The module: Molecules, Genes and Diseases (MGD)

Session 5

Lecture 10

Duration: 1 hour

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Lecture Title: The genetic code and translation

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- **Relevant reading can be found in, for instance:**
- ***Human Heredity*** **Chapter 9**
- ***Marks' Basic Medical Biochemistry*** **Chapters 14, 15**
- ***Medical Biochemistry*** **Chapters 32, 33**
- ***Lippincott's Illustrated Reviews: Cell and Molecular Biology*** **Chapters 8, 9, 10**

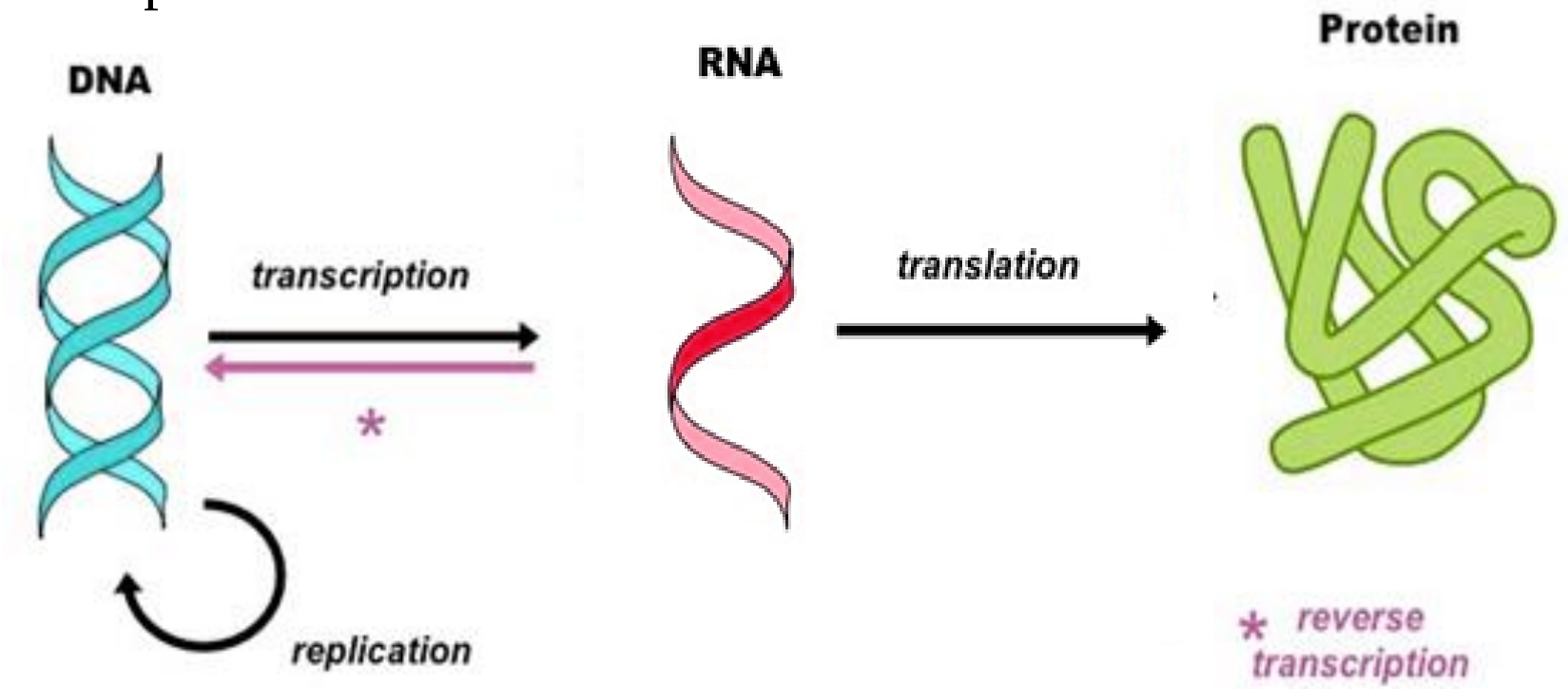
The Learning Outcomes

- Describe the process and role of translation. (LO 5.5)
- Explain the nature of the triplet code and be able to apply the genetic code. (LO 5.6)
- Comprehend the implications of the degeneracy of the genetic code. (LO 5.7)
- Compare and contrast gene expression in mammalian and bacterial cells and explain how the differences can be exploited clinically. (LO 5.8)
- Predict the effects of various mutations in a gene. (LO 5.9)
- Explain how mutations outside the coding region can affect gene expression. (LO 5.10)

The Central Dogma of Molecular biology

(LO.1)

In most organism DNA is the storage of genetic information with exception of RNA viruses.



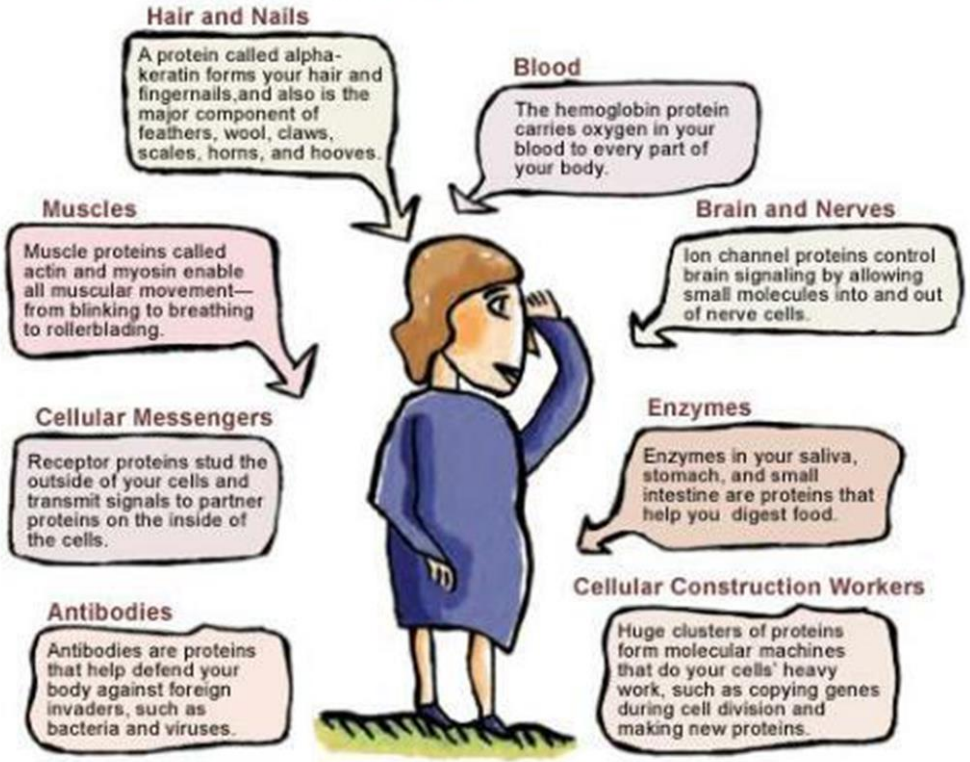
The Central Dogma: is the flow of information from DNA to RNA to Protein

Genotype —(Protein / Link)→ **Phenotype**

Protein Synthesis (Gene Expression) Notes

Proteins (Review)

- Proteins make up all **living** materials



The Process and Role of Translation (LO. 5)

- ✓ Genetic information, stored in chromosome and transmitted to daughter cells through replication is expressed through transcription to RNA, and through translation of mRNA a protein is formed.
- ✓ Any change in nucleic acid sequence may result in an improper amino acid (a.a.) insertion so causing disease or even death.
- ✓ DNA itself is not directly used in protein synthesis. Instead the genetic information is passed down to RNA molecules that play a direct role in protein synthesis
- ➢ Post-translational modification is important to achieve the functional form of the protein

The Process and Role of Translation

(LO. 5)

- ✓ Translation is conversion of information encoded in the nucleotide sequence of an mRNA molecule into the linear sequence of amino acids in a protein that occur at cytoplasm.
- ✓ **Components required for translation**
  - ❖ mRNA, the template for protein synthesis
  - ❖ Amino Acids
  - ❖ Charged tRNAs
  - ❖ Ribosomes
  - ❖ Amino acyl tRNA synthetases
  - ❖ Large number of proteins (factors)

The Process and Role of Translation

There are three phases in the translation process:

I- Initiation

II- Elongation

III- Termination

The mRNA is translated from its 5'-end to its 3'end, producing protein synthesized from its amino terminal end to its C-terminal end.

