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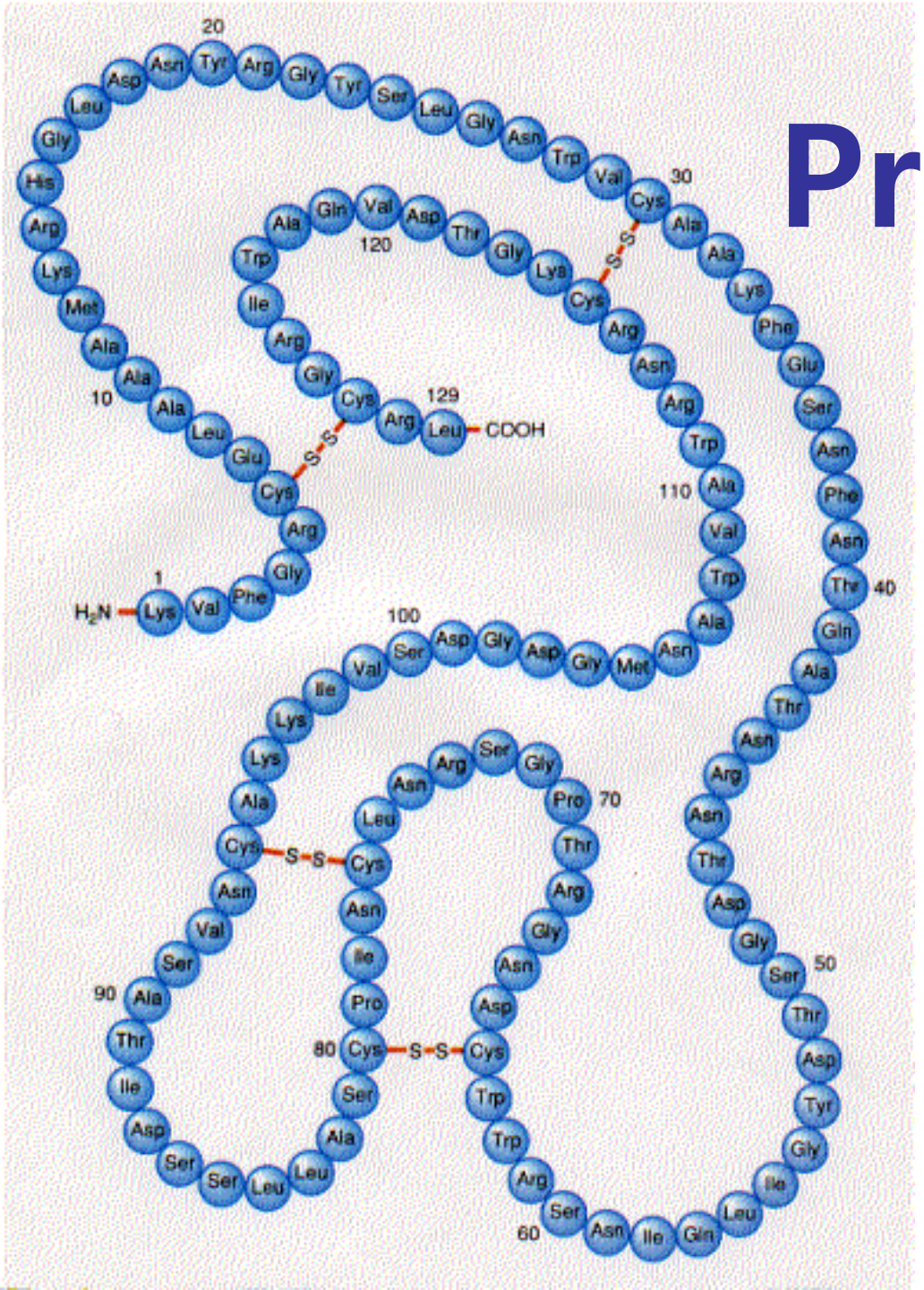
Steps of Protein Biosynthesis

&

Protein Biosynthesis Inhibitors

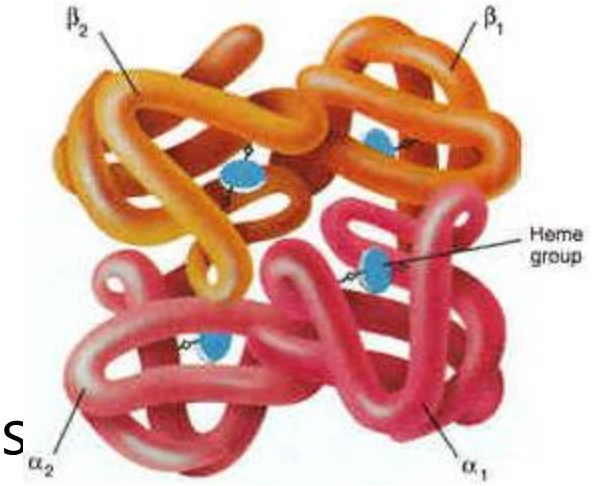


Protein Synthesis

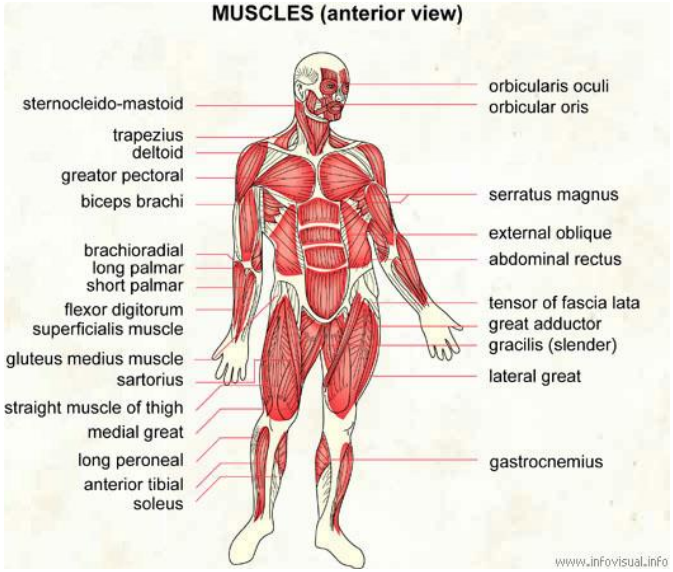
How do we get proteins from a bunch of A's, T's, C's and G's in DNA??

DNA contains the code of life…

The sequence of DNA codes for **proteins.**



Proteins are essential parts of <u>all</u> living things



Hormones, antibodies, enzymes, and body parts like muscles, ligament, cartilage and more are all made from proteins that our DNA codes for.

Remember that…

Proteins are made at the **ribosomes**, which are located in the **cytoplasm** of the cell.

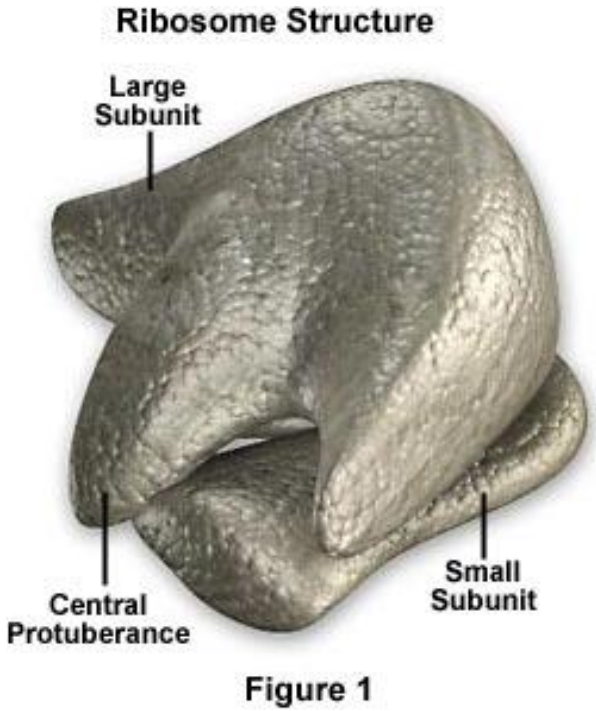


Figure 1

So how does the genetic code get from DNA in the <u>nucleus</u> to the ribosomes way out in the cytoplasm?!

RNA!!!

Ribo**N**ucleic **A**cid

3 Basic Parts of RNA:

1. **Ribose** Sugar
2. **Phosphate** group
3. Nitrogenous bases

RNA is **single-stranded.**

RNA contains the nitrogenous base **uracil** instead of **thymine**.

