

# Gene Expression

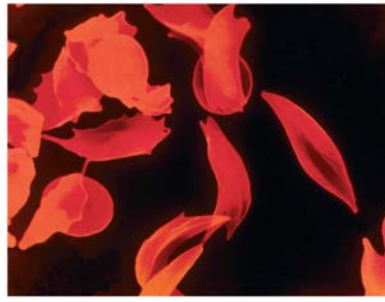
- One Gene – One Polypeptide
- Central Dogma
- Transcription
- Translation
- Mutations

## One Gene – One Polypeptide

- Sickle Cell Anemia
  - Two versions (Alleles) of the gene
    - Healthy allele – makes normal hemoglobin
    - Disease allele – makes alter hemoglobin



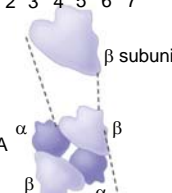
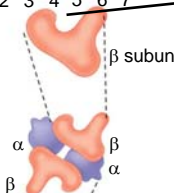
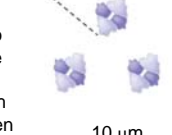
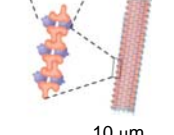


(a)



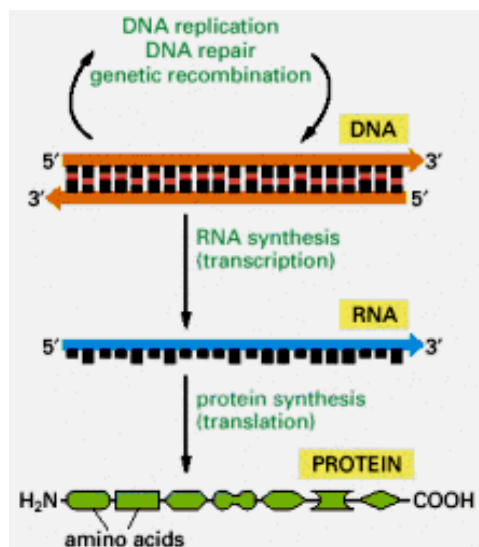
(b)

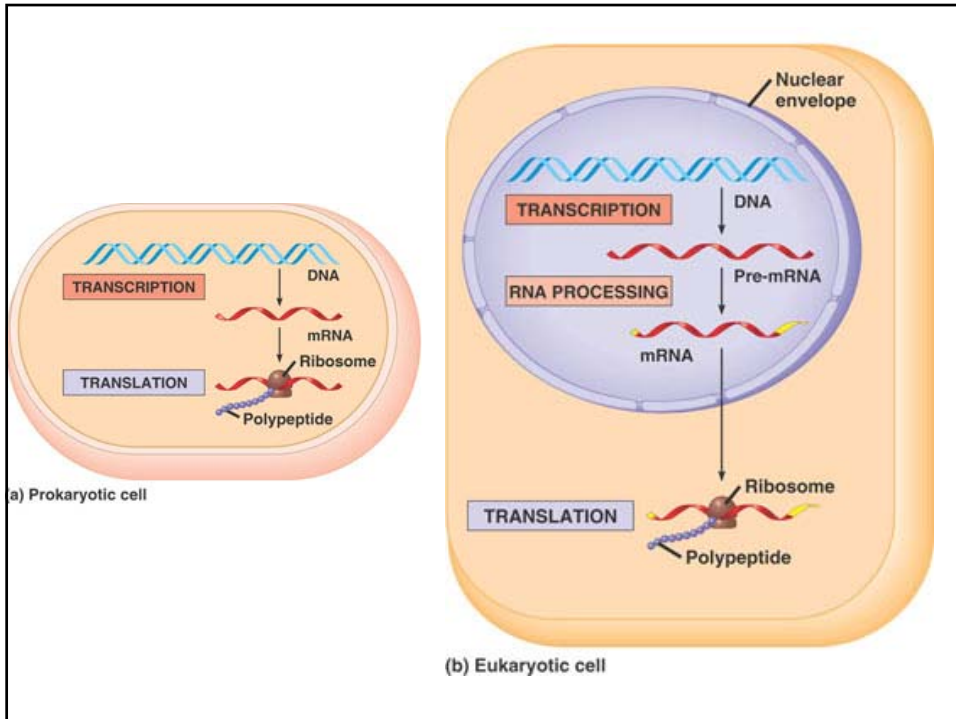
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# One Gene One Polypeptide

