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Biology

Chapter 17

Expression of genes

Med learn

❖ Introducton

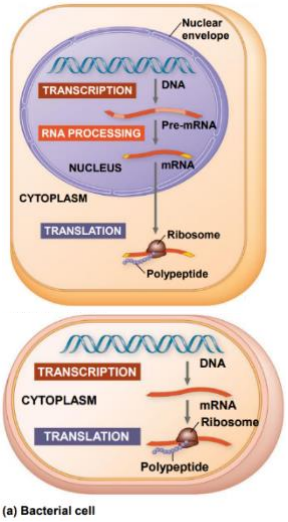
- **Proteins** are the links between genotype and phenotype
- **Gene expression:** The process by which DNA directs protein synthesis includes (transcription and translation)

❖ 17.1: [Genes specify proteins via transcription and translation]

- **Archibald Garrod** **first suggested that genes dictate phenotypes through enzymes** that catalyze specific chemical reactions
  - Cells synthesize and degrade molecules in a series of steps, a metabolic pathway in which each chemical reaction in a sequence is catalyzed by a specific enzyme
  - He thought symptoms of an inherited disease reflect an inability to synthesize a certain enzyme
- **George Beadle and Edward Tatum** exposed **bread mold (Neurospora crassa)** to X-rays creating mutations affecting the enzymes catalyzing chemical pathways
  - Neurospora is haploid (having only 1 copy from each gene)
  - It can normally live in the minimal medium → but the mutants created by Beadle & Tatum can't survive in these conditions because certain enzymes become inactive
- Their colleagues **Adrian Srb and Norman Horowitz** identified three classes of **arginine-deficient mutants** of Neurospora → each lacked a different enzyme necessary for synthesizing arginine
- The results of the experiments provided support for the one gene–one enzyme hypothesis
  - The hypothesis states that the function of a gene is to dictate production of a specific enzyme
- Not all proteins are enzymes, so researchers later revised the hypothesis: one gene–one protein
  - For example: Keratin (the structural protein of animal hair) and insulin are non-enzyme proteins
- Many proteins are composed of several polypeptides, each of which has its own gene
  - For example: hemoglobin contains two kinds of polypeptides and thus two genes encoding it
  - So, This hypothesis is now restated as the **one gene-one polypeptide hypothesis**
- **Genes** provide the instructions for making specific proteins, but a gene does not build a protein directly
  - The bridge between DNA and protein synthesis is **RNA**
- RNA differs from DNA that it is **single** stranded, its sugar is **ribose** and use **U instead of T**
- Nucleic acids and proteins are polymers with specific sequences of monomers that convey information

- **Transcription**
  - It is the **synthesis of RNA** using information in the DNA
    - The information is transcribed or rewritten from DNA to RNA
  - Transcription produces **messenger RNA (mRNA)**
    - It carries a genetic message from the DNA to the protein-synthesizing machinery of the cell
- **Translation**
  - It is the **synthesis of a polypeptide** using the information in the mRNA
  - Translating the nucleotide sequence of mRNA into amino acid sequence of a polypeptide
- **Ribosomes** → the **sites of translation** → they are molecular complexes that facilitate the orderly linking of amino acids into polypeptide chains

- Transcription and translation occur in **all organisms**
- The basic mechanics of transcription and translation are **similar** for bacteria and eukaryotes, but:
  - **Eukaryotic cells** have nuclei → **nuclear envelope separates** transcription from translation in space and time → **transcription** occurs in the **nucleus**, but the mRNA must be transported to the cytoplasm (ribosomes) for translation
  - **Bacteria** do not have nuclei → **No nuclear envelope** → allowing translation of mRNA begin before transcription has finished



(a) Bacterial cell

- Notice that before a eukaryotic RNA leaves the nucleus, they are **modified** in various ways to produce the final functional mRNA
  - ➢ **Primary transcript (pre-mRNA):** is the **initial RNA** transcript from any gene (prior to processing)

- The central dogma is the concept that cells are governed by a cellular chain of command:

- **How are the instructions for assembling amino acids into proteins encoded in DNA?**
  - There are 20 amino acids, but there are only four nucleotide bases in DNA
  - A **triplet** code (three nucleotides of DNA) encodes for a certain amino acid
  - The words of a gene are transcribed into complementary words of mRNA → Then translated into a chain of amino acids, forming a polypeptide

- For each gene, we have **two DNA strands** and one of them will be transcribed into mRNA:
  - ♦ **Template strand**
  - Is the strand that will be **transcribed** → **complementary to the mRNA**

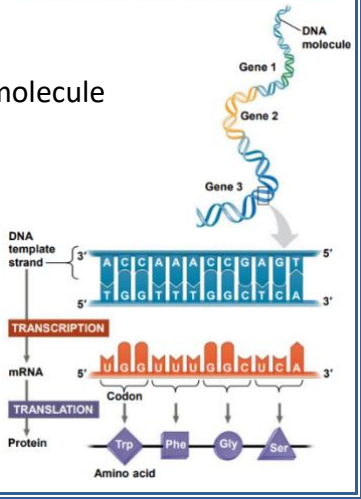
  - It is always the same strand for a given gene
    - ➢ The strand used as the template is determined by the **orientation of the enzyme** that transcribes the gene → depends on the **DNA sequences** associated with the gene

  - ♦ **Non-template strand**
  - Is the **identical strand to mRNA** (except U instead T & ribose instead of deoxyribose in mRNA)
  - It is called **coding strand** because the sequence of nucleotides of this strand is identical to the mRNA

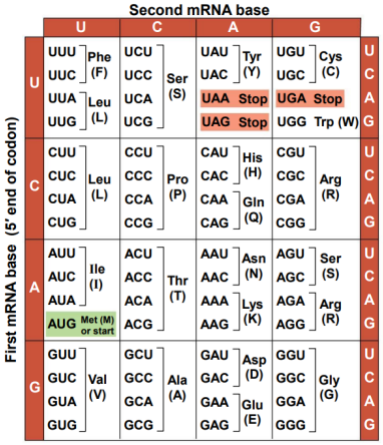
  - The sequence of the coding strand is used when a gene's sequence is reported

