

# Protein Synthesis – 3 basic steps

transcription → RNA processing → translation

## 2. RNA processing – the mRNA is modified before leaving the nucleus

- The mRNA made in the previous step is considered heterogeneous nuclear RNA (hnRNA) which contains extra nucleotides
  - Meaning it contains both coding regions and non-coding regions in the sequence
    - Regions that express code for the polypeptide are exons
    - Regions that do not express code are introns
  - An RNA complex called a spliceosome removes the introns.
- A poly(A) tail is added to the 3' end and a 5' cap is added to the 5' end

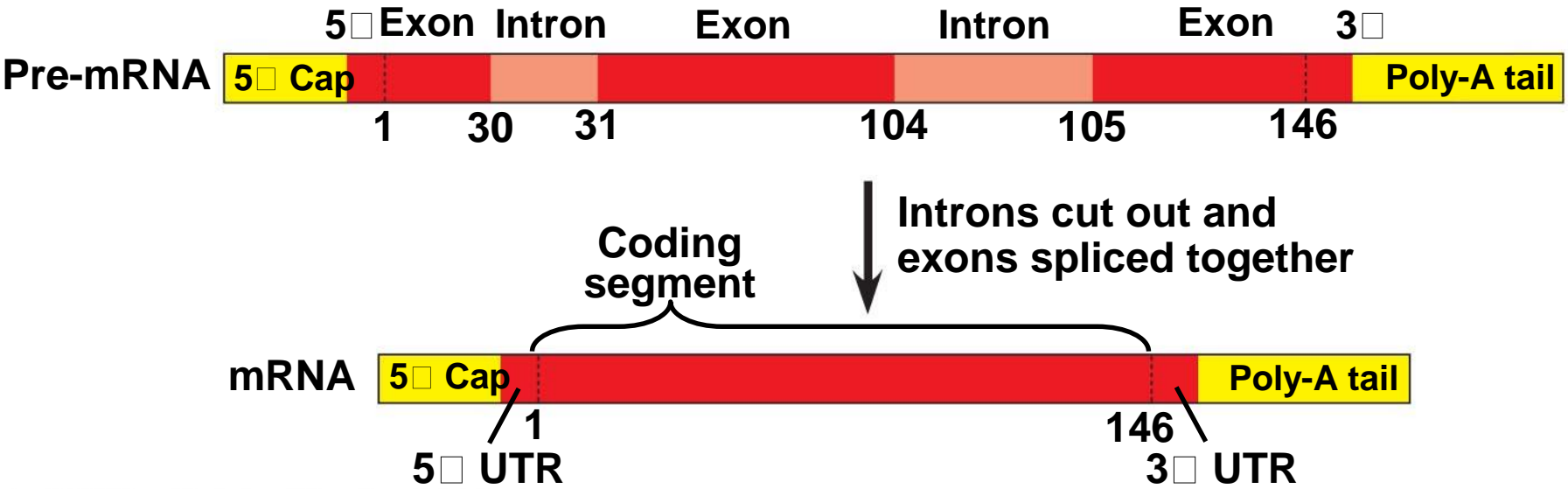
# Eukaryotic cells modify RNA after transcription

- Enzymes in the eukaryotic nucleus modify pre-mRNA before the genetic messages are dispatched to the cytoplasm
- During RNA processing, both ends of the primary transcript are usually altered
- Also, usually some interior parts of the molecule are cut out, and the other parts spliced together
- Each end of a pre-mRNA molecule is modified in a particular way:
  - The 5' end receives a modified nucleotide **5' cap** (a modified guanine nucleotide)
    - It is added onto the 5' end after transcription of the first 20-40 nucleotides
  - The 3' end gets a **poly-A tail**
    - Enzyme adds 50-250 adenines

# Split Genes and RNA Splicing

- Most eukaryotic genes and their RNA transcripts have long noncoding stretches of nucleotides that lie between coding regions
- These noncoding regions are called intervening sequences, or **introns**
- They get cut out of the mRNA
- The other regions are called **exons** because they are eventually expressed, usually translated into amino acid sequences
- **RNA splicing** removes introns and joins exons, creating an mRNA molecule with a continuous coding sequence
- (introns/exons are included in the primary transcript of RNA, the introns are removed during mRNA processing, the exons then join together allow for continuous translation