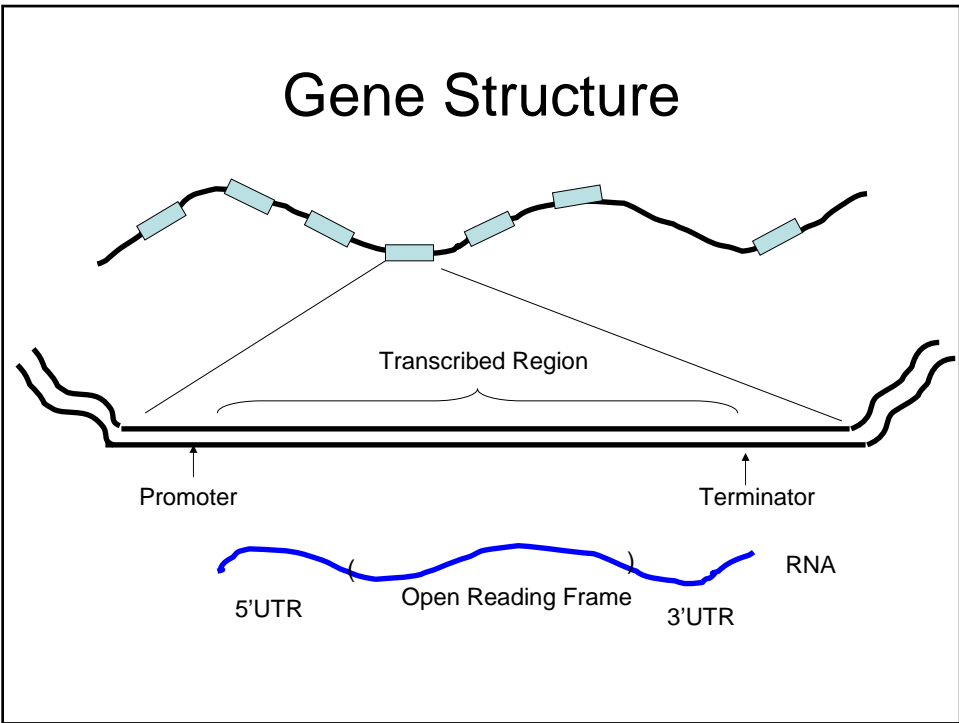
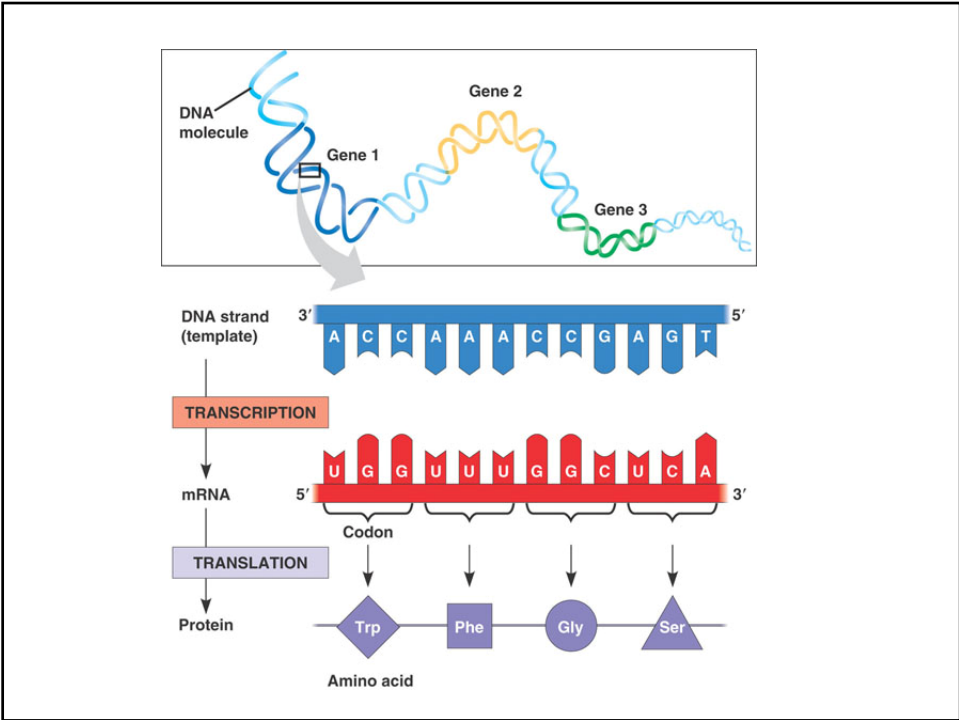
	Normal hemoglobin	Sickle-cell hemoglobin
<b>Primary structure</b>	Val   His   Leu   Thr   Pro   Glu   Glu ... 1 2 3 4 5 6 7	Val   His   Leu   Thr   Pro   <b>Val</b>   Glu ... 1 2 3 4 5 6 7
<b>Secondary and tertiary structures</b>	 <p>β subunit</p>	 <p>β subunit</p>
<b>Quaternary structure</b>	Hemoglobin A 	Hemoglobin S 
<b>Function</b>	Molecules do not associate with one another; each carries oxygen	Molecules interact with one another to crystallize into a fiber, capacity to carry oxygen is greatly reduced
<b>Red blood cell shape</b>	Normal cells are full of individual hemoglobin molecules, each carrying oxygen 	Fibers of abnormal hemoglobin deform cell into sickle shape 

