Cell Biology, Genetics and Evolution

Translation

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CENTRAL DOGMA

5′-ATGCCTAGGTACCTATGA-3′

3′-TACGGATCCATGGATACT-5

DNA

Transcription

5′-AUGCCUAGGUACCUAUGA-3

mRNA

Decoded as

5′-AUG CCU AGG UAC CUA UGA-

Translation

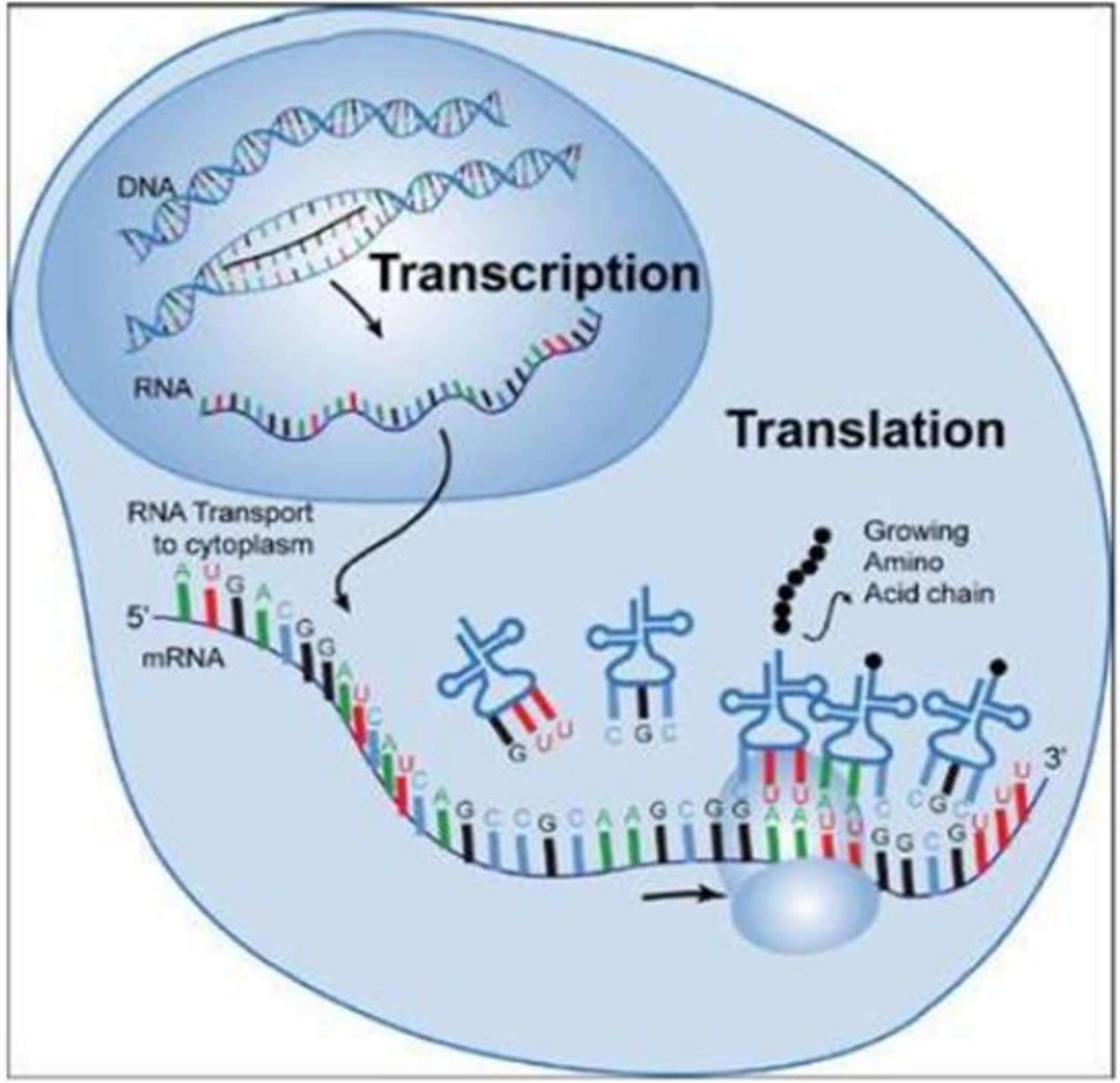
MET-PRO-ARG-TYR-LEU

Protein

Polypeptide chain

Translation (Definition)

- Translation in biology is the process by which cells create proteins from the instructions encoded in mRNA (messenger RNA).
- It is one of the key steps in gene expression, following transcription (when DNA is copied into mRNA).


