Protein Synthesis

Learning Objectives:

- ❖ Define the terms “Codons”, “Anticodon”, “ Exons”, “Introns”, “Genetic code”, “Coding & non Coding strands”.
- ❖ Describe briefly the processes of transcription & translation.
- ❖ Describe the role of DNA, mRNA, tRNA, and the ribosomes in the process of protein synthesis.

Protein Synthesis:

- ❖ In addition to directing its own replication, DNA serves as the master blueprint for protein synthesis.

- ❖ Recall from previous lectures that proteins are composed of polypeptide chains, which in turn are made up of amino acids.

- ❖ Lets call a ***"gene"*** ***as a segment of a DNA molecule that carries instructions for creating one polypeptide chain***.

- ❖ The four nucleotide bases (A, G, T, and C) are the "letters" used in the genetic alphabet, and the information of DNA is found in the sequence of these bases.

- ❖ Each sequence of three bases, called a triplet ***(Codon)***, can be thought of as a "word" that specifies a particular amino acid. For example, the triplet AAA calls for the amino acid phenylalanine, and CCT calls for glycine.

Protein Synthesis:

- The sequence of triplets in each gene forms a "sentence" that tells exactly how a particular polypeptide is to be made: It specifies the number, kinds, and order of amino acids needed to build a particular polypeptide.

- Most genes of higher organisms contain ***exons***, ***which are amino acid–specifying informational sequences.*** Exons are often separated by ***introns***, ***which are noncoding, often repetitive, segments that range from 60 to 100,000 nucleotides.***

- Once considered a type of "junk DNA," ***intron DNA is believed to serve as a reservoir or scrapyard of ready-to-use DNA segments for genome evolution, as well as a rich source of small RNA molecules***.

Nucleic Acids – *Role of RNA:*

- ❖ By itself, DNA is like a CD recording: The information it contains cannot be used without a decoding mechanism (a CD player).

- ❖ Furthermore, most polypeptides are manufactured at ribosomes in the cytoplasm, but in interphase cells, DNA never leaves the nucleus. ***So, DNA requires not only a decoder, but a messenger as well.***

- ❖ The decoding and messenger functions are carried out by RNA, the second type of nucleic acid of 3 types (mRNA, rRNA, tRNA).

- ❖ All types of RNA are formed on the DNA in the nucleus in much the same way as DNA replicates itself: The DNA helix separates and one of its strands serves as a template for synthesizing a complementary RNA strand.

- ❖ Once formed, the RNA molecule is released from the DNA template and migrates into the cytoplasm. Its job done, the DNA recoils into its helical, inactive form.

- ❖ Essentially, polypeptide synthesis involves two major steps: ***Transcription, in which DNA's information is encoded in mRNA*** & ***Translation, in which the information carried by mRNA is decoded and used to assemble polypeptides***.

Nucleic Acids – *Transcription:*

- A transcriptionist converts a message from a recording or shorthand notes into a written copy. In other words, information is transferred from one form or format to another.

- In cells, transcription transfers information from a DNA base sequence to the complementary base sequence of an mRNA molecule. The form is different, but the same information is being conveyed.

- Once the mRNA molecule is made, it detaches and leaves the nucleus via a nuclear pore, and heads for the protein synthesis machinery, the ribosome.

- Transcription cannot begin until gene-activating chemicals called ***transcription factors*** stimulate histones at the site-to-be of gene transcription to loosen.

Nucleic Acids – *Transcription:*

- The transcription factors then bind to ***the promoter***. *The promoter is a special DNA sequence that contains the start point (beginning of the gene to be transcribed).* It specifies where mRNA synthesis starts and which DNA strand is going to serve as the template strand.

- The uncoiled DNA strand not used as a template is called the ***coding strand*** because it has the same (coded) sequence as the mRNA to be built (except for the U in mRNA in place of T in DNA).

- The transcription factors also help position ***RNA polymerase***, the enzyme that oversees the synthesis of mRNA, correctly at the promoter. Once these preparations are made, RNA polymerase can initiate transcription.