I- Initiation (LO. 5)

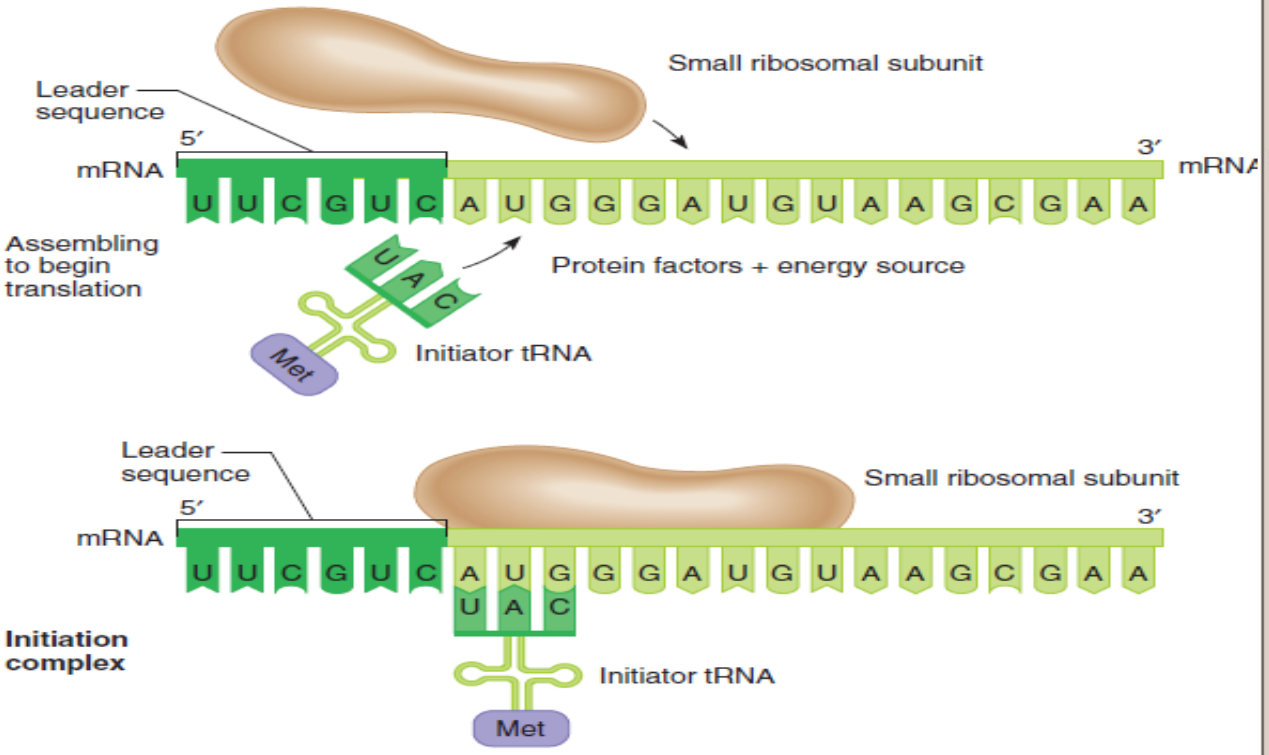
Initiation factors are required:

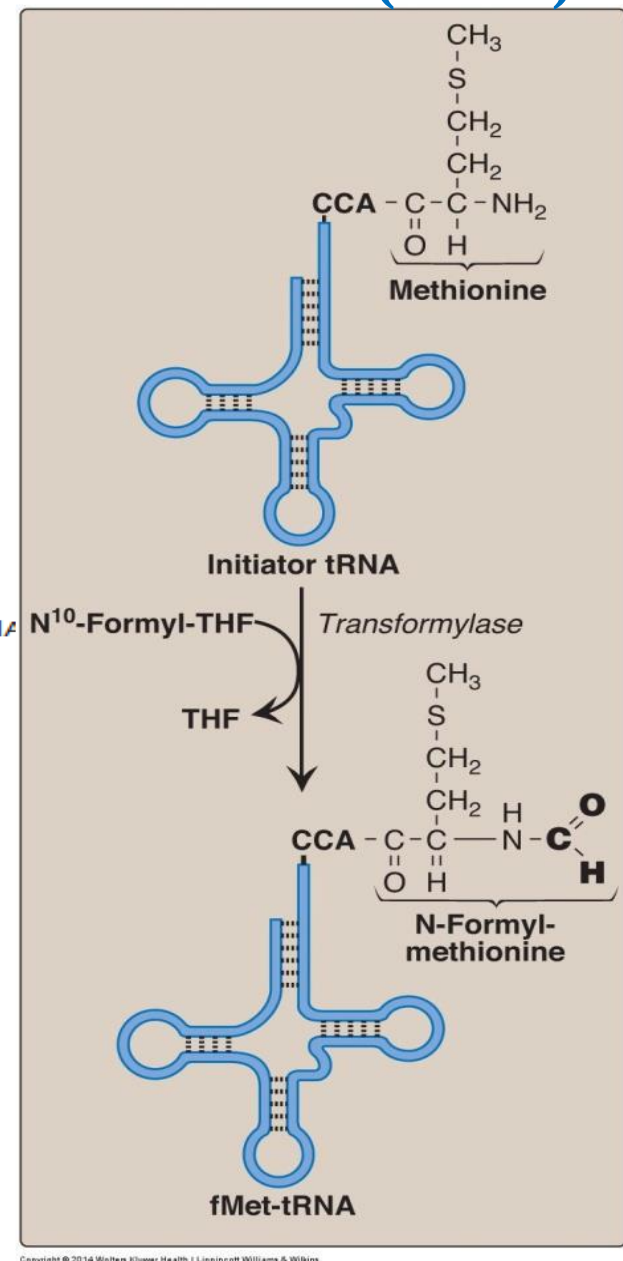
- In Eukaryotes: at least ten initiation factors are required (eIF).
- The small subunit of ribosomes (40 S) with the initiator tRNA (Met-tRNA Met) and other factors binds to cap structure at 5'end of mRNA forming complex,
- This complex migrates down the mRNA until it reach the initiator codon **AUG**. This scan requires energy.
- **AUG** codon recognition and binding, and formation of a functional ribosome.
- Then, the **UAC anticodon** sequence of the initiator Met-tRNAMet base pairs with the AUG sequence of the mRNA, the migration stops, and the **larger ribosomal subunit** joins the complex.

