**Unit 4: Molecular Genetics**
**Content Outline: Protein Synthesis (4.2) – Part 1**

I. George Beadle and Edward Tatum (1934)
   A. They develop *the one gene-one enzyme hypothesis*. This proposes that a *single gene* has the genetic information for making *one enzyme*. This is later changed to become the **one gene - one polypeptide** (protein) **hypothesis**; as enzymes are a *type* of polypeptide (protein).

II. **Transcription** (means " the process of making a *working copy* of an original")
   A. This process is the making of a *recyclable, workable copy* of DNA but in the form of **RNA.** (The recyclable copy will become known as **mRNA – messenger RNA**. It is a *recyclable copy* of the "Million Dollar DNA Blueprint".)
      1. mRNA is synthesized (made) by an *enzyme* called **RNA Polymerase**
      2. The *message* (mRNA) will be sent to the *construction site (ribosomes)* for *building* the protein.
      3. RNA nucleotides use Ribose instead of Deoxyribose as the *five carbon sugar.*
      4. In RNA, Uracil replaces Thymine. (Thymine can't exit nuclear pores. Remember, ribosomes are out in the cytoplasm, so Thymine needs to be *substituted* by Uracil.)
      5. mRNA is a single-stranded molecule, therefore it is *less stable* than DNA

   B. DNA serves as a *template (guide)* for making the mRNA. A = U and C = G (Still can use Chargaff's Rule.)
   *C. Transcription is considered the first part of Protein Synthesis.*

III. **Translation** (means "The process of taking from one language and *changing* to another language") (A good example would be "adios" in Spanish going to "good-bye" in English or "hola" to "hello".)
   A. In this process the cell is *turning* nucleotide language (DNA/RNA) *into* amino acid language to make proteins. Remember, amino acids are the *building blocks of proteins.*
   B. This process occurs at the Ribosome. The ribosome has a nickname… "the Translator". It is also considered a "construction site" since the cell is *building* a protein using the *copied "blueprint"* that was provided.
   *C. Translation is considered the second part of Protein Synthesis.*

IV. **Codon** "A.K.A Triplet Code" (This is the *RNA language* that will be translated into polypeptides.)
   A. Codons are a "three letter" or three nucleotide sequence of RNA (*determined* by the template strand of DNA/ Important Blueprint Information) but are *read on the RNA*! (The mRNA is being translated; <u>not</u> the DNA.)
      *1. The codons <u>must</u> be read 5' 3' on the mRNA! (Because this is how the mRNA was made. You do not write a sentence and then read it backwards do you. It would make no sense.)*
   B. **RNA Codon Chart** for Amino Acids (Contains the 20 known amino acids for living organisms.)
      1. There are three essential things you need to know about the genetic code (RNA Codon Chart)
         a. The RNA referred to is *mRNA* and it <u>must</u> be read in a **5' 3'** orientation.
         b. Each 3 letter codon (e.g. GCU) *codes for* one, and only one, amino acid.
         c. *Most* amino acids have more than one codon.
         d. Therefore the genetic code is *redundant*, but it is not ambiguous.
      2. 61of the 64 possible codons ($4^3 = 64$) codes for an Amino Acid.
         a. 4 refers to the four nucleotides *possible* (A, C, U, G); 3 refers to the number of pieces in a *unit* (codon).
      3. **AUG** is the **start codon** and is the codon for the amino acid Methionine (It depends on the *position* of Methionine in the mRNA. If it is the first codon on the 5' end, it will be the start codon. If it is not the first, it will be regular methionine.)
      4. **UAA, UAG**, and **UGA** are the **stop codons.** (These codons *stop the process* of transcription.)
      5. *This chart is <u>universal</u> for <u>all</u> living organisms, and viruses***.** (Viruses are *not considered* living.) (This hits on the theme of Unity and Diversity. Unity in that it indicates Common Ancestry among <u>all</u> organisms and viruses. Diversity is in the <u>differences</u> of the sequences of amino acids strung together to make a protein.) (Please make sure students understand this very important concept. It will be really important in the Evolution Unit.)
      6. The codon will *match* the anti-codon sequence in the translation phase of protein synthesis.
   C. **Reading Frame** (This term refers to a set of **3** *consecutive nucleotides*. They are read in 5' 3' direction.) (The sentence "The big dog ran") is a good device to use in making this clear.)