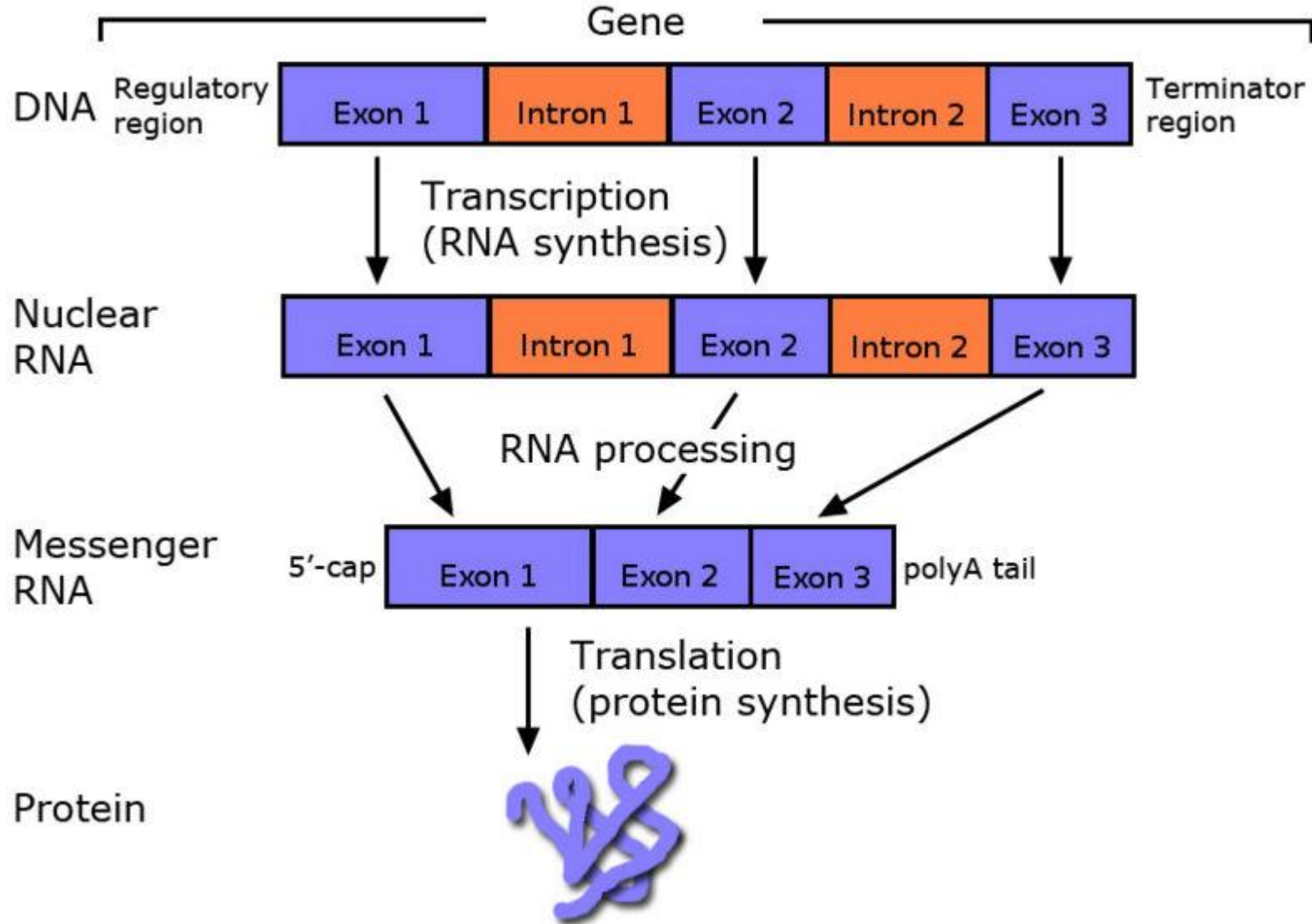
Fig. 14-10



- A **primary transcript** is the initial RNA transcript from any gene (before it undergoes processing to be the “final” version of mRNA that gets translated to protein)
- The central dogma is the concept that cells are governed by a cellular chain of command:  
DNA → RNA → protein