- **RNA** molecule is synthesized in an **antiparallel** direction to the **template** strand of DNA
  - ➢ The nucleotide triplet ACC along the DNA template strand (written as 3'-ACC-5') provides a template for 5'-UGG-3' in the mRNA molecule

- **Codons:** The **mRNA base triplets,** each codon specifies a certain amino acid
  - ➢ The number of nucleotides making up a genetic message must be 3 times the number of amino acids in the protein product
  - ✓ For example, 300 nucleotides are required along an mRNA strand to code 100 amino acids along the polypeptide chain



- **Marshall Nirenberg deciphered the first codon**
  - Nirenberg synthesized an artificial mRNA containing only one codon (**UUU**) over and over
  - When the poly-U polynucleotide is added to a test-tube mixture containing amino acids and ribosomes → it is translated into a polypeptide containing many units **phenylalanine** (Phe or F)

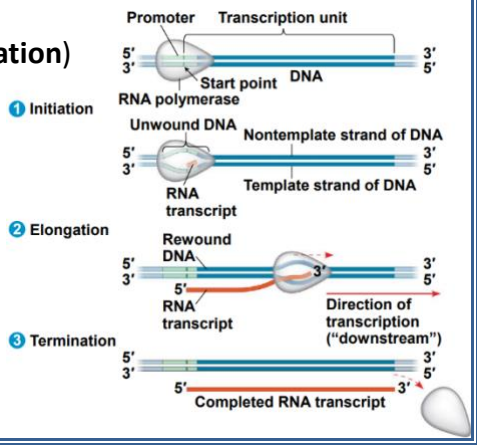


- There are 64 codon are divided into:
  - **61 code for amino acids**
    - ➢ including **AUG** → encodes **methionine** (Met, or M) and functions as a **start codon, or initiation codon** → start the translation
  - **3 code are stop codons** (UAG,UGA,UAA) → signals to end translation
- Polypeptides begin with Met because it is encoded by the start codon but an enzyme may remove this starter amino acid from the chain
- The genetic code is **redundant** → more than one codon may specify a particular amino acid
- But **not ambiguous** → no codon specifies more than one amino acid
- In many cases, codons that encodes for a particular amino acid differ only in the third nucleotide base of the triplet (GAA and GAG both specify glutamic acid)
- The message must be read in the correct reading frame as a series of **non-overlapping three-letter** words and not as a series of overlapping words

❖ 17.2: [Transcription is the DNA-directed synthesis of RNA: a closer look]

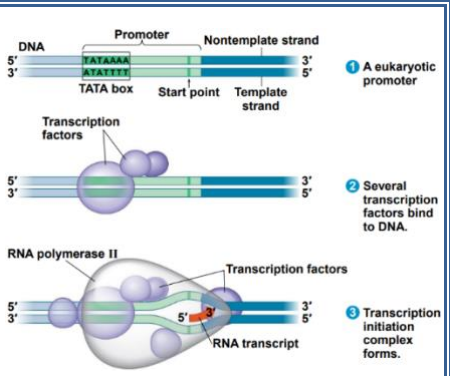
- Transcription is the **first** stage of gene expression
- RNA synthesis is catalyzed by **RNA polymerase**, which **pries the DNA strands apart** and **joins the RNA nucleotides together**
  - RNA polymerase does **not need any primer**
  - It assembles a polynucleotide only in its **5'→ 3' direction**, adding nucleotides to **its 3' end**
- **Promoter:** The DNA sequence where RNA polymerase attaches and initiates transcription
  - ➢ It extends several dozens of nucleotides **upstream (before)** from the coding region
- **Terminator:** The sequence signaling the end of transcription in bacteria
- **Transcription unit:** The stretch of DNA that is transcribed
- **Bacteria** have a **single type of RNA polymerase** that synthesizes mRNA and other types of RNA that (such as ribosomal RNA)
- **Eukaryotes** have **at least three types of RNA polymerase**, the one used for pre-mRNA synthesis is called **RNA polymerase II**
- The three stages of transcription (**Initiation → Elongation → Termination**)

1) RNA Polymerase Binding and Initiation of Transcription



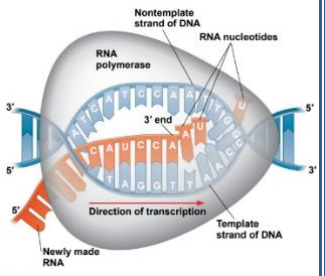
- **In bacteria** a part of the RNA polymerase itself specifically recognizes and **binds** to the promoter
- **In eukaryotes** the transcription factors mediate the binding of RNA polymerase and the initiation of transcription
  - ➢ Transcription factors are **proteins** that aid RNA polymerase

- **Transcription initiation complex:** Transcription factors + RNA polymerase II bound to a promoter
  - The protein-protein interaction between RNA polymerase II and transcription factors is a interactions which controls eukaryotic transcription
  - **TATA box:** A sequence of the promoter is crucial in forming the initiation complex



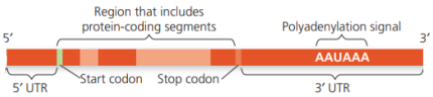
2) Elongation of the RNA Strand

- As RNA polymerase moves along the DNA, it untwists the double helix, exposes 10 to 20 bases at a time
- The enzyme adds nucleotides to the 3' end of the growing RNA molecule
- Behind the polymerase, the new RNA peels away from the template strand, which re-forms a double helix with the non-template strand
- Transcription progresses at a rate of 40 nucleotides per second in eukaryotes
- **A gene can be transcribed simultaneously by several RNA polymerases, Why?**
  - increasing the amount of mRNA transcribed from it, which helps the cell make the encoded protein in large amounts