- Transcription involves three basic phases: ***initiation, elongation, and termination (explained in the following slide image).***

TRANSCRIPTION

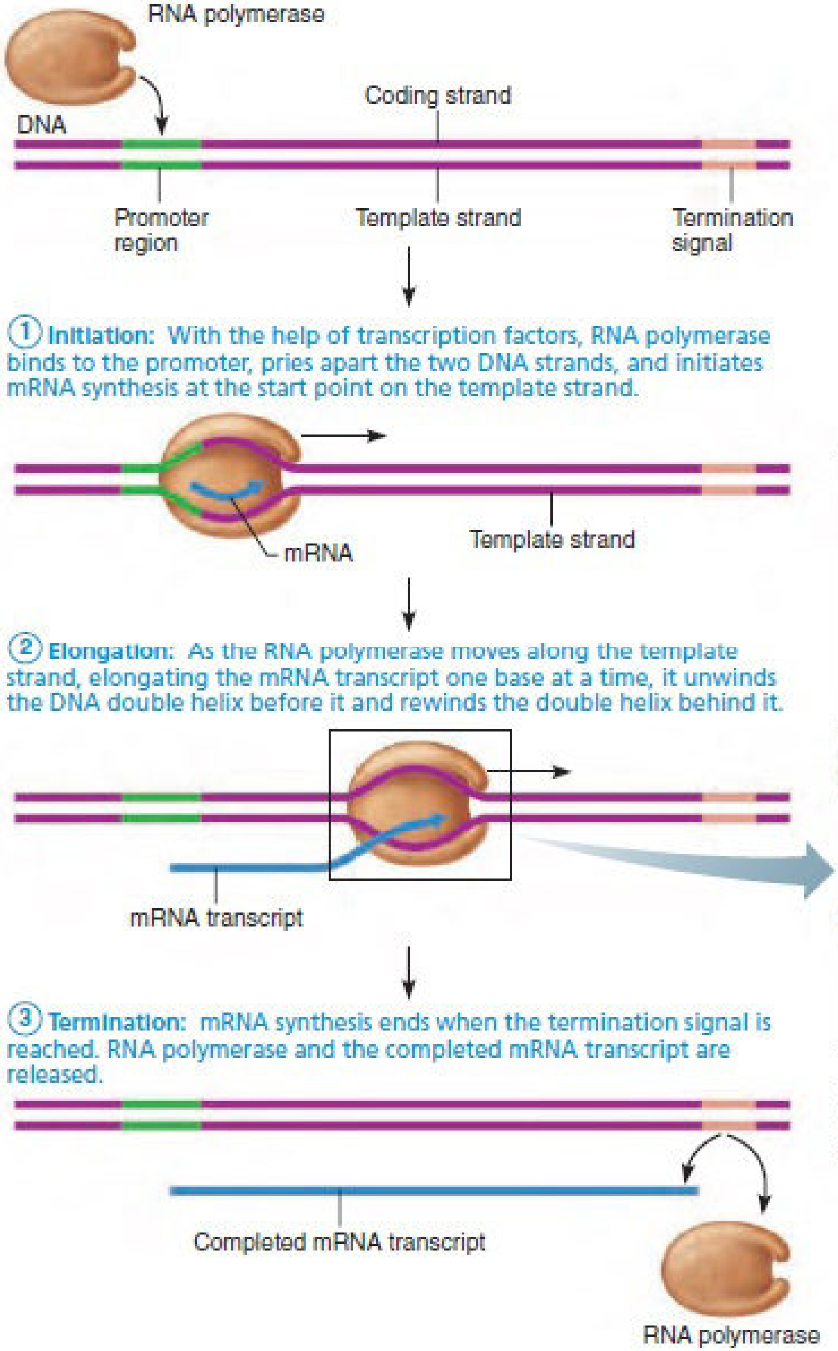
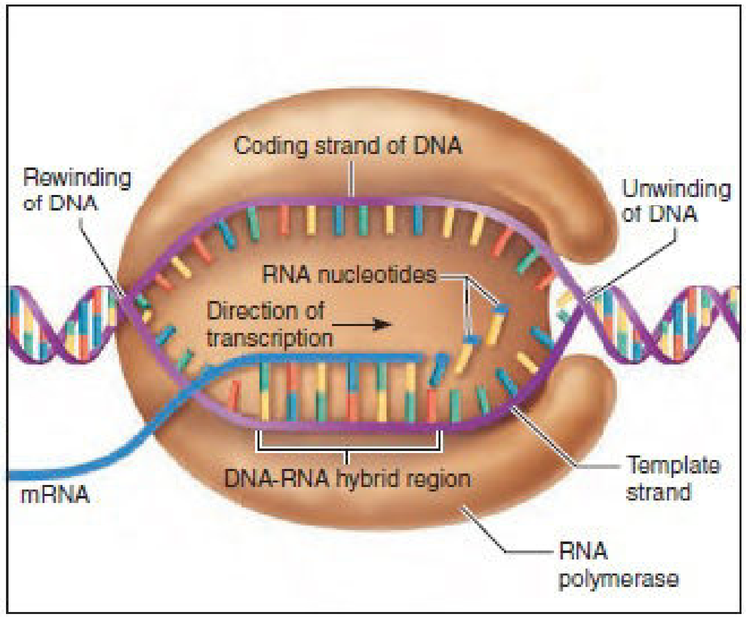


