Genetic code:

Def. Genetic code is the nucleotide base sequence on DNA (and subsequently on mRNA by transcription) which will be translated into a sequence of amino acids of the protein to be synthesized.
The code is composed of codons
Codon is composed of 3 bases (e.g. ACG or UAG). Each codon is translated into one amino acid.

The 4 nucleotide bases (A,G,C and U) in mRNA are used to produce the three base codons. There are therefore, 64 codons code for the 20 amino acids, and since each codon code for only one amino acids this means that, there are more than one cone for the same amino acid.

How to translate a codon (see table):

This table or dictionary can be used to translate any codon sequence. Each triplet is read from 5′ → 3′ direction so the first base is 5′ base, followed by the middle base then the last base which is 3′ base.

Examples: 5′- A UG- 3′ codes for methionine
5′- UCU- 3′ codes for serine
5′ - CCA- 3′ codes for proline

Termination (stop or nonsense) codons:

Three of the 64 codons; UAA, UAG, UGA do not code for any amino acid. They are termination codes which when one of them appear in mRNA sequence, it indicates finishing of protein synthesis.

Characters of the genetic code:

1- Specificity: the genetic code is specific, that is a specific codon always code for the same amino acid.

2- Universality: the genetic code is universal, that is, the same codon is used in all living organisms, procaryotics and eucaryotics.

3- Degeneracy: the genetic code is degenerate i.e. although each codon corresponds to a single amino acid,one amino acid may have more than one codons. e.g arginine has 6 different codons (give more examples from the table).

First base (5′ end)	Second base: U	Second base: C	Second base: A	Second base: G	Third base (3′ end)
U	UUU Phe	UCU Ser	UAU Tyr	UGU Cys	U
	UUC Phe	UCC Ser	UAC Tyr	UGC Cys	C
	UUA Leu	UCA Ser	UAA Stop	UGA Stop	A
	UUG Leu	UCG Ser	UAG Stop	UGG Trp	G
C	CUU Leu	CCU Pro	CAU His	CGU Arg	U
	CUC Leu	CCC Pro	CAC His	CGC Arg	C
	CUA Leu	CCA Pro	CAA Gln	CGA Arg	A
	CUG Leu	CCG Pro	CAG Gln	CGG Arg	G
A	AUU Ile	ACU Thr	AAU Asn	AGU Ser	U
	AUC Ile	ACC Thr	AAC Asn	AGC Ser	C
	AUA Ile	ACA Thr	AAA Lys	AGA Arg	A
	AUG Met or start	ACG Thr	AAG Lys	AGG Arg	G
G	GUU Val	GCU Ala	GAU Asp	GGU Gly	U
	GUC Val	GCC Ala	GAC Asp	GGC Gly	C
	GUA Val	GCA Ala	GAA Glu	GGA Gly	A
	GUG Val	GCG Ala	GAG Glu	GGG Gly	G

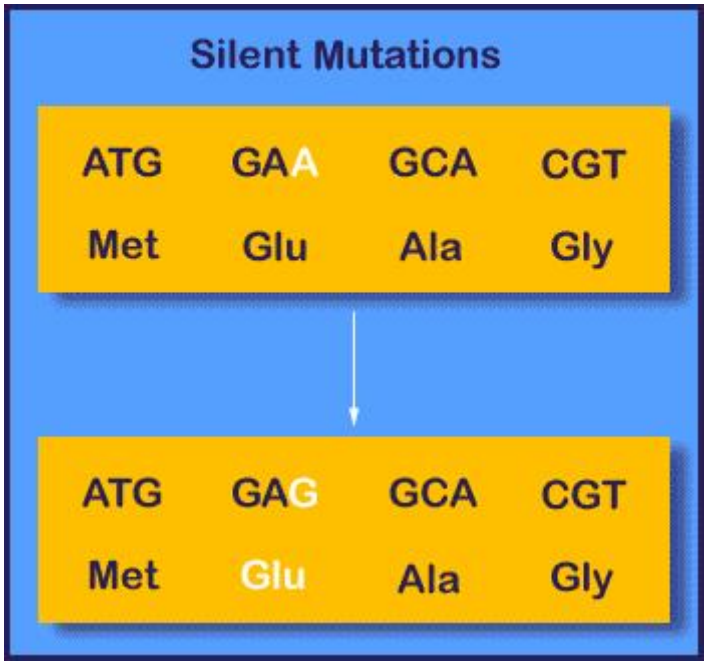
Gene mutation (altering the nucleotide sequence):