3) Termination of Transcription

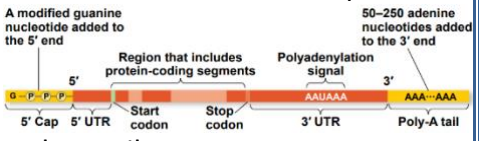
- In **bacteria** the polymerase stops transcription at the end of the **terminator** causing the polymerase to detach from the DNA & release the transcript → mRNA can be translated **without further modification**
- In **eukaryotes** RNA polymerase II stop transcription when reaches the **polyadenylation signal sequence** then the RNA is released 10–35 nucleotides downstream (after) this polyadenylation sequence
  - **Polyadenylation signal:** It is a sequence on the DNA which specifies a polyadenylation signal (AAUAAA) in the pre-mRNA



- Once this stretch of six RNA nucleotides appears, it is immediately bound by certain proteins in the nucleus which cut the RNA transcript free from the polymerase, releasing the pre-mRNA

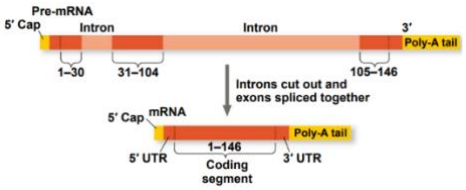
❖ 17.3: [Eukaryotic cells modify RNA after transcription]

- In **RNA processing** → enzymes in the **eukaryotic nucleus** modify pre-mRNA before the genetic messages are dispatched (sent) to the cytoplasm
- During RNA processing, both ends of the primary transcript are altered & certain interior sections of the molecule are cut out and the remaining parts spliced together
- The **5' end** of pre-mRNA receives a modified nucleotide **5' cap**
  - **5' cap:** It is a modified form of a **guanine (G)** nucleotide added onto the **5' end** after transcription of the first 20–40 nucleotides

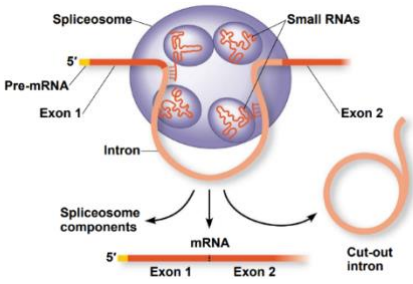


- The **3' end** gets a **poly-A tail**
  - An enzyme adds 50–250 more adenine (A) nucleotides, forming a poly-A tail
- These modifications (The 5' cap and poly-A tail) share several **functions**:
  - They seem to facilitate the **export of mature mRNA to the cytoplasm**
  - They **protect mRNA** from hydrolytic enzymes
  - They **help ribosomes attach to the 5' end** once the mRNA reaches the cytoplasm

- **UTRs:** are parts of the mRNA that will not be translated into protein, but they have other functions, such as **ribosome binding**
- Most eukaryotic genes and their RNA transcripts have long noncoding stretches of nucleotides that lie between coding regions
  - The non-coding regions → **intervening sequences**, or **introns**
  - The coding (expressed) regions → **exons**

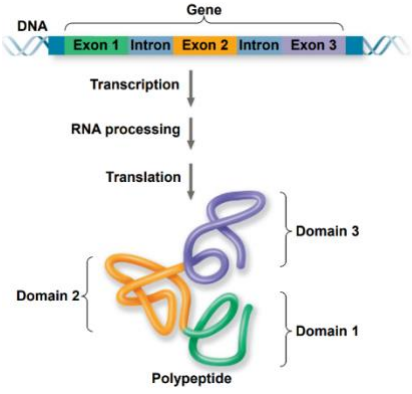


- **RNA splicing:** is a process which large portions of the RNA molecules are **removed (introns)** and the remaining portions are **reconnected (exons)**
  - RNA polymerase II transcribes both introns and exons from the DNA, but the mRNA molecule that enters the cytoplasm undergoes RNA splicing → which removes introns and joins exons, creating an mRNA molecule with a continuous coding sequence



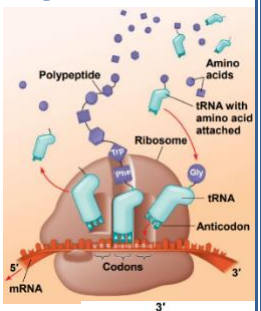
- The removal of introns is accomplished by **spliceosome**
  - **Spliceosome:** a large complex made of proteins and small RNAs that recognize the splicing sites
  - The **RNAs** of the spliceosome also catalyze the splicing reaction
- **Ribozymes:** Catalytic RNA molecules that function as enzymes and can splice RNA
- RNA splicing may occur without proteins or even additional RNA molecules
  - The intron RNA can function as a ribozyme and catalyze its own excision (self splicing)
  - For example, in the **ciliate protist Tetrahymena**, self-splicing occurs in the production of ribosomal RNA (**rRNA**), the pre-rRNA actually removes its own introns
- Three properties of RNA enable it to function as an enzyme:
  - It can form a **3D structure** because it can base-pair with itself complementary region
  - Some **bases in RNA contain functional groups** that may participate in catalysis
  - RNA may **hydrogen-bond** with other nucleic acid molecules (RNA or DNA)
- Complementary base pairing between the RNA of the spliceosome and pre-mRNA precisely locates the region where the ribozyme catalyzes splicing

- **The Importance of introns:**
- Some introns contain sequences that may **regulate gene expression**
- Some genes can encode more than one kind of polypeptide, depending on which segments are treated as exons during splicing ➔ **alternative RNA splicing**
  - So, the number of proteins an organism can produce is **much greater** than its number of genes

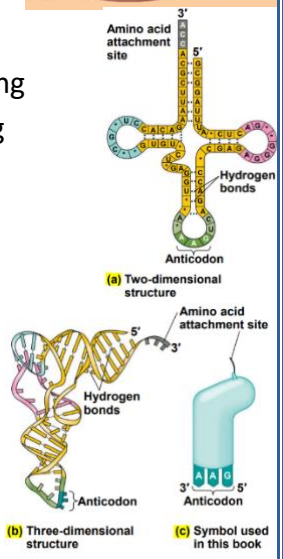


- **Domains:** Discrete **regions** in the proteins architecture
  - Different exons can code for the different domains in a protein
- Exon shuffling may result in the evolution of new proteins
  - Introns increase the probability of producing new combinations of exons and proteins with altered structure and function