Figure 3.35 **Overview of stages of transcription.**



The DNA-RNA hybrid: At any given moment, 16–18 base pairs of DNA are unwound and the most recently made RNA is still bound to DNA. This small region is called the DNA-RNA hybrid.

Nucleic Acids – *Transcription:*

- **Processing of mRNA:** Before translation can begin, editing and further processing are needed to clean up the mRNA transcript. Recall that mammalian DNA like ours has coding regions (exons) separated by non-protein-coding regions (introns).

- Because the DNA is transcribed sequentially, the mRNA initially made, called ***pre-mRNA or primary transcript, is still littered with introns***. Before the newly formed RNA can be used as a messenger, it must be processed, or edited—that is, sections corresponding to introns must be removed.

- Large RNA-protein complexes called ***spliceosomes*** snip out the introns and splice together the remaining exon-coded sections in the order in which they occurred in the DNA, producing functional mRNA.

Nucleic Acids – ***Translation:***

- A translator takes a message in one language and restates it in another. In the translation step of protein synthesis, the language of nucleic acids (base sequence) is translated into the language of proteins (amino acid sequence).

- **The Genetic Code:** The rules by which the base sequence of a gene is translated into an amino acid sequence are called the genetic code. ***For each triplet, or three-base sequence on DNA, the corresponding three-base sequence on mRNA is called a codon.***

- Since there are four kinds of RNA (or DNA) nucleotides, there are 4^3, or ***64, possible codons***. ***Three of these 64 codons are "stop signs" that call for termination of polypeptide synthesis***. ***All the rest code for amino acids.***

- ***Because there are only about 20 amino acids, some are specified by more than one codon.*** This redundancy in the genetic code helps protect against problems due to transcription (and translation) errors.

The Genetic Code

FIRST BASE	SECOND BASE: U	SECOND BASE: C	SECOND BASE: A	SECOND BASE: G	THIRD BASE
U	UUU, UUC — Phe UUA, UUG — Leu	UCU, UCC, UCA, UCG — Ser	UAU, UAC — Tyr UAA Stop UAG Stop	UGU, UGC — Cys UGA Stop UGG Trp	U C A G
C	CUU, CUC, CUA, CUG — Leu	CCU, CCC, CCA, CCG — Pro	CAU, CAC — His CAA, CAG — Gln	CGU, CGC, CGA, CGG — Arg	U C A G
A	AUU, AUC, AUA — Ile AUG Met or Start	ACU, ACC, ACA, ACG — Thr	AAU, AAC — Asn AAA, AAG — Lys	AGU, AGC — Ser AGA, AGG — Arg	U C A G
G	GUU, GUC, GUA, GUG — Val	GCU, GCC, GCA, GCG — Ala	GAU, GAC — Asp GAA, GAG — Glu	GGU, GGC, GGA, GGG — Gly	U C A G

Nucleic Acids – *Role of tRNA:*

- tRNA is well suited to its dual function of binding to both an amino acid and an mRNA codon.

- The amino acid (picked up from the cytoplasmic pool) is bound to one end of tRNA, at a region called ***the stem***. At the other end, ***the head***, is its anticodon sequence complementary to the mRNA codon calling for the amino acid carried by that particular tRNA.