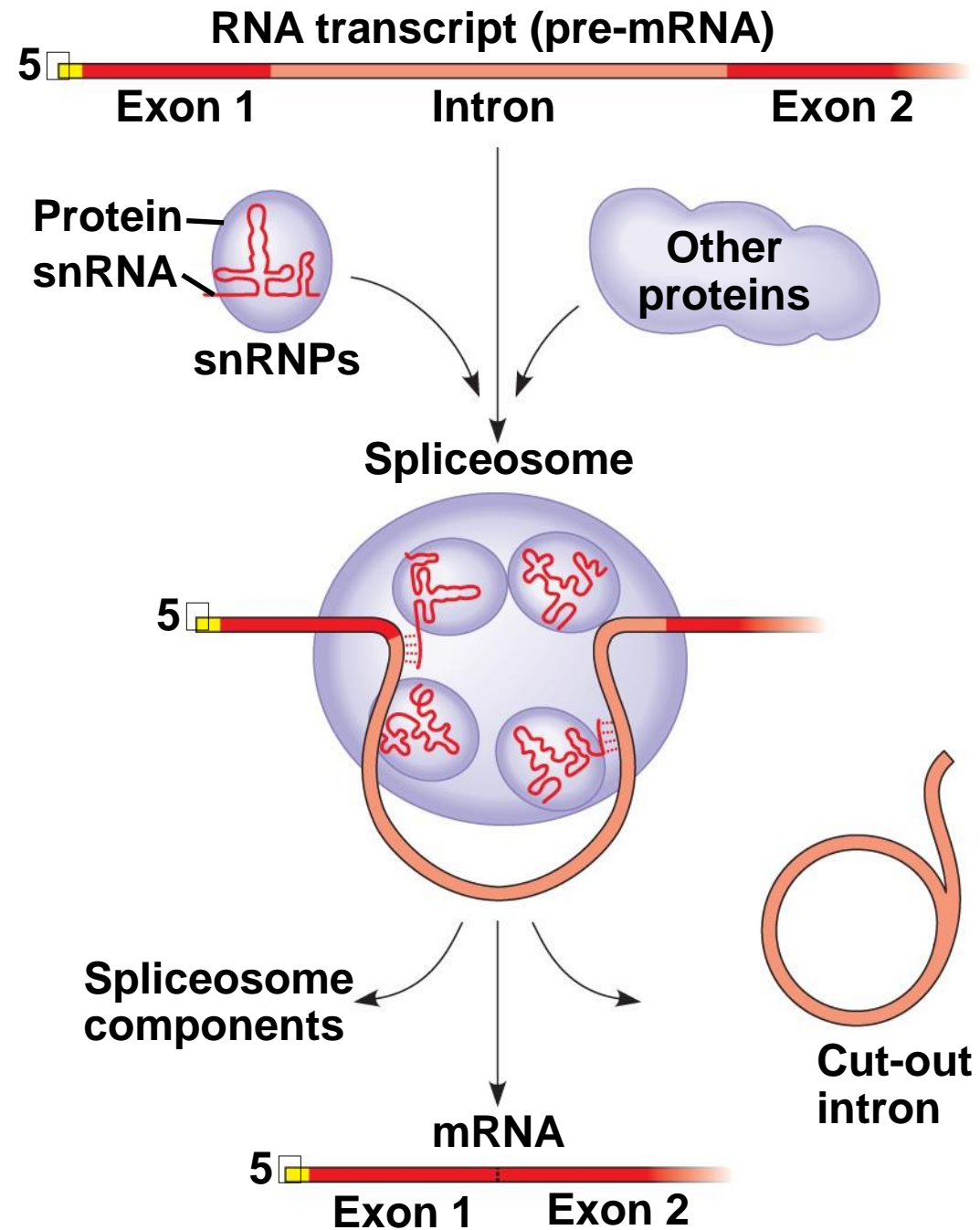
# Protein Synthesis – 3 basic steps

transcription → RNA processing → translation



- In some cases, RNA splicing is carried out by spliceosomes
- **Spliceosomes** consist of a variety of proteins and several small nuclear ribonucleoproteins (snRNPs are thought to catalyze the process) that recognize the splice sites
- They interact with sites along an intron, release the intron and join the exons together

