Review Article

DNA translation

S. Bavana Sri[1], R. Sarah Sathiyawathie[1]*, Deepa Gurunathan[2]

ABSTRACT

The process of translation can be seen as the decoding of instructions for making proteins, involving messenger RNA in transcription as well as transfer RNA. The genes in DNA encode protein molecules, which are the "workhorses" of the cell, carrying out all the functions necessary for life. For example, enzymes, including those that metabolize nutrients and synthesize new cellular constituents, as well as DNA polymerases and other enzymes that make the copies of DNA during cell division, are all proteins. In the simplest sense, expressing a gene means manufacturing its corresponding protein, and this multilayered process has two major steps.

KEY WORDS: Anticodons, Nucleotide, RNA polymerase

INTRODUCTION

The genes in DNA encode protein molecules, which are the "workhorses" of the cell, carrying out all the functions necessary for life. For example, enzymes, including those that metabolize nutrients and synthesize new cellular constituents, as well as DNA polymerases and other enzymes that make copies of DNA during cell division, are all proteins. In the simplest sense, expressing a gene means manufacturing its corresponding protein, and this multilayered process has two major steps. In the first step, the information in DNA is transferred to a messenger RNA (mRNA) molecule by way of a process called transcription. During transcription, the DNA of a gene serves as a template for complementary base pairing, and an enzyme called RNA polymerase II catalyzes the formation of a pre-mRNA molecule, which is then processed to form mature mRNA. The resulting mRNA is a single-stranded copy of the gene, which next must be translated into a protein molecule. During translation, which is the second major step in gene expression, the mRNA is "read" according to the genetic code, which relates the DNA sequence to the amino acid sequence in proteins.[1] Each group of three base pairs in mRNA constitutes a codon, and each codon specifies a particular amino acid (hence, it is a triplet code). The mRNA sequence is thus used as a template to assemble - in order - the chain of amino acids that form a protein.

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WHERE TRANSLATION OCCURS

Within all cells, the translation machinery resides within a specialized organelle called the ribosome. In eukaryotes, mature mRNA molecules must leave the nucleus and travel to the cytoplasm, where the ribosomes are located. On the other hand, in prokaryotic organisms, ribosomes can attach to mRNA while it is still being transcribed. In this situation, translation begins at the 5' end of the mRNA, while the 3' end is still attached to DNA.

In all types of cells, the ribosome is composed of two subunits: the large (50S) subunit and the small (30S) subunit (S, for Svedberg unit, is a measure of sedimentation velocity and, therefore, mass). Each subunit exists separately in the cytoplasm, but the two join together on the mRNA molecule. The ribosomal subunits contain proteins and specialized RNA molecules - specifically, ribosomal RNA (rRNA) and transfer RNA (tRNA). The tRNA molecules are adaptor molecules - they have one end that can read the triplet code in the mRNA through complementary base pairing and another end that attaches to a specific amino acid.[2] The idea that tRNA was an adaptor molecule was first proposed by Crick, codiscoverer

[1]Department of Research, Saveetha Dental College and Hospital, Saveetha Institute of Medical and Technical Sciences, Chennai, Tamil Nadu, India, [2]Department of Pedodontics, Saveetha Dental College and Hospital, Saveetha Institute of Medical and Technical Sciences, Chennai, Tamil Nadu, India

***Corresponding author:** Dr. R. Sarah Sathiyawathie, Department of Research, Saveetha Dental College and Hospital, Saveetha Institute of Medical and Technical Sciences, 162, Poonamallee High Road, Chennai - 600 077, Tamil Nadu, India. Phone: +91-9884156513. E-mail: dr.sarahrobin@gmail.com

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of DNA structure, who did much of the key work in deciphering the genetic code.[3]

Within the ribosome, the mRNA and aminoacyl-tRNA complexes are held together closely, which facilitate base pairing. The rRNA catalyzes the attachment of each new amino acid to the growing chain.