DNA
Transcription
RNA
Translation
RNA Transport
to cytoplasm
5'
mRNA
Growing
Amino
Acid chain
3'

Components of Translation

- 1. mRNA
- 2. Ribosomes (rRNA)
- 3. tRNA
- 4. Amino Acids (20 Types)
- 5. Mg2+ (Activator)
- 6. Amino acyl tRNA Synthetases
- 7. Initiation, Elongation and Termination Factors

mRNA

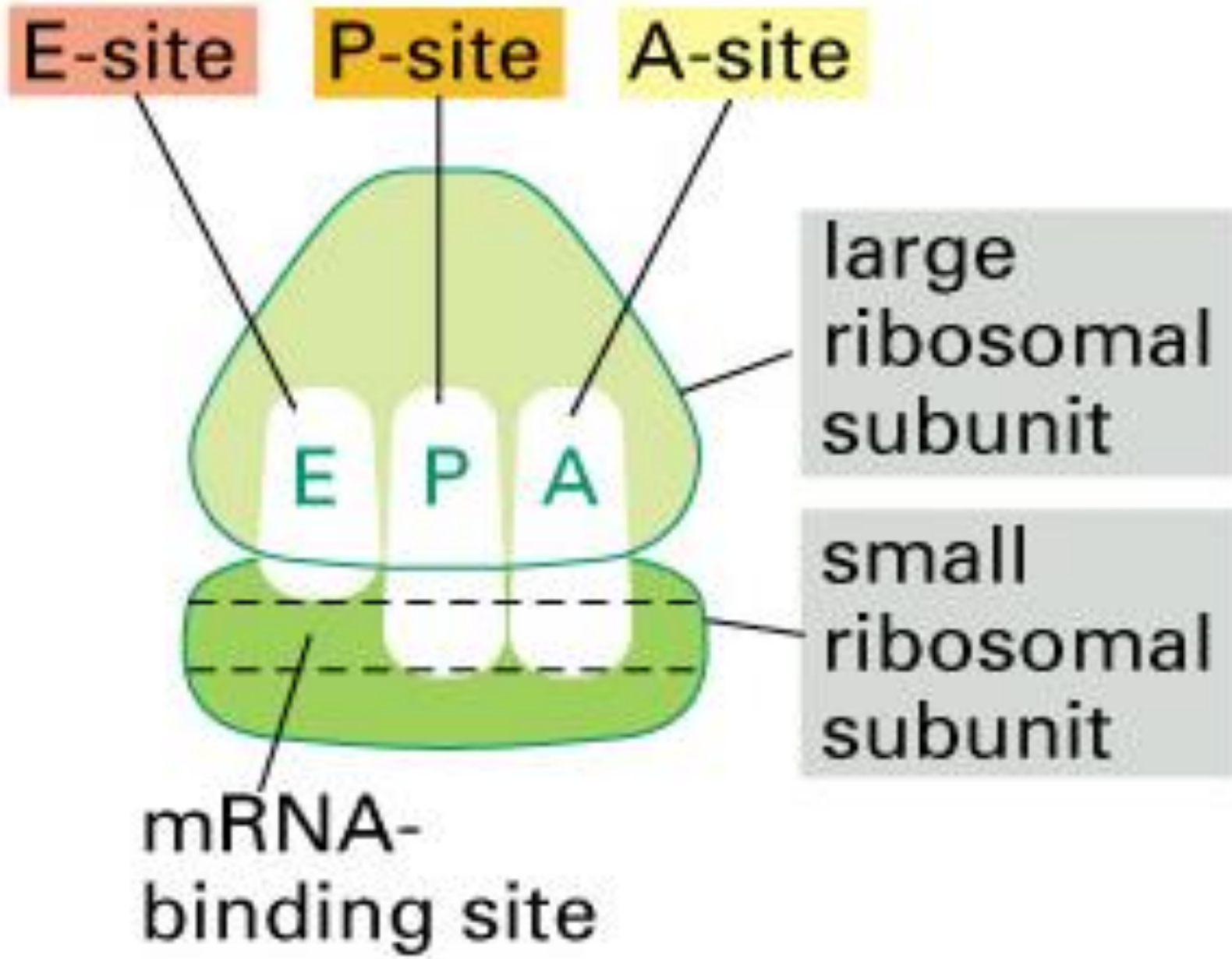
- mRNA carries the genetic information from DNA in the nucleus to the cytoplasm, where proteins are synthesized. The sequence of nucleotide bases (adenine (A), uracil (U), guanine (G), and cytosine (C)) on the mRNA dictates the sequence of amino acids in a protein.
- mRNA is read in codons, which are groups of three nucleotides. Each codon corresponds to a specific amino acid or a stop signal.