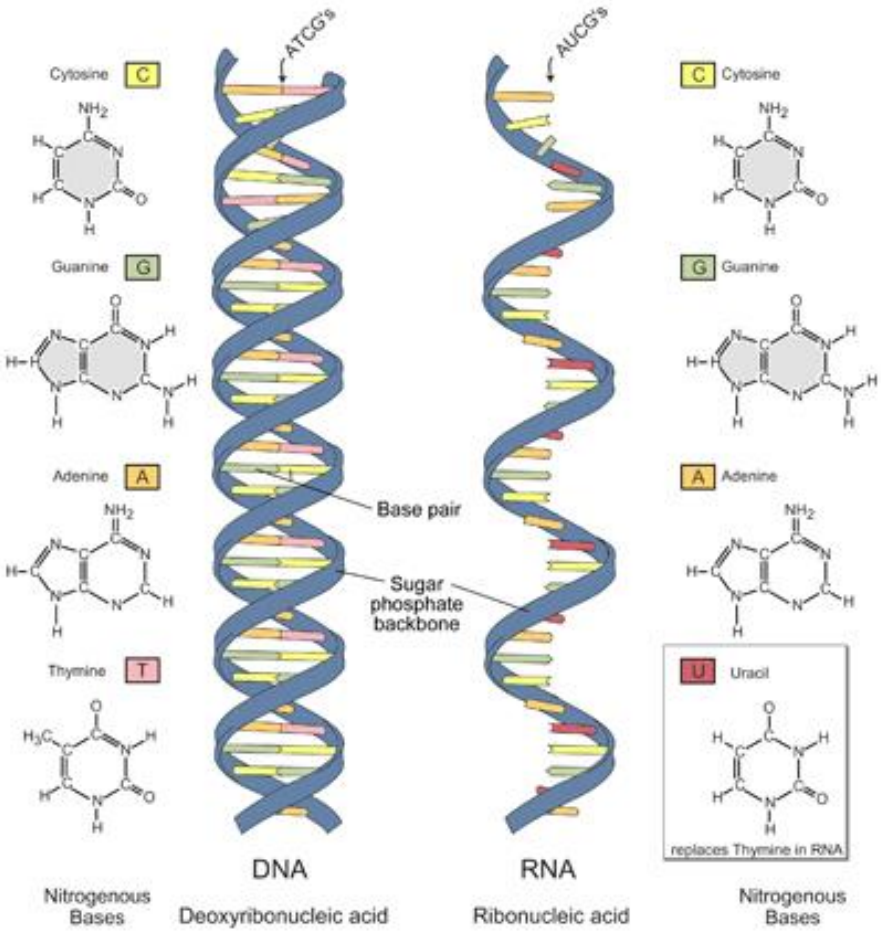
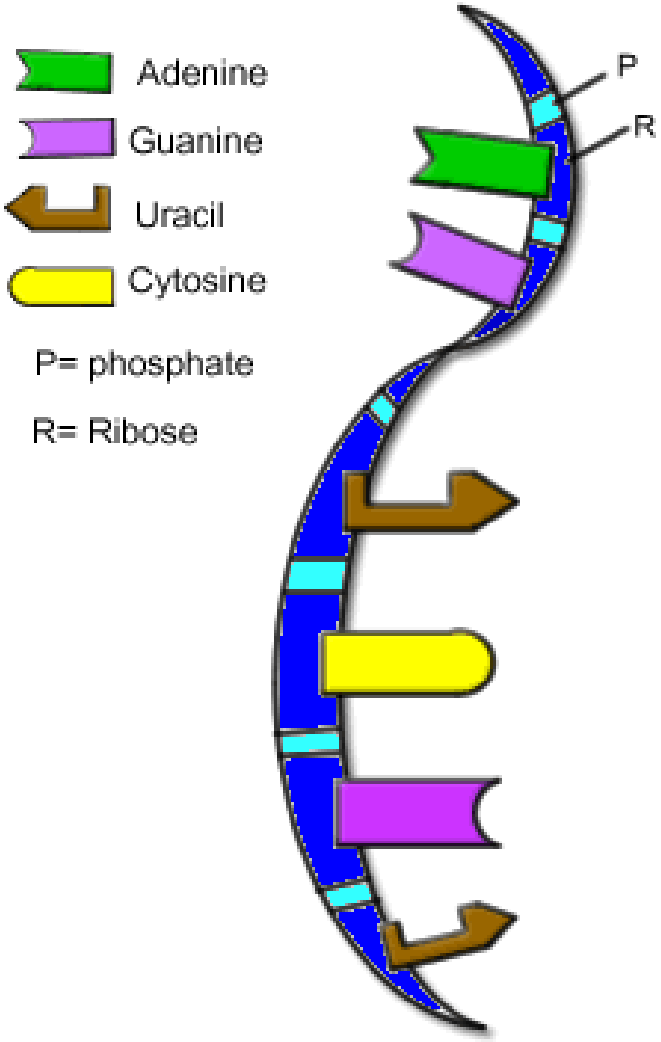


Image adapted from: National Human Genome Research Institute.

RNA is a disposable copy of a segment of DNA.



There are 3 main types of RNA.

1. Messenger RNA (mRNA)
2. Ribosomal RNA (rRNA)
3. Transfer RNA (tRNA)

Messenger RNA (mRNA)

mRNA is a **copy** of the genetic code that can travel out into the cytoplasm to the **ribosomes**.

DNA is too big and too important to go out into the cytoplasm itself.

mRNA is **short** and **disposable** (more can easily be made), so it is perfect for traveling out into the cytoplasm to the ribosomes.

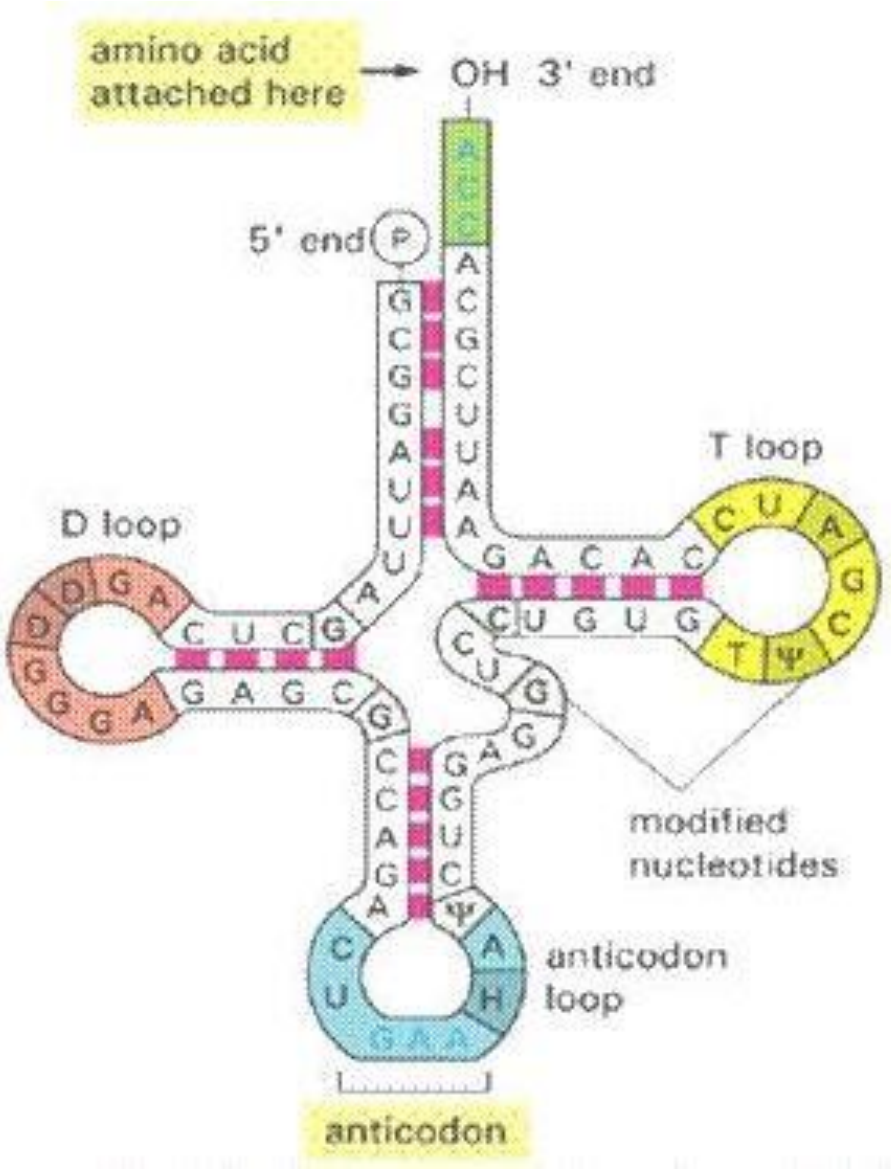
Ribosomes

Ribosomes are made up of another type of RNA, **ribosomal RNA (rRNA).**

Ribosomes **translate** the code that mRNA carries into a **protein**.

