

# BIEN 500

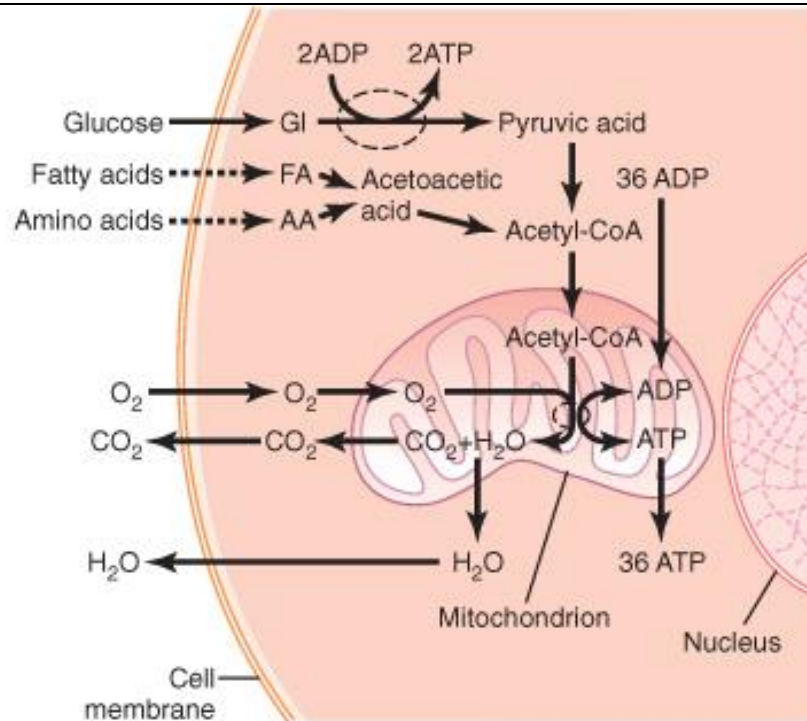
## Lecture 2

### Dr. DeCoster

Introduction to Physiology: The cell and General Physiology.

- Finish up of Chap 2. The cell and its functions.
- Chap 3. Genetic control of protein synthesis, cell function, and cell reproduction.

# Extraction of energy from nutrients- function of the mitochondria



© Elsevier. Guyton & Hall: Textbook of Medical Physiology 11e - [www.studentconsult.com](http://www.studentconsult.com)

- In the human body, essentially all carbohydrates are converted to glucose by the digestive tract and liver before they reach the other cells of the body. Similarly, proteins are converted into amino acids and fats into fatty acids- Figure 2-14. Almost all of these **oxidative** reactions occur inside the mitochondria, and the energy that is released is used to form the high-energy compound ATP. Then, ATP, not the original foodstuffs, is used throughout the cell to energize almost all the subsequent intracellular metabolic reactions.

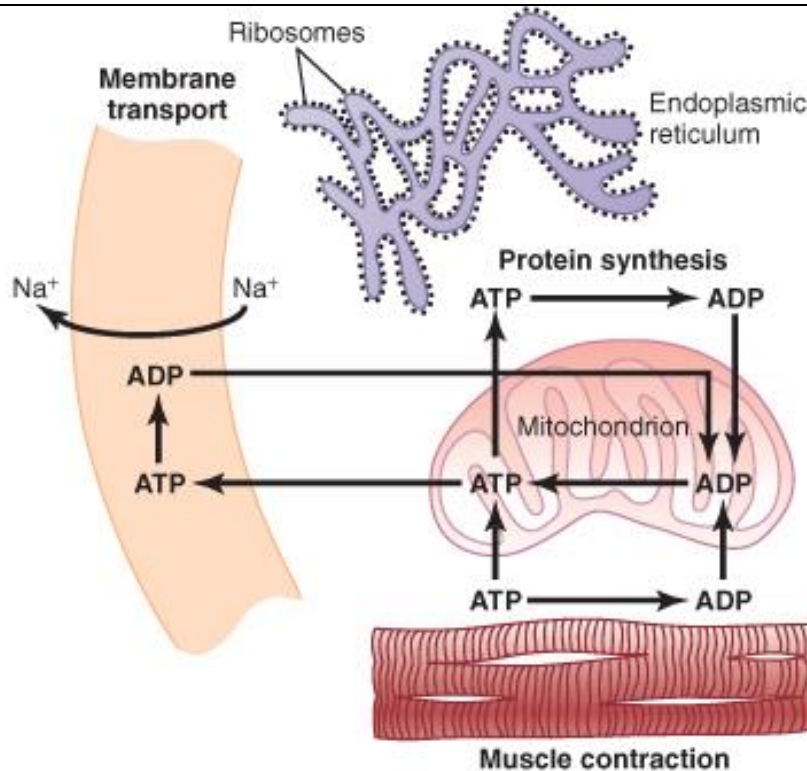
# Chemical processes in the formation of ATP- role of the mitochondria

