

# Chapter 14 Warm-Up

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1. Explain the contribution that Beadle and Tatum made to understanding the role of DNA.
2. Compare and contrast DNA to RNA.
3. What is the difference between replication, transcription and translation?



# Ch. 14 Warm-Up

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1. What are similarities between DNA and RNA?
2. What are differences between DNA and RNA?
3. What is a ribozyme?
4. How many different codons (3-letter RNA nucleotide combinations) are possible?
5. If there are all of the possibilities (in #4) , how come there are only 20 amino acids?



# Ch. 14 Warm-Up

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1. Describe the steps in transcription.
2. Contrast transcription in prokaryotes vs. eukaryotes.
3. What is the minimum # of nucleotides needed in an mRNA molecule to code for a protein with 200 amino acids?



# Chapter 14 Warm-Up

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1. How does mRNA differ from pre-mRNA?
2. What is the difference between introns and exons?
3. Describe how spliceosomes modify mRNA.
4. An original hypothesis was One Gene = One Protein. But how is it possible to have 22,000 genes but over 100,000+ different proteins??



# Chapter 14 Warm-Up

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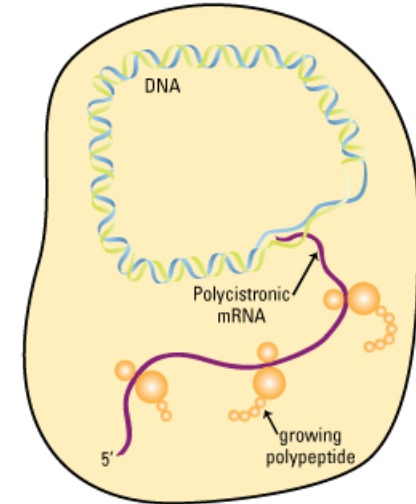
1. Describe the steps of translation.
1. If the DNA sequence is: 3' - T A C G A T C A G - 5'
  - ▶ the cDNA would be:
  - ▶ the mRNA is:
  - ▶ the tRNA is:
  - ▶ the amino acid sequence is:
2. How does the cell determine the ultimate destination of a polypeptide being synthesized?



# Chapter 14 Warm-Up

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1. What are some examples of point mutations?
2. Contrast a missense vs. nonsense mutation.
3. What is a frameshift mutation? How can it impact protein synthesis?
4. What kind of cell is shown below? Provide 3 pieces of evidence to support your claim.



# Chapter 14 Warm-Up

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*Refer to page 296. Fill in the chart comparing prokaryotic and eukaryotic gene expression:*

<b>Prokaryotes</b>	<b>Eukaryotes</b>





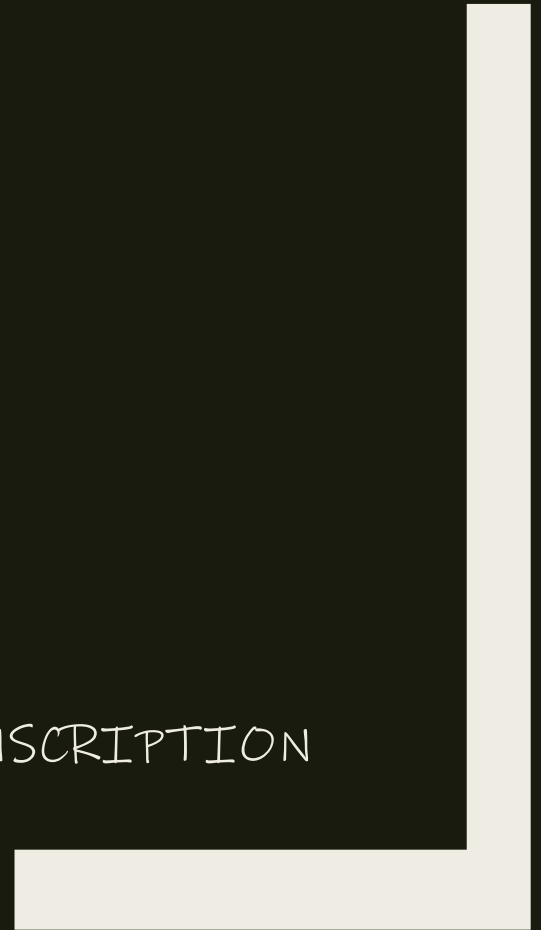
# Gene Expression: From Gene to Protein

Chapter 14



# CONCEPT 14.1:

GENES SPECIFY PROTEINS VIA TRANSCRIPTION  
AND TRANSLATION



**Gene Expression:** process by which DNA directs the synthesis of proteins (or RNAs)

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▶ **Old idea:** *one gene-one enzyme hypothesis*

- ▶ *Proposed by Beadle & Tatum – mutant mold experiments*
- ▶ *Function of a gene = dictate production of specific enzyme*

▶ **Newer idea:** *one gene-one polypeptide hypothesis*

▶ **Most accurate:** *one gene-one RNA molecule (which may or may not be translated into a polypeptide)*

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# Flow of genetic information

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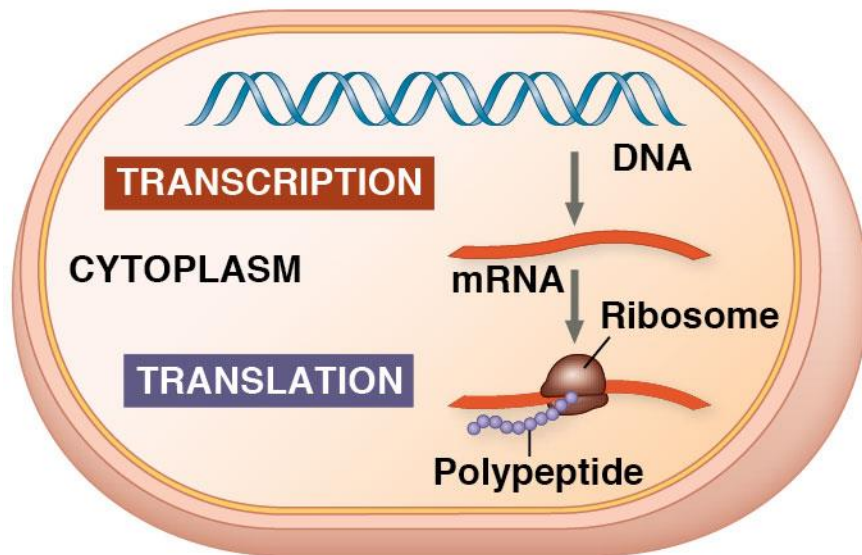


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- ▶ *Central Dogma:* DNA → RNA → protein
  - ▶ **Transcription:** DNA → RNA
  - ▶ **Translation:** RNA → protein
  
- ▶ Ribosome = site of translation

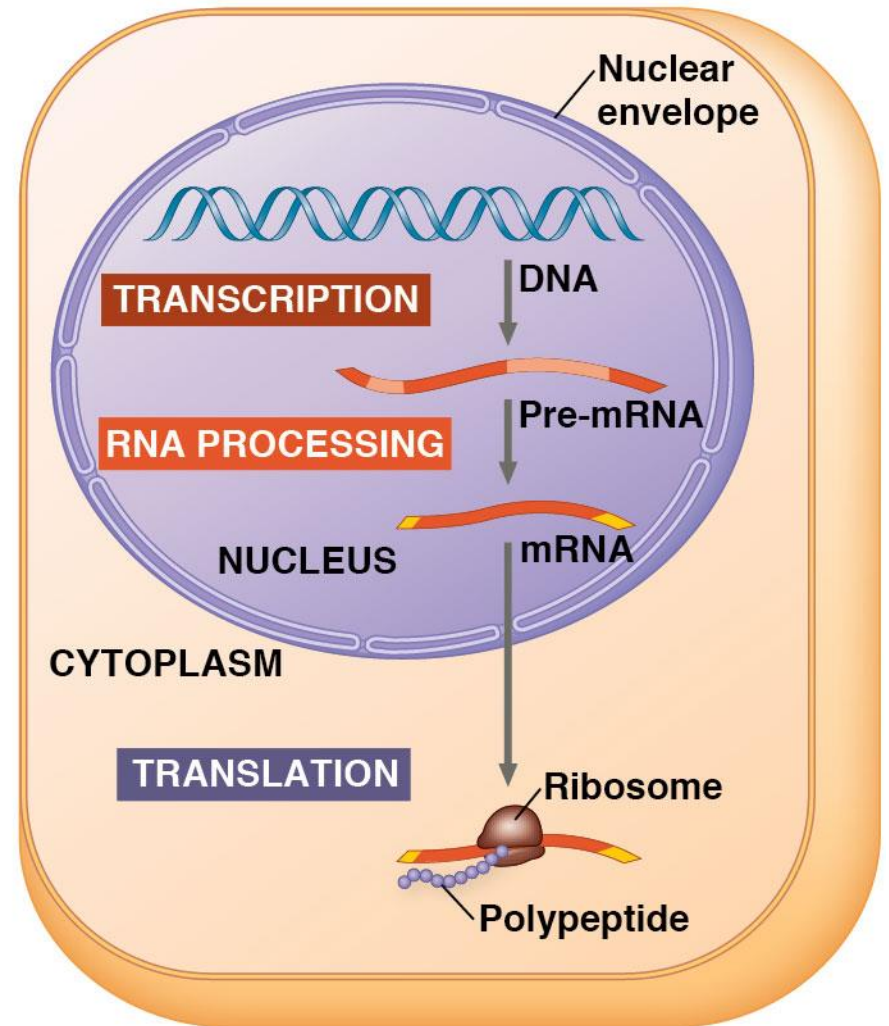


# Flow of Genetic Information in Prokaryotes vs. Eukaryotes



(a) Bacterial cell

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(b) Eukaryotic cell

# One gene = One RNA molecule

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## DNA

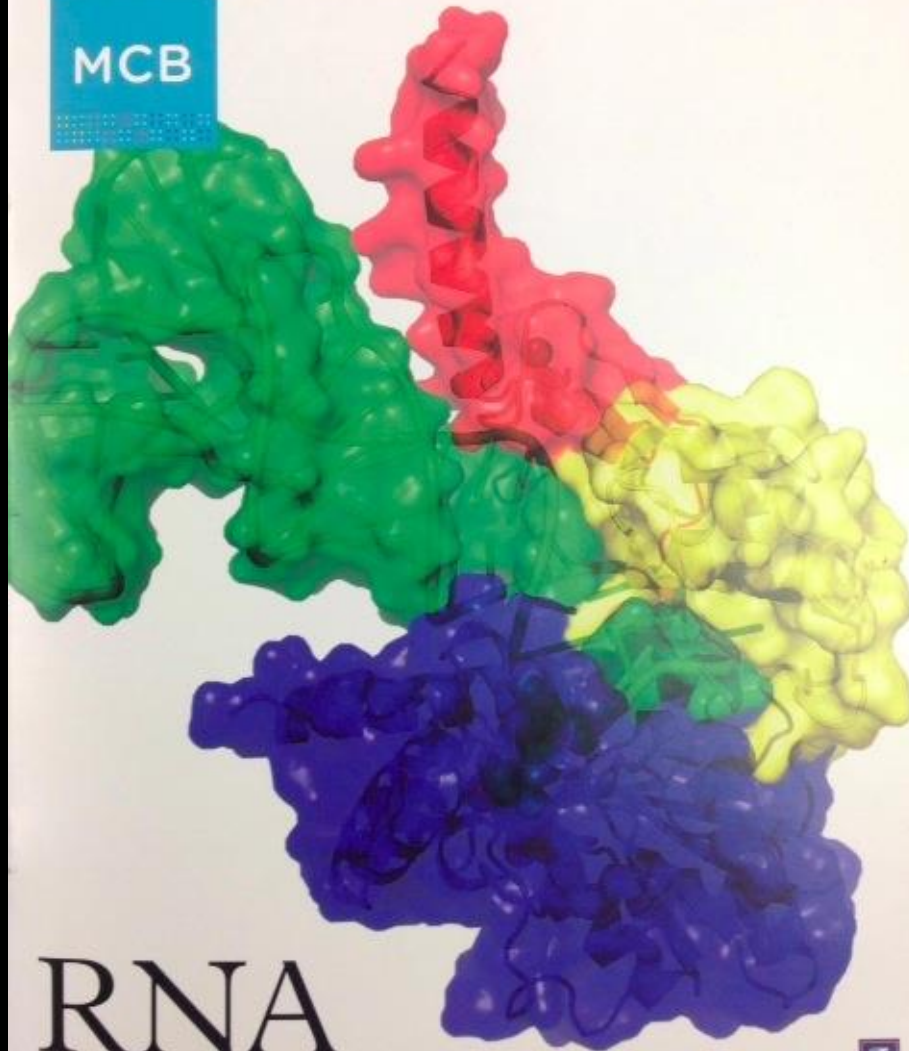
- ▶ Nucleic acid composed of nucleotides
- ▶ Double-stranded
- ▶ Deoxyribose=sugar
- ▶ Thymine
- ▶ Template for individual

## RNA

- ▶ Nucleic acid composed of nucleotides
- ▶ Single-stranded
- ▶ Ribose=sugar
- ▶ Uracil
- ▶ Many different roles!



MCB



RNA

BIOLOGY'S NEXT BIG STAR

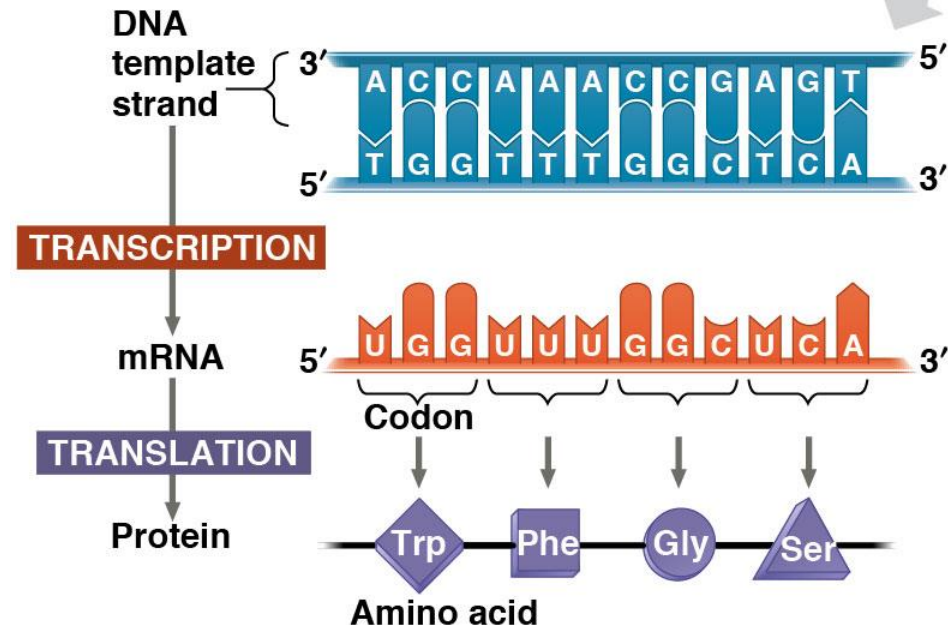
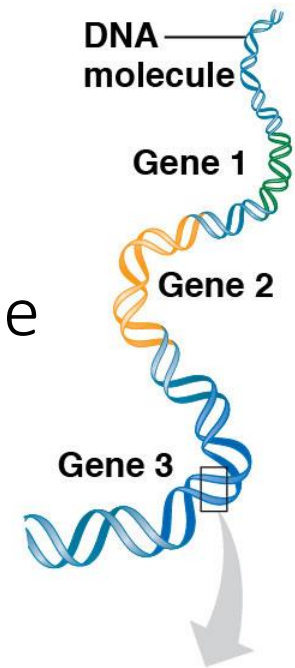


# RNA plays many roles in the cell

1. **pre-mRNA**=precursor to mRNA, newly transcribed and not edited
2. **mRNA**= edited version; carries the code from DNA that specifies amino acids
3. **tRNA**= carries a specific amino acid to ribosome based on its anticodon to mRNA codon
4. **rRNA**= makes up 60% of the ribosome; site of protein synthesis
5. **snRNA**=small nuclear RNA; part of a spliceosome; structural and catalytic roles
6. **srpRNA**= signal recognition particle that binds to signal peptides
7. **RNAi**= interference RNA; a regulatory molecule
8. **miRNA/siRNA**= micro/small interfering RNA; binds to mRNA or DNA to block it, regulate gene expression, or cut it up
9. **ribozyme**= RNA that functions as an enzyme

# The Genetic Code

- For each gene, one DNA strand (3' → 5') is the **template strand** (*aka: noncoding, minus or antisense strand*)
- mRNA (5' → 3') complementary to template
- mRNA triplets (**codons**) code for amino acids in polypeptide chain





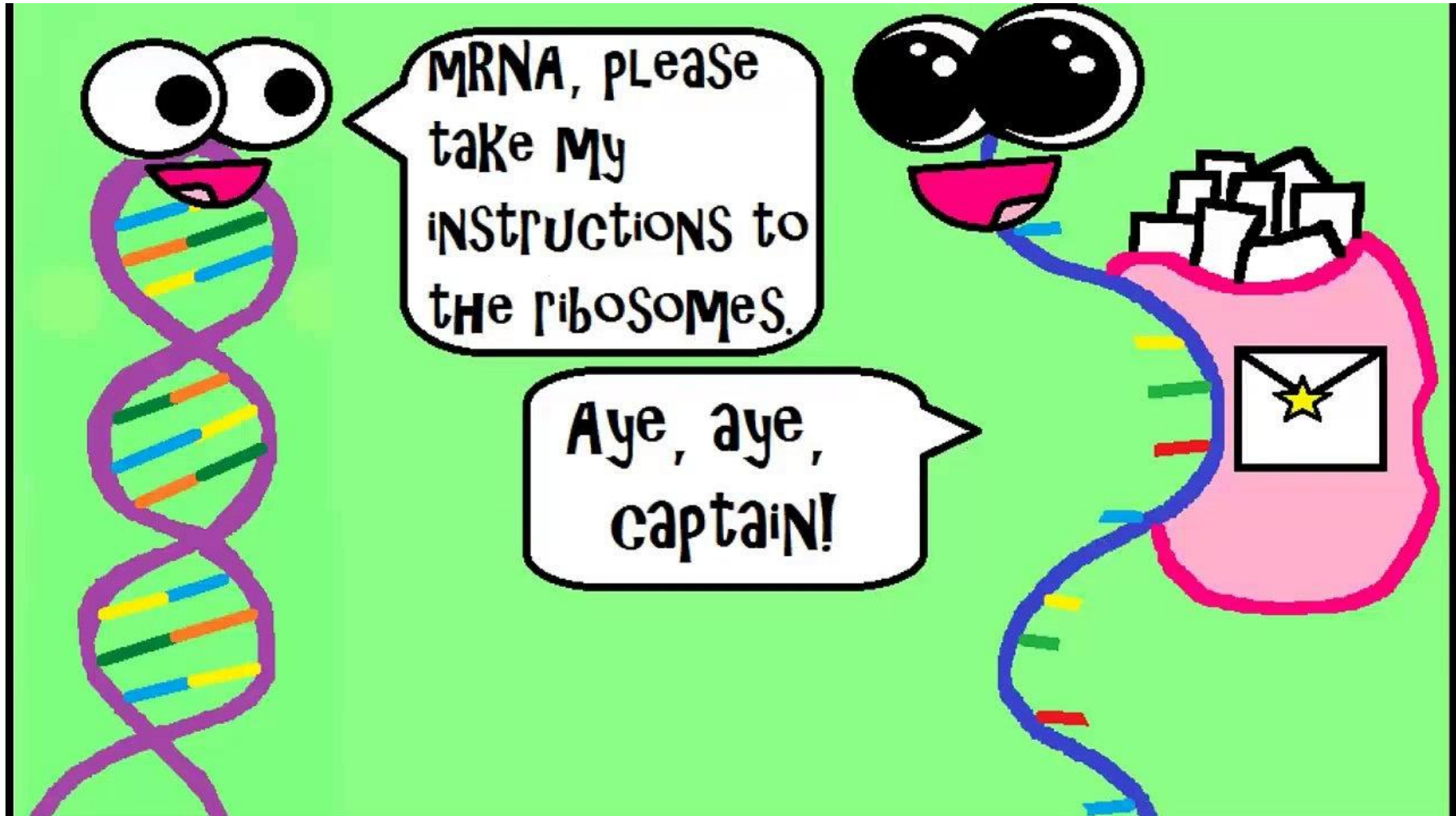
# The Genetic Code

- **64** different codon combinations
- **Redundancy:** 1+ codons code for each of 20 AAs
- **Reading frame:** groups of 3 must be read in correct groupings
- *This code is universal: all life forms use the same code.*

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

## CONCEPT 14.2:

TRANSCRIPTION IS THE DNA-DIRECTED  
SYNTHESIS OF RNA



MRNA, please  
take My  
iNSTRUCTIONS to  
the rIBOSOMES.