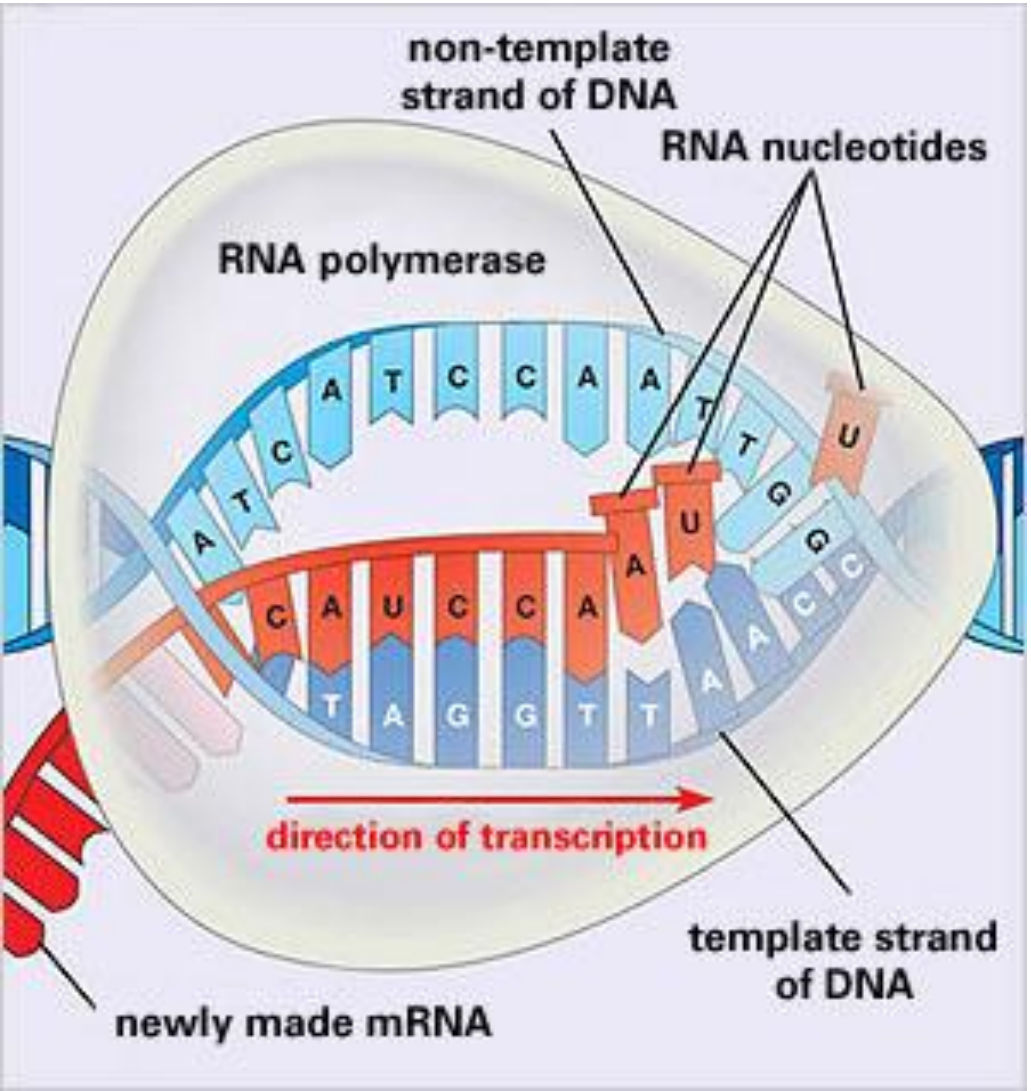
Transfer RNA (tRNA)

- tRNA carries **amino acids** to the ribosomes where they are linked together to form a protein
- Each tRNA has a specific **anticodon** that is complementary to a codon on mRNA.
- The anticodons match up with the codons to ensure that the correct amino acid is added to the polypeptide chain.



How is RNA made?

Transcription!

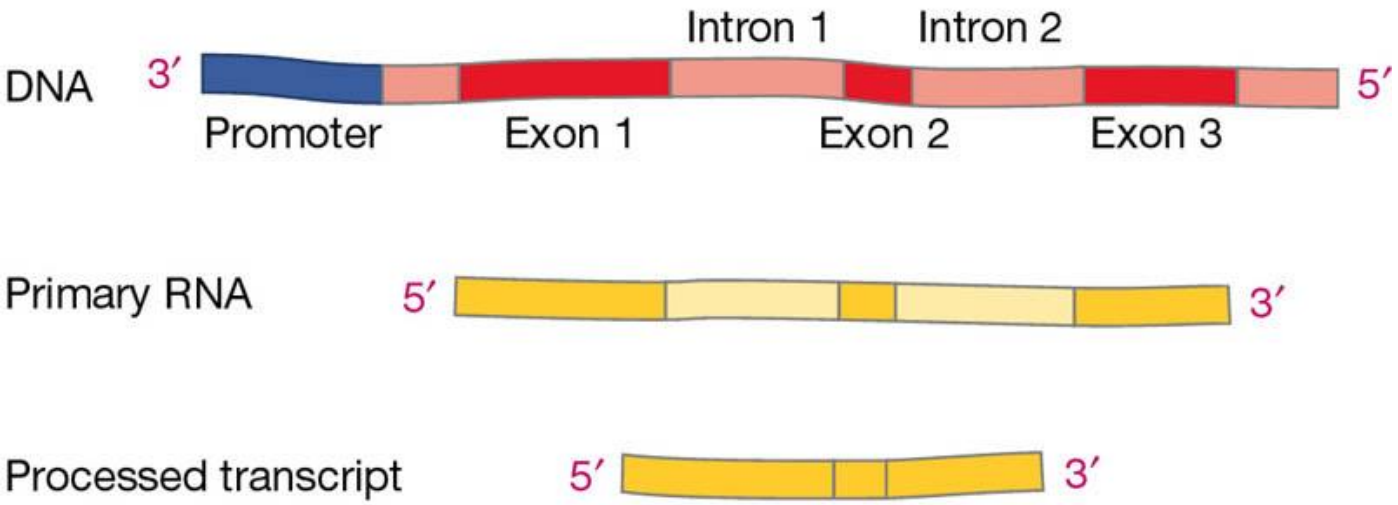


A lot like the process of DNA Replication…

1. **RNA Polymerase** unzips the DNA molecule.
2. **RNA Polymerase** then adds **nucleotides** to one side of the DNA making an RNA molecule.
3. The RNA molecule detaches from the DNA strand and makes its way out of the nucleus to perform its different jobs

***** Remember that there are no T's in RNA. Uracil (U) is used in place of thymine (T)*****

Before the mRNA can go to the ribosomes, it must be edited…



There are some parts of the DNA sequence that aren't involved in coding for proteins. These parts are called **introns**, and the introns must be removed from mRNA.

Introns are **in**-between…

Exons are **ex**pressed…

How Does a Code Work?

Pick a word that has at least 5 different letters… **DON'T TELL ANYONE YOUR WORD!!!**

Using the shapes on the board, come up with a code for your word.

We will exchange codes with each other and try to figure them out…

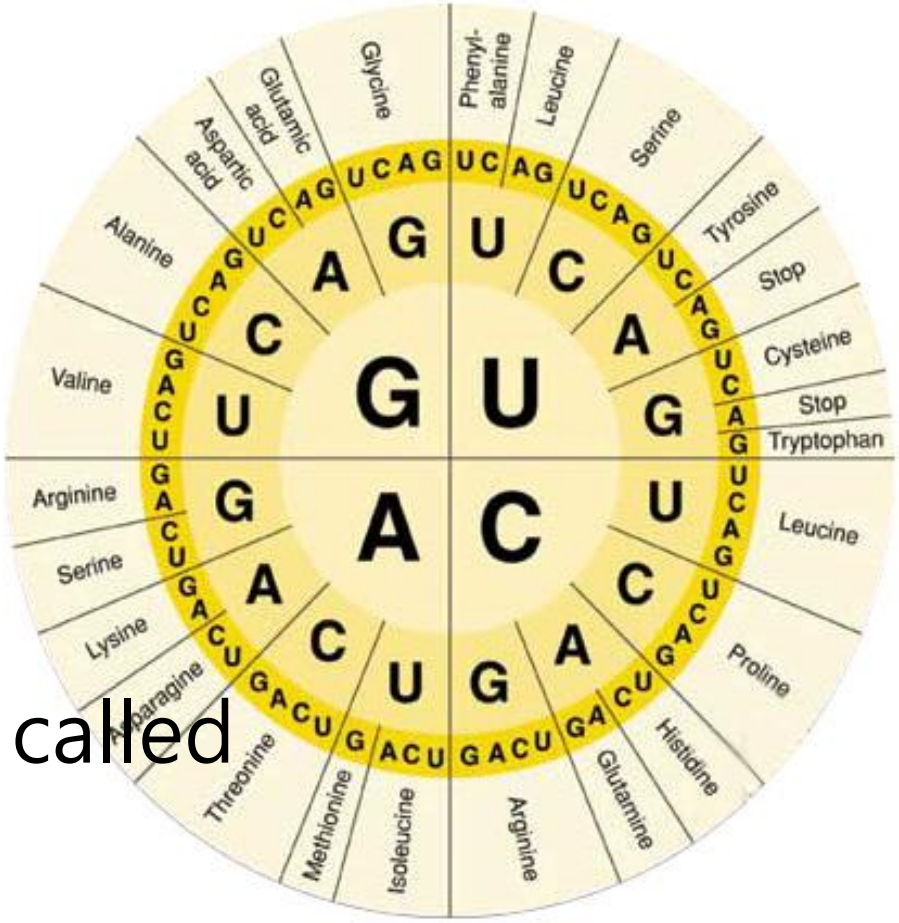
How were you able to encode 5 different letters using only 4 different colored beads?