(LO. 5)

Initiation

STEPS IN TRANSLATION (PROTEIN SYNTHESIS)





(LO. 5)

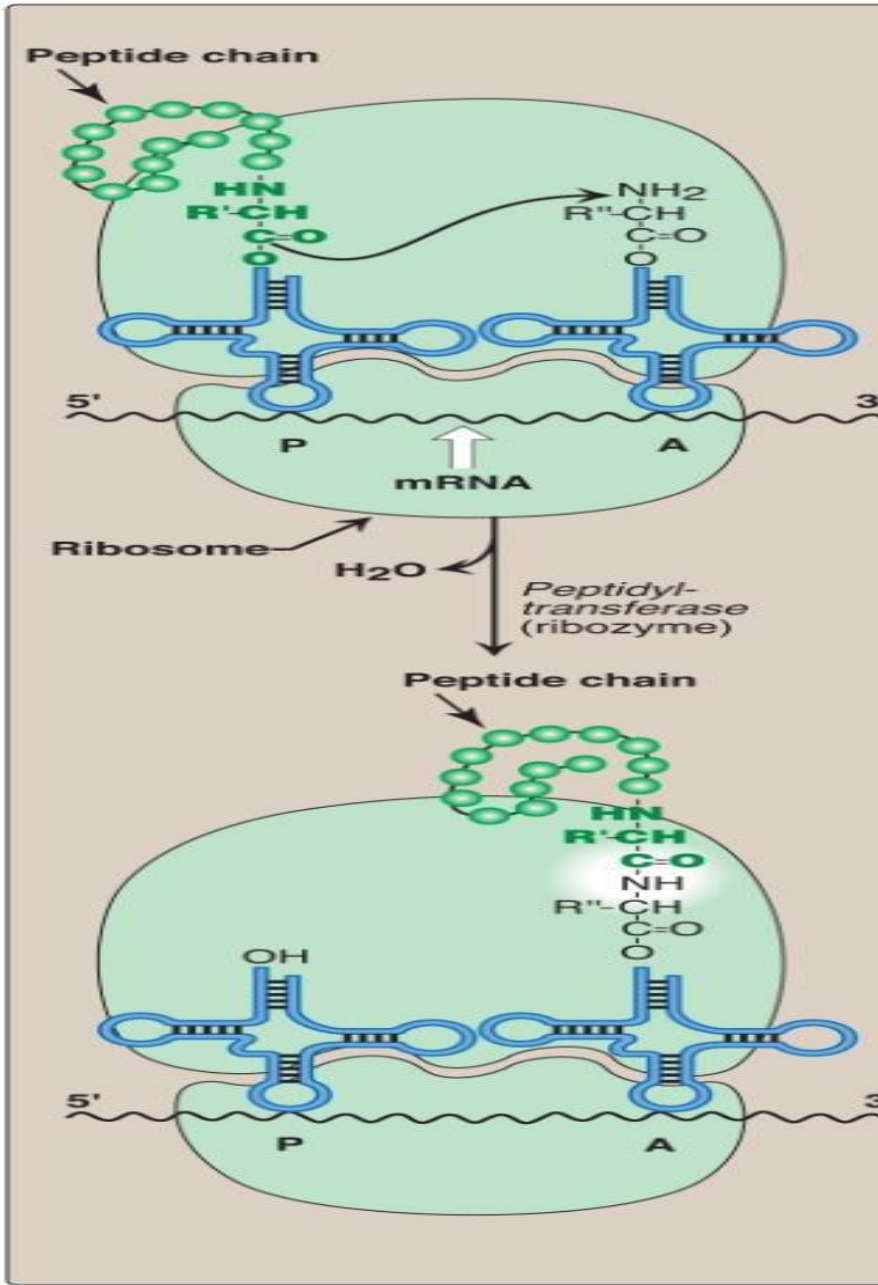
II- Elongation

The actual process of 'translating' the RNA message into protein.

- ✓ The tRNA charged by second a.a. enter in **A-**site. Then the first a.a. is linked to it by its COOH group to form peptide bond. This is helped by elongation eEF.

- ✓ After this translocation take place by movement of ribosome so peptidyl-tRNA is now in **P-**site and uncharged tRNA is in **E**-site from where it leaves the ribosome. This process is repeated.

Elongation


Peptide chain
HN
R'-CH
C=O
O
NH2
R''-CH
C=O
O
5'
3
P
A
mRNA
Ribosome
H2O
Peptidyl-transferase (ribozyme)
Peptide chain
HN
R'-CH
C=O
NH
R''-CH
C=O
O
OH
5'
3
P
A

III- Termination

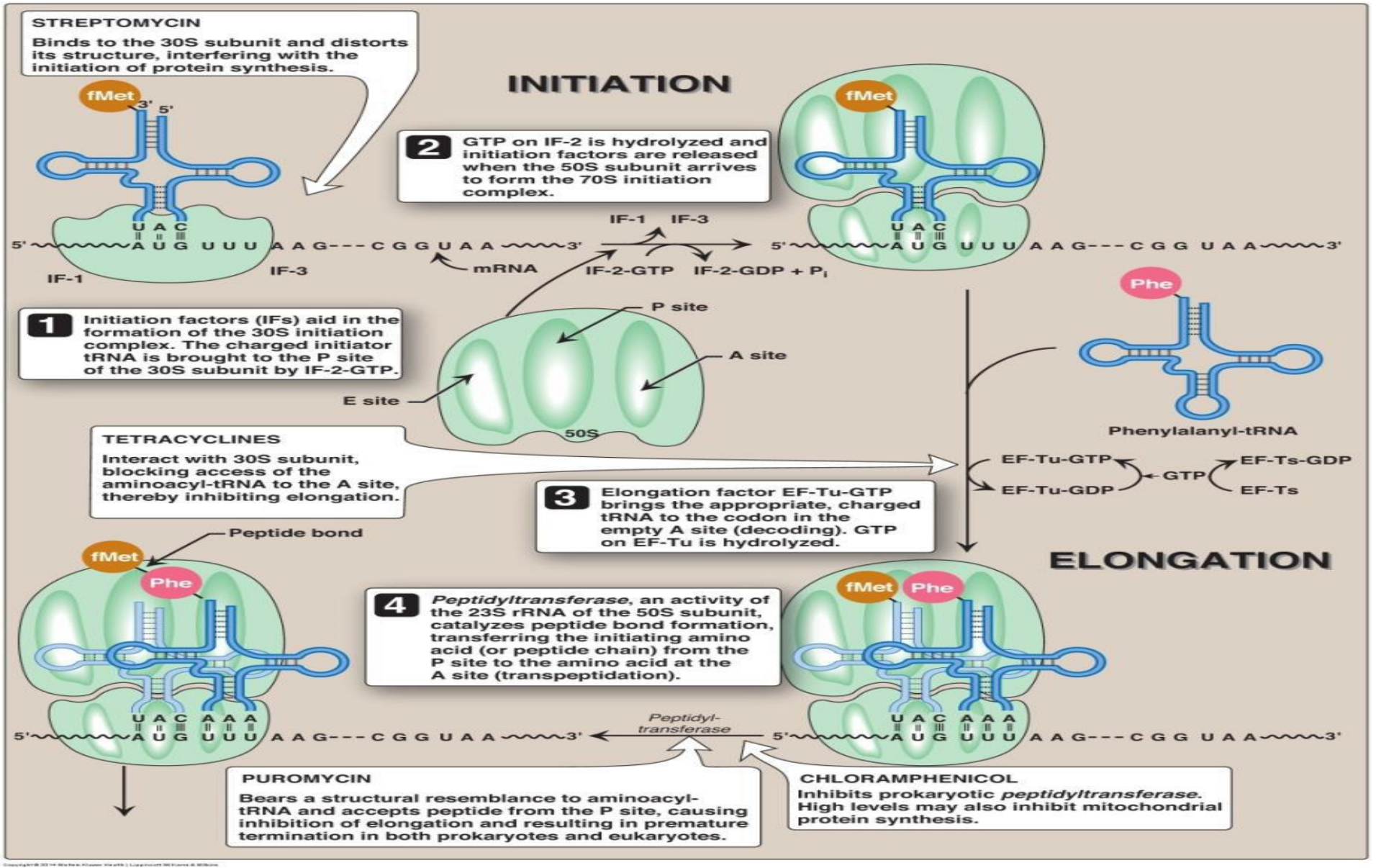
(LO. 5)

- It occur when one of the termination codon appear in **A** site.
- There are no naturally occurring tRNAs with anticodons that are complementary to UAA, UAG, or UGA (stop codons, termination codons).
- The termination process required releasing factors,