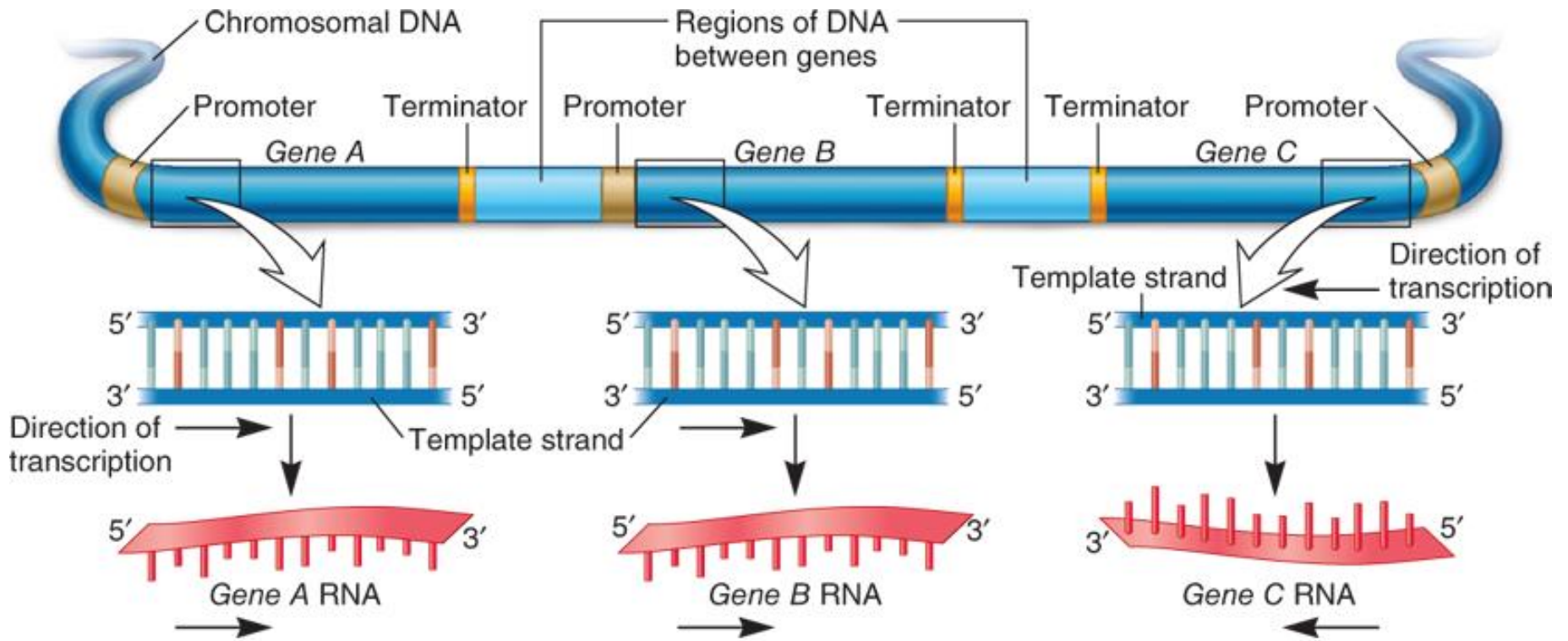
Aye, aye,  
captain!

# Transcription

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- ▶ **Transcription unit**: stretch of DNA that codes for a polypeptide or RNA (eg. tRNA, rRNA)
- ▶ **RNA polymerase**:
  - ▶ Separates DNA strands and transcribes mRNA
  - ▶ mRNA elongates in 5' → 3' direction
  - ▶ **Uracil (U)** replaces thymine (T) when pairing to adenine (A)
  - ▶ Attaches to **promoter** (start of gene) and stops at **terminator** (end of gene)





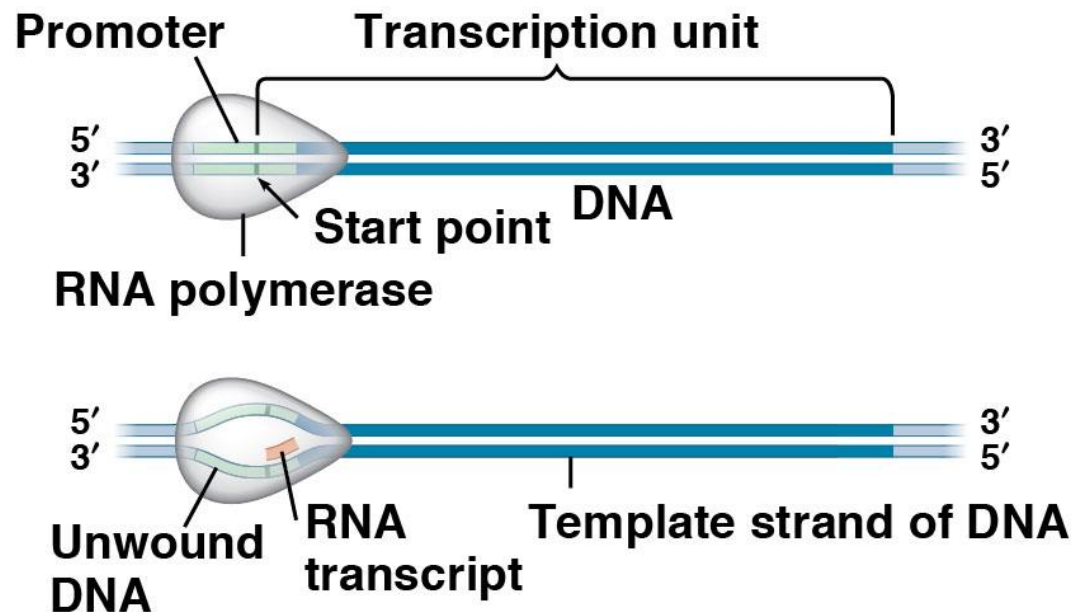
Source: G. Bradley Schaefer, James N. Thompson, Jr.:  
 Medical Genetics: An Integrated Approach  
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# 1. Initiation

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Bacteria: RNA polymerase binds directly to **promoter** in DNA

## 1 Initiation



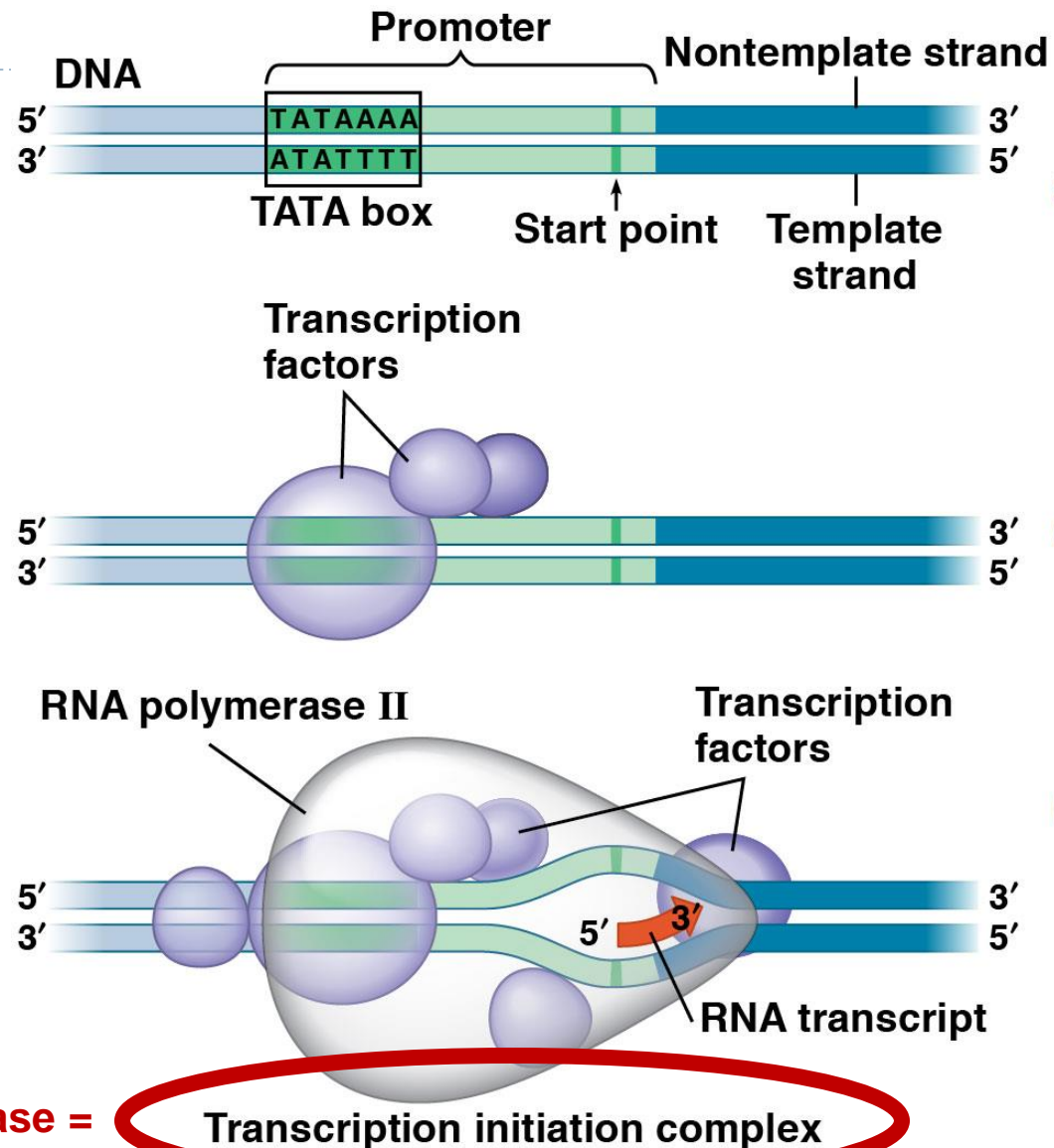
# 1. Initiation

## Eukaryotes:

**TATA box** = DNA sequence (TATAAAA) in **promoter region** *upstream* from transcription start site

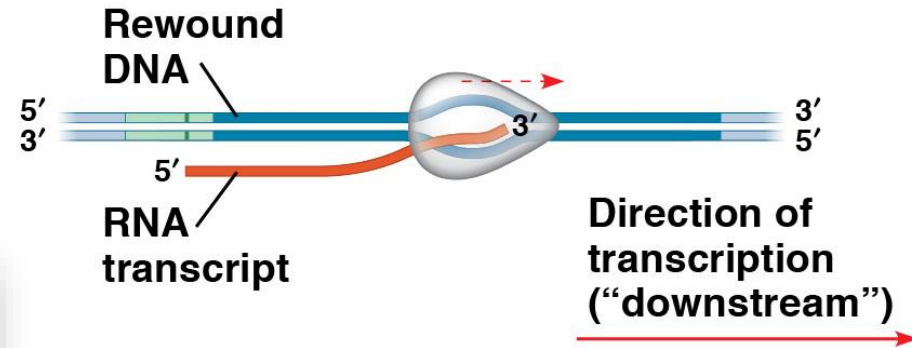
**Transcription factors** must recognize TATA box before RNA polymerase can bind to DNA promoter

**Transcription Factors + RNA Polymerase =**

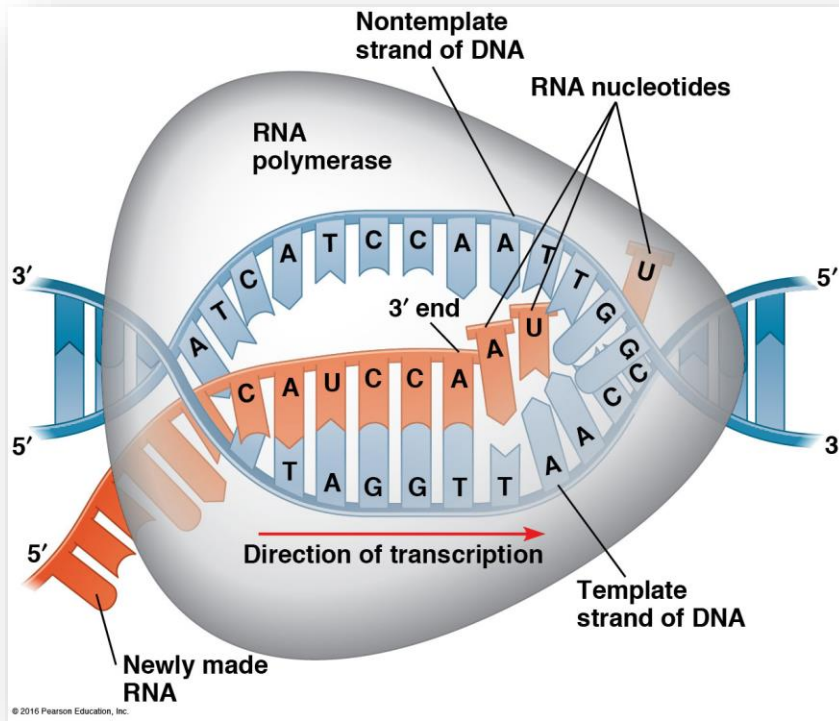


# 2. Elongation

## 2 Elongation



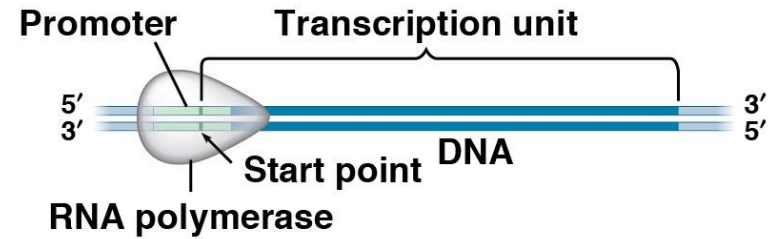
**RNA polymerase** adds RNA nucleotides to the 3' end of the growing chain (A-U, G-C)