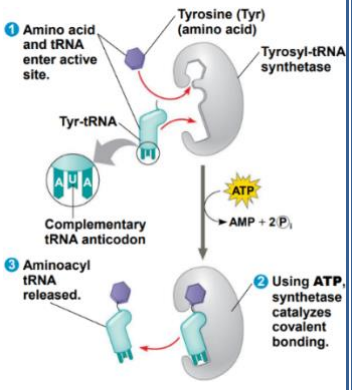
❖ 17.4: [Translation is the RNA-directed synthesis of a polypeptide: a closer look]



- Genetic information flows from mRNA → protein through the process of **translation**
- **Transfer RNA (tRNA):** It is the translator molecule which **transfer an amino acid** from the cytoplasm to the growing polypeptide in a ribosome during translation
  - ➢ A cell keeps its cytoplasm stocked with all 20 amino acids, either by synthesizing them or by taking them from the surrounding
  - ➢ Each tRNA molecule enables translation of a given mRNA codon into a certain amino acid
- A tRNA molecule consists of a single RNA strand that is only about 80 nucleotides long
  - Has a 3D structure (roughly L-shaped) → due to the complementary base pairing
  - Flattened into one plane to reveal its base pairing → looks like a **cloverleaf**
  - 5' and 3' both located near one end of the structure
    - ✓ **3' end** → acts as the attachment site for an **amino acid**



- Each tRNA has an **anticodon** on the other end which base-pairs with a **complementary codon on mRNA**
- Anticodons (3'→ 5') align properly with codons (5'→ 3')
  - ➢ For example: the mRNA codon 5'-GGC-3', which is translated as the amino acid glycine → the tRNA has 3'-CCG-5' as its anticodon and carries glycine at its other end
- Codon by codon, the genetic message is translated as tRNA position each amino acid in the order prescribed, and the ribosome adds that amino acid onto the growing polypeptide chain
- Transfer RNA molecules are transcribed from DNA templates
  - In **eukaryotic** cells tRNA is made in the nucleus and then travels to the cytoplasm, where it function
- In both bacterial and eukaryotic cells → each tRNA molecule is used repeatedly
- Accurate translation requires two steps:
  - ♦ **A correct match between a tRNA and an amino acid**

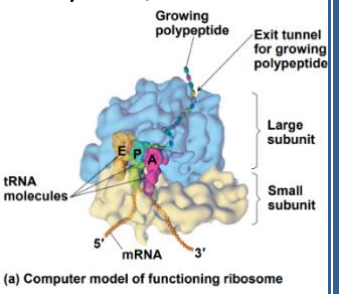


- done by the enzyme **aminoacyl-tRNA synthetase:** an enzyme catalyzes the covalent attachment (joins) a given **amino acid** to an appropriate **tRNA**
  - ➢ Its active site fits only a specific combination of amino acid and tRNA
- There is **20 different synthetases** (one for each amino acid)
  - The resulting tRNA is called **aminoacyl tRNA** or **charged tRNA**
  - This process is driven by the hydrolysis of ATP
  - ♦ **A correct match between the tRNA anticodon and an mRNA codon**
- **Flexible pairing at the third base** of a codon is **wobble** → it allows some tRNAs (attached to certain amino acids) to bind to more than one codon (coding the same amino acid)

❖ Ribosomes and their structure

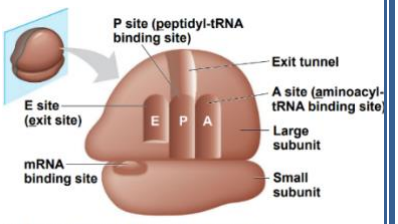
- Ribosomes facilitate specific coupling of tRNA anticodons with mRNA codons in protein synthesis
- A ribosome consists of **two ribosomal subunits**: large and small subunits are made of proteins and ribosomal RNA (rRNA)
  - ➢ rRNAs are primarily responsible for both the structure and the function of the ribosome
  - ➢ **rRNA is the most abundant type of cellular RNA**

- Bacterial and eukaryotic ribosomes are somewhat similar but have significant differences:
  - In **eukaryotes**, the subunits are made in the **nucleolus** and then exported to the cytosol, but in bacteria they are synthesized in the cytosol
  - Eukaryotic ribosomes have **4 rRNA**
  - Bacterial ribosomes have **3 rRNA**
  - Eukaryotic ribosomes are slightly larger



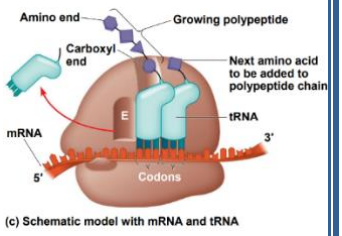
(a) Computer model of functioning ribosome

- In both bacteria and eukaryotes, large and small subunits join to form a functional ribosome only when attached to an mRNA molecule
- The differences are medically significant
  - Certain **antibiotic drugs** can inactivate bacterial ribosomes without affecting eukaryotic ribosomes
  - These drugs, including **tetracycline and streptomycin**, are used to combat bacterial infections
- **A ribosome has three binding sites for tRNA**
  1. **The P site (peptidyl tRNA binding site)**
     - Holds the tRNA that carries the growing polypeptide chain
  2. **The A site (aminoacyl-tRNA binding site)**
     - Holds the tRNA that carries the next amino acid to be added to the chain
  3. **The E site**
     - It is the exit site, where discharged tRNAs leave the ribosome



(b) Schematic model showing binding sites

- The ribosome holds the tRNA and mRNA in close proximity and positions the new amino acid so that it can be added to the **carboxyl end** of the growing polypeptide → it then catalyzes the formation of the peptide bond
- As the polypeptide becomes longer, it passes through an exit tunnel in the ribosome's large subunit → When the **polypeptide** is complete, it is **released through the exit tunnel**
- **rRNA** is the main constituent of the A and P sites and of the interface between the two subunits and it acts as the **catalyst** of peptide bond formation