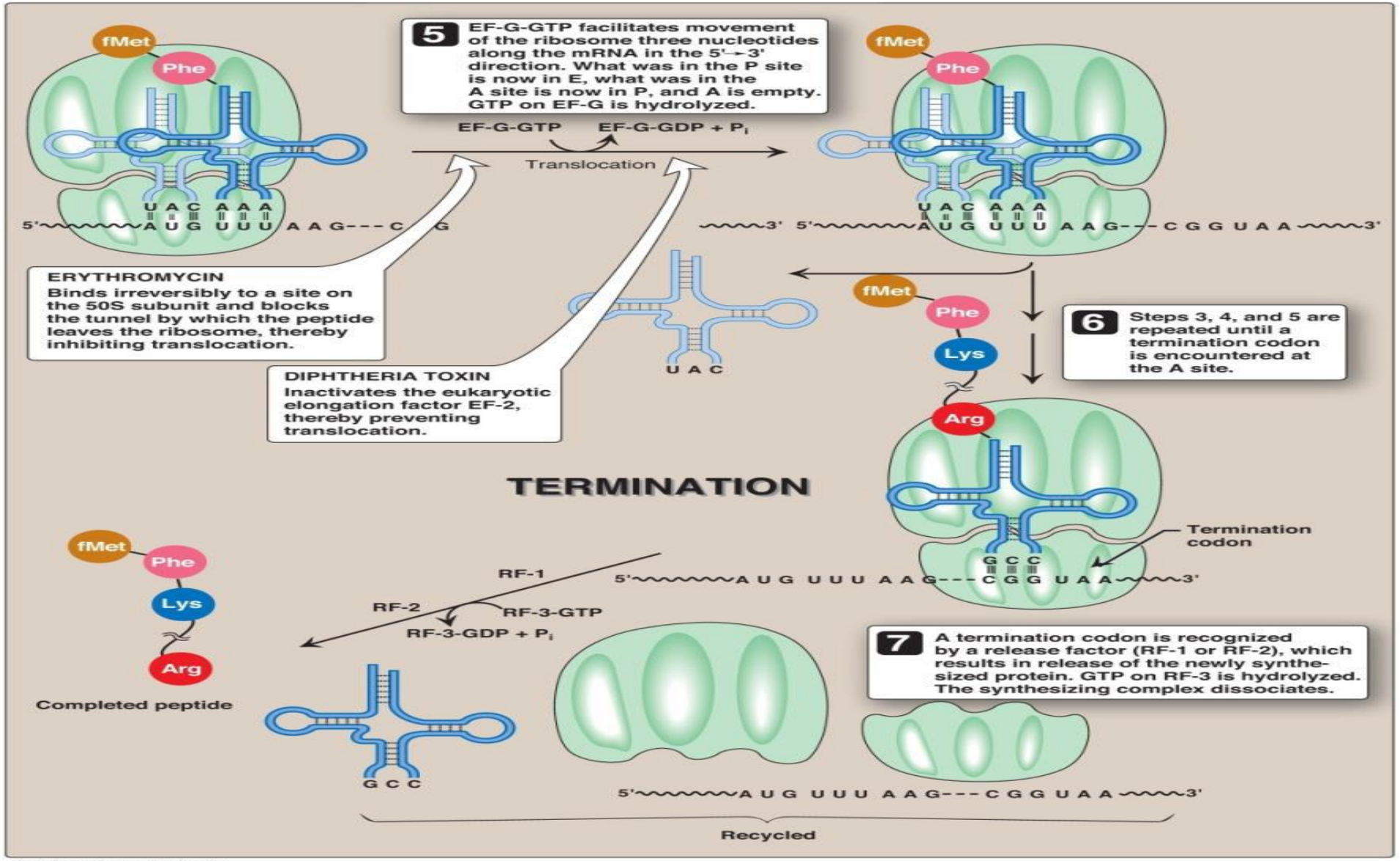
  - eRF & GTP → **in eukaryotes**

- These factors cause the newly synthesizes protein to be released from ribosomal complex.

STEPS IN PROTEIN SYNTHESIS



STEPS IN PROTEIN SYNTHESIS



THE **GENETIC** CODE (LO. 6)

- *The Genetic Code:* the sequence of nucleotides in deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) that determines the amino acid sequence of proteins.

- *Codon*: Sequence of three nucleotides in DNA or mRNA that specifies a particular amino acid during protein synthesis; also called *triplet or* 3-letter "words"

- (amino acid is the building blocks of proteins).

  - ✓ There are 64 codons (4^3)
  - ✓ 61 codon: for different a.a.
  - ✓ Three codon: for stop (UAG, UAA, UGA)
  - ✓ Strat codon : AUG for methionine

(LO. 6)

THE GENETIC CODE

First letter	Second letter: U	Second letter: C	Second letter: A	Second letter: G	Third letter
U	UUU Phe (F)	UCU Ser (S)	UAU Tyr (Y)	UGU Cys (C)	U
	UUC Phe (F)	UCC Ser (S)	UAC Tyr (Y)	UGC Cys (C)	C
	UUA Leu (L)	UCA Ser (S)	UAA Stop	UGA Stop	A
	UUG Leu (L)	UCG Ser (S)	UAG Stop	UGG Trp (W)	G
C	CUU Leu (L)	CCU Pro (P)	CAU His (H)	CGU Arg (R)	U
	CUC Leu (L)	CCC Pro (P)	CAC His (H)	CGC Arg (R)	C
	CUA Leu (L)	CCA Pro (P)	CAA Gln (Q)	CGA Arg (R)	A
	CUG Leu (L)	CCG Pro (P)	CAG Gln (Q)	CGG Arg (R)	G
A	AUU Ile (I)	ACU Thr (T)	AAU Asn (N)	AGU Ser (S)	U
	AUC Ile (I)	ACC Thr (T)	AAC Asn (N)	AGC Ser (S)	C
	AUA Ile (I)	ACA Thr (T)	AAA Lys (K)	AGA Arg (R)	A
	AUG Met (M)	ACG Thr (T)	AAG Lys (K)	AGG Arg (R)	G
G	GUU Val (V)	GCU Ala (A)	GAU Asp (D)	GGU Gly (G)	U
	GUC Val (V)	GCC Ala (A)	GAC Asp (D)	GGC Gly (G)	C
	GUA Val (V)	GCA Ala (A)	GAA Glu (E)	GGA Gly (G)	A
	GUG Val (V)	GCG Ala (A)	GAG Glu (E)	GGG Gly (G)	G

