

Translations is the RNA-directed synthesis of a polypeptide: *a closer look*

- In the process of translation, a cell interprets a series of codons along a mRNA molecule.
- **Transfer RNA (tRNA)** transfers amino acids from the cytoplasm's pool to a ribosome.
- The ribosome adds each amino acid carried by tRNA to the growing end of the polypeptide chain.
- During translation, each type of tRNA links a mRNA codon with the appropriate amino acid.
- Each tRNA arriving at the ribosome carries a specific amino acid at one end and has a specific nucleotide triplet, an **anticodon**, at the other.
- The anticodon base-pairs with a complementary codon on mRNA.
 - If the codon on mRNA is UUU, a tRNA with an AAA anticodon and carrying phenylalanine will bind to it.
- Codon by codon, tRNAs deposit amino acids in the prescribed order and the ribosome joins them into a polypeptide chain.
- Like other types of RNA, tRNA molecules are transcribed from DNA templates in the nucleus.
- Once it reaches the cytoplasm, each tRNA is used repeatedly
 - to pick up its designated amino acid in the cytosol,
 - to deposit the amino acid at the ribosome, and
 - to return to the cytosol to pick up another copy of that amino acid.
- A tRNA molecule consists of a strand of about 80 nucleotides that folds back on itself to form a three-dimensional structure.
 - It includes a loop containing the anticodon and an attachment site at the 3' end for an amino acid.
- Ribosomes facilitate the specific coupling of the tRNA anticodons with mRNA codons.
 - Each ribosome has a large and a small subunit.
 - These are composed of proteins and ribosomal RNA (rRNA), the most abundant RNA in the cell.

- After rRNA genes are transcribed to rRNA in the nucleus, the rRNA and proteins form the subunits in the nucleolus.
- The subunits exit the nucleus via nuclear pores.
- The large and small subunits join to form a functional ribosome only when they attach to an mRNA molecule.
- Each ribosome has a binding site for mRNA and three binding sites for tRNA molecules.
 - The **P site** holds the tRNA carrying the growing polypeptide chain.
 - The **A site** carries the tRNA with the next amino acid.
 - Discharged tRNAs leave the ribosome at the **E site**.
- Translation can be divided into three stages:
 - initiation
 - elongation
 - termination
- **Initiation** brings together mRNA, a tRNA with the first amino acid, and the two ribosomal subunits.
 - First, a small ribosomal subunit binds with mRNA and a special initiator tRNA, which carries methionine and attaches to the start codon.
 - *Initiation factors* bring in the large subunit such that the initiator tRNA occupies the P site.
- **Elongation** consists of a series of three step cycles as each amino acid is added to the proceeding one.
 1. During **codon recognition**, an *elongation factor* assists hydrogen bonding between the mRNA codon under the A site with the corresponding anticodon of tRNA carrying the appropriate amino acid.
 2. During **peptide bond formation**, an rRNA molecule catalyzes the formation of a peptide bond between the polypeptide in the P site with the new amino acid in the A site.
 3. During **translocation**, the ribosome moves the tRNA with the attached polypeptide from the A site to the P site.
 - The three steps of elongation continue codon by codon to add amino acids until the polypeptide chain is completed.

- **Termination** occurs when one of the three stop codons reaches the A site.
- A *release factor* binds to the stop codon and hydrolyzes the bond between the polypeptide and its tRNA in the P site.
- This frees the polypeptide and the translation complex disassembles.
- During and after synthesis, a polypeptide coils and folds to its three-dimensional shape spontaneously.
 - The primary structure, the order of amino acids, determines the secondary and tertiary structure.
- In addition, proteins may require *posttranslational modifications* before doing their particular job.
 - This may require additions like sugars, lipids, or phosphate groups to amino acids.
 - Enzymes may remove some amino acids or cleave whole polypeptide chains.
 - Two or more polypeptides may join to form a protein.

Point mutations can affect protein structure and function

- **Mutations** are changes in the genetic material of a cell (or virus).
- These include large-scale mutations in which long segments of DNA are affected (for example, translocations, duplications, and inversions).
- A chemical change in just one base pair of a gene causes a **point mutation**.
- If these occur in gametes or cells producing gametes, they may be transmitted to future generations.
- A point mutation that results in replacement of a pair of complimentary nucleotides with another nucleotide pair is called a **base-pair substitution**.
- Some base-pair substitutions have little or no impact on protein function.
 - In *silent mutations*, alterations of nucleotides still indicate the same amino acids because of redundancy in the genetic code.
 - Other changes lead to switches from one amino acid to another with similar properties.
 - Still other mutations may occur in a region where the exact amino acid sequence is not essential for function.

- Other base-pair substitutions cause a readily detectable change in a protein.
 - These are usually detrimental but can occasionally lead to an improved protein or one with novel capabilities.
 - Changes in amino acids at crucial sites, especially active sites, are likely to impact function.
- **Missense mutations** are those that still code for an amino acid but change the indicated amino acid.
- **Nonsense mutations** change an amino acid codon into a stop codon, nearly always leading to a nonfunctional protein.
- **Insertions and deletions** are additions or losses of nucleotide pairs in a gene.
 - These have a disastrous effect on the resulting protein more often than substitutions do.
- Unless these mutations occur in multiples of three, they cause a **frameshift mutation**.
 - All the nucleotides downstream of the deletion or insertion will be improperly grouped into codons.
 - The result will be extensive missense, ending sooner or later in nonsense - premature termination.
- Mutations can occur in a number of ways.
 - Errors can occur during DNA replication, DNA repair, or DNA recombination.
 - These can lead to base-pair substitutions, insertions, or deletions, as well as mutations affecting longer stretches of DNA.
 - These are called *spontaneous mutations*.
- **Mutagens** are chemical or physical agents that interact with DNA to cause mutations.
- Physical agents include high-energy radiation like X-rays and ultraviolet light.
- Chemical mutagens may operate in several ways.
 - Some chemicals are base analogues that may be substituted into DNA, but that pair incorrectly during DNA replication.
 - Other mutagens interfere with DNA replication by inserting into DNA and distorting the double helix.
 - Still others cause chemical changes in bases that change their pairing properties.
- Researchers have developed various methods to test the mutagenic activity of different chemicals.
 - These tests are often used as a preliminary screen of chemicals to identify those that may cause cancer.
 - This makes sense because most carcinogens are mutagenic and most mutagens are carcinogenic.

What is a gene? *revisiting the question*

- The Mendelian concept of a gene views it as a discrete unit of inheritance that affects phenotype.
- Morgan and his colleagues assigned genes to specific loci on chromosomes.
- We can also view a gene as a specific nucleotide sequence along a region of a DNA molecule.
- We can define a gene functionally as a DNA sequence that codes for a specific polypeptide chain.
- Transcription, RNA processing, and translation are the processes that link DNA sequences to the synthesis of a specific polypeptide chain.
- ***A gene is a region of DNA whose final product is either a polypeptide or an RNA molecule.***