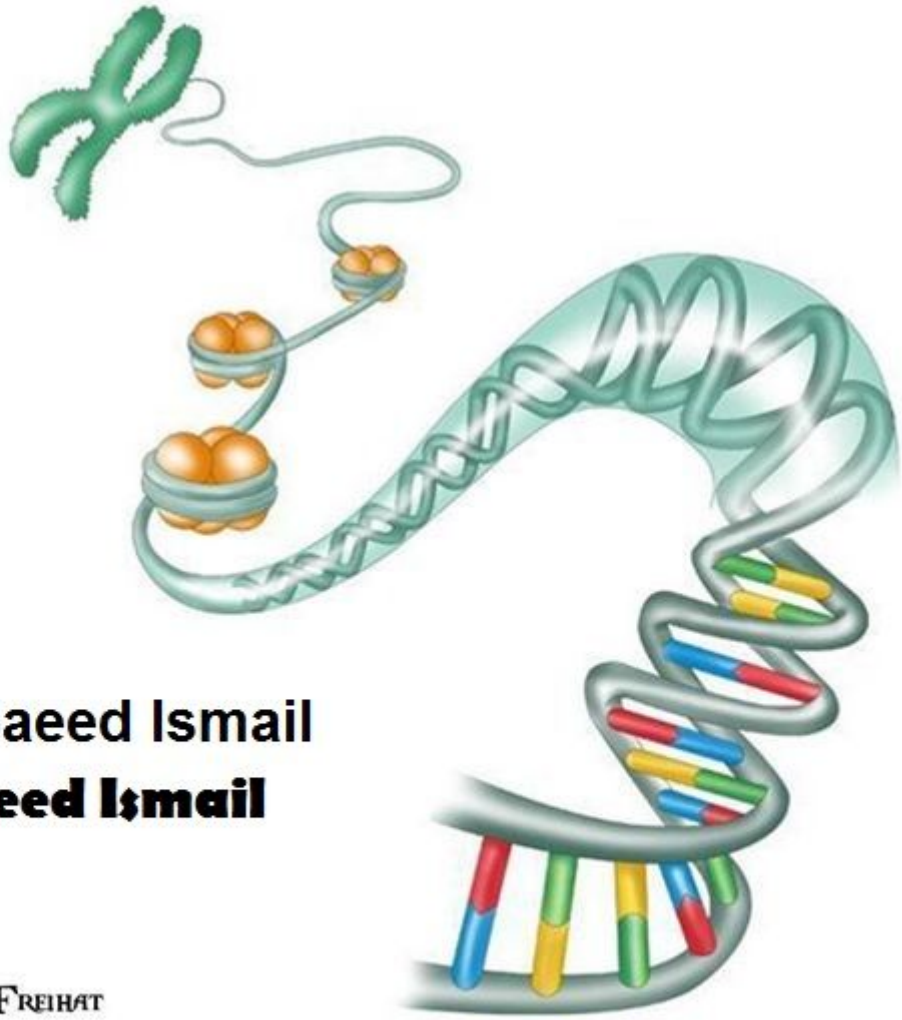
University of Jordan
Faculty of Medicine
Batch 2013-2019

Medical Committee
The University of Jordan

Genetics & Molecular Biology

○ Slides ○ Sheet ○ Handout ○ other.....