Fig. 14-11-3



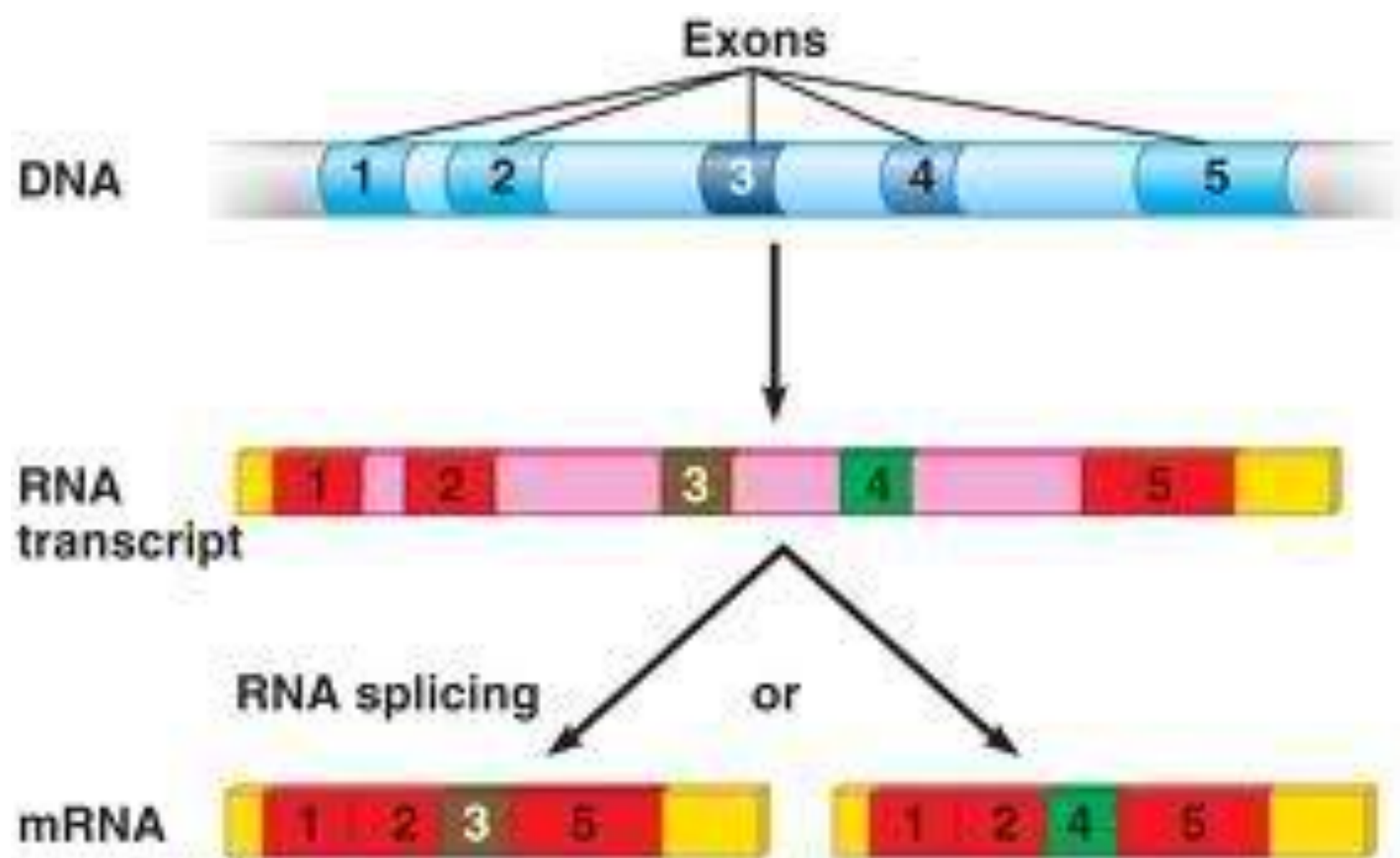


# Evolutionary importance

- Prokaryotes have DNA and undergo a similar process as eukaryotes in transmitting the genetic code into a product
- In prokaryotes, mRNA produced by transcription is immediately translated without more processing
- So, parts of the mRNA are being translated into a protein while other segments are still being transcribed from DNA to mRNA
- This is because there is no separation due to the lack of a nucleus
- In a eukaryotic cell, the nuclear envelope separates transcription from translation
- Eukaryotic RNA transcripts are modified through **RNA processing** to yield finished mRNA

# *The Functional and Evolutionary Importance of Introns*

- Some genes can encode more than one kind of polypeptide, depending on which segments are treated as exons during RNA splicing
- Such variations are called **alternative RNA splicing**
- Because of alternative splicing, the number of different proteins an organism can produce is much greater than its number of genes

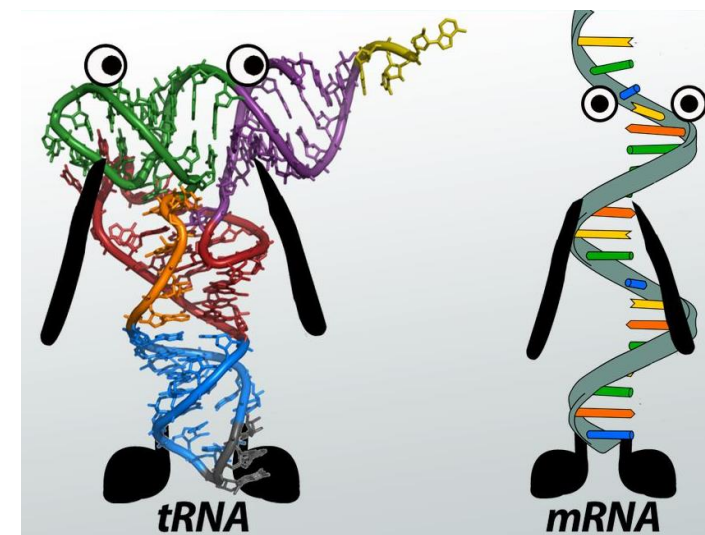
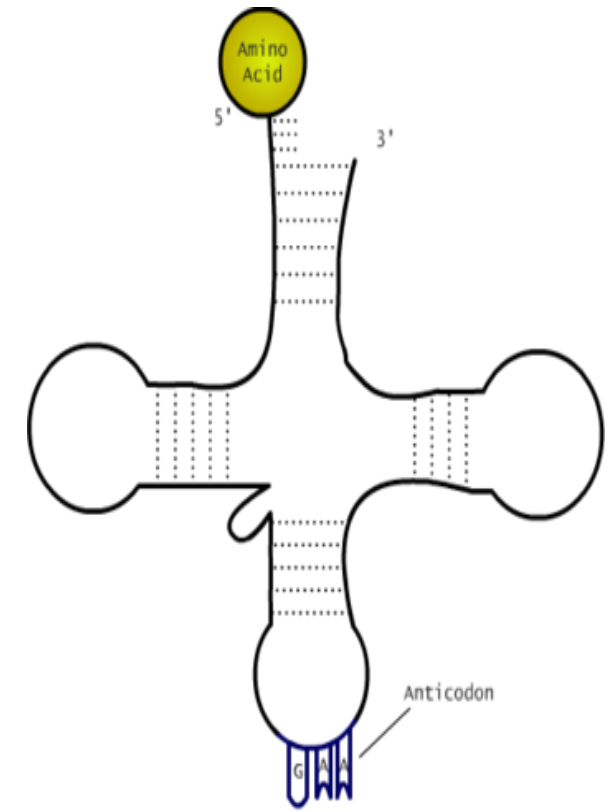