The Genetic Code

3-letter "words" code for amino acids.

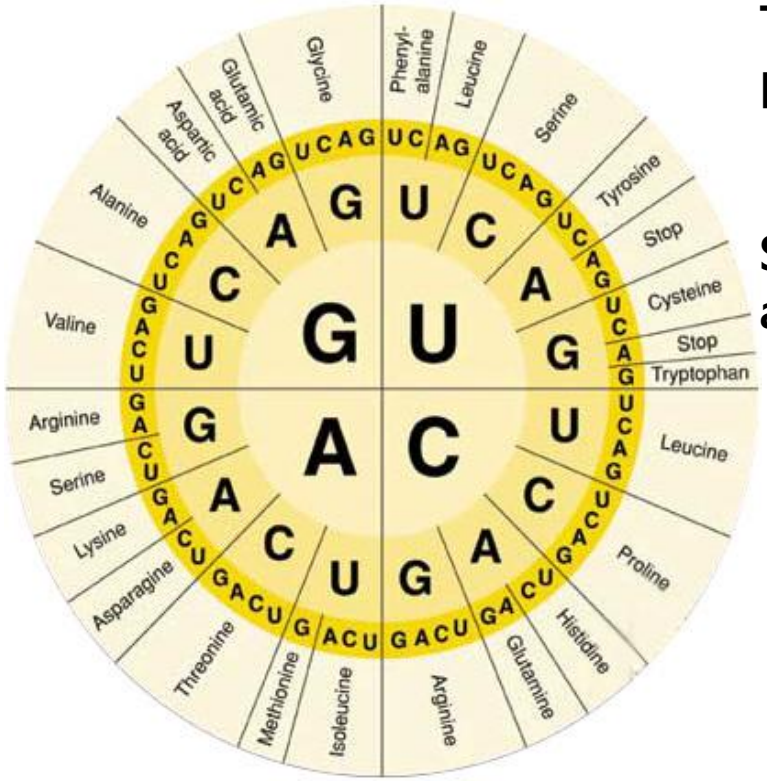
Amino acids are the building blocks of proteins.

The "words" of DNA are called **codons.**



CODONS

3-letter "words" of the DNA sequence that code for amino acids.



There are 64 codons… because there are 4 possible bases for each slot (4x4x4=64!)

Since there are only 20 amino acids, some amino acids are coded for by more than one codon.

mRNA code

UCGCACGGUCAGGUGCAC

codons

UCG-CAC-GGU-CAG-GUG-CAC

Amino acids

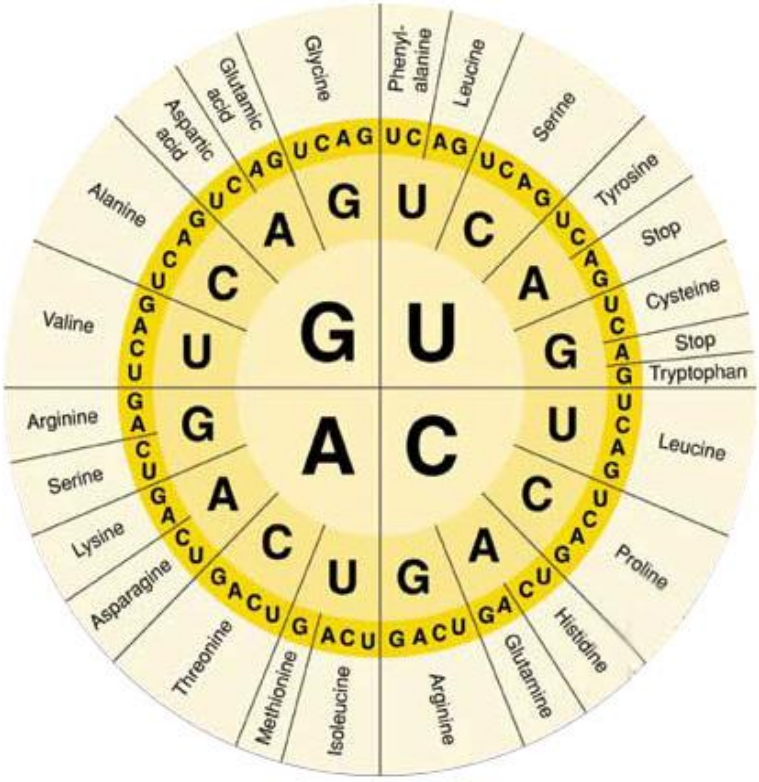
Serine-Histidine-Glycine-Glutamine-Valine-Histidine

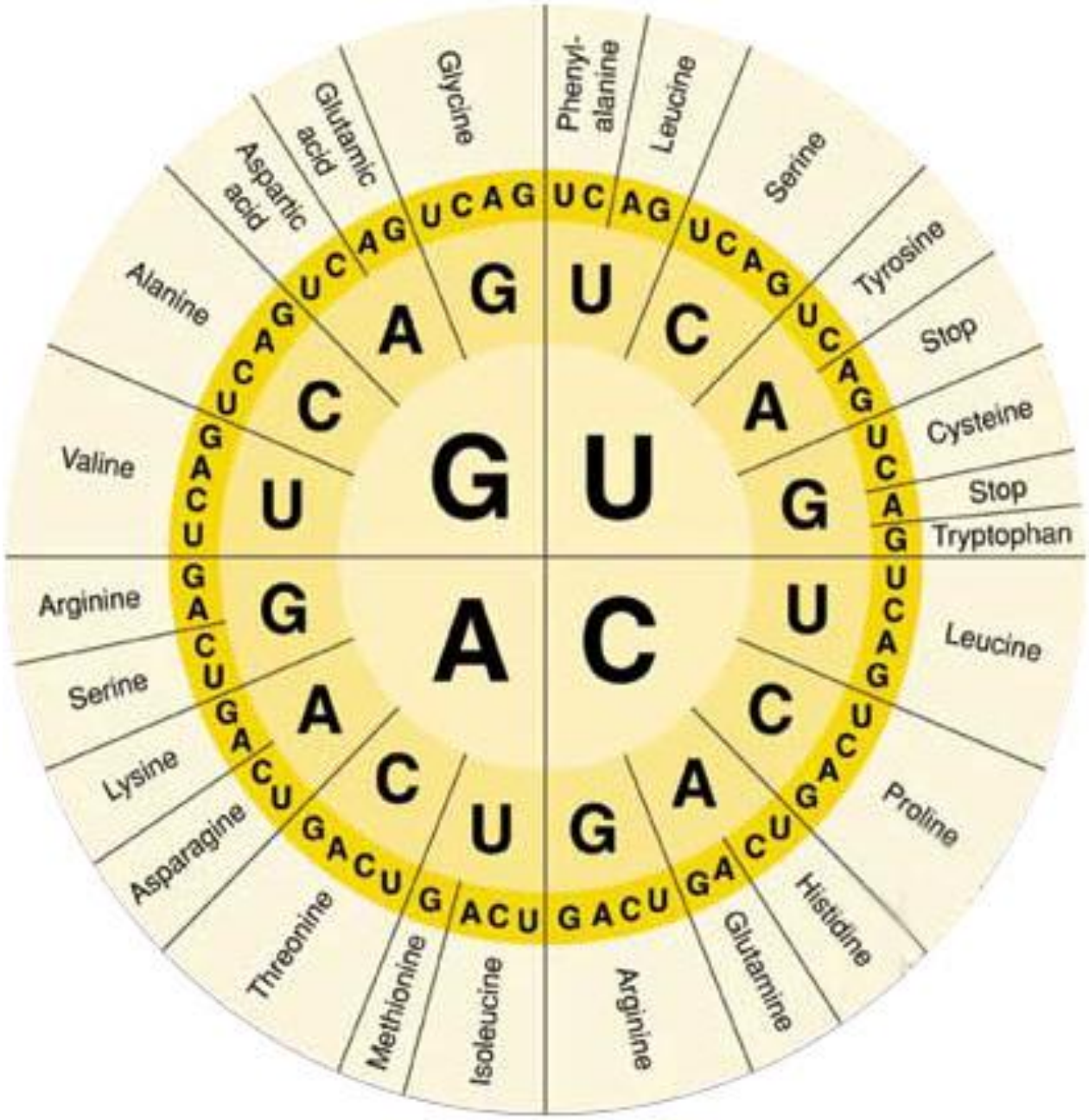
Your Turn!