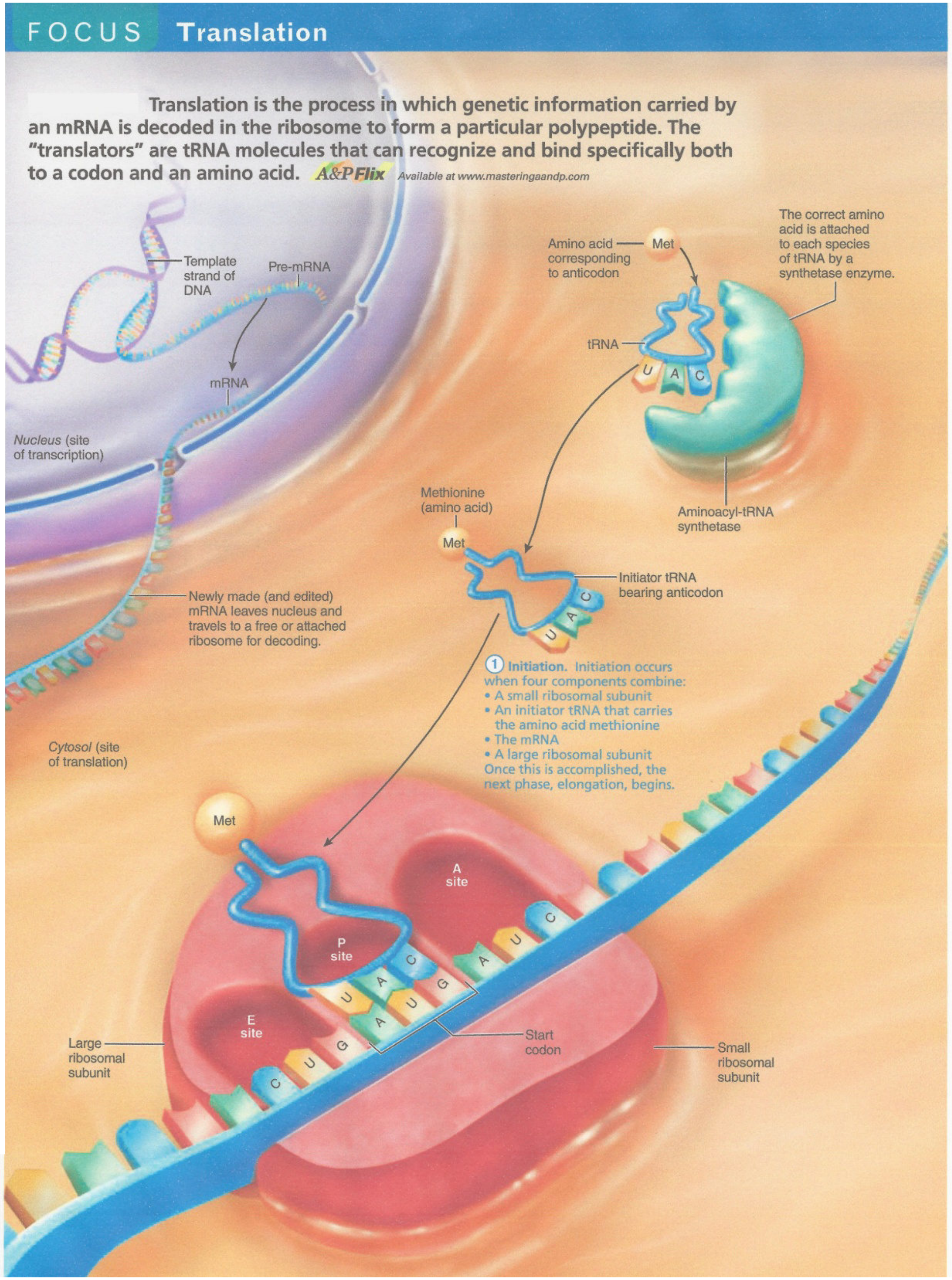
- Because anticodons form hydrogen bonds with complementary codons, tRNA is the link between the language of nucleic acids and the language of proteins.

- For example, if the mRNA codon is AUA, which specifies isoleucine, the tRNAs carrying isoleucine will have the anticodon UAU, which can bind to the AUA codons.

- **Translation** also involves three phases: ***initiation, elongation, and termination (explained in the following slide image).***