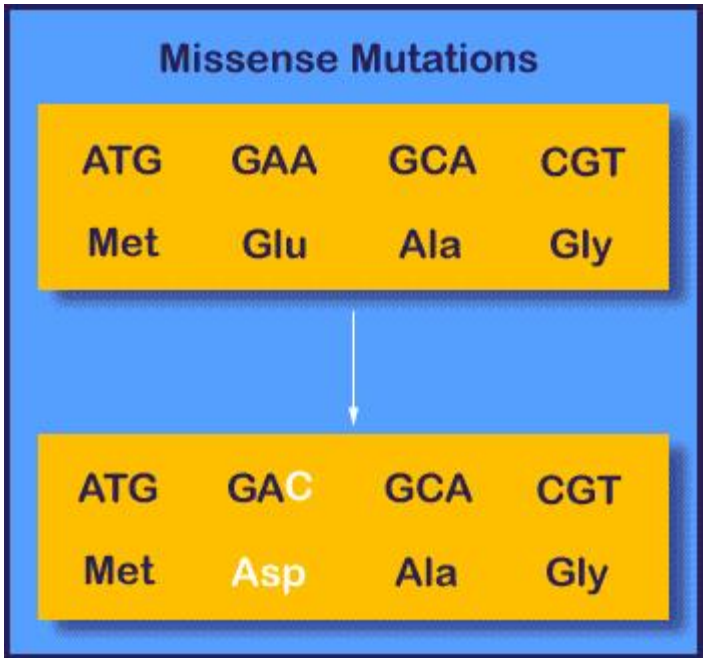
1- Point mutation: changing in a single nucleotide base on the mRNA can lead to any of the following 3 results:

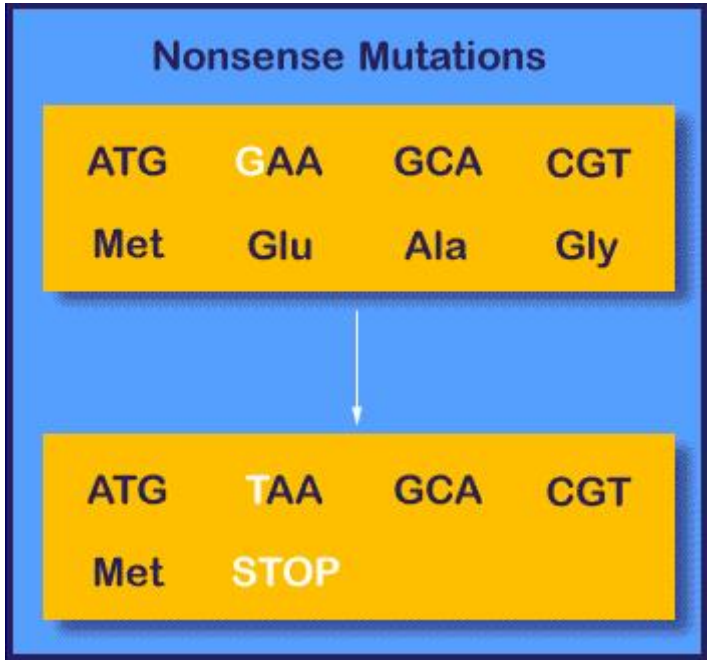
i- Silent mutation: i.e. the codon containg the changed base may code for the same amino acid. For example, in serine codon UCA, if A is changed to U giving the codon UCU, it still code for serine. See table.

ii- Missense mutation: the codon containing the changed base may code for a different amino acid. For example, if the serine codon UCA is changed to be CCA (U is replaced by C), it will code for proline not serine leading to insertion of incorrect amino acid into polypeptide chain.

iii- Non sense mutation: the codon containing the changed base may become a termination codon. For example, serine codon UCA becomes UAA if C is changed to A. UAA is a stop codon leading to termination of translation at that point.


