بسم الله الرحمن الرحيم

كل هالبروتين وين يروح L

هذه المذكرة كافية تماما وهي اتمام لما بدأته قبل سنتين

هي اهداء لدفعة ٤٢٨ الرائعين J

واهداء لأغلى انسان لي في هذه الدفعة خاصة J

اهداء الى كل الدفعات القادمة . . .

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Overview

- Protein Synthesis called **" Translation "**
- Translation needs **Genetic Code** .

- Genetic Information :

- Stored In Chromosomes .
- Transmitted to daughter cells by DNA replication .

- **Genetic Information** is expressed through Transcription to RNA **à** mRNA - **à** Subsequent translation into proteins .

Note :

- Any alter in the nucleic acid sequence may result in an improper Amino Acid being inserted into protein chain ,potentially cuasing Disease or even death

- **Many Proteins are covalently modified to :**

- Activate them
- Alter their activities
- Target them to extracellular or intracellular destination

The Genetic Code

* Each Individual word in the code is composed of *three* Nucleotide bases .
*These Genetic words are called " *Codons* "

A - Codons

- Present In mRNA .
- They are presented by the language of : C, G , A , U
- Their nucleotides should be written from 5'-end to 3'-end
- there are 64 different combinations of bases

كل ثلاثة منهم تترتب بترتيب معين ويسووا كودن جديد

- Adenine (A)
- Guanine (G)
- Cytosine (C)
- Uracil (U)

NO T (thymine) (MCQ) **J** >>>

How To Translate a Codon

you can translate the codons
to Amino acid .
- For Example , 5'-AUG-3' codes for methionine .
- 61 of 64 are coded for the 20 common amino acid

Termination (or " stop " or " nonsense ") codons :

{ UAG - UGA - UAA }هاااام

If One of these amino acid appears in mRNA :
termination will occur and they do not code for Amino acid
à
sending signals that the process is complete

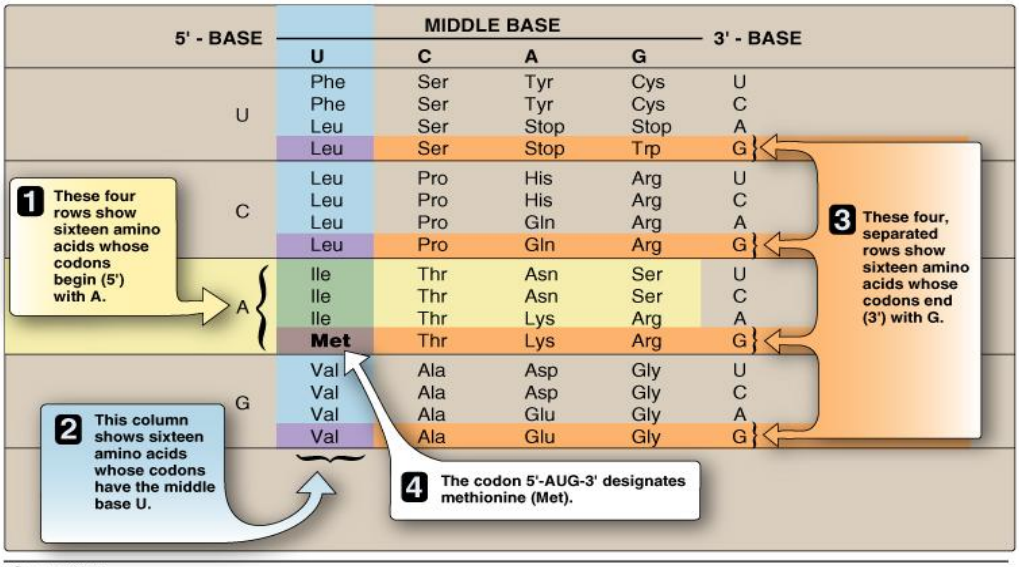

Figure 31.2
Use of the genetic code table to translate the codon AUG.

