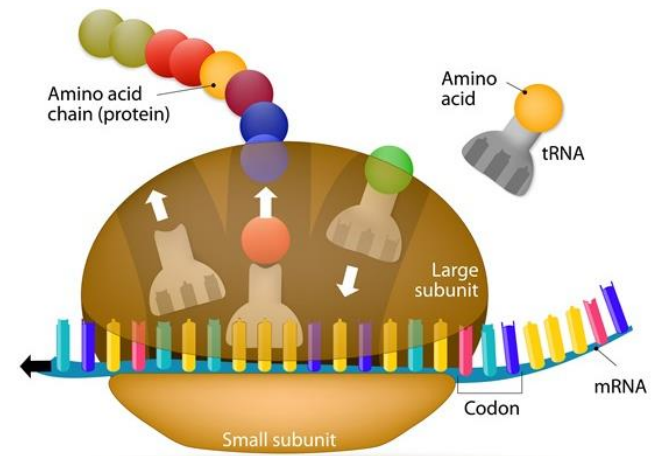


DNA & Protein Synthesis

UNIT D & E



How this Unit is broken down

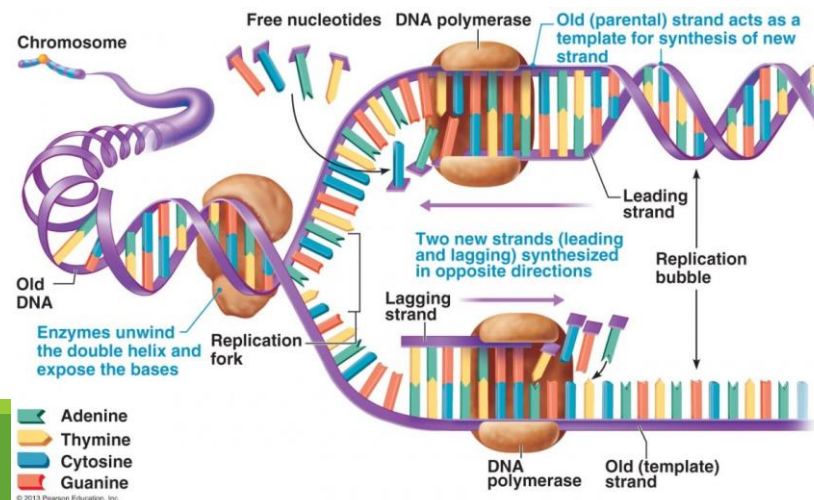
Chapter 10.1 – 10.3 – The structure of the genetic material

Chapter 10.4 & 10.5 – DNA replication

Chapter 10.6 – 10.15 – The flow of genetic information from the DNA to RNA to protein (Protein Synthesis)

Chapter 10.16 – Review (summary)

Chapter 12.1 – 12.3 – Bacterial plasmids and gene cloning



Standards

Unit E

I can provide an overview of the events involved in protein synthesis.

I can use a CODON table accurately.

I can name examples of mutagens.

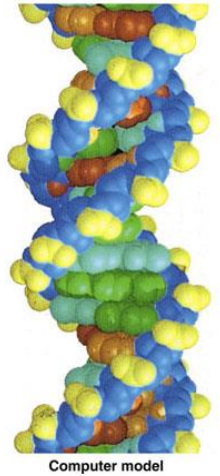
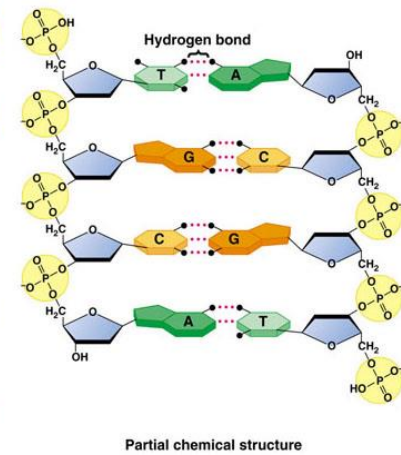
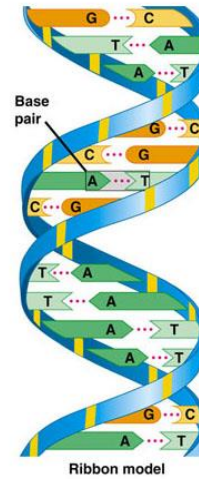
I can explain how a mutation in DNA can cause a genetic disorder.

I can explain how a genetic disorder impacts protein structure.

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

Key:

Ala = Alanine (A)
Arg = Arginine (R)
Asn = Asparagine (N)
Asp = Aspartate (D)
Cys = Cysteine (C)
Gln = Glutamine (Q)
Glu = Glutamate (E)
Gly = Glycine (G)
His = Histidine (H)
Ile = Isoleucine (I)
Leu = Leucine (L)
Lys = Lysine (K)
Met = Methionine (M)
Phe = Phenylalanine (F)
Pro = Proline (P)
Ser = Serine (S)
Thr = Threonine (T)
Trp = Tryptophan (W)
Tyr = Tyrosine (Y)
Val = Valine (V)

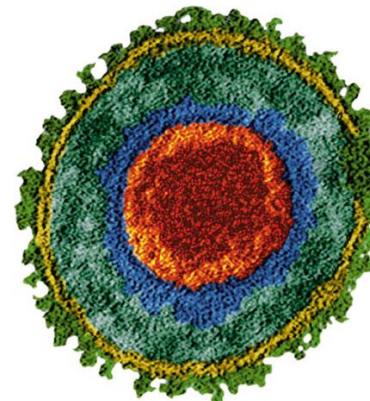


Chapter 10

MOLECULAR BIOLOGY OF THE GENE

Sabotage Inside Our Cells

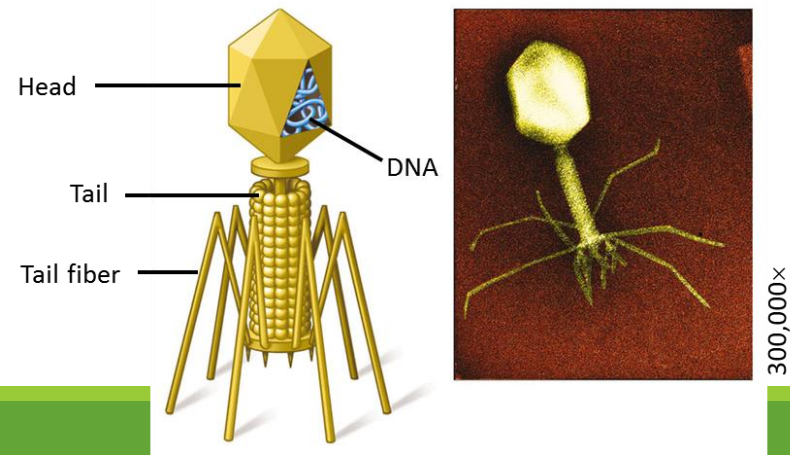
- A saboteur: Lies low waiting for the right moment to strike
- Viruses are biological saboteurs
 - Hijacking the genetic material of host cells in order to reproduce themselves
- Viruses provided some of the earliest evidence
 - That genes are made of DNA



THE STRUCTURE OF THE GENETIC MATERIAL

10.1 Experiments showed that DNA is the genetic material

- The Hershey-Chase experiment showed that certain viruses reprogram host cells
 - To produce more viruses by injecting their DNA
- The Hershey-Chase results, added to earlier evidence, convinced scientists that DNA is hereditary material
- What happened next was one of the most celebrated quests in history of science: to determine the structure of DNA and how that structure enables the molecule to store genetic information and transmit it from parent to offspring.



