to form 80S initiation complex.
- As the 80S complex is formed, the initiation factors bound to 48S initiation complex are released and recycled

Fig. 25.17 : A diagrammatic representation of initiation of protein biosynthesis (translation) in eukaryotic cells (The eukaryotic initiation factors are represented by symbols □ △ and ○. By prefixing with eIF, the full names of the factors are obtained e.g. □ represents eIF-3).

Elongation of translation:

- Ribosomes elongate the polypeptide chain by sequential addition of amino acids.
- Elongation process involves use of certain elongation factors (EF).

Steps:

(1) Binding of aminoacyl tRNA to A-site.

- The 80 S initiation complex contains met tRNA in the P-site, and the A-site is free. Another aminoacyl-tRNA is placed in the A-site.

(2) Peptide bond formation.

- The enzyme peptidyltransferase catalyses the formation of peptide bond

(3) Translocation.

- As the peptide bond formation occurs, the ribosome moves to the next codon of the mRNA (towards 3'-end).
- Translocation involves the movement of growing peptide chain from A-site to P-site.
- Translocation requires EF-2 and GTP.

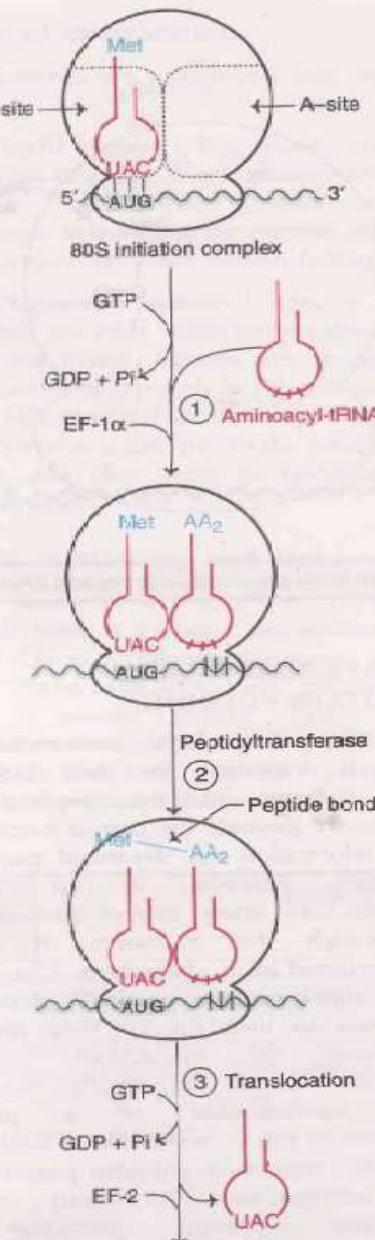
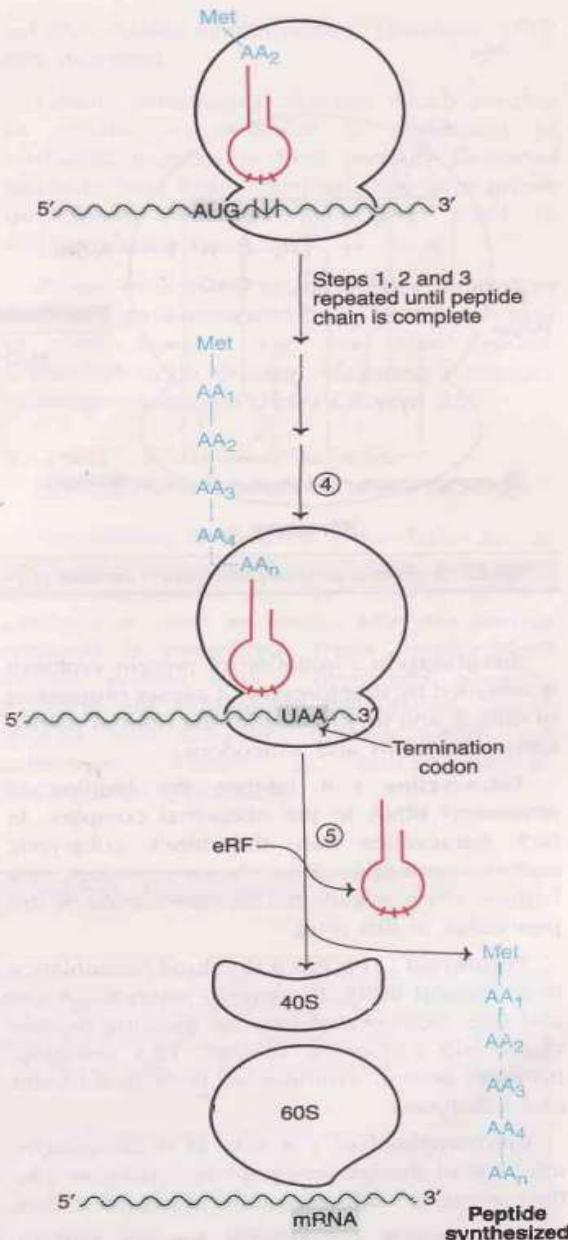


