بسم الله الرحمن الرحيم

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Today we will talk about **Gene Translation (protein synthesis)**; this sheet will cover the following:

**A: Introduction to molecules involved in translation process.**

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**B: The basis of translation :( Basis of coding).**

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**C: Features of the genetic code:**

- **Degenerate.**
- **Unambiguous.**
- **Almost universal.**

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**D: t-RNA (overview).**

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**E: Reading frame:**

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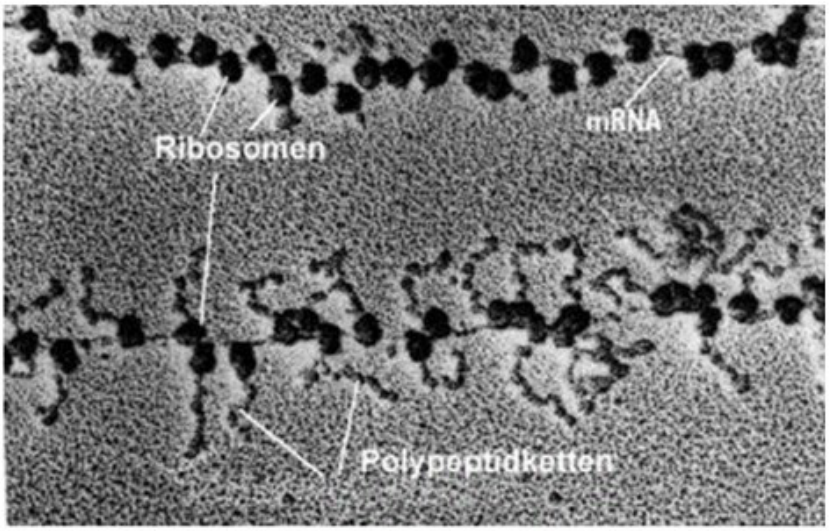
**F: Translation process:**

- **Initiation.**
- **Elongation.**
- **Termination.**
- **Posttranslational modifications.**

# A: Introduction to molecules involved in the translation process:

The **translation** process occurs in the **cytoplasm** of the cell, where there are complexes called **Ribosomes** which will translate **m-RNA** that is coming from our genome. Look at the following picture which is showing a real electron microscopy image and notice the following:




1) It represents multiple Ribosomes translating single m-RNA.

2) The **thin** filament is the **messenger RNA (m-RNA)** which is to be translated.

3)the dark, round bodies represent **ribosomes**.

4) The threads extending from ribosomes are **polypeptides**.

5) notice that the polypeptide chains being produced on the left are longer from that on the right, indicating that ribsomes start from the 5' end on the left.

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**Ribosomes** translate single m-RNA **simultaneously; once** it started **translation of m-RNA**, it will run continuously, it won't wait!

Q: Why Ribosomes are in rush?!

A: Because the half life of mRNA is very short in cytoplasm. The shortness of mRNA half life is actually due to **RNase**(s), which are one of the most aggressive nucleases ever, they will break RNA rapidly, so **ribosomes** are stimulated for any mRNA that comes out of the genome to decrease the time of RNA exposure to **RNase**. one of the factors that slow the degradation of mRNA is the **Poly-A-tail ;** because RNAse breaks the **3' tail** until reaching the coding region , by the time they have broken it, Ribosomes finish their job ! that's why they are working simultaneously.

Remember: translation direction is from **5'➔3'**.

The **aggregation** of many ribosomes that are working (translating) on one single m-RNA is called **Polysome**.

**::: End of Introduction:::**

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## B: The basis of translation: (Basis of coding)

We deal with **nucleic acids sequence** as a language; they will form a three litter words known as **Codons**.

Until the late 40's and the early 50's, no one was seriously considering DNA as the coding material ; because if you want to build something as complicated as human body, you have to have a very complicated language consisting of so many letters. Every time they were looking in the nucleus and studying DNA they found that it consists of repeated **phosphate sugars** that will not code for anything, in addition to **4 nitrogenous bases** that will code only for 4 different things.

Q: how have scientists discovered it that way?

