Module 12 / Protein Synthesis

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Describe what post-transcriptional modification must take place before translation.	Define the role of each RNA molecule used in translation.	Distinguish between prokaryotic and eukaryotic translation.
Define the genetic code.	Describe the process of translation as a step-wise process.	

The Code

Translation involves the conversion of a sequence of RNA to a corresponding sequence of amino acids. To perform the conversion a code is needed to translate from the four nucleotides (AUGC) of mRNA to the 20 naturally occurring amino acids. The question then is what combination of nucleotides can code for at least twenty different amino acids? Four nucleotides taken two at a time would generate 16 possible unique sequences. Not enough to code for 20 different amino acids. However, four nucleotides taken 3 at a time would generate 64 different unique sequences. Clearly this is enough to code for the 20 naturally-occurring amino acids. In fact, the abundance of codes means that there is redundancy or degeneracy in the code with more than one triplet code representing a single amino acid.

Through experimentation it was found that the universal start code or codon is AUG and three stop codons (UAG, UGA and UAA) were identified. The remaining 60 codons represented the 20 amino acids. Having elucidated the entire code it was found that for many of the amino acids, the first two nucleotides in the sequence defined the amino acid with the third nucleotide being any of the four nucleotides. For example the codon for the amino acid leucine is CUX where the X represents any one of the four nucleotides, and the codon for the amino acid valine is GUX. This third base then became known as the wobble base signifying the flexibility the system has in identifying the third base. This also demonstrates the fact that a single amino acid can be coded by several triplet codes but a triplet code only represents a single amino acid. This triplet code for converting the sequence of mRNA to a sequence of amino acids is referred to as the **Genetic Code**.

The Starting Materials

Having identified a code to perform the translation, it is now necessary to describe the process by which the genetic code is used. Four major ingredients are necessary to carry out translation: m-RNA, t-RNA, the ribosome and the initiation factors.

Messenger RNA (mRNA) was discussed in the last section with a description of the post-transcriptional modification that convert the pre-mRNA in the nucleus to mature-mRNA in the cytoplasm.

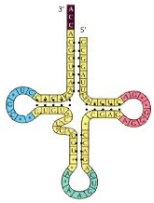
Transfer-RNA (tRNA) was introduced in the section on the structure of DNA and RNA and its production and post-transcriptional modification were briefly described in the previous section. As seen in the illustration below, tRNA is produced as a primary transcript in a linear primary structure. Following

processing the tRNA folds into the cloverleaf secondary structure. In this structure it is easy to see the 3' end

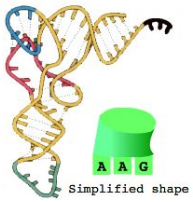
processing the tRNA folds into the cloverleaf secondary structure. In this structure it is easy to see the 3' end of the structure with its ACC sequence that is common to all tRNAs. In addition the bottom loop in the structure (the anticodon loop) contains the sequence that is complementary and antiparallel to a sequence on the mRNA. This secondary structure folds to a tertiary structure in the form of an inverted L. The 3' end is at one end of the structure and is the site that will carry a specific amino acid that corresponds to the sequence of nucleotides in the anticodon at the other end of the molecule. The process by which the correct amino acid is added to the correct tRNA is referred to as the charging of the tRNA. The formation of the charged tRNA is a two-step process as depicted in the "Charging" animation below.

tRNA Structures

Primary Sequence



Secondary Sequence



Tertiary Sequence

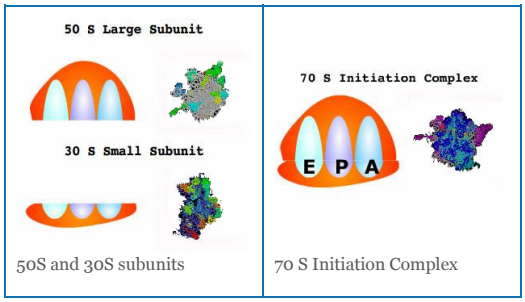
The Following Learn by Doing contains an animation describing the tRNA structures.

learn by doing

Flash Player needed! Please click here to install Flash Player.

learn by doing

- **Ribosomes** are quaternary complexes of rRNA and proteins. When they are not translating RNA to protein, the ribosomes exist as two separated subunits: a large (50S) subunit and a small (30S) subunit as depicted in the figure below. During the formation of the 70S initiation complex that starts translation, the two subunits come together to form the complete ribosome.



50S and 30S subunits | 70 S Initiation Complex

- **Initiation Factors** are a set of proteins used to facilitate the specific binding of mRNA to the small subunit of the ribosome.

Protein Synthesis

The following animation describes the formation of the initiation complex, the elongation of the peptide during synthesis and the termination of the synthesis at the termination or stop codon. The process is fundamentally the same for prokaryotes and eukaryotes. The one notable exception is in the binding of the mRNA with the small subunit of the ribosome during formation of the initiation complex. Prokaryotes do not have a 5'cap to identify the end of the mRNA but they do have a consensus sequence called the Shine-Dalgarno-Sequence at the 5' end of the mRNA. This sequence is used to align the mRNA with the appropriate site on the ribosomal subunit. In eukaryotic organisms the 5'cap provides the alignment along with multiple initiation factors. Following formation of the initiation complex, the synthesis of protein follows the same sequence in both organisms.

learn by doing

The Consequence or Error

During both replication and transcription errors can be made in the incorporation of the correct bases during the complementary copying of the DNA. In a previous section a discussion of the methods used by the system to minimize these errors has been presented. However, even with editing functions, some errors are generated and result in changing of the reading code used during translation to a protein sequence. These changes are referred to as mutations and can be categorized into four different categories described by the end result of the mutation or change.

- **Silent mutation** – Because of the degeneracy of the genetic code, multiple triplet codes represent the same amino acid. Thus, a change in the sequence for a code may not result in a change in amino acid. This particularly applies to the wobble or third base in a triplet code sequence. Thermophylic bacteria that operate optimally at high temperatures have optimized the use of the degeneracy to include codons with high G and C content to increase the thermal stability (higher melting temperature) of the resulting duplex DNA.
- **Missense mutation** – Some mutations result in the changing of a codon to represent a different amino acid. Missense mutations that change the amino acid can have no effect on the structure of a protein or may have a dramatic effect on the folding of a protein causing loss of function.
- **Nonsense mutation** – Another class of mutations may result in the changing of a codon to one of the three termination or stop codons. This will result in premature stop in the translation of a protein. Such a mutation at the beginning of the translation sequence will generally result in total loss of function which some nonsense mutations near the normal termination of the coding sequence may have little or no effect on the function of the resulting protein.
- **Frame-shift mutations** – Occasionally a mutation will occur that results in either the insertion or deletion of an extra base in the coding sequence. This type of mutation results in a shifting of the "reading" frame for the triplet codes after the insertion or deletion and production of a meaningless sequence of protein after that point. Again depending on where the insertion or deletion occurs, the effect can vary on the final product. It should also be noted that this reading frame shift will also change the position of the termination codon giving either a premature termination of the translation or an extended coding sequence.

did I get this

Which of the following mRNA sequences could be bound to the tRNA anticodon 3'GGC5'

- 3'CCG5'
- 5'UGA3'
- 5'UUA3'
- 5'CCG3'
- 3'UGC5'

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