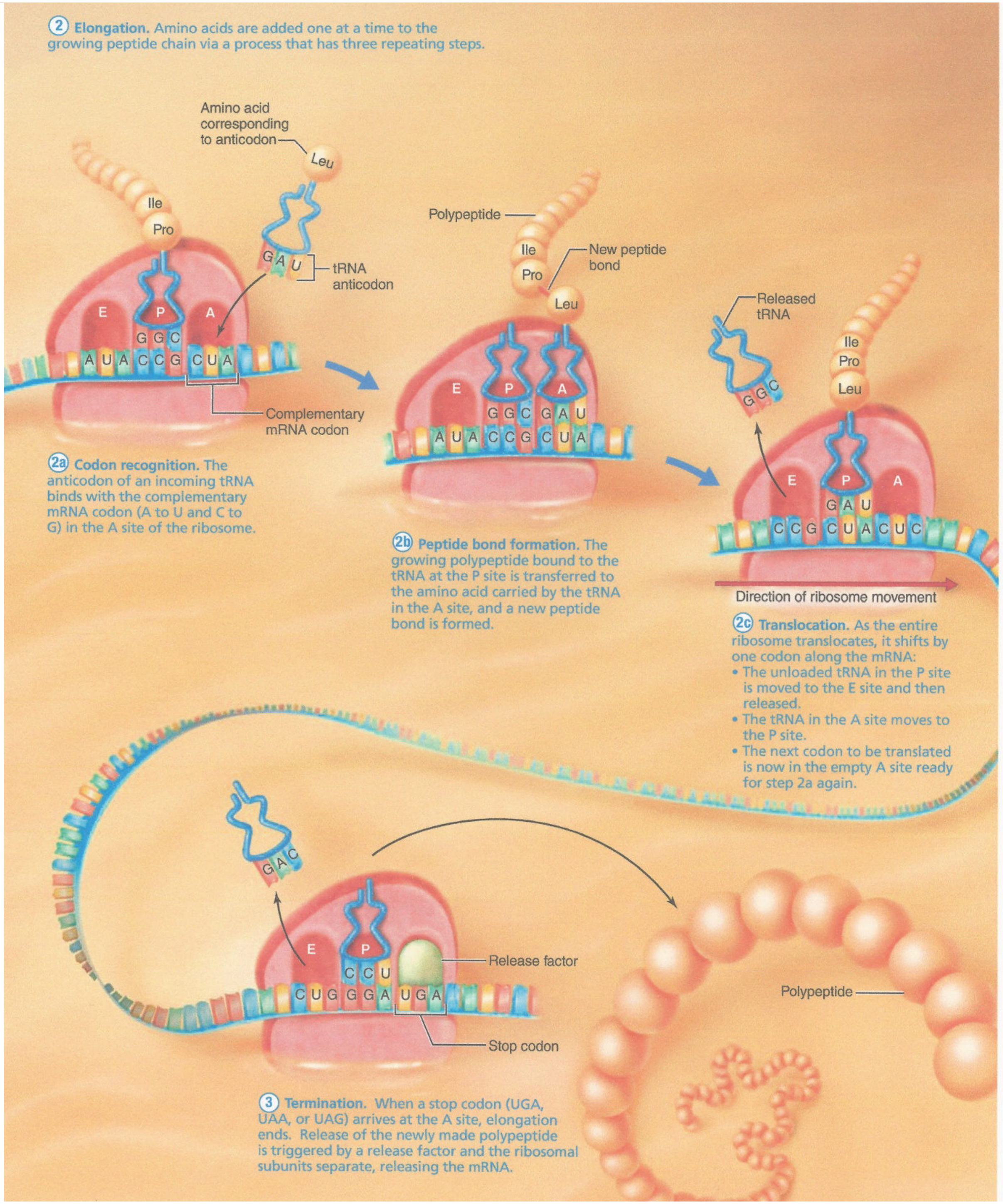
1. Initiation: A small ribosomal subunit binds to a special methionine-carrying initiator tRNA, and then to the "new" mRNA to be decoded. With the initiator tRNA still in tow, the small ribosomal subunit scans along the mRNA until it encounters the *start codon—the first AUG triplet it meets.* When the initiator tRNA's UAC anticodon "recognizes" and binds to the start codon, a large ribosomal subunit unites with the small one, forming a functional ribosome.

At the end of this phase the mRNA is firmly positioned in the groove between the ribosomal subunits, the initiator tRNA is sitting in the P site, and the A site is vacant, ready for the next aminoacyl tRNA to deliver its cargo. The next phase, elongation of the polypeptide, now begins.



2. Elongation: During the three-step cycle (2a, 2b, 2c in the image) of elongation, the mRNA is moved through the ribosome in one direction and one amino acid at a time is added to the growing Polypeptide.

3. Termination: The mRNA strand continues to be read sequentially until its last codon, the *stop codon (one UGA,* UAA, or UAG) enters the A site. The stop codon is the "period" at the end of the mRNA sentence—it tells the ribosome that translation of that mRNA is finished. As a result a ***protein release factor*** *binds to the stop codon at the A site* and directs the addition of water (instead of an amino acid) to the polypeptide chain. This hydrolyzes (breaks) the bond between the polypeptide and the tRNA in the P site.