◦ The Hershey-Chase experiment

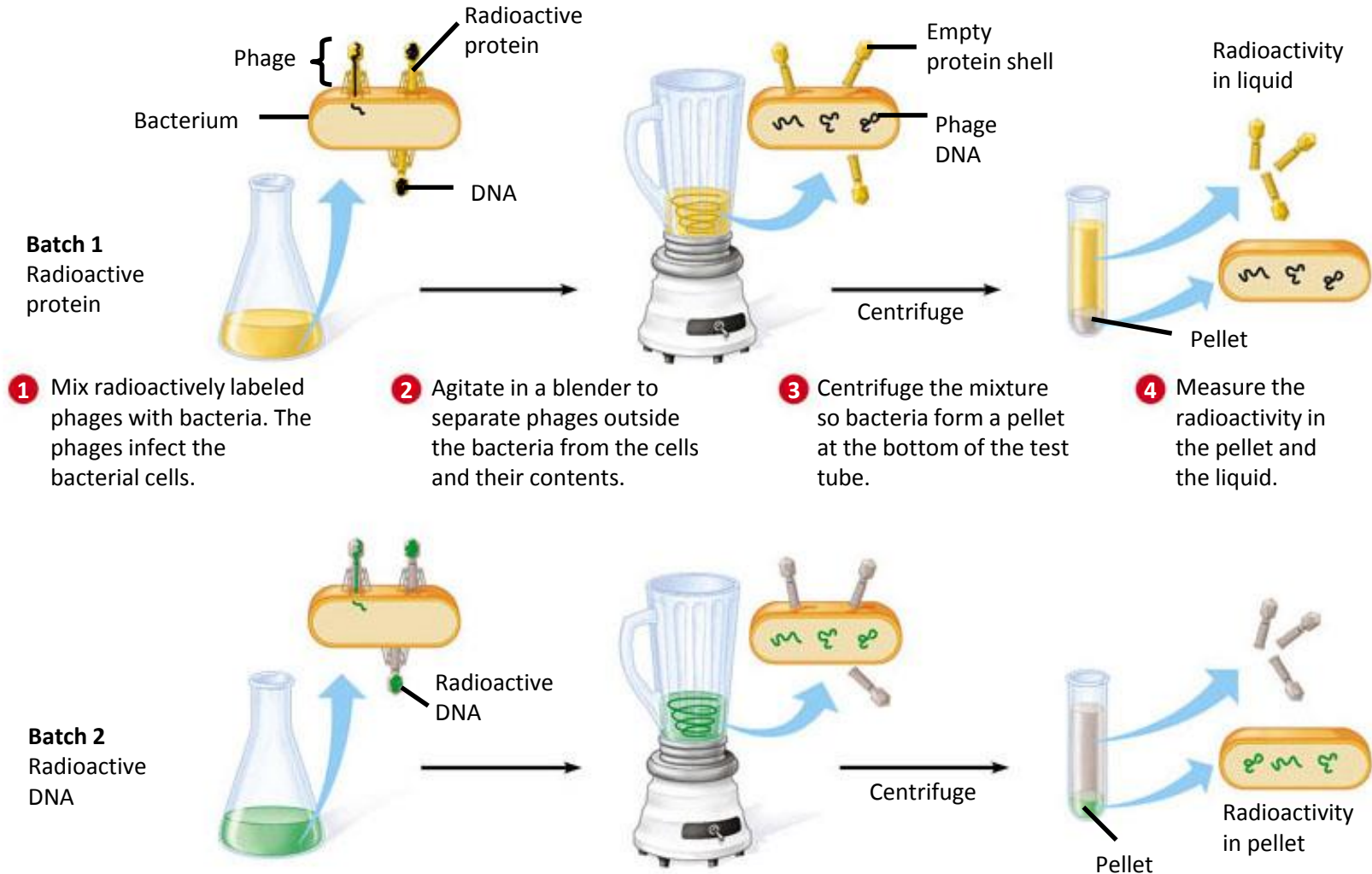


Figure 10.1B

- Phage reproductive cycle

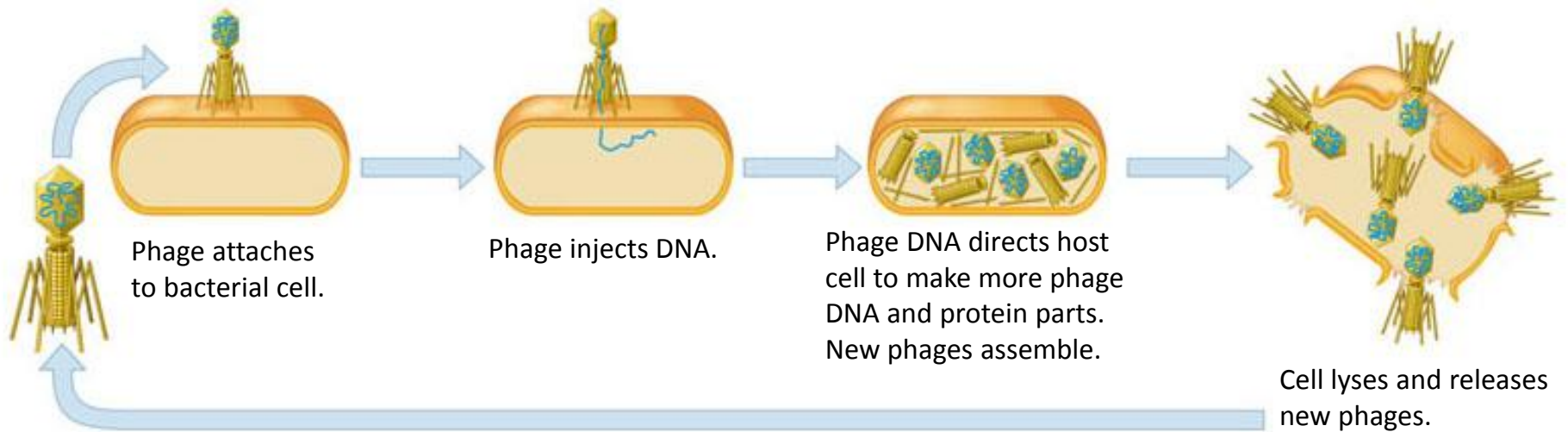
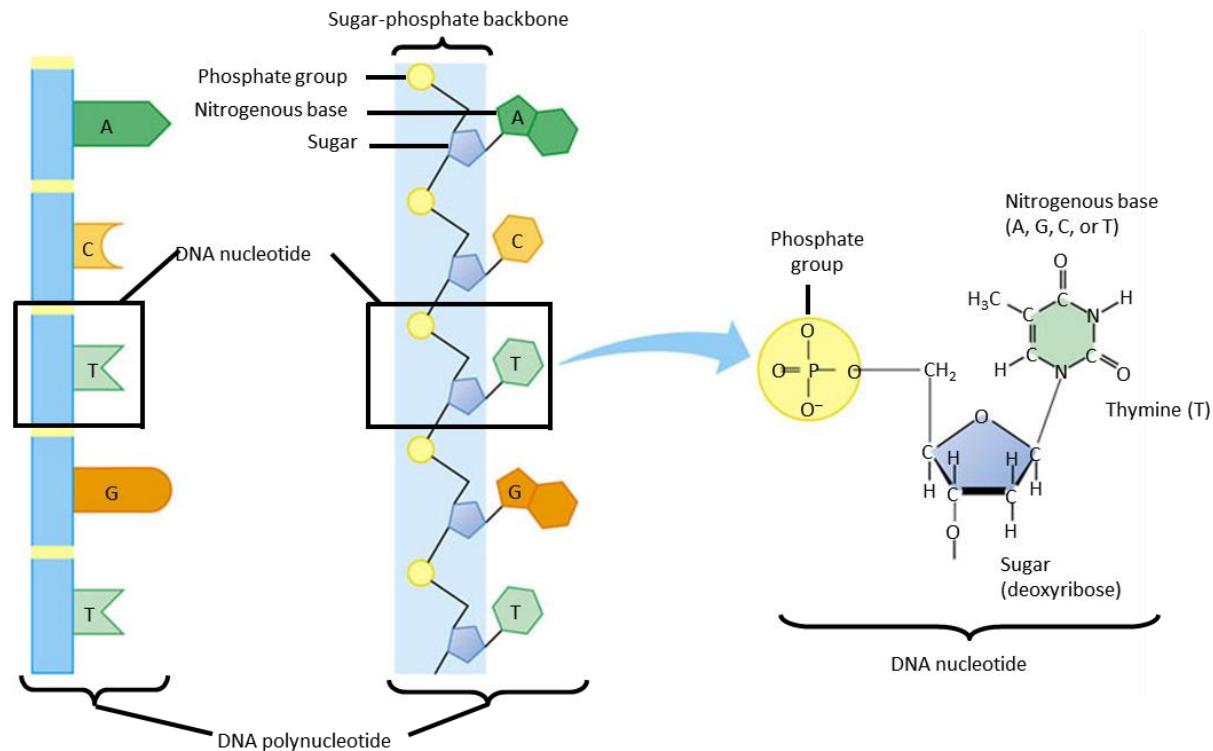


Figure 10.1C

10.2 DNA and RNA are polymers of nucleotides

- DNA is a nucleic acid
 - Made of long chains of nucleotide monomers



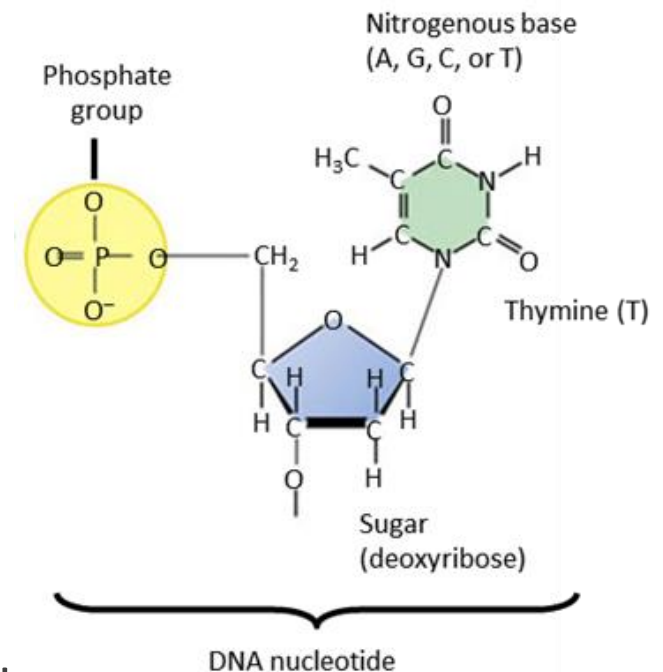
DNA

Within each of the DNA nucleotide there are three important components

1. A nitrogenous base (A, C, T, G)
2. A sugar
3. A phosphate group

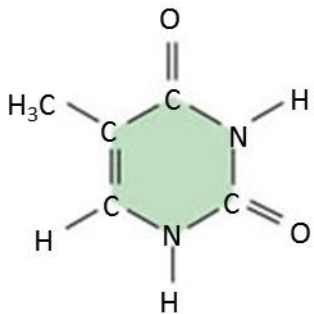
These are joined with covalent bonds between the sugar of one nucleotide and the phosphate of the next

This results in the sugar-phosphate backbone!

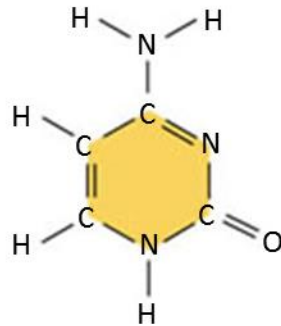


Nitrogenous Bases

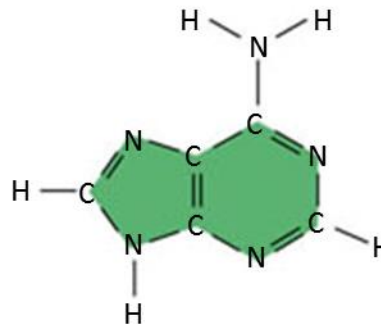
- DNA has four kinds of nitrogenous bases in two groups
 - Pyrimidines: Thymine and Cytosine
 - Purines: Adenine and Guanine



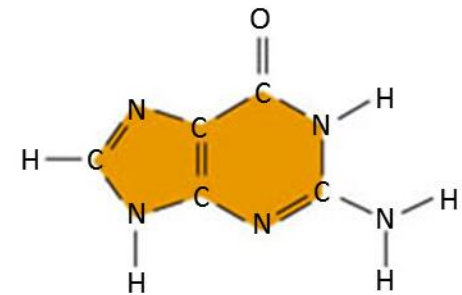
Thymine (T)



Cytosine (C)



Adenine (A)



Guanine (G)

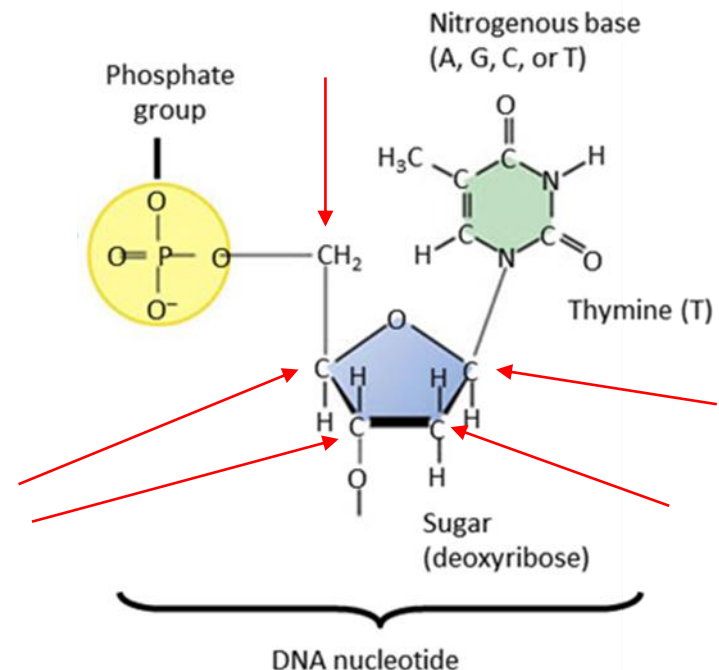
Pyrimidines

Purines

Sugar & the Phosphate Group

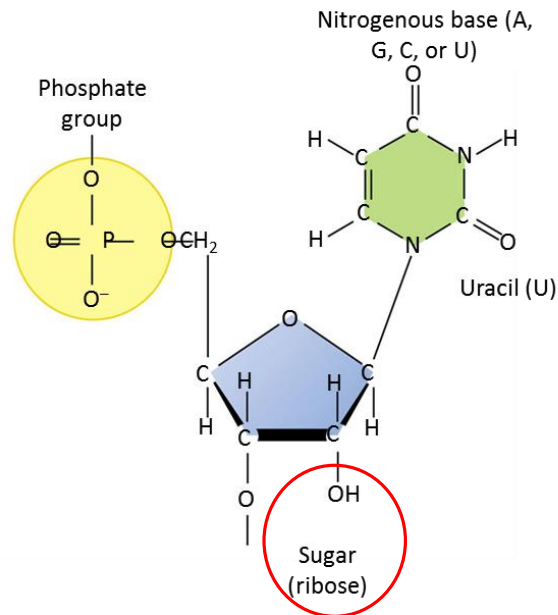
The sugar has five carbon atoms,
four in the ring and one that
extending above the ring

Has a phosphorus atom at its centre
and is the source of the acid in
nucleic acid



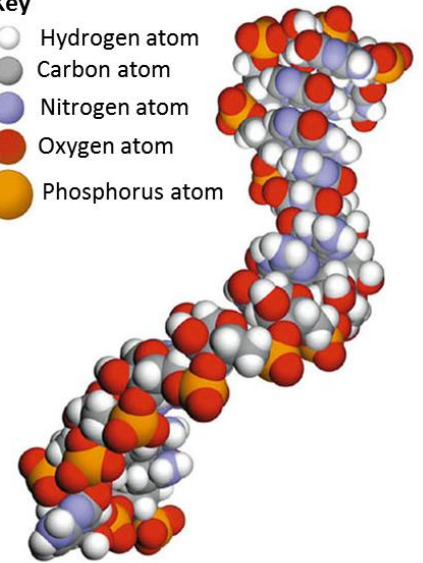
RNA

- RNA is also a nucleic acid
 - But has a slightly different sugar, with oxygen
 - And has Uracil instead of Thymine