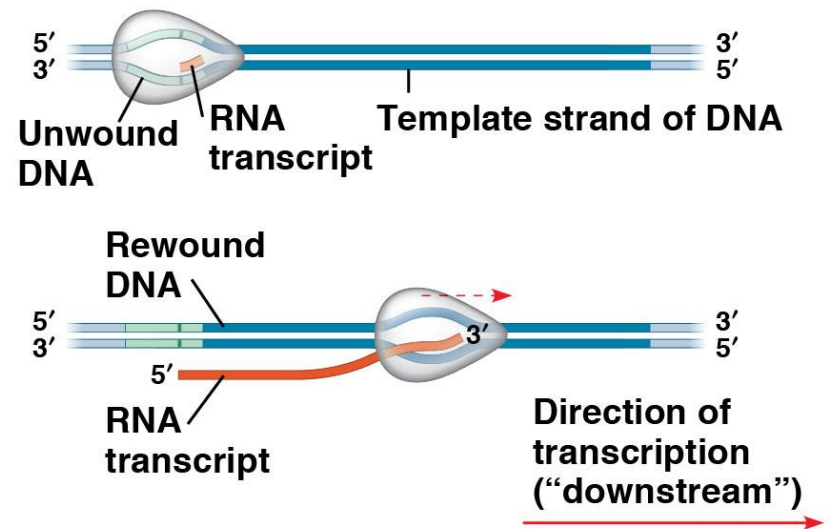


# 2. Elongation

## 1 Initiation



## 2 Elongation



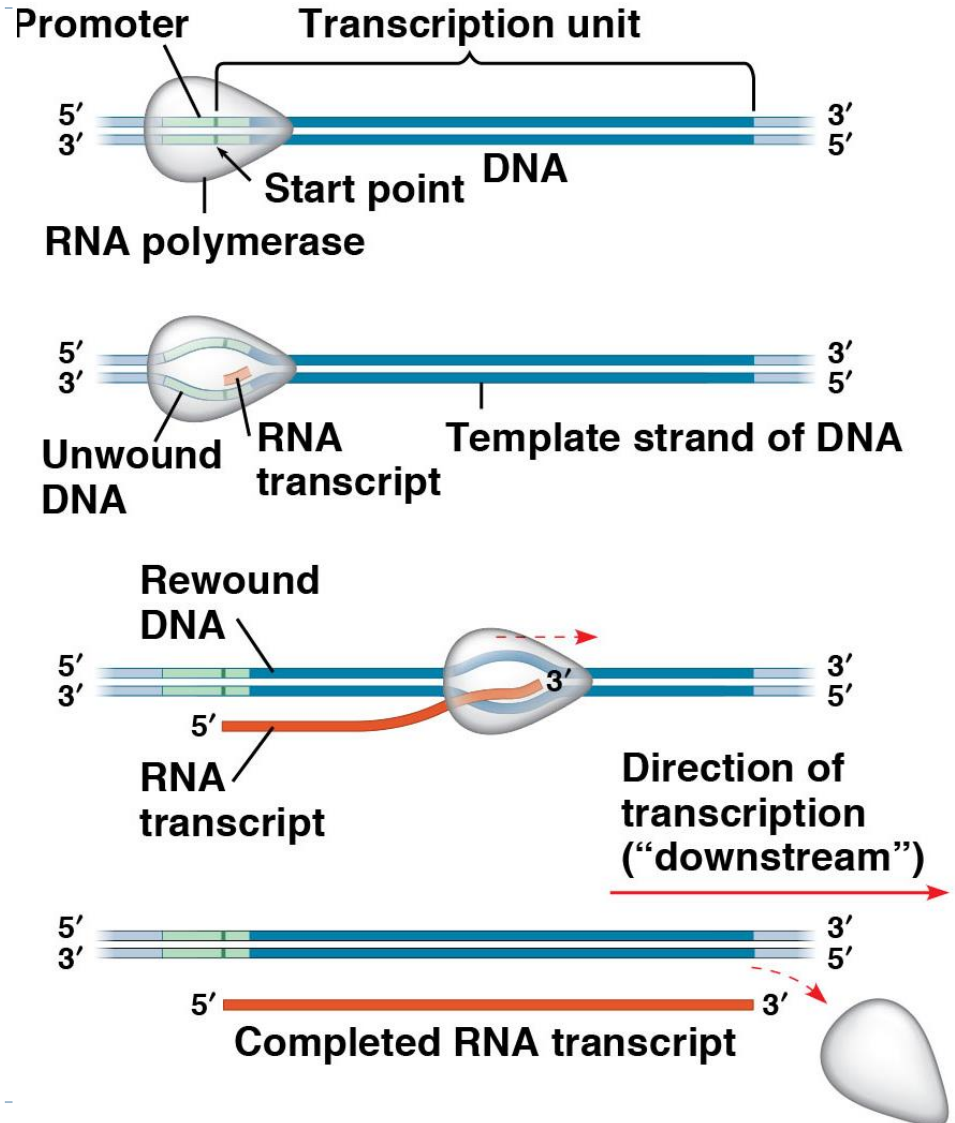
As RNA polymerase moves, it untwists DNA, then rewinds it after mRNA is made

# 3. Termination

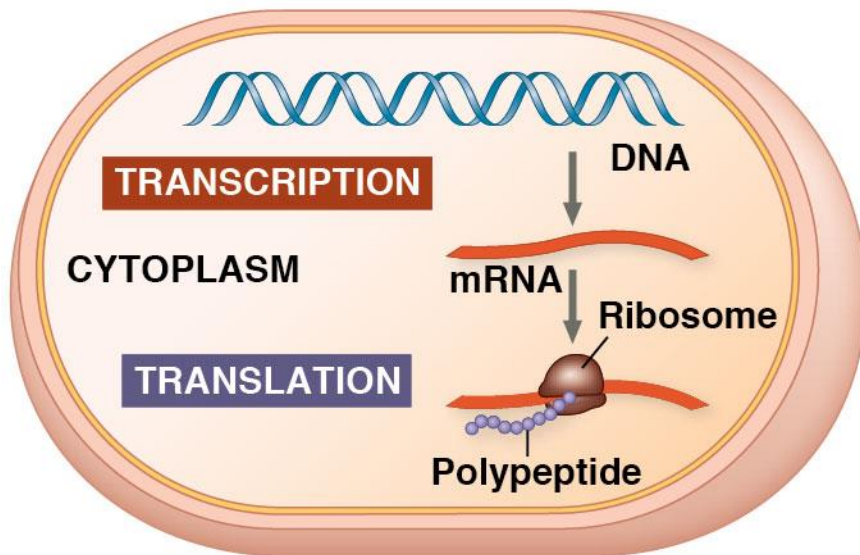
RNA polymerase transcribes a **terminator** sequence (prok) or **polyadenylation signal** sequence (euk), then mRNA and polymerase detach.

It is now called **pre-mRNA** for eukaryotes.

Prokaryotes = mRNA ready for use

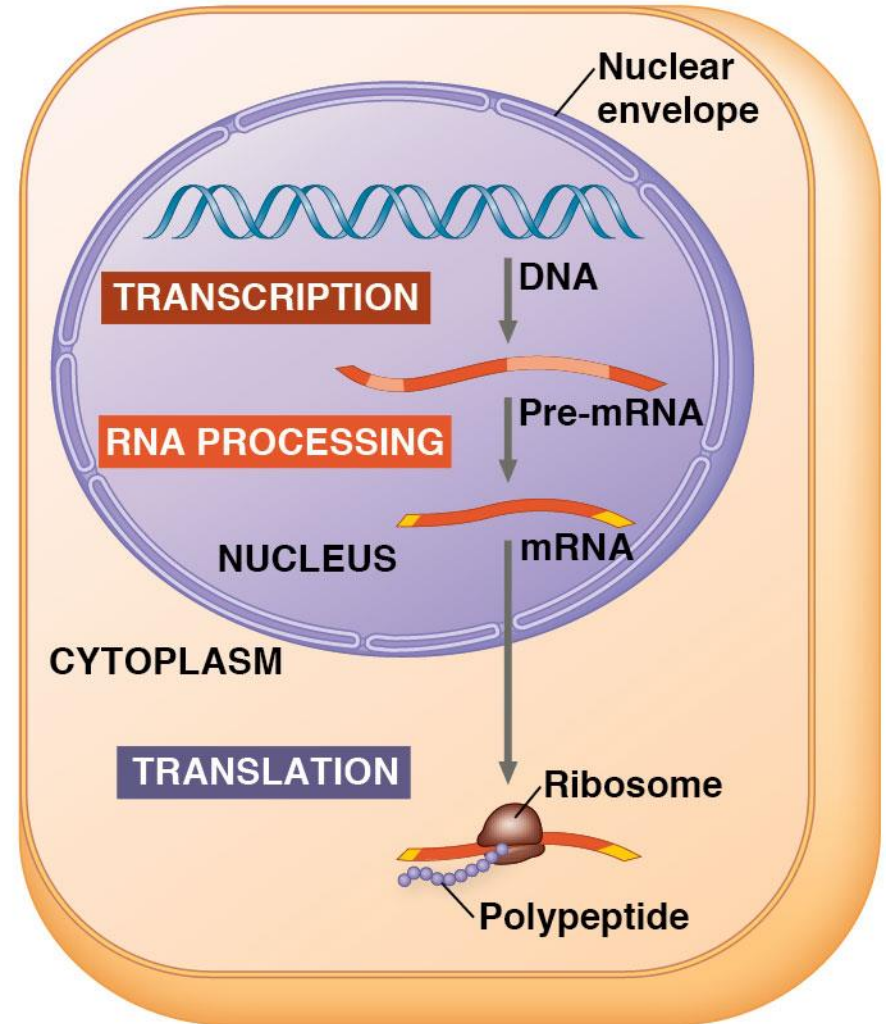


# Flow of Genetic Information in Prokaryotes vs. Eukaryotes



(a) Bacterial cell

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(b) Eukaryotic cell

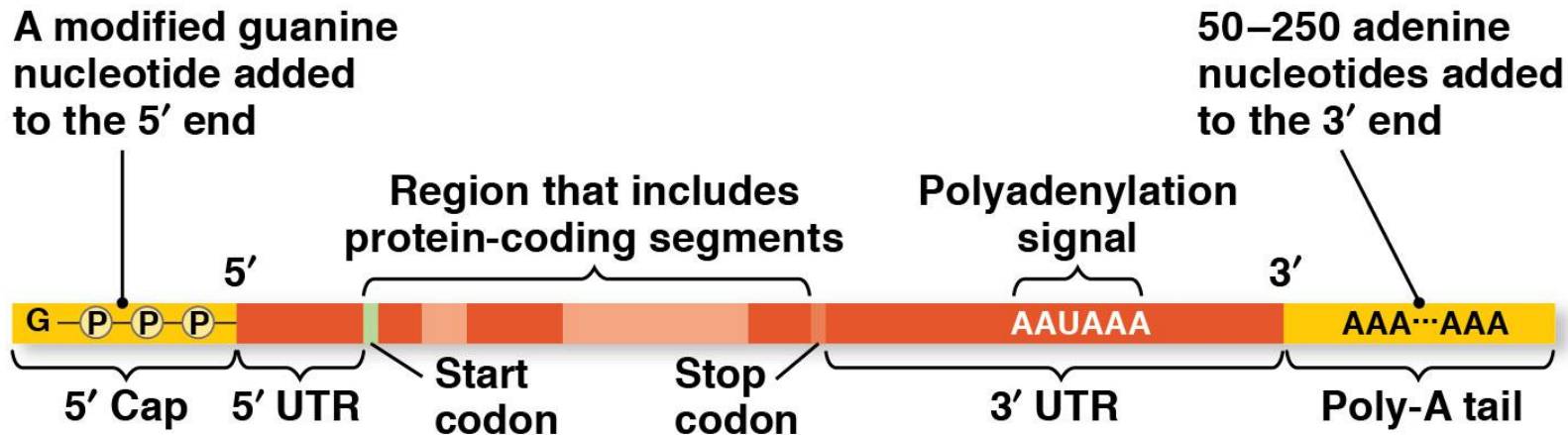
Concept 14.3:

Eukaryotic cells modify RNA

after transcription

# Additions to pre-mRNA:

- ▶ **5' cap** (modified guanine) and 3' **poly-A tail** (50-250 A's) are added

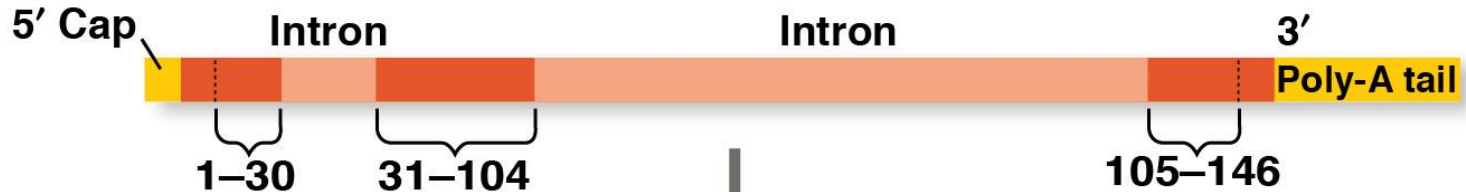


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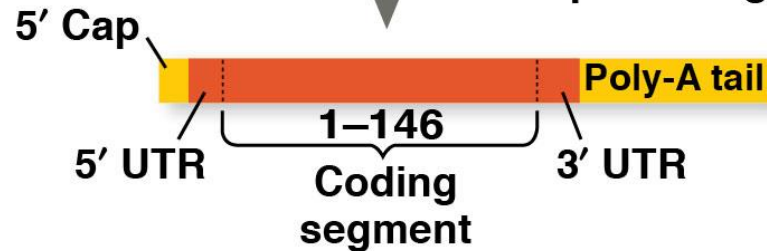
- Functions:**
1. Export from nucleus
  2. Protect mRNA from enzyme degradation
  3. Attach mRNA to ribosomes in cytoplasm

# RNA Splicing

Pre-mRNA



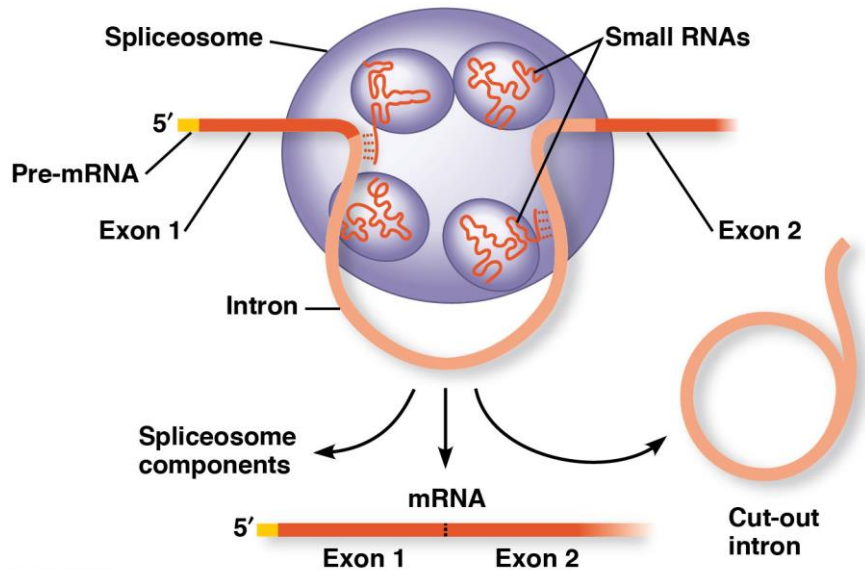
mRNA



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- ▶ Pre-mRNA has **introns** (noncoding sequences) and **exons** (codes for amino acids)
- ▶ **Splicing** = introns cut out, exons joined together

# RNA Splicing



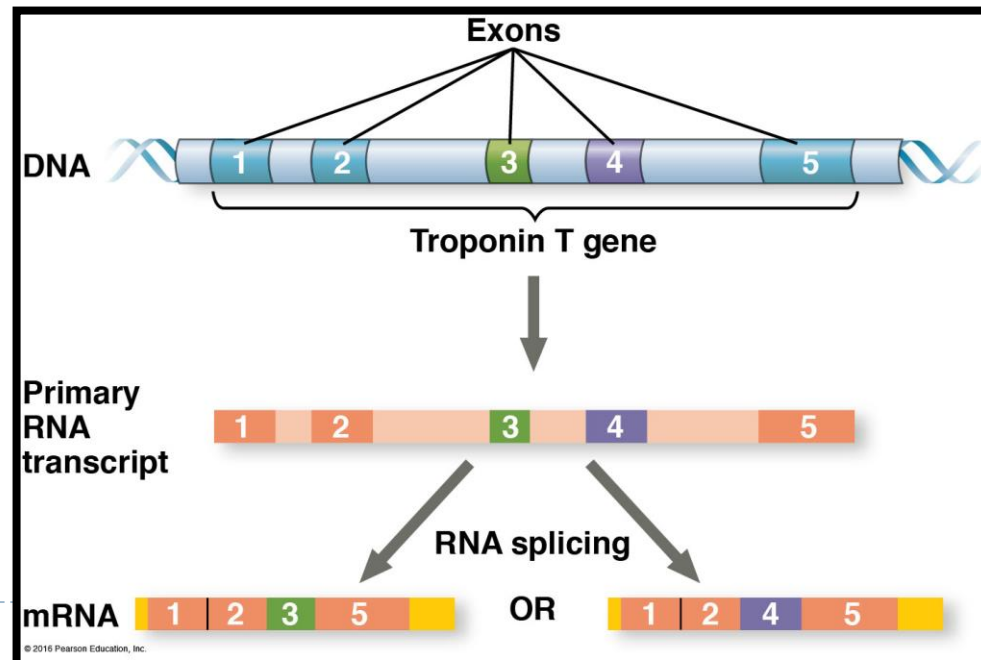
- ▶ **small nuclear ribonucleoproteins = snRNPs**
- ▶ snRNP = snRNA + protein
- ▶ Pronounced “snurps”
- ▶ Recognize splice sites
- ▶ snRNPs join with other proteins to form a spliceosome

- ▶ **Spliceosomes** catalyze the process of removing introns and joining exons
- ▶ **Ribozyme = RNA acts as enzyme (catalytic role)**



# Why have introns?

- ▶ Some regulate gene activity
- ▶ **Alternative RNA Splicing**: produce different combinations of exons
- ▶ One gene can make more than one polypeptide!
- ▶ 20,000 genes → 100,000 polypeptides



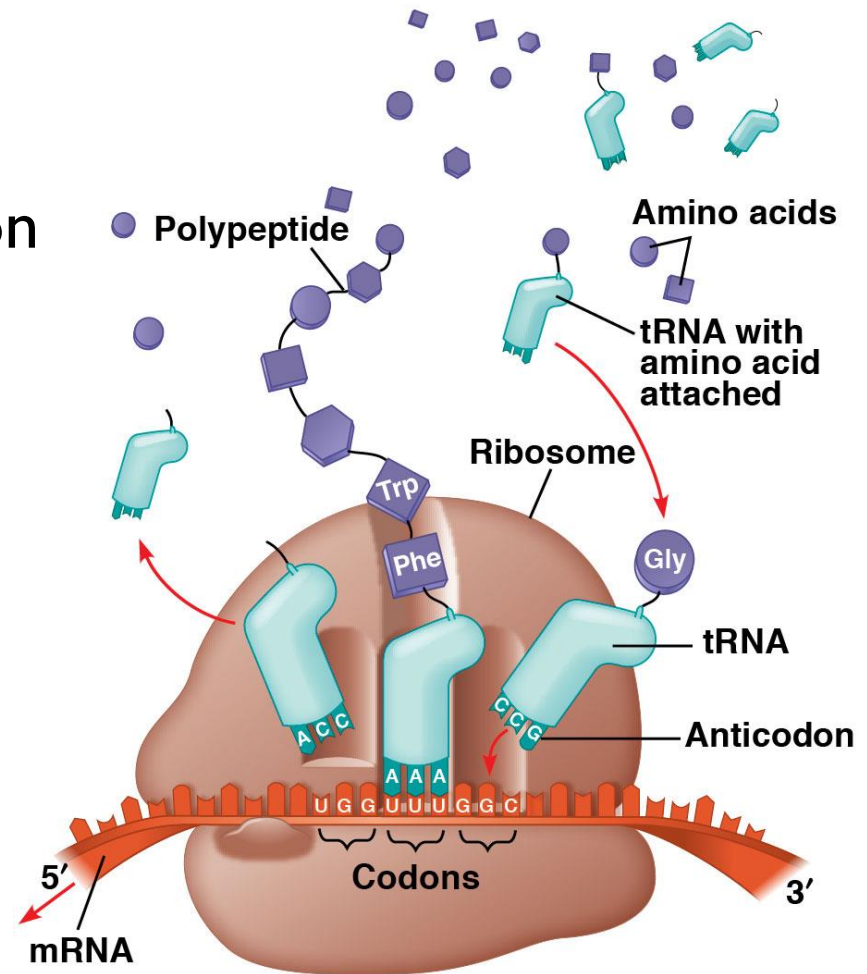


Concept 14.4:

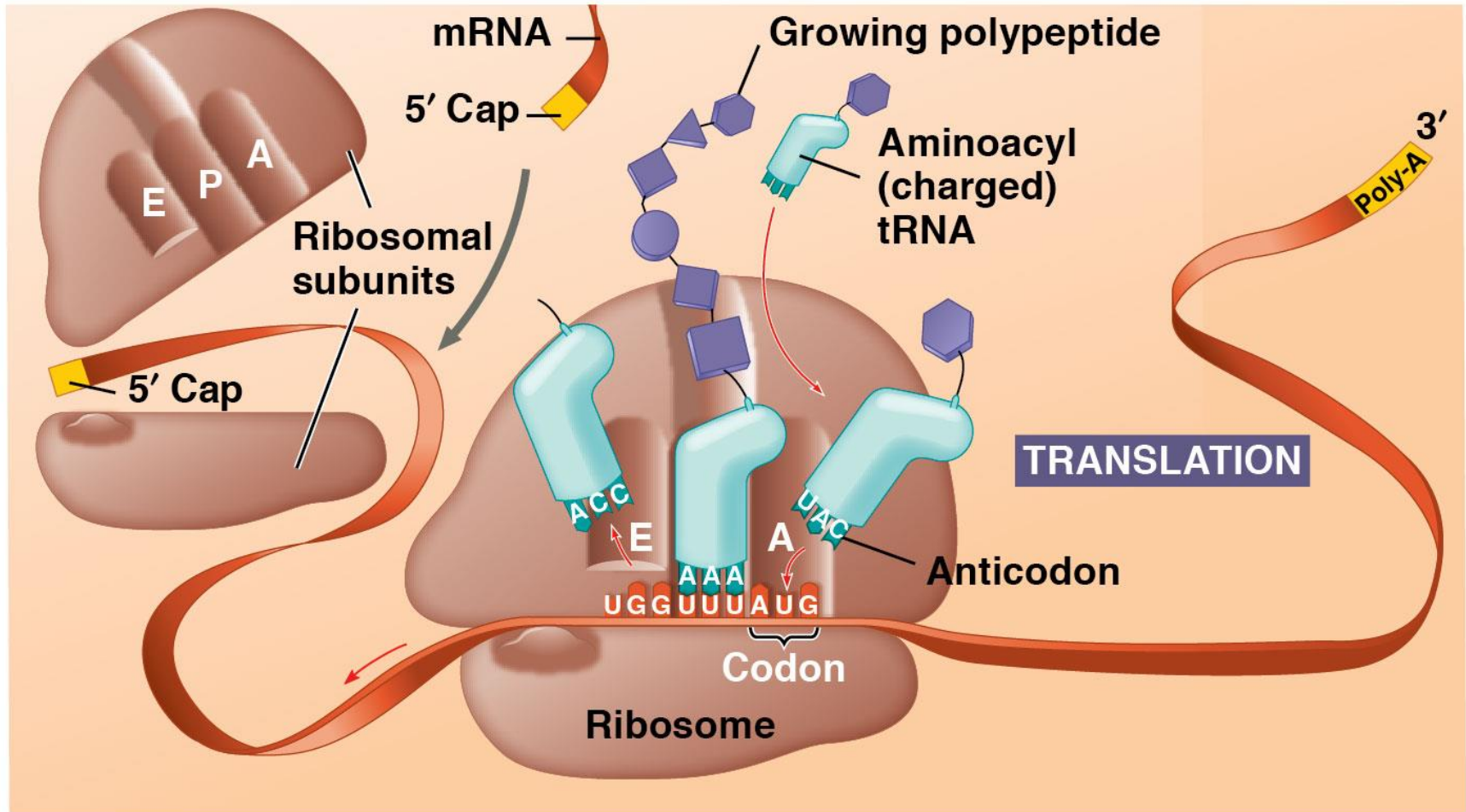
Translation is the RNA-directed synthesis of a polypeptide

# Components of Translation

1. **mRNA** = message
2. **tRNA** = interpreter
3. **Ribosome** = site of translation

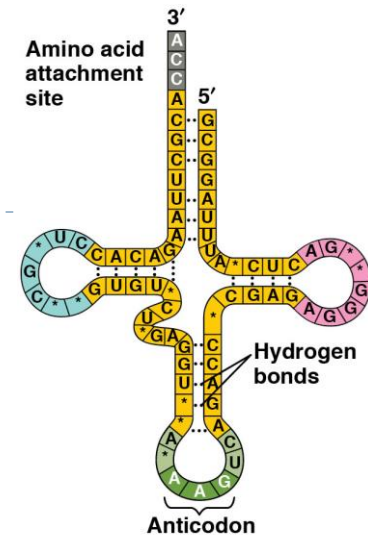


# Summary of Translation



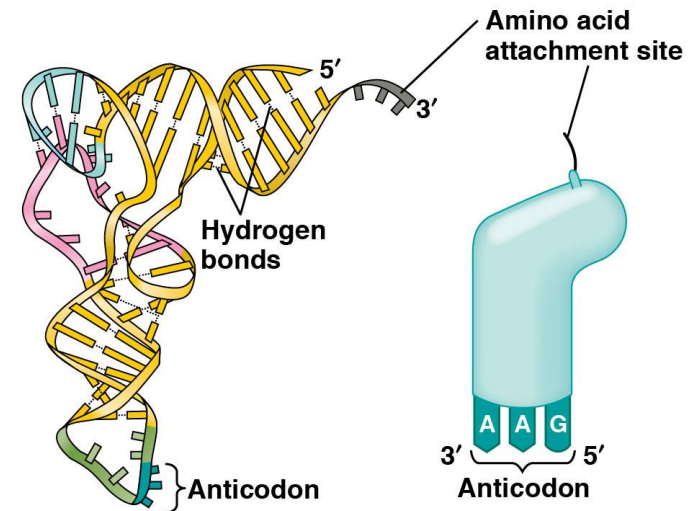
# tRNA

- ▶ Transcribed in nucleus
- ▶ Specific to each amino acid
- ▶ Transfer AA to ribosomes
- ▶ Anticodon: pairs with complementary mRNA codon
- ▶ Base-pairing rules between 3<sup>rd</sup> base of codon & anticodon are not as strict. This is called wobble.



(a) Two-dimensional structure

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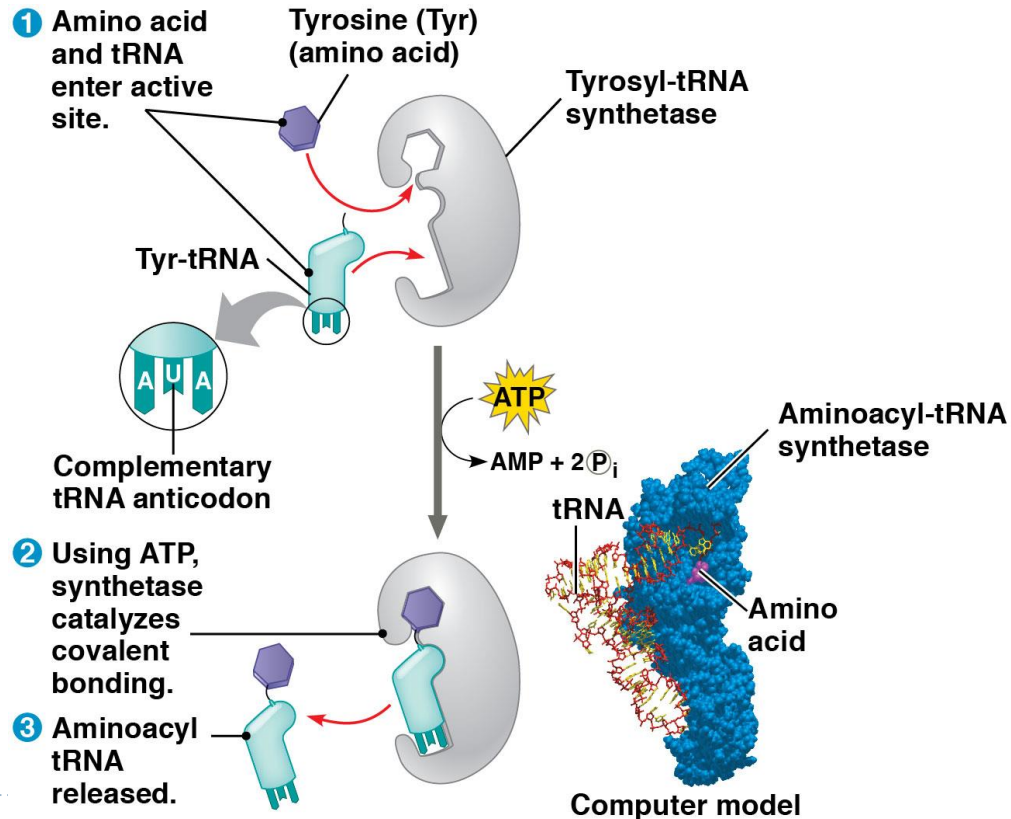
(b) Three-dimensional structure

(c) Symbol used in this book

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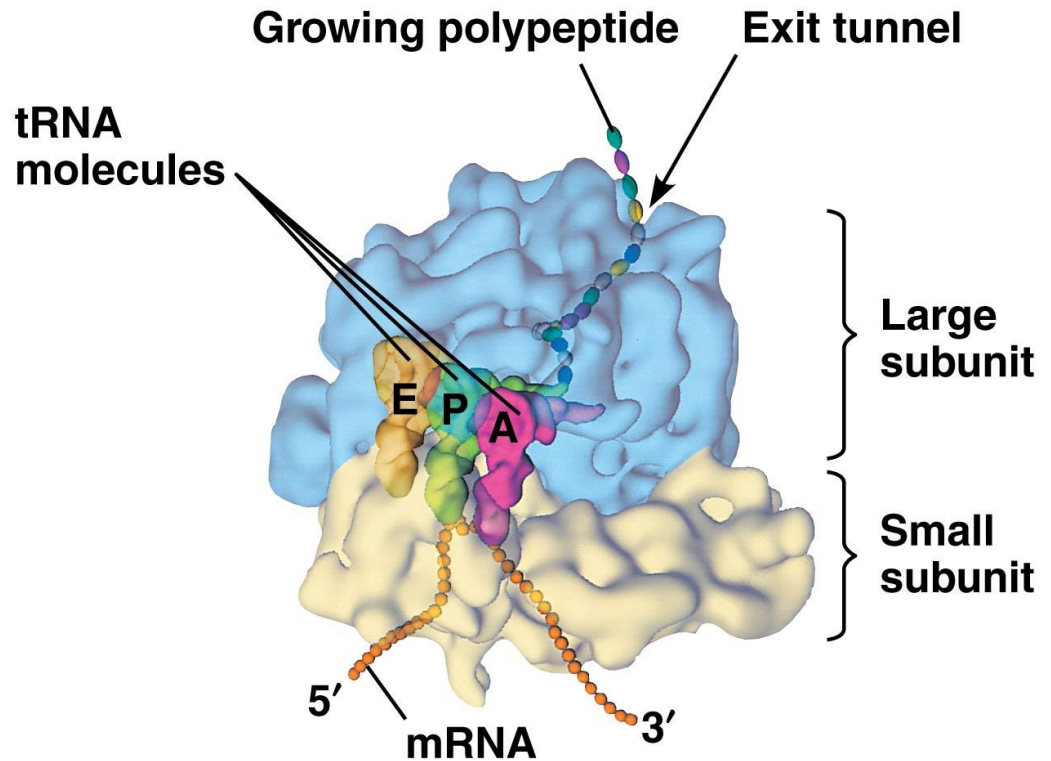
# tRNA

- ▶ Aminoacyl-tRNA-synthetase: enzyme that binds tRNA to specific amino acid



# Ribosomes

- ▶ Ribosome = rRNA + proteins
- ▶ made in nucleolus
- ▶ 2 subunits

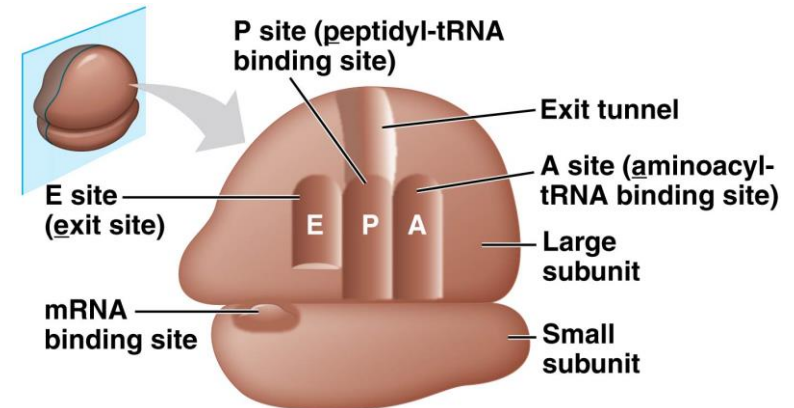


(a) Computer model of functioning ribosome

# Ribosomes

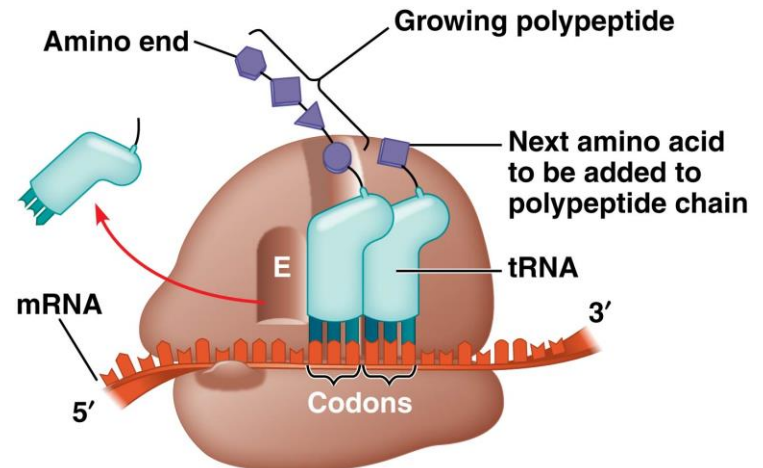
## Active sites:

- ▶ **A site:** holds **AA** to be added
- ▶ **P site:** holds growing polypeptide chain
- ▶ **E site:** exit site for tRNA



(b) Schematic model showing binding sites

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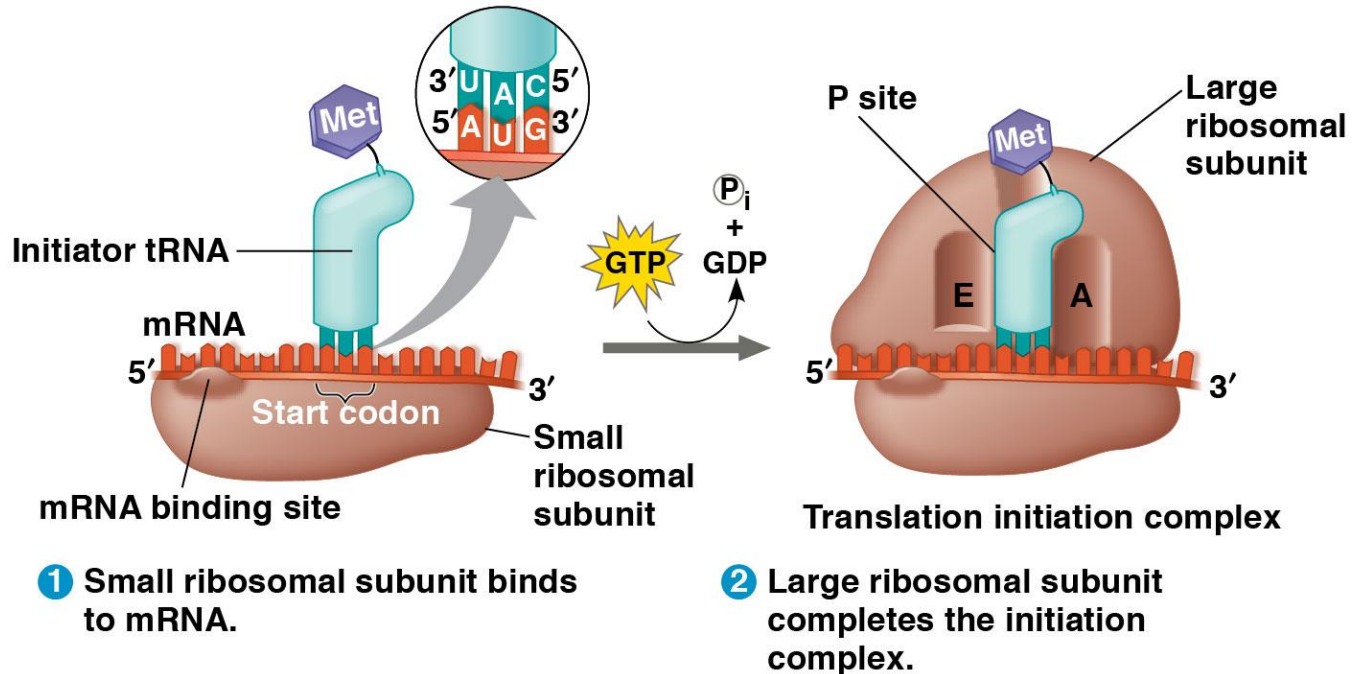


(c) Schematic model with mRNA and tRNA

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# Translation:

## 1. Initiation



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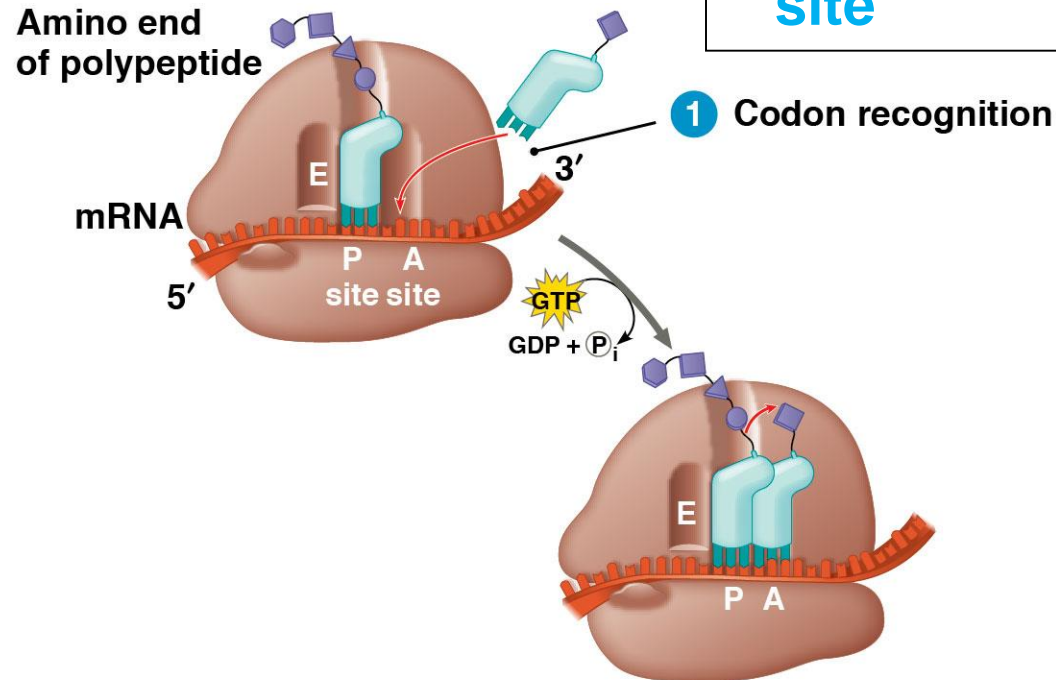
- Small subunit binds to start codon (AUG) on mRNA
- tRNA carrying Met attaches to P site
- Large subunit attaches



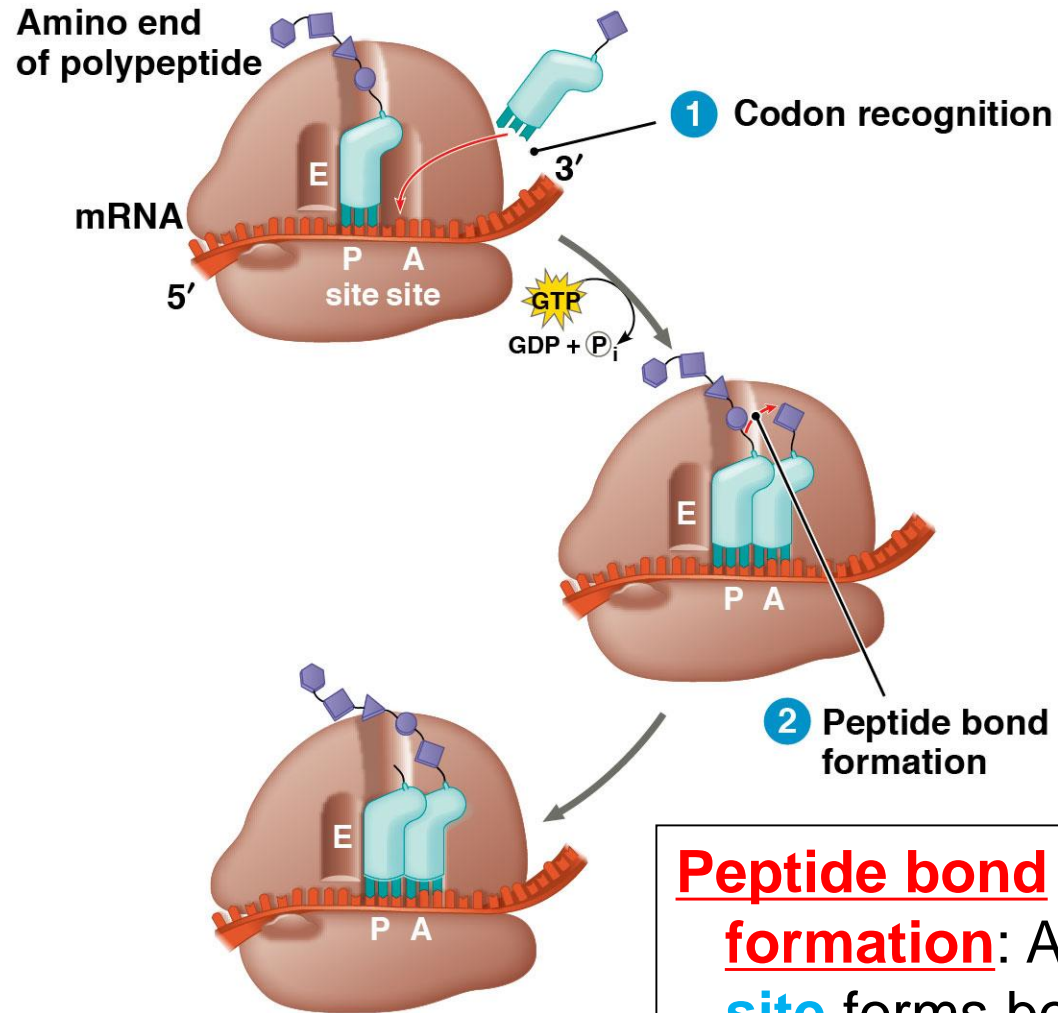
# 2. Elongation

## Codon recognition:

tRNA anticodon  
matches codon in **A**  
**site**

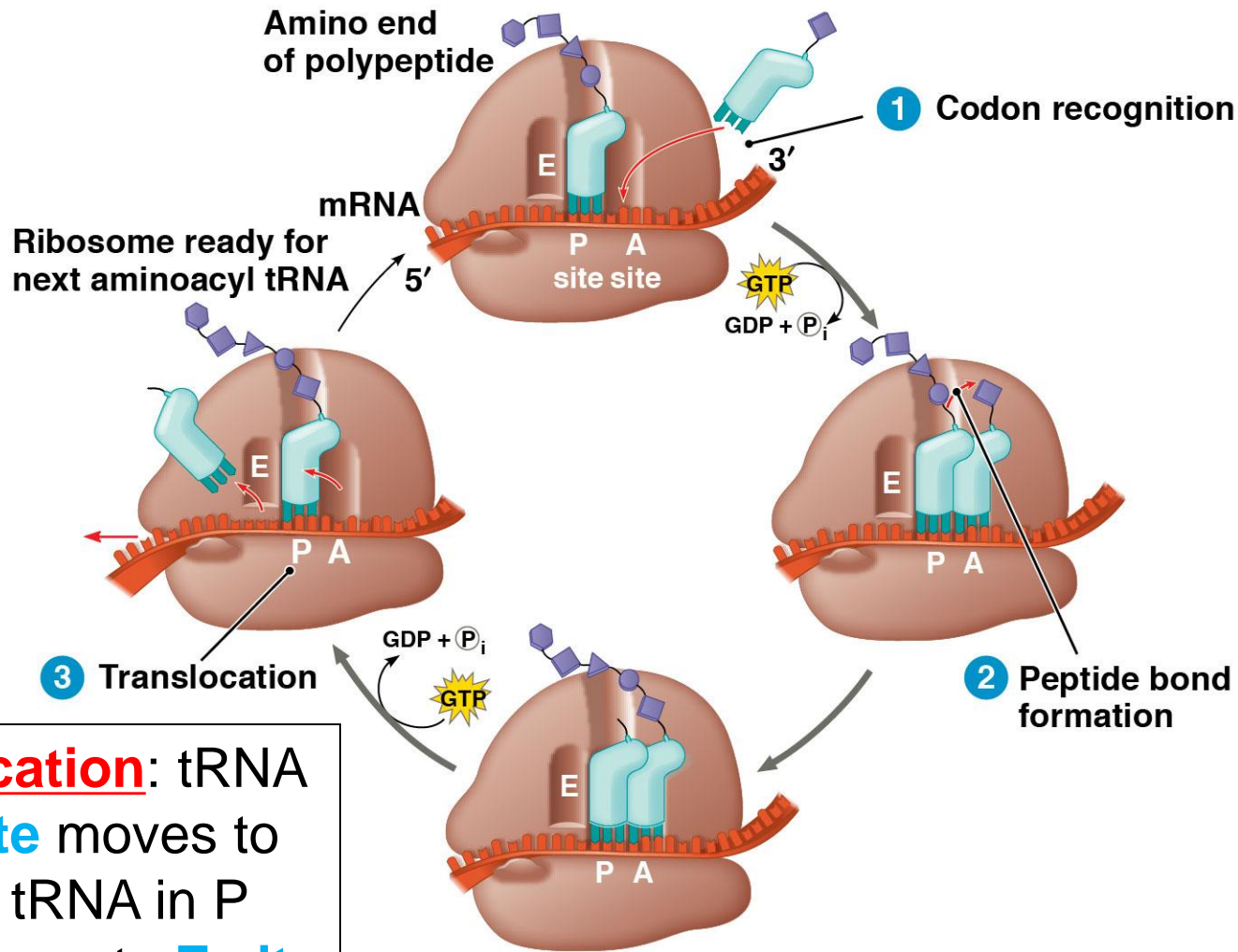


# 2. Elongation



**Peptide bond formation:** AA in **A site** forms bond with peptide in **P site**

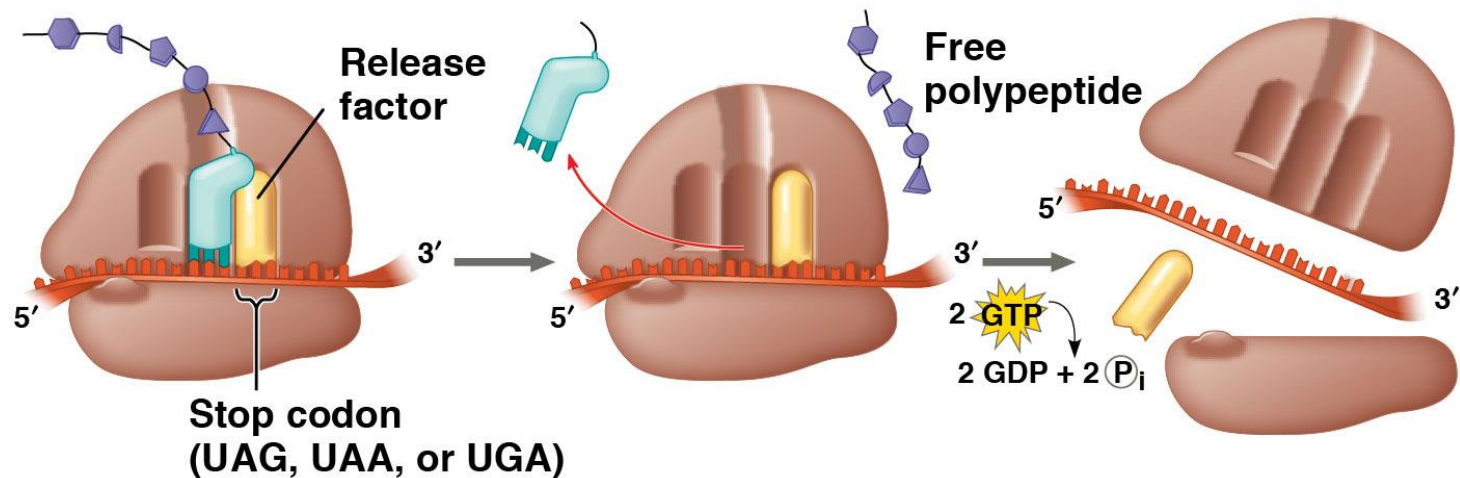
# 2. Elongation



**Translocation:** tRNA in **A site** moves to **P site**; tRNA in P site moves to **E site** (then exits)

# 3. Termination

- ▶ **Stop codon** reached and translation stops
- ▶ **Release factor** binds to stop codon; polypeptide is released
- ▶ Ribosomal subunits dissociate



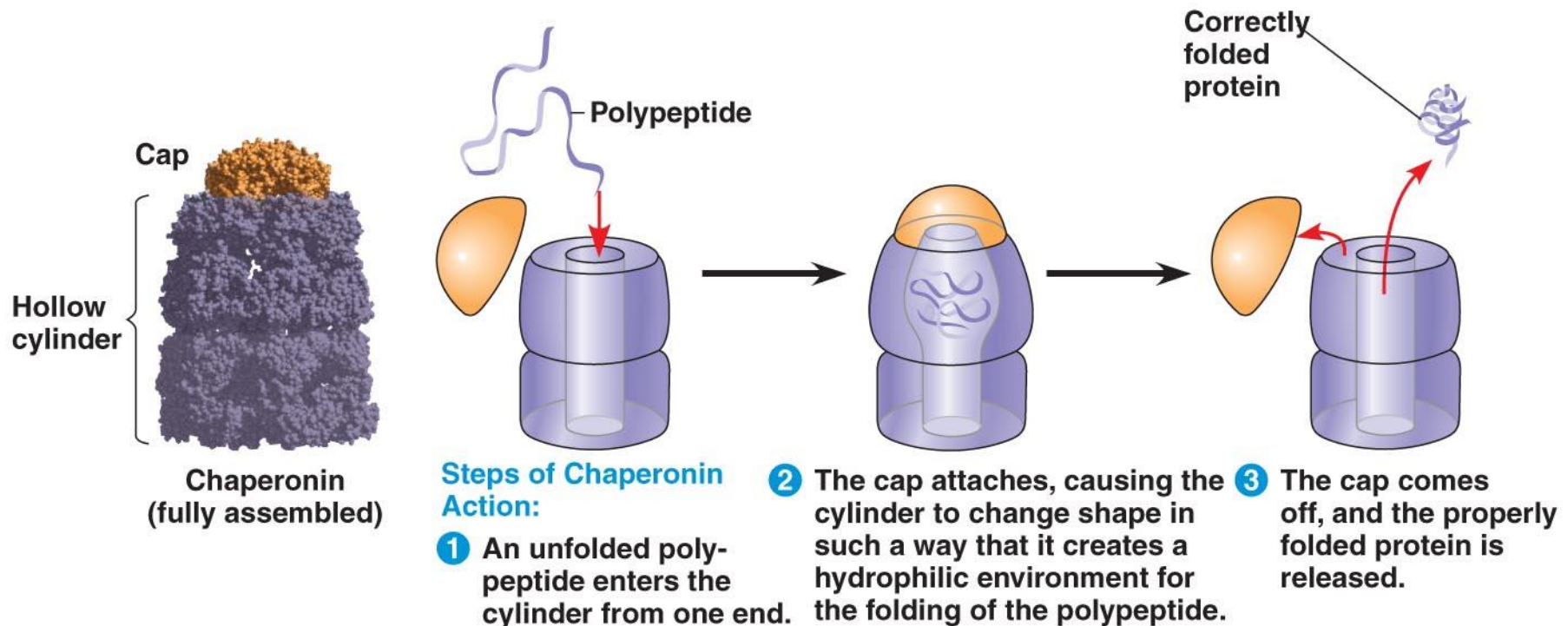
**1** Ribosome reaches a stop codon on mRNA.

**2** Release factor promotes hydrolysis.

**3** Ribosomal subunits and other components dissociate.

# Protein Folding

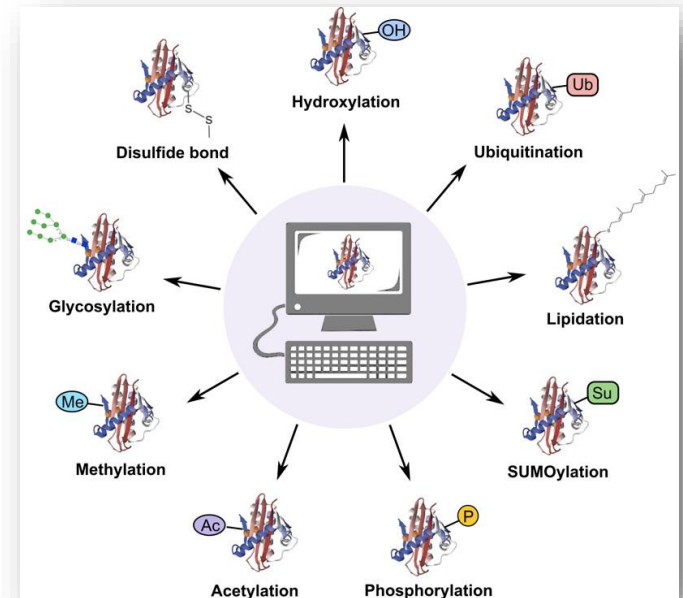
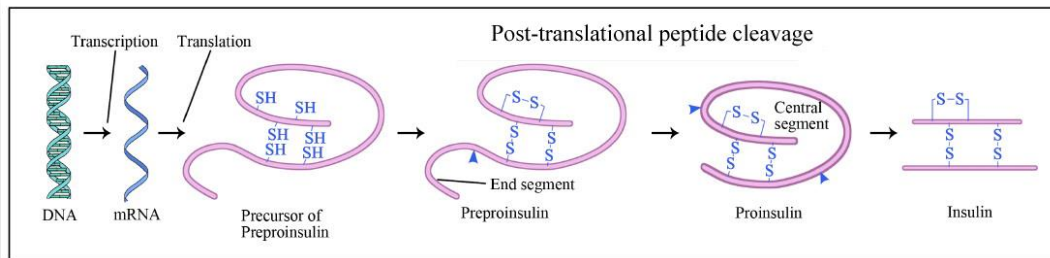
- ▶ During synthesis, polypeptide chain coils and folds spontaneously
- ▶ **Chaperonin**: protein that helps polypeptide fold correctly



# Post-Translational Modifications

- ▶ Attach sugars, lipids, phosphate groups, etc.
- ▶ Remove amino acids from ends
- ▶ Cut into several pieces
- ▶ Subunits come together