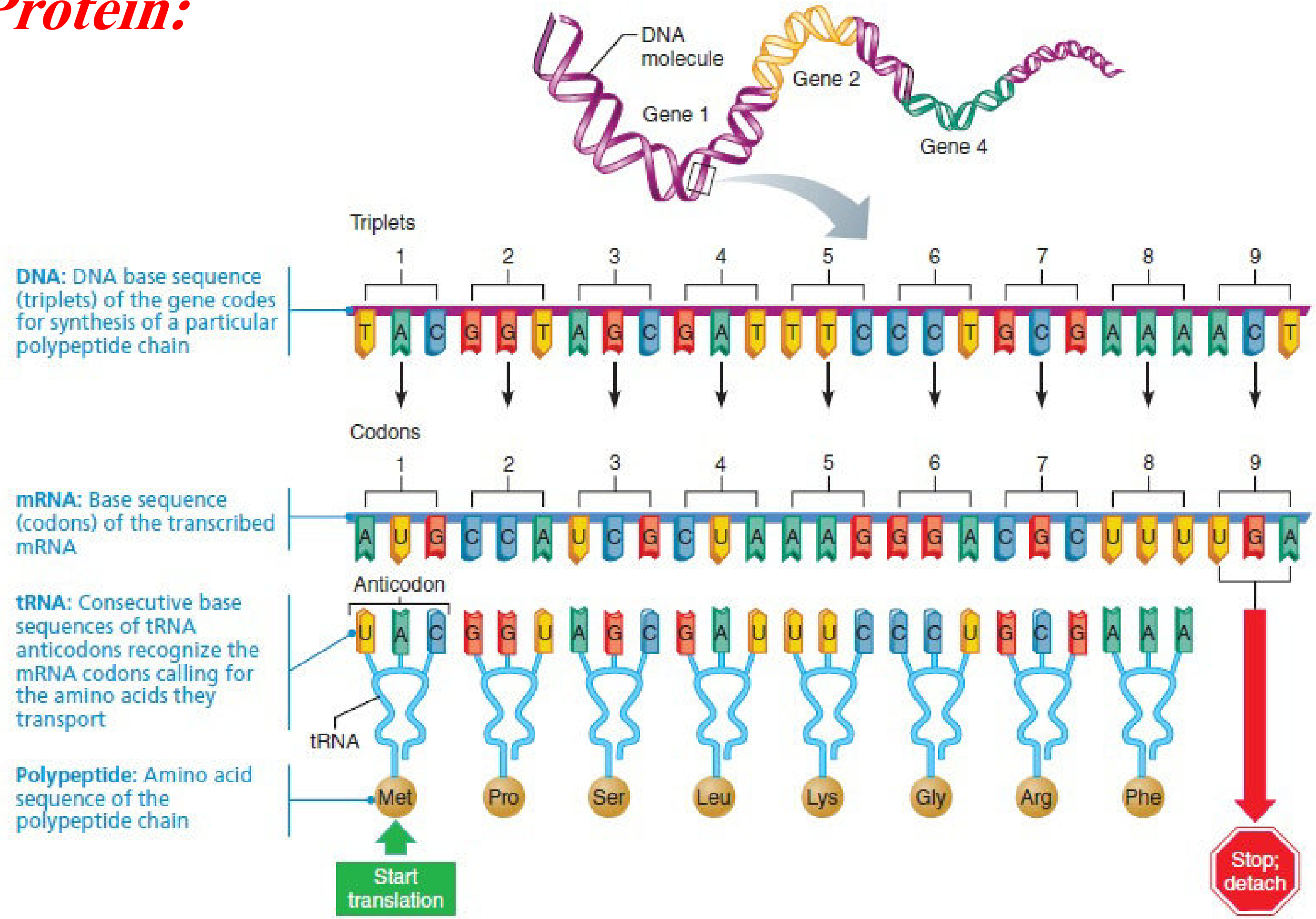


Summary-*From DNA to Proteins:*

- The genetic information of a cell is translated into the production of proteins via a sequence of information transfer that is completely directed by complementary base pairing.

- The transfer of information goes from DNA base sequence (triplets) to the complementary base sequence of mRNA (codons) and then to the tRNA base sequence (anticodons), which is identical to the template DNA sequence except for the substitution of uracil (U) for thymine (T)

From DNA to Protein:



Information transfer from DNA to RNA to polypeptide. Information is transferred from the DNA of the gene to the complementary messenger RNA molecule, whose codons are then "read" (translated) by transfer RNA anticodons. ***Notice that the "reading" of the mRNA by tRNA anticodons reestablishes the base (triplet) sequence of the DNA genetic code (except that T is replaced by U).***