Silent Mutations
ATG GAA GCA CGT
Met Glu Ala Gly
ATG GAG GCA CGT
Met Glu Ala Gly


Missense Mutations
ATG GAA GCA CGT
Met Glu Ala Gly
ATG GAC GCA CGT
Met Asp Ala Gly


Nonsense Mutations
ATG GAA GCA CGT
Met Glu Ala Gly
ATG TAA GCA CGT
Met STOP

Types of point mutation:

U A A (termination codon) — Nonsense mutation

↑

U C A → U C U — Silent mutation

(codon for serine) (codon for serine)

↓

C C A (codon for proline) — Missense mutation:

Give other examples on missense mutation which leads to some Hb disease.

2- Frame- shift mutation:

deletion or addition of one or two base to message sequence, leading to change in reading frame (reading sequence) and the resulting amino acid seuence may become completely different from this point.

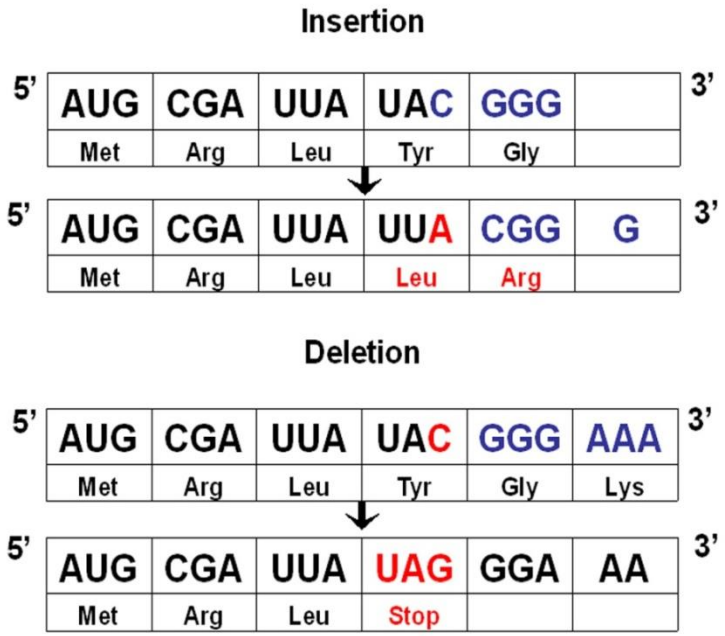
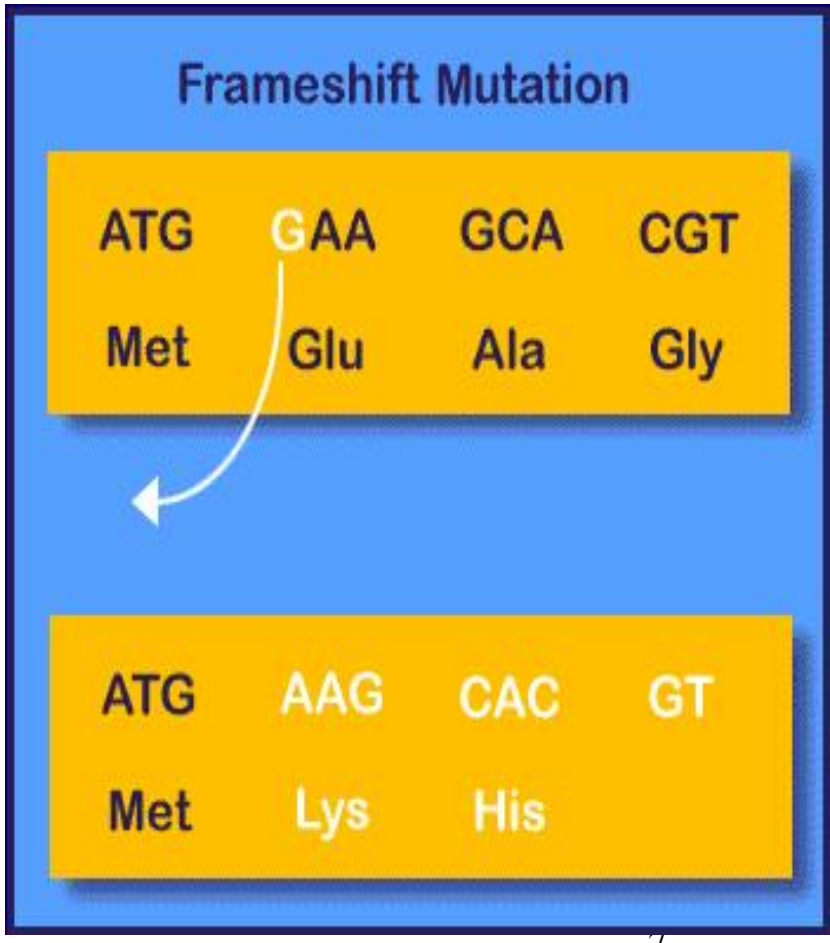