# Protein Synthesis – 3 basic steps

transcription → RNA processing → translation

## 3. Translation – mRNA leaves the nucleus and searches for a ribosome

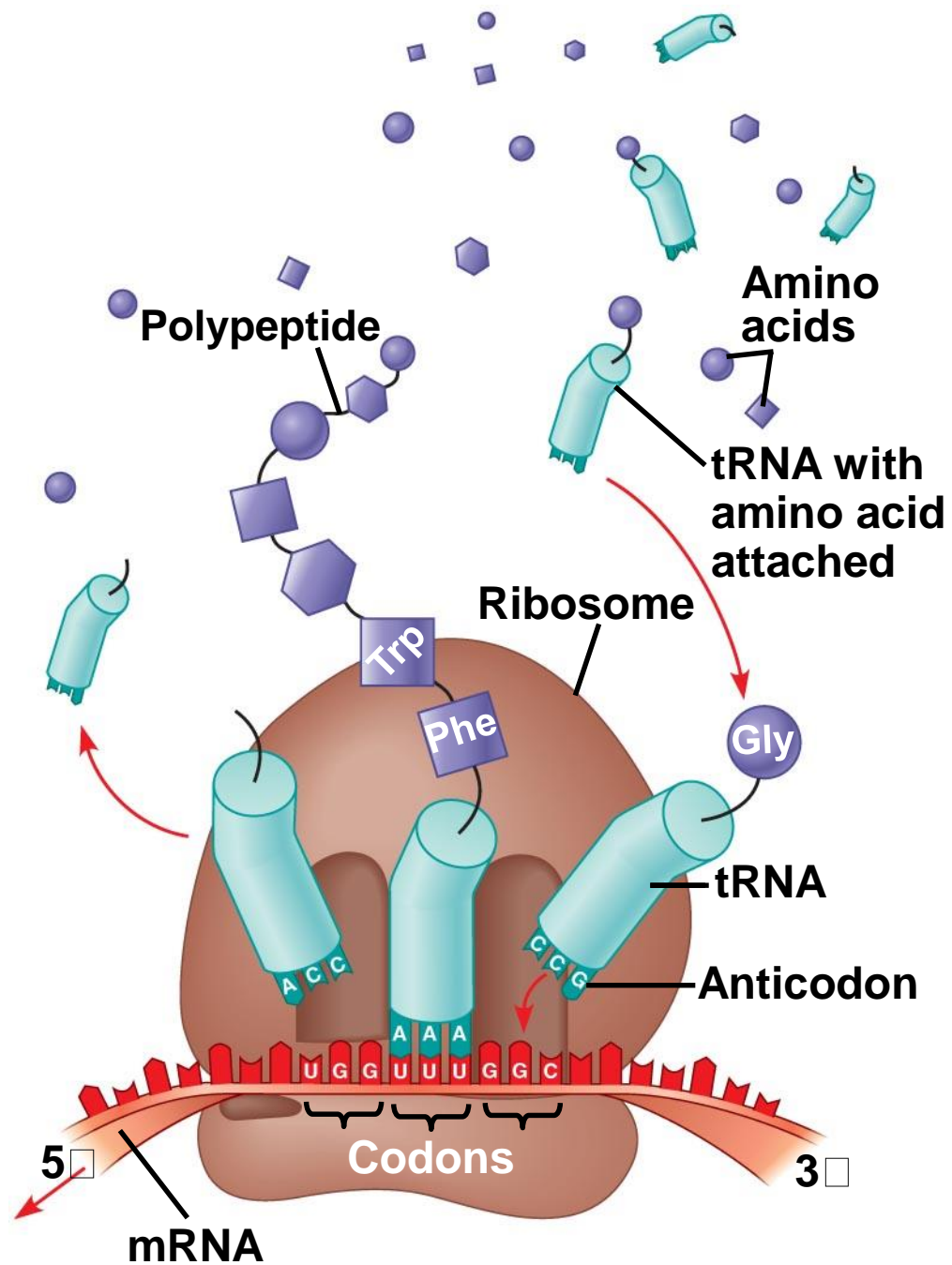
- The mRNA is organized into a sequence of three letter codons that correspond to one of the 20 amino acids
  - Some amino acids are specified by more than one codon
- The amino acids are carried to the mRNA/ribosome by tRNA
  - ATP charges the enzymatic attachment of the amino acids to the tRNA so that it can be “shuttled” over to the mRNA and attached to the amino acids chain
  - The tRNA has a three letter anticodon that is complimentary to the codons of the mRNA



# Molecular Components of Translation

- A cell translates an mRNA message into protein with the help of **transfer RNA (tRNA)**
- Molecules of tRNA are not identical:
  - Each carries a specific amino acid on one end
  - Each has an **anticodon** on the other end; the anticodon base-pairs with a complementary codon on mRNA