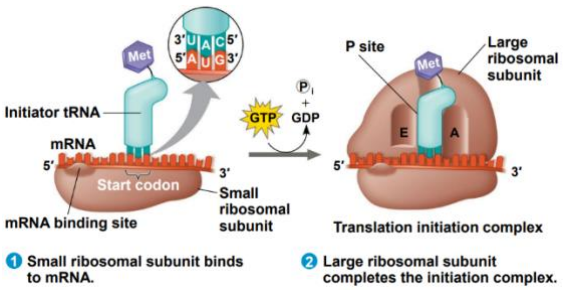


(c) Schematic model with mRNA and tRNA

- The three stages of translation (Initiation → Elongation → Termination)
  - All three stages require protein (factors) that aid in the translation process
  - **Energy** is required for some steps, provided by the hydrolysis of guanosine triphosphate (**GTP**)

♦ Ribosome Association and Initiation of Translation

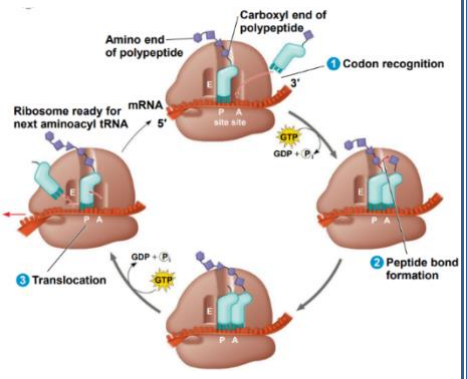
- A small ribosomal subunit binds with mRNA → Then it moves along the mRNA until reaching (AUG)
- The start codon (AUG) signals the start of translation → a special initiator tRNA which carries (Met)
  - In bacteria, the small subunit binds the mRNA at a **specific RNA sequence upstream of the AUG**
  - In eukaryotes, the small subunit with the initiator tRNA (already bound) binds to the **5' cap** of the mRNA
- **After the binding** of the small ribosomal subunit, tRNA (carrying Met) and mRNA → large ribosomal subunit is attached
  - **Initiation factors:** proteins bring the large subunit completing the translation initiation complex



- This step spends energy obtained by hydrolysis of a GTP molecule to form the initiation complex
- At the completion of the initiation process, the initiator tRNA sits in the P site of the ribosome, and the A site is ready for the next aminoacyl tRNA

♦ Elongation of the Polypeptide Chain

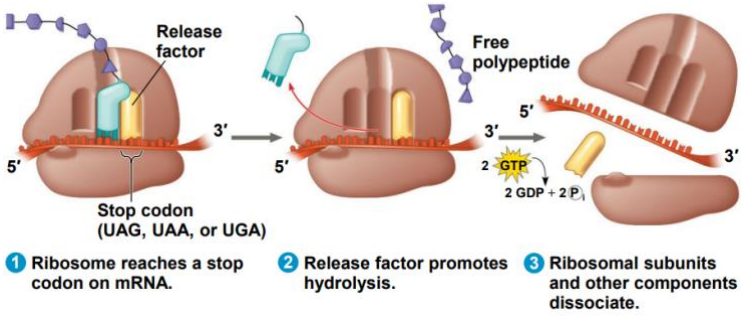
- During elongation, amino acids are added one by one to the **C-terminus** of the growing chain
  - Each addition involves proteins called **elongation factors**
  - The polypeptide is always synthesized in one direction, from the initial methionine at the **amino end (N-terminus) toward** the final amino acid at the **carboxyl end (C-terminus)**
- Elongation occurs in three steps:
  - **codon recognition → peptide bond formation → translocation**



- Energy expenditure (hydrolysis of GTP) occurs in the first and third steps (codon recognition & translocation)
- Translation proceeds along the **mRNA in a 5' → 3' direction**
- The ribosome & mRNA move **uni-directionally** (relative to each other)
- The empty tRNAs released from the E site return to the cytoplasm where they will be reloaded with the appropriate amino acid

♦ Termination of Translation

- Elongation continues until a **stop codon** in the mRNA reaches the A site of the ribosome
  - The nucleotide base triplets **UAG, UAA, and UGA (stop codons)** → do not code for amino acids but instead act as signals to stop translation
- **Release factor:** It is a protein shaped like an aminoacyl tRNA, binds directly to the stop codon in the A site → causing the **addition of a water** molecule instead of an amino acid
  - So, breaking (hydrolysis) the bond between the completed polypeptide and the tRNA in the P site, releasing the polypeptide through the exit tunnel
- The translation assembly then comes apart in a multistep process, aided by other protein factors
- Breakdown of the translation assembly requires the hydrolysis of **2 more GTP molecules**



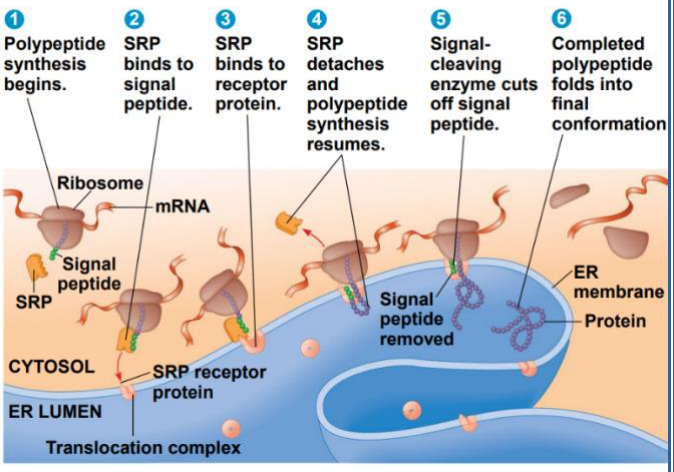
- Often translation is not sufficient to make a functional protein → Polypeptide chains are modified after translation or targeted to specific sites in the cell
- During its synthesis, a polypeptide chain begins to coil and fold spontaneously into a specific 3D shape with secondary and tertiary structure
  - A gene determines → primary structure → determines secondary & tertiary → determines the shape