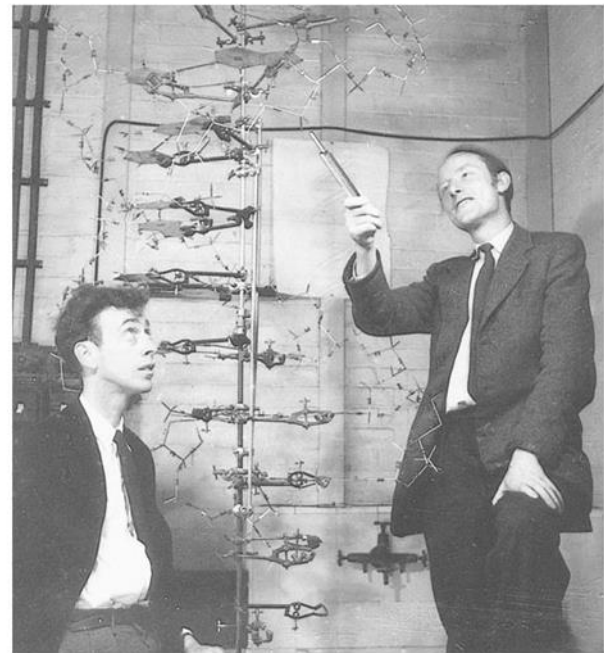
Key

- Hydrogen atom
- Carbon atom
- Nitrogen atom
- Oxygen atom
- Phosphorus atom



10.3 – DNA is a double-stranded helix

- James Watson and Francis Crick
 - Worked out the three-dimensional structure of DNA, based on work by Rosalind Franklin



The Structure

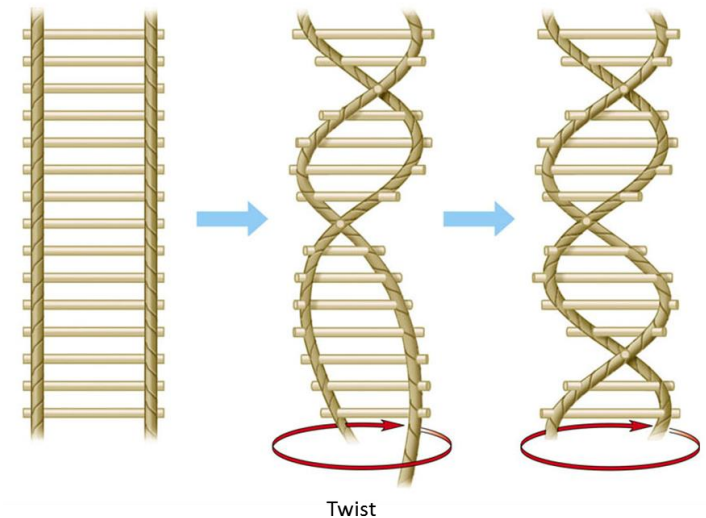
Consists of two polynucleotide strands wrapped around each other in a double helix

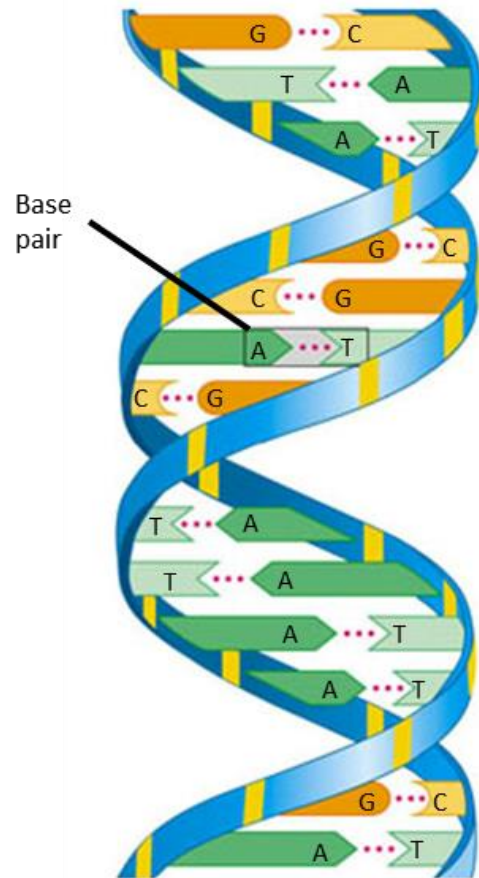
Hydrogen bonds between bases

- Hold the strands together

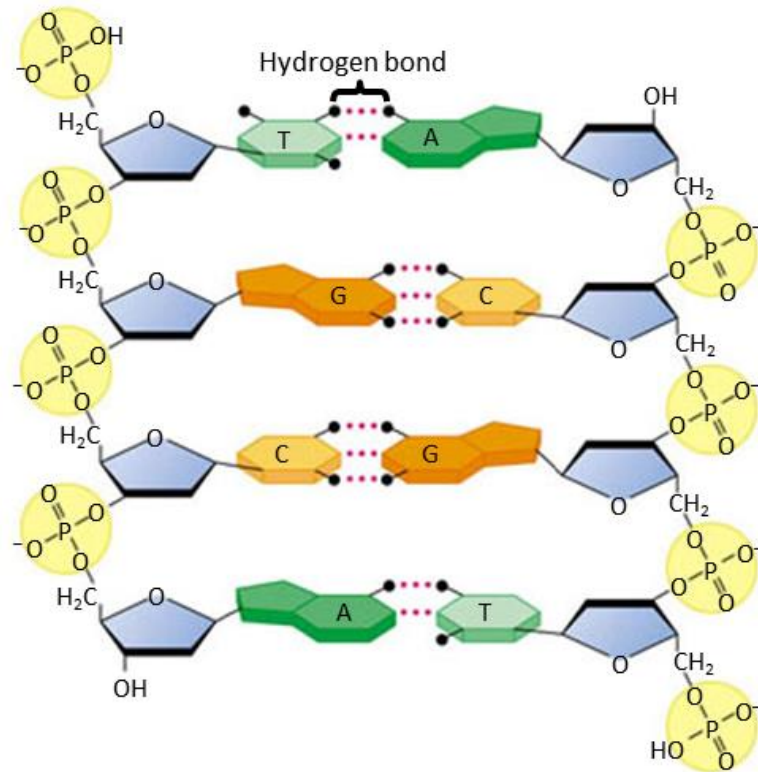
Each base pairs with a complementary partner

- A with T, and G with C

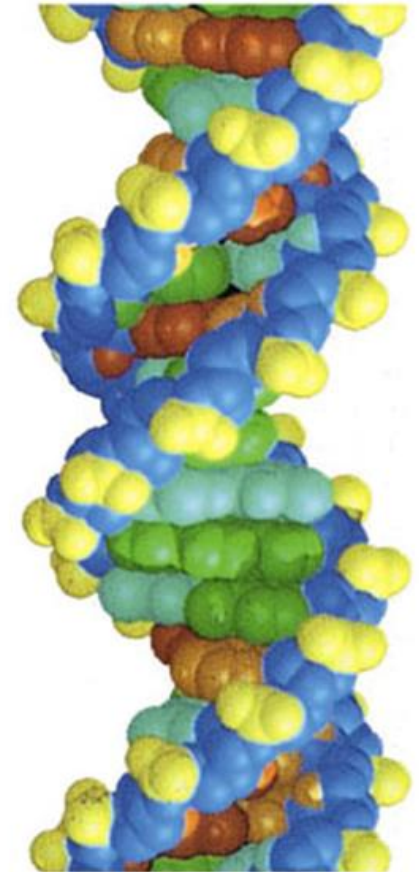




Ribbon model



Partial chemical structure

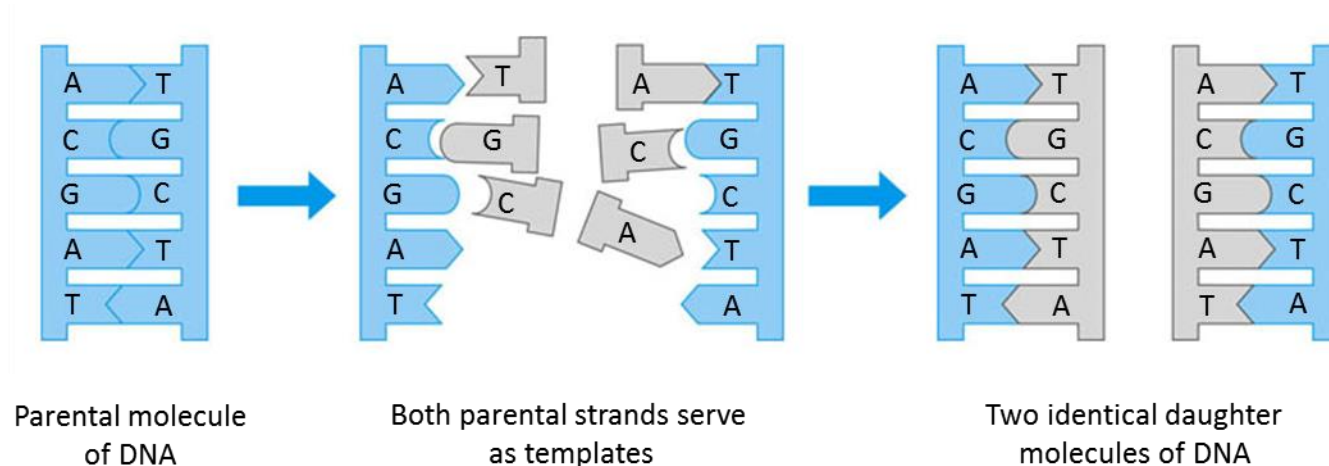


Computer model

10.4 - DNA Replication

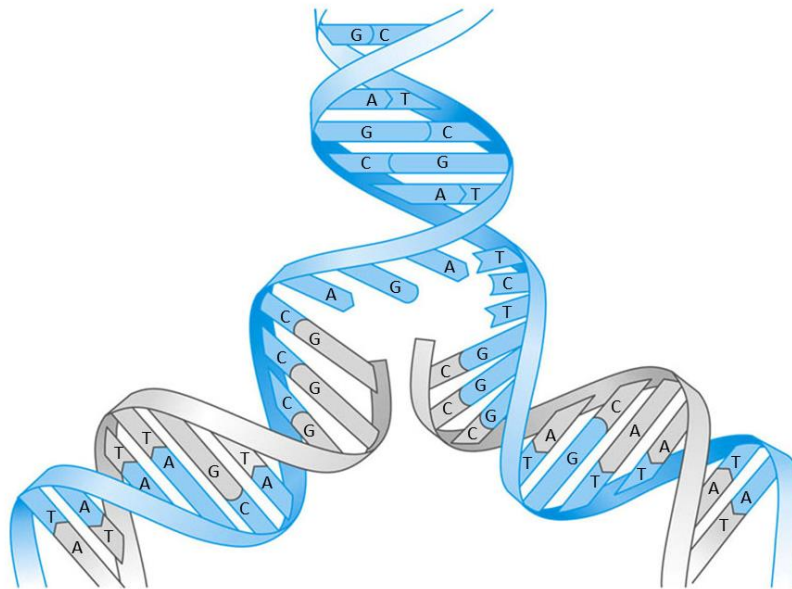
DNA replication depends on specific base pairing

- DNA replication
 - Starts with the separation of DNA strands
 - Then enzymes use each strand as a template
 - To assemble new nucleotides into complementary strands (semi-conservative)



DNA Replication

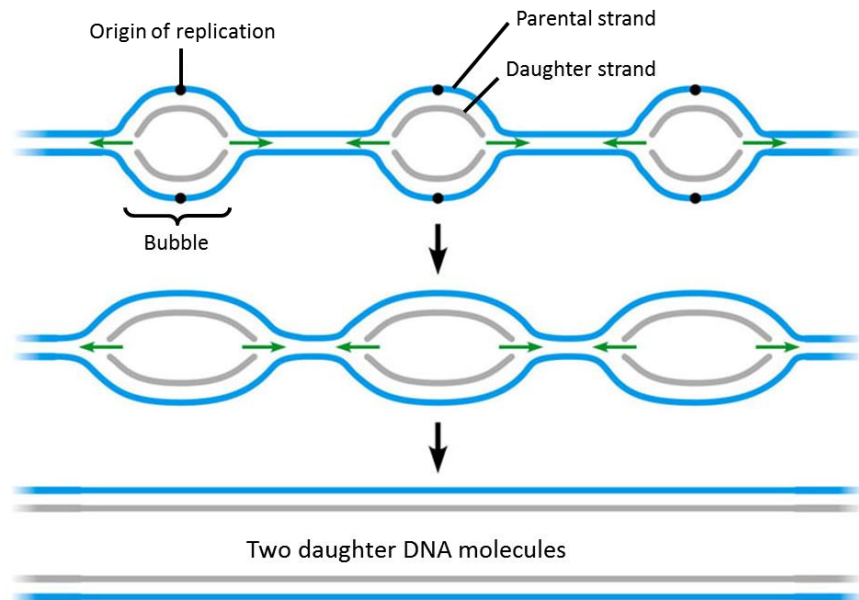
- DNA replication is a complex process
 - Due in part to the fact that some of the helical DNA molecule must untwist
 - Occurs quickly, 50 nucleotides per second. 500 per sec in bacteria!