- **Mathematically:**

**Keep in mind that we have <u>20 amino acids</u> in our body**

**Since we have 20 amino acids, how can 4 nitrogenous bases code for them?!**

1) If the codon consists of one letter (I:E one nitrogenous base) then it will code for only **4 amino acids** which is less than 20! ➔Not accepted. (4^1=4)

2) If the codon consists of two letters (I.E: two nitrogenous bases) then it will code for only **16 amino acids** which is again less than 20! ➔Not accepted. (4^2=16)

3) If the codon consists of three letters (I.E: three nitrogenous bases) then it will code for **64 amino acids** which is a lot more than 20! ➔ This was **accepted** because scientists have discovered that **one amino acid can be coded by more than one codon so it seems logic.** (4^3=64)

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- **Experimentally:**

They worked on a DNA and <u>they knew the protein (original)</u> that was coded by it, then they started adding nucleotides in the **coding frame** and comparing its newly translated proteins with the original protein coded by this DNA molecule as the following:

**1st** by adding one nucleotide; they find out that **the protein completely differs from the original one.**

**2nd** by adding two nucleotides; they found that **there was downstream shift with completely different amino acids**.

**3rd** by adding 3 nucleotides; the result was that they got **the same protein** but with **one extra amino acid**.

(When adding three nucleotides they have to be **in-frame**<I.E:<u>between codons</u>> not out-frame).

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After they prove it mathematically & experimentally, **they have to know what each codon codes for.** They did so by making strands and putting them in bacteria and observing amino acid sequence for the coded protein.

For example: they made strand that are composed of completely A's **(AAA)** they came up with **lysine**, etc,and they tried all combinations to know the coded amino acids till they discovered **the genome**.

## ::: End of the basis of coding :::

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## C: Features of the genetic code:

### A) Degenerate (redundant):

It means **repetition** in function (more than one codon code for the **same amino acid**).

We have **3 stop codons** that aren't coding for amino acids, these are: **UGA, UAG, or UAA.**

**So from the 64 codons ; 61 are coding , 3 are non-coding ,**and the 61 codons are not equally distributed on all amino acids, for example **Methionine** has **one codon**, while Serine has **6 codons** ,**so it differs from one amino acid to another.**

- Different codons that code for the same amino acid usually differ in **the third nucleotide** (TC**C,**TC**G,**TC**T,**TC**A** these will code for serein).
- That's why they say that if mutation occurs in the third nucleotide it will be **less dangerous** because mostly it will end up coding for the same amino acid.

Note: we have **one start codon** that code for **methionine** which is **AUG**.

**B) Unambiguous:**

It means that each codon codes **only for one amino acid** (despite that more than one codon can code for the same amino acid)

For example, imagine if each codon can code for different amino acids each time, it will be **impossible for us to resolve the genetic code**, and it will be extremely **mysterious.**

**C) Almost universal:**

In all living creatures you'll find that codon will give the same amino acids, for example AAG is the codon for lysine in humans, animal, bacteria, and viruses. However recently scientists discovered some **exceptions**, for example certain viruses' or Bactria's AUG will not code for methionine but different amino acid **,that's why it's "almost" universal.**

## ::: End of the features :::

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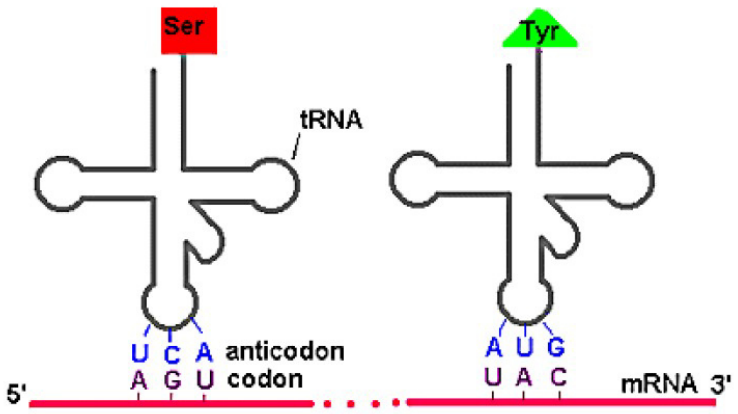
## D: t-RNA

- Look at following figure:




- Here is the t-RNA ,notice that on **loop#2** you'll find the **Anticodon,** by which it will recognize the codon then an

amino acid will be synthesized .

- **Aminoacyl t-RNA synthetase** is an enzyme that will put the amino acid sequence on the t-RNA.

- t-RNA+Amino acid = **Aminoacylt-RNA** , it's also called **charged t-RNA.**

- The following figure illustrates the process of binding the right t-RNA with the right amino acid sequence by **Aminoacyl t-RNA synthetase**.
- We have **more than one type** of this enzyme , each one is specific for **certain t-RNA** depending on the type of **anti-codon** of that t-RNA, producing a new amino acid bounded to **3'prime end of t-RNA**.