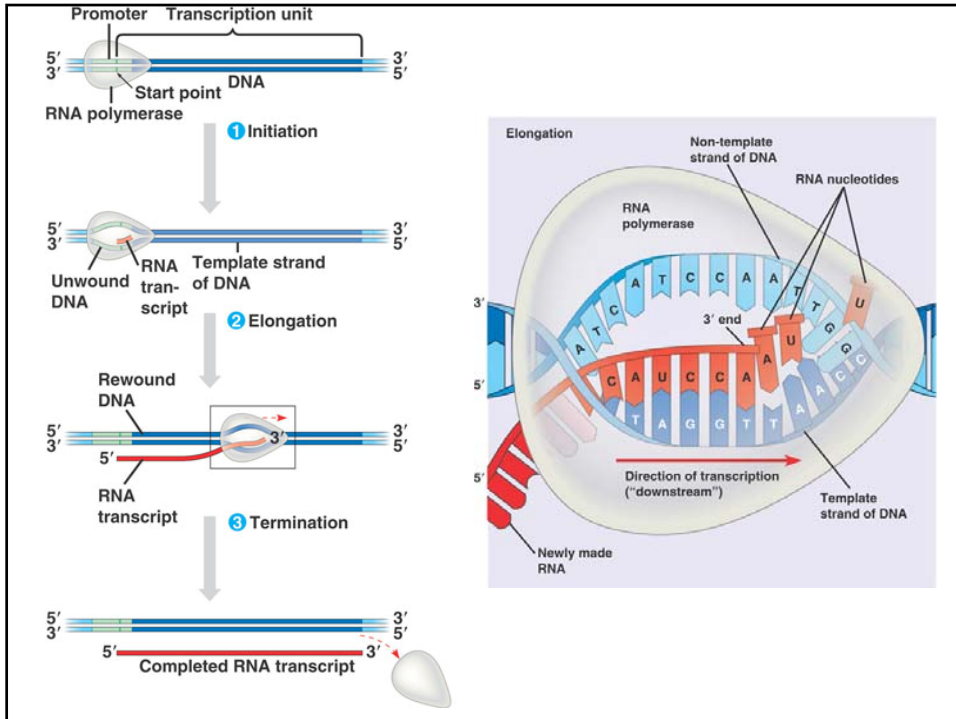
# Central Dogma of Molecular Biology





	DNA	RNA
<b>Strands</b>	2	1
<b>Sugar</b>	deoxyribose	ribose
<b>Types of bases</b>	adenine (A), thymine (T) cytosine (C), guanine (G)	adenine (A), uracil (U) cytosine (C), guanine (G)
<b>Base pairs</b>	DNA:DNA A-T T-A C-G G-C	RNA:DNA A-T U-A C-G G-C  RNA:RNA A-U U-A C-G G-C
<b>Function</b>	Contains genes; sequence of bases in most genes determines the amino acid sequence of a protein	<b>Messenger RNA (mRNA):</b> carries the code for a protein-coding gene from DNA to ribosomes <b>Ribosomal RNA (rRNA):</b> combines with proteins to form ribosomes, the structures that link amino acids to form a protein <b>Transfer RNA (tRNA):</b> carries amino acids to the ribosomes





## Three Parts to Transcription

- **Transcriptional Initiation** –
  - RNA polymerase binds to promoter
  - DNA strands separate
  - RNA synthesis begins as ribonucleotides complementary to template strand are linked
- **Transcriptional Elongation**
  - RNA polymerase moves down DNA unwinding a small window of DNA.
  - Nucleotides are added to the growing RNA chain
- **Transcriptional Termination**
  - When the RNA polymerase reaches terminator the RNA and the RNA polymerase are released from the DNA.