AUGGUGCCACGAAGGUGA

AUG-GUG-CCA-CGA-AGG-UGA

Methionine-Valine-Proline-
Arginine-Arginine-Stop




G
U
A
C
Glycine
Glutamic acid
Aspartic acid
Alanine
Valine
Phenyl-alanine
Leucine
Serine
Tyrosine
Stop
Cysteine
Stop
Tryptophan
Leucine
Proline
Histidine
Glutamine
Arginine
Isoleucine
Methionine
Threonine
Asparagine
Lysine
Serine
Arginine

Special Codons

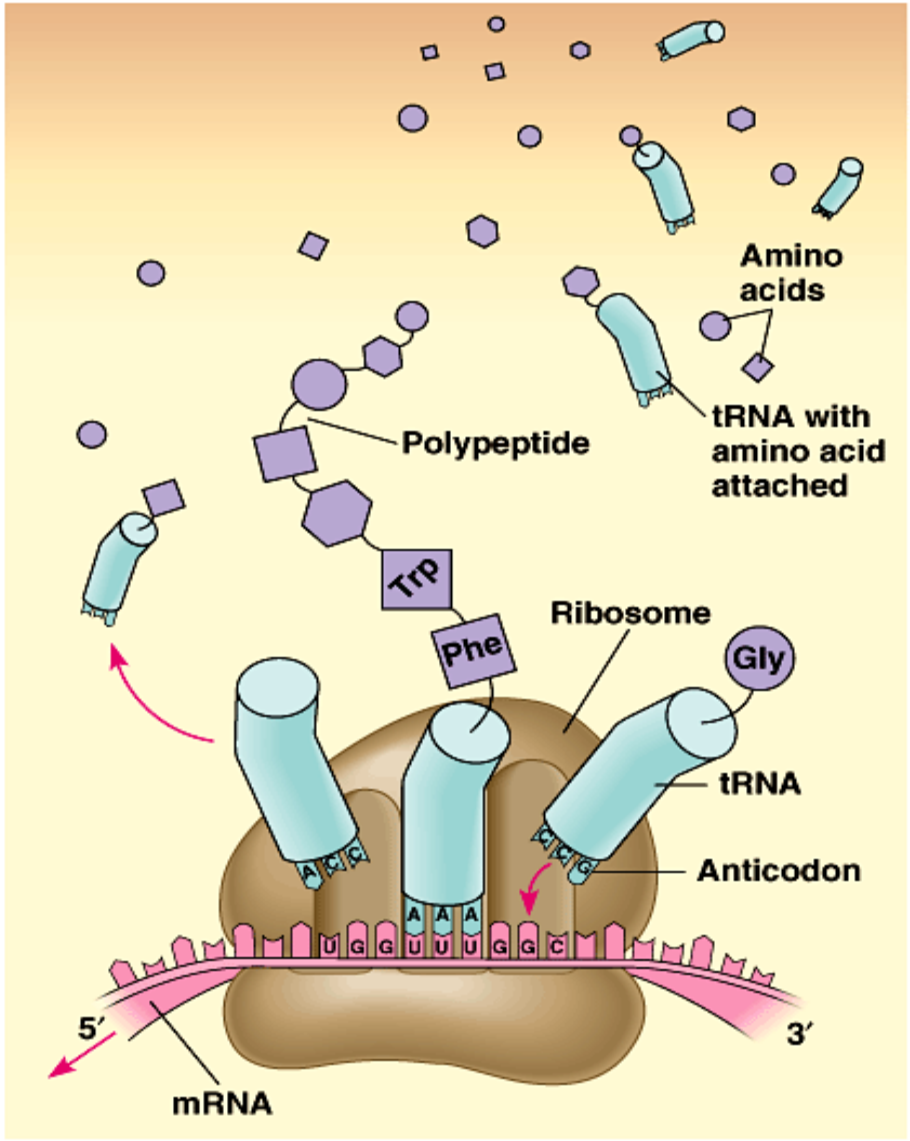
- Some codons don't code for an amino acid.

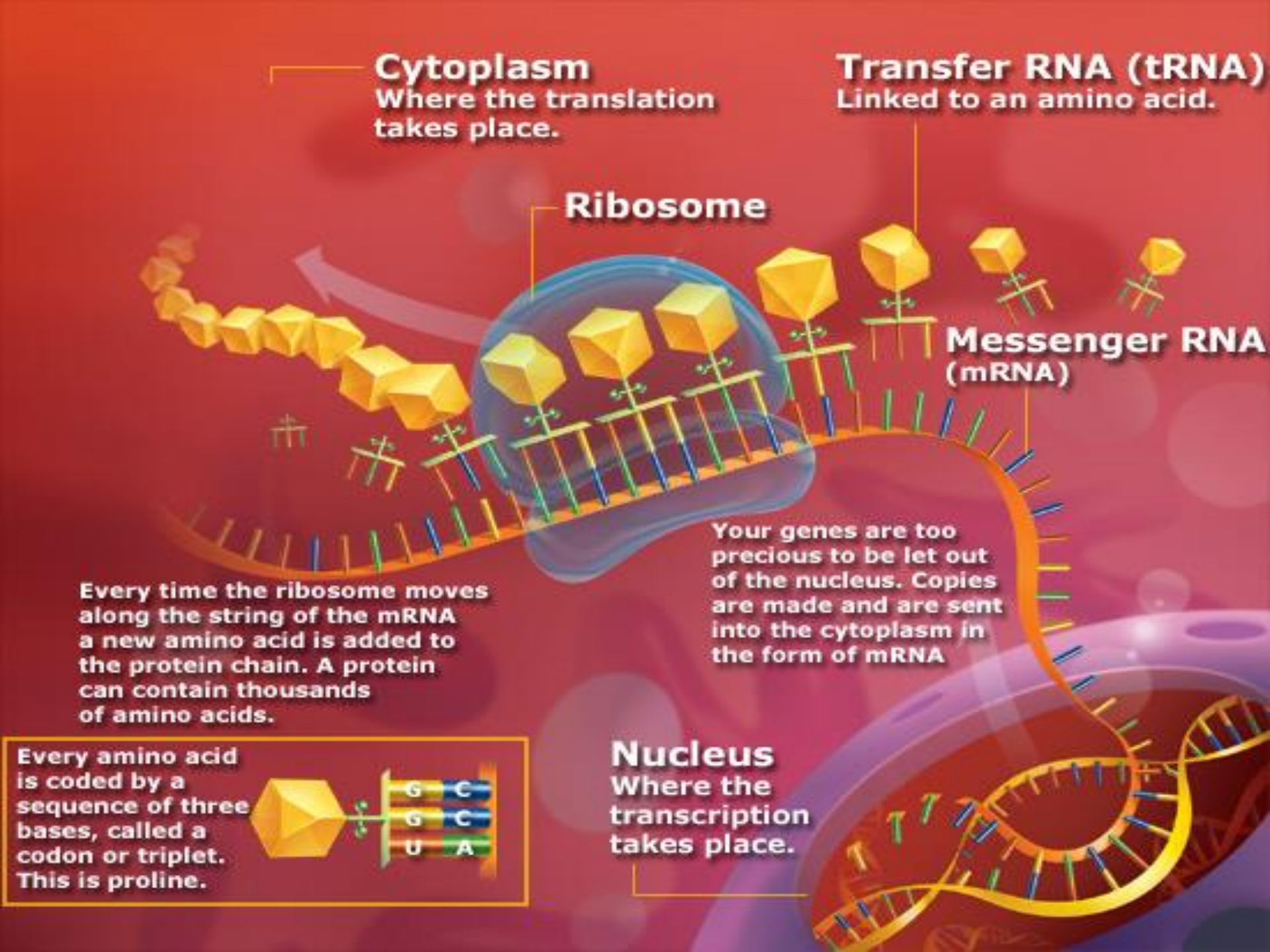
- Instead they signal the start of the protein or they code for synthesis to stop→ like the period at the end of a sentence!