10.5 – DNA replication: A closer look

DNA replication

- Begins at specific sites on the double helix creating replication 'bubbles'
- These bubbles can form simultaneously, shortening the time needed for this process.
- Bubbles merge, yielding two completed daughter DNA molecules



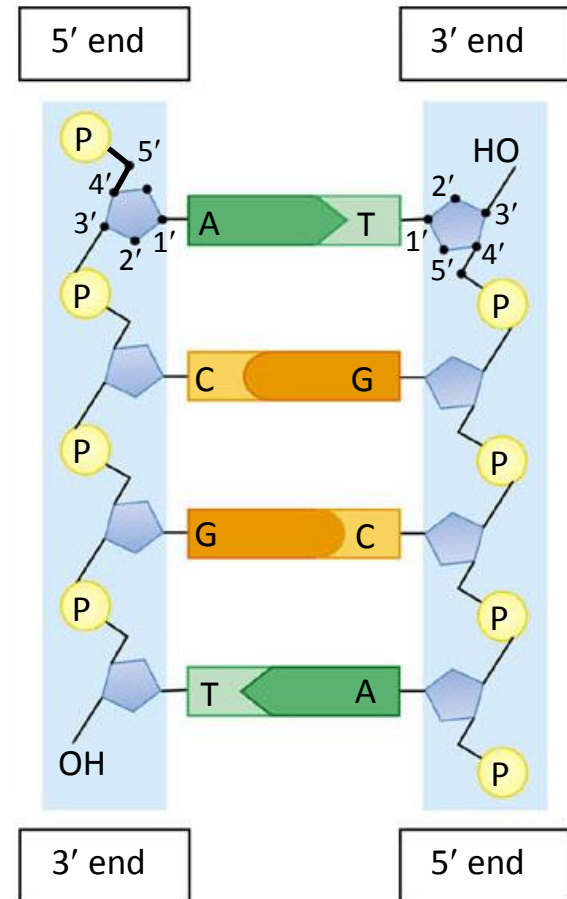
Opposite directions

Each strand of the double helix

- Is oriented in the opposite direction

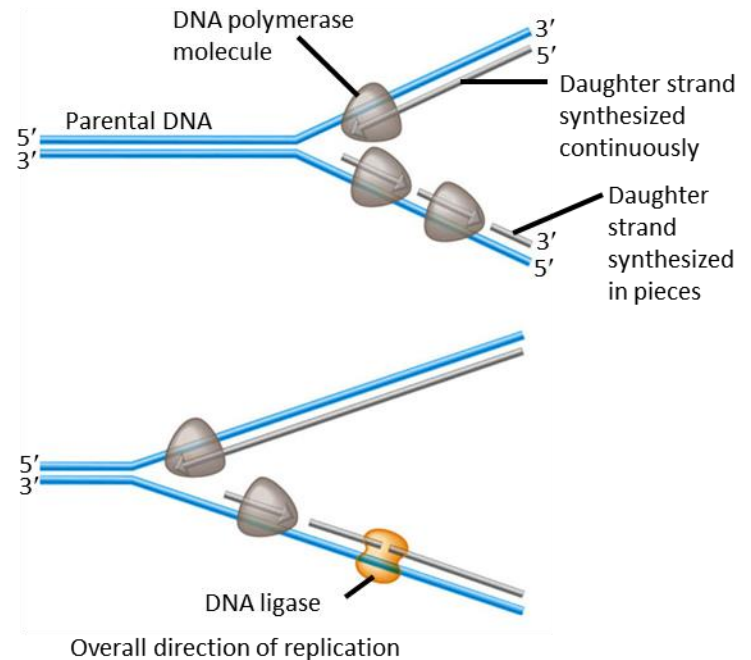
The primed numbers refer to the carbon atoms of the nucleotide sugars

- At one end of each DNA strand, the sugar's 3' carbon atom is attached to an –OH group; at the other end, the sugar's 5' carbon has a phosphate group



DNA Polymerases

- Using the enzyme DNA polymerase
 - The cell synthesizes one daughter strand as a continuous piece
- The other strand is synthesized as a series of short pieces
 - Which are then connected by the enzyme DNA ligase



THE FLOW OF GENETIC INFORMATION FROM DNA TO RNA TO PROTEIN (Protein synthesis)

10.6 – 10.16

10.6 The DNA genotype is expressed as proteins, which provide the molecular basis for phenotypic traits

The information constituting an organism's genotype

- Is carried in its sequence of its DNA bases

A particular gene, a linear sequence of many nucleotides

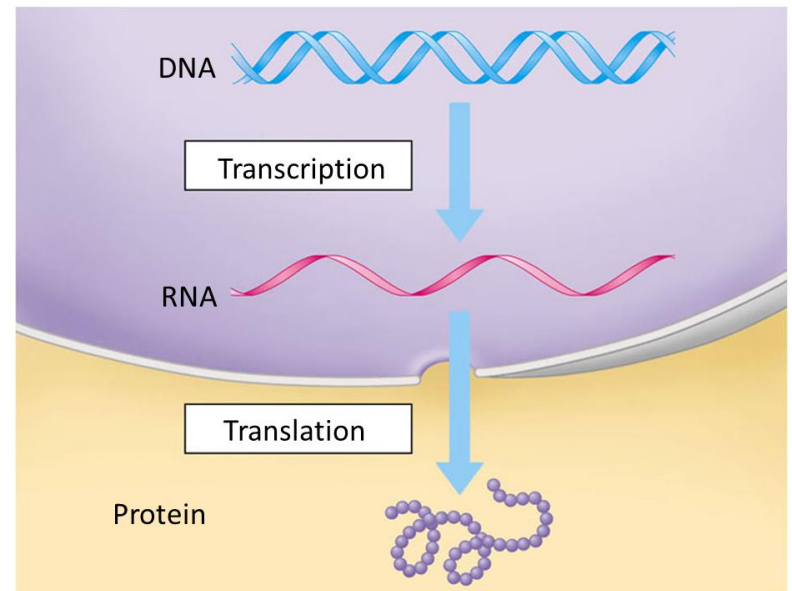
- Specifies a polypeptide

Transcription and Translation

The chain of command is from DNA in the nucleus of the cell to RNA to protein synthesis in the cytoplasm

The two main stages are:

- Transcription, the transfer of genetic information of the gene is transcribed into RNA
- Translation, the transfer of information in the RNA molecule into a protein



Enzymes!

Garrod observed 'inborn errors of metabolism' and attributed them to the lack of function or presence of an enzyme through a metabolic pathway

As a result, lacking an enzyme would result in a missing amino acid which could inhibit the function of a specific gene.

This led to the thought of 'gene-one enzymes' to dictate the production of a specific enzyme.

This thought extended beyond enzymes to all types of proteins

- Studies of inherited metabolic disorders in mold
 - First suggested that phenotype is expressed through proteins



Figure 10.6B

10.7 Genetic information written in codons is translated into amino acid sequences

- The “words” of the DNA “language”
 - Are triplets of bases called codons
- The codons in a gene
 - Specify the amino acid sequence of a polypeptide

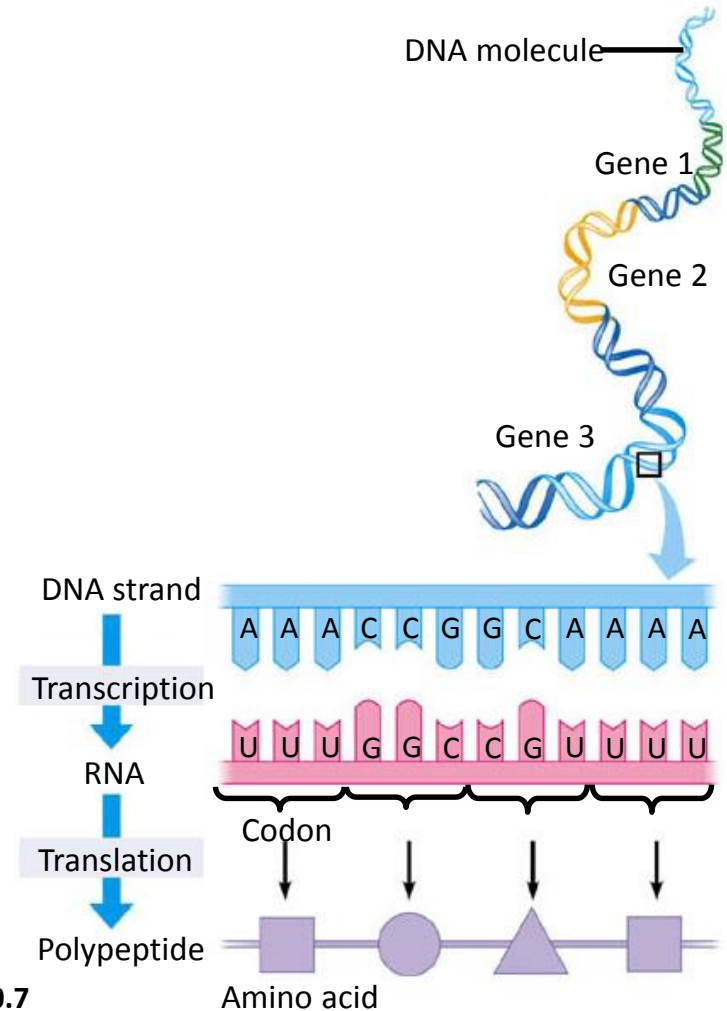
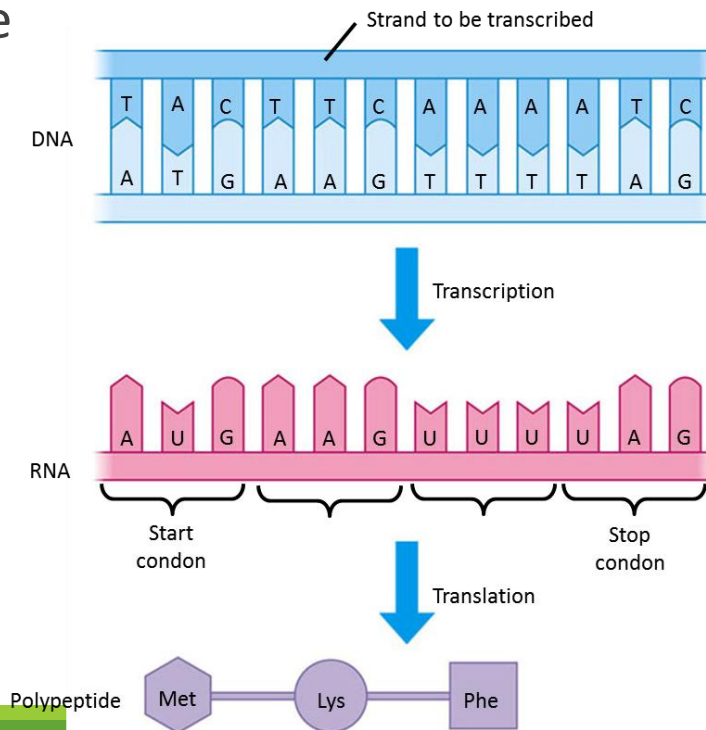


Figure 10.7

10.8 The genetic code is the Rosetta stone of life

- Nearly all organisms
 - Use exactly the same genetic code
- An exercise in translating the genetic code



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

10.9 - Transcription produces genetic messages in the form of RNA

A close-up view of transcription

As with replication, the two DNA strands must first separate at the place where the process will start

In transcription, however, only one of the DNA strands serves as a template for the newly forming molecule

The RNA nucleotides are linked by the transcription enzyme RNA polymerase.