من الجدول اعرف التالي :

1) Met & Trp is the only amino acids that form by only one codon
2) others amino acids formed by more than one codon as u see
3) Not in every protein we find Met

any mutation that altered the manner in which the code was translated would have caused the alteration of most, if not all, protein sequences, which would certainly have been lethal

Characteristics of the genetic code

Specificity

- The genetic code is specific
- a particular codon always codes for the same amino acid

Universality

في أي مكان من الجسم أي ترتيب للبيبس يعطي نفس الامينو اسيد بأي مكان ثاني بالجسم ولهذا استثناء الميتوكندريا **J**

- the specificity of the genetic code has been conserved from very early stages of evolution [Note: An exception occurs in mitochondria, in which a few codons have different meanings like , UGA codes for trp.]

Degeneracy (Redunduncy)

- a given amino acid may have more than one triplet coding for it. For example, arginine is specified by six different codons.

كل امين ممكن يكونه اكثر من كودون بس كل كودن يكون أمين واحد

لا تنسوا ال *Met* يكونه كودن واحد تتذكروه ؟

Nonoverlapping and commaless

- The genetic code is nonoverlapping and commaless, that is, the code is read from a fixed starting point as a continuous sequence of bases, taken three at a time. For example, ABCDEFGHIJKL is read as ABC/DEF/GHI/JKL without any “punctuation” between the codons.

C. Consequences of altering the nucleotide sequence:

- Alteration in single nucleotide base (point mutation) :

1. silent mutation :
the codon containing changed base may code for the *same amino acid*
(e.g. UCA **è** UCU = serine)

2. missense mutation :
the codon containing changed base may code for *different amino acid*
(e.g. UCA =serine **è** CCA = proline)

3. Nosense mutation :
the codon containing changed base may become *termination codon*
(e.g. UCA = serine **è** UAA = termination codon)

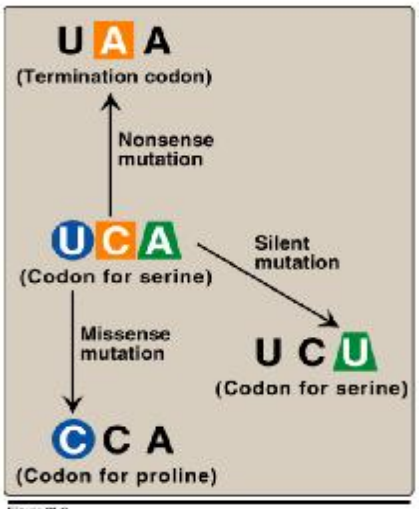

Figure 31.3
Possible effects of changing a single nucleotide base in the coding region of an mRNA chain.

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Alteration in amount or structure of protein produced by translation :

A. *Trinucleotide repeat expansion :(MCQ)*

Occasionally, a sequence of three bases that is repeated in tandem will become amplified in number, so that too many copies of the triplet occur.

If this occurs:

1) *Within coding region of gene* :
the protein will contain many extra copies of one amino acid .

I. Huntington protein (11-34 CAG = 11-34 glutamine) **è** huntingon disease (MCQ) (neurogenrative).
* N.B : Huntington protein is unstable

2) ***In untranslated portion of gene*** **è** decrease in produced protein :

I. Fragile X syndrome (7-50 CGG)
II. Myotonic dystrophy (5-35 CTG)

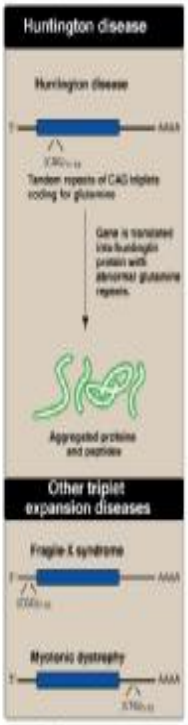

Figure 31.4
Role of tandem triplet repeats in mRNA causing Huntington disease and other gene expansion diseases.

