

Transcription and Translation

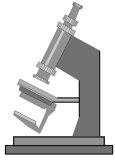
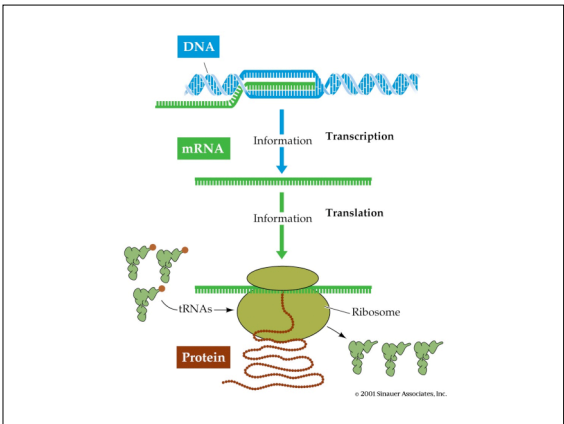
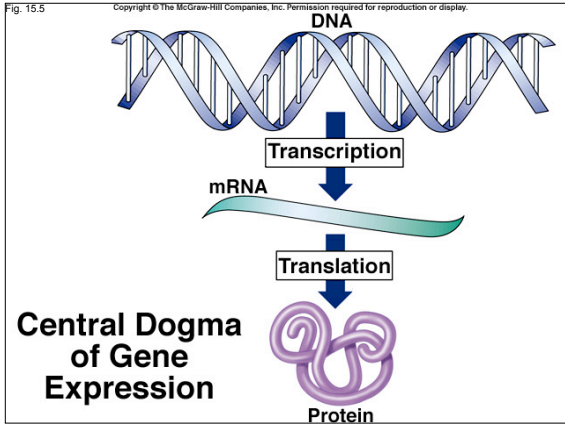
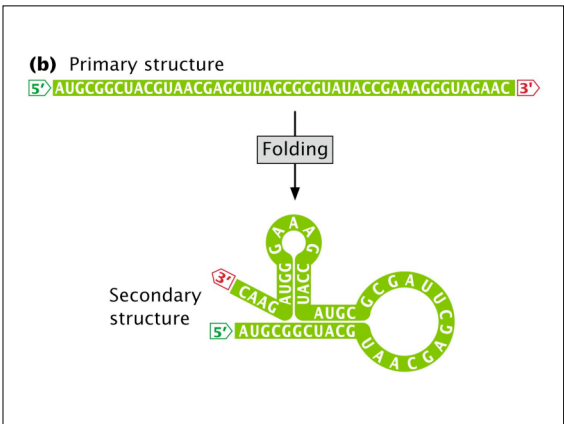



Table 13.1 The structures of DNA and RNA compared

Characteristic	DNA	RNA
Composed of nucleotides	Yes	Yes
Type of sugar	Deoxyribose	Ribose
Presence of 2'-OH group	No	Yes
Bases	A, G, C, T	A, G, C, U
Nucleotides joined by phosphodiester bonds	Yes	Yes
Double or single stranded	Usually double	Usually single
Secondary structure	Double helix	Many types
Stability	Quite stable	Easily degraded

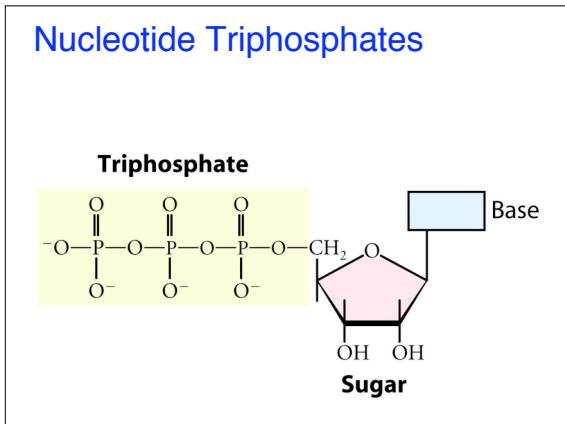
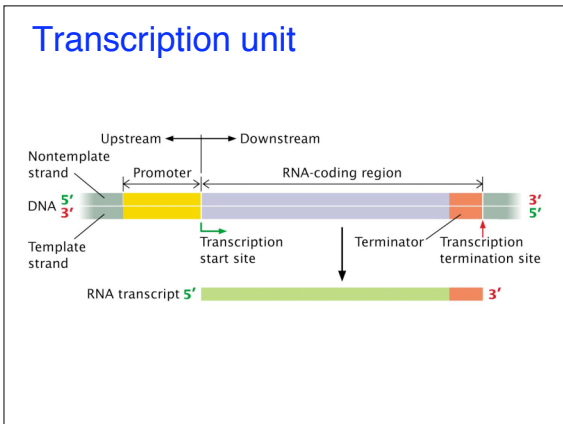
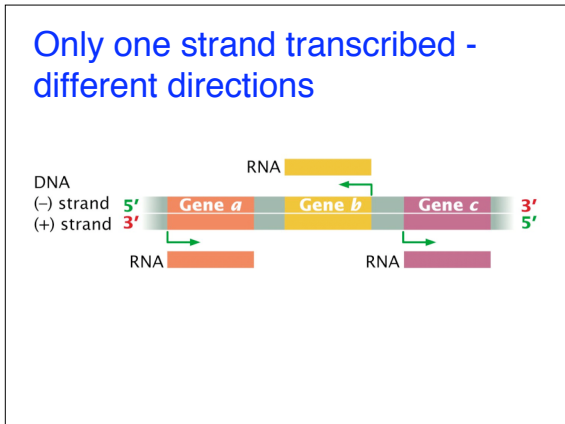
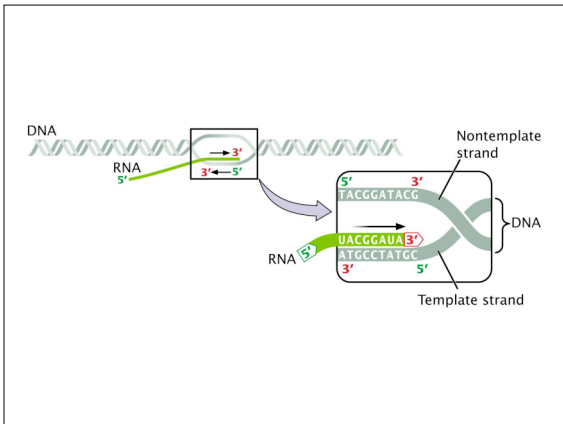
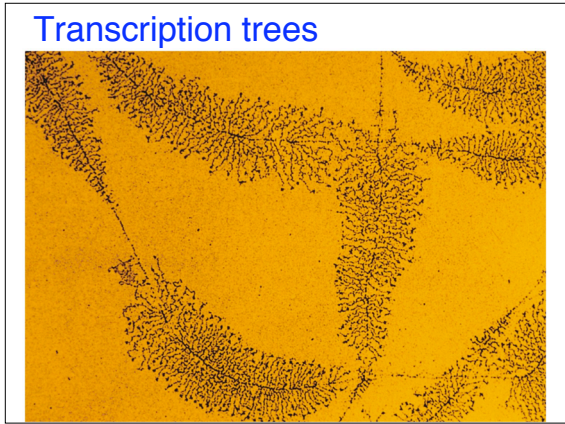
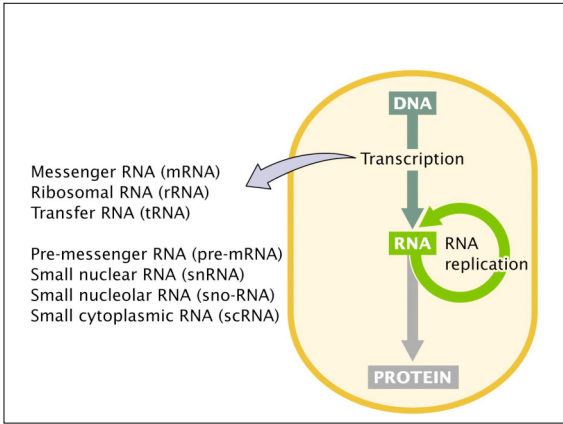


Types of RNA

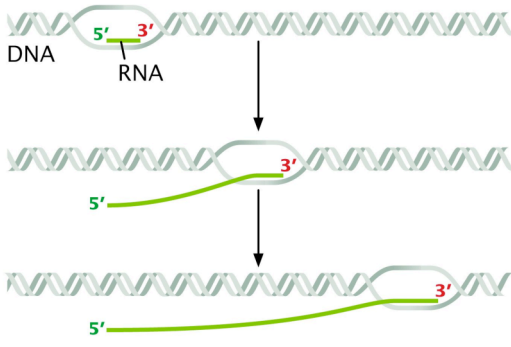
Table 13.2 Locations and functions of different classes of RNA molecules

Class of RNA	Cell Type	Location of Function* in Eukaryotic Cells	Function
Ribosomal RNA (rRNA)	Bacterial and eukaryotic	Cytoplasm	Structural and functional components of the ribosome
Messenger RNA (mRNA)	Bacterial and eukaryotic	Nucleus and cytoplasm	Carries genetic code for proteins
Transfer RNA (tRNA)	Bacterial and eukaryotic	Cytoplasm	Helps incorporate amino acids into polypeptide chain
Small nuclear RNA (snRNA)	Eukaryotic	Nucleus	Processing of pre-mRNA
Small nucleolar RNA (snoRNA)	Eukaryotic	Nucleus	Processing and assembly of rRNA
Small cytoplasmic RNA (scRNA)	Eukaryotic	Cytoplasm	Variable

*All eukaryotic RNAs are transcribed in the nucleus.



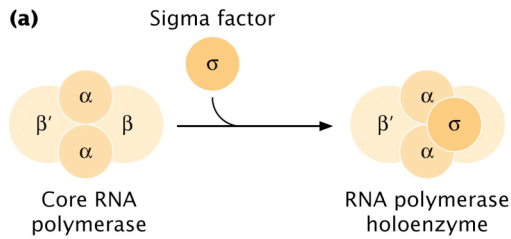
Transcription 5' to 3'



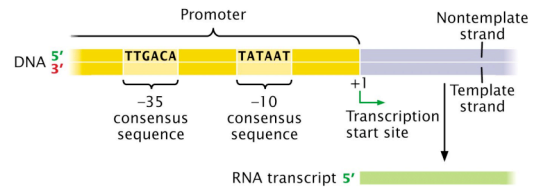
RNA Polymerase



Core enzyme to holoenzyme

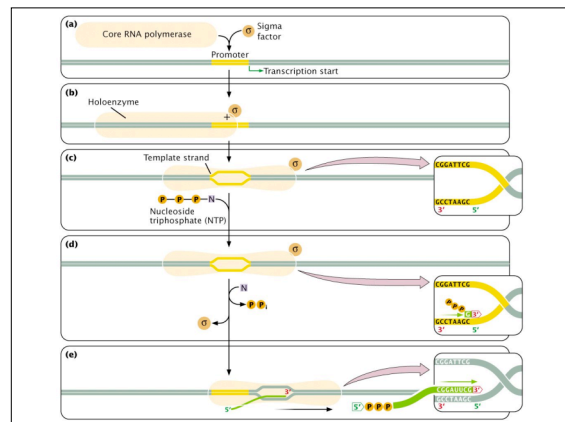


Bacterial promoters

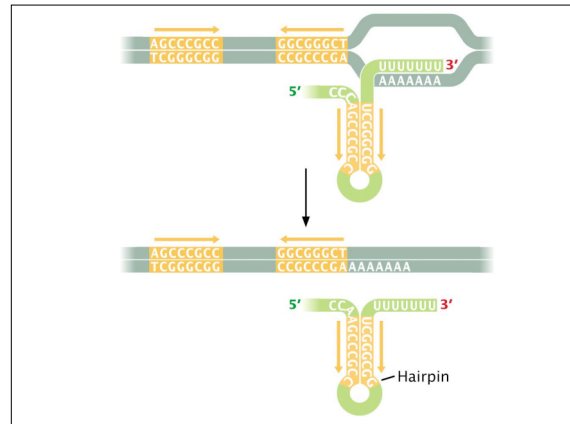
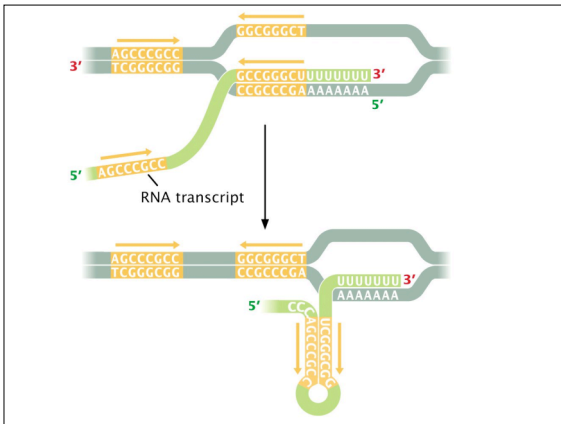
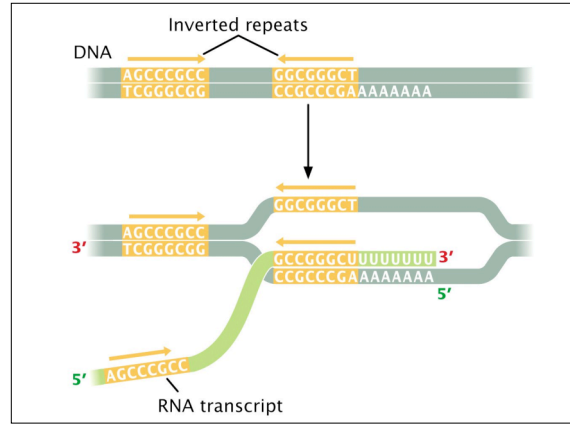
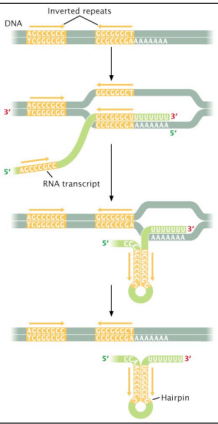