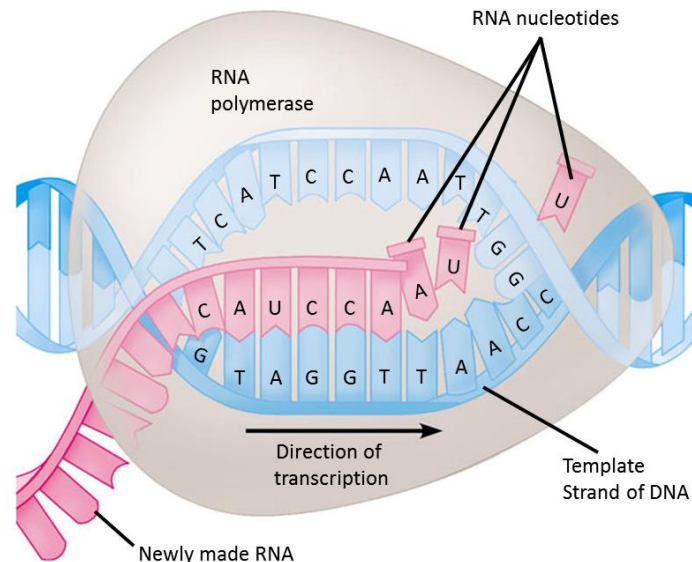


Figure 10.9A

Transcription of a gene

- In the nucleus, the DNA helix unzips
 - And RNA nucleotides line up along one strand of the DNA, following the base pairing rules
- As the single-stranded messenger RNA (mRNA) peels away from the gene
 - The DNA strands rejoin

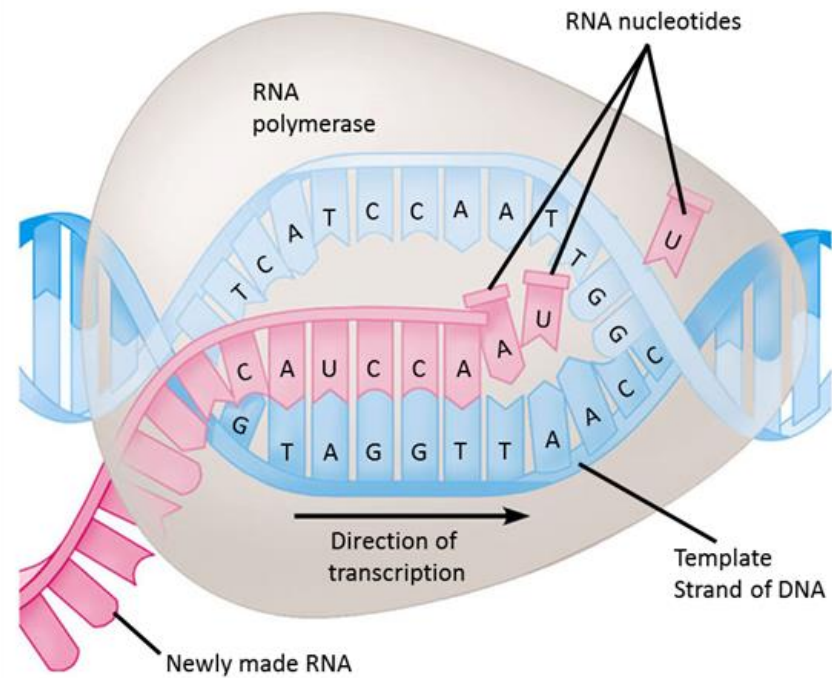


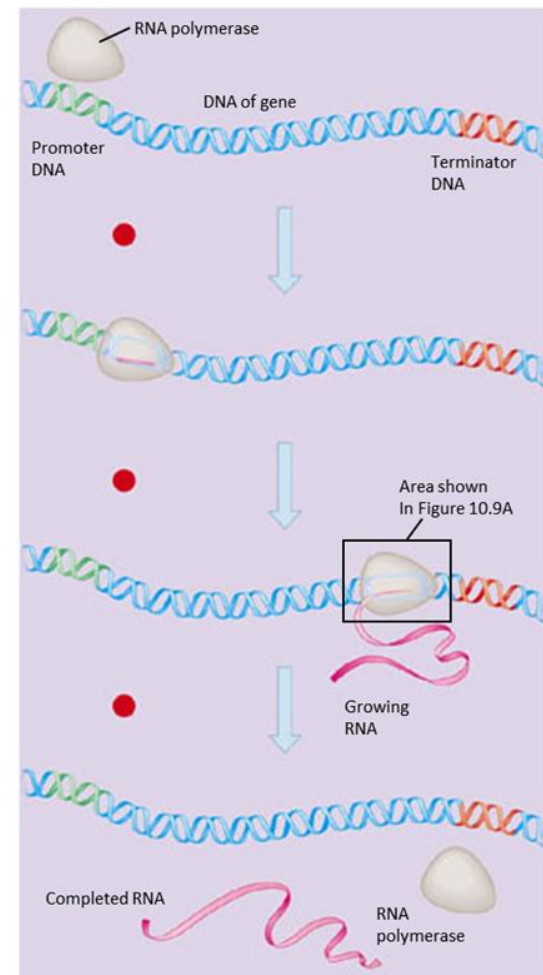
Figure 10.9A

Transcription of a gene

As discussed, there are specific sequences of nucleotides along the DNA that mark where transcription of a gene begins and ends

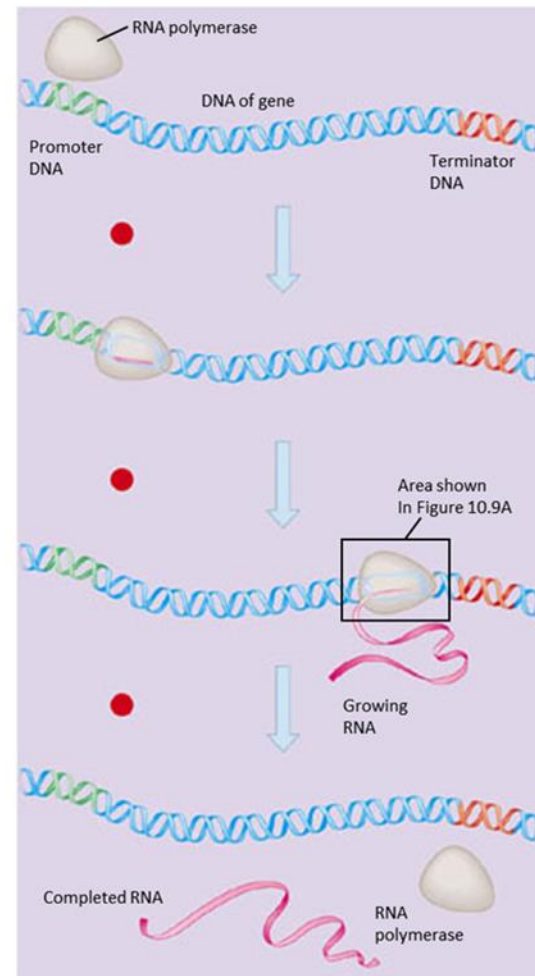
The 'start transcribing' signal is a sequence called the promoter

This is the binding site for the RNA polymerase and one of the strands is used to transcription.



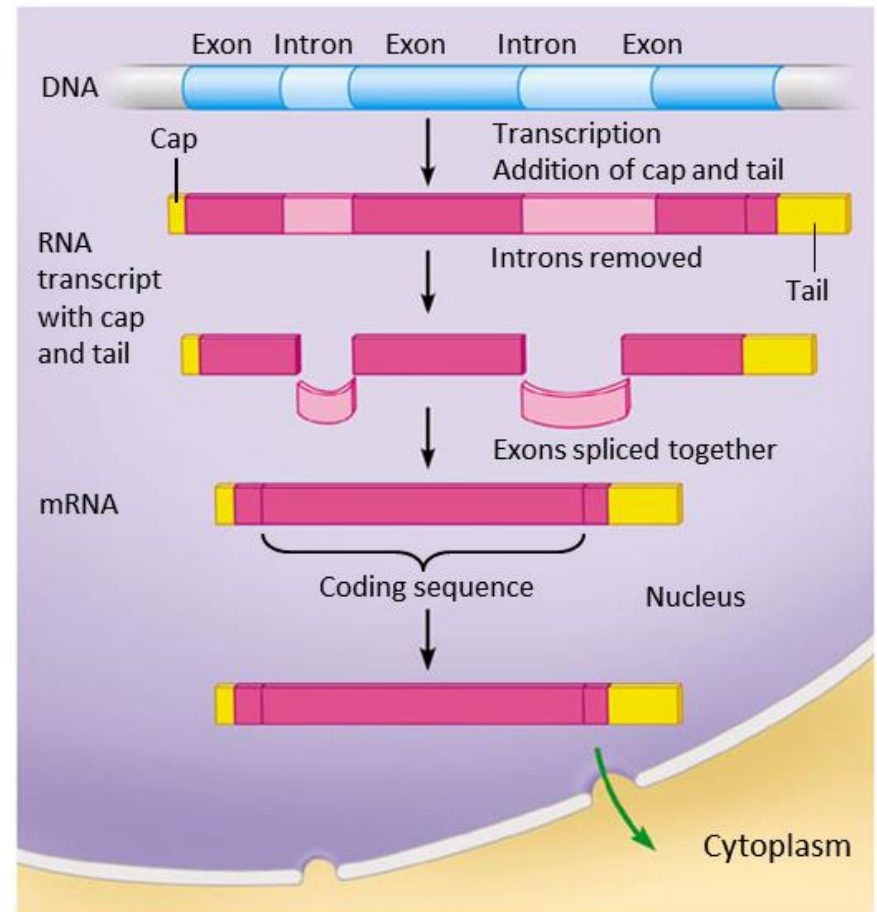
Phases of transcription

1. Initiation: attachment of RNA polymerase to the promotor and is the start of RNA synthesis
2. Elongation: RNA elongates, RNA synthesis continues, RNA peels away from DNA, allowing DNA to come back together
3. Termination: The RNA polymerase reaches a sequence of bases in DNA called a terminator. This sequence signals the end of the gene. RNA polymerase detaches from RNA and the gene



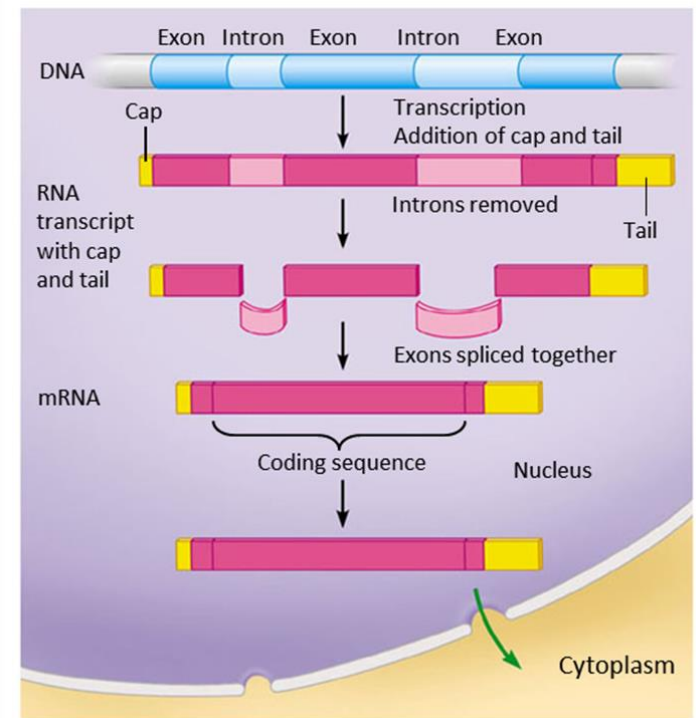
10.10 Eukaryotic RNA is processed before leaving the nucleus

- Before leaving the nucleus as mRNA, eukaryotic transcripts are modified, or processed, in several ways.
- One kind of RNA processing is the addition of extra nucleotides to the ends of RNA transcript
- These additions include a small cap (a single G nucleotide) at one end and a long tail (a chain of 50 to 250 A's) at the other end
- The cap and tail facilitate the export of the mRNA from the nucleus, protect from enzymes, and help ribosomes bind to the mRNA for translation into proteins.