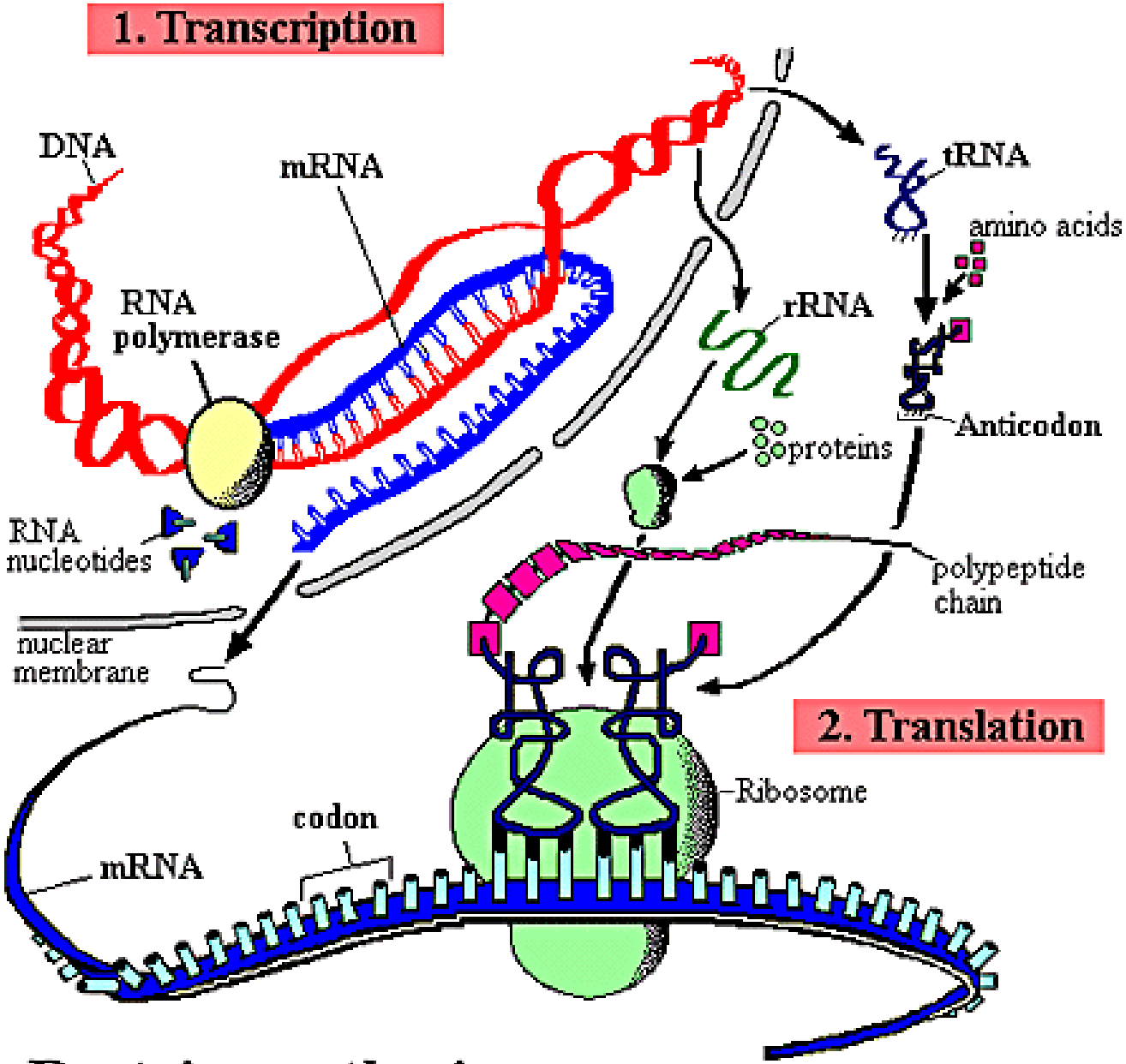
Translation

The process where the genetic code is read and a protein is created at the ribosomes.

1. mRNA travels from the nucleus to the ribosomes
2. Ribosomes begin "reading" the mRNA
3. Transfer RNA (tRNA) carries amino acids to the ribosomes where they are joined together in the correct order




Cytoplasm
Where the translation takes place.
Transfer RNA (tRNA)
Linked to an amino acid.
Ribosome
Messenger RNA (mRNA)
Your genes are too precious to be let out of the nucleus. Copies are made and are sent into the cytoplasm in the form of mRNA
Every time the ribosome moves along the string of the mRNA a new amino acid is added to the protein chain. A protein can contain thousands of amino acids.
Every amino acid is coded by a sequence of three bases, called a codon or triplet. This is proline.
G C
G C
U A
Nucleus
Where the transcription takes place.

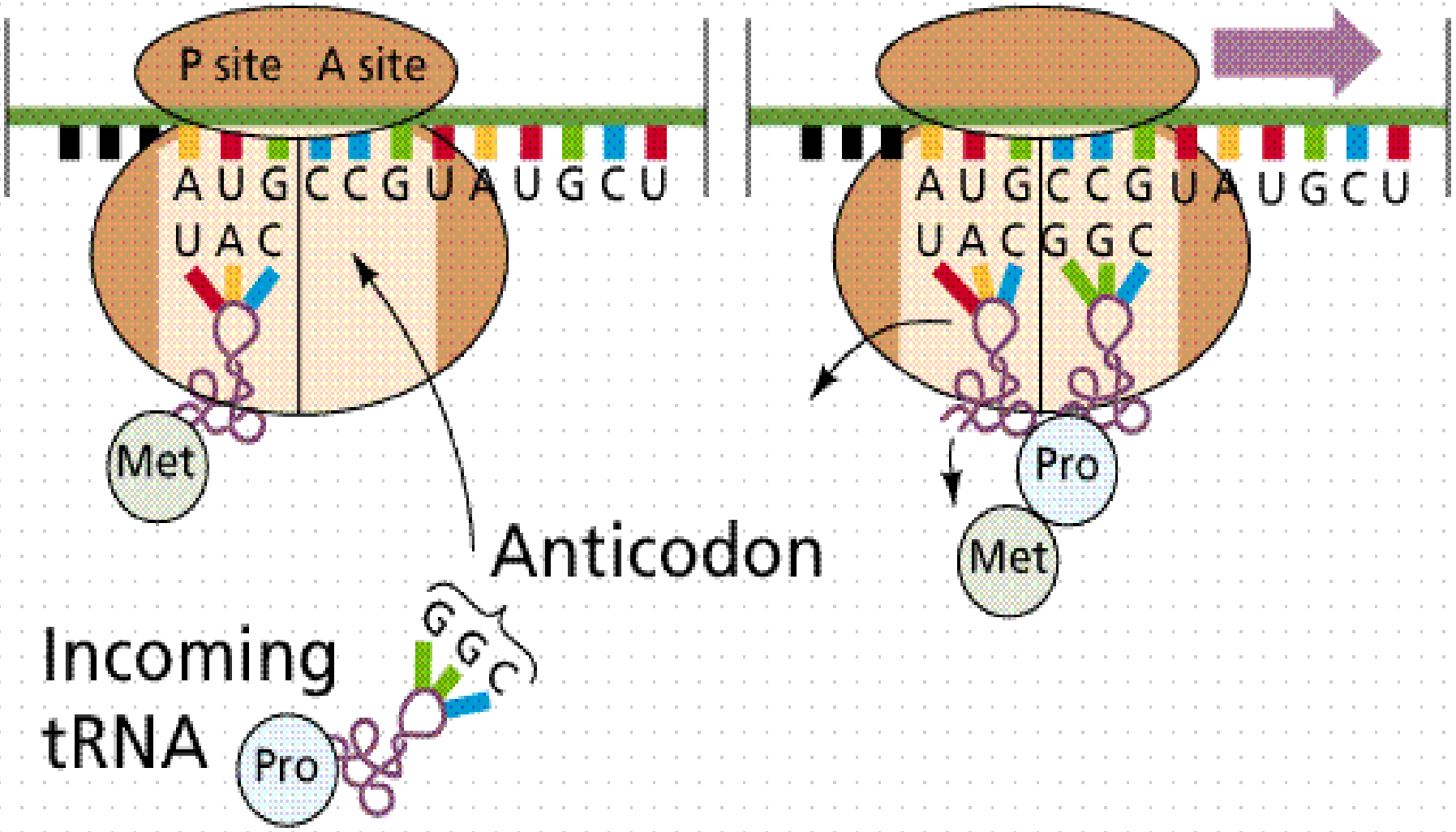


Protein synthesis

STEP 1: The first step in protein synthesis is the transcription of mRNA from a DNA gene in the nucleus. At some other prior time, the various other types of RNA have been synthesized using the appropriate DNA. The RNAs migrate from the nucleus into the cytoplasm.

Prior to the beginning of the protein synthesis, all of the component parts are assembled in the ribosome which is the brown/tan structure in the left graphic.