Ribosomes

- **Structure:** Ribosomes are composed of two subunits: a large subunit (50S in prokaryotes, 60S in eukaryotes) and a small subunit (30S in prokaryotes, 40S in eukaryotes). Together, they form a 70S ribosome in prokaryotes and an 80S ribosome in eukaryotes.
- **Function:** Ribosomes facilitate the binding of tRNA to mRNA and catalyze the formation of peptide bonds between amino acids.

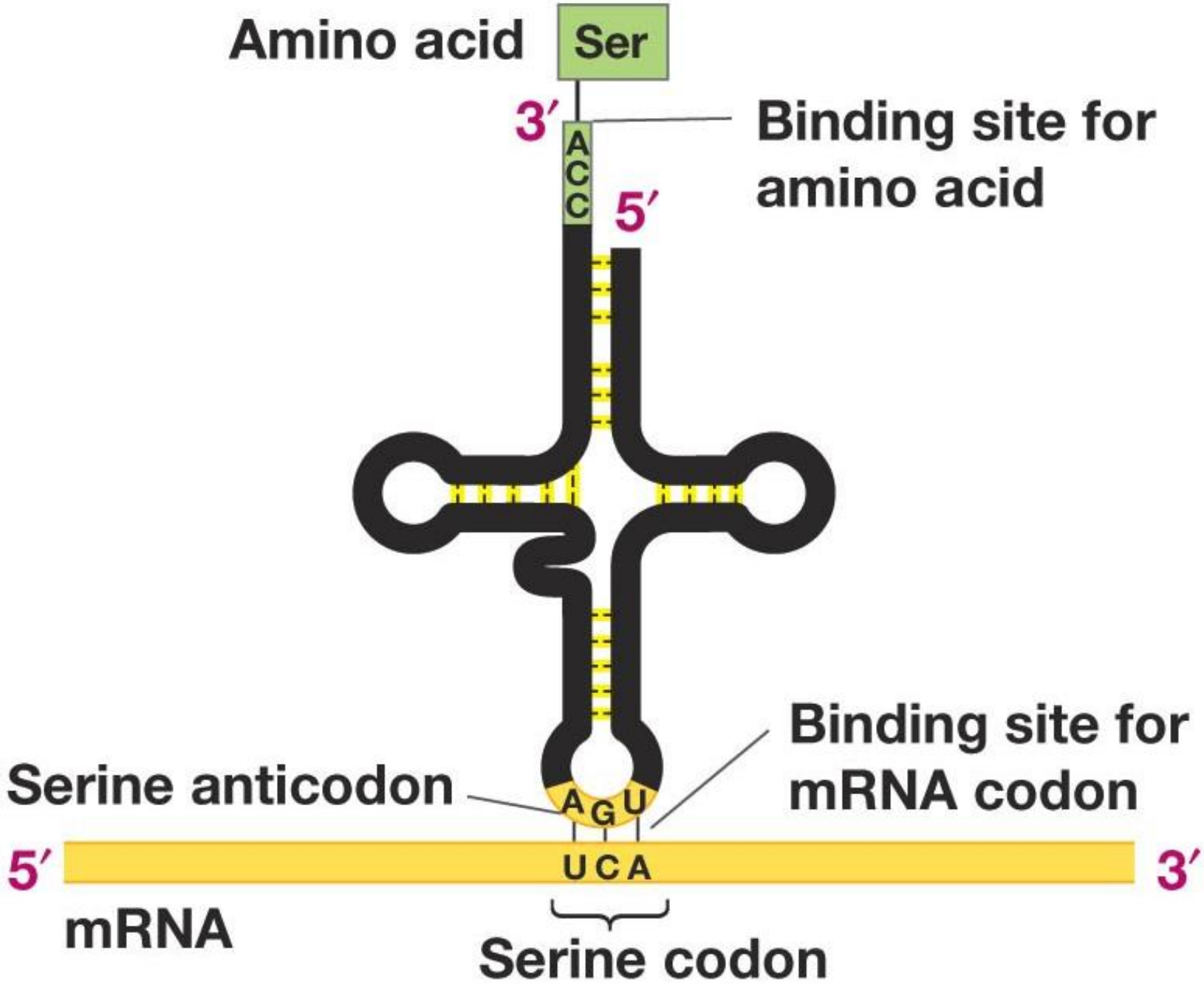
Sites of Ribosomes

- They have three key sites:
- A site (Aminoacyl site): Where incoming tRNA carrying the next amino acid binds.
- P site (Peptidyl site): Holds the tRNA with the growing polypeptide chain.
- E site (Exit site): Where the empty tRNA exits the ribosome after transferring its amino acid.