Consensus sequences

	-35 region	-10 region	Transcription start site
Promoter	16-18 base pairs	6-7 base pairs	
<i>trp</i>	TTGACA	TTAACT	
tRNA ^{Tyr}	TTTACA	TATGAT	
<i>lac</i>	TTTACA	TATGTT	
<i>recA</i>	TTGATA	TATAAT	
<i>rrnD1</i>	TTGTGC	TATAAT	
<i>araB,A,D</i>	CTGACG	TACTGT	
Consensus sequences	TTGACA	TATAAT	



Termination-
rho
independent



Rho
dependent
termination

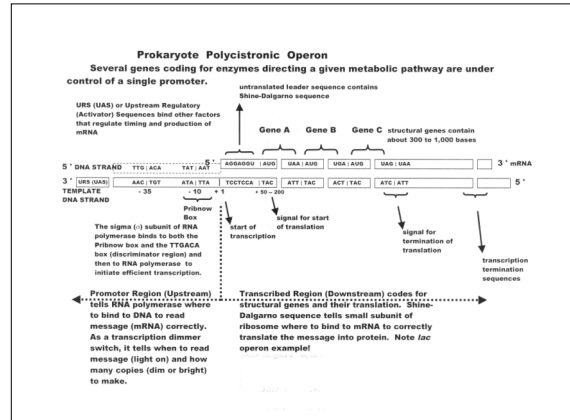
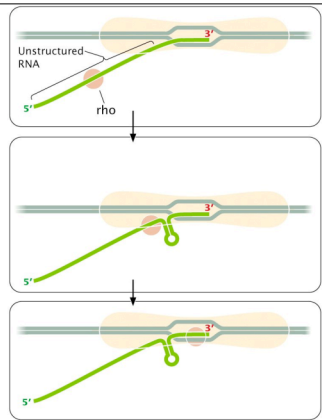
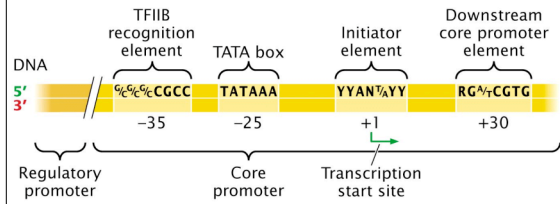


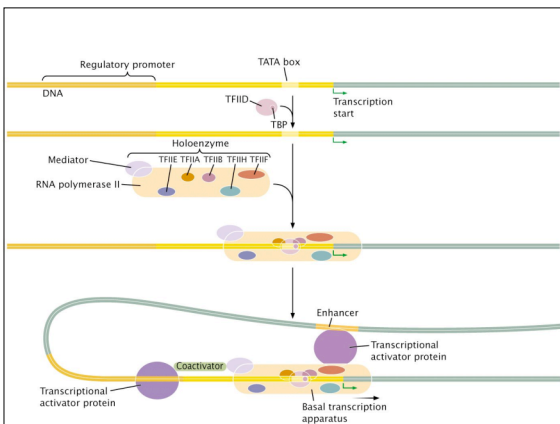
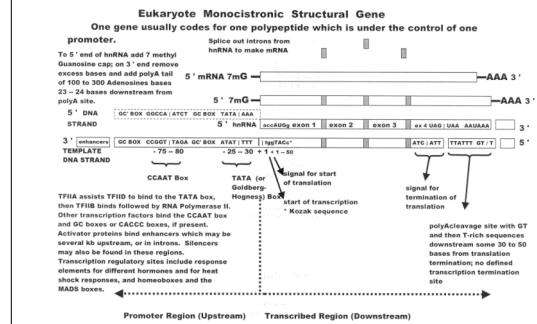
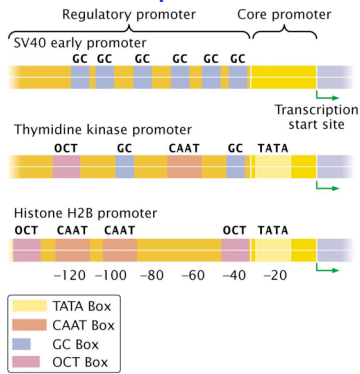
Table 13.3 Eukaryotic RNA polymerases

Type	Transcribes
RNA polymerase I	Large rRNAs
RNA polymerase II	Pre-mRNA, some snRNAs, snoRNAs
RNA polymerase III	tRNAs, small rRNA, snRNAs

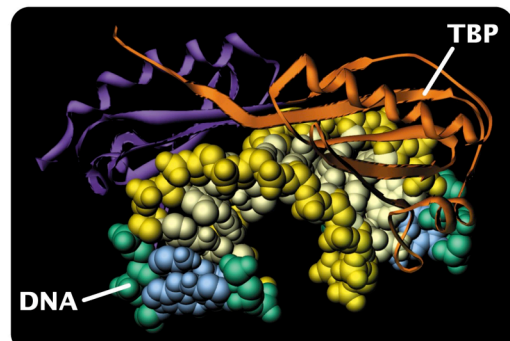
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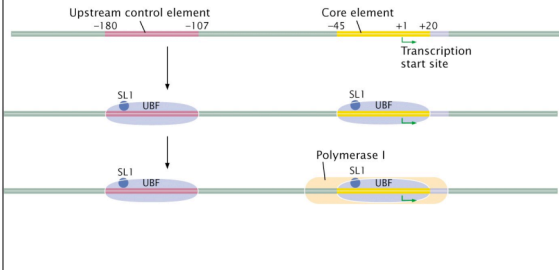
Consensus sequences



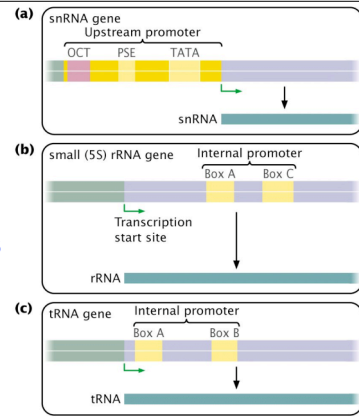
RNA Polymerase II



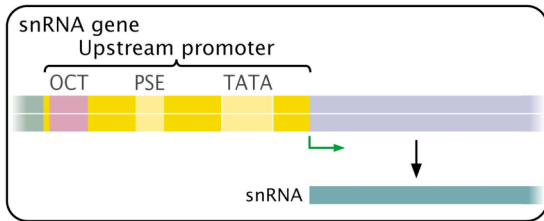
RNA polymerase I promoters



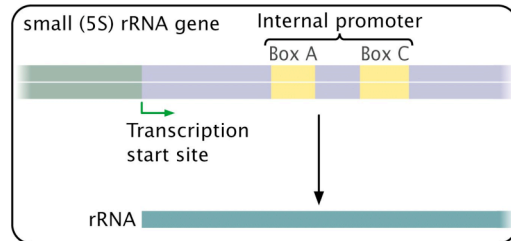
RNA Polymerase III promoters



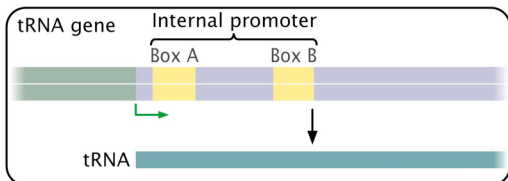
RNA pol III



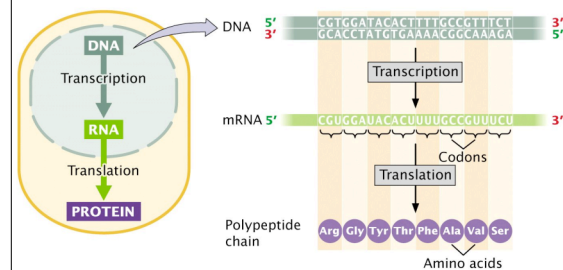
RNA pol III



RNA pol III



Colinearity - Number and kind of nucleotides corresponds to the number & kind of amino acids



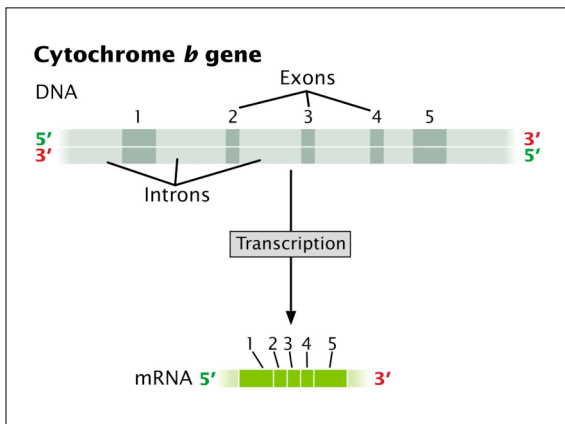
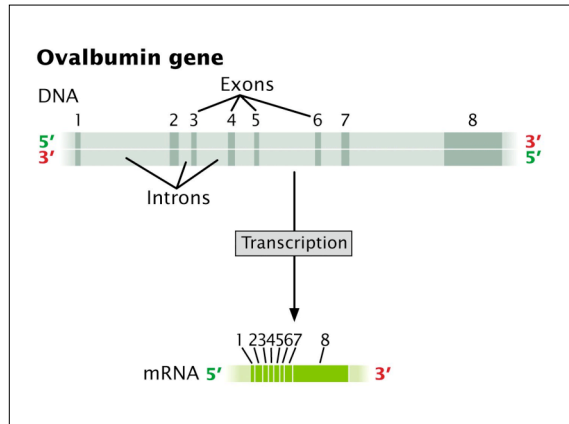
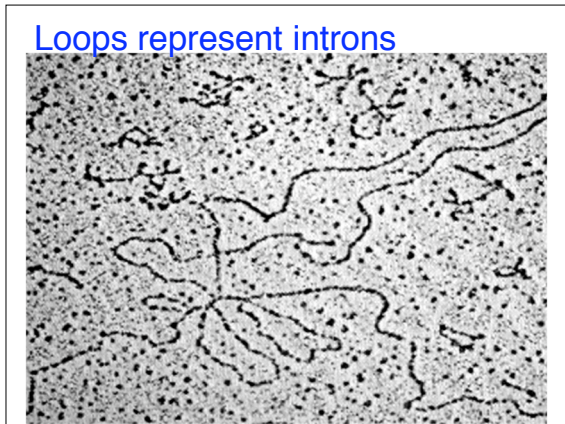
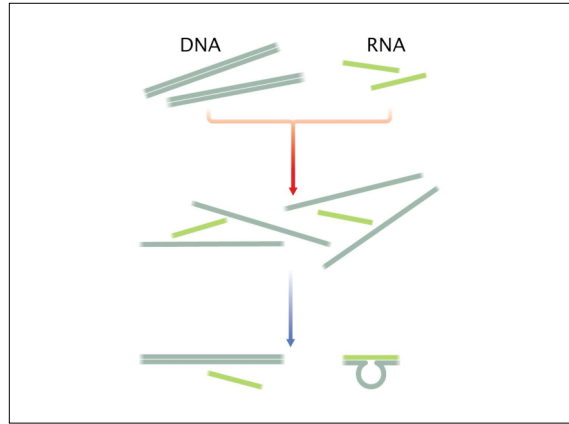
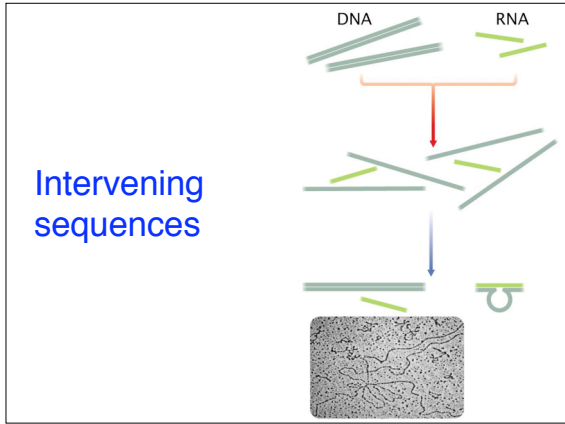


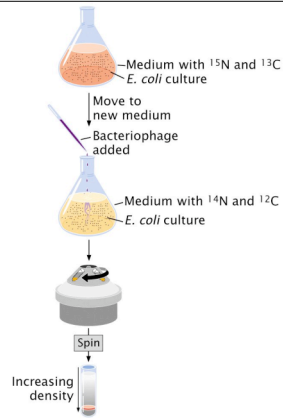
Table 14.1 Major types of introns

Type of Intron	Location	Type of Splicing
Group I	Some rRNA genes	Self-splicing
Group II	Protein-encoding genes in mitochondria and chloroplasts	Self-splicing
Nuclear pre-mRNA	Protein-encoding genes in the nucleus	Spliceosomal
tRNA	tRNA genes	Enzymatic

Note: There are also several types of minor introns, including group III introns, twintrons, and archaean introns.

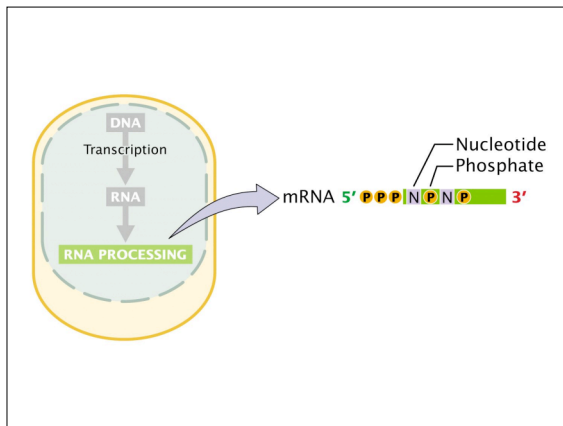
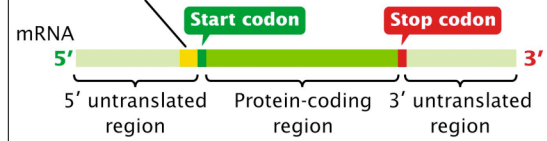
Do ribosomes carry genetic information?