Elongation (translation)



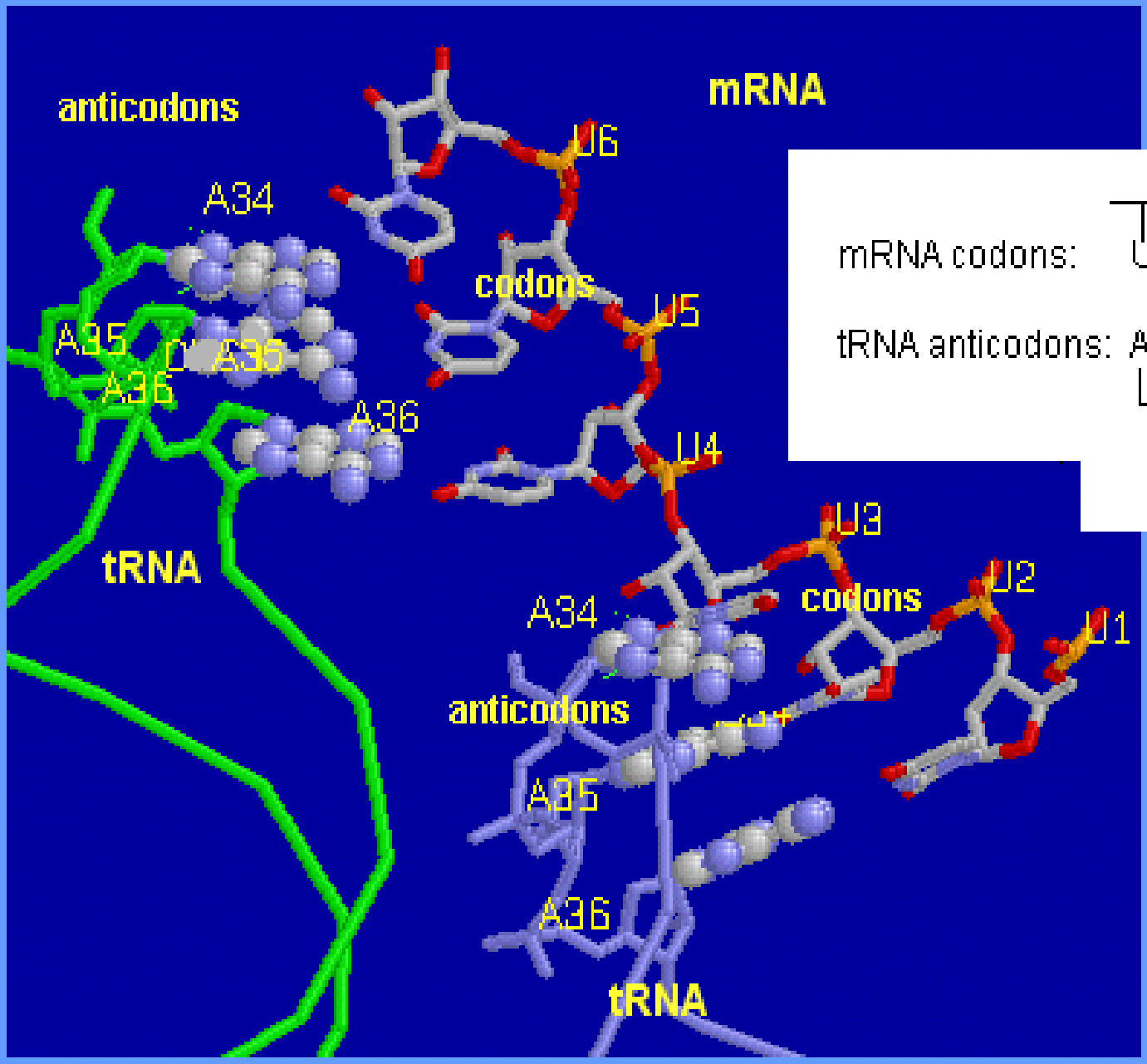
STEP 2: Initiation:

In the cytoplasm, protein synthesis is actually initiated by the AUG codon on mRNA. The AUG codon signals both the interaction of the ribosome with m-RNA and also the tRNA with the anticodons (UAC). The tRNA which initiates the protein synthesis has N-formyl-methionine attached. The formyl group is really formic acid converted to an amide using the $-NH_2$ group on methionine (left most graphic)

The next step is for a second tRNA to approach the mRNA (codon - CCG). This is the code for proline. The anticodon of the proline tRNA which reads this is GGC. The final process is to start growing peptide chain by having amine of proline to bond to the carboxyl acid group of methinone (met) in order to elongate the peptide.

The next codon is UAU. What is the next amino acid to be added?

Interaction of tRNA and mRNA

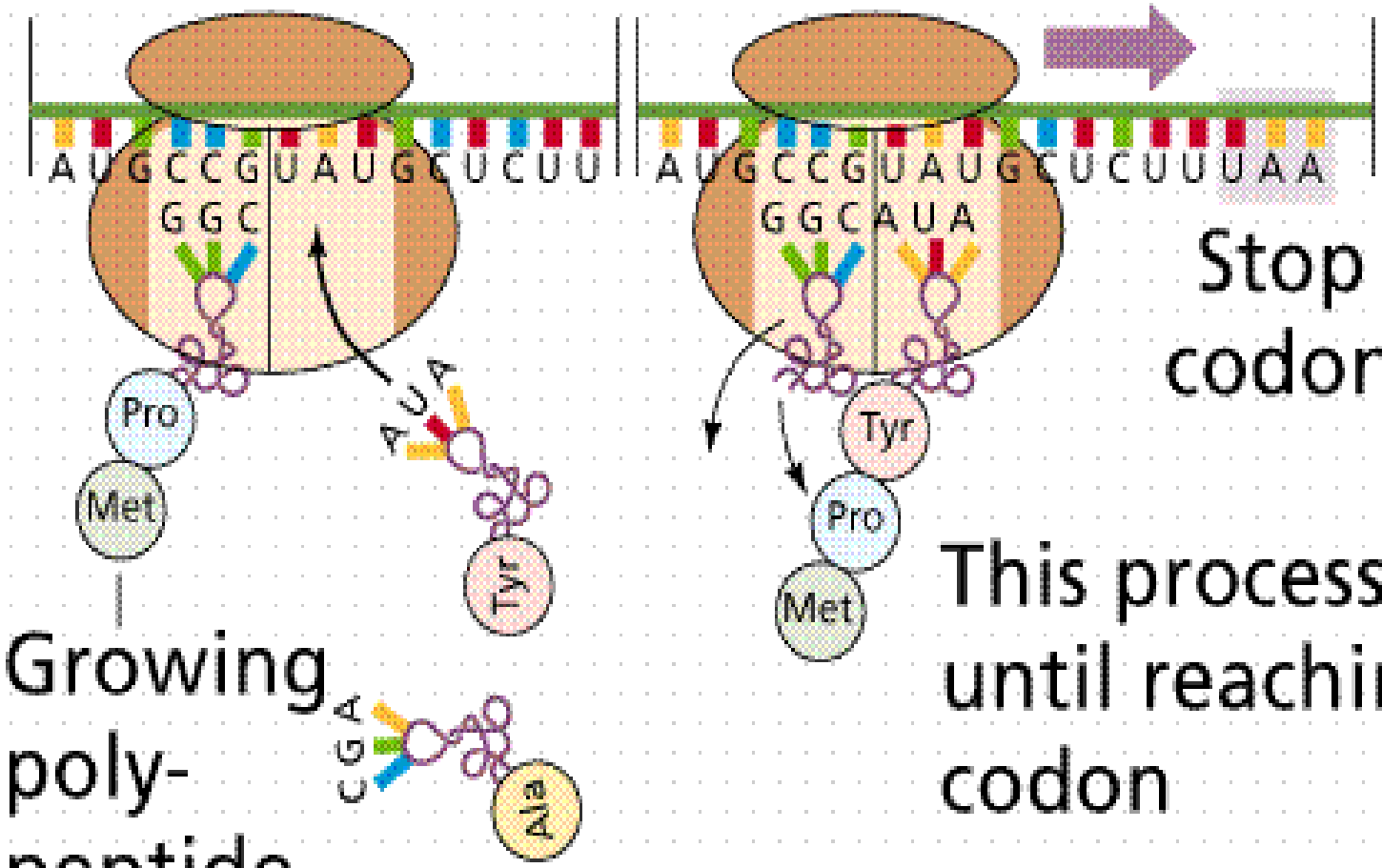


STEP 3: Elongation:

Elongation of the peptide begins as various tRNA's read the next codon. In the example on the left the next tRNA to read the mRNA is tyrosine. When the correct match with the anticodons of a tRNA has been found, the tyrosine forms a peptide bond with the growing peptide chain .

The proline is now hydrolyzed from the tRNA. The proline tRNA now moves away from the ribosome and back into the cytoplasm to reattach another proline amino acid. *The next codon is GCU. What is the next amino acid to be added?*

Elongation continues



Stop codon

This process repeats until reaching a stop codon

Growing poly-peptide

When the stop signal on mRNA is reached, the protein synthesis is terminated. The last amino acid is hydrolyzed from its t-RNA. The peptide chain leaves the ribosome. The N-formyl-methionine that was used to initiate the protein synthesis is also hydrolyzed from the completed peptide at this time.
The ribosome is now ready to repeat the synthesis several more times.