# Genetic Code

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

## Identifying ORF

5' GACGACGGAUGCGCAAUGCGUCUCUAUGAGACGUAGCUCAC

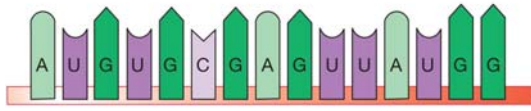
- Locate start codon (1st ATG from 5' end)
- Identify Codons (non overlapping units of three codons including and following start codon)
- Stop at stop codon (remember stop codon doesn't encode amino acid)
- Nucleotides before start codon – 5'UTR
- Nucleotides after stop codon - 3'UTR
- [MetArgAsnAlaSerLeu]

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

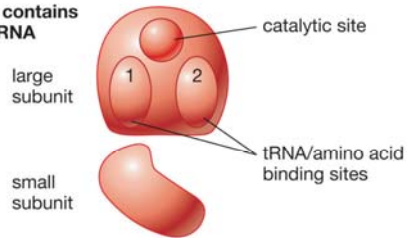
# Players in Translation

mRNA – Genetic Code  
 Ribosome – synthesizes protein  
 tRNA – adaptor molecule

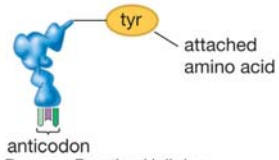
(a) Messenger RNA (mRNA)



(b) Ribosome: contains ribosomal RNA (rRNA)

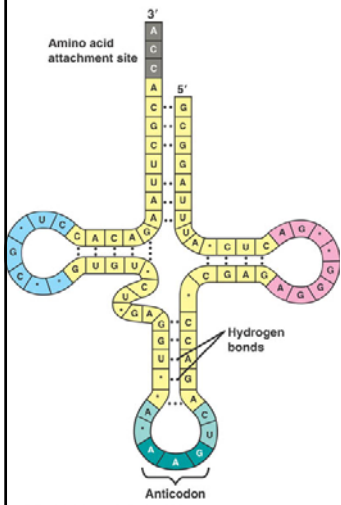


(c) Transfer RNA (tRNA)