**Protein Synthesis – Part 2**

**I. mRNA Synthesis** and **Modification** (The making of mRNA.)(This process occurs at the nucleolus. Remember, the nucleolus is "like" a copy machine because we are making a *cheap recyclable copy* of the DNA sequence.)

A. Three Phases of *Production* to **a transcription unit** (a piece of mRNA.):

1. **Initiation** (This is building our *factory to make* mRNA basically.)
   a. A protein called a **Transcription Factor** attaches to *promoter* sequence of the gene being transcribed. Then additional transcription factors (proteins and enzymes) are added in the building process.
   b. The whole "factory" is called a **Transcription Initiation Complex**. (Can you *see* the definition in the term? Transcription is the process being done. Initiation refers to the beginning process. Complex indicates we have *many* parts involved in making the structure.)
2. **Elongation** (This refers to the *actual making* of the mRNA molecule.)
   *a. This must be made in the 5' → 3' direction!*
   b. RNA Polymerase II separates the DNA Double Helix to make *room to work*, and *adds nucleosides* to the growing molecule.
   c. Cells can make *multiple* copies of RNA because the DNA is left *intact and protected* in the nucleus.
3. **Termination** (Just like it sounds… *stop* the transcription.)
   a. A stop codon is made (for the ribosome) and the "factory" molecule slows down.
   b. RNA Polymerase II slows down until it stops transcription by forming an AAUAAA sequence and is then released from the DNA. (Please tell students to not try and memorize the sequence. It will not be on the test. Please make sure the understand what is happening in each step.)

B. **Modification** of the **Primary Transcript** for *Eukaryotic* Cells (This also occurs in the nucleus.)

1. *Front end (5') modification* of the mRNA molecule.
   a. A 5' protective cap is added. (This would be like you putting on a hard hat to protect your head when you go outside into a "construction site".)
2. *Back end (3') modification* of the mRNA molecule.
   a. A Poly A Tail added. ("poly" means "many"; 50-250 Adenines will be added onto the tail. The more As the *longer* the mRNA will last.)
   b. This acts as protection against digestive enzymes in the cytoplasm. (Remember, it is a construction site and things are being broken down as well as being built.)
3. *Middle modification* of the mRNA molecule.
   a. During this step, **remove the non-coding introns** (These act as spacers) using **Spliceosomes**. A spliceosome is a type of enzymes that act as *scissors.*
   b. Then *rearrange* the *separated* **coding exons**. The reaaranging allows for *different sequences of exons.* (A good way to demonstate is to use the exons "A", "B", and "C". The make the following sequences: ABC, ACB, BAC, BCA, CAB, CBA. Students should understand that this rearranging *increases* the number of proteins/enzymes that can be made; but without, increase the *amount of DNA.*
   c. Spliceosomes "Stitch" the pieces together to make the *finalized* **secondary mRNA** transcript that is know ready for transport to the ribosomes for translation into proteins.

**Protein Synthesis – Part 3**

I. **Translation** (Protein *Synthesis* - This is the part *of actually making the protein.*)

A. This process occurs at the Ribosome "the Translator".

B. The process turns the mRNA into a **primary (1') sequence** of amino acids for making of the protein.

C. This process needs the *assistance* of **tRNA (transfer RNA)** to *transfer free amino acids* from the cytoplasm to the construction site of the Ribosome.

1. Remember, that the **anticodon** is found on the **tRNA** molecule, not the mRNA.
2. The Anticodon *"matches"* the codon on the mRNA molecule ensuring the *proper amino acid* is brought to the construction site of the Ribosome. If they do not match … it is the *wrong* Amino Acid!
3. The amino acid is connected to the 3' end of the tRNA molecule.
   a. Remember, the tRNA molecule is a nucleotide sequence; so there is a phosphate on the 5' end and an *open bound* on the 3' end… so this is where the amino acid gets *attached* so that it can be *transported* to the ribosome (construction site).