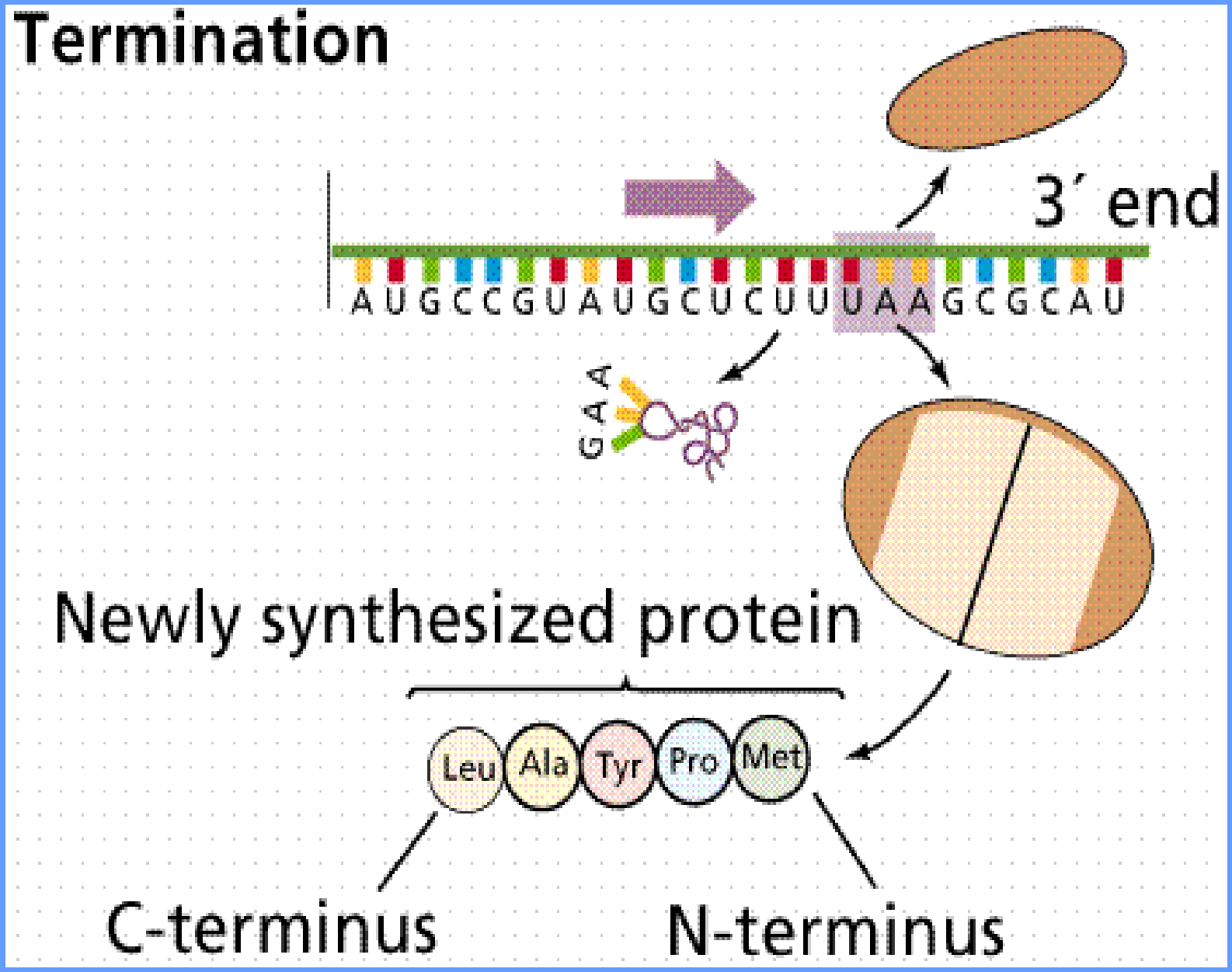
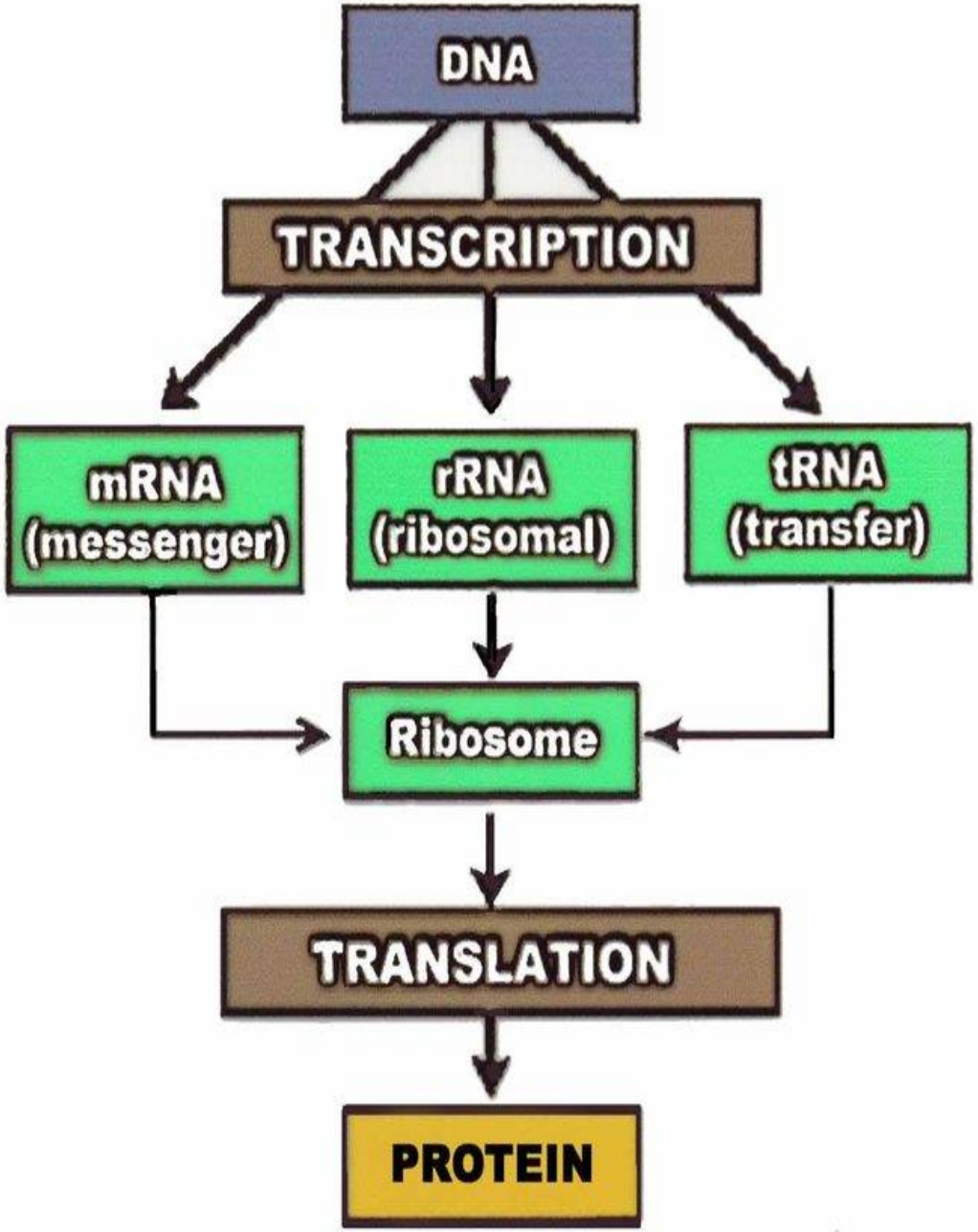


Image from Purves et al., Life: The Science of Biology, 4th Edition, by Sinauer Associates (www.sinauer.com) and WH Freeman (www.whfreeman.com), used with permission.



Draw a graphic organizer or flow chart to show the path from DNA to protein!

Antibacterial Antibiotics Inhibitors of Protein Synthesis

- **Protein synthesis** - different ribosomes 70s good site of attack
  - Aminoglycosides - (streptomycin, gentamicin) bind to 30s subunit blocks translation and misreading of mRNA
  - **Tetracyclines** - bind to 30s subunit and block attachment of tRNA
  - **Chloramphenicol** - binds to 50S subunits and prevents peptide bonds from being formed
  - Macrolides - bind to 50s subunits and prevents the continuation of protein synthesis - used in many G(+) and walking atypical pneumonia instead of penicillin

Antibacterial Antibiotics Inhibitors of Protein Synthesis

- **Tetracyclines**
  - Broad spectrum
    - Interferes with tRNA attachment
- **Macrolides**
  - Gram-positives
    - Binds 50S, prevents translocation
    - **Common macrolides**
      - Azithromycin (Zithromax)
      - Clarithromycin (Biaxin, Fromilid)
      - Dirithromycin (Dynabac)
      - Erythromycin
  - Gram-positives
    - Binds 50S, prevents translocation

Antibacterial Antibiotics Inhibitors of Protein Synthesis

- Streptogramins
  - Gram-positives
    - Binds 50S subunit, inhibits translation
- Synercid
  - Gram-positives
    - Binds 50S subunit, inhibits translation
- Oxazolidinones
  - Linezolid
    - Gram-positives
      - Binds 50S subunit, prevents formation of 70S ribosome