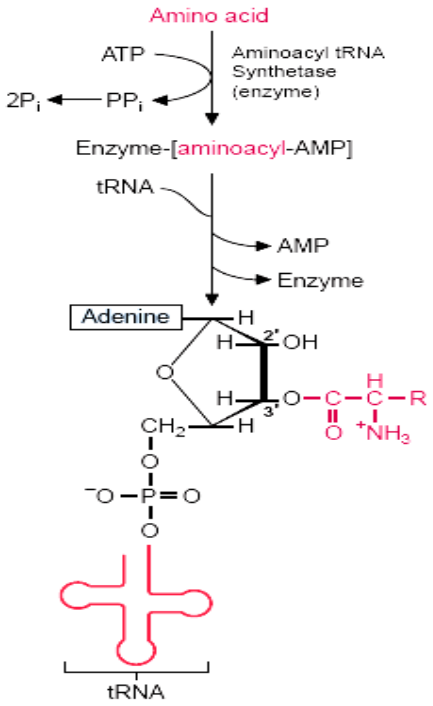



*FIG. 15.5.* Formation of aminoacyl-tRNA. The amino acid is first activated by reacting with ATP. The amino acid is then transferred from the aminoacyl-AMP to tRNA.

----------::**End of the t-RNA**::----------

## E: Reading frame:

a reading frame is a way of dividing the sequence of nucleotides in a nucleic acid (DNA or RNA) molecule into a set of consecutive, non-overlapping **triplets.(Wikipedia)**


- It's no necessary that the first nucleotide in RNA will be translated into a protein**,** the ribosome will look for **Start codon**(**AUG** that codes for methionine) and then it will start translating**.** The region before the start codon is called **5'UTR (5' Untranslated region).**

- **Ribosome** will continue translating until reaching a **STOP** codon which is not necessarily the last codon**.** The region after the stop codon is called **3'UTR (3' Untranslated region).**

- **Reading frame** is detected by **the first AUG**: from the 1st AUG, reading frame will start ,it can be after 4 or 3 ,2,6,... codons anywhere . Also their maybe more than one AUG but what determine the reading frame is **the 1st AUG**.

- In some genes it will ignore the first AUG, and start from the 2nd or another one, however this not the case in most genes.

## ::: End of Reading frame :::

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## F: Translation process:

- **Ribosomes** are responsible for translation process, they are composed of **large & small subunits**; each contains number of **proteins** and **r-RNA molecules**.

- We can divide translation process into 3 parts : **Initiation** , **Elongation** , **Termination**.

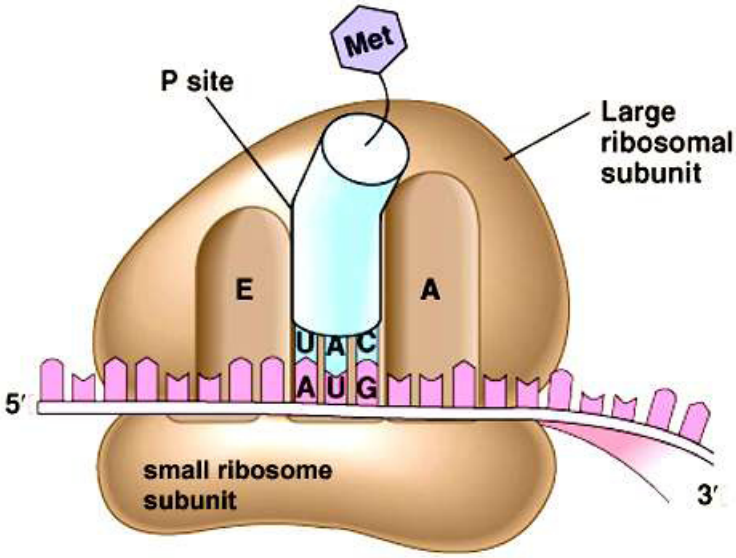
### 1| Initiation:

- **Translation initiation complex** consists of : m-RNA ,Small & Large subunits, the first t-RNA which contain methionine "**met t-RNA**", and proteins called **initiation factors** which will combine these components together.

- Initiation complex will combine as the following :
  **small subunit** will come, it will bind at **5' end of m-RNA ,** it will recognize it {5' end} fast; because there is a **large CAP** on the 5' end of m-RNA, then it{small subunit} will start scanning looking for **AUG**, once it reach it ; it will stop.

  Then **large subunit & met t-RNA** will come, all the components will be combined by **Ifs** (initiation factors).

- When this initiation translation complex is formed, there will **three sites** where t-RNA can bind to it, they are: **A site, P site, E site**.




