How Proteins are Made

Genetic Transcription, Translation, and Regulation

Introduction and Review of Proteins

- Protein Review.
  - Polypeptides (proteins) are large organic macromolecules made up of strands of hundreds or thousands of amino acids joined together by peptide bonds.
  - Although there are tens of thousands of different proteins, there are only 20 different amino acids; like letters in an alphabet, they can be used to create millions of different words. .

Introduction and Review of Proteins

- Protein Review.
  - Every protein has the identical amino acids in order along its length, just as every time the word *automobile* is written, it has the same letters in the same order along its length.

Protein Synthesis Overview: Two Major Stages

- First Stage.
  - Problem—DNA resides in the nucleus, but proteins are made in the cytoplasm.
  - Solution—DNA is the master set of instructions for the cell, so it needs to stay protected and isolated in the nucleus. Analogy—Precious reference book in the library.

Protein Synthesis Overview: Two Major Stages

- First Stage.
  - Instead of allowing DNA to leave the nucleus and

travel to the cytoplasm, the cell makes a cheap copy of DNA in a smaller and less permanent form called RNA and lets that leave the nucleus.
  - The process of copying DNA into RNA copy is called transcription.

Protein Synthesis Overview: Two Major Stages

- Second Stage.
  - Problem—How is one language (nucleotides) translated into the other (amino acids)?
  - Proteins are assembled from amino acids on ribosomes.
  - The correct amino acid is added at the correct time by using the information on the RNA message from the nucleus.
  - Process of assembling proteins from RNA instructions is called translation.
  -

Step 1: Transcription

- RNA differs from DNA.
  - Sugars are different—ribose in RNA, deoxyribose in DNA.
  - RNA has nitrogen-containing bases, A, G, C, and U instead of T.
  - RNA is single-stranded, not a duplex.

Step 1: Transcription

- Three types of RNA are transcribed.
  - mRNA (messenger RNA) carries instructions for sequence of amino acids in a protein.
  - rRNA (ribosomal RNA) is an important component of ribosomes.
  - tRNA (transfer RNA) is involved in matching the correct amino acid to specific instructions in mRNA.

Step 1—Transcription

- Mechanism of Transcription.
  - Just like replication, base pairing, **Figure 14.4,** is the mechanism used to copy DNA in transcription, but here into RNA and not DNA.
  - DNA is unwound and used as a template to match complementary bases, C to G and A to U (not T) to make a new daughter strand.

Step 1: Transcription

- Mechanism of Transcription.
  - Enzyme critical to catalyzing this process is RNA polymerase.
  - The new nucleotides are covalently linked together by the same enzyme to make a single strand of RNA (called a transcript) from one strand of the double helix.

Step 1: Transcription

- RNA processing.
  - mRNA is not ready directly after transcription, but must be edited further.
  - Parts to be cut out are called introns.
  - The remaining pieces (called exons) are joined together to make the finished product.
- Essay: Making Sense of ‘Junk’ DNA.

Step 2: The Importance of the Genetic Code

- How many bases signify one amino acid?
  - Four bases in DNA, 20 amino acids in protein, not one to one,

clearly.
  - Not two to one either—there are only 16 possible combinations of two bases of DNA (AA, AT, AC, AG, CA, etc.).
  - Sydney Brenner suggested it worked as a triplet code—three nucleotides (called a codon) signifying one amino acid. There are 64 different possible combinations of the four nucleotides, more than enough for the 20 different amino acids.

Step 2: The Importance of the Genetic Code

- Which three bases signify which amino acid?
  - Analogy to Morse code: **. _ .** = letter P
  - UCC = what amino acid?
  - The code is redundant (several different codons signify the same amino acid).
  - The code carries instruction codons for stopping and starting.
  - The genetic code is universal (same for bacteria and humans) and is good evidence for a common inheritance (evolution).

Translation

- Necessary Molecules.
  - mRNA (carries the instructions in the codons, like a recipe).
  - Amino acids.
  - Ribosomes, location of protein synthesis, **Figure 14.9**, are a large conglomerate of enzymes and ribosomal RNA (rRNA) in two subunits with A and P sites.

Translation

- Necessary Molecules.
  - tRNA molecules (transfer RNA) are “translator” molecules; they can match the appropriate amino acid with the codon in the mRNA. Part of the molecule binds an amino acid, and the other end has three nucleotides (anticodon) that form a base pair with the codon in the mRNA.

Translation

- Steps in Translation.
  - mRNA binds to the small subunit of the ribosome. Start codon, AUG, brings in initiator tRNA with the amino acid methionine, and then large subunit binds.

Translation

- Steps in Translation.
  - tRNA that matches the next codon ferries in the appropriate amino acid into the “A” site. The ribosome catalyzes the peptide bond between the first two amino acids at the “A” site; then the ribosome jumps along the mRNA to the next codon, moving the newly formed peptide to the “P” site. This continues until a stop codon is reached.

Translation

- Steps in Translation.
  - At the stop codon, no new tRNA comes into the “A” site, and the whole complex falls apart, releasing the new protein.
  - Five amino acids are added every second, and multiple ribosomes move along a transcript simultaneously.

Translation

- Steps in Translation.
  - Five amino acids are added every second, and multiple ribosomes move along a transcript simultaneously.
  - What is a gene?

Genetic Regulation

- What are the start and stop signals for the whole process from transcription to translation? Proteins.
- Example of protein regulation of gene expression—the lac operon (multipart genetic system) in *E. coli*.

The Lac Operon

- Monod and Jacob in France in the late 1950s used the knowledge that bacteria synthesize certain enzymes only if the substrate for that enzyme is present (example is sugar lactose, called an inducer).
- Three genes involved, *y* (permease enzyme to help lactose enter the cell), *z* (β-galactosidase enzyme to cut lactose into galactose and glucose), and the *a* gene.

The Lac Operon

- Upstream from these three genes is a promoter (stretch of DNA that acts as a binding site for RNA polymerase) to copy all three genes as one transcript.
- Between promoter and first gene is a region called the operator, a sequence of DNA that can act in two different states.
  - The operator can bind a repressor (protein from the *i* gene; only role is to regulate transcription of another gene) and prevent DNA polymerase from binding the promoter.
  - If the repressor binds lactose, it will not bind the operator, so

transcription ensues.

Genetic Regulation

- Alternate splicing.
  - Number of genes for humans, versus *C. elegans*.

Genetic Regulation

- Alternate splicing.
  - Splicing process.

The Magnitude of the Metabolic Operation

- Genome size for humans is 3.2 billion, about 30,000 genes.
  - It would take 1,000 telephone books (each 1,000 pages long) to print all the bases.
  - What is a gene? A segment of DNA that makes a transcript.