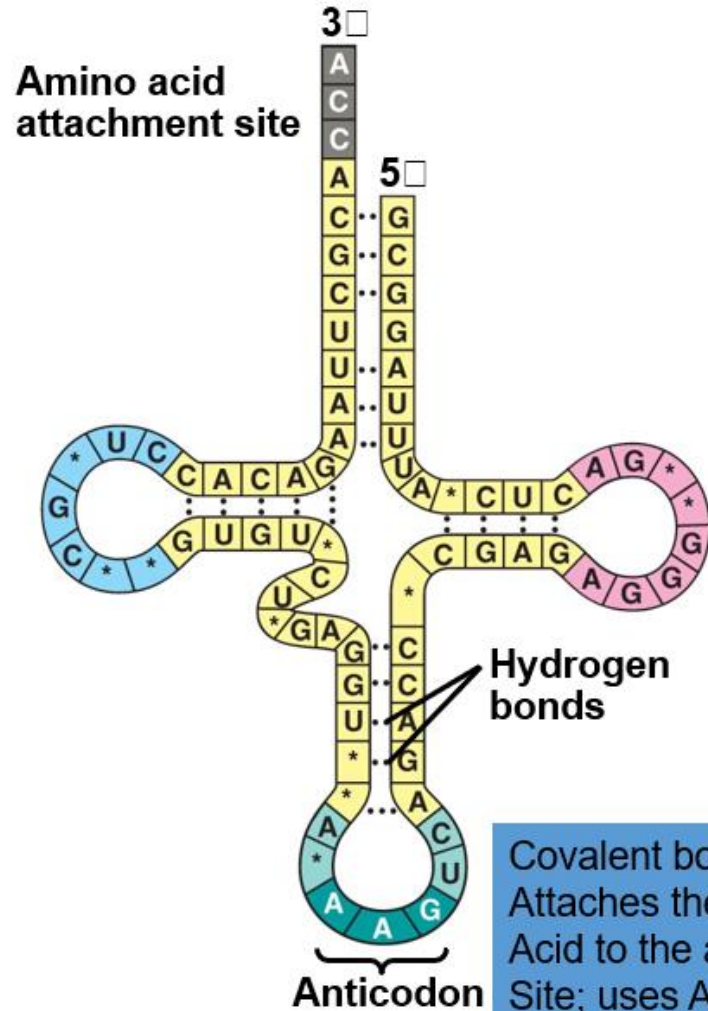
Fig. 14-13



# *The Structure and Function of Transfer RNA*

- A tRNA molecule consists of a single RNA strand that is only about 80 nucleotides long
- Flattened into one plane to reveal its base pairing, a tRNA molecule looks like a cloverleaf
- It forms into this shape because 1) it is single stranded 2) can fold up on itself and have complementary “patches” that allow distinct spots on the RNA to form sections that are double stranded

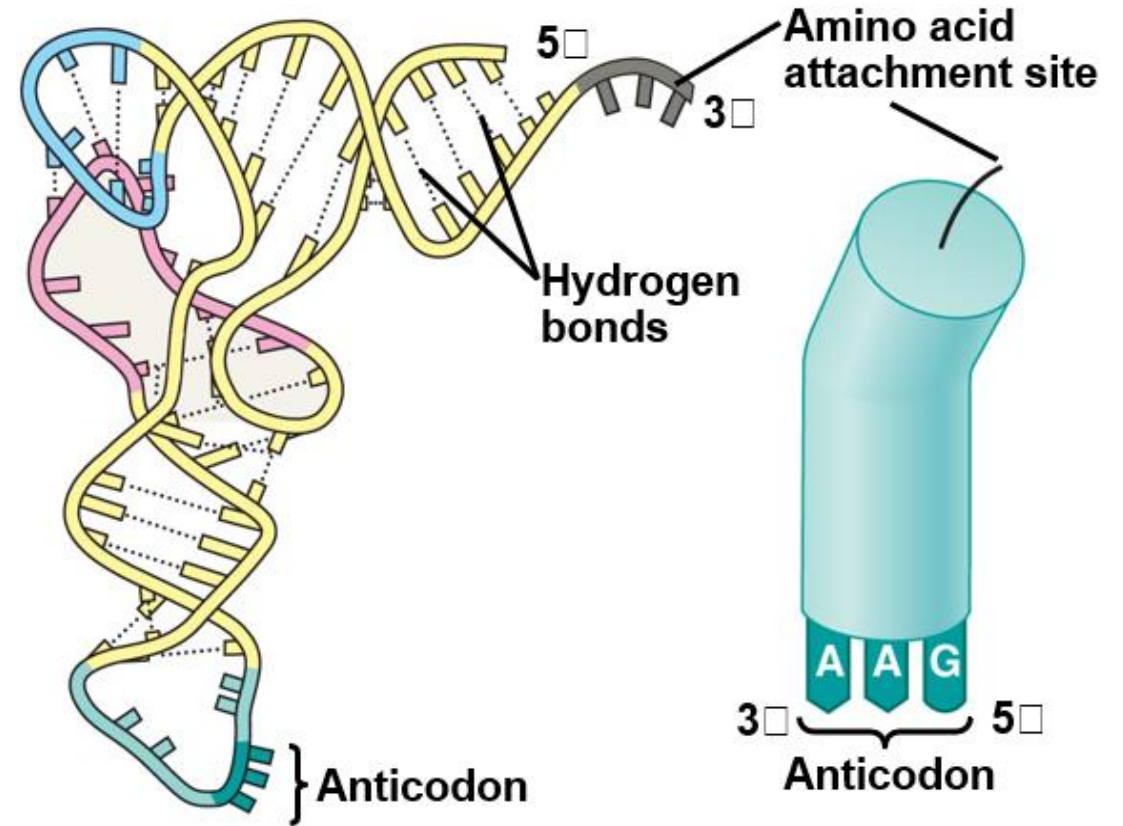




Covalent bond  
Attaches the amino  
Acid to the attachment  
Site; uses ATP as the  
Energy source; this is catalyzed  
By aminoacyl-tRNA synthetases

(a) Two-dimensional structure

Copyright © 2008 Pearson Education, Inc., publishing as Pearson Benjamin Cummings.