Only old ribosomes were found in culture

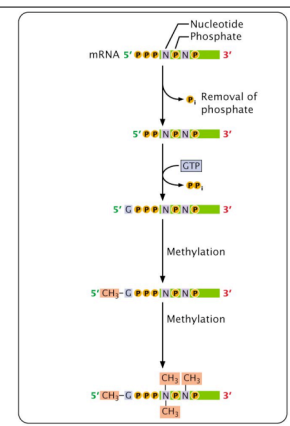


RNA structure

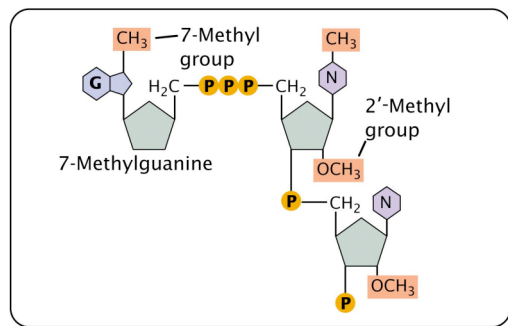
Shine-Dalgarno sequence in prokaryotes only



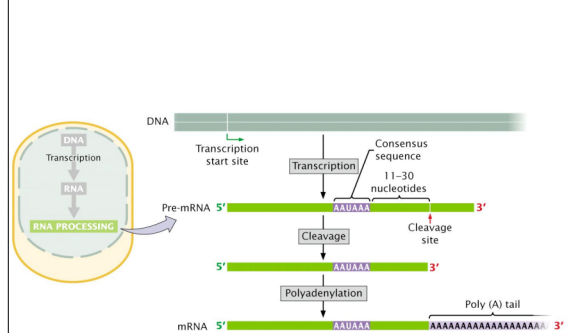
5' cap

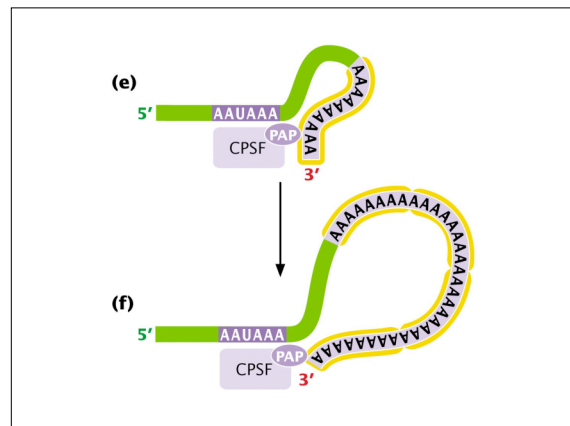
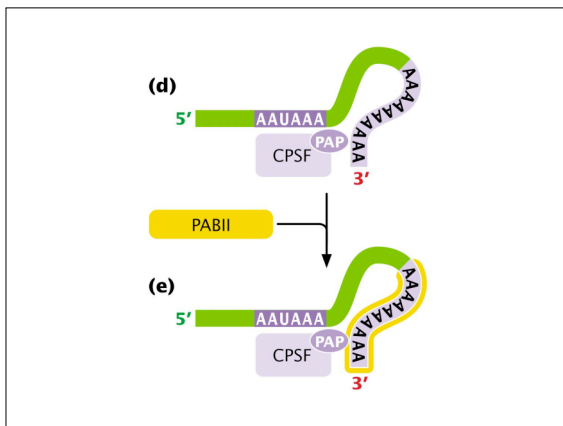
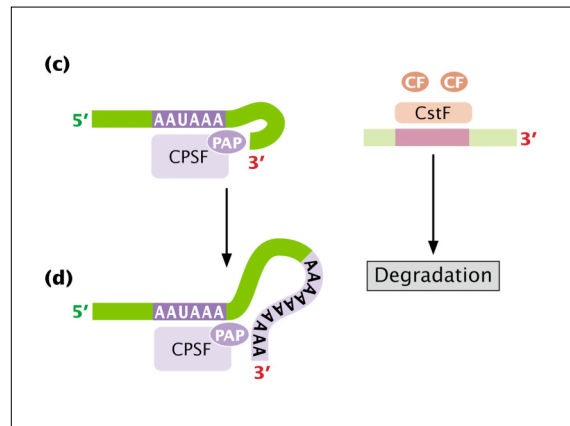
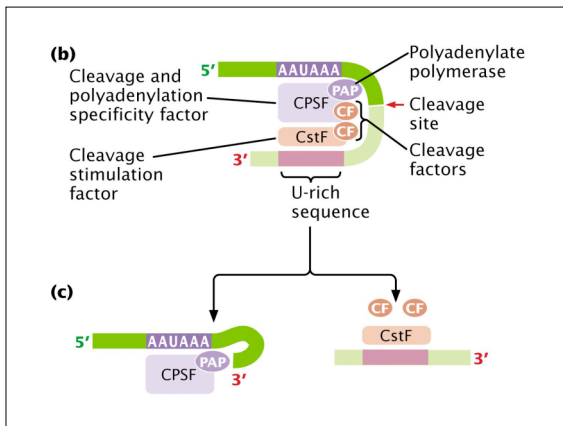
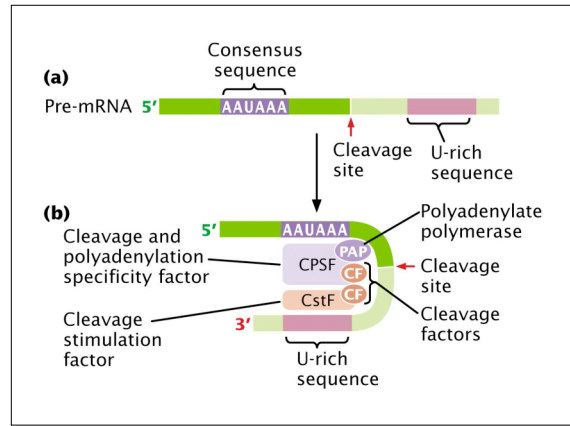
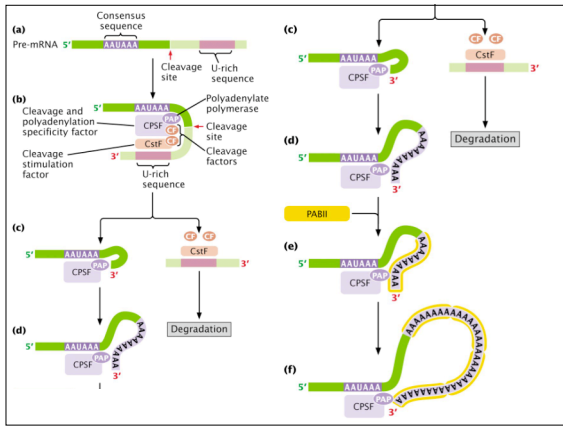


7 mG cap

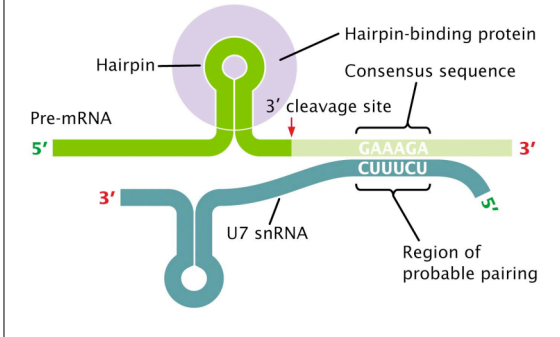


Poly A cleavage

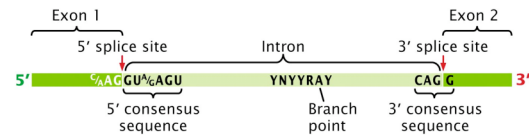




Non poly A splicing



Intron structure



Intron splicing

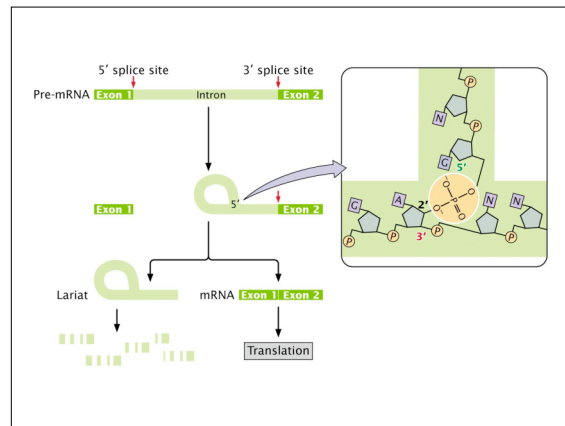
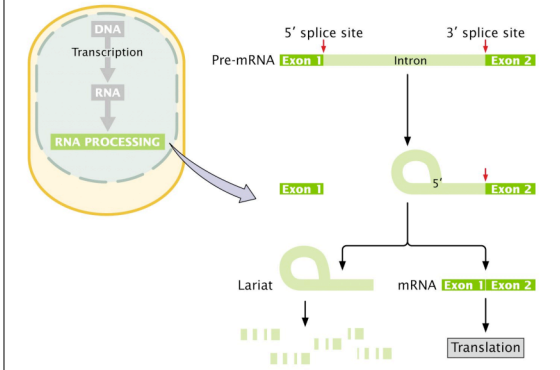
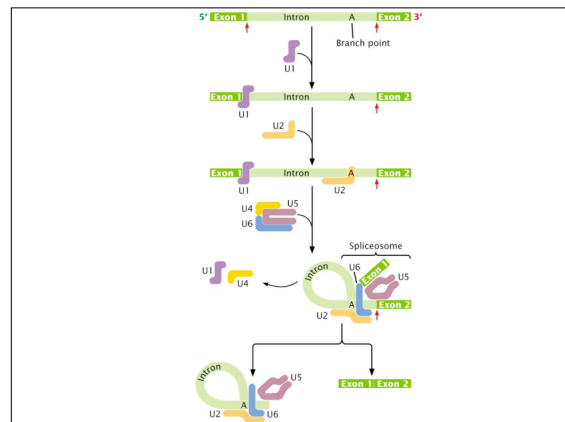
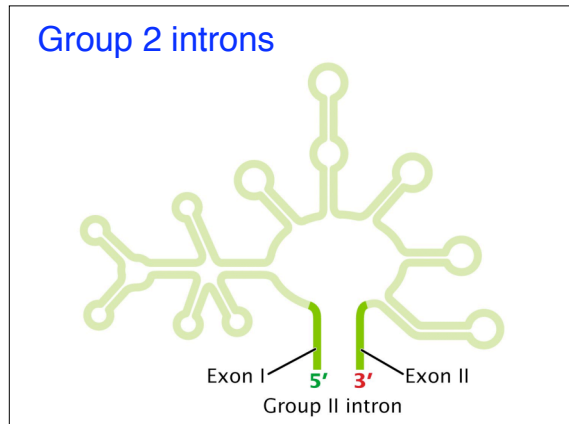
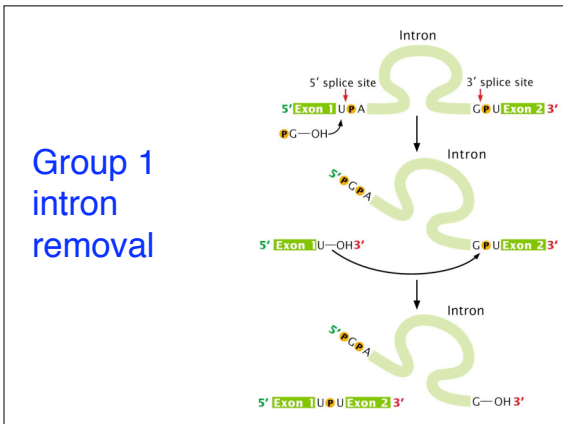
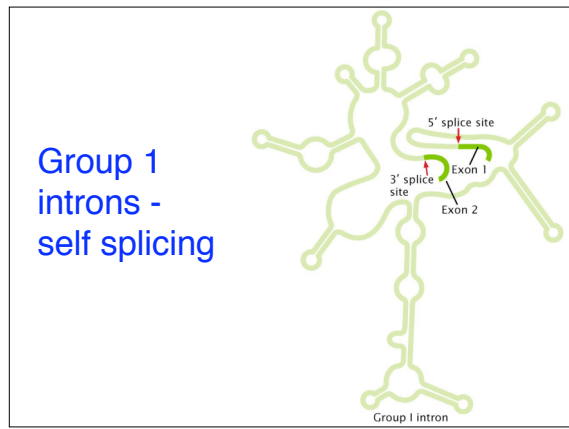
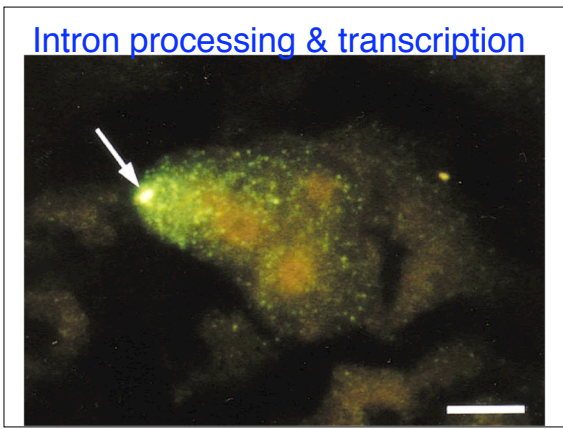
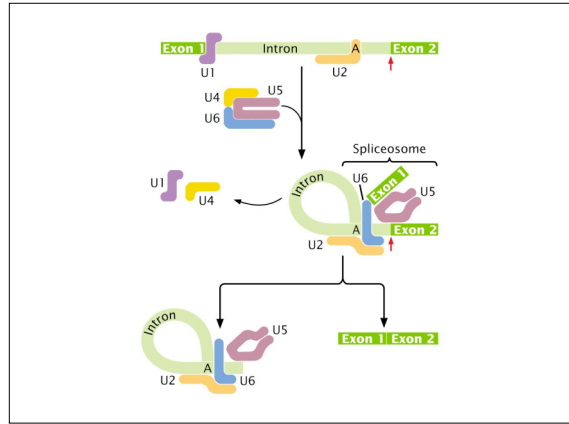
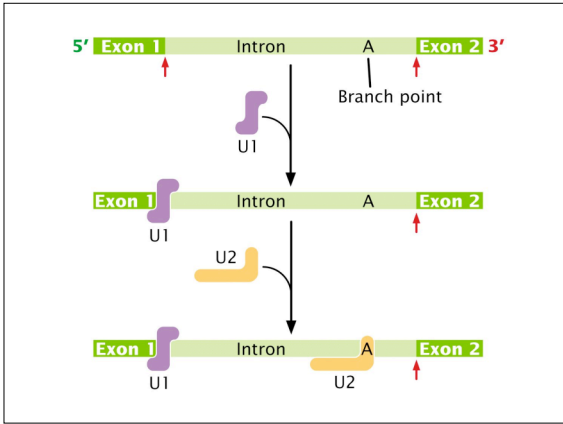