Sheet#: 17

Dr. Name: Saeed Ismail

Done By: **Saeed Ismail**

Designed by Nadeen Al-Freihat

بسم الله الرحمن الرحيم

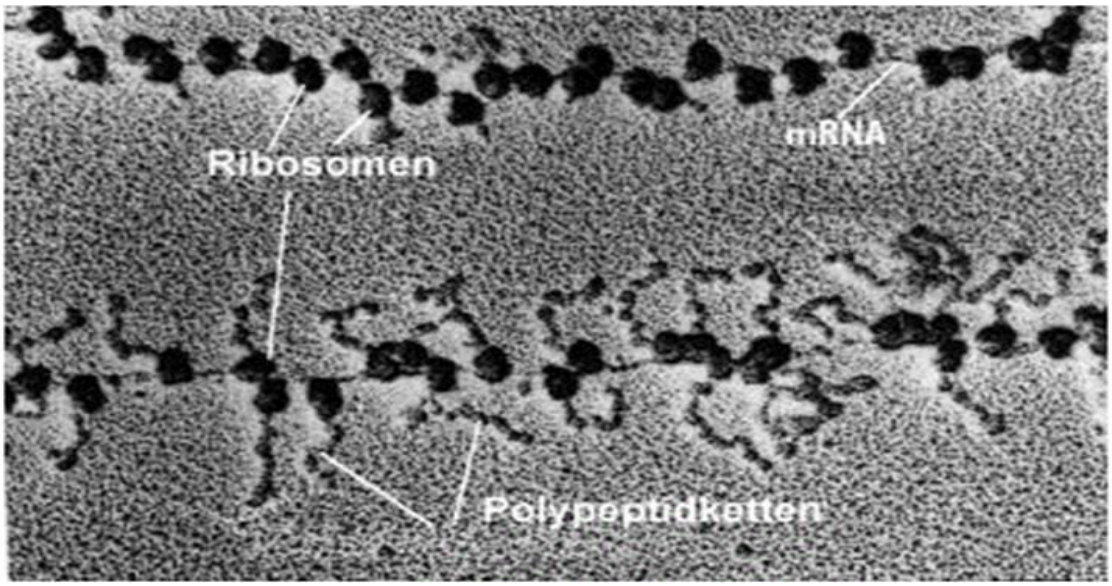
Chapter 15

Translation and synthesis of proteins

** Unlike other sheet writers who claim that their sheet is easy, this one is really the easiest and shortest sheet you will ever see in koleyet el teb.

- This is a real electron microscopy photo that shows you the mRNA and the Ribosomes (dark globes), you can see the growing polypeptide coming out of each ribosome.

-This whole picture we are seeing is called **Polysome** which means several ribosomes translating a single mRNA simultaneously, the reason why they do not wait is because the mRNA is short lived, so ribosome #2 won't wait until ribosome #1 finishes its translation process ,in order to synthesize more polypeptide chains.



-Bases on which Translation from mRNA to proteins is done (nucleic acid language to amino acid language):

-according to a genetic code which is simply:

*Each 3 nucleotides make a codon which encodes for a certain amino acid.

The genetic Story:

From the doctor's point of view, this is the most important discovery of all times; to know how life is encoded and then decoded is amazing, and it took them thousands of years to know this . it is really amazing how the genetic information are encoded in the DNA and then they are translated into functional proteins .the question was how a piece of DNA is translated into a functional protein ?! the answer was : mRNA takes the msg from the DNA to the cytosol to be translated . then the other question is how the msg is translated into amino acids ? the first crack to the answer was from mathematicians (which the doctor thinks they are the biggest minds in history…. Yalla el kol y7awel mathematics)

So the question was: how would 4 different nucleotides encode for 20 amino acids?!

A mathematician said that it has to be triplets→ and you can make 64 different combinations, even though it's more than the number of amino acids, it is the only way (if each two makes one amino acid , it will not be enough (combination will give us 16 amino acid) and if each 4 gives us one amino acid , the possible # of amino acids will be 256 , so the most convenient solution is that 3 nucleotides give us one amino acid).

In the early 60's Marshall Nirenberg solved the whole puzzle biologically by bringing a stretch of RNA made of UUUUUUUUU…, injects it in the bacteria and observes the resulting proteins and he found that it was phenylalanine-phenylalanine-… (poly phenylalanine , so he discovered the first codon (UUU gives us phenylalanine).