Figure 2. Schematic representation of nucleotide insertion and deletion

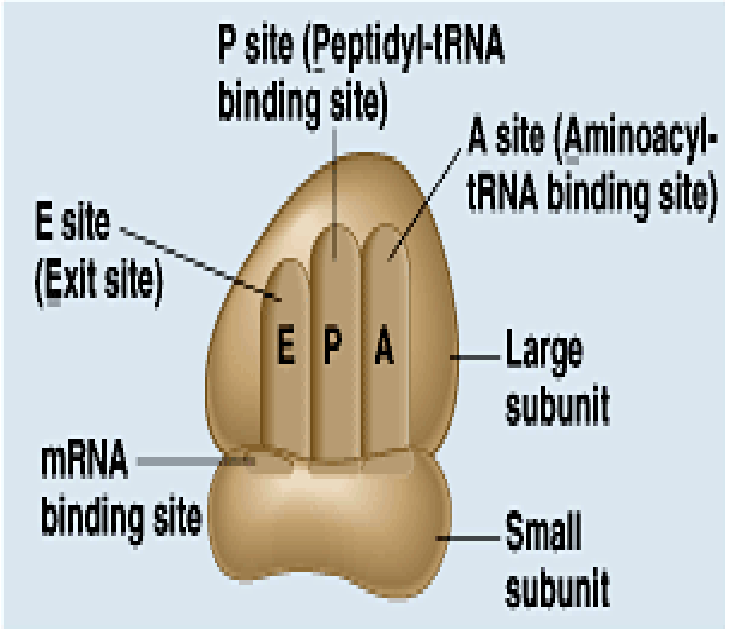


Translation

Components required for protein synthesis:

1- Amino acids: all amino acids involved in the finished protein must be present at the time of protein synthesis.

2- Ribosomes: the site of protein synthesis. They are large complexes of protein and rRNA. In human, they consist of two subunits, one large (60S) and one small (40S).



(b) Schematic model showing binding sites

3- tRNA: at least one specific type of tRNA is required to transfer one amino acid. There about 50 tRNA in human for the 20 amino acids, this means some amino acids have more than one specific tRNA. The role of tRNA in protein synthesis is discussed before. (amino acid attachment and anticodon loop).

4- aminoacyl-tRNA synthetase: This is the enzyme that catalyzes the attachment of amino acid with its corresponding tRNA forming aminoacyl tRNA

5- mRNA: that carry code for the protein to be synthesized

6- protein factors: Initiation, elongation and termination (or release) factors are required for peptide synthesis