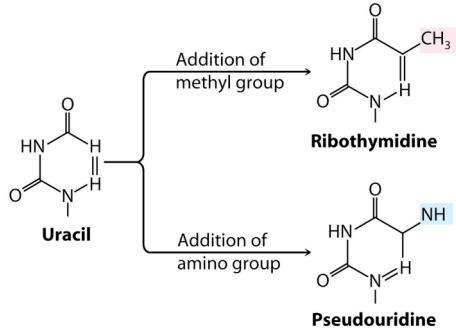
Table 14.2 RNA-RNA interactions in pre-mRNA splicing

Interaction	Function
U1 with 5' splice site	U1 attaches to 5' end of intron; commits intron to splicing; no direct role in splicing
U2 with branch point	Positions 5' end of intron near branch point for lariat formation
U2 with U6	Holds 5' end of intron near branch point
U6 with 5' splice site	Positions 5' end of intron near branch point
U5 with 3' end of first exon	Anchors first exon to spliceosome subsequent to cleavage; juxtaposes two ends of exon for splicing
U5 with 3' end of one exon and 5' end of the other	Juxtaposes two ends of exon for splicing
U4 with U6	Delivers U6 to intron; no direct role in splicing

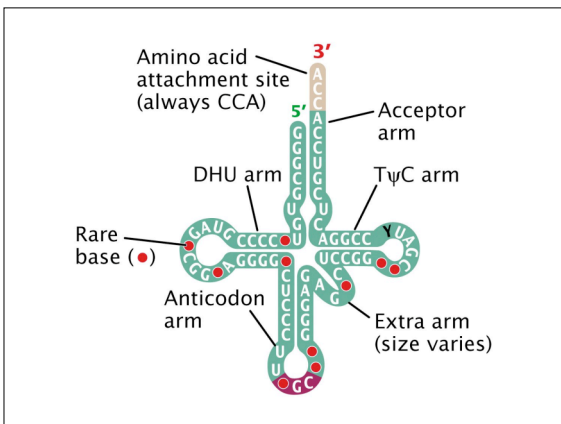
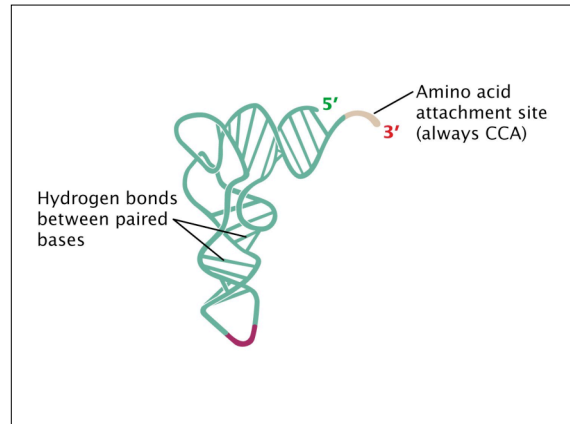
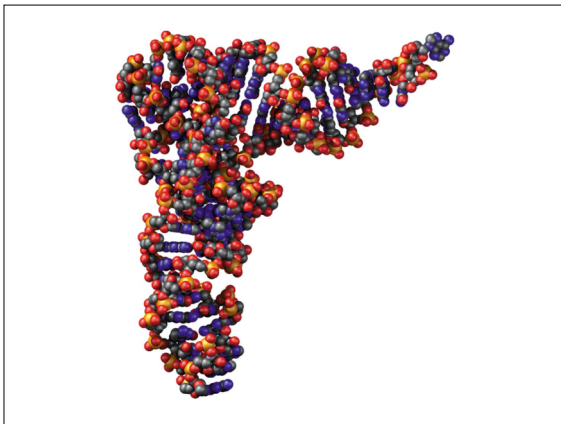
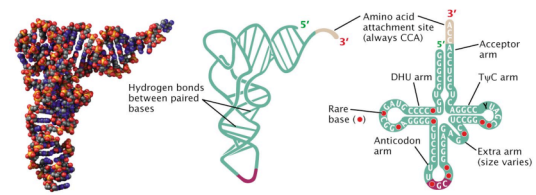




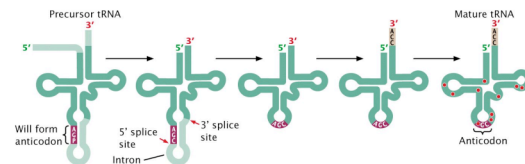
Modified bases in tRNA



tRNA structure



tRNA processing



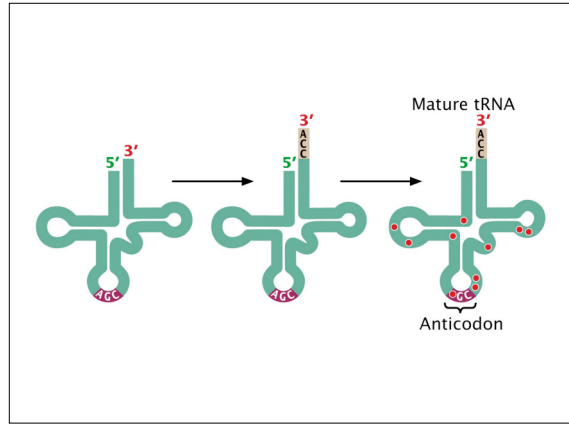
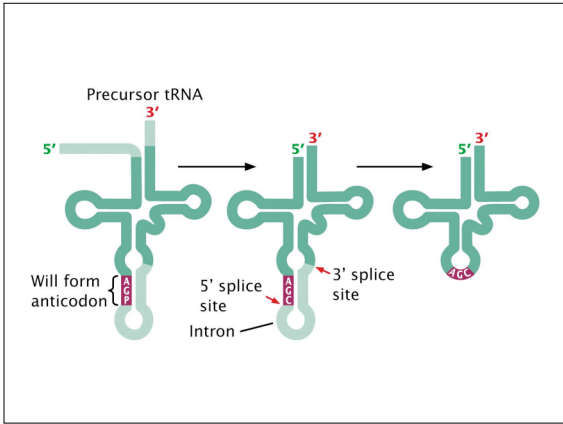


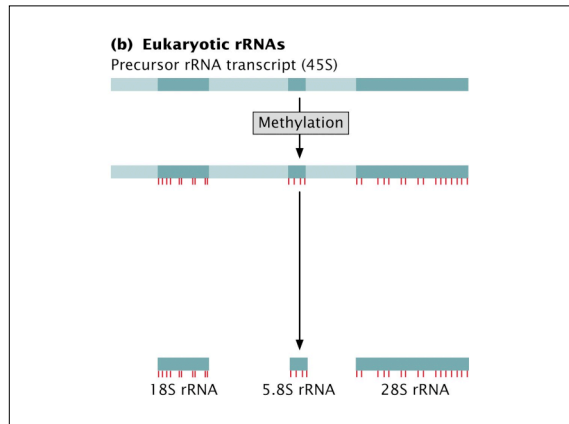
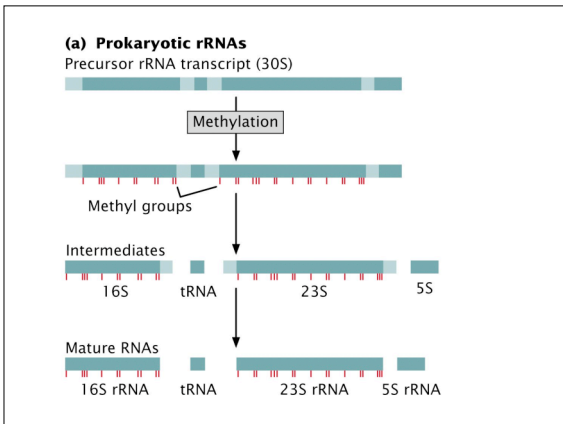
Table 14.3 Composition of ribosomes in bacterial and eukaryotic cells

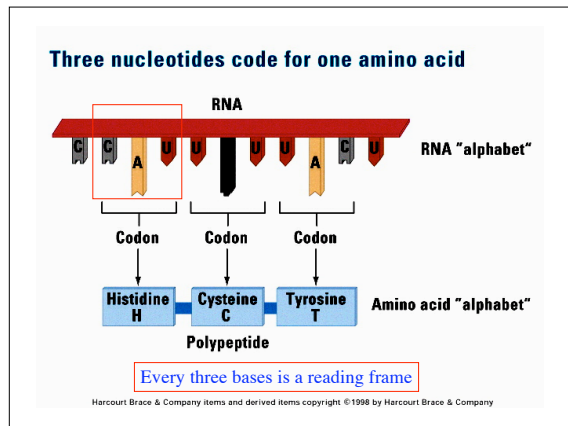
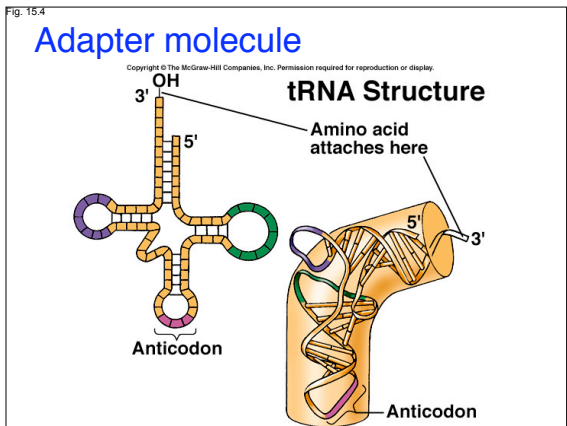
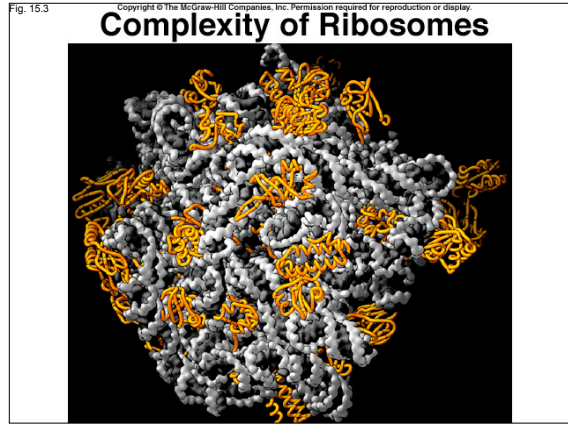
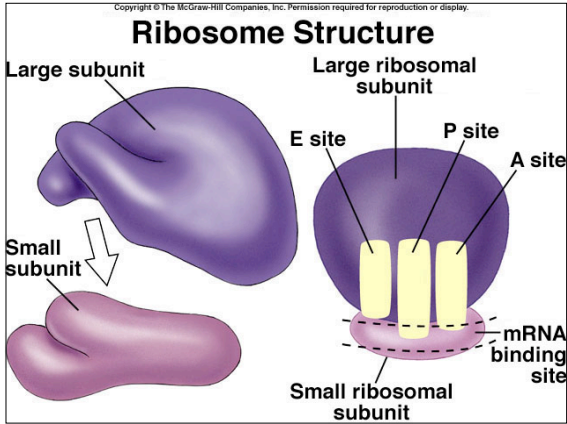
Cell Type	Ribosome Size	Subunit	rRNA Component	Proteins
Bacterial	70S	Large (50S)	23S (2900 nucleotides) 5S (120 nucleotides)	31
		Small (30S)	16S (1500 nucleotides)	21
Eukaryotic	80S	Large (60S)	28S (4700 nucleotides) 5.8S (160 nucleotides)	49
		Small (40S)	5S (120 nucleotides)	33
			18S (1900 nucleotides)	

Note: The letter S stands for Svedberg unit.

Table 14.4 Number of rRNA genes in different organisms

Species	Copies of rRNA Genes or Genome
<i>Escherichia coli</i>	1
Yeast	100–200
Human	280
Frog	450





12.1 Signals that Start and Stop Transcription and Translation

	TRANSCRIPTION	TRANSLATION
Initiation	Promoter sequence in mRNA	AUG start codon
Termination	Terminator sequence in DNA	UAA, UAG, or UGA stop codon in mRNA

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Reading-Frame Alterations

Delete 1 base
 WHYDIDTHEREDBATEATTHEFATRAT?
Hypothesis A : Delete T unpunctuated
 WHY DID HER EDB ATE ATT HEF ATR AT?
 — (Nonsense) —
Hypothesis B : Delete T punctuated
 WHY DID HE O EDO ATO ATO HE O ATO AT?
 — (Nonsense) —

Delete 3 bases
Hypothesis A : unpunctuated
 WHYDIDTHEREDBATEATTHEFATRAT?
 Delete T, R, and A
 WHY DID HEE DBT EAT THE FAT RAT?
 — (Sense) —
Hypothesis B : punctuated
 WHYDIDOTHEOREDOBATOEOATOTHEOFATORAT?
 Delete T, R, and A
 WHY DID HEO DOB OEA OTH OFA ORA?
 — (Nonsense) —

Breaking the genetic code

EXPERIMENT

Question: What are the amino acids specified by the triplet codons UUU, AAA, and CCC?

METHOD

RESULTS

Phe Phe Phe
 Lys Lys Lys
 Pro Pro Pro

Conclusion: UUU is an mRNA codon for phenylalanine.
 AAA is an mRNA codon for lysine.
 CCC is an mRNA codon for proline.

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Genetic code

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

The genetic code is redundant
 2 bases per codon $4 \times 4 = 16$
 3 bases per codon $4 \times 4 \times 4 = 64$

Four different codons code for the same amino acid. Not difference is in last base.