B. *Splice site mutations:*

- Mutation at splice site **è** no removal of introns from pre-mRNA **è** apparent protein production

C. *Frame – shift mutations :*

- *frame – shift mutations :*
  - ü Addition or deletion of 1 or 2 nucleotides to interior of message sequence (not 3) (MCQ) هالم
  - ü Reading frame of mRNA is altered
  - ü Resulting amino acid sequence may become different from this point on

- *Addition or deletion of amino acid:*
  - ü Addition or deletion of 3 nucleotides (amino acid)
  - ü Not frame – shift mutations
  - ü Reading frame of mRNA is not altered

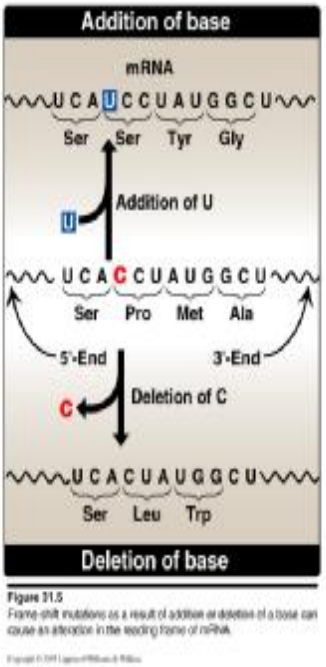

Figure 31.5
Frame-shift mutations as a result of addition or deletion of a base can cause an alteration in the reading frame of mRNA.

Loss of three nucleotides maintains the reading frame, but can result in serious pathology.

For example, *cystic fibrosis (CF)*:
- *a hereditary disease*
- primarily affects the *pulmonary and digestive systems*
- is most commonly caused by deletion of three nucleotides from the coding region of a gene, resulting in the loss of *phenylalanine* at the 508th position (ΔF508) in the protein encoded by that gene. This ΔF508 mutation *prevents normal folding of the CF transmembrane conductance regulator (CFTR) protein*, leading to its destruction by the proteasome .

Note :

CFTR normally functions as a chloride channel in epithelial cells, and its loss results in the production of thick, sticky secretions in the lungs and pancreas, leading to lung damage and digestive deficiencies . In over seventy percent of patients with CF, the ΔF508 mutation is the cause of the disease.

III. Components Required for Translation:

1- all the amino acids that are found in the finished product

2- the mRNA (to be translated)

3- transfer RNA (tRNA) .

4- functional ribosomes .

5- energy sources .

6- enzymes

7- protein factors

Amino acids

All the amino acids must be present at the time of protein synthesis

(If one amino acid is missing (for example, if the diet does not contain an essential amino acid), translation stops at the codon specifying that amino acid.)

Transfer RNA

-At least one specific type of tRNA is required per amino acid
-In humans, there are at least fifty species of tRNA
-some amino acids have more than one specific tRNA molecule.
-But every single tRNA is directed for one amino acid

Amino acid attachment site

- Each tRNA molecule has an attachment site for a specific (cognate) amino acid at its 3′-end.

- charged : tRNA has a covalently attached amino acid

- Uncharged :tRNA is not bound to an amino acid

When an amino acid become activated ?
- when it attached to t- RNA

Anticodon:

Each tRNA molecule also contains a three-base nucleotide sequence—the anticodon—that recognizes a specific codon on the mRNA

tRNA are able to carry a specific amino acid and to recognize the codon for that amino acid. tRNA, therefore, function as adaptor molecules. (MCQ)