(b) Three-dimensional structure

Copyright © 2008 Pearson Education, Inc., publishing as Pearson Benjamin Cummings.

(c) Symbol used  
in this book

This is the "complementary" sequence That  
recognizes the correct Corresponding sequence of the  
Correct amino acid



- Accurate translation requires two steps:
  - First: a correct match between a tRNA and an amino acid, done by the enzyme **aminoacyl-tRNA synthetase**
  - The enzymes have active sites that are specific to a certain combination of amino acids and tRNA
  - There are 20 different synthetases that correspond to the 20 different amino acids and the tRNAs
  - These synthetases bring the appropriate amino acid to the tRNA
  - Second: a correct match between the tRNA anticodon and an mRNA codon
  - If there were a tRNA that existed for each way to make every amino acid, we would need 61 different tRNAs.
  - There are only 45. This means that some tRNAs must be able to bind to more than one codon.

# *Codons: Triplets of Bases*

- The flow of information from gene to protein is based on a **triplet code**: a series of nonoverlapping, three-nucleotide words
- These triplets are the smallest units of uniform length that can code for all the amino acids
- Flexible pairing at the third base of a codon is called **wobble** and allows some tRNAs to bind to more than one codon
- That is why, when you look at the amino acid chart, there are several ways that can result in the same amino acid

nonpolar polar basic acidic (stop codon)

# Standard genetic code

1st base	2nd base								3rd base
	U		C		A		G		
U	UUU	(Phe/F) Phenylalanine	UCU	(Ser/S) Serine	UAU	(Tyr/Y) Tyrosine	UGU	(Cys/C) Cysteine	U
	UUC		UCC		UAC		UGC		C
	UUA		UCA		UAA	Stop (Ochre)	UGA	Stop (Opal)	A
	UUG		UCG		UAG	Stop (Amber)	UGG	(Trp/W) Tryptophan	G
C	CUU	(Leu/L) Leucine	CCU	(Pro/P) Proline	CAU	(His/H) Histidine	CGU	(Arg/R) Arginine	U
	CUC		CCC		CAC		CGC		C
	CUA		CCA		CAA	(Gln/Q) Glutamine	CGA		A
	CUG		CCG		CAG		CGG		G
A	AUU	(Ile/I) Isoleucine	ACU	(Thr/T) Threonine	AAU	(Asn/N) Asparagine	AGU	(Ser/S) Serine	U
	AUC		ACC		AAC		AGC		C
	AUA		ACA		AAA	(Lys/K) Lysine	AGA	(Arg/R) Arginine	A
	AUG <sup>[A]</sup>	(Met/M) Methionine	ACG		AAG		AGG		G
G	GUU	(Val/V) Valine	GCU	(Ala/A) Alanine	GAU	(Asp/D) Aspartic acid	GGU	(Gly/G) Glycine	U
	GUC		GCC		GAC		GGC		C
	GUA		GCA		GAA	(Glu/E) Glutamic acid	GGA		A
	GUG		GCG		GAG		GGG		G

		Second Position					
		U	C	A	G		
First Position [5' end]	U	UUU } Phe UUC } UUA } Leu UUG }	UCU } UCC } Ser UCA } UCG }	UAU } Tyr UAC } UAA } Stop UAG } Stop	UGU } Cys UGC } UGA } Stop UGG } Trp	U C A G	Third Position [3' end]
	C	CUU } CUC } Leu CUA } CUG }	CCU } CCC } Pro CCA } CCG }	CAU } His CAC } CAA } Gln CAG }	CGU } CGC } Arg CGA } CGG }	U C A G	
	A	AUU } Ile AUC } AUA } AUG } Met	ACU } ACC } Thr ACA } ACG }	AAU } Asn AAC } AAA } Lys AAG }	AGU } Ser AGC } AGA } Arg AGG }	U C A G	
	G	GUU } GUC } Val GUA } GUG }	GCU } GCC } Ala GCA } GCG }	GAU } Asp GAC } GAA } Glu GAG }	GGU } GGC } Gly GGA } GGG }	U C A G	

- Example: AGT at a particular position on a DNA strand results in the placement of the amino acid serine at the corresponding position of the polypeptide to be produced
- AGT (this is the triplet code that is the DNA segment that is transcribed to...)
- UCA (the mRNA codon)
- Serine amino acid

# WHAT IF SOMETHING MESSES UP?

- It is possible that the correct tRNA could attach to an incorrect amino acid
- The ribosome is only paying attention to the anticodon of the tRNA but not to the amino acid it is carrying so an incorrect amino acid could get placed onto a growing polypeptide chain