## Insulin Production



# Types of Ribosomes

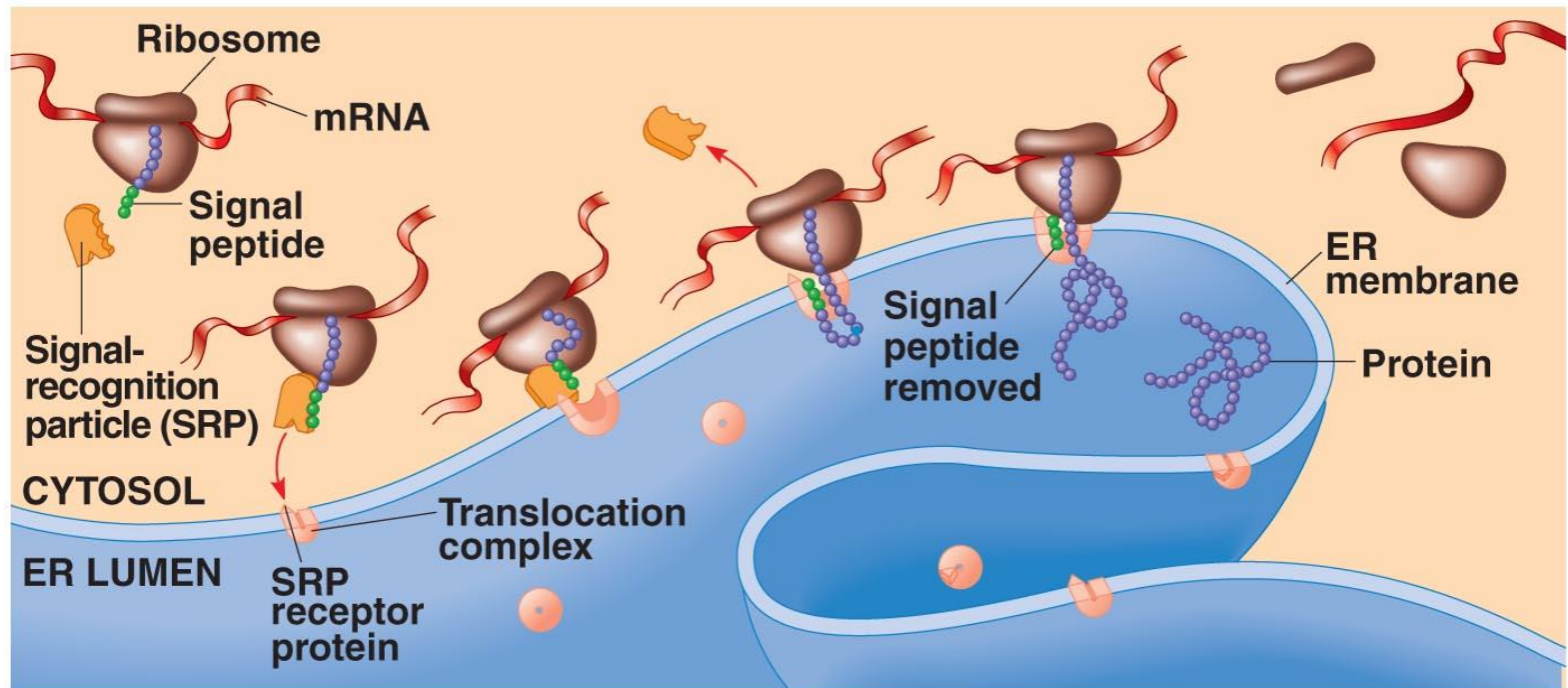
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- ▶ **Free ribosomes**: synthesize proteins that stay in cytosol and function there
- ▶ **Bound ribosomes** (to ER): make proteins of endomembrane system (nuclear envelope, ER, Golgi, lysosomes, vacuoles, plasma membrane) & proteins for secretion
  - ▶ Uses **signal peptide** to target location



# Cellular “Zip Codes”

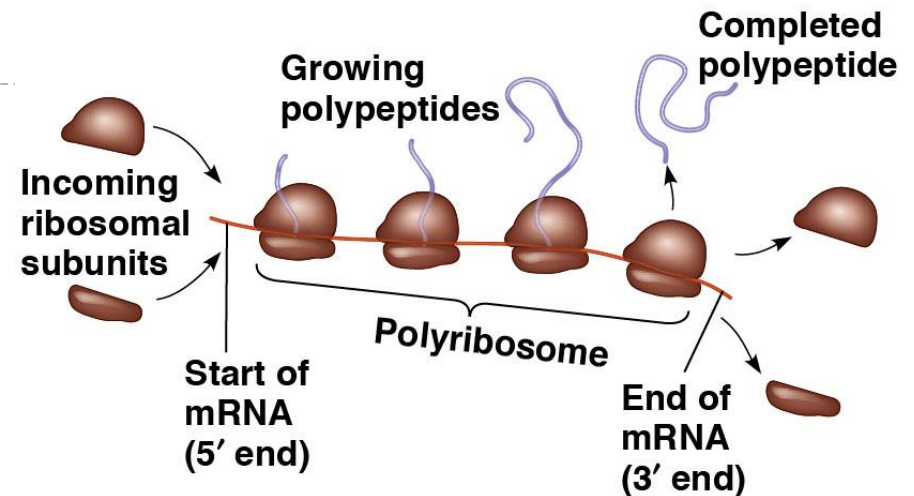
- ▶ Signal peptide: 20 AA at leading end of polypeptide determines destination
- ▶ Signal-recognition particle (SRP): brings ribosome to ER



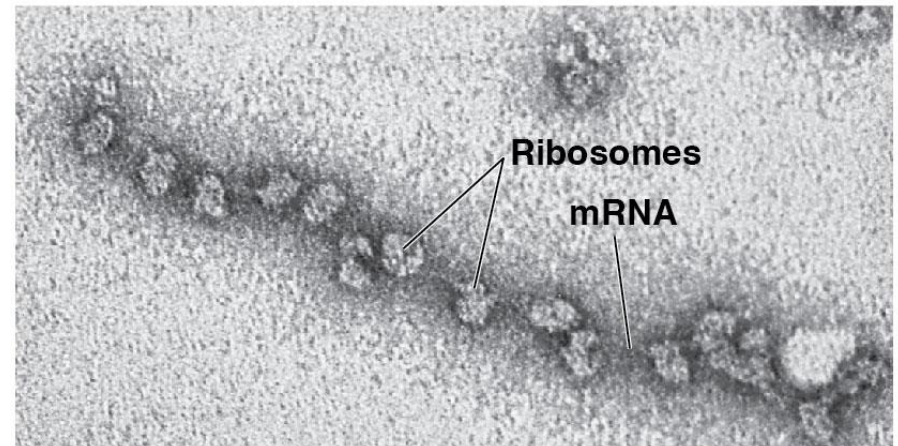


# Polyribosomes

- ▶ A single mRNA can be translated by several ribosomes at the same time



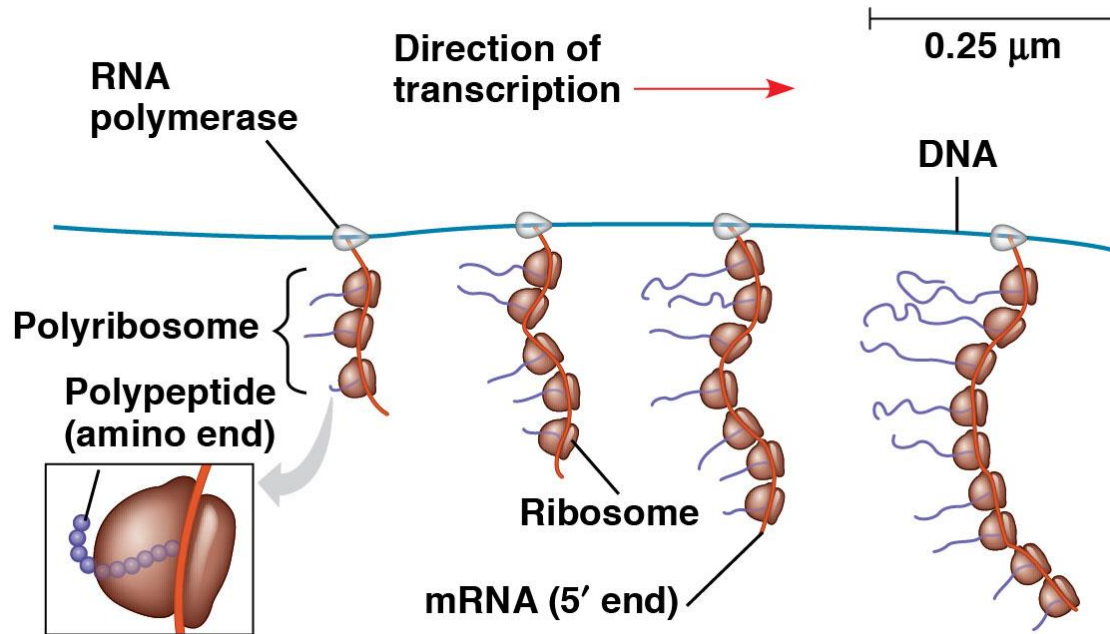
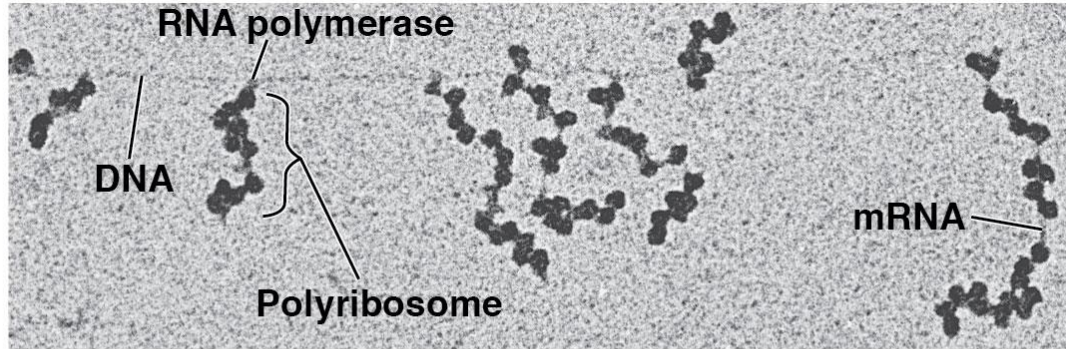
(a) An mRNA molecule translated simultaneously by several ribosomes



(b) A large polyribosome in a bacterial cell (TEM)

0.1 μm

# Prokaryotes can transcribe + translate

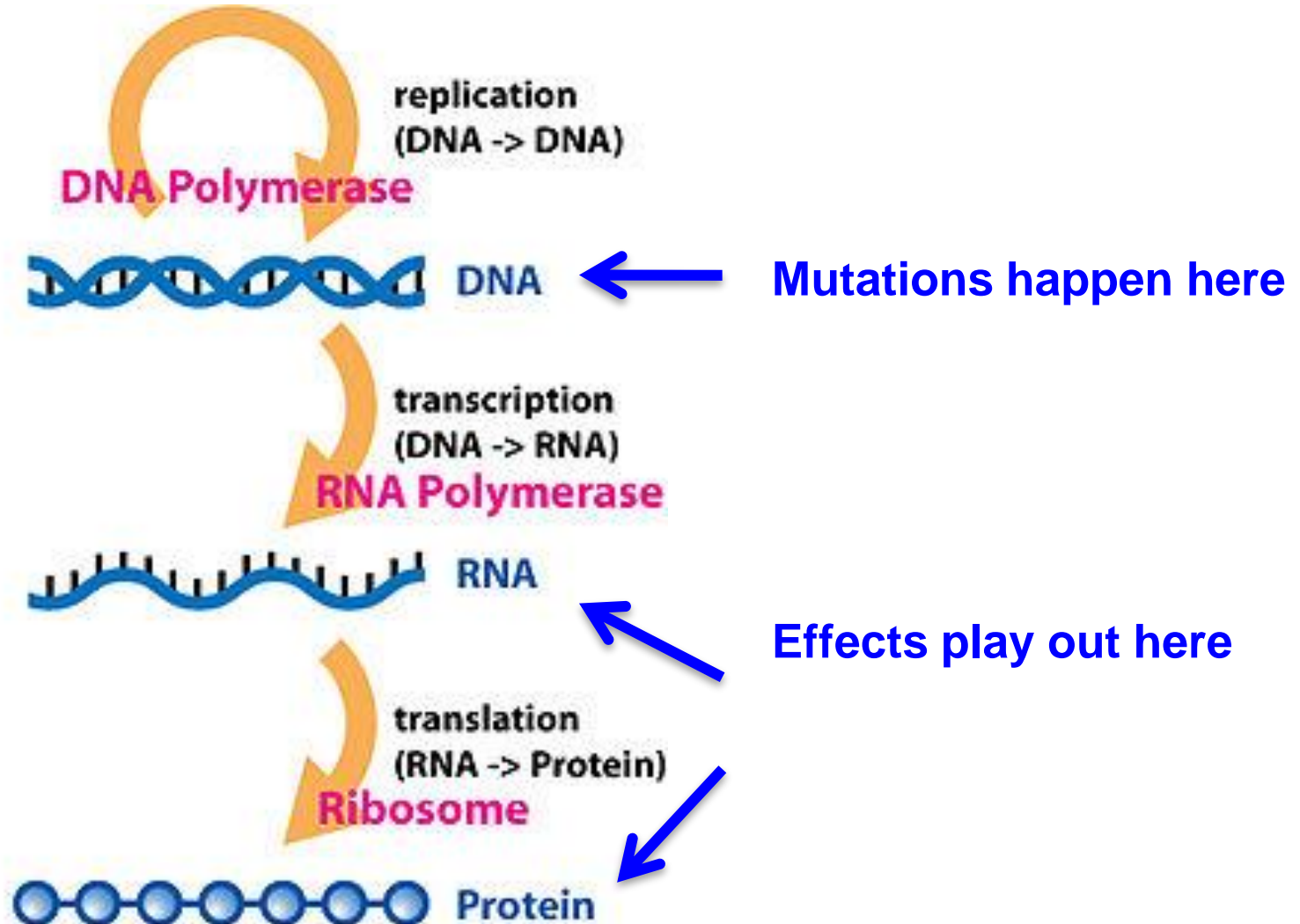


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Concept 14.5:

Mutations of one or a few nucleotides can affect protein structure and function

# The Central Dogma



Mutations = changes in the genetic material of a cell

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- ▶ **Chromosomal**: large-scale; always causes disorders or death (eg. nondisjunction, translocation, inversions, duplications, large deletions)
- ▶ **Point Mutations**: change single **nucleotide pair** of a gene
  1. **Substitution** – replace 1 with another
    - ▶ Silent: same amino acid
    - ▶ Missense: different amino acid
    - ▶ Nonsense: stop codon, not amino acid
  2. **Frameshift (insertion/deletion)** – mRNA read incorrectly; nonfunctional proteins



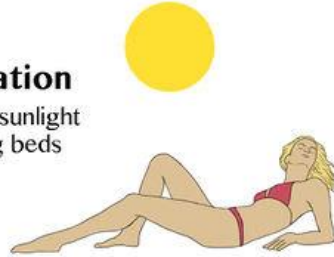
# Mutagens: substances or forces that cause mutations in DNA

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## Radiation

### UV Radiation

Both natural sunlight and tanning beds



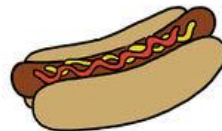
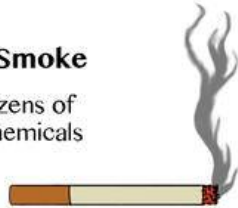
### X-Rays

Medical, dental, airport security screening

## Chemicals

### Cigarette Smoke

Contains dozens of mutagenic chemicals



**Nitrate & Nitrite Preservatives**  
In hot dogs and other processed meats

**Barbecuing**  
Creates mutagenic chemicals in foods



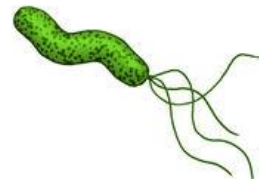
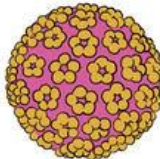
### Benzoyl Peroxide

Common ingredient in acne products

## Infectious Agents

### Human Papillomavirus (HPV)

Sexually transmitted virus

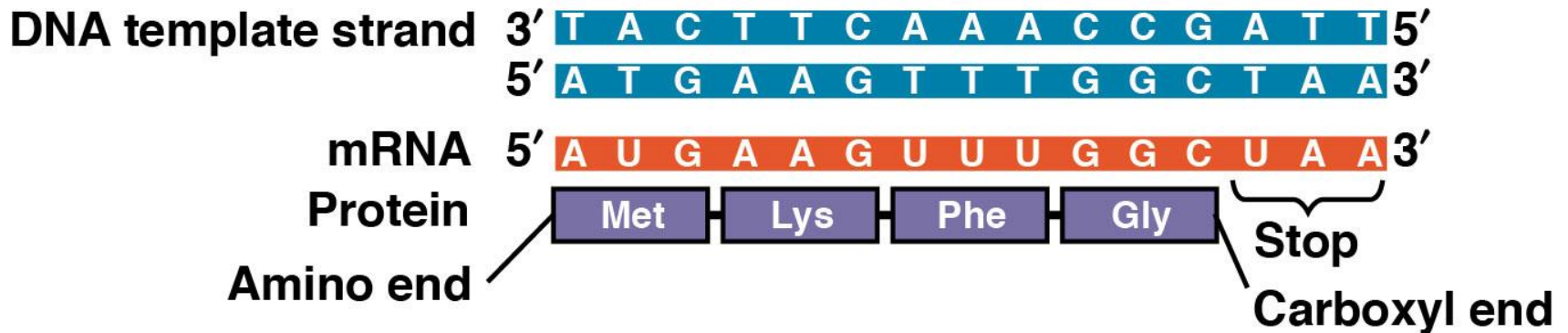


### *Helicobacter pylori*

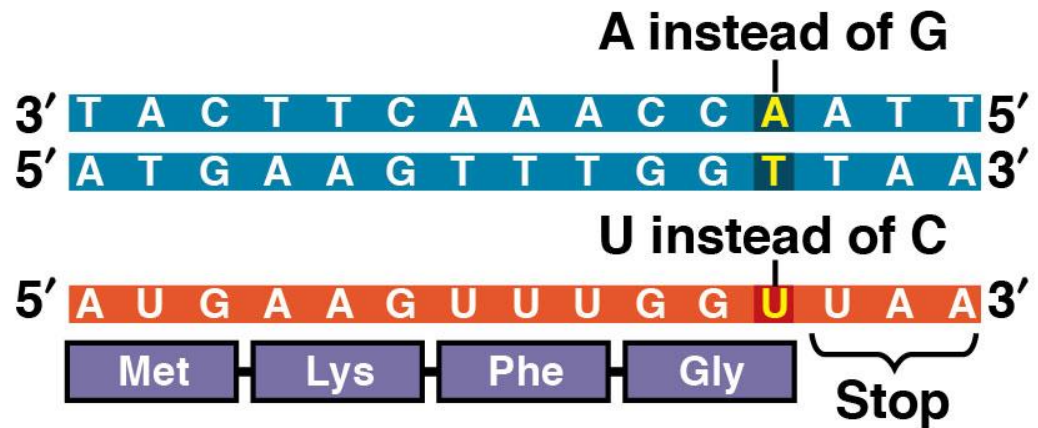
Bacteria spread through contaminated food