AAAAAA… → glycine and so on, then he started making different combinations and observed the resulting protein, to make a strand that you control its sequence was a miracle back then (60's).

So Marshall Nirenberg was able to know the codons and the amino acids coded by them.

-Features of the genetic codons:

A. 1 start codon → encodes Methionine
B. 3 stop codons → do not encode any amino acid
C. Degenerate (redundant)التكرار → we have 61codons (64-3 stop codons) for 20 amino acids so there will be different codons for the same amino acid, but, **they are not distributed equally** because you can have 6 codons for serine and one codon for Methionine.
D. Unambiguous غير غامض→ it means that it's true that there are different codons for the same amino acid *but a codon can't give you different amino acid each time it is translated* (every time you translate AUC it gives serine, it can't give you serine once and the other time you get glycine, this is not logical , as if the ribosome faces AUC and AUC was coding for serine and glycine , what to add ?? so it's logical that the genetic code is not ambiguous).
E. Almost universal → in the past it was called universal but because of some exceptions (very few) that were discovered in some bacteria they added "almost" . so almost universal means that the *same codon will be translated into the same amino acid in all organisms starting from simple viruses to humans* (AUG gives Methionine in viruses and humans), but in some *few cases* , for example ,a codon coding for serine in bacteria could give you glycine in human (for example).

-**Translation process:** the real translator is not the Ribosomes, it is the tRNA (in fact it is the enzyme called aminoacyl tRNA synthetase, which makes the **ester bond** between the amino acid and the tRNA on its 3') that has an anticodon that binds the codon on the mRNA bringing with it the specific amino acid for that codon (for example AGU –anti codon→UCA on the tRNA bringing serine with it).

- There must be a reading frame to translate mRNA to a protein. The start of the reading frame is determined by the start codon AUG, meaning that the ribosome will attach from the 5' cap of mRNA and read the codes but it doesn't translate until it reads the AUG codon.

-Charging tRNAs:

*Charging the tRNA with right amino acid.

*Done by the enzyme **Aminoacyl tRNA synthetase** (there are more than 5o of these enzymes each one charges a different tRNA).

-Stages of translation:

I. Initiation
II. Elongation
III. Termination

-**Initiation:** it is the stage at which the translation complex assembles over the start codon.

- The small ribosomal subunit binds the 5' end of mRNA and it starts reading. when it reads the start codon (AUG) ,the tRNA (with the anti codon UAC) comes and bind coding for Methionine, then the large subunit comes.

-The whole complex is combined together with the Help of proteins called **initiation factors**.

To sum up : *the small ribosomal subunit identifies the 5' end of mRNA and scans for the start codon, the first tRNA comes with Methionine, then comes the large subunit and assemble at the start codon with the help of initiation factors.

- **Elongation:** after the assembly of the complex ,we have 3 binding sites in the large subunit:

A site (from Amino acid): the site where the new tRNA comes.

P site (peptide): the site where the polypeptide is held.

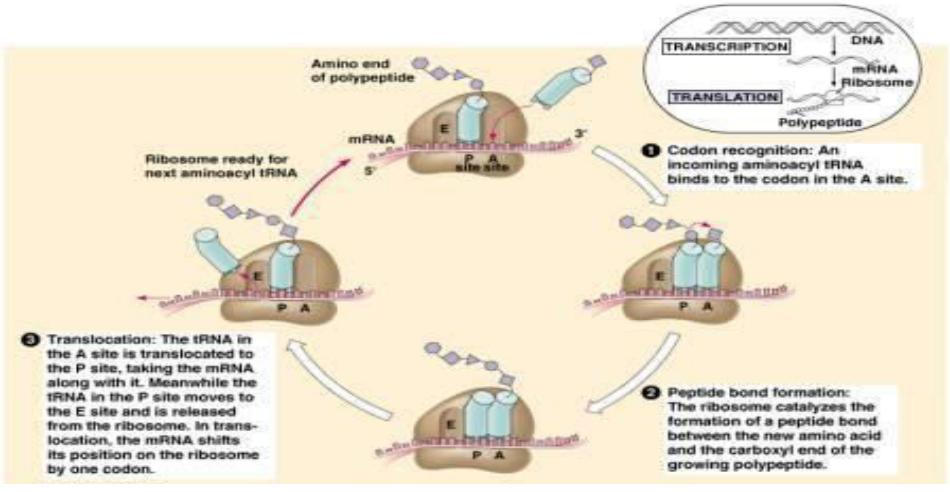
E site (Exit): the site where the tRNA exits after delivering the amino acid.