Fig. 25.18 contd. next column



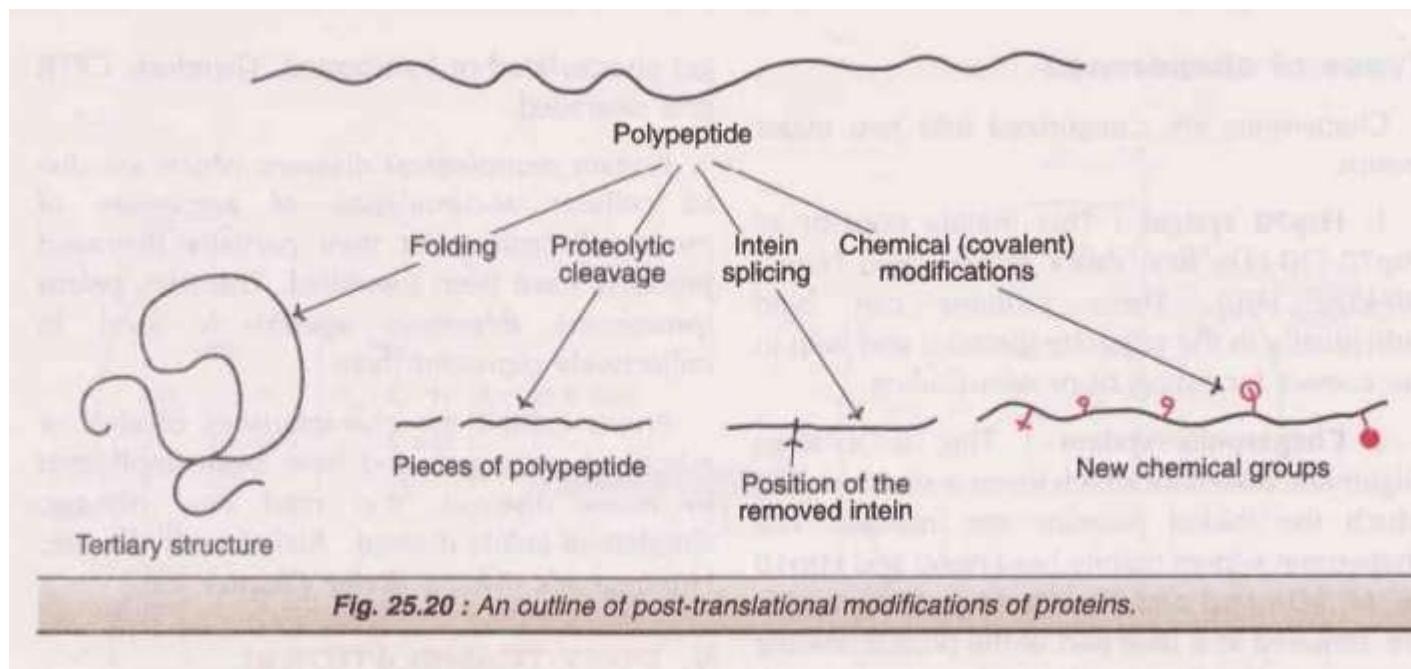
Termination of translation:

- After successive addition of amino acids, ribosome reaches the termination codon sequence (UAA, UAG or UGA) on the mRNA.
- As the **termination codon** occupies the ribosomal A-site, the release factor eRF recognizes the stop signal.
- The 80S ribosome dissociates to form 40S and 60S subunits which are recycled.
- The mRNA is also released.

Fig. 25.18 : Protein biosynthesis — Elongation and termination (for initiation See Fig. 25.17). Met-Methionine; P-site — Peptidyl tRNA binding site; A-site — Aminoacyl tRNA binding site. AA-Amino acid; EF-Elongation factor; RF-Releasing factor.

Post-translational processing:

- The proteins synthesized in translation are, as such, not functional. so some changes are needed
- These modifications include **protein folding** , **trimming by proteolytic degradation**, **intein splicing** and **covalent changes** which are collectively known as Post-translational modification.





Inhibitors of protein synthesis

- Majority of the **antibiotics** interfere with the bacterial protein synthesis.
- **Streptomycin** inhibit initiation of protein synthesis. It causes misreading of mRNA and interferes with the normal pairing between codons and anticodons.
- **Tetracycline** inhibits the binding of aminoacyl tRNA to the ribosomal complex.
- **Puromycin** enters into the growing peptide chain and causes its release
- **Chloramphenicol** acts as a competitive inhibitor of peptidyltransferase and thus interferes with elongation of peptide chain.
- **Erythromycin** inhibits translocation by binding with 50S subunit of bacterial ribosome.
- **Diphtheria toxin** prevents translocation in protein synthesis by inactivating elongation factor