E-site
P-site
A-site
E
P
A
large ribosomal subunit
small ribosomal subunit
mRNA-binding site

tRNA

- Each tRNA molecule has an anticodon that is complementary to the codon on the mRNA. The anticodon allows tRNA to bring the correct amino acid into the ribosome.
- At the other end of the tRNA molecule is the amino acid attachment site, where the corresponding amino acid is covalently linked.


Amino acid
Ser
3′
A C C
5′
Binding site for amino acid
Binding site for mRNA codon
Serine anticodon
A G U
5′
U C A
3′
mRNA
Serine codon

Amino Acids

- Amino acids are linked together by peptide bonds to form a polypeptide chain.
- There are 20 standard amino acids, each with distinct side chains that determine the protein's structure and function.

Aminoacyl-tRNA Synthetase

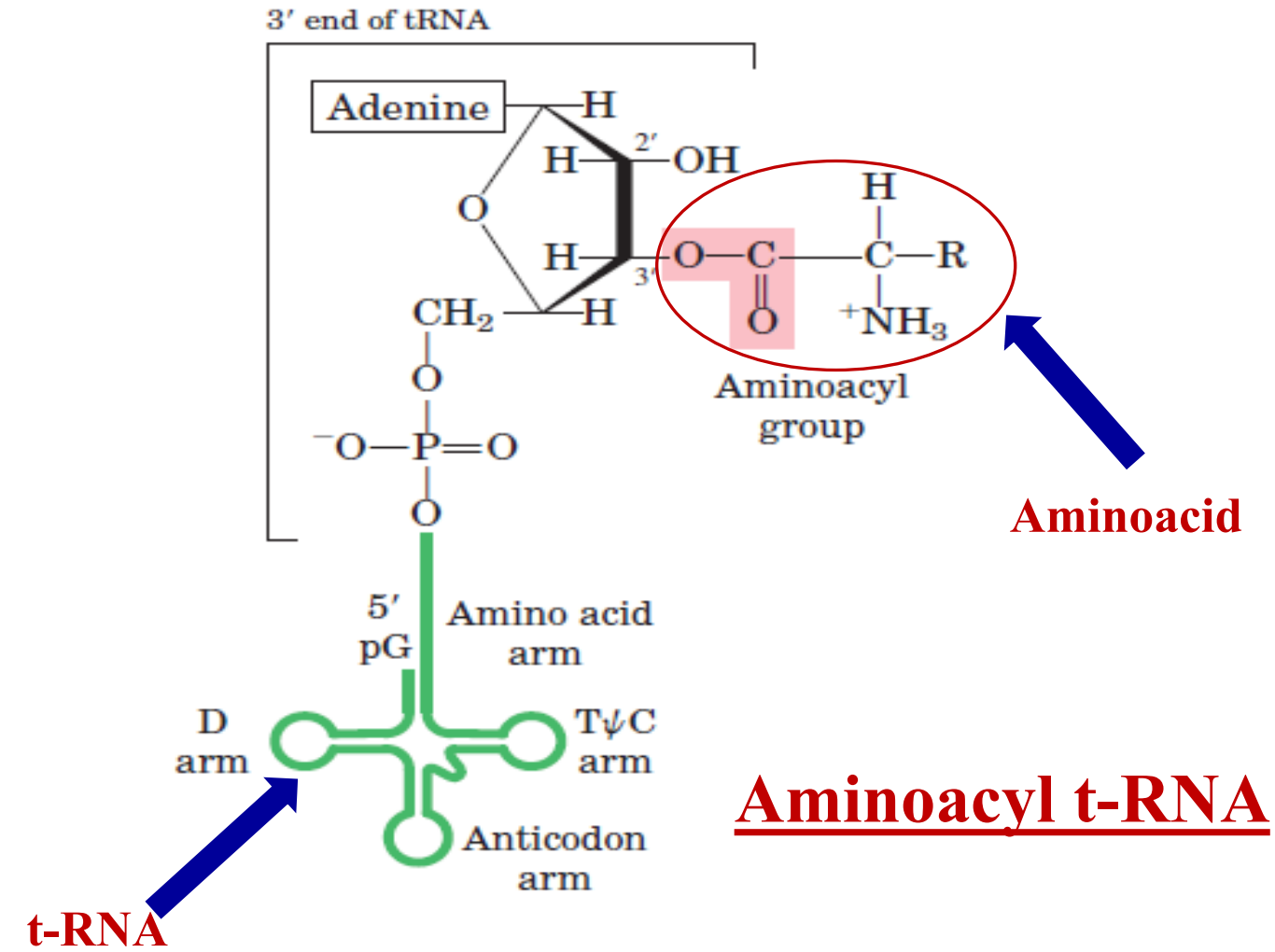
- The enzyme aminoacyl-tRNA synthetase ensures the correct amino acid is attached to the appropriate tRNA, a process known as "charging" the tRNA.

