Gene Expression by Dr. Ty C.M. Hoffman

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Gene expression is the process in which the code stored in a gene (DNA nucleotides) is used to indirectly assemble a polypeptide. Gene expression occurs in two major steps:

- In transcription, the sequence of nucleotides (known as a gene) within a DNA molecule is read. A strand of RNA nucleotides is assembled wherein each RNA nucleotide is complementary to the corresponding DNA nucleotide in the gene. Thus, C in DNA specifies G in RNA; G specifies C; T specifies A; and A specifies U (because RNA uses uracil instead of thymine). The resulting strand is messenger RNA (mRNA), and it is called the mRNA transcript.
- In translation, the mRNA transcript that was produced during transcription is used as a set of instructions for how to assemble a polypeptide. The transcript joins with a ribosome, which reads the transcript, and the polypeptide is assembled one amino acid at a time.

A prokaryotic cell lacks membrane-bounded organelles, so it has just one compartment. In these cells, both transcription and translation occur in the cytoplasm. In eukaryotic cells, transcription occurs in the nucleoplasm (where the DNA is found), and translation occurs in the cytoplasm (where ribosomes are found). In addition, the mRNA produced in eukaryotic cells must be modified before it can function for translation.

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Transcription features a one-to-one correspondence between DNA nucleotides in the gene and RNA nucleotides in the RNA transcript. However, the four nucleotide types used in RNA are insufficient to individually specify all twenty biological amino acids during translation. Instead, a sequence of three mRNA nucleotides (collectively called a codon) specifies a single amino acid. Since there are three nucleotide positions within a codon, and each position can be occupied by any of four types of nucleotide, there are sixty-four possible codons. This is more than enough to specify the twenty biological amino acids.

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The genetic code is universal in that all organisms (with very few exceptions) use the same code for specifying amino acids with mRNA codons. The genetic code is redundant in that more than one codon can specify the same amino acid. This is because there are more types of codons than there are types of amino acids used by organisms. The genetic code is not ambiguous, however, because each codon always specifies the same amino acid. Four of the codons serve special functions. One operates as a start codon (signaling initiation of translation), and three codons operate as stop codons (signaling the termination of translation).

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Transgenesis is the process by which a gene from some organism is transferred to some unrelated organism. In these examples, the tobacco plant and the pig acquire a new trait (the ability to glow) that was present in the organism from which the gene was taken. This demonstrates the universality of the genetic code, because a gene specifies the same polypeptide, regardless of what type of organism expresses that gene.

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Translation takes place at a ribosome, which is formed when two ribosomal subunits (a small subunit and a large subunit) come together, clamping the mRNA transcript between them. The ribosome then travels along the length of the transcript, one codon at a time, and each codon that is read specifies which kind of transfer RNA (tRNA) molecule is allowed to bring in the next amino acid to be added to the growing polypeptide. A triplet of nucleotides on each tRNA, called the anticodon, is able to recognize a specific and complementary codon in the mRNA transcript. There are therefore many different versions of tRNA, each having its own anticodon. Any given tRNA is able to carry only one type of amino acid, ensuring proper correspondence between mRNA codon and choice of amino acid, according to the unambiguous genetic code.

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In the elongation phase of translation, the polypeptide is enlarged one amino acid at a time. The tRNA that occupies the P slot on the ribosome is carrying the string of amino acids that have been joined so far. A new tRNA (with the appropriate anticodon and therefore carrying the appropriate amino acid) recognizes the mRNA codon at the A slot, and enters the slot, bringing in the next amino acid. The string of amino acids on the tRNA in the P slot is then transferred to the amino acid on the tRNA in the A slot, leaving the P-slot tRNA uncharged (empty). As the ribosome shifts along the transcript by one codon, the uncharged tRNA is put into the E slot and exits the ribosome. At the same time, the tRNA carrying the growing strand is put into the P slot, and the A slot is now open, reading the next codon. Assembly of a polypeptide is expensive, requiring energy in the form of two GTP molecules for each amino acid that is added during elongation.

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Termination of translation occurs when any of three stop codons appears at the A slot. In this case, no tRNA enters the A slot; instead, a special protein called a release factor enters, and this causes disintegration of the translation complex. The two ribosomal subunits separate, the mRNA transcript is released, and the completed polypeptide is freed from the tRNA that was carrying it.

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A mutation is an accidental change in the DNA nucleotide sequence of a gene. A change at even one nucleotide position can have drastic effects, as is illustrated by sickle cell disease. Just one of the DNA triplets (CTT) in the normal gene mutates into CAT. Transcription occurs as usual for either the normal person or the one with the mutation. But transcription of the normal CTT triplet specifies GAA as an mRNA codon, whereas the mutant DNA triplet (CAT) specifies GUA. During translation, the normal codon (GAA) specifies glutamic acid as the amino acid, but the mutant codon (GUA) specifies valine as the amino acid. This incorrect amino acid gives hemoglobin a different shape, making hemoglobin much less able to effectively carry oxygen within red blood cells of people with sickle cell disease.