- **A site = Amino acid site.**
- **P site = Peptide site.**
- **E site = Exit site.**

**::: End of initiation:::**

## 2|Elongation:

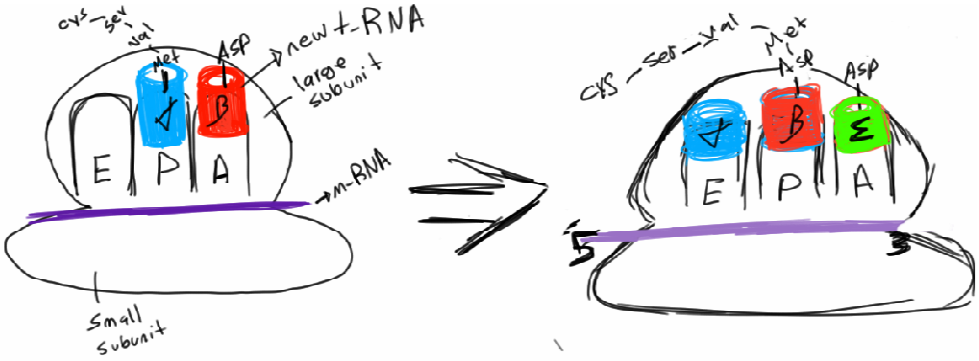
Elongation process is simply combining **translation initiation complex** on m-RNA**.**

- During the elongation stage the **P site** will have **t-RNA** with polypeptide bounded to it, and this polypeptide is **4 amino acid long for example.**

- New Amino acid will bind to **A site**; then the previous 4 amino acids will bind to the new one by **peptide bond**.

- **t-RNA** that donated the 4 amino acids will move from **P site to E** .

To illustrate this example I drew the following figure just to make the picture clearer **(this is not a professional figure it's just for illustration purposes :P)**




**We have 3 t-RNAs,** I named them "**Alpha, Beta, and Epsilon".**

**1) Alpha t-RNA** is on **P site** and bounded to it is a polypeptide consisting of **4** amino acids.

**2)** Then a **new t-RNA which is "beta t-RNA"** will sit on the **A site**, bounded to it a new amino acid (amino acid #5).

**3)** Polypeptide will break from the **Alpha t-RNA** ,and it will bind to the **Beta t-RNA**.

**::So it was 4 amino acids polypeptide now its 5 amino acids, meaning it have been elongated.::**

**4)** Now the **Alpha t-RNA will go to the E site to exit, Beta t-RNA will come to P site.**

**5)** A new t-RNA will occupy **the A site** which is "**Epsilon t-RNA** in our illustration "which Carries (amino acid #6) and the cycle continues.

When t-RNA move from **A** site to **P** site it's called **translocation**.

Peptide bonds are formed by an enzyme called **peptidyl transferase** which is a component of the **large subunit**, and it's one of the **r-RNA** molecules with catalytic activity and it will actually bind amino acids together.

**::: End of Elongation:::**

## 3|TERMINATION:

- The **complex** is still moving and for example we reached codon#1250 and it was **UGA** (stop codon), **there is no t-RNA carrying an anticodon for the UGA**, instead there is another protein waiting to unveil on **A site** called the **releasing factor**.

- Once this releasing factor see **stop codon** on the A site it will **occupy** it and **break** this complex (I mean translation complex) into large & small subunits, m-RNA, and the **newly synthesized polypeptide**.

**::: End of termination:::**

## ❖ Posttranslational modification:

In bacteria, translation occurs **simultaneously** with transcription, once mRNA is produced from DNA, immediately Ribosomes start synthesis to produce functional polypeptide chains (no modifications).

In human cells (eukaryotic cells) **posttranslational modification** to polypeptides will occur such as ribosylation , carboxylation ...etc.

**Table 15.4 Posttranslational Modifications of Proteins**

| |
|---|
| Acetylation |
| ADP-ribosylation |
| Carboxylation |
| Fatty acylation |
| Glycosylation |
| Hydroxylation |
| Methylation |
| Phosphorylation |
| Prenylation |

- Also some of them will **conjugate** to become functional, others will make **quaternary structure** like **hemeoglobulin** by combining **4 polypeptides** in addition to conjugating with **heme.**

- Others need **cleavage** like **insulin** which is translated as a very long polypeptide, so its **middle part** will be cut, and the terminal parts will bind to each other by **disulfide bridges.**

- We will be talking more about phosphorylation in one of the chapters.

- **We can say that most of our proteins will be modified to become functional.**

**::: End of Post Translational Modification:::**

**::: END OF TRANSLATION PROCESS :::**

بعتذر عن أي خطأ لغوي أو علمي.

زميلكم | علاء الدين دحبور .