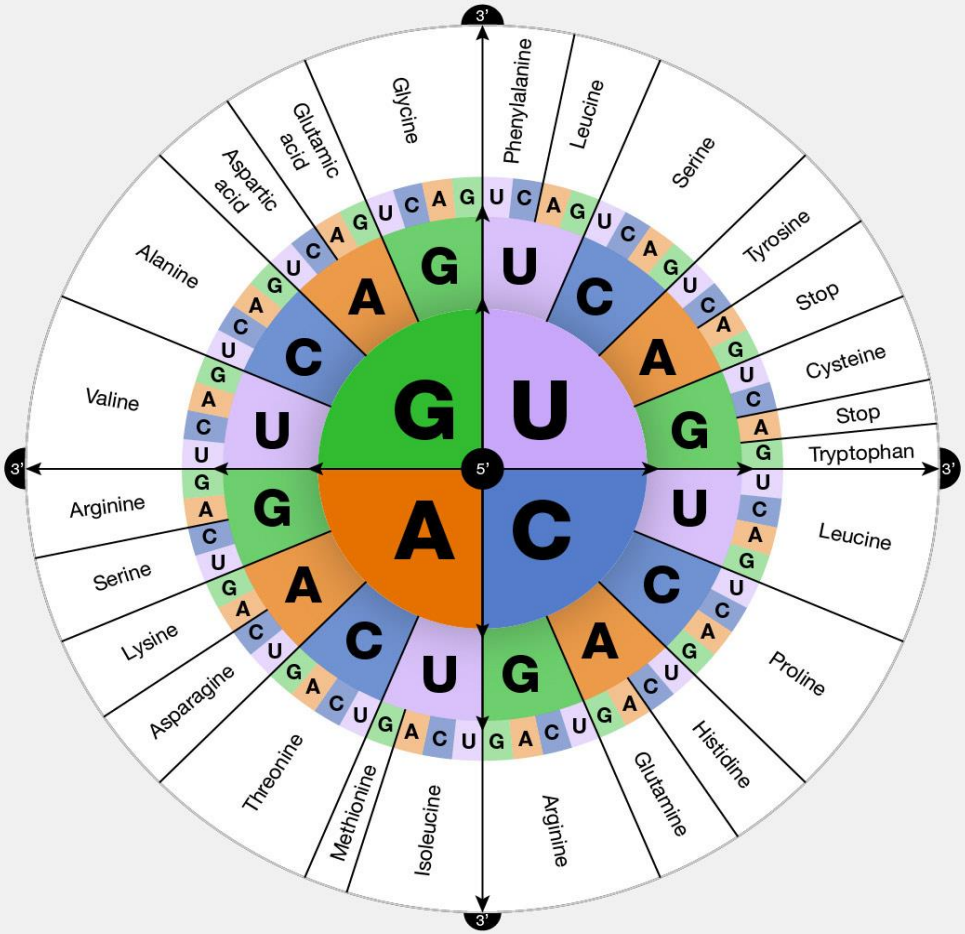
= Chain termination codon (stop)

= Initiation codon

Stop codons do not specify amino acids.

(LO. 6)

THE **GENETIC** CODE



Characteristic of The Genetic Code

(LO. 6)

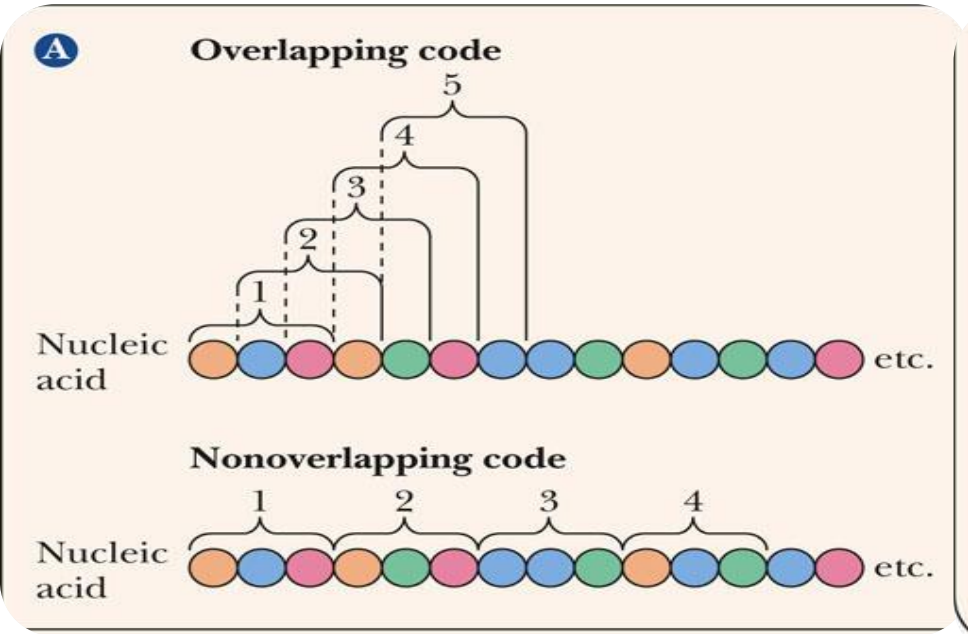
- ✓ *Specificity*: The genetic code is specific, that is, a particular codon always codes for the same amino acid.
- ✓ *Universality*: The genetic code is virtually universal, that is, the specificity of the genetic code has been conserved from very early stages of evolution, with only **slight** differences in the manner in which that code is translated.

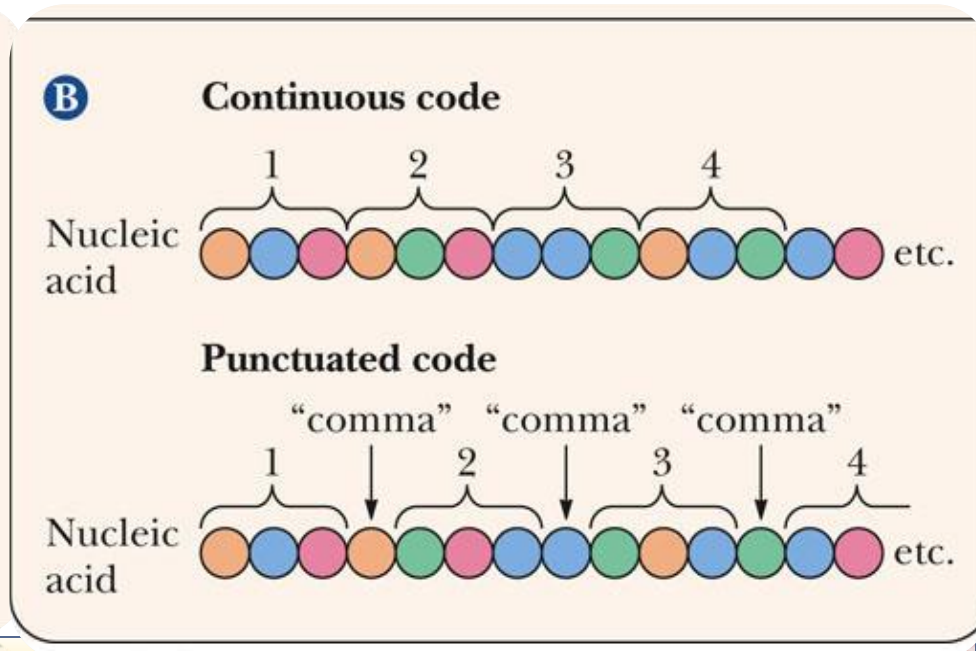
Note

Because of the universal codes, it is possible to express cloned copies of genes encoding useful protein in different host organism. Example, human insulin expression in bacteria)

Characteristic of the genetic code – conti. (LO. 6)

- ✓ *Non-overlapping:* It is read from fixed starting point every three base together.
- ✓ *Commaless:* It is read in continous manner without punctuation.

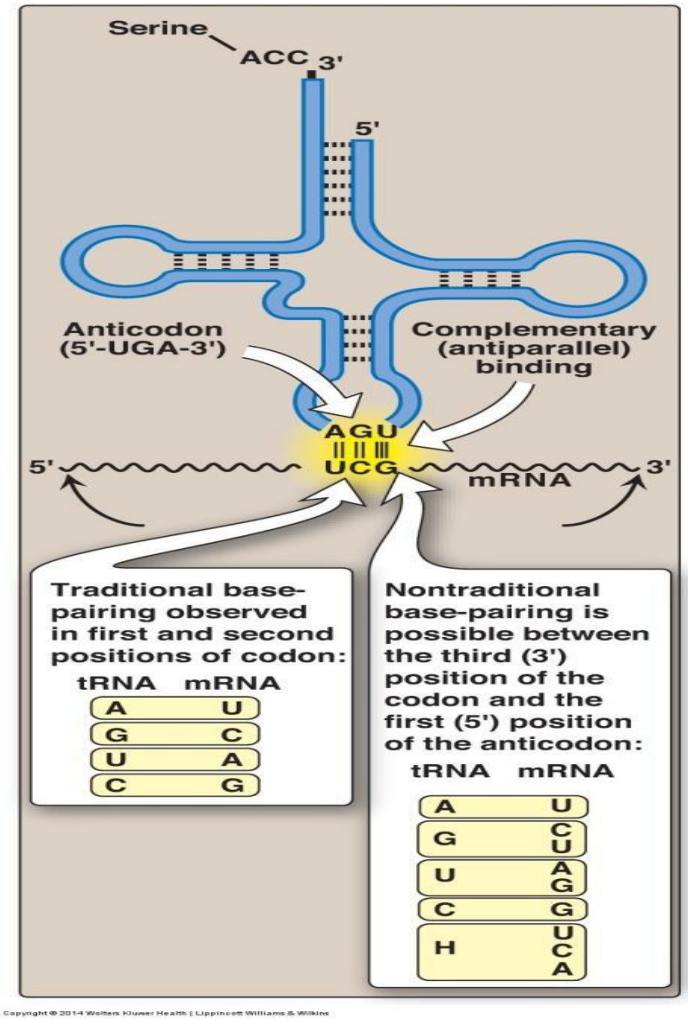




Characteristic of the genetic code – conti. (LO. 6)