- On entry into the cells, glucose is subjected to enzymes in the cytoplasm that convert it into pyruvic acid (a process called glycolysis). A **small** amount of **ADP (what is this?)** is changed to ATP by glycolysis, but this accounts for less than 5% of the overall energy metabolism of the cell: **THIS IS DONE W/O OXYGEN.**
- By far, the major portion of the ATP formed in the cell, about 95%, is formed in the mitochondria. The pyruvic acid derived from carbohydrates, fatty acids from lipids, and amino acids from proteins are eventually converted into the compound **acetyl-CoA** in the matrix of the mitochondrion.
- This substance in turn is further altered to extract energy by another series of enzymes in the mitochondrion matrix, in a sequence of chemical reactions called the citric acid cycle or Krebs cycle.

# ATP- Mitochondria-2

- In this citric acid cycle, acetyl-CoA is split into its component parts, hydrogen atoms and carbon dioxide. The carbon dioxide diffuses out of the mitochondria and eventually out of the cell; finally it is excreted from the body through the lungs.
- The hydrogen atoms, conversely, are highly reactive, and they combine instantly with oxygen that has also diffused into the mitochondria. This releases a tremendous amount of energy which is used by the mitochondria to convert very large amounts of ADP to ATP, with the byproduct being water.
- Newly formed ATP is transported out of the mitochondria into all parts of the cell cytoplasm and nucleoplasm, where its energy is used to energize multiple cell functions.

# How is ATP used?: Uses of ATP for cellular function

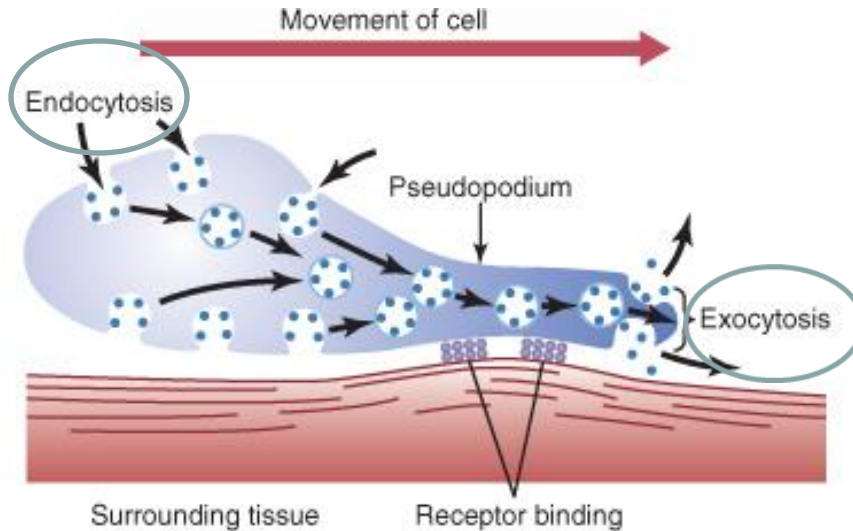


© Elsevier. Guyton & Hall: Textbook of Medical Physiology 11e - [www.studentconsult.com](http://www.studentconsult.com)

- Energy from ATP is used to promote three major categories of cellular functions: 1) transport of substances through multiple membranes in the cell, 2) synthesis of chemical compounds throughout the cell, and 3) mechanical work. These uses of ATP are illustrated by examples in fig. 2-15.
- -Membrane transport is so important to cell function that some cells- the renal tubular cells for instance, use as much as 80% of the ATP that they form for this purpose alone.
- Some cells use as much as 75% of all the ATP formed in the cell simply to synthesize new chemical compounds, especially protein molecules; this is particularly true during the growth phase of cells.
- -mechanical work includes muscle contraction and ciliary and amoeboid motion.

# Another example of ATP use:

## Locomotion of cells



© Elsevier. Guyton & Hall: Textbook of Medical Physiology 11e - [www.studentconsult.com](http://www.studentconsult.com)

Amoeboid movement is movement of an entire cell in relation to its surroundings, such as movement of white blood cells through tissues. Figure 2-16 shows schematically the process of amoeboid movement by a cell. The basic principal of amoeboid motion is the result of **continual formation** of new cell membrane at the leading edge of the pseudopodium and **continual absorption** of the membrane in mid and rear portions of the cell.