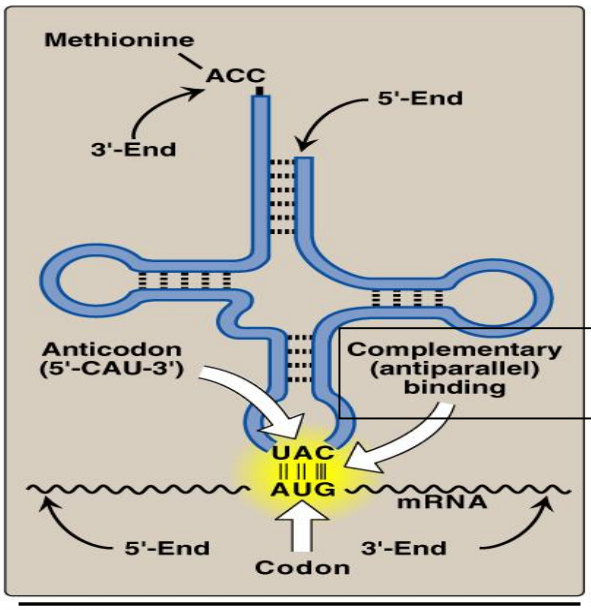

Figure 31.6
Complementary, antiparallel binding of the anticodon for methionyl-tRNA (CAU) to the mRNA codon for methionine (AUG).

Aminoacyl-tRNA synthetases:

- This family of enzymes is required for attachment of amino acids to their corresponding tRNA .
- Each member of this family recognizes a specific amino acid and the tRNA that correspond to that amino acid (isoaccepting tRNA).

Aminoacyl-tRNA synthetases:

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- catalyzes a two-step reaction
- The overall reaction requires adenosine triphosphate (ATP), which is cleaved to adenosine monophosphate (AMP) and inorganic pyrophosphate (PP_i)
- The extreme specificity contributes to the high fidelity of translation of the genetic message .
- have a "proofreading" or "editing" activity that can remove mischarged amino acids from the enzyme or the tRNA molecule.

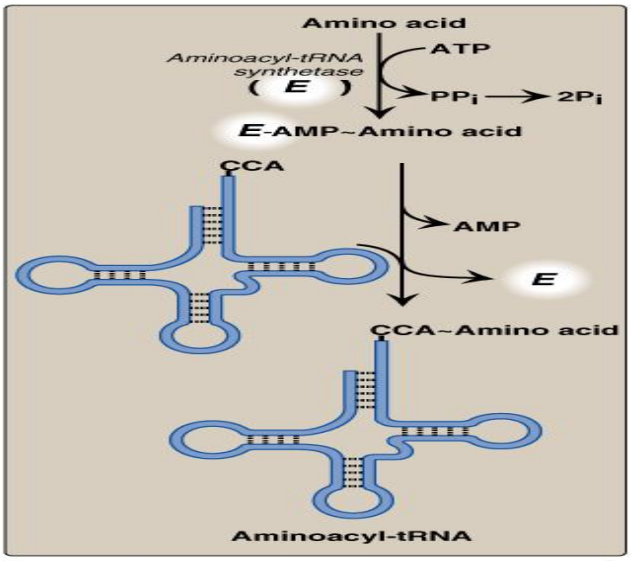


Figure 31.7
Attachment of a specific amino acid to its corresponding tRNA by *aminoacyl-tRNA synthetase* (*E*).

Messenger RNA

The specific mRNA required as a template for the synthesis of the desirec polypeptide chain must be present

Functionally competent ribosome

-Ribosomes are large complexes of protein and ribosomal RNA (rRNA)

-They consist of two subunits —one large and one small— .

-Their relative sizes are generally given in terms of their sedimentation coefficients, or S (Svedberg) values.

- Because the S values are determined both by shape as well as molecular mass, their numeric values are not strictly additive. For example, the prokaryotic 50S and 30S ribosomal subunits together form a 70S ribosome. The eukaryotic 60S and 40S subunits form an 80S ribosome.] (MCQ)(IMP)

- Prokaryotic and eukaryotic ribosomes are similar in structure, and serve the same function, namely, as the “factories” in which the synthesis of proteins occurs.