✓ *Degeneracy:* more than one triplet can code for the same amino acid, for example

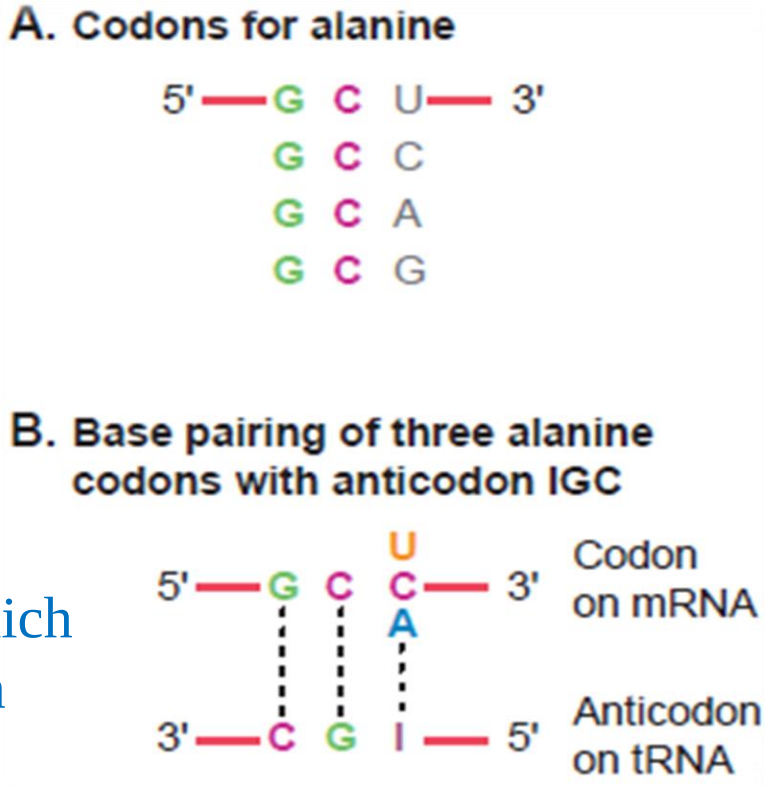
- Leu, Ser, and Arg are each coded for by six triplet
- AGA (Arg) and AGG (Arg) fit with UCU anticodon also UCG (Ser) and UCA (Ser) fit with AGU anticodon.



(LO. 7)

The Implications of The Degeneracy of The Genetic Code

- ✓ In most instances of multiple codons for a single amino acid, the variation occurs in the third base of the codon.
- ✓ the pairing between the 3' base of the codon and the 5' base of the anticodon does not always follow the strict base-pairing rules of Watson-Crick, i.e., A pairs with U, and G pairs with C. This observation called "Wobble hypothesis".



Wobble hypothesis It is the mechanism by which one tRNA can recognize more than one codon for a specific amino acid

- ✓ Because of wobble between the codon and anticodon, fewer than 61 tRNAs are required to translate the genetic code.

(LO. 8)

	Eukaryotic	Prokaryotic
Gene regions	• Always monocistronic. That is, mRNA is transcribed from a single gene and codes for only a single protein. • Genes have exons and intrans. • Large spacer (noncoding) DNA between Genes.	• May be polycistronic. The mRNA in this case contains information from several genes and codes for several different proteins • Genes are continuous coding regions. • Very little spacer (noncoding) DNA between genes.
RNA polymerase	• Three types of RNA polymerase	• has single type of RNA polymerase
Initiation of transcription	• Large set of Promoter including TATA box	•Three promoter elements including TATAAT

	Eukaryotic	Prokaryotic
Posttranscriptional processing of (pre-mRNA)	In nucleus: • Removal of introns from pre-mRNA	None
Ribosomes	• 80S (40S and 60S) • rRNA and protein	• 70S (30S and 50S)
Site of gene expression	Transcription occurs in nucleus while translation occurs in cytoplasm.	Transcription and translation are coupled in cytoplasm.

(LO. 8)

(LO. 9)

Mutations

I. Point Mutation

II. Frame shift Mutation

III. Trinucleotides Repeat

(LO. 9)

1. Point Mutation

1. Missense mutation: An alternation that changes a codon specific for one amino acid to a codon specific for another amino acid.

Effect on protein: Possible decrease in function; variable effects.

2. Nonsense or stop mutation: An alternation causing a change to a chain-termination codon.

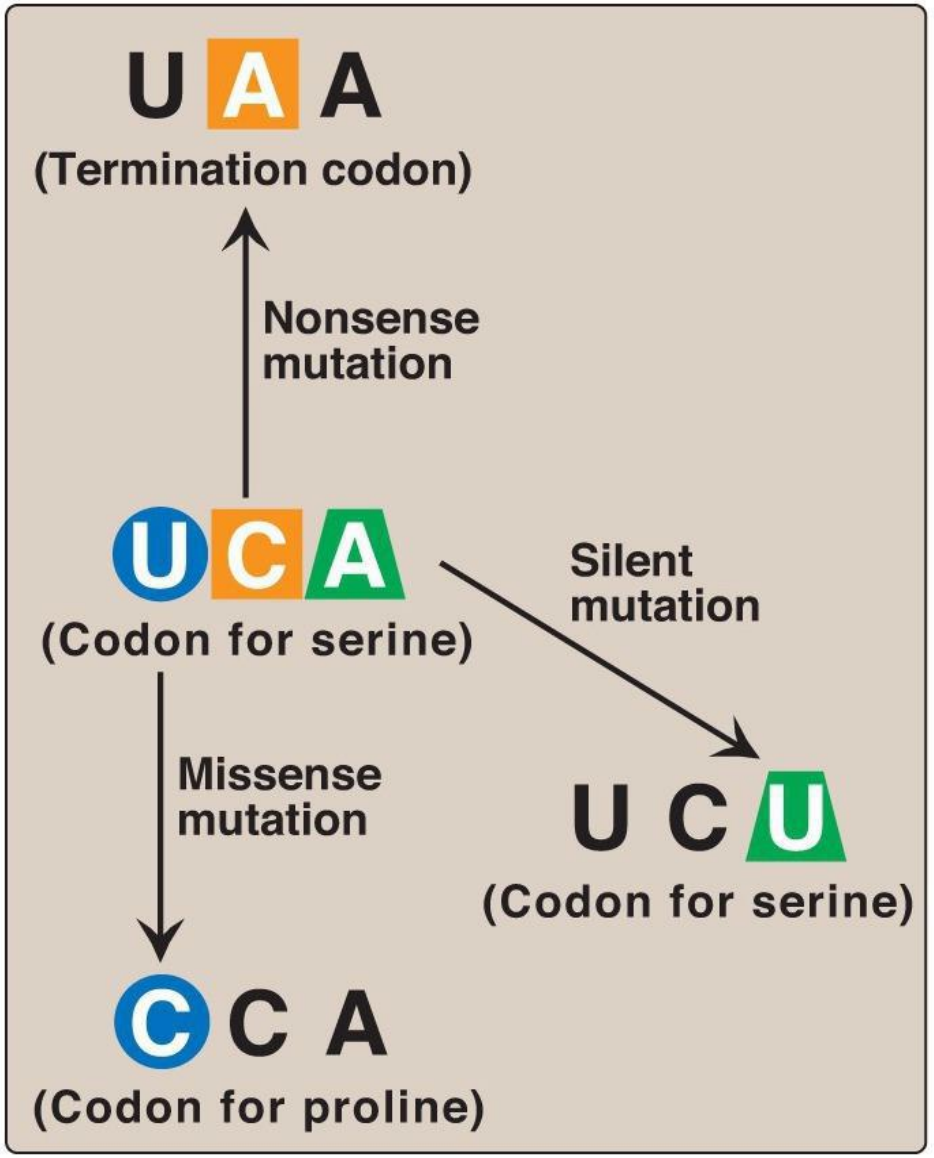
Effect on protein: Shorter than normal; usually nonfunctional.