Hartwell et al., & Cougle, From Cell to Organism, Copyright © 2005 by Sinauer Associates, Inc. & Company.

Mixed copolymers decipher the code

- ✓ Synthesize RNA
 - ⇒ Add A and C at a ratio of 1:5
 - ⇒ 1/6 chance for A
 - ⇒ 5/6 chance for C
 - ⇒ AAA = $(1/6)^3$ or 0.4% chance
 - ⇒ AAC = $(1/6)^2 (5/6)$ or 2.3%
- ✓ Determine the amino acids produced compare to the expected base upon the reading frame

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The Genetic Code

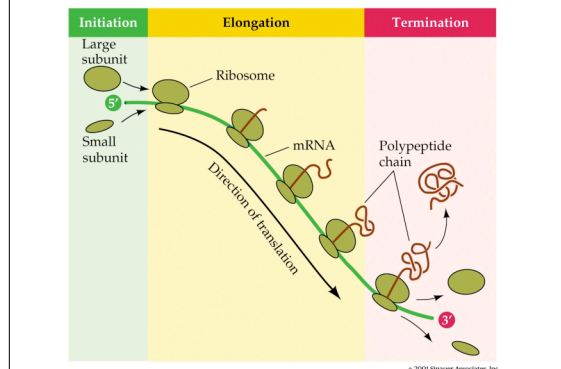
First Letter	Second Letter			Third Letter
	U	C	A	G
U	UUU Phenylalanine UUC Phenylalanine UUA Leucine UUG Leucine	UCU Serine UCC Serine UCA Serine UCG Serine	UAU Tyrosine UAC Tyrosine UAA Stop UAG Stop	UGU Cysteine UGC Cysteine UGA Stop UGG Tryptophan
C	CUU Leucine CUC Leucine CUA Leucine CUG Leucine	CCU Proline CCC Proline CCA Proline CCG Proline	CAU Histidine CAC Histidine CAA Glutamine CAG Glutamine	CGU Arginine CGC Arginine CGA Arginine CGG Arginine
A	AUU Isoleucine AUC Isoleucine AUA Methionine; Start AUG Start	ACU Threonine ACC Threonine ACA Threonine ACG Threonine	AAU Asparagine AAC Asparagine AAA Lysine AAG Lysine	AGU Serine AGC Serine AGA Arginine AGG Arginine
G	GUU Valine GUC Valine GUA Valine GUG Valine	GCU Alanine GCC Alanine GCA Alanine GCG Alanine	GAU Aspartate GAC Aspartate GAA Glutamate GAG Glutamate	GGU Glycine GGC Glycine GGA Glycine GGG Glycine

Exceptions to the universal code

TABLE 12-5 Exceptions to the Universal Code

Triplet	Normal Code Word	Altered Code Word	Source
UGA	termination	trp	Human and yeast mitochondria <i>Mycoplasma</i>
CUA	leu	thr	Yeast mitochondria
AUA	ile	met	Human mitochondria
AGA	arg	termination	Human mitochondria
UAA	termination	gln	<i>Paramecium</i> <i>Tetrahymena</i> <i>Stylonychia</i>
UAG	termination	gln	<i>Paramecium</i>

Translation summary



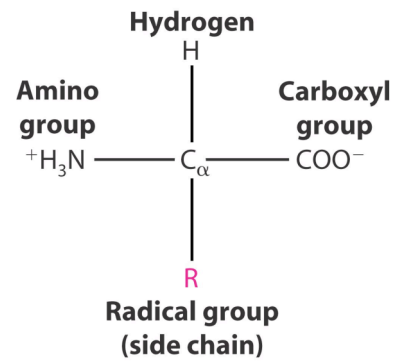
Luciferin + ATP (Luciferase)



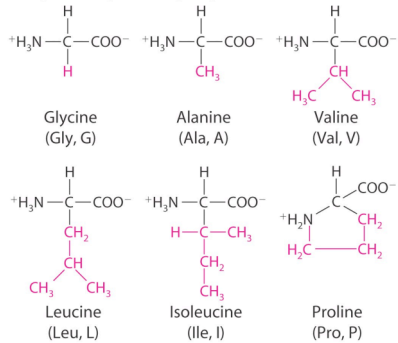
Fibroin (spider webs)



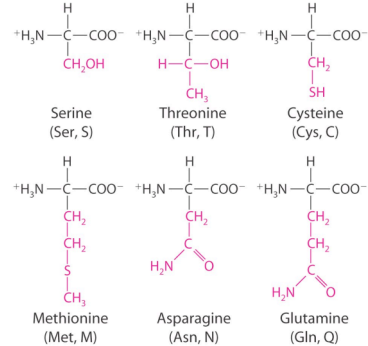
Caster beans (Ricin)



Nonpolar, aliphatic R groups



Polar, uncharged R groups



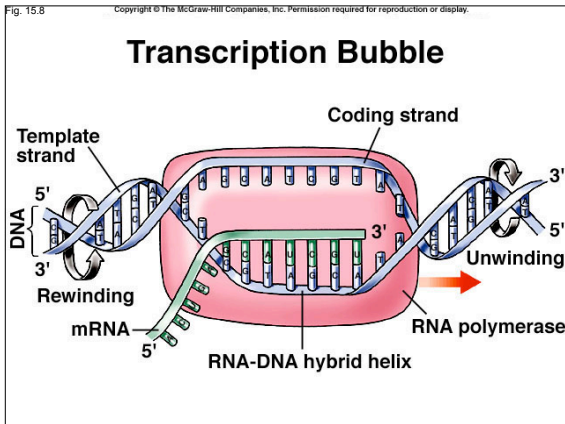
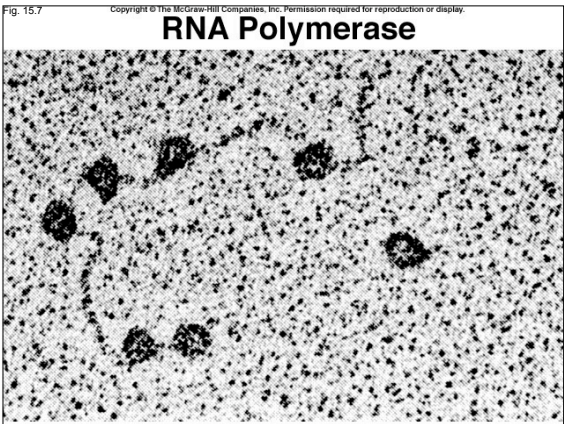
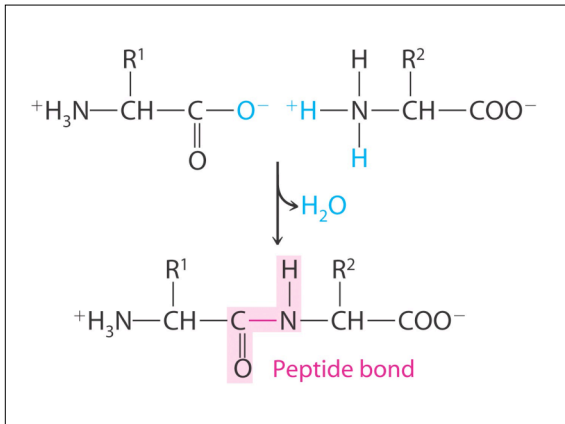
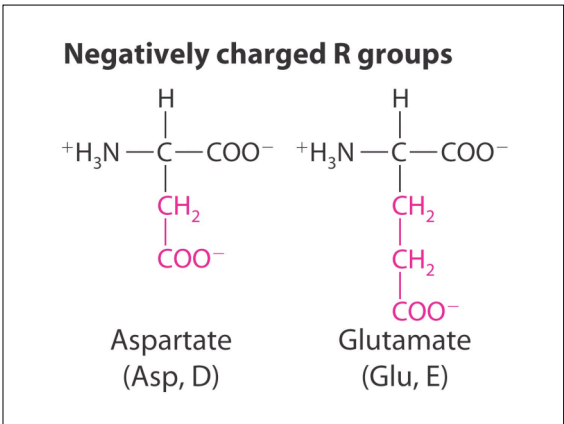
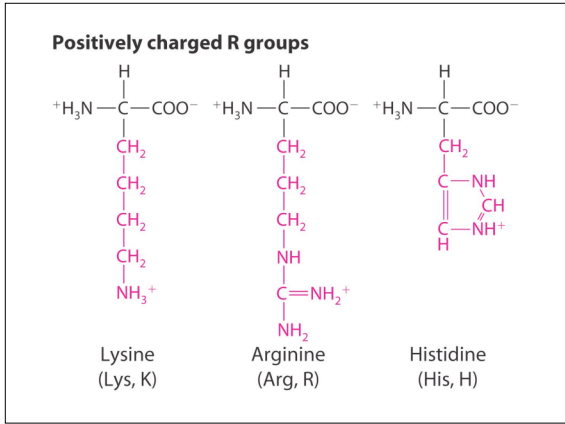
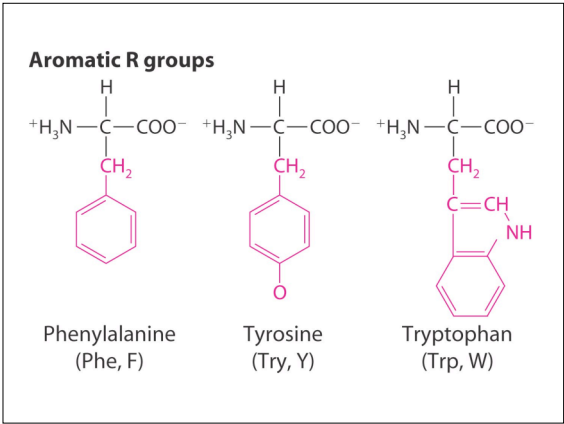


Fig. 15.10

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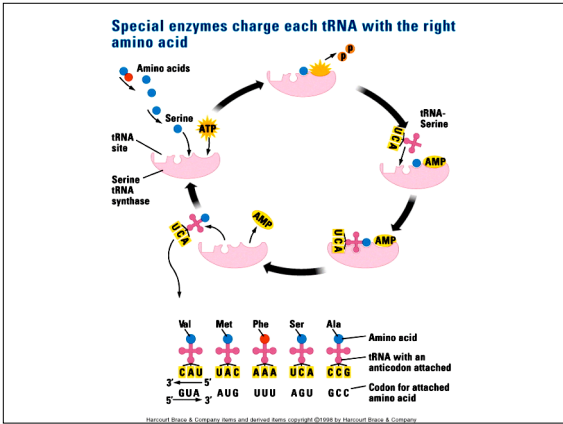
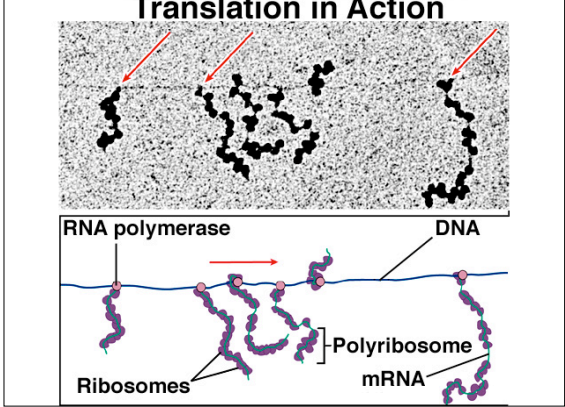


Fig. 15.11

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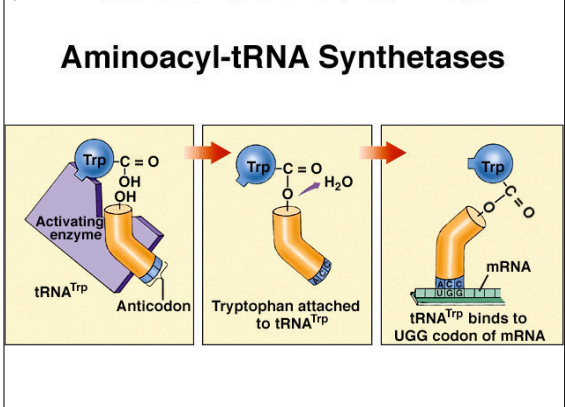
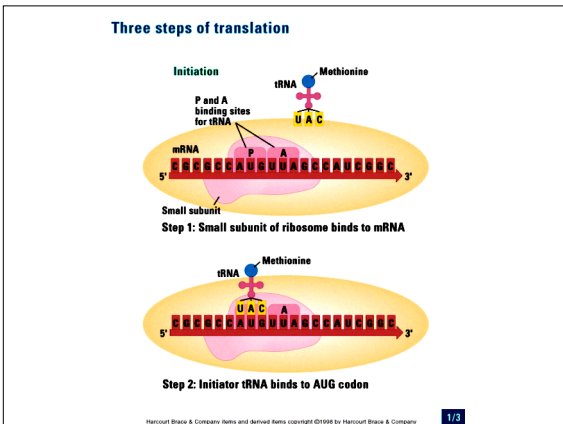
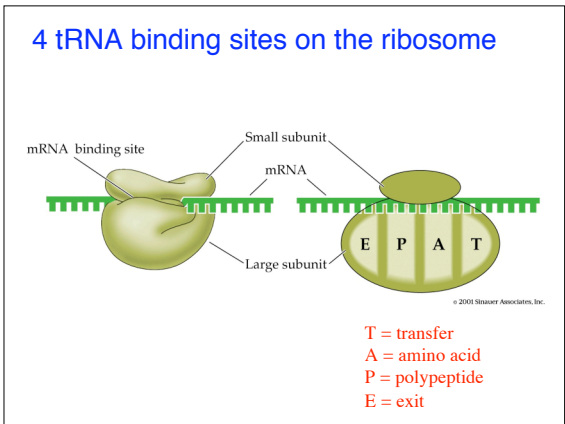
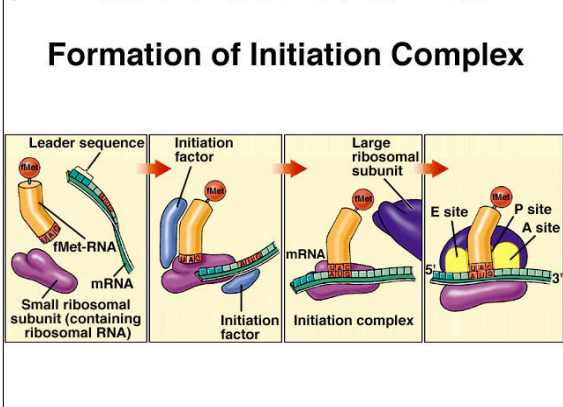
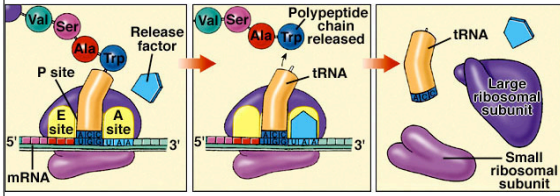