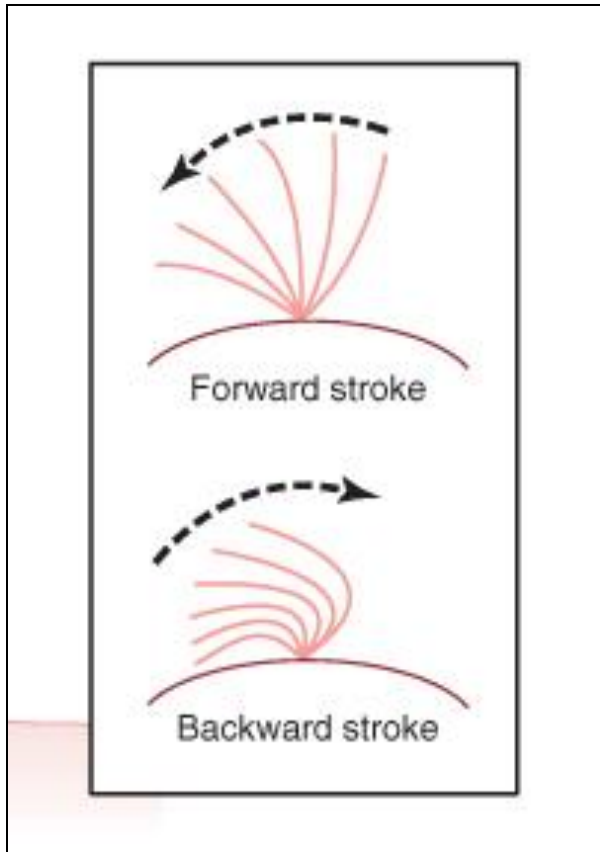
**Examples:** Types of cells that exhibit amoeboid locomotion.

- The most common cells that exhibit amoeboid locomotion in the human body are the white blood cells when they move out of the blood into the tissues in the form of tissue macrophages.
- Some other cell types are mobile such as fibroblasts which move into an area of injury.
- Finally, cell locomotion is especially important in development of the embryo and fetus where embryonic cells often must migrate long distances from their sites of origin to new areas to form target tissues.

# Control of ameboid locomotion-chemotaxis

- The most important initiator of ameboid locomotion is the process called chemotaxis. This process is caused by chemical substances called chemotactic substances.
- Most cells that exhibit ameboid locomotion move toward the source of a chemotactic substance, that is, from an area of lower concentration toward an area of higher concentration- which is called positive chemotaxis.
- Some cells move away from the source, which is called negative chemotaxis.

# Cilia and ciliary movements



- Ciliary movement is a whiplike motion of cilia on the surfaces of cells. This occurs in the human body on the surfaces of the respiratory airways and on the inside surfaces of the uterine tubes (fallopian tubes) of the reproductive tract.
- Figure 2-17. in the inset of Figure 2-17, movement of the cilium is shown. The cilium moves forward with a sudden, rapid whiplike stroke 10-20 times per second, bending sharply where it projects from the surface of the cell. Then it moves backward slowly to its initial position.
- The rapid forward-thrusting, whiplike movement pushes the fluid lying adjacent to the cell in the direction that the cilium moves; the slow, dragging movement in the backward direction has almost no effect on fluid movement.
- As a result, the fluid is continually propelled in the direction of the fast-forward stroke. Because most ciliated cells have large numbers of cilia on their surfaces and because all of the cilia are oriented in the same direction, this is an effective means for moving fluids from one part of the surface to another.