- **Post-translational modifications** may be required before the protein can begin doing its particular job :
  - Chemical modifications by the attachment of sugars, lipids, phosphate groups
  - Enzymes may remove one or more amino acids from the **leading (amino) end** of the polypeptide
  - Enzymatically cleaved the polypeptide chain into two or more pieces
  - Join 2 or more polypeptides that are synthesized separately

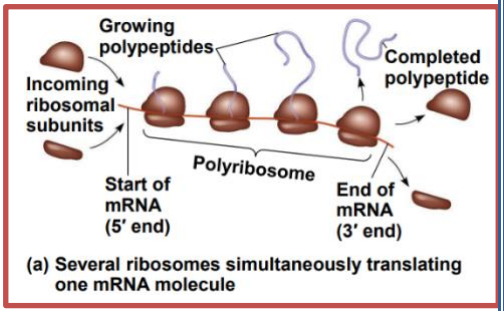
- Two populations of ribosomes are evident in cells:
  - **Free ribosomes** → in the cytosol → synthesize proteins that stay and function there
  - **Bound ribosomes** → attached to the ER or to the nuclear envelope → make proteins of the endomembrane system and secreted proteins
    - Ribosomes are identical and can switch from free to bound

- Polypeptide synthesis **always begins in the cytosol** in a free ribosome
- Then the synthesis can be completed in the cytosol (free) or on the ER (bound)
- Synthesis finishes in the cytosol unless the polypeptide **signals** the ribosome to attach to the ER
  - **Signal peptide:** a sequence of about 20 amino acids at or near the leading end (N-terminus) of the polypeptide → directs the polypeptide to the ER or for secretion
  - **Signal-recognition particle (SRP):** A protein-RNA complex recognizes the signal peptide as it emerges from the ribosome → then it escorts the ribosome to SRP receptor on ER
  - SRP receptor is a protein built into the ER membrane and it is a part of a multiprotein **translocation complex**
  - Polypeptide synthesis continues and the growing polypeptide snakes across the membrane into the ER lumen via a protein pore

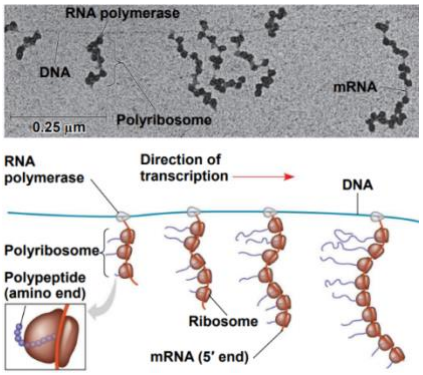
- Then if the polypeptide is intended to:
  - be **secreted** from the cell → the polypeptide is released into the solution within the ER lumen then forming a vesicle for secretion
  - be a **membrane protein** → it remains partially embedded in the ER membrane → then travel by a vesicle to the intended membrane
- Other kinds of signal peptides are used to target polypeptides of organelles that are not part of the endomembrane system



- When a polypeptide is required in a cell → the need is for many copies, not just one
- Many copies can be rapidly obtained by:
  - **Transcribing multiple mRNAs from the same gene**
  - **Multiple ribosomes can translate a single mRNA** simultaneously forming a **polyribosome (or polysome)** enabling the cell to rapidly make many copies of a polypeptide

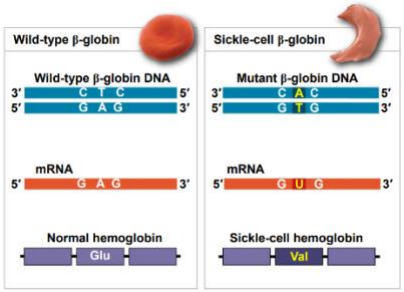


- **Note:**
  - ✓ In bacteria, **transcription and translation are coupled directly** in a streamlined process, and RNA is not processed before translation
  - ✓ In eukaryotes, **nuclear envelope separates the processes of transcription and translation** and **RNA undergoes processing before leaving the nucleus**



❖ 17.5: [Mutations of one or a few nucleotides can affect protein structure and function]

- Mutations are changes in the genetic information of a cell
- Mutations, are responsible for the **huge diversity** of genes found among organisms because mutations are the ultimate **source of new genes**
- If a mutation occurs in a gamete (germ cell), it may be transmitted to future generations
- Mutations can be either:
  - ➢ **Large-scale** mutations affecting a large segment in the **chromosome**
  - ➢ **Small-scale** mutations affecting only a **few nucleotides** such as point mutations
- **Point mutations:** are changes in just one nucleotide pair of a gene
- If the mutation has an adverse effect on the phenotype of a person, the mutant condition is referred to as a genetic disorder or hereditary disease. For example:
  - **Sickle-cell disease:** A mutation of a **single nucleotide** pair in the gene that encodes the **β-globin** polypeptide of hemoglobin
  - **Familial cardiomyopathy:** a heart condition leads to sudden death
- The change of a single nucleotide in a DNA template strand can lead to the production of an abnormal protein

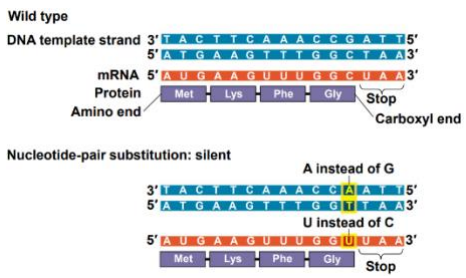


❖ Types of Small-Scale Mutations

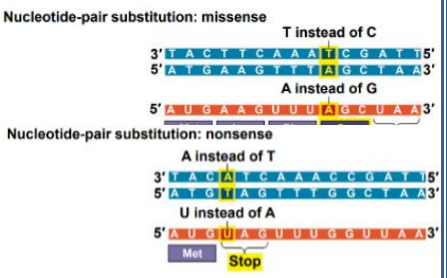
- They can be divided into two general categories:
  - Single nucleotide-pair **substitutions**
  - Nucleotide-pair **insertions or deletions**