3. Silent mutation: The codon containing the changed base may code for the same amino acid.

Effect on protein: None.

(LO. 9)

Point Mutations



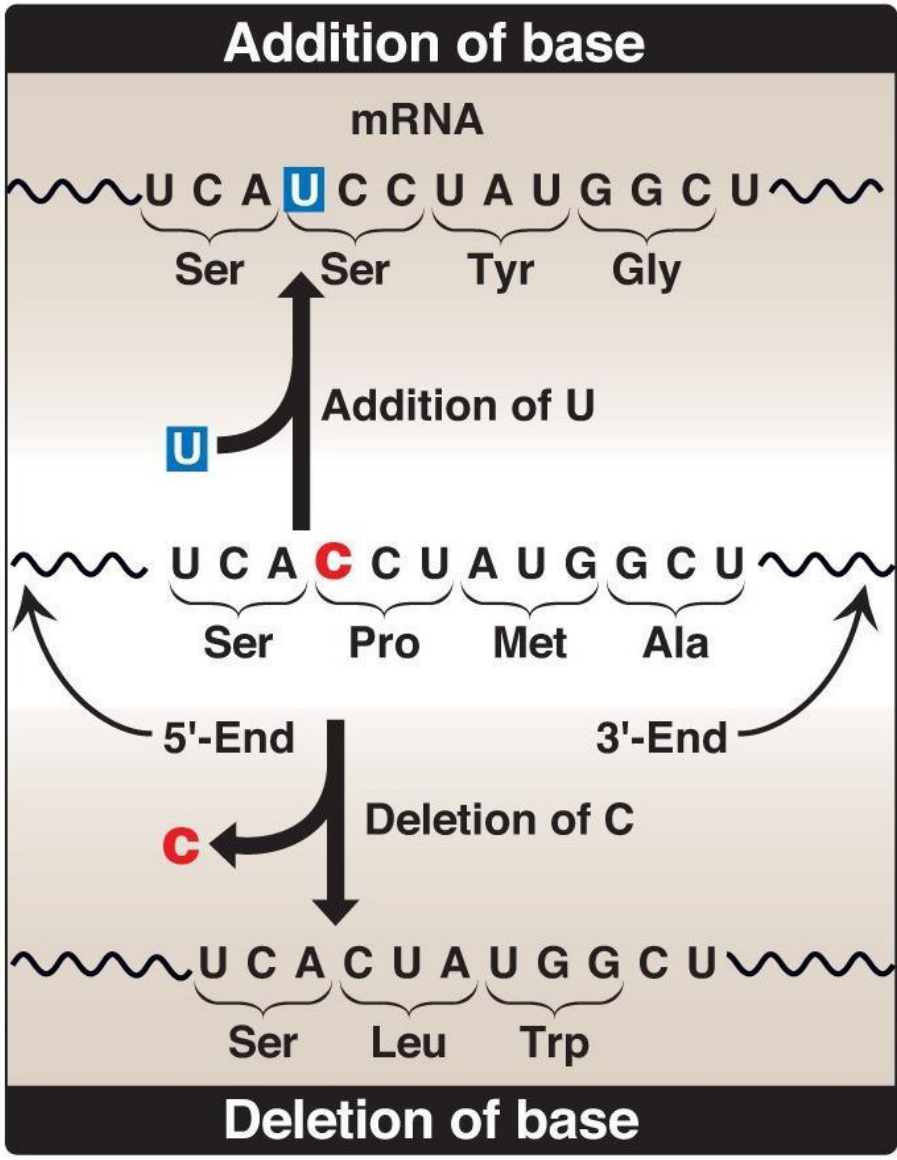
II- Frame-Shift Mutation

(LO. 9)

1. Added or deleted base lead to alter of a.a. sequences.
2. If 3 bases are added ----new a.a. is inserted.
3. If 3 bases are deleted ---lose of one a.a. e.g. cystic fibrosis.

Effect on protein

Usually nonfunctional; often shorter than normal.



(LO. 9,10)

III. Trinucleotide repeat expansion

1. Repeats in coding sequences.

Tandem repeat of CGA triplet coding for glutamine lead to toxic gain of function by alterations of protein structure

e.g. **Huntington disease**

2. Repeats in non-coding sequences:

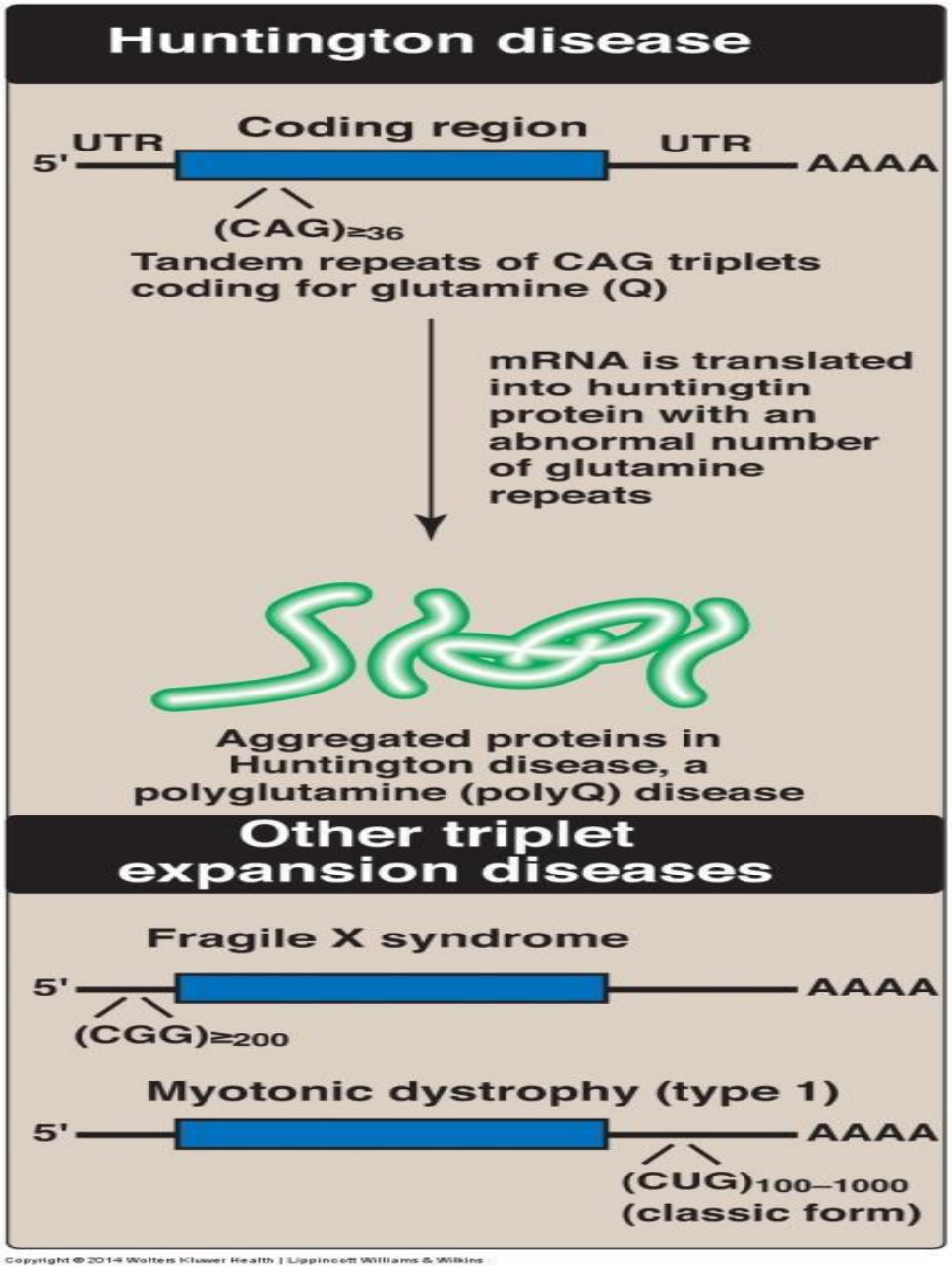
A sequence of three bases that is repeated in tandem will become amplified in number resulted in too many copies of the triplet.