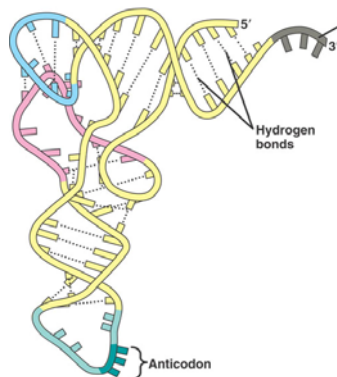


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## tRNA



a) Two-dimensional structure



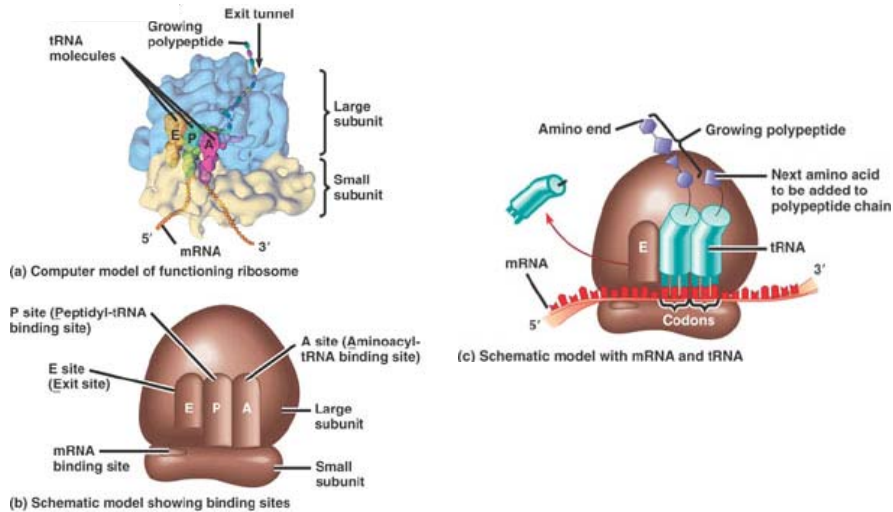
(b) Three-dimensional structure



(c) S

ol used in this book

# Ribosomes



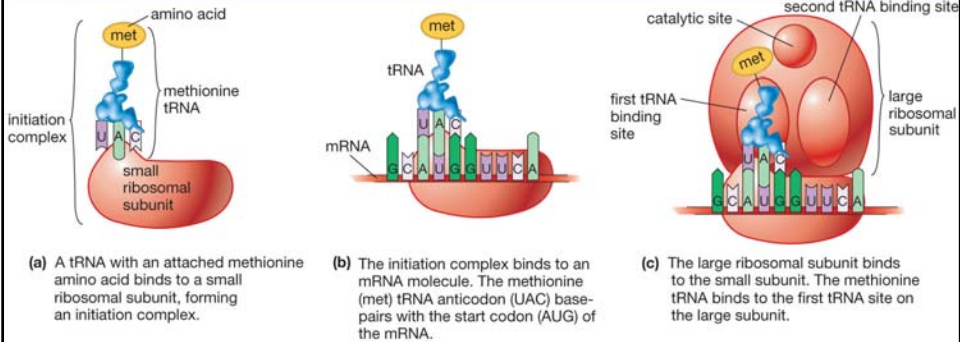
## Three parts to Translation

- **Initiation**
  - Delivery of Ribosome with first tRNA to start codon.
- **Elongation Cycle**
  - Three Parts of Elongation Cycle
    - Delivery of tRNA to A site
    - Transpeptidase Activity – Amino acids on tRNA in P site cleaved from tRNA and attached to amino acid on tRNA in A site.
    - Translocation – Ribosome ratchets over on codon. The tRNA that was in the A site is moved to the P site. The uncharged tRNA in the P site exits the ribosome through the E site.
- **Termination**
  - When ribosome reaches the stop codon a release factor binds to the A site and triggers the release of the polypeptide. The ribosome releases the tRNA and the mRNA.



# Translational Initiation

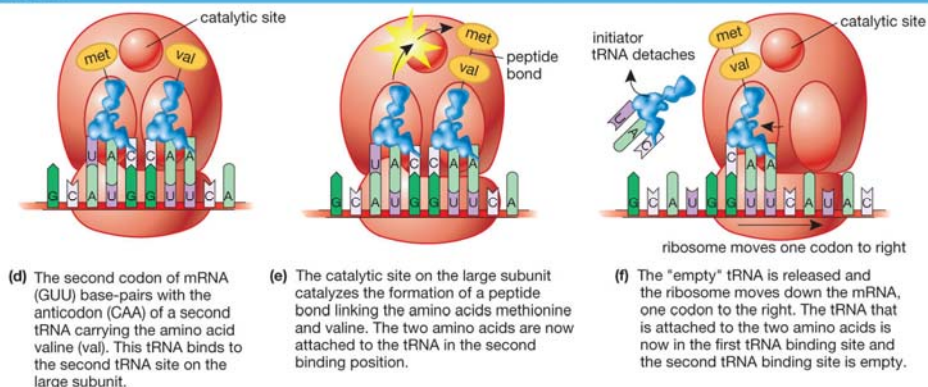
## Initiation:



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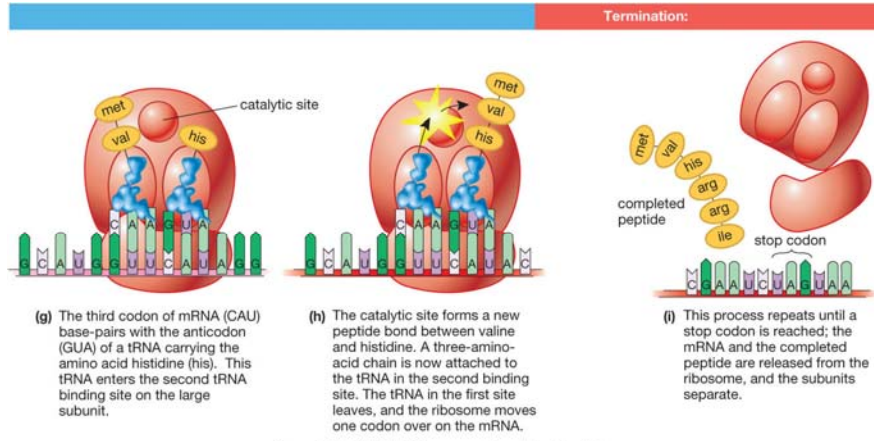
# Translational Elongation