D. Ribosome Structure (This cellular *particle* has 2 parts.) (Please remind students that these are not organelles.)

1. The Small sub-unit (This part acts as a *platform for work*; much like your desk.)
2. The Large sub-unit (This part is the *factory* for making the protein.)
   a. The **A** site (This is where the next tRNA molecule is *added* in the "factory".)
   b. The **P** site (This is the part of the "factory" where the *protein* is attached.)
   c. The **E** site (This is where the "*used tRNA* molecule" *exits* the "factory" to be recycled.)
3. The ribosome **translocates** ("walks") down the mRNA *one codon at a time* until it gets to the stop codon at the end of the mRNA molecule. Thus having completed the "message" on how to make that particular protein.
4. *Remember, these are not membrane-bound organelles. All cells possess these structures.*

E. The process of translation has three phases: (They are the same 3 as Transcription.)

1. **Initiation** - This is *building the factory* needed to make the protein.
   a. The *small sub-unit* attaches to the **5' cap.** (This *signals* the large sub unit.)
   b. **AUG** (the start codon on the mRNA molecule) brings in the tRNA (using the anticodon) molecule with Methionine attached. This *starts production* of the protein.
   c. The large sub-unit is *aligned* so that Methionine is in the P site. The A site *is open* for the *addition* of the next tRNA molecule.
2. **Elongation** - This is the actual making of the primary(1') sequence of amino acids.
   a. The ribosome "walks" down the mRNA one codon at a time
3. **Termination**
   a. This occurs when a termination codon reaches the A site.
   b. A **release factor** (enzyme) enters the A site causing a *hydrolysis reaction* to occur that *releases* the protein from the last tRNA molecule (which is sitting in the P site). (Please remind students that hydrolysis reactions break apart molecules and dehydration synthesis reactions put molecules together.)
   c. After the hydrolysis reaction occurs, the protein *detaches* and the sub units *separate* to be reused.
4. The mRNA may be reused to make more of that particular protein or it may be broken down and the nucleotides recycled.
   a. Polyribosomes (many ribosomes) can also occur on a single strand of mRNA.
   b. This allows for a cell to make *many copies* of the *same* protein very quickly. (Such as might be needed during repair.)

II. Post (means "after") Translation Modification (This is the *protein folding* that must occur for the protein to be functional.)

A. If the 1' sequence enters a **Chaperonin** to fold, the protein *will stay inside* the cell. (Please help students see that this is a smaller water free container for protein folding. Please help students "see" the word by asking them what Chaperons do?... Watch over and protect.

*B.* If the 1' sequence enters the Rough Endoplasmic Reticulum (RER) to fold, the protein *will be exported out of the cell.*

**Part 4**

I. **Mutations**

A. *Change in the nucleotide sequence* of DNA or mRNA that code for a protein.

B. Caused by **Mutagens** (Means to "**gen**erate a **muta**tion".)

1. These are a *physical or chemical interactions* that changes the nucleotide sequence of DNA.
2. Examples of mutagens:
   a. Ultraviolet radiation (UV Radiation) from the sun
   b. Cigarette Smoke
   c. Alcohol in excess
   d. Viruses
   e. Car Exhaust
   f. Chemicals (Laboratory, Pesticides, insecticides, poisons)

C. Two major **TYPES** of Mutations:

1. **Point mutations** (A *single nucleotide mutates* thus affecting *a single codon*.)
   a. **Silent Point Mutation**– The mutation causes *no change in the amino acid coded for.* *(We would never know because it has no effect.)*
   b. **Missense Point Mutation** – The mutation *changes the amino acid* coded for. (MIStake) (This is best seen in the mutation that causes Sickle cell.)
   *c.* **Nonsense Point Mutation** – The mutation *changes from coding for an amino acid to coding for a STOP codon* (No protein will be made.) (NONsense)
   *d.* (Please help students "see" the words.)
2. **READING FRAMESHIFT** Mutation (The whole DNA "sentence" is *changed behind the mutation*.)
   a. These mutations alter the codon sequence.
   b. **Insertion** – *adding* nucleotides to the sequence.
      **For Example**: THE BIG TAN DOG RAN
      **with Inserted Letter:** THE B**O**I GTA NDO GRA N
   c. **Deletion** – *taking out* nucleotides from the sequence.
      **For Example**: THE BIG TAN DOG RAN
      **with Deleted Letter**: THE BGT AND OGR AN
   (Please help students see the difference between one codon and many codons being effected and what that means to the organism or cell.)

D. Gametes vs. Somatic – Who is affected? If a mutation occurs in somatic cells, the only one affected by the mutation is the person that the mutation occurred to. If the mutation occurs in gametes (sex cells), the only one affected *will* be the organism *created* from that sex cell. This is how *future* generations may be affected and *this is a cause of evolution. Change in the DNA over time*. (Please make sure students understand the difference between somatic and germ cells and who is *affected.* This will be helpful when you get to the Evolution unit.)