e.g. **fragile X syndrome and myotonic dystrophy**

the trinucleotide repeat expansion occurs in the untranslated portion of a gene, the result can be a decrease in the amount of protein produced

(LO. 9,10)

Trinucleotide repeat expansion

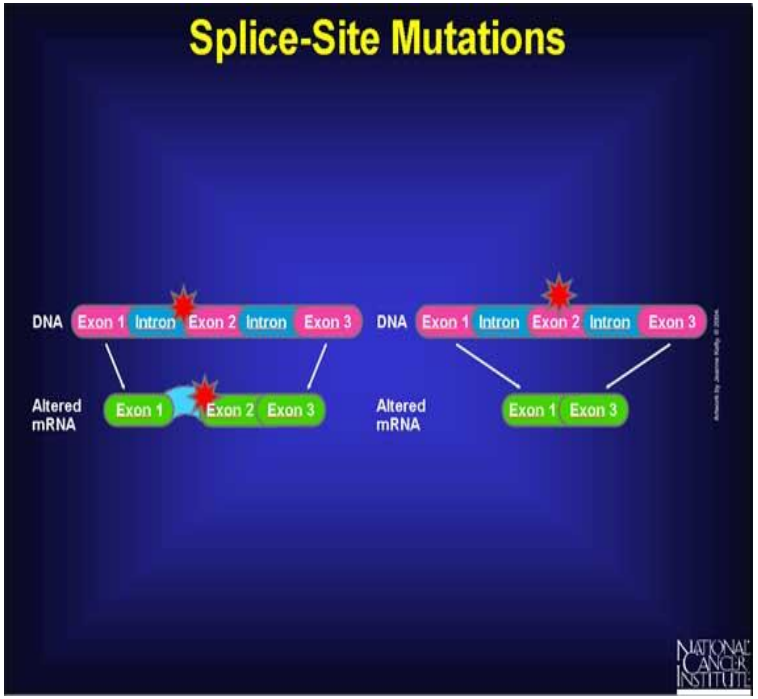


Other mutation outside the coding region. (LO. 10)

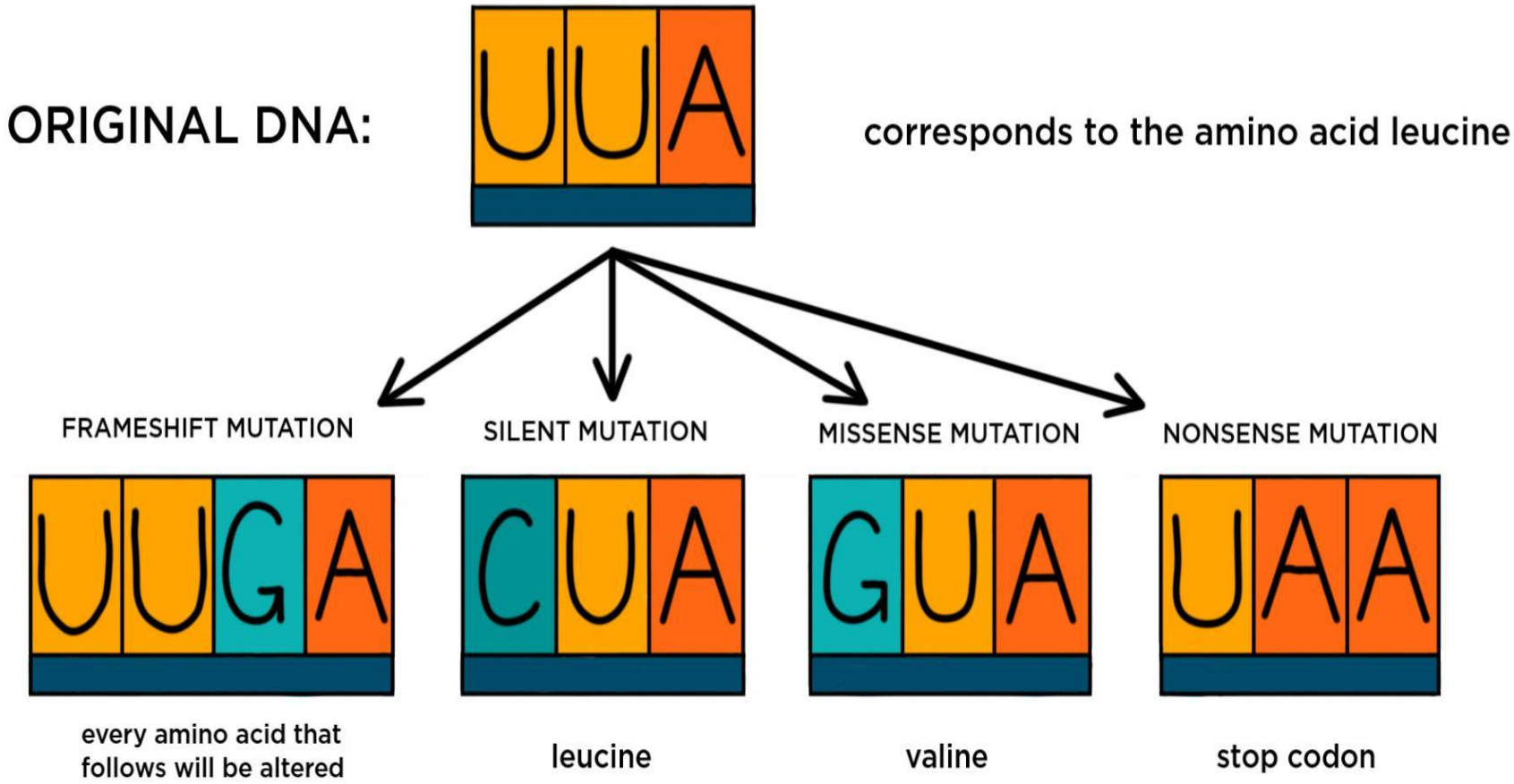
Splice site mutations:

- Proper splicing of pre-mRNA is essential for normal gene function.
- Splicing defects cause several human genetic disorders.

- e.g. ß-thalassemia,
  - mutations at the intron/exon border
  - result in a deficiency in the amount of ß-globin mRNA and
  - lower than-normal amounts of the ß-globin protein,
  - producing anemia as a phenotype.



What Are Point Mutations?



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