THE BEGINNING OF mRNA

Interestingly, not all regions of an mRNA molecule correspond to particular amino acids. In particular, there is an area near the 5' end of the molecule that is known as the untranslated region (UTR) or leader sequence. This portion of mRNA is located between the first nucleotide that is transcribed and the start codon (AUG) of the coding region, and it does not affect the sequence of amino acids in a protein. Hence, what is the purpose of the UTR? It turns out that the leader sequence is important because it contains a ribosome-binding site. In bacteria, this site is known as the Shine-Dalgarno box (AGGAGG), after scientists Shine and Dalgarno, who first characterized it. A similar site in vertebrates was characterized by Kozak and is thus known as the Kozak box. In bacterial mRNA, the 5' UTR is normally short; in human mRNA, the median length of the 5' UTR is about 170 nucleotides. If the leader is long, it may contain regulatory sequences, including binding sites for proteins, that can affect the stability of the mRNA or the efficiency of its translation.[4-6]

TRANSLATION OF mRNA

The translation of mRNA begins with the formation of a complex on the mRNA. First, three initiation factor proteins (known as IF1, IF2, and IF3) bind to the small subunit of the ribosome. This pre-initiation complex and a methionine-carrying tRNA then bind to the mRNA, near the AUG start codon, forming the initiation complex.

Although methionine (Met) is the first amino acid incorporated into any new protein, it is not always the first amino acid in mature proteins - in many proteins, Met is removed after translation. In fact, if a large number of proteins are sequenced and compared with their known gene sequences, Met (or formylmethionine) occurs at the N-terminus of all of them. However, not all amino acids are equally likely to occur second in the chain, and the second amino acid influences whether the initial Met is enzymatically removed. For example, many proteins begin with Met followed by alanine. In both prokaryotes and eukaryotes, these proteins have the Met removed so that alanine becomes the N-terminal amino acid. However, if the second amino acid is lysine, which is also frequently the case, Met is not removed (at least in the sample proteins that have been studied thus far). These proteins, therefore, begin with Met followed by lysine.[7]

THE ELONGATION PHASE

The next phase in translation is known as the elongation phase. First, the ribosome moves along the mRNA in the 5'-to-3' direction, which requires the elongation factor G, in a process called translocation. The tRNA that corresponds to the second codon can then bind to the A site, a step that requires elongation factors (in *Escherichia coli*, these are called EF-Tu and EF-Ts), as well as guanosine triphosphate (GTP) as an energy source for the process. On binding of the tRNA-amino acid complex in the A site, GTP is cleaved to form guanosine diphosphate and then released along with EF-Tu to be recycled by EF-Ts for the next round.

Next, peptide bonds between the now-adjacent first and second amino acids are formed through a peptidyl transferase activity. For many years, it was thought that an enzyme catalyzed this step, but recent evidence indicates that the transferase activity is a catalytic function of rRNA (Pierce, 2000). After the peptide bond is formed, the ribosome shifts or translocates, again, thus causing the tRNA to occupy the E site. The tRNA is then released to the cytoplasm to pick up another amino acid. In addition, the A site is now empty and ready to receive the tRNA for the next codon. This process is repeated until all the codons in the mRNA have been read by tRNA molecules, and the amino acids attached to the tRNAs have been linked together in the growing polypeptide chain in the appropriate order. At this point, translation must be terminated, and the nascent protein must be released from the mRNA and ribosome.[8]

TERMINATION OF TRANSLATION

There are three termination codons that are employed at the end of a protein-coding sequence in mRNA: UAA, UAG, and UGA. No tRNAs recognize these codons. Thus, in the place of these tRNAs, one of the several proteins, called release factors, binds and facilitates the release of the mRNA from the ribosome and subsequent dissociation of the ribosome.

COMPARING EUKARYOTIC AND PROKARYOTIC TRANSLATION

The translation process is very similar in prokaryotes and eukaryotes. Although different elongation, initiation, and termination factors are used, the genetic code is generally identical. As previously noted, in bacteria, transcription and translation take place simultaneously, and mRNAs are relatively short-lived. In eukaryotes, however, mRNAs have highly variable half-lives, are subjected to modifications, and

must exit the nucleus to be translated; these multiple steps offer additional opportunities to regulate the levels of protein production and thereby fine-tune gene expression.[9]

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