Aminoacyl-tRNA Synthetase

- One synthetase for each amino acid a single synthetase may recognize multiple tRNAs or the same amino acid
- Two classes of synthetases
- **Class I -** monomeric, acylates the 2´-OH on the terminal ribose
- Arg, Cys , Gln, Glu, Ile, Leu, Met, Trp Tyr, Val
- **Class II -** dimeric, acylates the 3´-OH on the terminal ribose
- Ala, Asn, Asp, Gly, His, Lys, Phe, Ser, Pro, Thr

Activation of Amino acid (By Mg2+)

$$\text{Amino acid} + \text{tRNA} + \text{ATP} \xrightleftharpoons{Mg^{2+}} \text{aminoacyl-tRNA} + \text{AMP} + PP_i$$



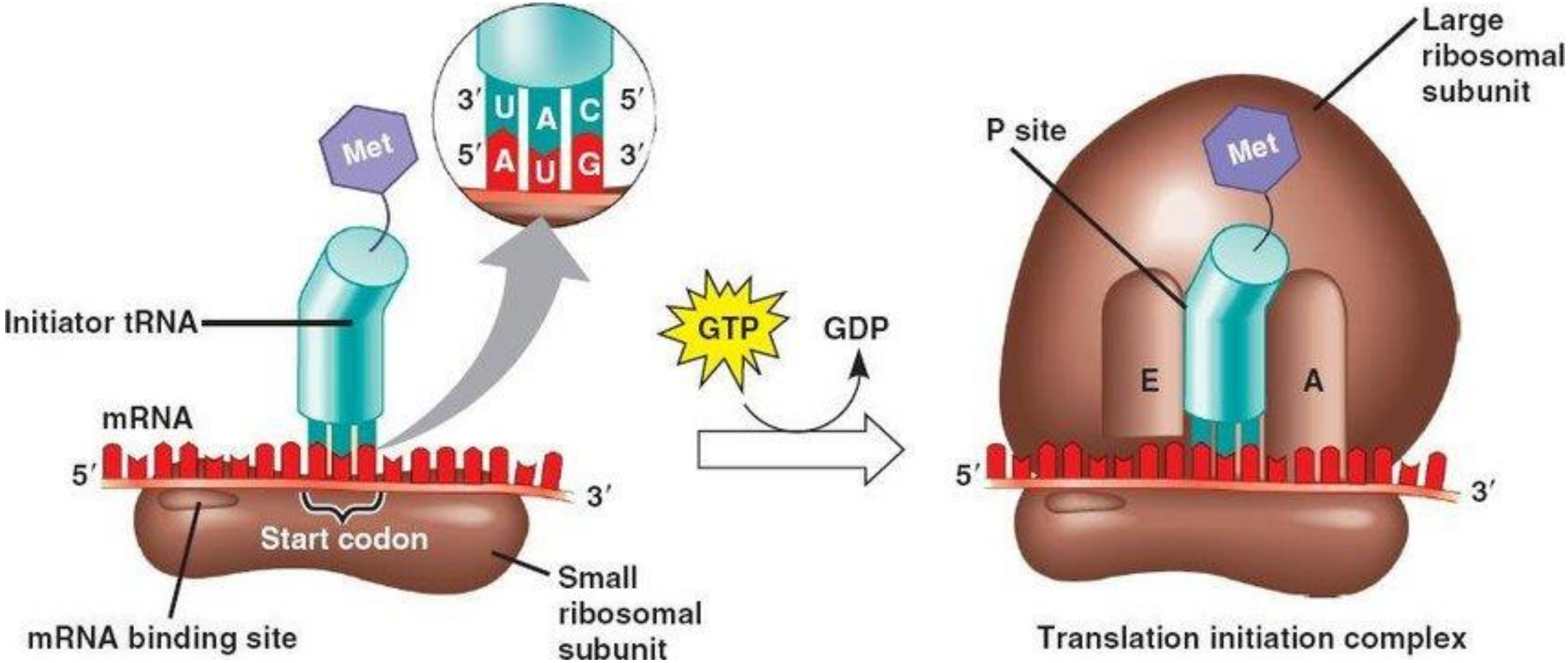
Aminoacyl t-RNA

Stages of Translation

- 1. Initiation
- 2. Elongation
- 3. Termination

Initiation

- Translation begins when the initial portion of an mRNA molecule binds to rRNA molecule in a ribosome.
- The mRNA lies on the ribosome in such a way that only one of its codons is exposed at the polypeptide site at any time.

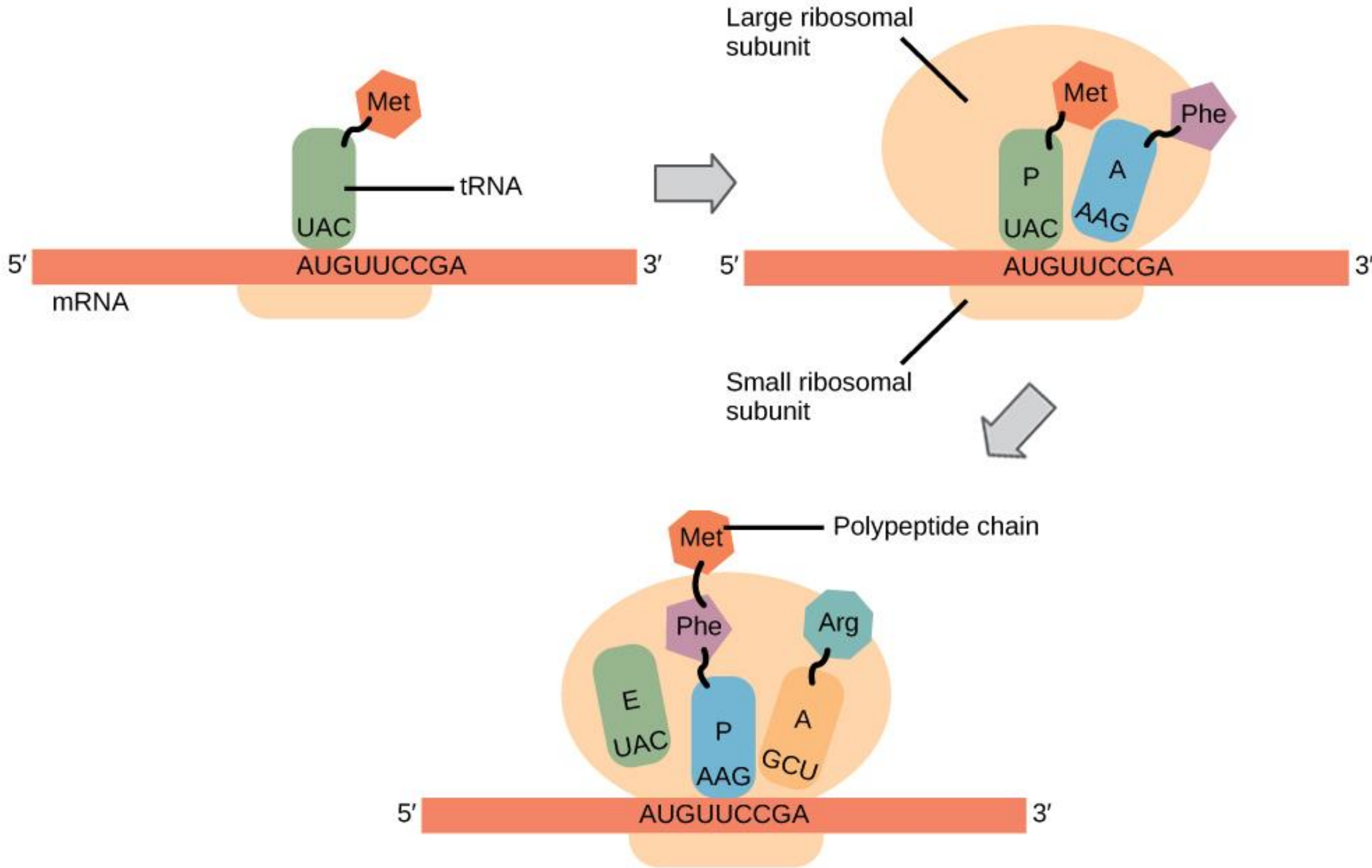

3′ U A C 5′
5′ A U G 3′
Met
Initiator tRNA
mRNA
5′
3′
Start codon
mRNA binding site
Small ribosomal subunit
GTP
GDP
Large ribosomal subunit
P site
Met
E
A
5′
3′
Translation initiation complex