10.10 Eukaryotic RNA is processed before leaving the nucleus

- Noncoding segments called introns are spliced out
- The parts of the gene that are expressed as amino acids are called exons
- The cutting and pasting process is called RNA splicing
- Catalyzed by a complex set of proteins or its own RNA and remove its own introns!



10.10 Eukaryotic RNA is processed before leaving the nucleus

We are now ready to see how the translation process works. Translation of mRNA into protein involves more complicated machinery than transcription

Key points:

Transfer RNA, another kind of RNA molecule

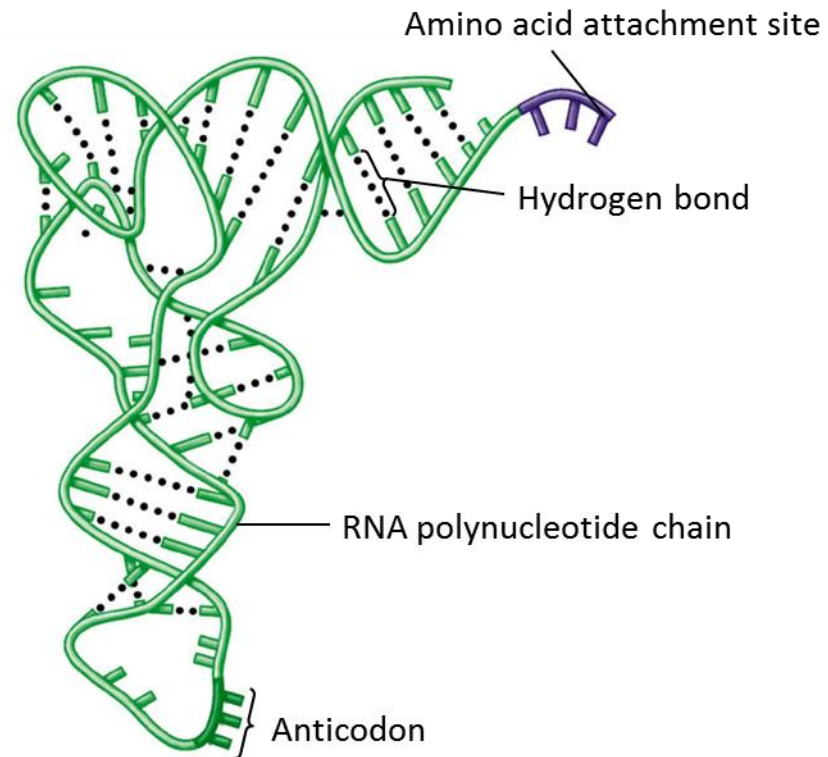
Ribosomes, the organelle where translation occurs

Enzymes and a number of protein 'factors'

Sources of chemical energy, such as ATP

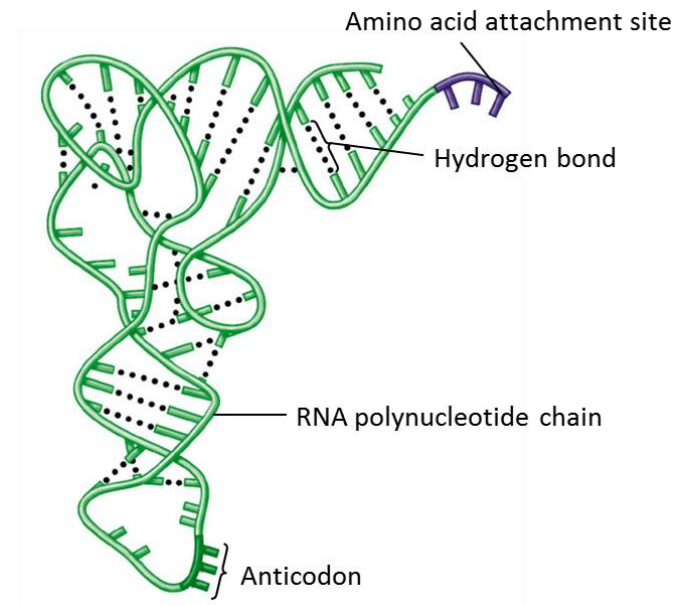
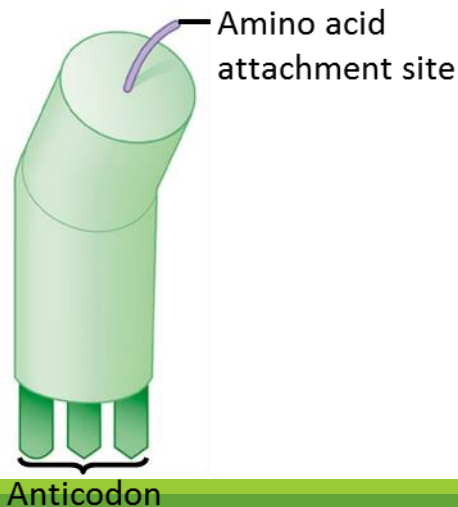
10.11 Transfer RNA molecules serve as interpreters during translation

- Translation of any language requires an interpreter, this is the job of a molecular interpreter employed by the cell
- This special type of RNA is called transfer RNA (tRNA)
- Its primary job is to convert three-letter words (codons) of nucleic acids to the one-letter, amino acids words of proteins.
- To perform this task, tRNA molecules must carry out two functions:
 - 1. picking up the appropriate amino acids
 - 2. recognizing the appropriate codons in the mRNA
- The unique structure of tRNA molecules enable them to perform both tasks



10.11 Transfer RNA molecules serve as interpreters during translation

- A ribosome attaches to the mRNA
 - And translates its message into a specific polypeptide aided by transfer RNAs (tRNAs)
- Each tRNA molecule
 - Is a folded molecule bearing a base triplet called an anticodon on one end
- A specific amino acid
 - Is attached to the other end



10.12 Ribosomes build polypeptides

- A ribosome consists of two subunits
 - Each made up of proteins and a kind of RNA called ribosomal RNA
- There are some antibacterial medications that can inactivate prokaryotic ribosomes while leaving eukaryotic ribosomes to combat infections!

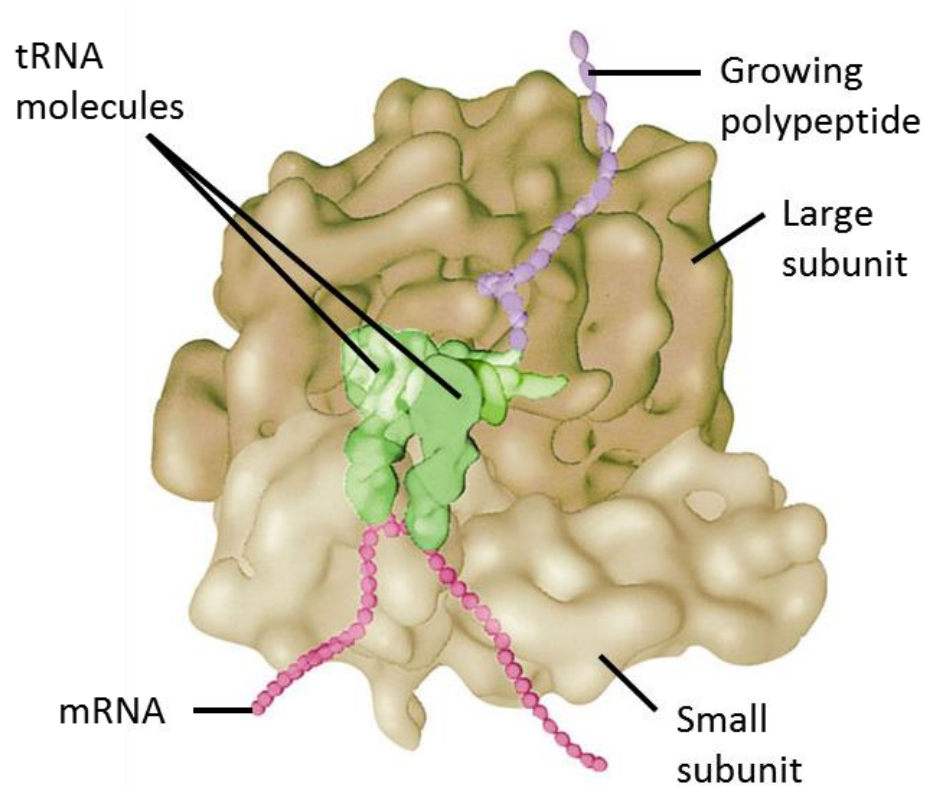
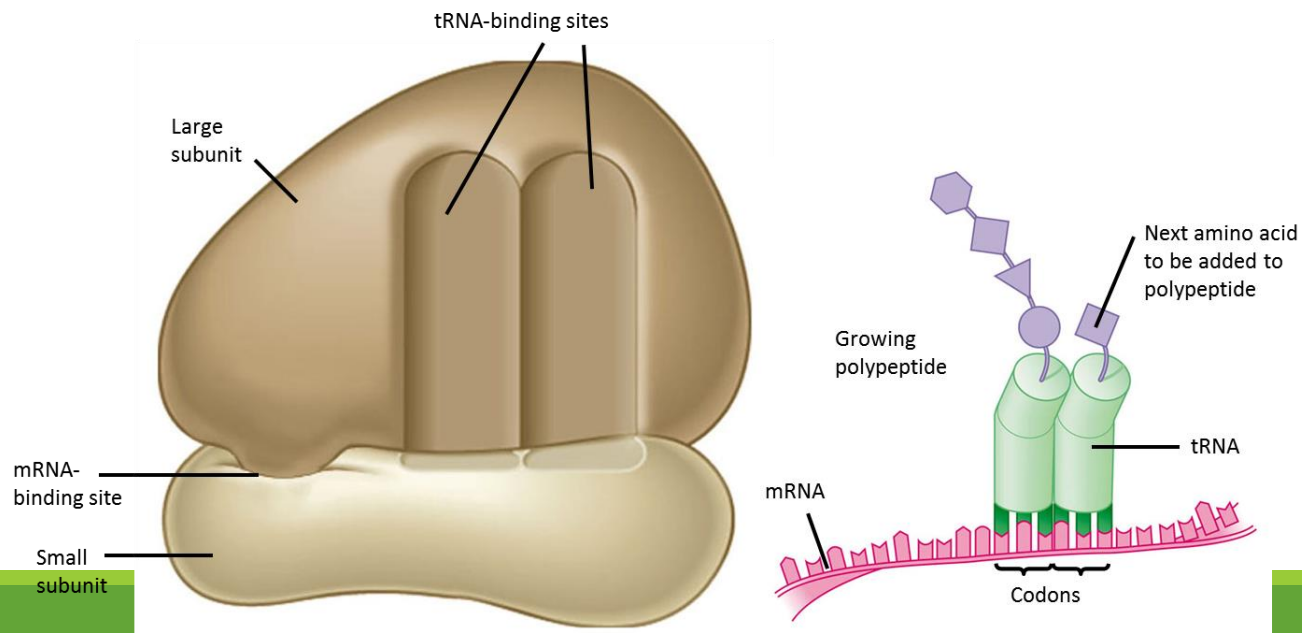


Figure 10.12A

Ribosomes

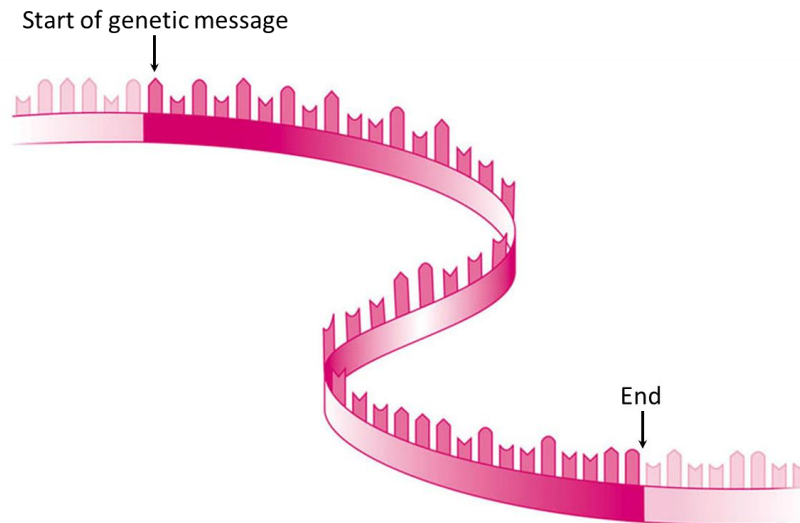
- The subunits of a ribosome
- The subunits of the ribosome act like a vice by holding the tRNA and mRNA close together during translation
- This allows for the polypeptide chain to grow connected.