• Substitutions

- A nucleotide-pair substitution **replaces** one nucleotide and its partner with another pair of nucleotides
- It can be classified into:
  - ➢ **Silent mutations:** have **no effect on the amino acid** produced by a codon because of redundancy in the genetic code → translated into the same amino acid)
    - Usually occur in the **wobble position (3rd nucleotide)**
    - Some silent mutations may indirectly affect where or at what level the gene gets expressed

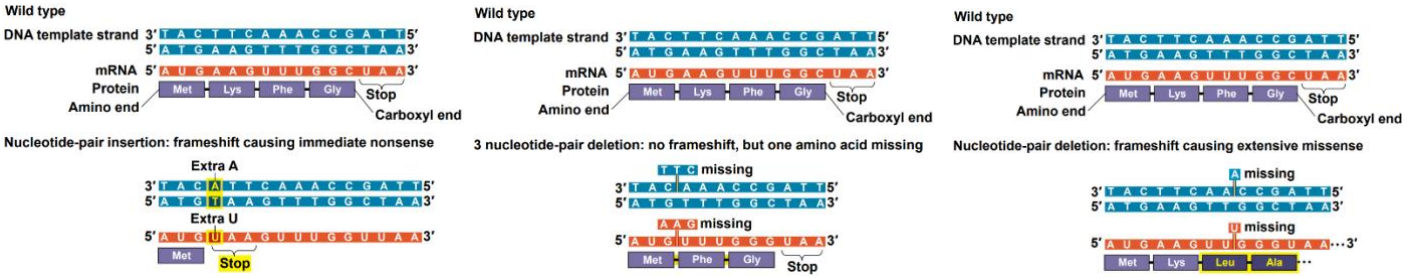


- **Missense mutations:** still code for an amino acid, but **<u>not the correct amino acid</u>** (may have little effect on the protein)
- **Nonsense mutations:** change an amino acid codon **<u>into a stop codon</u>** → most lead to a nonfunctional (premature) protein because its translation is terminated prematurely



Insertions and Deletions

- Insertions and deletions are additions or losses of nucleotide pairs in a gene
- These mutations often have a <u>more disastrous effect on the resulting protein than substitutions</u>
- **Frameshift mutations:** They occur whenever the number of nucleotides inserted or deleted is **<u>not a multiple of three</u>** → so they alter the reading frame



- **Spontaneous mutations** can occur during errors in <u>DNA replication, recombination, or repair</u>
- **Mutagens** are <u>physical or chemical agents</u> that can cause **non-spontaneous mutations**
  - **Physical mutagens** → include **X-rays**, **high-energy radiation** and **ultraviolet (UV)** light
  - **Chemical mutagens** → include **nucleotide analogs** are chemicals that pair incorrectly during DNA replication → they insert themselves into the DNA and distorting the double helix
- Most **carcinogens** (cancer-causing chemicals) are **mutagens**, and most mutagens are carcinogenic

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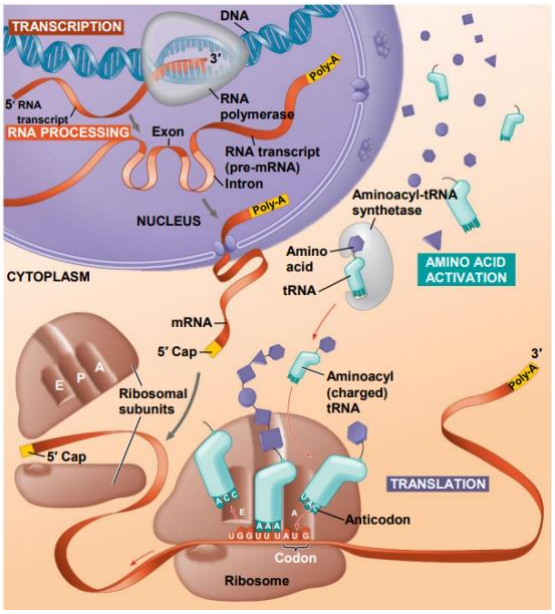
- The idea of the gene has evolved through the history of genetics:
- A gene is considered as → A discrete unit of inheritance → A region of specific nucleotide sequence in a chromosome → A DNA sequence that codes for a specific polypeptide chain

- **Gene:** It is a region of DNA that can be expressed to produce a final functional product that is either a polypeptide or an RNA molecule
  - A given type of cell expresses only a subset of its genes
  - Proteins in turn bring about an organism's observable phenotype



Past Papers

1. **Which is the energy rich molecule required for the initiation of translation?**
   A. ATP
   B. GTP
   C. CTP
   D. AMP
   E. Glucose

   Answer: B

2. **Which of the following molecules is not normally found in a ribozyme?**
   A. Uracil
   B. Thiamine
   C. guanine
   D. Cytosine
   E. none of the following

   Answer: B

3. **As a ribosome translocate along an mRNA molecule by one codon, which of the following occurs?**
   A. The tRNA that was in the A site moves into the P site
   B. the tRNA that was in the P site moves into the A site
   C. the tRNA that was in the A site moves into the E site and is released
   D. the tRNA that was in the A site departs from the ribosome via a tunnel
   E. the polypeptide enters the E site

   Answer: A

4. **During normal translation, where would you expect to find tRNA attached to single amino acid?**
   A. E site
   B. P site
   C. A site
   D. Both E and P
   E. Both A and P

   Answer: E

5. **Which of the following components does not form part of the transcription initiation complex in eukaryotic promoter?**
   A. TATA box
   B. Start point
   C. Transfer RNA
   D. Transcription factors
   E. RNA polymerase