Elongation

- **Codon Recognition:** After initiation, elongation begins when a new tRNA binds to the ribosome's A site. This tRNA has an anticodon that is complementary to the next codon on the mRNA.
- **Elongation Factors (EFs):** These proteins assist in bringing the correct tRNA into the A site and ensure the tRNA is positioned properly. EFs also help move the ribosome along the mRNA.

Elongation

- **Peptide Bond Formation:** The ribosome's peptidyl transferase activity (an enzymatic function of the large ribosomal subunit) catalyzes the formation of a peptide bond between the amino acid on the tRNA in the A site and the growing polypeptide chain in the P site.
- The growing polypeptide chain is now transferred to the tRNA in the A site, leaving the tRNA in the P site empty.


Met
tRNA
UAC
5′
AUGUUCCGA
3′
mRNA
Large ribosomal subunit
Met
Phe
P
A
UAC
AAG
5′
AUGUUCCGA
3′
Small ribosomal subunit
Met
Polypeptide chain
Phe
Arg
E
UAC
P
AAG
A
GCU
5′
AUGUUCCGA
3′

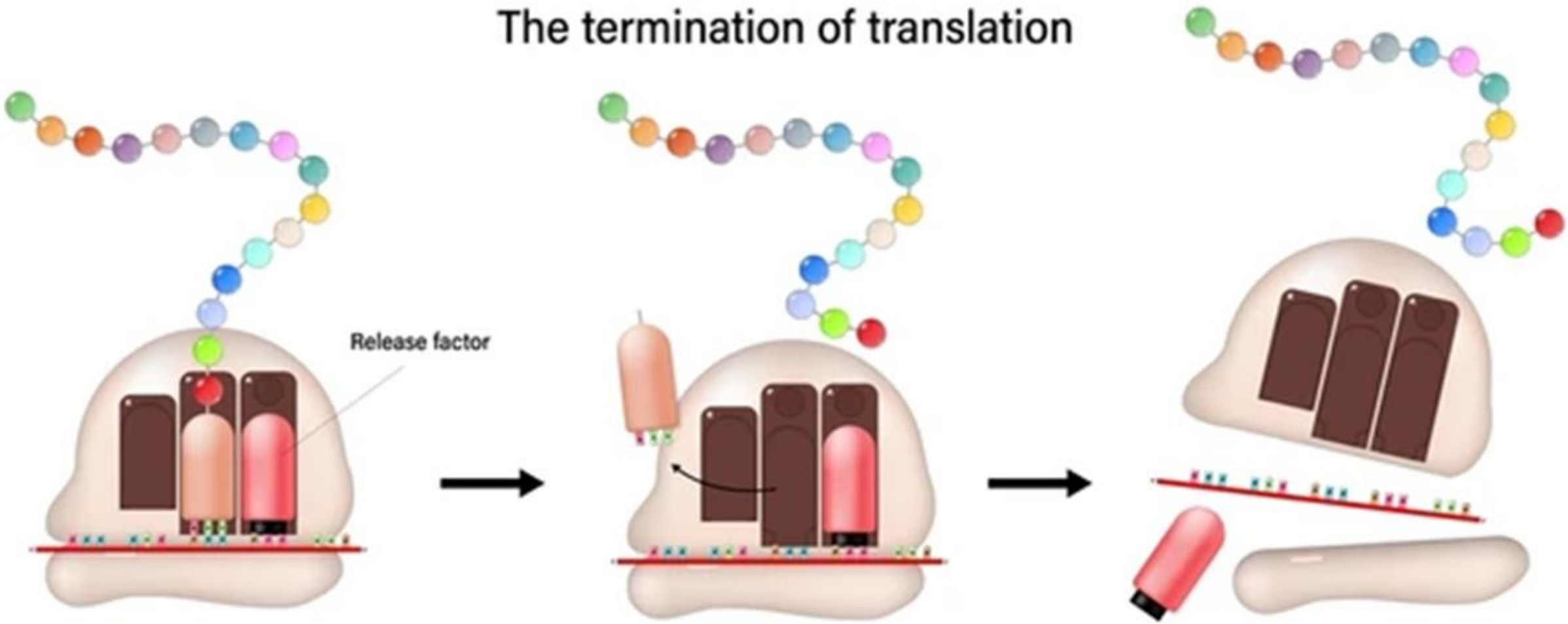
Elongation

- **Translocation:** After the peptide bond is formed, the ribosome moves one codon down the mRNA in a process called translocation. This shifts the tRNA with the growing peptide chain from the A site to the P site, and the now-empty tRNA from the P site moves to the E site before being released. GTP is hydrolyzed to provide energy for this step.
- This process continues as the ribosome moves along the mRNA, reading codons, and adding the corresponding amino acids to the growing chain.