10.13 An initiation codon marks the start of an mRNA message

Translation can be divided into the same three phases as transcription: initiation, elongation and termination.

Initiation: brings together the mRNA. A tRNA with its first amino acid, and the two subunits of a ribosome.



Initiation

Initiation takes place in two steps.

- 1. An mRNA molecule binds to a small ribosomal subunit. A special tRNA binds to a specific codon (start codon) and translation begins. The initiator tRNA carries the amino acid methionine (Met).
 - UAC binds to the start codon AUG
- 2. Next, a large ribosomal subunit binds to a small one, creating a functional ribosome. The initiator tRNA fits into one of the two tRNA-binding sites. (P site)
 - P site will hold the growing peptide.
 - The A Site is vacant and ready for the next amino-acid-bearing tRNA

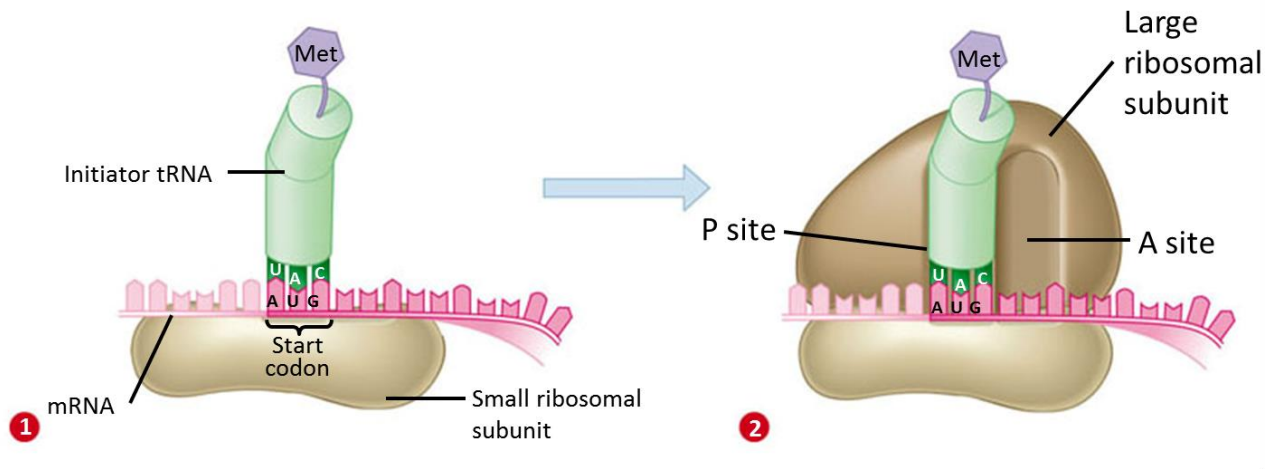


Figure 10.13B

- mRNA, a specific tRNA, and the ribosome subunits
 - Assemble during initiation

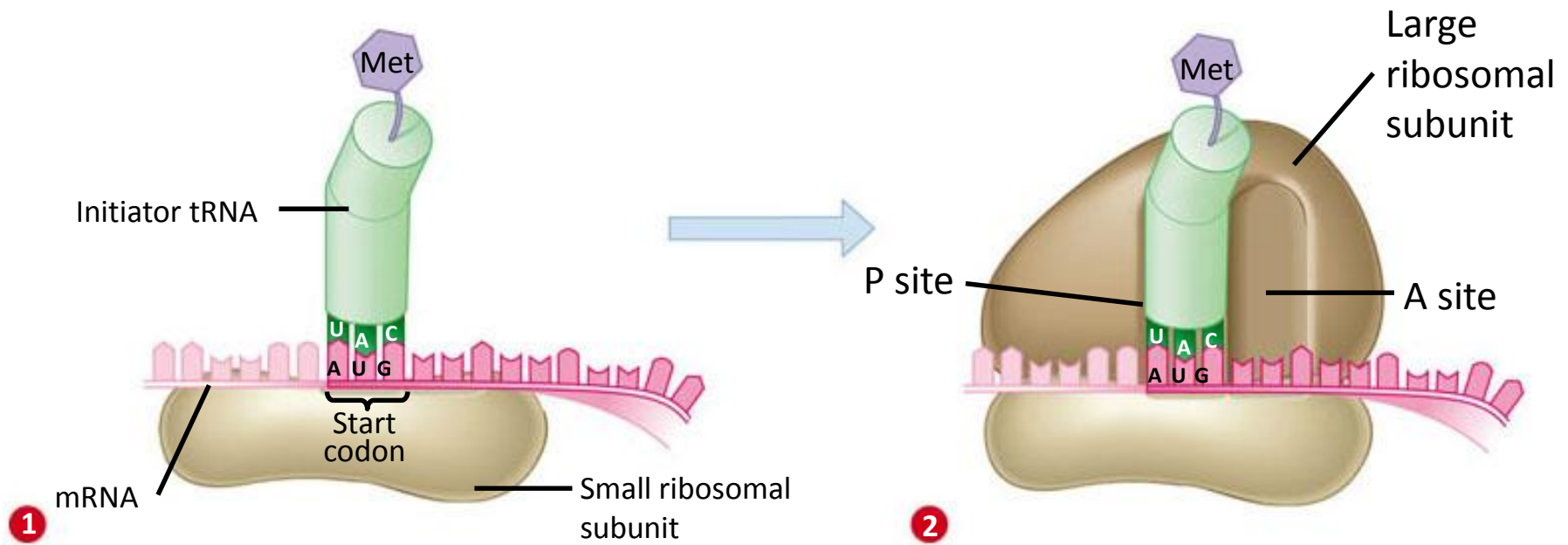


Figure 10.13B

10.14 Elongation adds amino acids to the polypeptide chain until a stop codon terminates translation

- Once initiation is complete
 - Amino acids are added one by one to the first amino acid
- Each addition of an amino acid
 - Occurs in a three-step elongation process
- 1. Codon recognition – anticodon with tRNA with it's a.a. pairs with mRNA codon at A site
- 2. Peptide bond formation – ribosome catalyzes the bond
- 3. Translocation – P-site tRNA now leaves and the ribosome moves (translocates) the tRNA in the A-site to the P-site with its attached polypeptide
- Elongation continues until a stop codon reaches the ribosomes A site. (UAA, UAG, UGA)

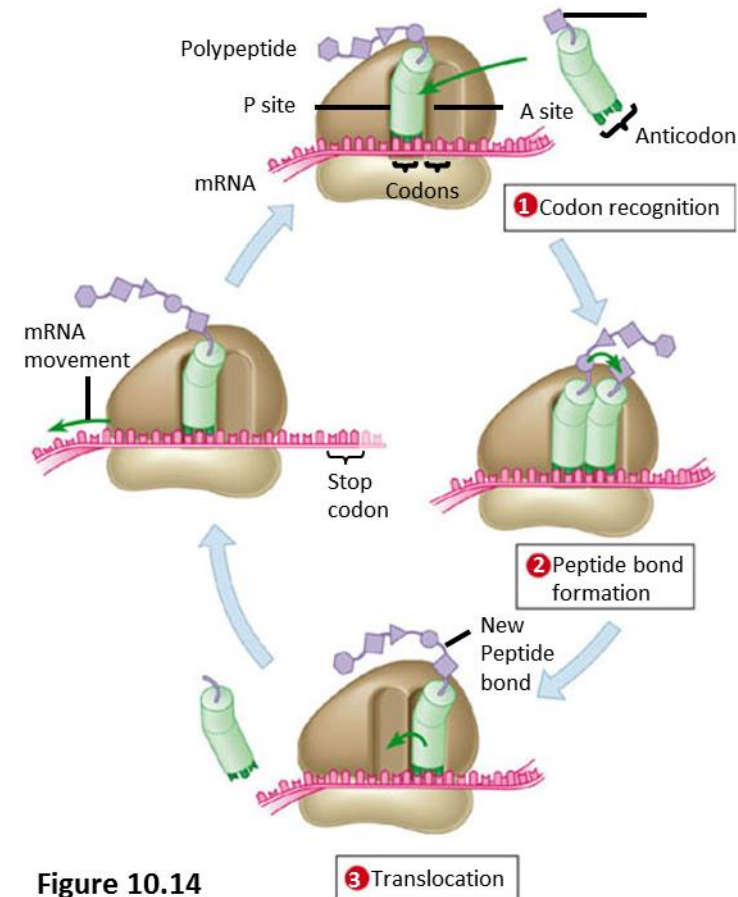
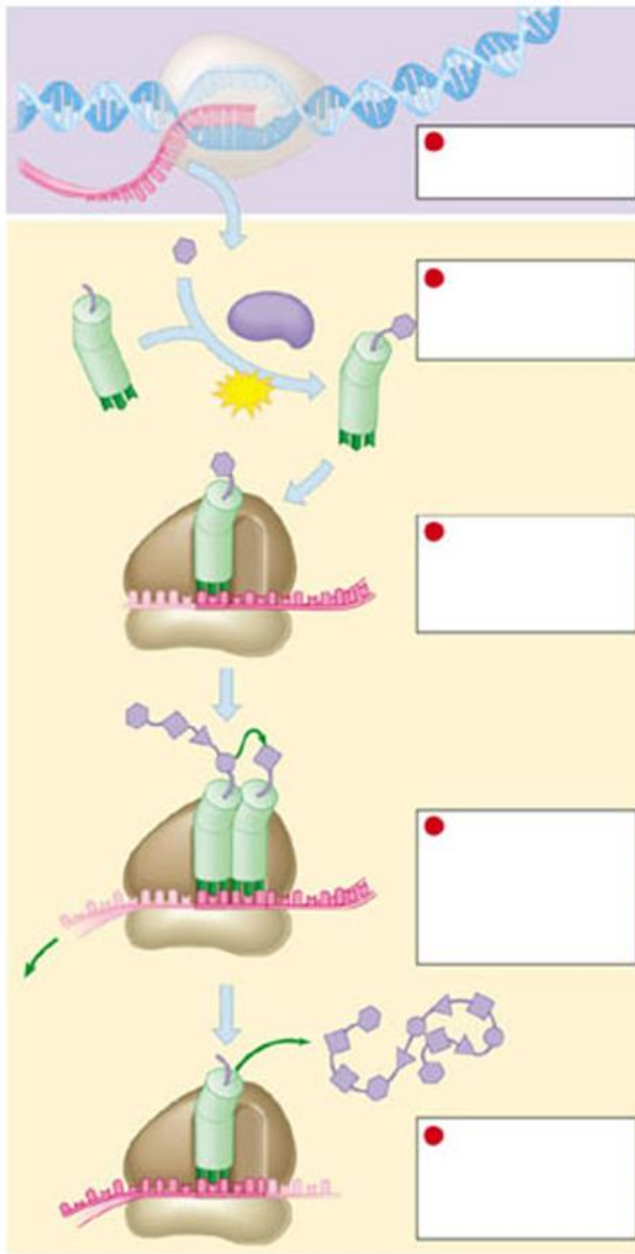