# Substitution = Silent (no effect)

## Wild type

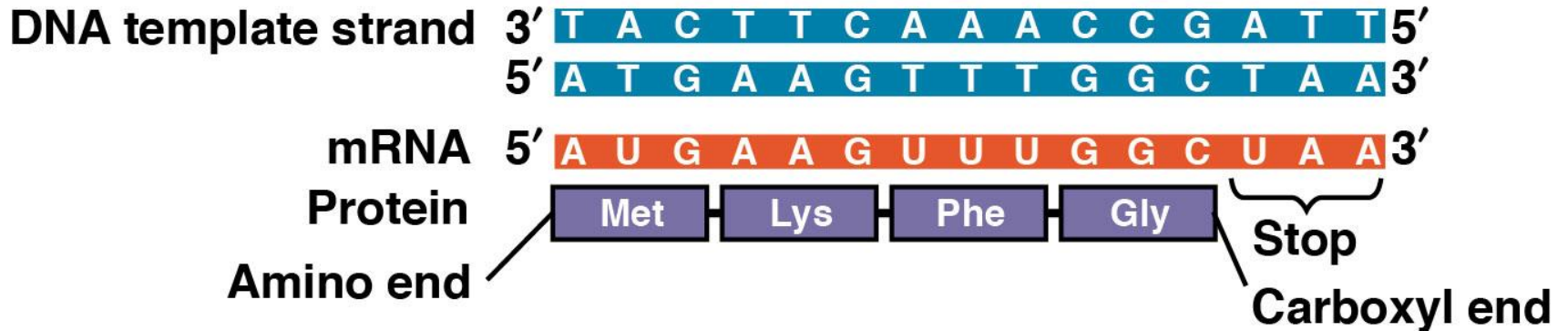


## Nucleotide-pair substitution: silent

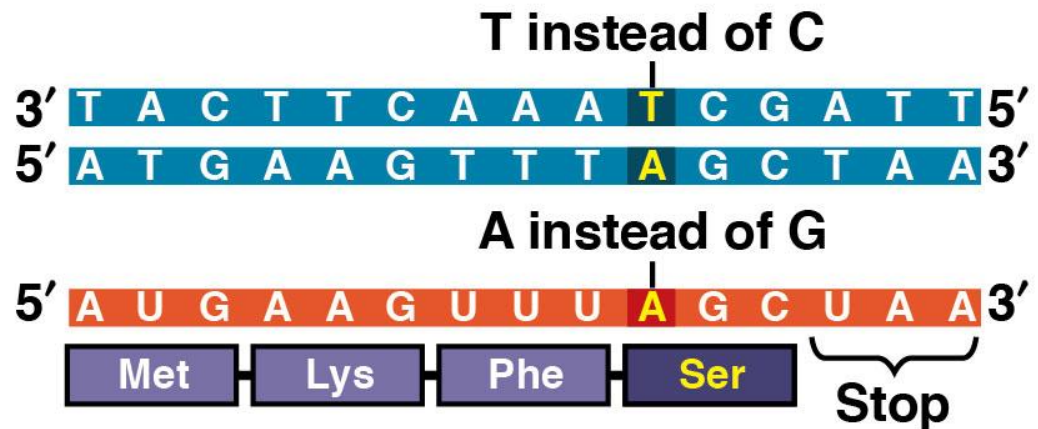


# Substitution = Missense

## Wild type



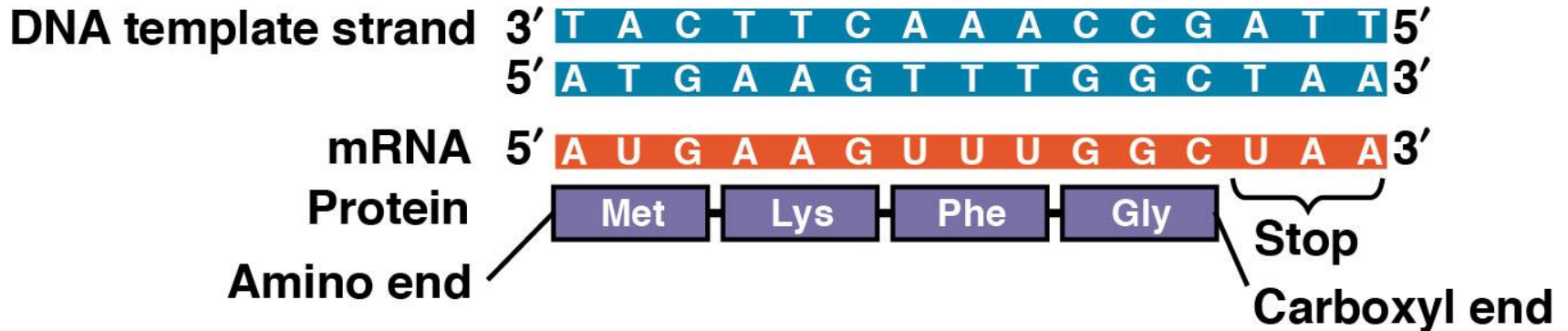
## Nucleotide-pair substitution: missense



