Mutation
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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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Mutation is a random change in the DNA sequence of nucleotides. Mutation can be purely accidental (by a mistake made during DNA replication), or mutation can result from exposure of DNA to a mutagen (something that causes mutation). Mutations can be classified into two major types:

- Base-pair substitutions do not change the number of nucleotides in the DNA, because one base pair is substituted for another. Because of the redundancy of the genetic code, it is possible for a base-pair substitution to have no effect (a silent mutation), because the mutant version of DNA will code for an mRNA codon that specifies the same amino acid as the wild-type. Therefore, the correct protein is made during translation, despite the silent mutation. A missense mutation results when a mutant DNA triplet codes for an mRNA codon that specifies a different amino acid compared to the wild type. All other amino acids will be correct. However, this results in a differently shaped protein that will function differently (usually worse or not at all). In a nonsense mutation, the mutated DNA triplet codes for one of the stop codons. This prematurely ends translation, so a shortened protein that has very little chance of functioning is made.
- Insertions and deletions do change the number of nucleotides in the DNA, and this has more drastic effects. Insertions add some number of base pairs, and deletions remove some number of base pairs without replacing them with substitutes. An insertion or deletion of some number of base pairs other than a multiple of three results in a frameshift, because mRNA is interpreted by the ribosome as codons that are three nucleotides in length. Frameshifts affect all codons downstream of the mutation, so they result in drastically different (and therefore usually worthless) proteins.

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A mutation 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.

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The shape of a polypeptide depends on its particular sequence of amino acids (i.e., its primary structure), because this determines how amino acids within that polypeptide interact. The primary sequence is determined by the sequence of nucleotides in the gene that codes for that polypeptide. If a change is made to even one of the many amino acids in a polypeptide, the shape can be profoundly affected. This is exemplified by sickle cell disease, in which a mutation (a change in the DNA sequence) causes the wrong amino acid to be placed in one of the positions within a polypeptide subunit of hemoglobin. Though all of the other amino acids are correct, the polypeptide is severely deformed.