# --Chapter 3: genetic control of protein synthesis, cell function and cell reproduction

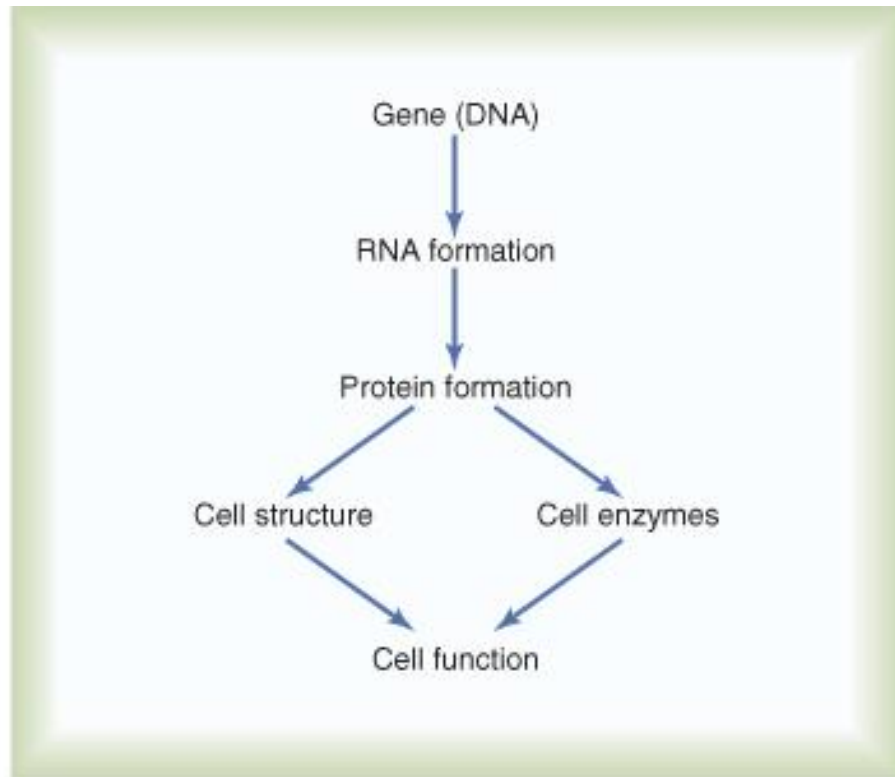
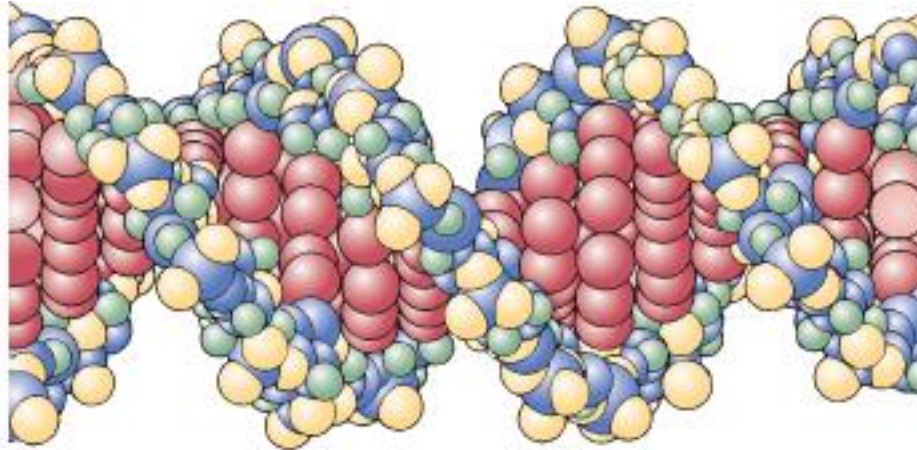


