Lecture 4. Translation of genetic information

Learning outcomes:

1. Explain the ribosome cycle and fidelity of translation.
2. Define the genetic code, tRNA, mRNA, codon, anticodon.
3. Describe the structure of tRNA and the mechanism of its charging.
4. Explain the scanning model of translation.
5. Explain the mechanism of translation and its phases.
6. Describe the structure of ribosomes and polysomes.

Translation, the synthesis of protein from RNA. Hereditary information is contained in the nucleotide sequence of DNA in a code. The coded information from DNA is copied faithfully during transcription into a form of RNA known as messenger RNA (mRNA), which is then translated into chains of amino acids. Amino acid chains are folded into helices, zigzags, and other shapes to form proteins and are sometimes associated with other amino acid chains.

The specific amounts of amino acids in a protein and their sequence determine the protein's unique properties; for example, muscle protein and hair protein contain the same 20 amino acids, but the sequences of these amino acids in the two proteins are quite different. If the nucleotide sequence of mRNA is thought of as a written message, it can be said that this message is read by the translation apparatus in "words" of three nucleotides, starting at one end of the mRNA and proceeding along the length of the molecule. These three-letter words are called codons. Each codon stands for a specific amino acid, so if the message in mRNA is 900 nucleotides long, which corresponds to 300 codons, it will be translated into a chain of 300 amino acids.

Translation takes place on ribosomes—complex particles in the cell that contain RNA and protein. In prokaryotes (organisms that lack a nucleus) the ribosomes are loaded onto the mRNA while transcription is still ongoing. The mRNA sequence is read three bases at a time from its 5' end toward its 3' end, and one amino acid is added to the growing chain from its respective transfer RNA (tRNA), until the complete protein chain is assembled. Translation stops when the ribosome encounters a termination codon, normally UAG, UAA, or UGA (where U, A, and G represent the RNA bases uracil, adenine, and guanine, respectively). Special release factors associate with the ribosome in response to these codons, and the newly synthesized protein, tRNAs, and mRNA all dissociate. The ribosome then becomes available to interact with another mRNA molecule.

Any one mRNA is translated by several ribosomes along its length, each one at a different stage of translation. In eukaryotes (organisms that possess a nucleus) ribosomes that produce proteins to be used in the same cell are not associated with membranes. However, proteins that must be exported to another location in the organism are synthesized on ribosomes located on the outside of flattened membranous chambers called the endoplasmic reticulum (ER). A completed amino acid chain is extruded into the inner cavity of the ER. Subsequently, the ER transports the proteins via small vesicles to another cytoplasmic organelle called the Golgi apparatus, which in turn buds off more vesicles that eventually fuse with the cell membrane. The protein is then released from the cell.

Translation has pretty much the same three parts, but they have fancier names: initiation, elongation, and termination.

Initiation ("beginning"): in this stage, the ribosome gets together with the mRNA and the first tRNA so translation can begin.

Elongation ("middle"): in this stage, amino acids are brought to the ribosome by tRNAs and linked together to form a chain.

Termination ("end"): in the last stage, the finished polypeptide is released to go and do its job in the cell.

The key components required for translation are mRNA, ribosomes, and transfer RNA (tRNA).

During translation, mRNA nucleotide bases are read as codons of three bases. Each ‘codon’ codes for a particular amino acid. Every tRNA molecule possesses an anticodon that is complementary to the mRNA codon, and at the opposite end lies the attached amino acid. tRNA molecules are therefore responsible for bringing amino acids to the ribosome in the correct order ready for polypeptide assembly

It is important to know that a single amino acid may be coded for by more than one codon. There are also specific codons that signal the start and the end of translation.

Aminoacyl-tRNA synthetases are enzymes that link amino acids to their corresponding tRNA molecules. The resulting complex is charged and is referred to as an aminoacyl-tRNA.

Initiation

For translation to begin, the start codon 5’AUG must be recognised. This is a codon specific to the amino acid methionine, which is nearly always the first amino acid in a polypeptide chain.

At the 5’ cap of mRNA, the small 40s subunit of the ribosome binds. Subsequently, the larger 60s subunit binds to complete the initiation complex. The next step (elongation) can now commence.

Elongation

The ribosome has two tRNA binding sites; the P site which holds the peptide chain and the A site which accepts the tRNA.

While Methionine-tRNA occupies the P site, the aminoacyl-tRNA that is complementary to the next codon binds to the A site, using energy yielded from the hydrolysis of GTP.

Methionine moves from the P site to the A site to bond to new amino acid there, and so the growth of the peptide has begun. The tRNA molecule in the P site no longer has an attached amino acid, and so leaves the ribosome.

The ribosome then translocates along the mRNA molecule to the next codon again using energy yielded from the hydrolysis of GTP. Now, the growing peptide lies at the P site and the A site is open for the binding of the next aminoacyl-tRNA, and the cycle continues. The polypeptide chain is built up in the direction from the N terminal (methionine) to the C terminal (the final amino acid).

Termination

One of the three stop codons enters the A site. No tRNA molecules bind to these codons so the peptide and tRNA in the P site become hydrolysed releasing the polypeptide into the cytoplasm.

The small and large subunits of the ribosome dissociate ready for the next round of translation.

The questions for self - control:

1. What is the genetic code and which properties it has?
2. What is biological translation? What are the main phases of translation? What happens at each phase?
3. What are the differences of translation process in eucariotes and procariotes?

Recommended readings:

1. Alberts et al., pp. 333-362;
2. Russell, pp. 102-130;
3. Weaver, pp. 522-601.