The large ribosomal subunit catalyzes formation of the peptide bonds that link amino acid residues in a protein. The small subunit binds mRNA and is responsible for the accuracy of translation by ensuring correct base-pairing between the codon in the mRNA and the anticodon of the tRNA

Ribosomal RNA :

prokaryotic ribosomes contain three molecules of rRNA, whereas eukaryotic ribosomes contain four molecules of rRNA

Ribosomal proteins :

Ribosomal proteins are present in considerably greater numbers in eukaryotic ribosomes than in prokaryotic ribosomes

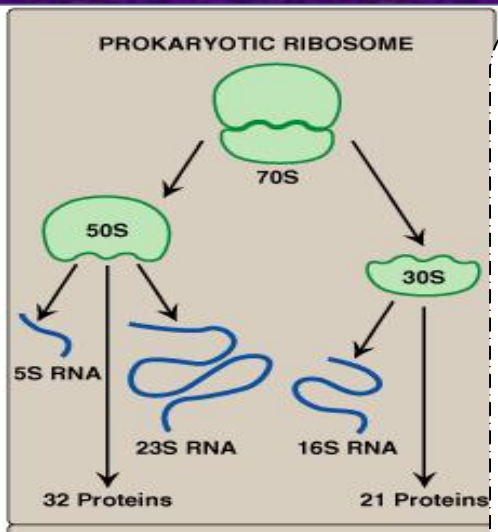
A, P, and E sites on the ribosome :

The ribosome has three binding sites for tRNA molecules—the A, P, and E sites—each of which extends over both subunits. Together, they cover three neighboring codons. During translation :

the A site binds an incoming aminoacyl-tRNA as directed by the codon currently occupying this site. This codon specifies the next amino acid to be added to the growing peptide chain. (MCQ)

The P-site codon is occupied by peptidyl-tRNA. This tRNA carries the chain of amino acids that has already been synthesized.(MCQ)

The E site is occupied by the empty tRNA as it is about to exit the ribosome. (MCQ)



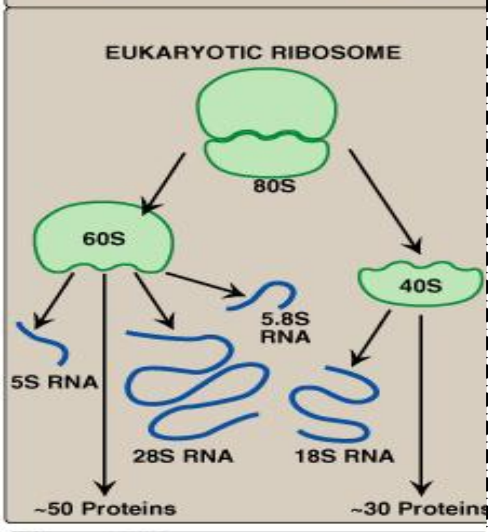


Figure 31.8
Ribosomal composition. (The numb of proteins in the eukaryotic ribosom subunits varies somewhat from spec to species.)

Cellular location of ribosomes :

- In eukaryotic cells the ribosomes are:

Free (cytosolic) (MCQ)

Cytosolic ribosomes synthesize proteins required in the cytosol itself, or destined for the nucleus, mitochondria, and peroxisomes

Associated with RER :

The RER-associated ribosomes areresponsible for synthesizing proteins that are:

1- to be exported from the cell .

2- destined to become integrated into plasma, endoplasmic reticulum, or Golgi membranes, or incorporated into lysosomes.

Note **: Mitochondria contain their own set of ribosomes and their own unique, circular DNA.**

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Protein factors

Initiation, elongation, and termination (or release) factors are required for peptide synthesis

ATP and GTP are required as sources of energy

Cleavage of ***four*** high-energy bonds (MCQ) is required for the addition of one amino acid to the growing polypeptide chain:

1- ***two*** from ATP in the *aminoacyl-tRNA synthetase* reaction:
   - one in the removal of PP_i
   - one in the subsequent hydrolysis of the PP_i to inorganic phosphate by *pyrophosphatas.*

2- two from GTP :
   - one for binding the aminoacyl-tRNA to the A site .
   - one for the translocation step .

[Note: Additional ATP and GTP molecules are required for initiation in eukaryotes, whereas an additional GTP molecule is required for termination in both eukaryotes and prokaryotes.]

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