Fig. 3-1 shows the general schema of genetic control

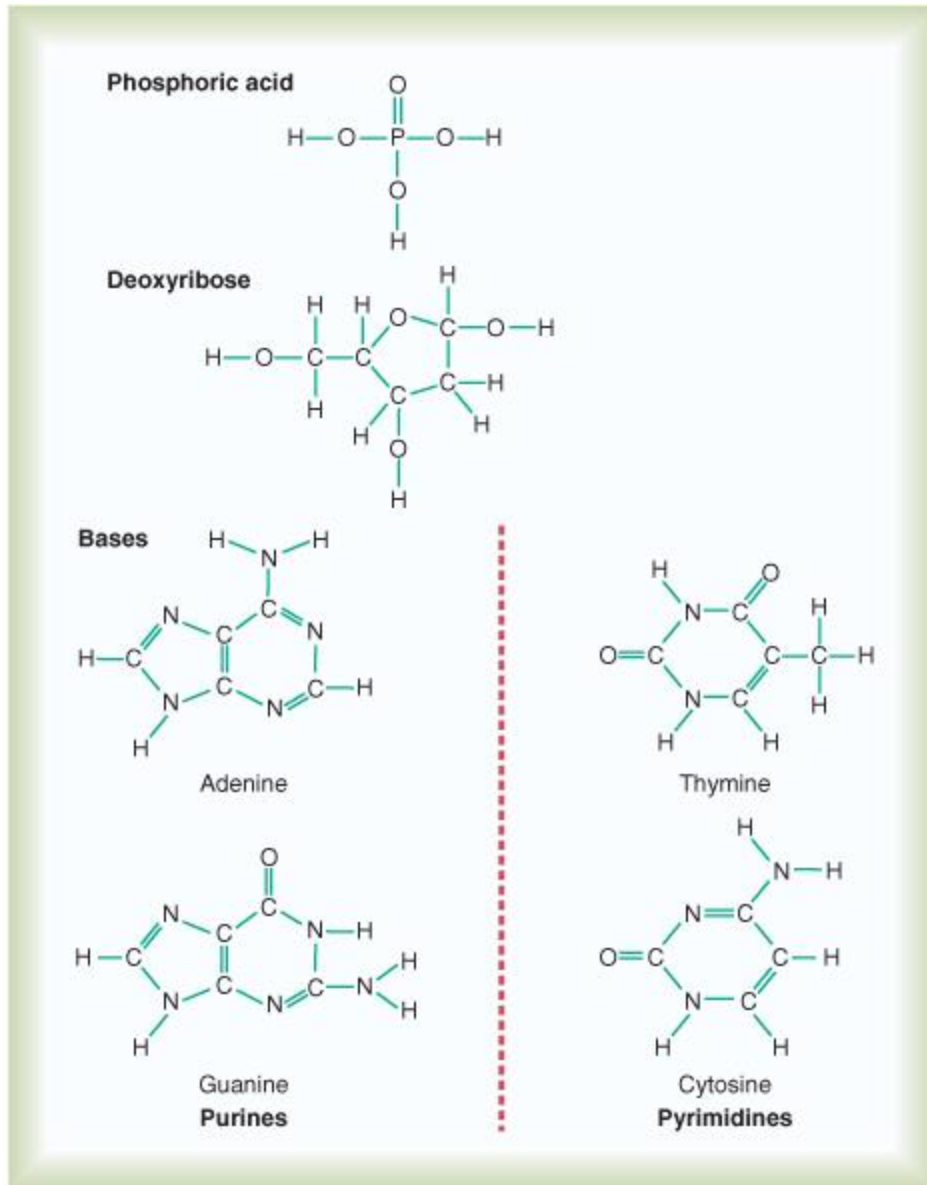
# DNA-1 → Protein



© Elsevier. Guyton & Hall: Textbook of Medical Physiology 11e - [www.studentconsult.com](http://www.studentconsult.com)

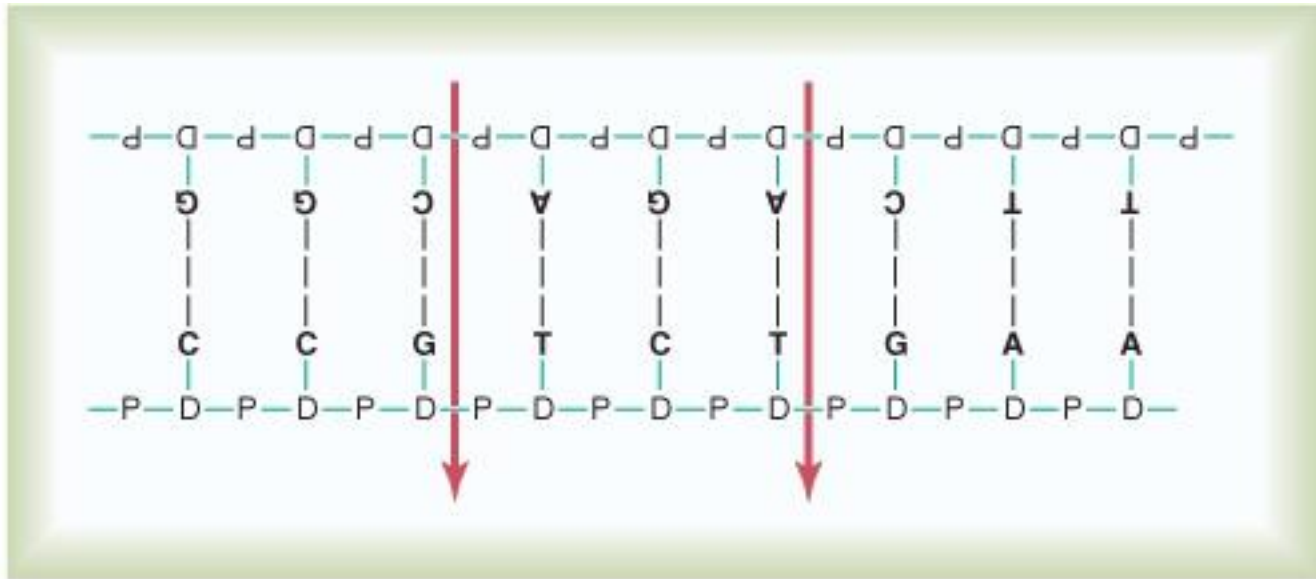
- In the cell nucleus large numbers of genes are attached end on end in extremely long double-stranded helical molecules of DNA. A very short segment of such a molecule is shown in fig. 3-2.