Fig. 15.12

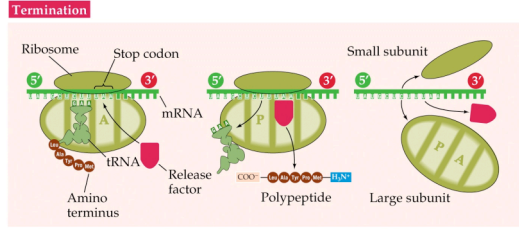
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Protein Synthesis Termination



Termination



12.2 Antibiotics that Inhibit Bacterial Protein Synthesis

ANTIBIOTIC	STEP INHIBITED
Chloromycetin	Formation of peptide bonds
Erythromycin	Translocation of mRNA along ribosome
Neomycin	Interactions between tRNA and mRNA
Streptomycin	Initiation of translation
Tetracycline	Binding of tRNA to ribosome

Wobble

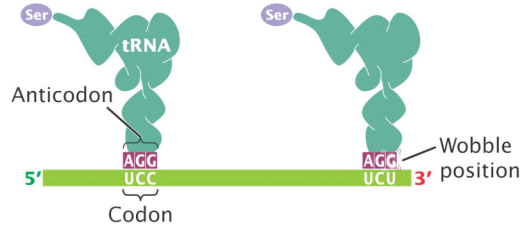


Table 15.2 The wobble rules, indicating which bases in the third position (3' end) of the mRNA codon can pair with bases at the first (5' end) of the anticodon of the tRNA.

First Position of Anticodon	Third Position of Codon	Pairing
C	G	Anticodon: 3'-X-Y-C-5' Codon: 5'-Y-X-G-3'
G	U or C	Anticodon: 3'-X-Y-G-5' Codon: 5'-Y-X-U-3' or 5'-Y-X-C-3'
A	U	Anticodon: 3'-X-Y-A-5' Codon: 5'-Y-X-U-3'
U	A or G	Anticodon: 3'-X-Y-U-5' Codon: 5'-Y-X-A-3' or 5'-Y-X-G-3'
I (inosine)	A, U, or C	Anticodon: 3'-X-Y-I-5' Codon: 5'-Y-X-A-3', 5'-Y-X-U-3', or 5'-Y-X-C-3'

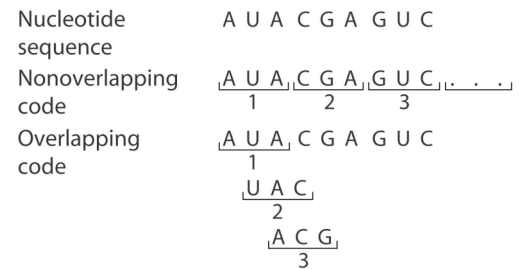
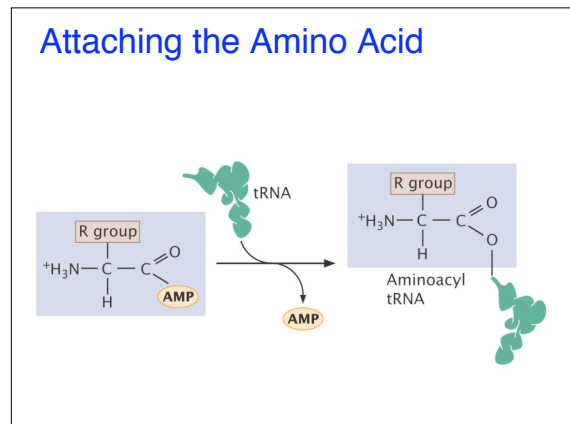
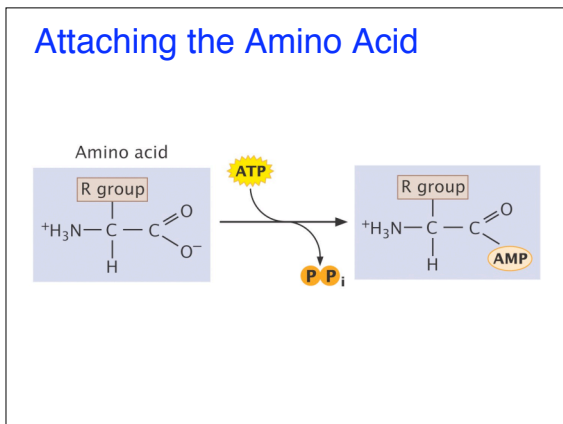
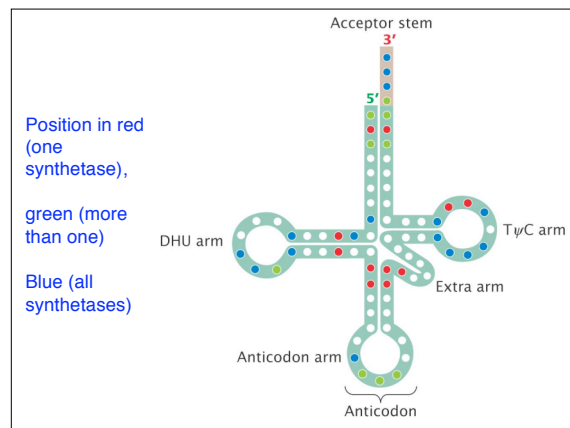
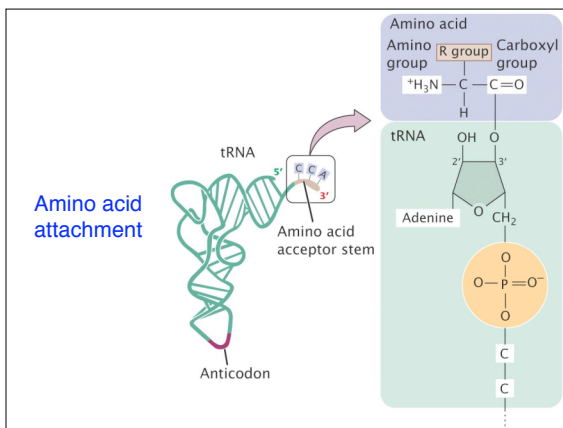
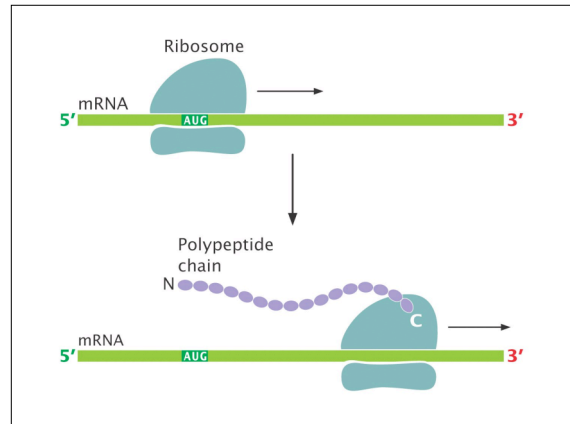
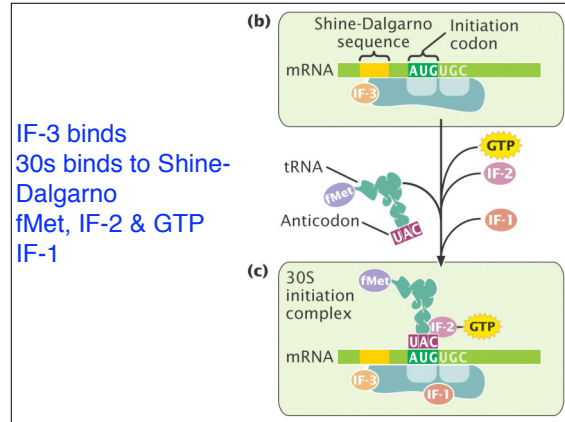
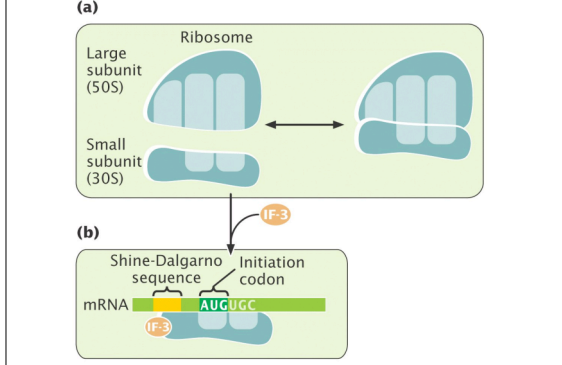


Table 15.3 Some exceptions to the universal genetic code

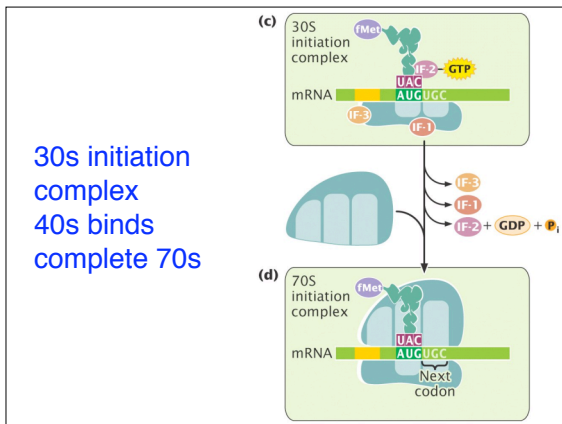
Genome	Codon	Universal Code	Altered Code
Bacterial DNA <i>Mycoplasma capricolum</i>	UGA	Stop	Trp
Mitochondrial DNA			
Human	UGA	Stop	Trp
Human	AUA	Ile	Met
Human	AGA, AGG	Arg	Stop
Yeast	UGA	Stop	Trp
Trypanosomes	UGA	Stop	Trp
Plants	CGG	Arg	Trp
Nuclear DNA			
<i>Tetrahymena</i>	UAA	Stop	Gln
<i>Paramecium</i>	UAG	Stop	Gln



Dynamic equilibrium



IF-3 binds
30s binds to Shine-Dalgarno
fMet, IF-2 & GTP
IF-1



30s initiation complex
40s binds
complete 70s

Shine Dalgarno consensus sequences

E. coli trpA gene 5' **AGCACGAGGGGAAU**CUG**AUGGAACGCUAC** 3'

E. coli araB gene **UUUGGAUGGAGUGAA**ACG**AUGGCGAUUGCA**

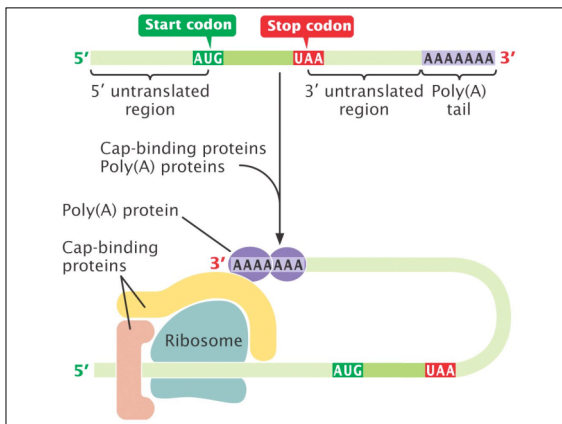
E. coli lacI gene **CAAUUCAGGUGGUG**AAU**CUGAAACCAGUA**

λ phage *CRO* gene **AUGUACUAAGGAGGU**UGU**AUGGAACAAGCG**

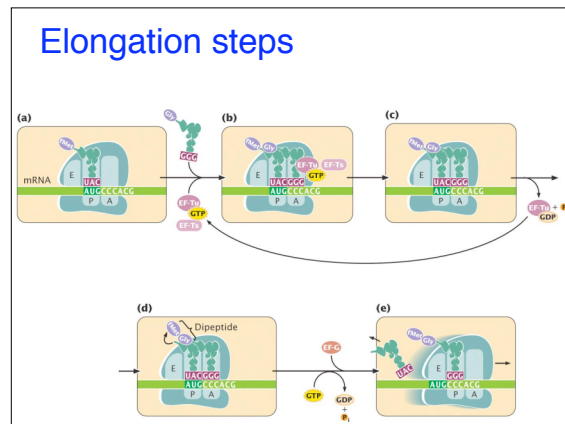
Shine-Dalgarno sequence Initiation codon; pairs with fMet-tRNA^{fMet}

mRNA 5' **AUGUACUAAGGAGGUUGU****AUGGAACAAGCG** 3'

16S rRNA 3' **AUCCUCCA** 5'