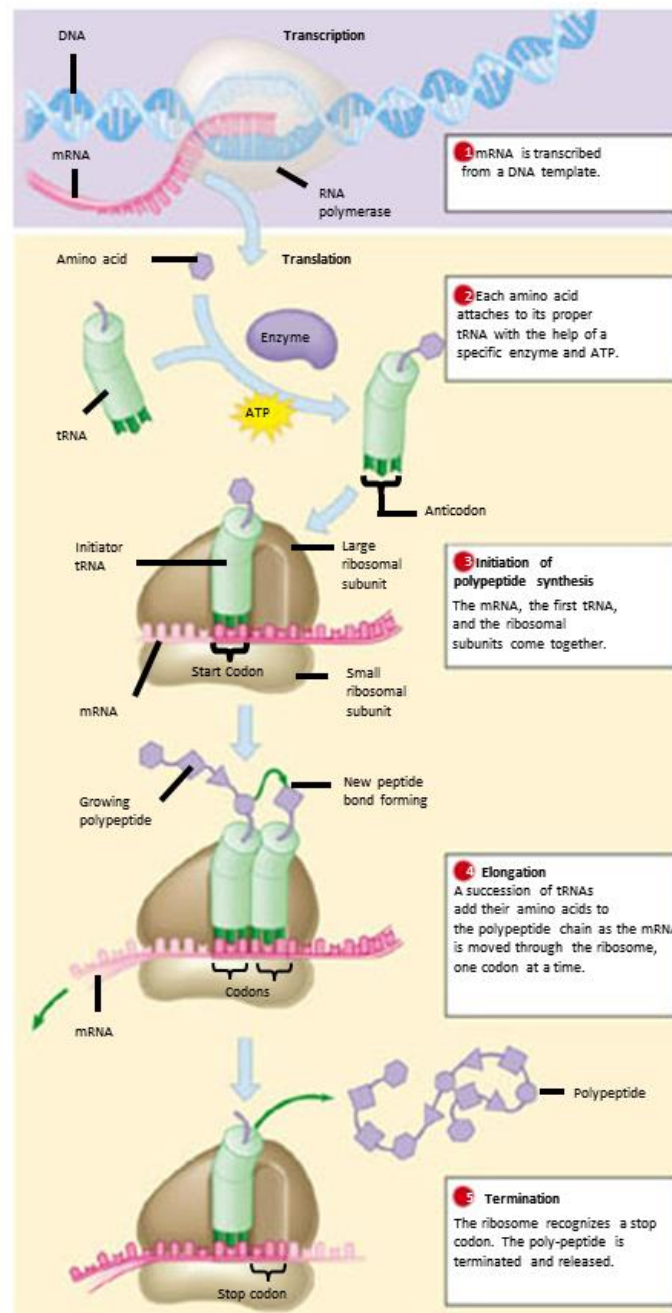
Figure 10.14

10.15 Review: The flow of genetic information in the cell is DNA→RNA→protein

- The sequence of codons in DNA, via the sequence of codons
 - Spells out the primary structure of a polypeptide

Summary of transcription
and translation





10.16 Mutations can change the meaning of genes

- Mutations are changes in the DNA base sequence
 - Caused by errors in DNA replication or recombination, or by mutagens
 - Mutagens include chemical (bases that are similar) or physical (radiation, x-rays, uv light)
 - Can be positive, negative or neutral
 - Single change can alter one amino acid causing sickle-cell from one change to a nucleotide

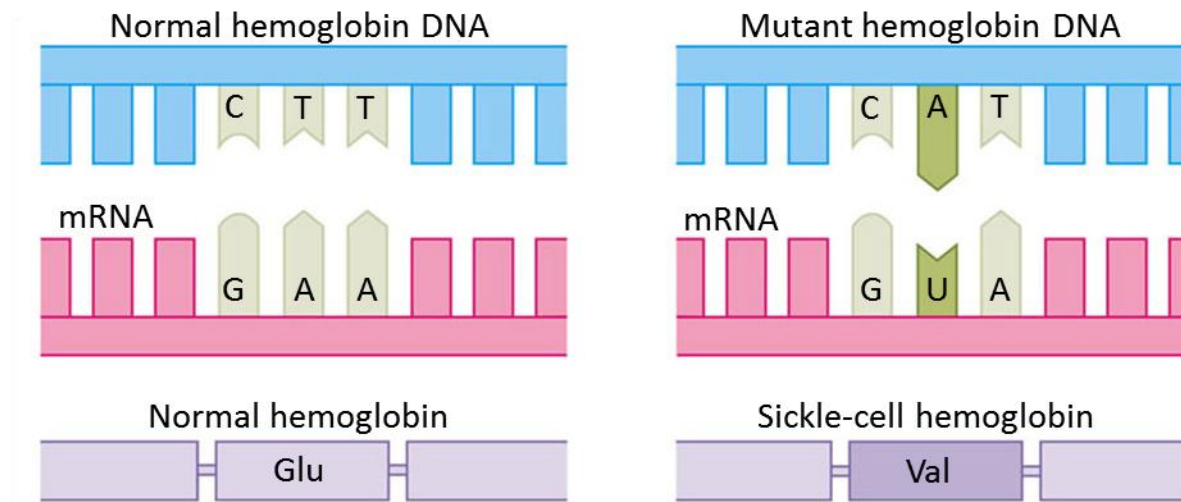


Figure 10.16A

Mutations

- Substituting, inserting, or deleting nucleotides alters a gene
 - With varying effects on the organism

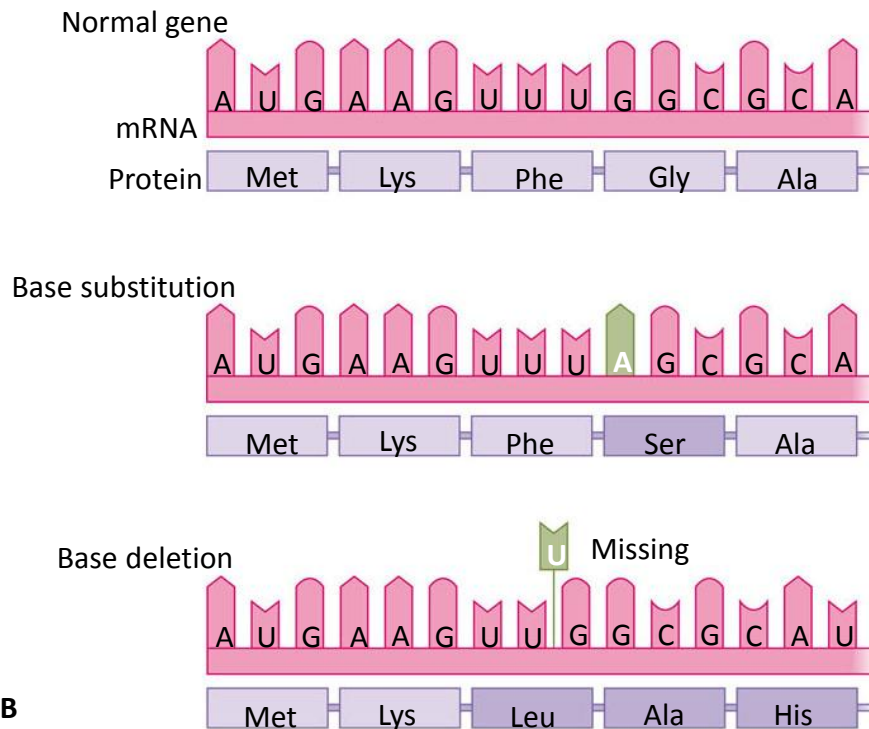


Figure 10.16B

Recombinant DNA technology

Is a set of laboratory techniques for combining genes from different sources – even different species – into a single DNA molecule

Recombinant DNA technology is widely used to alter the genes of many types of cells for practical purposes from cancer drugs to pesticides

Furthermore, genes have been transferred from bacteria to plants and from humans to farm animals

Ch. 12 – Recombinant DNA Technology

To manipulate genes in the lab,

- Bacterial plasmids may be used
- Enzymes can be used to 'cut and paste' DNA
- Genes can be cloned in recombinant plasmids
- Nucleic acid probes

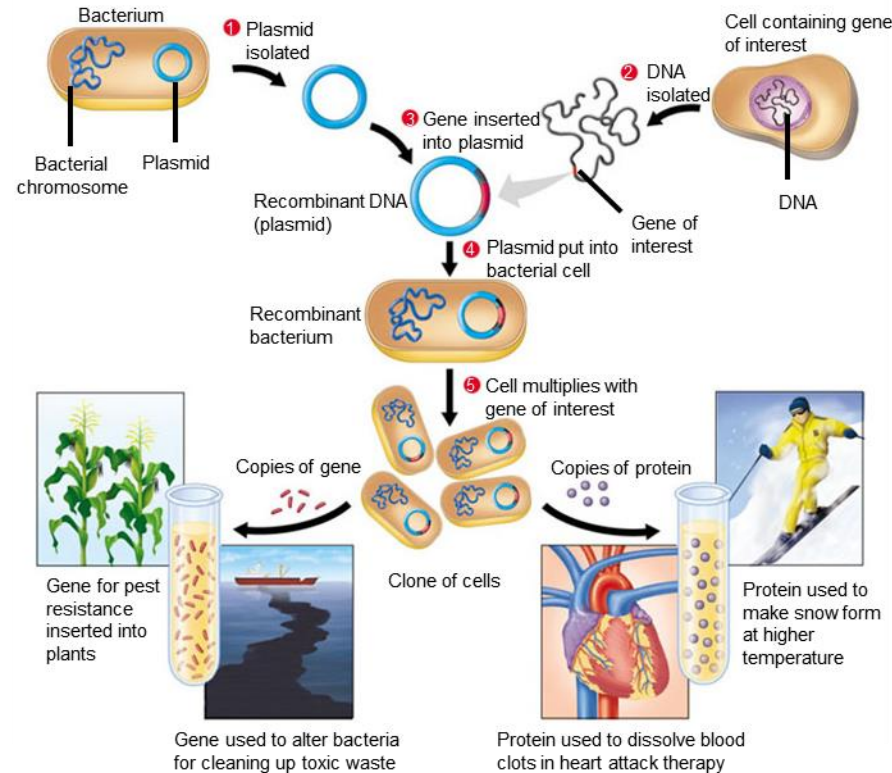


Figure 12.1

Recombinant DNA technology

TABLE 12.6 SOME PROTEIN PRODUCTS OF RECOMBINANT DNA TECHNOLOGY

Product	Made In	Use
Human insulin	<i>E. coli</i>	Treatment for diabetes
Human growth hormone (HGH)	<i>E. coli</i>	Treatment for growth defects
Epidermal growth factor (EGF)	<i>E. coli</i>	Treatment for burns, ulcers
Interleukin-2 (IL-2)	<i>E. coli</i>	Possible treatment for cancer
Bovine growth hormone (BGH)	<i>E. coli</i>	Improving weight gain in cattle
Cellulase	<i>E. coli</i>	Breaking down cellulose for animal feeds
Taxol	<i>E. coli</i>	Treatment for ovarian cancer
Interferons (alpha and gamma)	<i>S. cerevisiae</i> ; <i>E. coli</i>	Possible treatment for cancer and viral infections
Hepatitis B vaccine	<i>S. cerevisiae</i>	Prevention of viral hepatitis
Erythropoietin (EPO)	Mammalian cells	Treatment for anemia
Factor VIII	Mammalian cells	Treatment for hemophilia
Tissue plasminogen activator (TPA)	Mammalian cells	Treatment for heart attacks

Table 12.6

Other applications and Info

Recombinant DNA can lead to mass-produce gene products

Leads to change in pharmaceutical industry and medicine

- Therapeutic Hormones
- Diagnosis and treatment of disease
- Vaccines
- Gene therapy
- Genetically modifying in agriculture

There are risks associated with this that scientists don't know about.

Chapter 12 in your text has lots of additional information on the topics above.