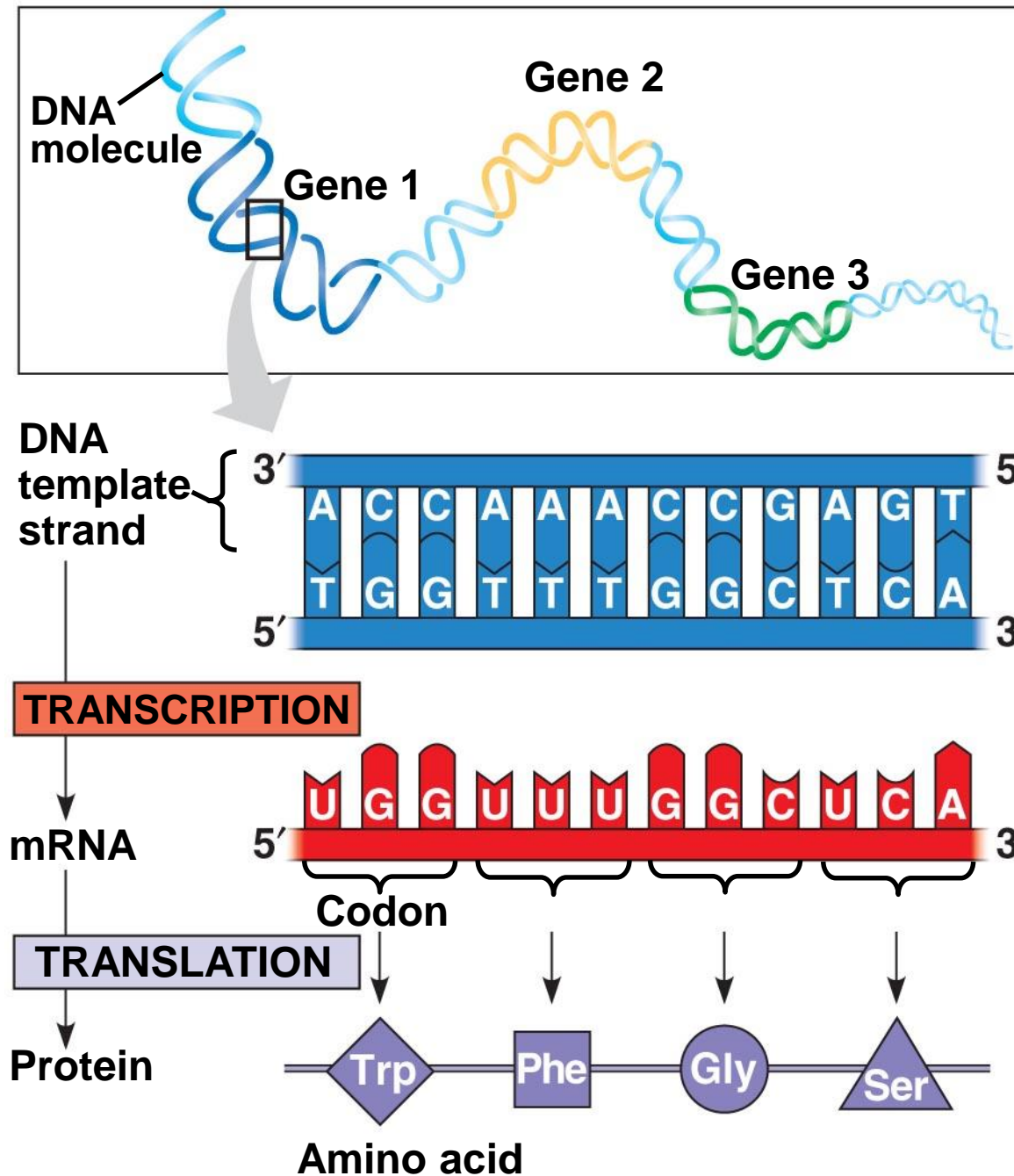
- The DNA template strand is read in the 3' to 5' direction (just like in DNA replication)
- The mRNA is MADE in the 5' to 3' direction (just like in DNA replication except you are substituting U for T)
- When the mRNA codons are read IT IS DONE IN THE 5' to 3' direction

- During transcription, one of the two DNA strands called the **template strand** provides a template for ordering the sequence of nucleotides in an RNA transcript
- During translation, the mRNA base triplets, called **codons**, are read in the 5' to 3' direction
- Each codon specifies the amino acid to be placed at the corresponding position along a polypeptide

- Codons along an mRNA molecule are read by translation machinery in the 5' to 3' direction
- Each codon specifies the addition of one of 20 amino acids
- Remember: DNA is replicated in the 5' to 3' direction, so new bases were being added at the 3' end and the template strand was being read in the opposite direction (kind of confusing but know the difference)



Fig. 14-4



Think of it  
This way;  
The mRNA  
Strand is just  
The complement  
Of the DNA  
template  
With "U"s  
instead of "T"s

# Cracking the Code

- All 64 codons were deciphered by the mid-1960s
- Of the 64 triplets, 61 code for amino acids; 3 triplets are “stop” signals to end translation
- The genetic code is redundant but not ambiguous;  
**no codon specifies more than one amino acid**
- Codons must be read in the correct **reading frame** (correct groupings) in order for the specified polypeptide to be produced
- Mutations can alter this reading frame and cause little (if we are lucky) or huge differences in the resulting polypeptides.

# *Evolution of the Genetic Code*

- The genetic code is **nearly** universal, meaning, the codon can be translated to the same amino acid across different species.
- From the simplest bacteria to the most complex animals
- Genes can be transcribed and translated after being transplanted from one species to another