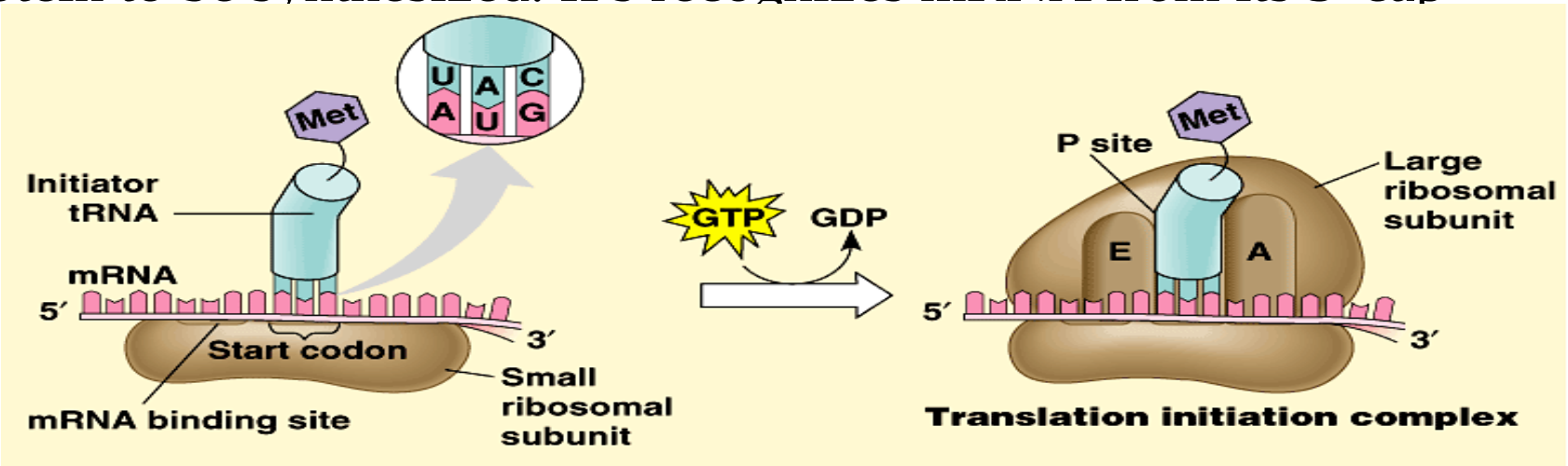
7- ATP and GTP : are required as source of energy.

Steps: **(movie)**

1- Initiation:

Initiation (start) codon is usually AUG which is the codon of methionine, so **the initiator tRNA** is methionnyl tRNA (Met. tRNA).

a- The initiation factors (IF-1, IF-2 and IF-3) binds the Met. tRNA with small ribosomal subunit then to mRNA containing the code of the protein to be synthesized. IFs recognizes mRNA from its 5' cap



b-This complex binds to large ribosomal subunit forming initiation complex in which Met. tRNA is present in P- site of 60 ribosomal subunit.

NB:- tRNA bind with mRNA by base pairing between codon on mRNA and anticodon on tRNA.

- mRNA is read from 5′ → 3′ direction

P-site: is the peptidyl site of the ribosome to which methionyl tRNA is placed (enter).

2- Elongation: elongation factors (EFs) stimulate the stepwise elongation of polypeptide chain as follow:

a- The next aminoacyl tRNA (tRNA which carry the next amino acid specified by recognition of the next codon on mRNA) will enter A site of ribosome

A site or acceptor site or aminoacyl tRNA site:

Is the site of ribosome to which each new incoming aminoacyl$_{10}$tRNA will enter.

b) **ribosomal peptidyl transferase** enzyme will transfer methionine from methionyl tRNA into A site to form a peptide bond between methionine and the new incoming amino acid to form dipeptidyl tRNA.