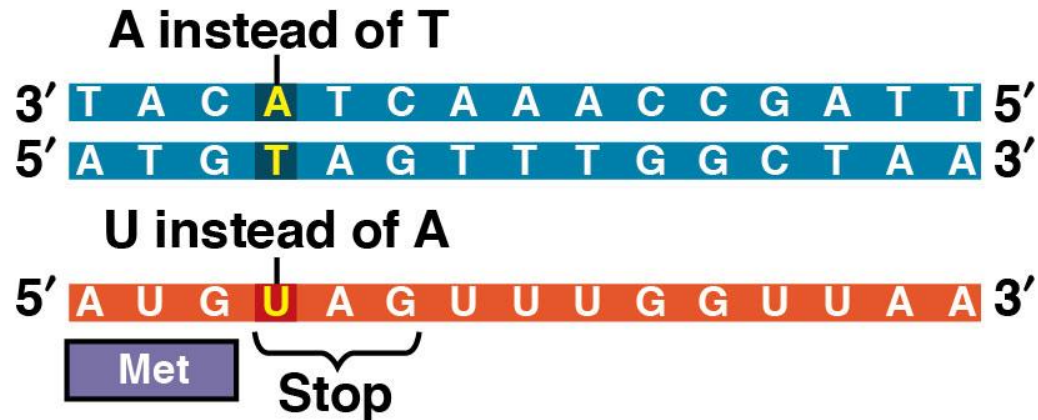


# Substitution = Nonsense (STOP)

## Wild type

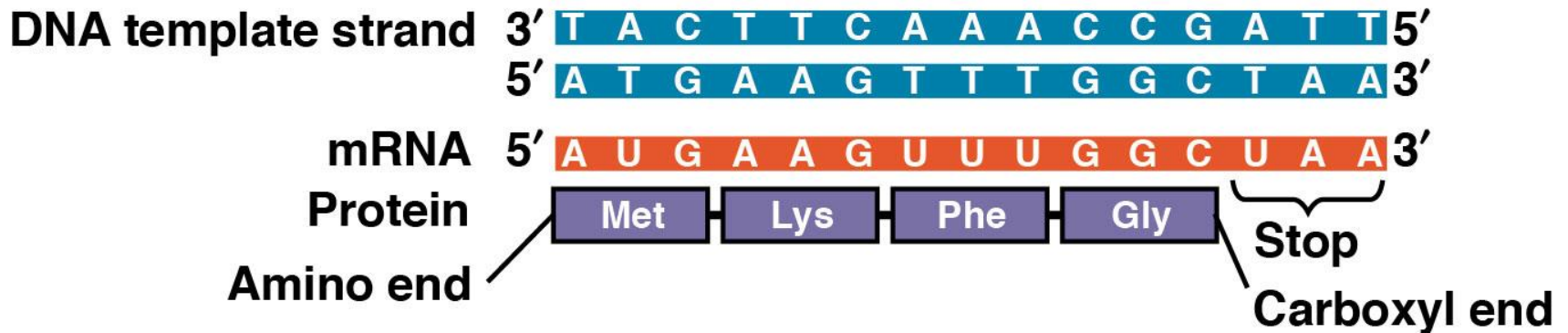


## Nucleotide-pair substitution: nonsense

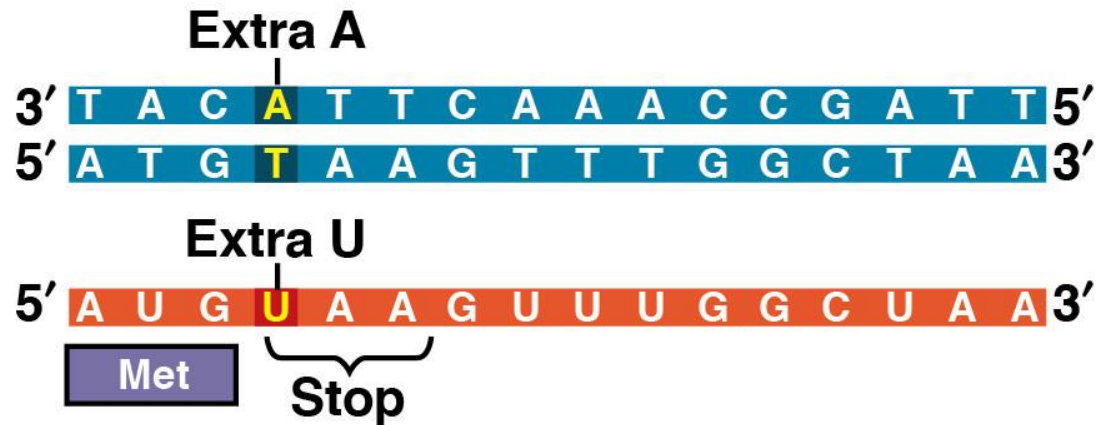


# Frameshift Mutation = Insertion/Deletion

## Wild type

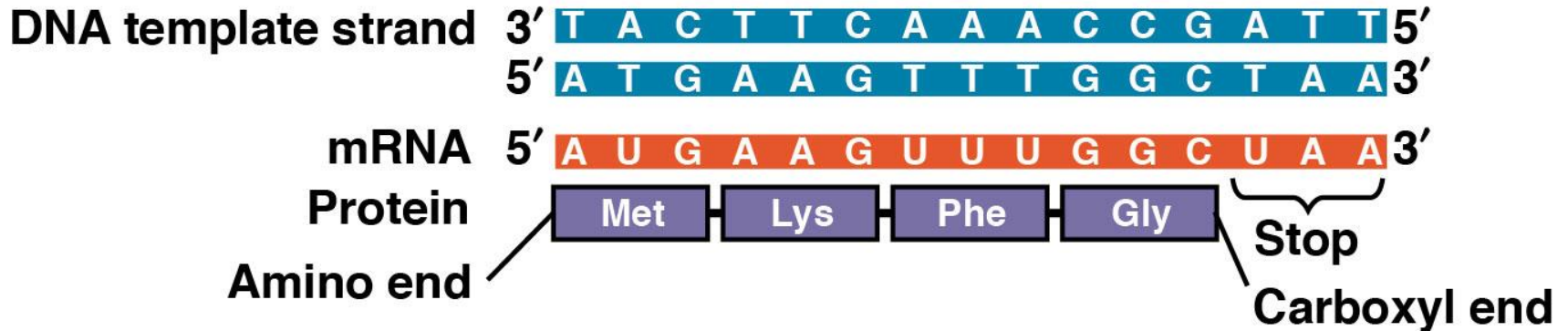


## Nucleotide-pair insertion: frameshift causing immediate nonsense

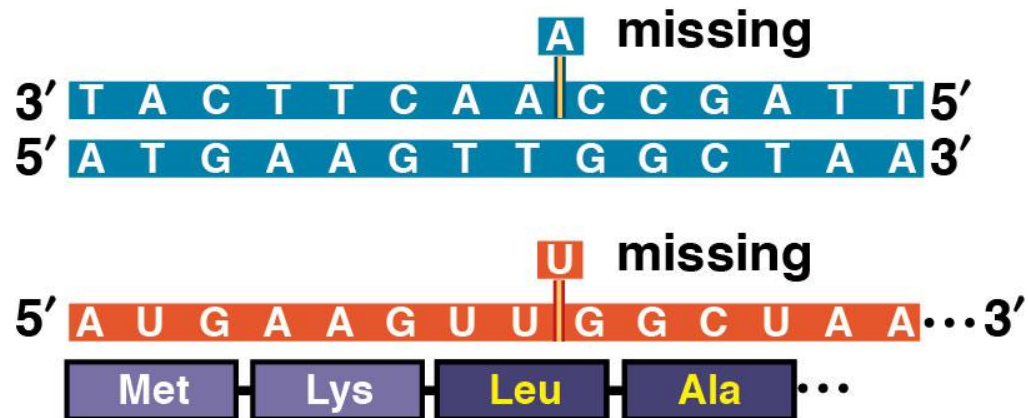


# Frameshift Mutation = Insertion/Deletion

## Wild type

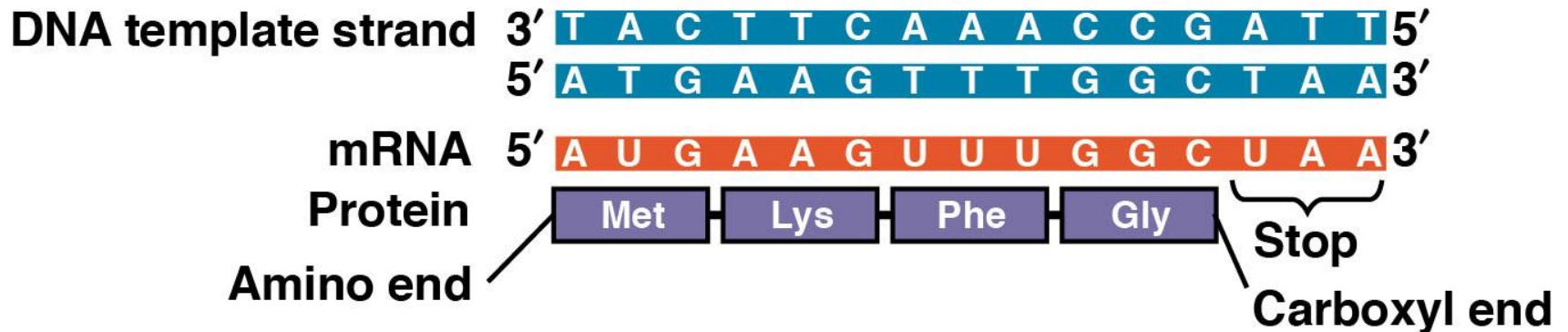


## Nucleotide-pair deletion: frameshift causing extensive missense

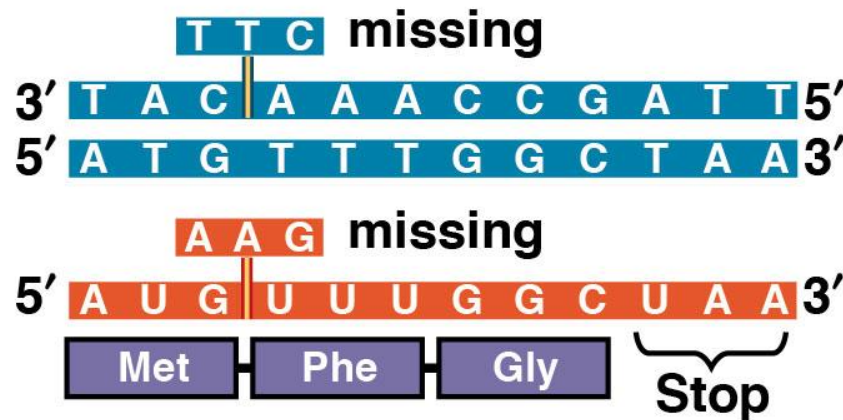


# 3-Nucleotide-Pair Deletion/Insertion

## Wild type



## 3 nucleotide-pair deletion: no frameshift, but one amino acid missing



# Sickle Cell Disease

## Symptoms

Anemia

Pain

Frequent infections

Delayed growth

Stroke

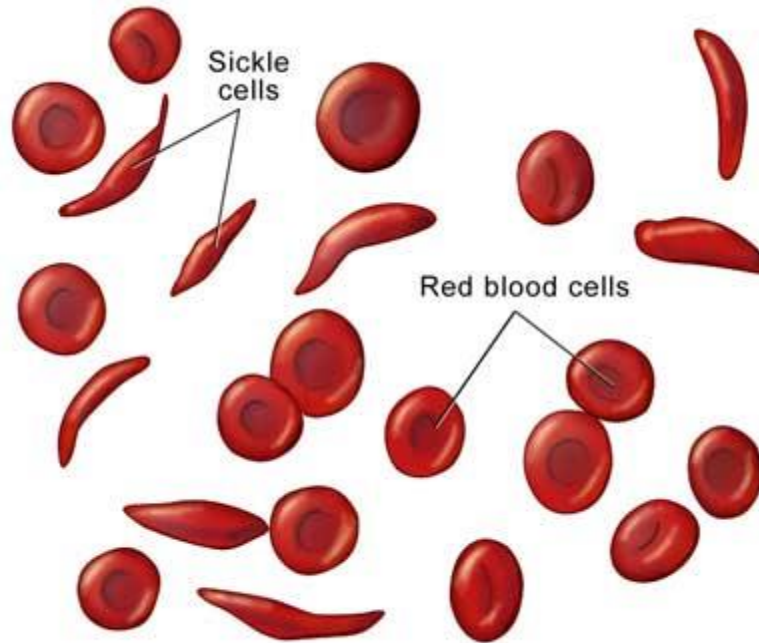
Pulmonary hypertension

Organ damage

Blindness

Jaundice

gallstones



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Caused by a genetic defect

Carried by 5% of humans

Carried by up to 25% in some regions of Africa

Life expectancy

42 in males 48 in females



# Sickle-Cell Disease = Point Mutation

Wild-type  $\beta$ -globin



Sickle-cell  $\beta$ -globin



Wild-type  $\beta$ -globin DNA



Mutant  $\beta$ -globin DNA



mRNA



mRNA

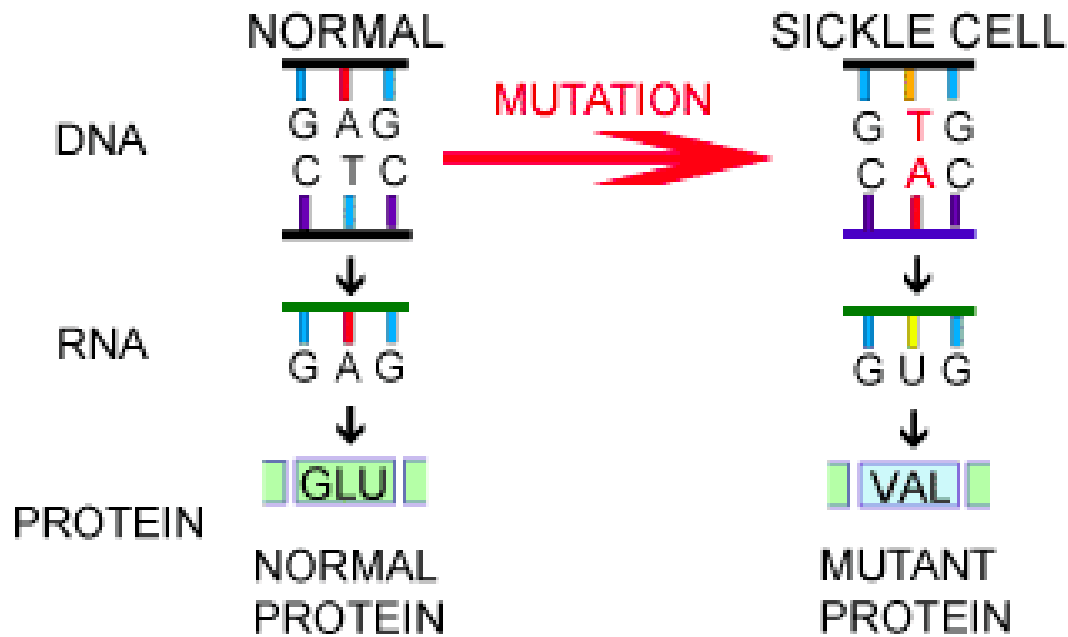
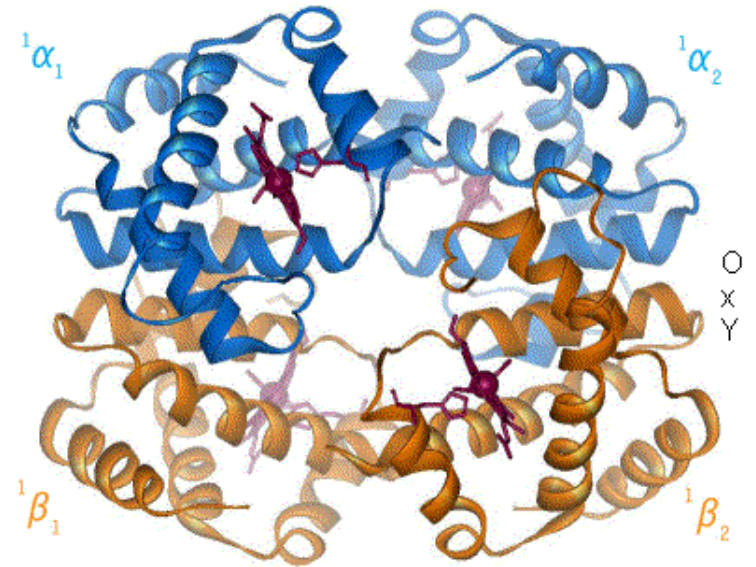
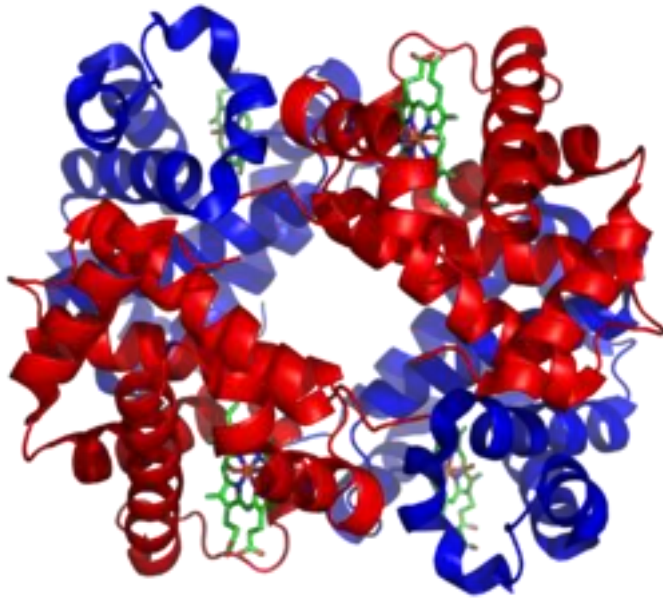


Normal hemoglobin

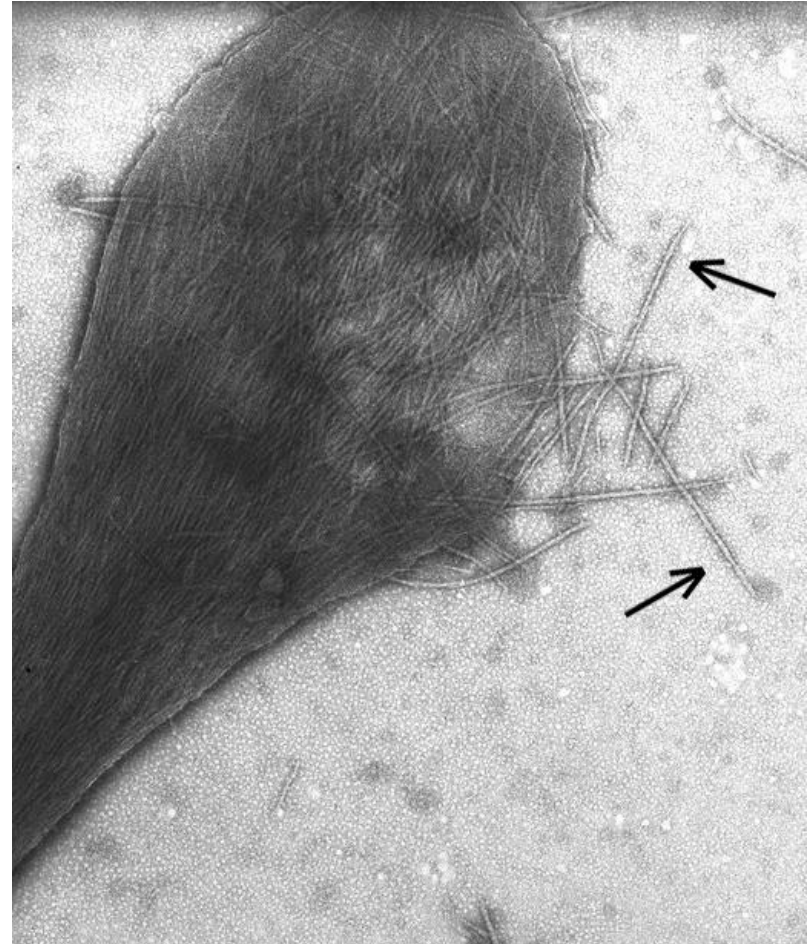
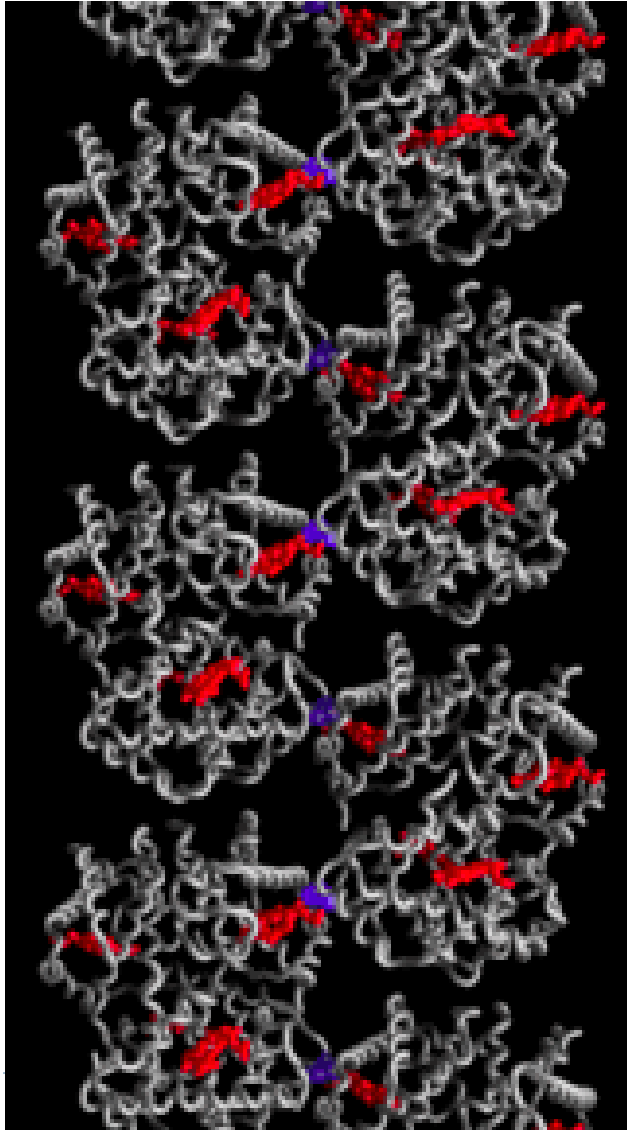


Sickle-cell hemoglobin



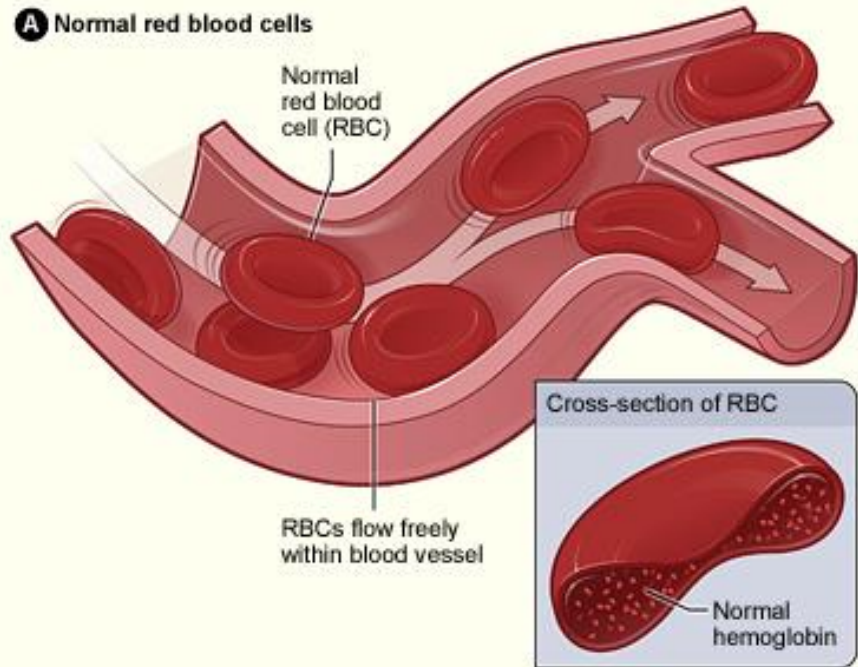


Sickle cell hemoglobin forms long, inflexible chains

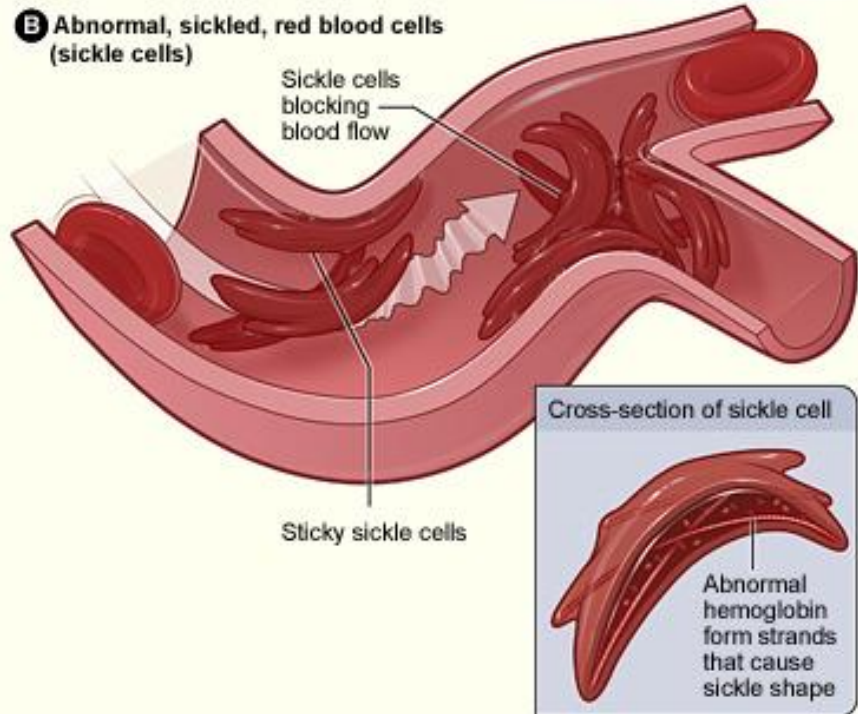




**A** Normal red blood cells



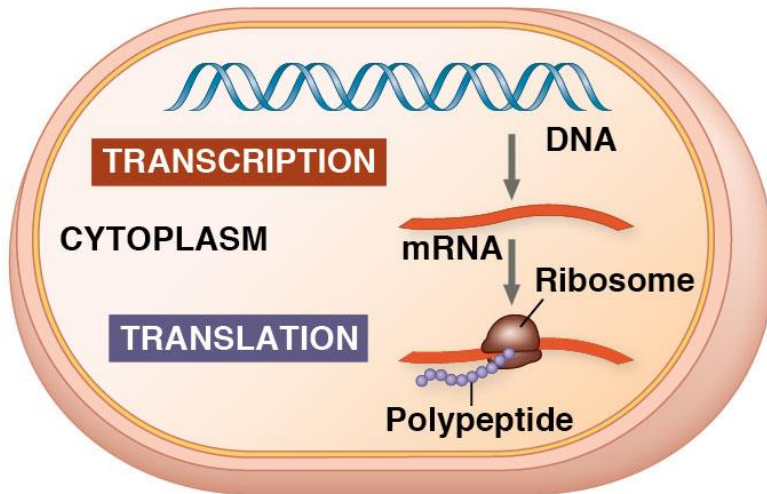
**B** Abnormal, sickled, red blood cells (sickle cells)



Coevolution of Genes and Culture:  
Got Lactase?

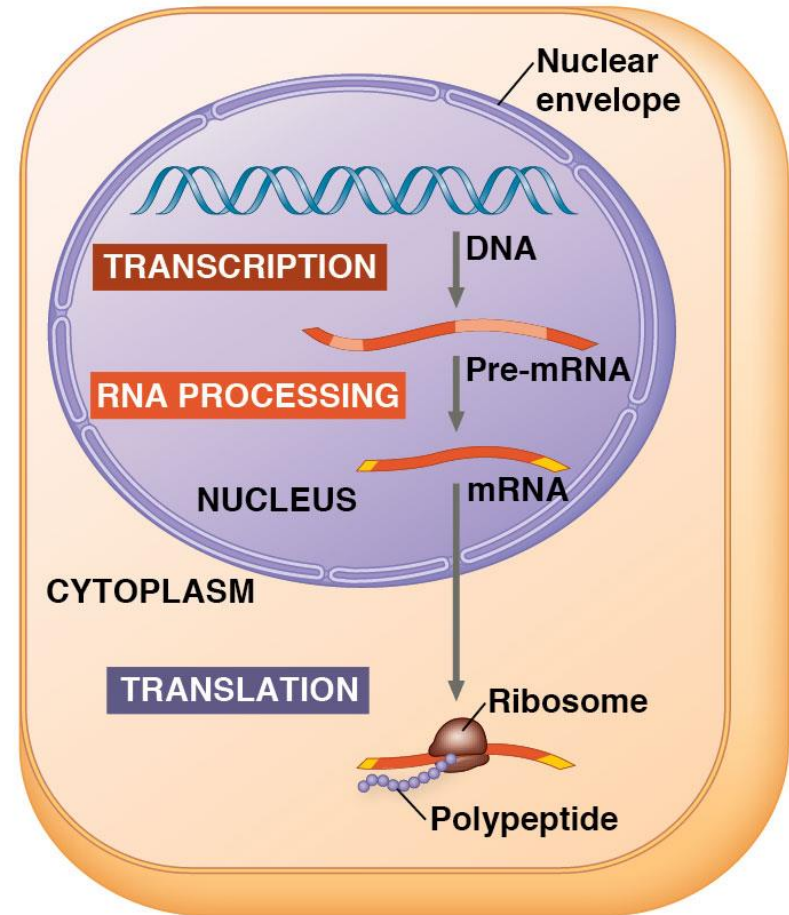
# Comparison: Prokaryotes vs. Eukaryotes

# Prokaryote vs. Eukaryote



**(a) Bacterial cell**

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**(b) Eukaryotic cell**

# Prokaryotes vs. Eukaryotes

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## Prokaryotes

- ▶ Transcription and translation both in cytoplasm
- ▶ DNA/RNA in cytoplasm
- ▶ RNA poly binds directly to promoter
- ▶ Transcription makes mRNA (not processed)
- ▶ No introns

## Eukaryotes

- ▶ Transcription in **nucleus**; translation in **cytoplasm**
- ▶ DNA in nucleus, RNA travels in/out nucleus
- ▶ RNA poly binds to TATA box & transcription factors
- ▶ Transcription makes pre-mRNA → **RNA processing** → final mRNA
- ▶ Exons, introns (cut out)



# A Summary of Protein Synthesis (p. 297)

## Most current definition for a GENE:

A region of DNA that can be expressed to produce a final product that is either a polypeptide or an RNA molecule