# Basic building blocks of DNA



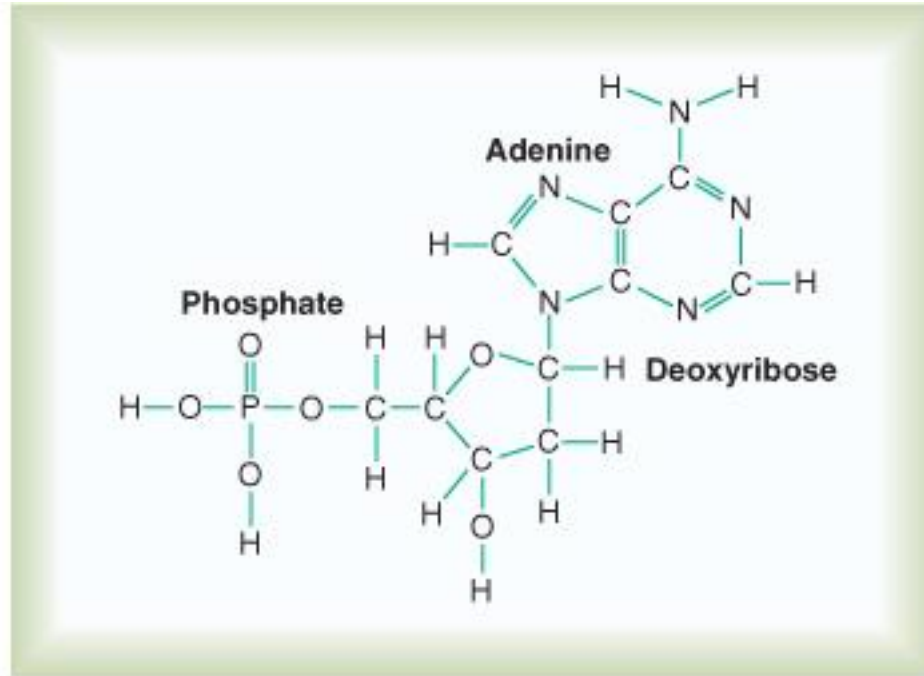
- Fig. 3-3. **COMPONENTS:** Basic building blocks include 1) phosphoric acid, 2) a sugar called deoxyribose, and 3) four nitrogenous bases (two purines—adenine and guanine and two pyrimidines—cytosine and thymine).
- The phosphoric acid and deoxyribose form the two helical strands that are the backbone of the DNA molecule, and the nitrogenous bases lie between the two strands and connect them (fig. 3-6).-Next Slide

Arrangement of deoxyribose nucleotides in a double strand of DNA (serves as a template).



© Elsevier. Guyton & Hall: Textbook of Medical Physiology 11e - [www.studentconsult.com](http://www.studentconsult.com)

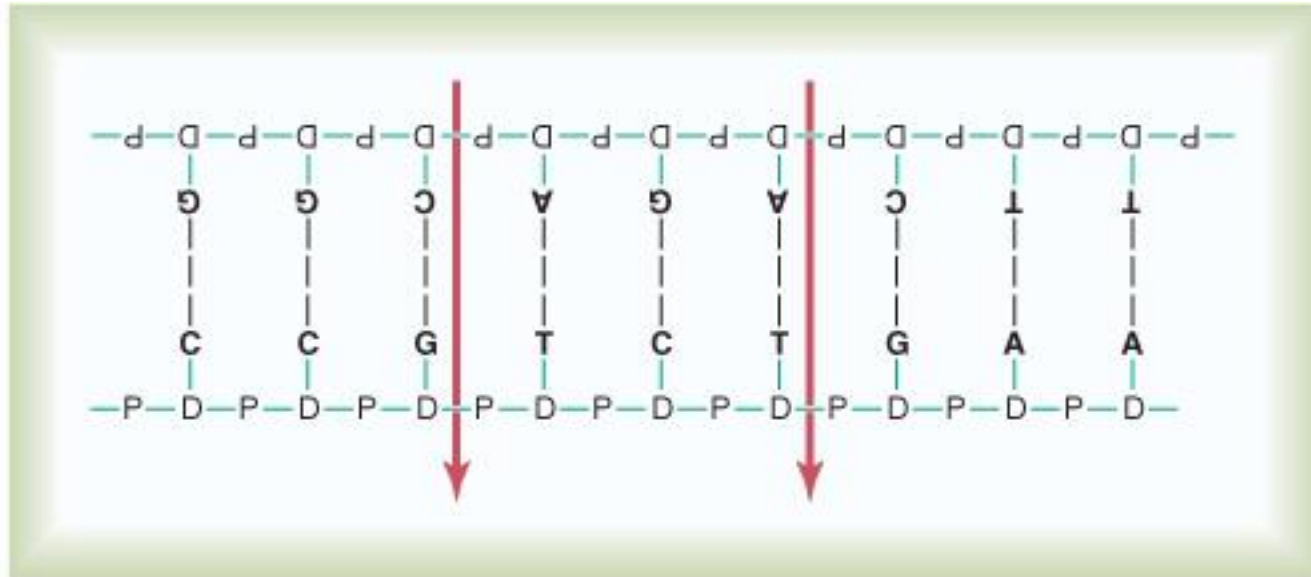
# Nucleotides.