Elongation steps



Termination

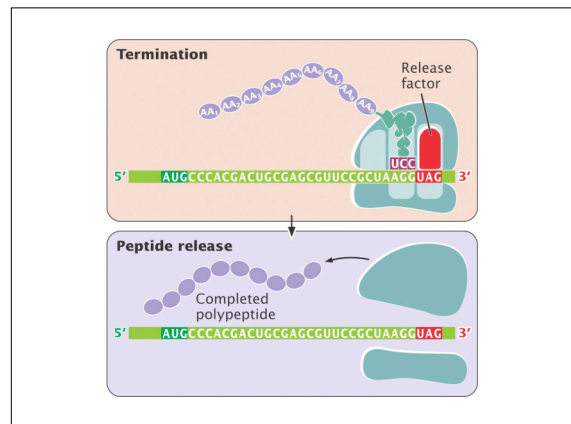
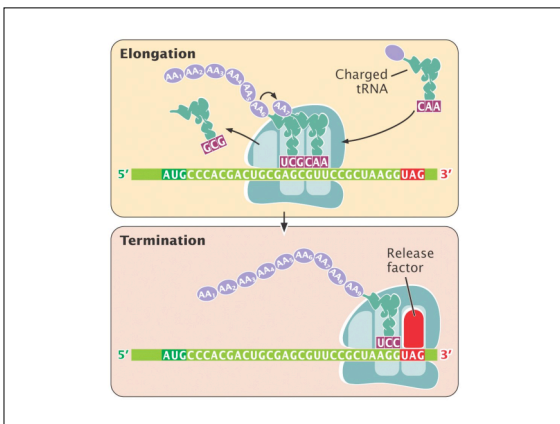
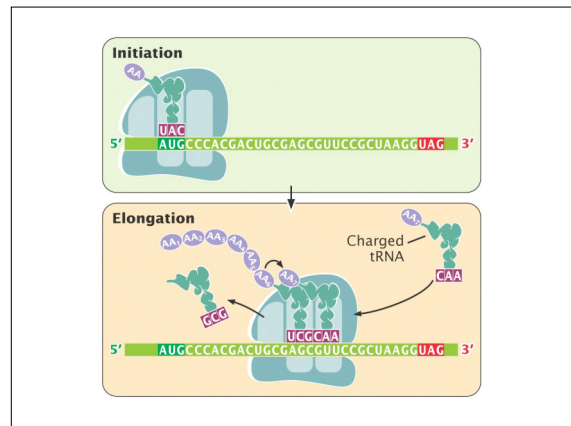
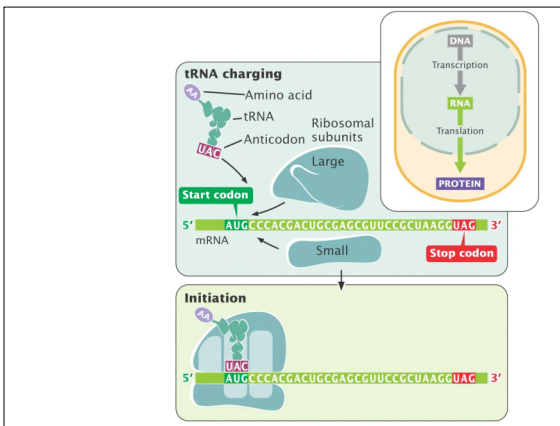
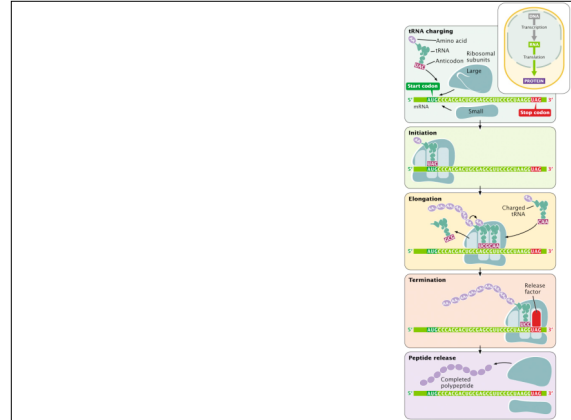
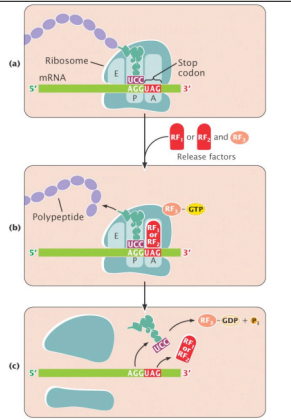
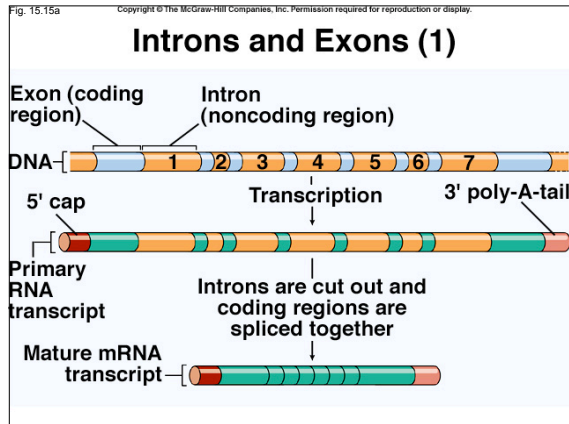
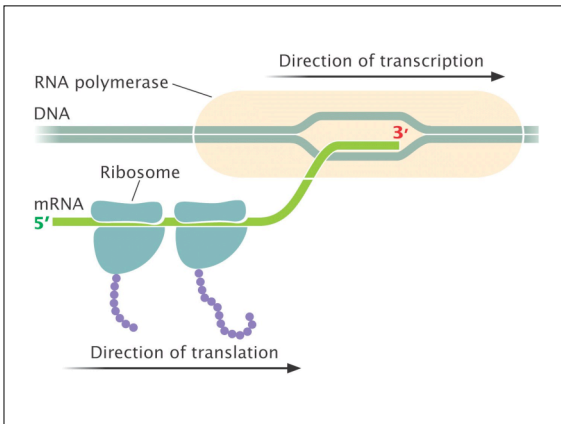
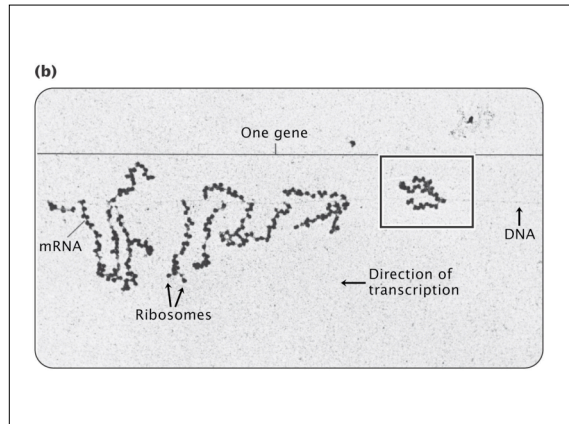
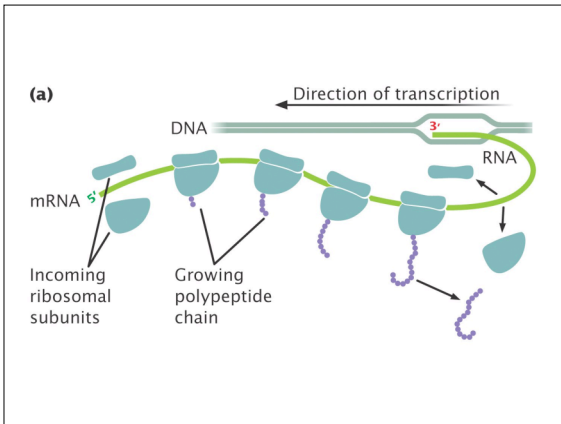
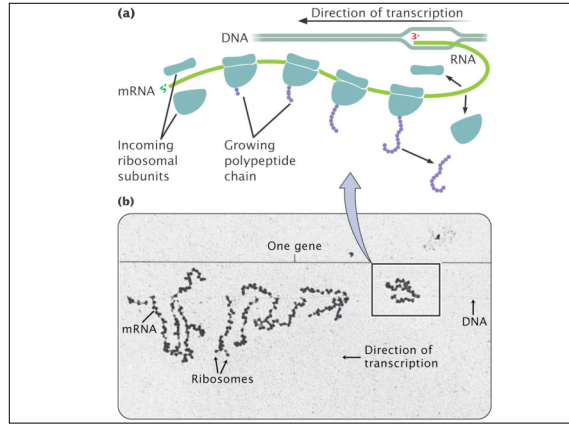
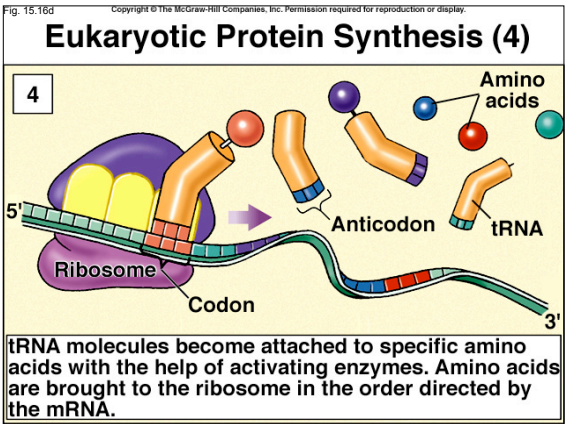
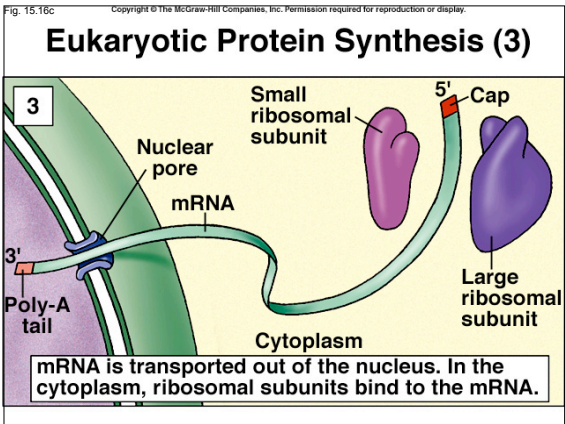
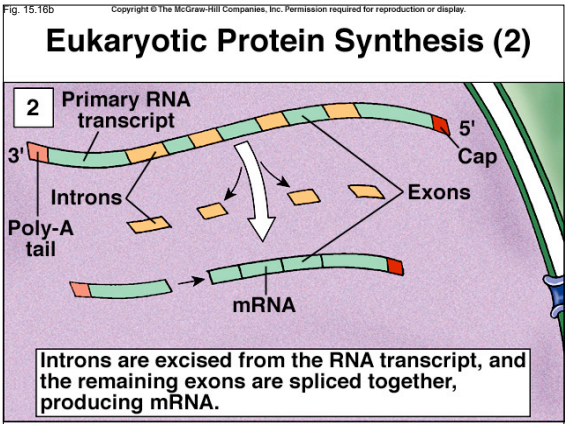
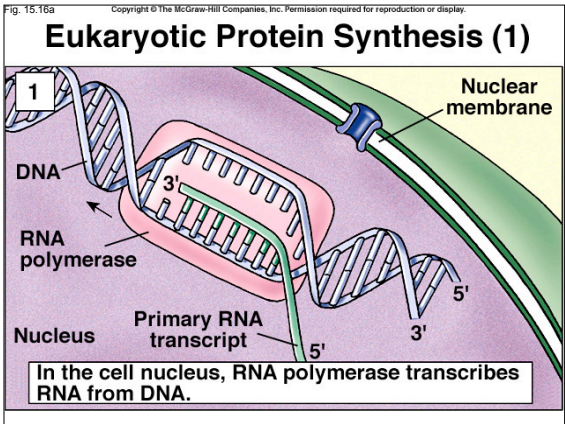
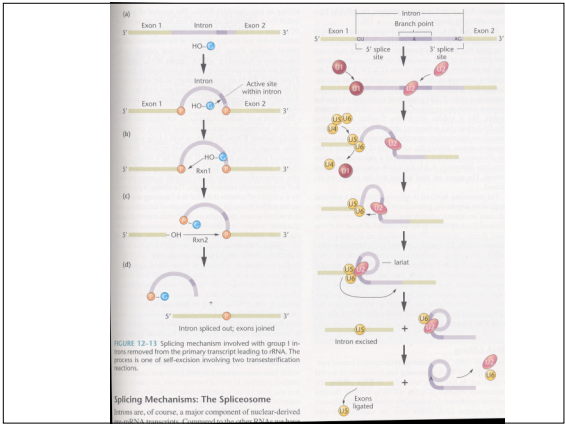
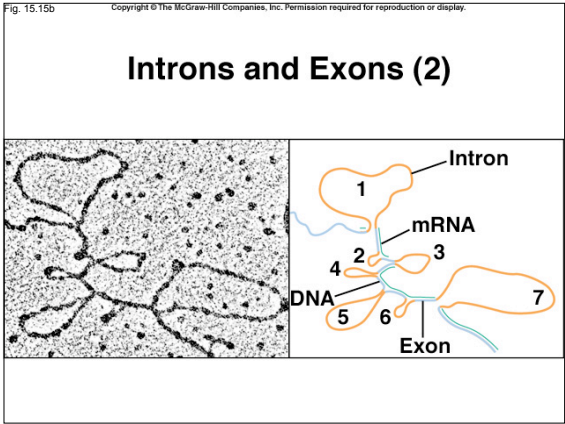
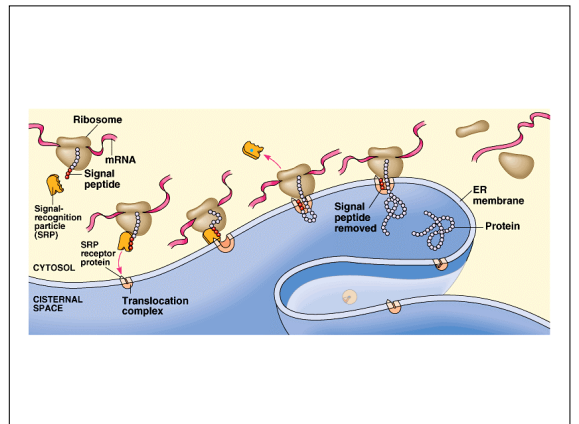
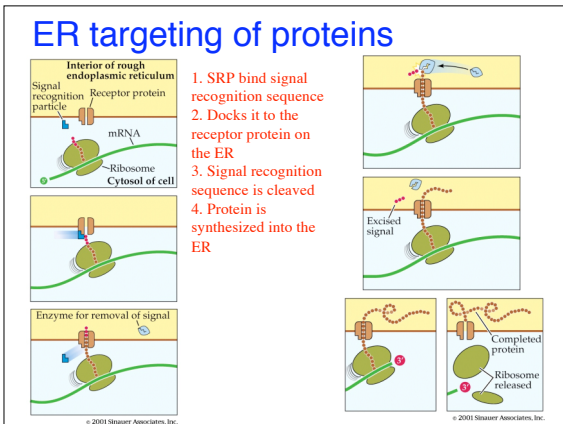
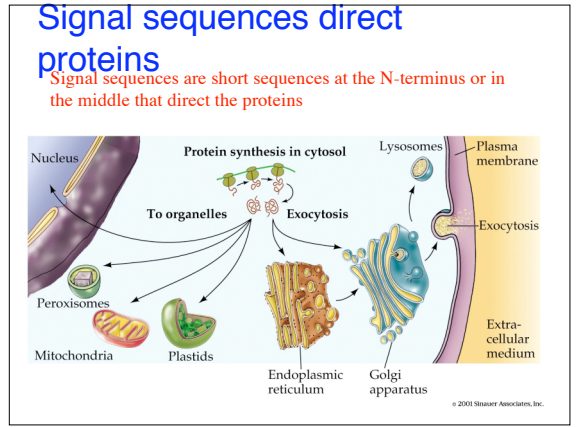
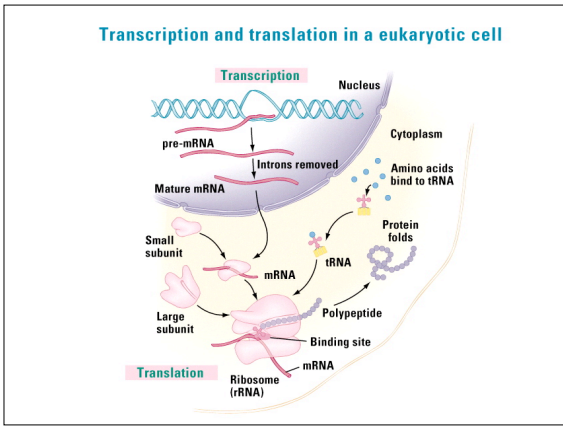
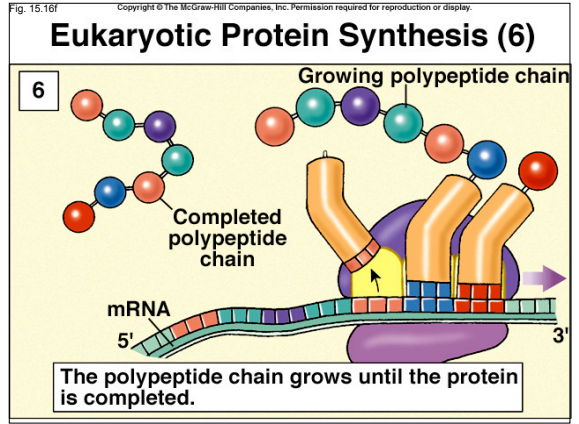
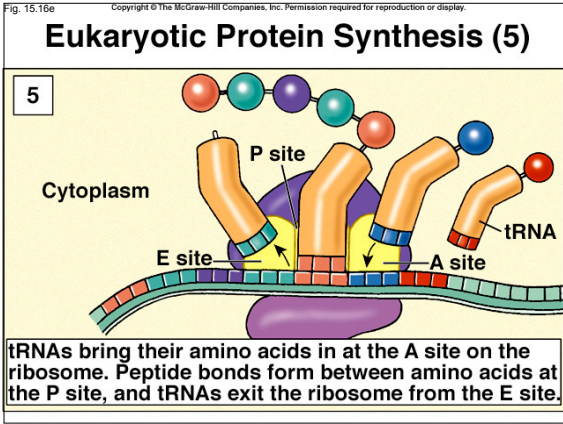