The new amino acid #2 comes on the next tRNA (which is #2)at the A site ,the first amino acid that is found at site P will attach to the second one at A (meaning the new one goes to the old one at site A , not the old goes to new at site P), then the tRNA at site P exits from site E and the tRNA at site A moves to site P.

The doctor explains the slide below (the pic below):

The elongating polypeptide chain has 4 amino acids at the **P site**, the 5th tRNA arrives at site A carrying amino acid #5, and the 4 amino acids will bind on the fifth amino acid making the growing polypeptide on **site A** (meaning that the peptide that is composed of 4 amino acids will move to the fifth one at site A **not** the 5 amino acid at site A moves to the growing peptide at site P) , the tRNA that holds nothing exits from the E site, and the tRNA with the 5 amino acid polypeptide will **translocate** to site P exposing the new A site for amino acid #6…and so on .

There was and still a big argument about how translocation occurs , the question was who moves?! is it the ribosome or the mRNA ? we don't know till now but the Dr. thinks that it is the mRNA.



-**Termination:** translation (elongation) continues until the ribosome reads one of the stop codons (UGA, UAA, and UAG) as there is no tRNA with an anticodon complementary for them, instead, a protein that is named **releasing protein** or **release factor** comes and binds to the A site and dismantle the whole complex to →small subunit, large subunit, mRNA, polypeptide chain.

-The resulting polypeptide chain is usually functional in ***prokaryotes***, all it needs is folding.

-In eukaryotes ,the resulting chain is called the *primary polypeptide* and it needs folding & modification before it becomes a functional protein (*each* protein will be modified *differently*, unlike the 3 processing steps that happen to *all* mRNAs <capping at 5' end, splicing, polyadenylation at 3' end>) ;meaning that some proteins get methylated, others will be glycosylated…and so on .

So , the Post-translational modifications are :

1-Folding: it is the three dimensional conformation of the polypeptide and it is Essential for protein function .some proteins will have just a tertiary structure , while others are formed from more than one polypeptide so they will have quaternary structure . folding Starts at N-terminus while polypeptide is still being synthesized. And it is mediated by Chaperons .

Disulfide bonds:

they stabilize 3° and 4° structure and are formed between Cysteine residues.

2-Modification: e.g.

- ✓ Removal of terminal Methionine (by a protease).
- ✓ Cleavage of the chain (like insulin protein ,which is primarily synthesized as a large polypeptide and then cleaved and rejoined , very complicated)
- ✓ Addition of final groups on specific a. a:
- ✓ Methylation of Lysine residues.
- ✓ Phosphorylation / de-phosphorylation: on/off control of many proteins : meaning that by the ability of the cell to modify the protein , it can control its function (for example it can phosphorylate a certain protein and make it active , then decides to inactivate it by removing the phosphate group)
- ✓ Glycosylation: (addition of sugar moieties) for membrane of secretory proteins.

The Dr recommended watching these videos to understand translation. ☺

Animation:

http://www.youtube.com/watch?v=5iS4CRPPDus

Or

http://www.youtube.com/watch?v=D5vH4Q_tAkY

Dedicated to: Ahmad masri, Ali halabi, Qusai sharief, Marah Atari, Nour hayek, Amal orabi

Done by: Saeed Ismail ☺