© Elsevier. Guyton & Hall: Textbook of Medical Physiology 11e - [www.studentconsult.com](http://www.studentconsult.com)

- The first stage in the formation of DNA is to combine one molecule each of phosphoric acid, deoxyribose, and one of four bases to form an acidic nucleotide example shown in fig. 3-4.

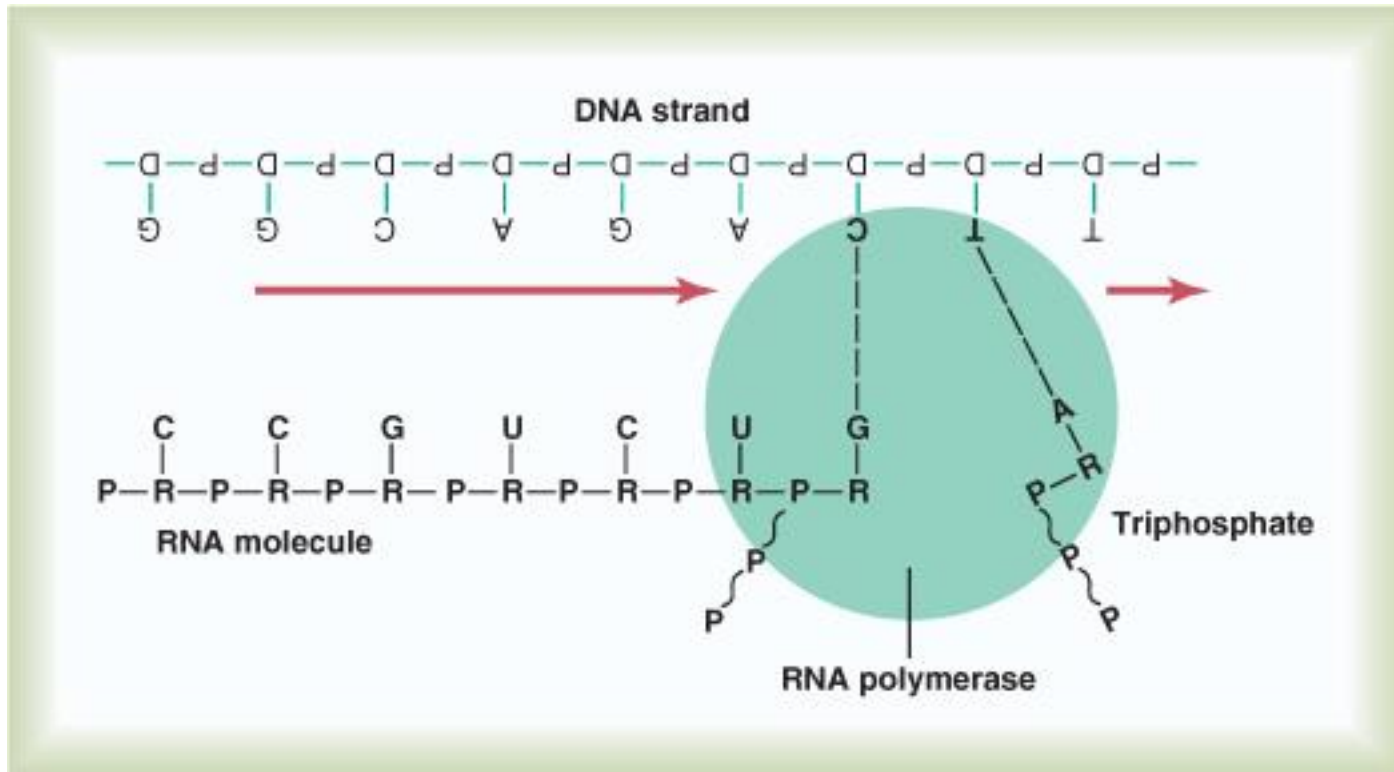
# Organization of the nucleotides to form two strands of DNA loosely bound to each other.