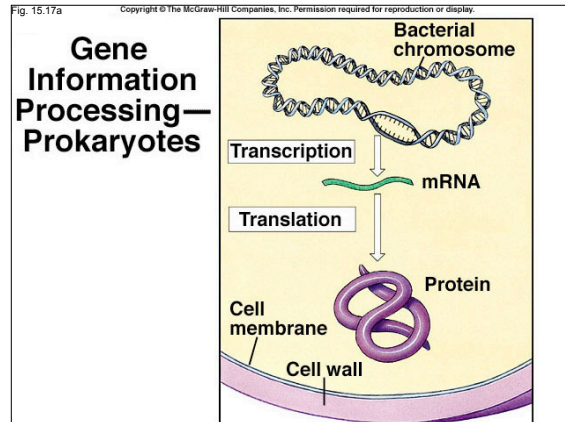
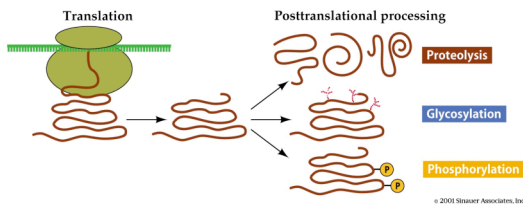
Table 15.4 Components required for protein synthesis in bacterial cells		
Stage	Component	Function
Binding of amino acid to tRNA	Amino acids	Building blocks of proteins
	tRNAs	Deliver amino acids to ribosomes
	aminoacyl-tRNA synthetase	Attaches amino acids to tRNAs
	ATP	Provides energy for binding amino acid to tRNA
Initiation	mRNA	Carries coding instructions
	fMet-tRNA ^{fMet}	Provides first amino acid in peptide
	30S ribosomal subunit	Attaches to mRNA
	50S ribosomal subunit	Stabilizes tRNAs and amino acids
	Initiation factor 1	Enhances dissociation of large and small subunits of ribosome
Elongation	Initiation factor 2	Binds GTP; delivers fMet-tRNA ^{fMet} to initiation codon
	Initiation factor 3	Binds to 30S subunit and prevents association with 50S subunit
	70S initiation complex	Functional ribosome with A, P, and E sites and peptidyl transferase activity where protein synthesis takes place
Termination	Charged tRNAs	Bring amino acids to ribosome and help assemble them in order specified by mRNA
	Elongation factor Tu	Binds GTP and charged tRNA; delivers charged tRNA to A site
	Elongation factor Ts	Generates active elongation factor Tu
	Elongation factor G	Stimulates movement of ribosome to next codon
	GTP	Provides energy
	Peptidyl transferase	Creates peptide bond between amino acids in A site and P site
	Release factors 1, 2, and 3	Bind to ribosome when stop codon is reached and terminate translation



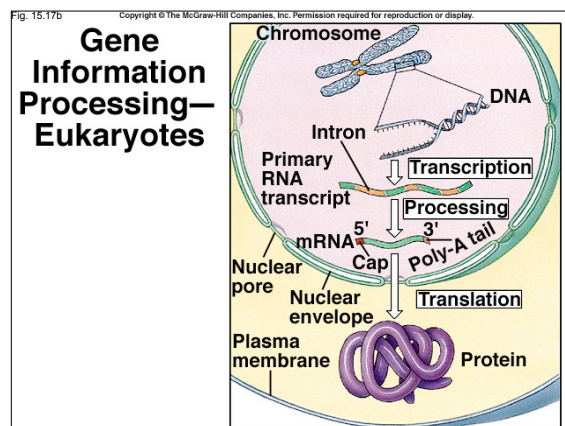
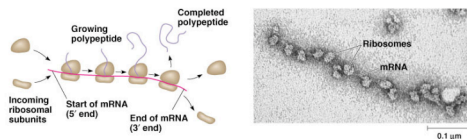




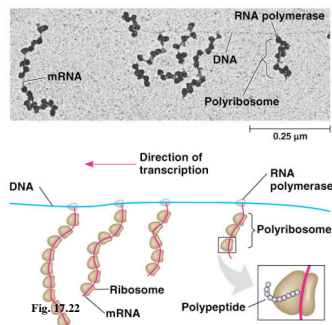
Post-translational modifications



- ✓ Typically a single mRNA is used to make many copies of a polypeptide simultaneously.
- ✓ Multiple ribosomes, **polyribosomes**, may trail along the same mRNA.
- ✓ A ribosome requires less than a minute to translate an average-sized mRNA into a polypeptide.



- ✓ In one big difference, prokaryotes can transcribe and translate the same gene simultaneously.
- ✓ The new protein quickly diffuses to its operating site.



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Table 17.1 Types of RNA in a Eukaryotic Cell

Type of RNA	Functions
Messenger RNA (mRNA)	Carries information specifying amino acid sequences of proteins from DNA to ribosomes.
Transfer RNA (tRNA)	Plays catalytic (ribozyme) roles and structural roles in ribosomes.
Ribosomal RNA (rRNA)	Plays structural and catalytic (ribozyme) roles in ribosomes.
Primary transcript	Serves as a precursor to mRNA, rRNA, or tRNA and may be processed by splicing or cleavage. In eukaryotes, pre-mRNA commonly contains introns, noncoding segments that are spliced out as the primary transcript is processed. Some intron RNA acts as a ribozyme, catalyzing its own splicing.
Small nuclear RNA (snRNA)	Plays structural and catalytic roles in spliceosomes, the complexes of protein and RNA that splice pre-mRNA in the eukaryotic nucleus.
SRP RNA	Is a component of the signal-recognition particle (SRP), the protein-RNA complex that recognizes the signal peptides of polypeptides targeted to the ER.

- ✓ **Missense mutations** are those that still code for an amino acid but change the indicated amino acid.
- ✓ **Nonsense mutations** change an amino acid codon into a stop codon, nearly always leading to a nonfunctional protein.

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Mutations

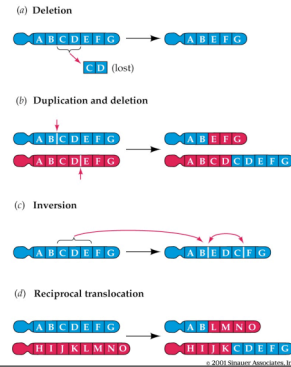
Permanent changes in the DNA sequence

Somatic - non gamete cells
Germ-line mutations

Point mutations - substitution or deletion/addition of a nucleotide

Silent (no change)
missense (sickle cell)
Nonsense (Stop)
Frame shift

Chromosome mutation - loss or change in a DNA segment

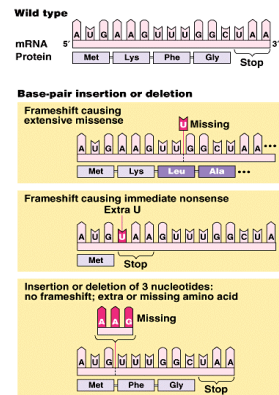


- ✓ **Insertions and deletions** are additions or losses of nucleotide pairs in a gene.
- ✓ Unless these mutations occur in multiples of three, they cause a **frameshift mutation**.

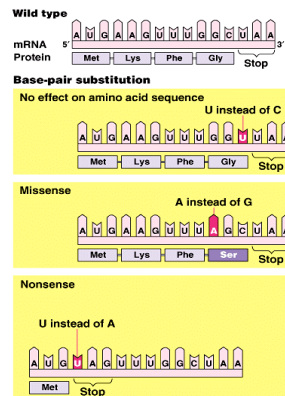
- ⇒ All the nucleotides downstream of the deletion or insertion will be improperly grouped into codons.
- ⇒ The result - missense, ending sooner or later in nonsense - premature termination.

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Insertion or deletion

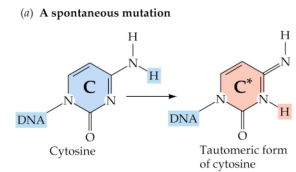


Substitution



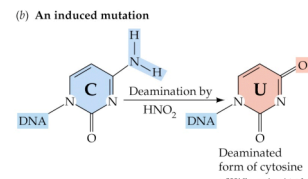
Spontaneous and induced mutations

Tautomeric C pairs with A



Base modifications by chemicals or radiation

benzpyrene
Nitrates
X-rays
UV light



- ✓ **Mutagens** are chemical or physical agents that interact with DNA to cause mutations.
- ✓ Physical agents include high-energy radiation like X-rays and ultraviolet light.
- ✓ Chemical mutagens
 - ⇒ base analogues
 - ⇒ DNA insertion - distorting the double helix.
 - ⇒ chemical changes in bases that change their pairing properties.

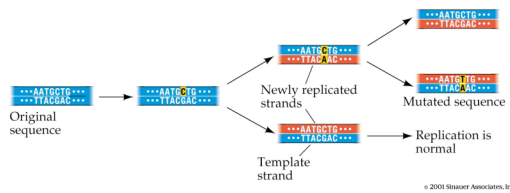
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- ✓ Researchers have developed various methods to test the mutagenic activity of different chemicals.
 - ⇒ preliminary screen of chemicals to identify those that may cause cancer.
 - ⇒ most carcinogens are mutagenic and most mutagens are carcinogenic.
- ✓ Ames Test

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Mutation propagation

(c) The consequences of either mutation



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- ✓ For example, sickle-cell disease is caused by a mutation of a single base pair in the gene that codes for one of the polypeptides of hemoglobin.
 - ⇒ A change in a single nucleotide from T to A in the DNA template leads to an abnormal protein.

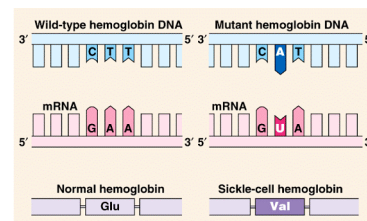
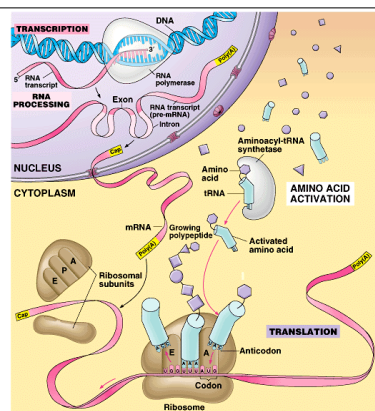


Fig. 17.23

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Overview



- ✓ The one gene-one polypeptide definition must be refined and applied selectively.
 - ⇒ Most eukaryotic genes contain large introns
 - ⇒ Promoters and other regulatory regions are not transcribed, but they must be present for transcription to occur
 - ⇒ must include RNA that is not translated into polypeptides.
- ✓ A gene is a region of DNA whose final product is either a polypeptide or an RNA molecule.

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The End.