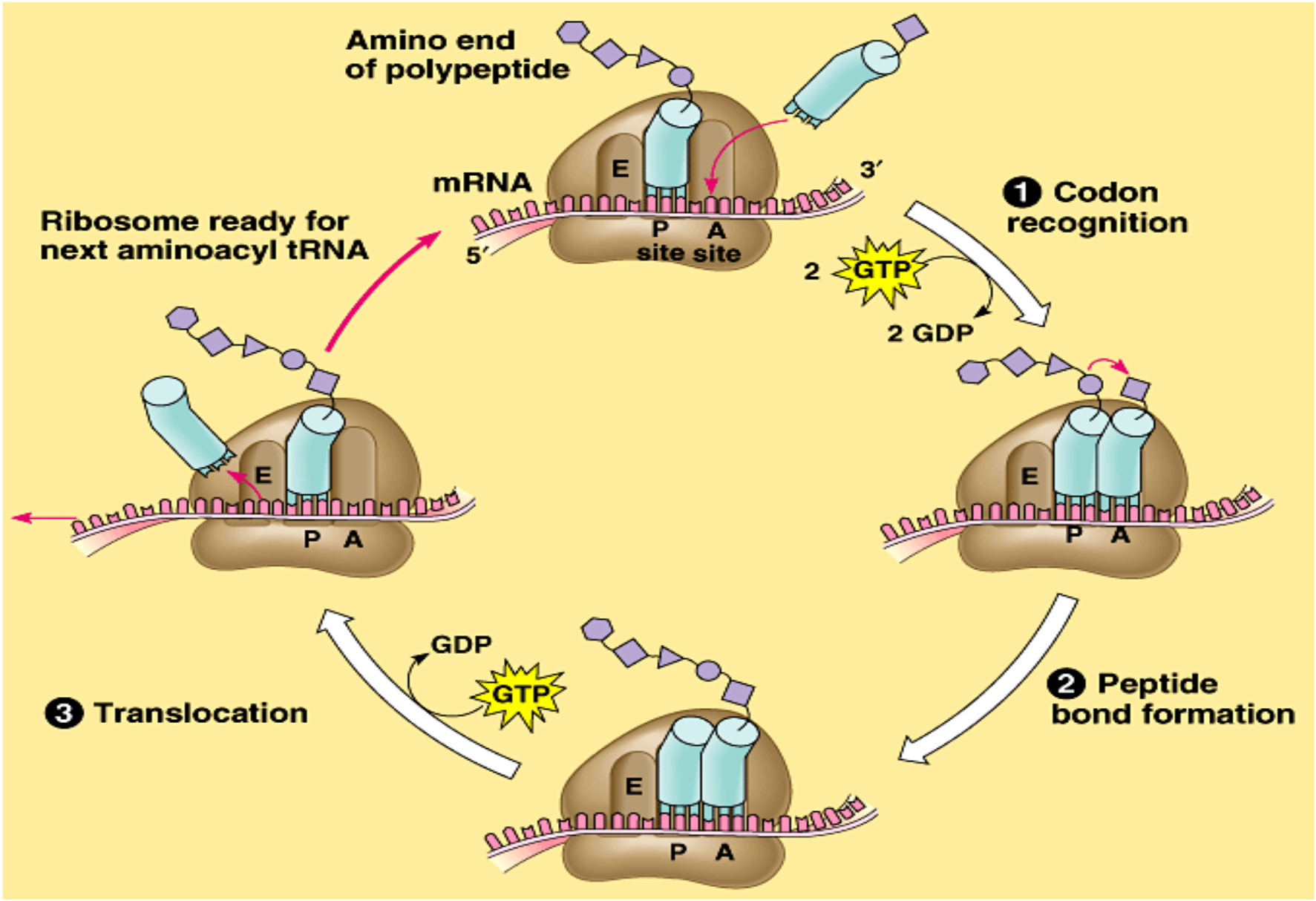
c) Elongation factor-2 (EF-2), (called also, translocase): moves mRNA and dipeptidyl tRNA from A site to P site leaving A site free to allow entrance of another new aminoacyl tRNA.

The figure shows the repetitive cycle of elongation of chain. Each cycle is consisting of

1) codon recognition and the entrance of the new aminoacyl tRNA acid (amino acid carried on tRNA) into A site,

2) The growing chain in P site will moved to A site with peptide bond formation with the new amino acid

3) Translocation of growing chain to P site allowing A site free for enterance of new amino acid an so on…….. Resulting in elongation of poly peptide chain.



repetitive cycle of elongation

3- Termination: occurs when one of the three stop codons (UAA, UAG or UGA) enters A site of the ribosome. These codons are recognized by release factors (RFs) which are RF-1, RF-2, RF-3. RFs cause the newly synthesized protein to be released from the ribosomal complex and dissociation of ribosomes from mRNA (i.e. cause dissolution of the complex)