   Answer: C

6. **After mRNA (5' -AUGUAUACAGCACAUCGAUGACAA- 3') translation is completed, what will be the first amino acid and the total number of amino acids in the synthesized polypeptide?**
   A. Methionine. 9 amino acids
   B. Methionine, 7 amino acids
   C. arginine, 8 amino acids
   D. methionine, 6 amino acids
   E. methionine, 8 amino acids

   Answer: D

7. What is a ribozyme?

A. A mutated ribosome
B. An RNA with enzymatic activity
C. A DNA sequence near the promoter that assists in the binding of RNA polymerase
D. A biological catalyst consisting of DNA
E. An enzyme that holds open the DNA double helix while RNA polymerase adds nucleotides

Answer: B

8. Aminoacyl-tRNA synthetases:

A. Binds the correct amino acid to the empty tRNA
B. Binds the tRNA to the anticodon
C. Binds the amino acids together
D. Binds the tRNA to the mRNA
E. Cuts and assemble the tRNA molecule

Answer: A

9. Transcription in eukaryotes requires which of the following in addition to RNA polymerase?

A. The protein product of primer
B. Start and stop codons
C. Ribosomes
D. Transcription factors
E. Aminoacyl synthetase

Answer: D

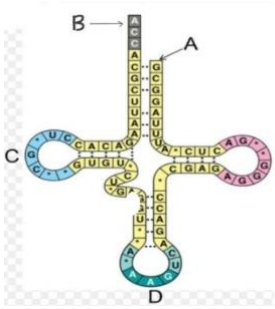
10. Once transcribed, eukaryotic mRNA typically undergoes alterations that include:

A. Union the ribosomes
B. Fusion into circular forms known as plasmid
C. Linkage to histone molecules
D. Excision of introns
E. Fusion with other newly transcribed mRNA

Answer: D

11. Which letter represent the amino acid attachment site?

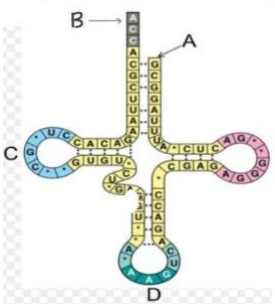
A. A
B. B
C. C
D. D
E. None of the above



Answer: B

12. The figure represents tRNA that recognizes and binds the amino acid phenylalanine. Which codon on the mRNA strand codes for this amino acid?

A. UGG
B. GUG
C. UUC
D. CUU
E. CAU



Answer: C

13. What are the components of a spliceosome?

A. DNA and protein
B. protein and small nuclear RNA
C. Exons and introns
D. proteins and mRNA
E. coding and noncoding RNAs

Answer: B

14. The transcription factors can:

A. Regulate the synthesis of DNA in response to a signal
B. Regulate the release of calcium from the endoplasmic reticulum
C. Compose the spliceosome which facilitates mRNA splicing
D. Mediate the binding of RNA polymerase to the parental strand of DNA
E. Facilitate the termination of the mRNA transcript

Answer: D

15. As a molecule of mRNA is moved through a ribosome, _____ are_____into_____, one by one until the top codon is reached

A. codons, translated, amino acids
B. codons, transcribed, amino acids
C. codons, replicated , amino acids
D. codons, translated , nucleotides
E. codons, transcribed, nucleotides

Answer: A

16. SRP molecules function involve:

A. Enhance the progress of translation by the ribosome
B. Dock the ribosome onto Golgi apparatus membrane
C. Arresting synthesis of a nascent membrane protein
D. Targeting proteins to ER
E. Acting as a chaperone

Answer: D

17. How many nucleotides are needed to code for a protein with 450 amino acids?

A. 450 × 1
B. 450 × 2
C. 450 × 3
D. 450 × 4
E. We cannot determine

Answer: C

18. Which component is the last to join the initiation complex during the initiation of translation?

A. the mRNA molecule
B. the small ribosomal subunit
C. the large ribosomal subunit
D. the initiator tRNA
E. both B and C

Answer: C

19. A nucleotide-pair substitution is

A. insertion of nucleotide pair in a gene
B. deletion of nucleotide pair in a gene
C. replacement of nucleotide pair with another pair of nucleotides
D. replacement of nucleotide pair with nucleotide analogs
E. C and D are correct

Answer: C

20. Sickle-cell disease is the result of which kind of mutation?

A. Point mutation
B. Silent mutation
C. Missense mutation
D. Nonsense mutation

Answer: A

21. During elongation which site in the ribosome represents the location where a codon being read?

A. P site
B. A site
C. The small ribosomal subunit
D. mRNA binding site

Answer: B

22. What is the effect of a nonsense mutation in a gene?

A. It changes an amino acid in the encoded protein
B. It has no effect on the amino acid sequence of the encoded protein
C. It introduces a stop codon into the mRNA, causes translation to be terminated prematurely
D. It alters the reading frame of the mRNA that prevents introns from being excised.

Answer: C

23. The change in a nucleotide pair may transform one codon into another that is translated into the same amino acid is described as……

A. silent mutation
B. nonsense mutation
C. missense mutation
D. frameshift mutation
E. all of the above

Answer: A

24. Which components not directly involved in translation:

A. mRNA
B. DNA
C. RNA
D. Ribosomes
E. GTP

Answer: B

25. Frameshift mutations result from:

A. Addition or deletion of nucleotides
B. Introducing a stop codon into the mRNA, causes translation to be terminated prematurely
C. Changing an amino acid in the encoded protein
D. It has no effect on the amino acid sequence of the encoded protein

Answer: A

26. The 5' end of pre-MRNA is modified by addition of:

A. A cap
B. An intron
C. An exon
D. Poly-A tail
E. Dose not modified

Answer: A

27. Which of the following protect mRNA from degradation?

A. Poly-A tail
B. 5’ cap
C. Introns
D. Exons
E. A and B only

Answer: E

28. Processing of pre-mRNA into mRNA occur in :

A. Cytoplasm
B. Cytosol
C. Nucleus
D. Nucleolus
E. None of the above

Answer: C

تم بحمد الله

أراكم الفصل القادم في مادتي الفسيولوجي و السايتولوجي