Lecture 5: From gene to protein: mRNA translation and the function of the ribosome

I. The genetic code and the central dogma of molecular biology

A. The Genetic code

The genetic code defines how DNA and RNA sequences are translated into proteins. This code is based on codons, which are triplet nucleotide sequences found in messenger RNA (mRNA). Each codon specifies either:

(1) One of 20 distinct standard amino acids, or (2) A translational stop signal.

Key characteristics of the genetic code include:

(1) **Triplet Characteristic:** Each codon consists of three nucleotides.
(2) **Degeneracy:** The genetic code has redundancy, meaning most amino acids are encoded by more than one codon.
(3) **Unambiguity:** Each codon corresponds to a single amino acid.
(4) **Highly Conserved:** The genetic code is consistent across nearly all organisms, indicating a shared evolutionary ancestor.
(5) **Non-Overlapping:** Genes are interpreted sequentially without overlapping codons or intervening punctuation.

B. The Central Dogma

The central dogma describes the directional flow of genetic information from DNA to protein:

DNA → RNA → Protein

⇔ DNA replication **ensures** the continuity of genetic information.
⇔ Transcription **converts** DNA information into RNA.
⇔ Translation **decodes** RNA information into functional proteins.

◎ Now we will focus on the events following transcription, specifically from mRNA export out of the nucleus to protein translation.

II. The cytoplasmic fate of mRNA

Once the mRNA is in the cytoplasm, it may have several outcomes:

(1) It may be translated immediately.
(2) It may be stored temporarily in ribonucleoprotein granules.
(3) It may undergo degradation, regulated by mechanisms that control mRNA stability.

For most mRNAs, the primary functional destination is translation on the ribosome.

III. Translation: Decoding mRNA into protein

A. What is translation

Translation is the process by which ribosomes synthesize polypeptides based on the instructions provided by mRNA.

Key molecular components include:

(1) **mRNA:** The template containing codons.
(2) **Ribosomes:** Ribozyme complexes made of ribosomal RNA (rRNA) and proteins.
(3) **tRNA:** Adapter molecules that link codons to their corresponding amino acids.
(4) **Aminoacyl-tRNA Synthetases:** Enzymes that charge tRNAs with the appropriate amino acids.

IV. The stages of translation

1- Translation initiation

- **Ribosomal subunits**

Eukaryotic ribosomes consist of:

a. A small (40S) subunit
b. A large (60S) subunit

- **Initiator tRNA**

a. Carries methionine (Met).
b. Recognizes the start codon AUG.

⇔ **Initiation process**

[1] The **5' cap of the mRNA** is recognized by the small ribosomal subunit.
[2] The ribosomal subunit moves along the mRNA in the 5' → 3' direction, looking for the start codon.
[3] Upon recognition of the start codon:
(A) The initiator tRNA binds to the P-site.
(B) The large ribosomal subunit associates, forming a fully assembled initiation complex.

B. Translation elongation

It occurs in three main steps:

(1) Codon recognition

a. An aminoacyl-tRNA enters the A site.
b. Codon–anticodon base pairing ensures specificity.

(2) Peptide bond formation

a. The ribosome contains rRNA that catalyzes peptide bond formation.
b. The nascent polypeptide chain transfers from the tRNA in the P-site to the A-site, enabling continued synthesis.

(3) Translocation

a. The ribosome moves by one codon along the mRNA.
b. tRNAs shift positions:
    i. A site → P site
    ii. P site → E site (exit)

◎ The polypeptide is progressively elongated from the N-terminus to the C-terminus through a sequential process.

C. Translation termination

(1) Termination occurs when a stop codon (UAA, UAG, or UGA) appears at the A-site.
(2) No corresponding tRNA exists for stop codons.
(3) Release factors bind to the stop codon, initiating:
    a. Hydrolysis of the polypeptide from the tRNA.
    b. Dissociation of the ribosomal subunits.
    c. The nascent polypeptide is released into the cytosol.

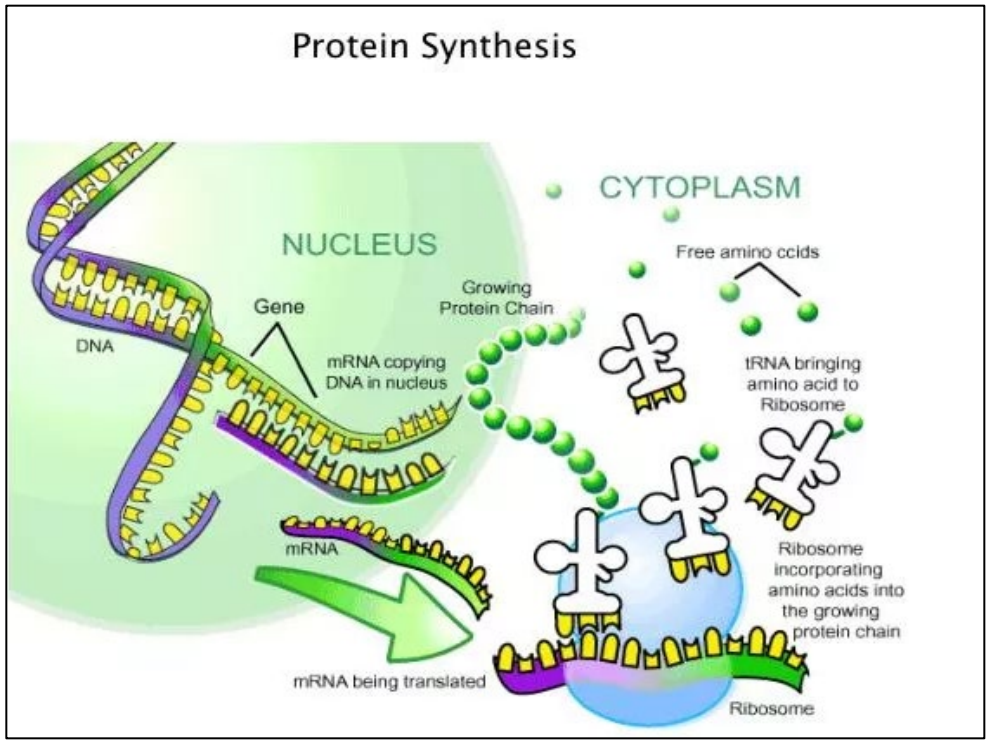

Figure 1: Schematic showing transcription of DNA into mRNA in the nucleus and translation of mRNA into a polypeptide by ribosomes and tRNAs in the cytoplasm.

V. post-translational events

Proteins typically undergo post-translational processing, which may include:

(A) Folding, facilitated by molecular chaperones.
(B) Post-translational modifications, such as phosphorylation, glycosylation, or ubiquitination.
(C) Targeting and localization, mediated by signal peptides and transport mechanisms.

These steps are essential for achieving full biological activity.