## Elongation:

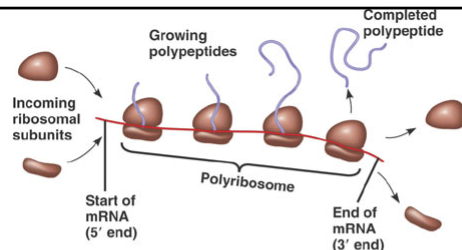


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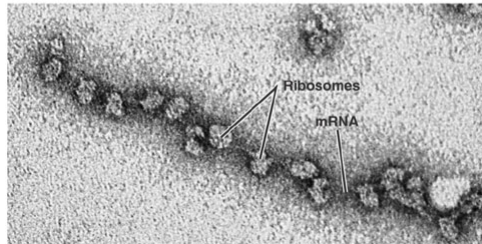
# Translational Termination



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(a) An mRNA molecule is generally translated simultaneously by several ribosomes in clusters called polyribosomes.



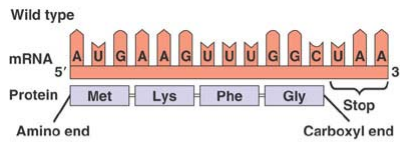
0.1 μm

(b) This micrograph shows a large polyribosome in a prokaryotic cell (TEM).

## Polysomes

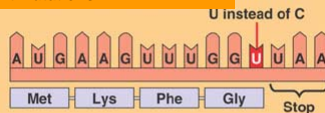
# Mutations

- Changes in DNA sequence
  - Example base substitution
    - G changed to an A
  - Mutations can affect proteins in several ways
  - Raw material for evolution
    - New forms of genes

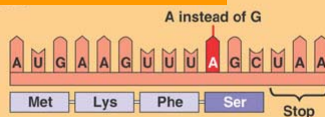


## Base-pair substitution

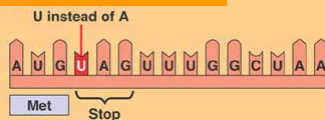
### Silent Mutations



### Missense Mutations



### Nonsense Mutations



# Regulating Gene Expression

- Gene expression highly regulated
- Different tissues express different genes
- Gene expression regulated by environmental cues

The diagram illustrates the mechanism of steroid hormone action. Testosterone (blue spheres) enters the cytoplasm and is converted to DHT (pink spheres) by the enzyme 5 $\alpha$ -reductase. DHT then binds to the Androgen receptor (pink spheres) in the cytoplasm. The complex enters the nucleus, where it binds to DNA, initiating transcription (indicated by green X's). The diagram is labeled 'Ellis, JA et al. (2002)'.

**Female lion**

CC1=C(C(=O)O)C=CC=C1

**Estrogen**

**Male lion**

CC12CCC3=C(C(=O)O)C=CC=C3C=C12

**Testosterone**

# Sex Determination in Mammals

## Typical Male

Y Chromosome includes critical SRY gene which produces SRY transcription factor in the embryonic gonad

SRY transcription Factor – binds to promoters of gonad genes turning genes on (and off)

This pattern of SRY induced gene expression results in the gonad developing into a testis

The testis secretes testosterone

Testosterone moves to other tissues and binds to the androgen receptor which moves into the nucleus turning on “male specific” genes.

Male secondary sexual characteristics, Male genitalia

Typical Female lack Y chromosome and SRY. Default gonad development ovaries. No testosterone, default secondary sexual characteristic female

## Two ways to have XY females

1. Mutation in SRY gene  
Ovaries – produce estrogen  
Usually reduced fertility
2. Mutation in androgen receptor  
Testes (has SRY)  
Large amounts of testosterone produced but no androgen receptor to bind

Testicular Feminization



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