Termination

- **Stop Codon Recognition:** When the ribosome encounters a stop codon (UAA, UAG, or UGA) on the mRNA, no tRNA corresponds to these codons. Instead, release factors (RFs) bind to the ribosome.
- **Release of the Polypeptide Chain:** Release factors promote the hydrolysis of the bond between the tRNA in the P site and the last amino acid of the polypeptide chain. This releases the newly synthesized protein (polypeptide chain).
- **Dissociation of the Ribosome:** After the polypeptide is released, the ribosome disassembles into its large and small subunits, and the mRNA is released. GTP hydrolysis again provides energy for this process.

The termination of translation

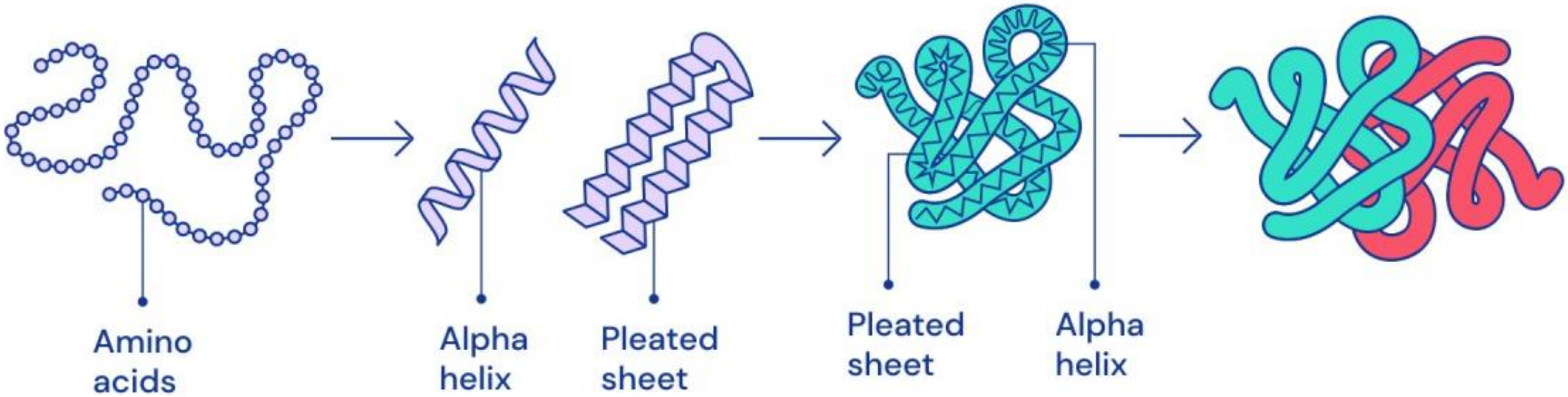


Proofreading

- **Proofreading Mechanisms:**
- Aminoacyl-tRNA synthetases have proofreading abilities to ensure that the correct amino acid is attached to the corresponding tRNA. If the wrong amino acid is attached, the enzyme can hydrolyze the incorrect product and attach the correct one.
- **GTP Hydrolysis:**
- Many steps in translation, especially the binding and translocation of tRNAs, are coupled with GTP hydrolysis. This coupling ensures that errors in codon recognition are minimized because GTP hydrolysis only occurs if the correct tRNA is bound.

Post-Translational Modifications

- Once a protein is synthesized, it often undergoes further modifications that are essential for its proper function. These modifications include:
- **1. Folding:** The protein must fold into its correct 3D shape.
- **2. Chemical Modifications:** Proteins can undergo phosphorylation, methylation, glycosylation, or acetylation, which regulate their function, localization, or interactions with other molecules.
- **3. Transportation:** Proteins may be transported to specific areas in the cell (e.g., the nucleus, mitochondria, or plasma membrane) to carry out their functions.


Amino acids
Alpha helix
Pleated sheet
Pleated sheet
Alpha helix


Thank
You!