© Elsevier. Guyton & Hall: Textbook of Medical Physiology 11e - [www.studentconsult.com](http://www.studentconsult.com)

Fig. 3-6 shows the manner in which multiple numbers of nucleotides are bound together to form two strands of DNA. The two strands are in turn, **loosely bonded** with each other by weak cross linkages (hydrogen **bonds-why is weak bonding important?**) illustrated in fig. 3-6 by the central dashed lines. 1) Each purine base **adenine** of one strand always bonds with pyrimidine base **thymine** of the other strand and 2) each purine base **guanine** always bonds with a **cytosine** pyrimidine base.

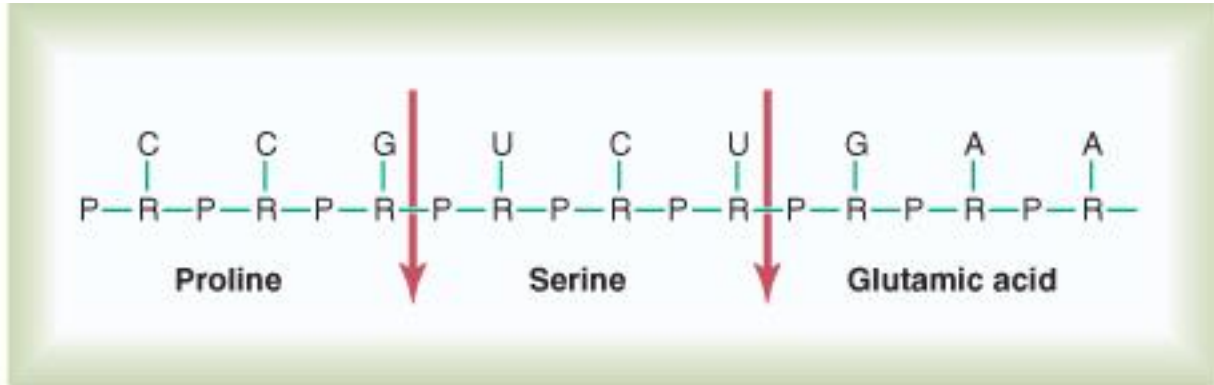
# Genetic code



© Elsevier. Guyton & Hall: Textbook of Medical Physiology 11e - [www.studentconsult.com](http://www.studentconsult.com)

- The importance of DNA lies in its ability to control the formation of proteins in the cell. It does this by means of the so called genetic code.
- Thus when the two strands of a DNA molecule are pulled apart, this exposes the bases projecting to the side of each DNA strand as shown in the top strand in fig. 3-7.

# Genetic code-2



© Elsevier. Guyton & Hall: Textbook of Medical Physiology 11e - [www.studentconsult.com](http://www.studentconsult.com)

- The genetic code consists of successive triplets of bases, that is, each three successive bases is a code word that results in an amino acid, the sequence of which make up the final protein.
- The RNA chain uses the triplet codons to form specific amino acids as shown in fig. 3-8.



# Genetic code-3

- The DNA code in the cell nucleus is transferred to an RNA code in the Cell cytoplasm—the process of **transcription**.
- The process of transferring the DNA code to RNA is called transcription, after this process, the RNA diffuses from the nucleus through nuclear pores (**lecture 1**) into the cytoplasm compartment, where it controls protein synthesis.
- Basic building blocks of RNA.
- Similar to DNA except that ribose is used rather than deoxyribose and thymine is replaced by another pyrimidine= uracil.
- Activation of the RNA nucleotides
- Nucleotides are added to the growing RNA molecule via addition of two high energy phosphate radicals to form triphosphates (shown in fig. 3-7)- these phosphates are derived from ATP in the cell. The energy from the ATP is thus used to add nucleotides to the growing RNA chain.

# Transcription details

- These steps are carried out under the influence of an enzyme RNA polymerase that has many functional properties necessary for formation of the RNA molecule.
- 1. The DNA strand immediately ahead of the initial gene is a sequence of nucleotides called the **promoter**. The RNA polymerase has an appropriate complementary structure that recognizes this promoter and becomes attached to it. *This is the essential step for initiating formation of the RNA molecule.*
- 2. After the RNA polymerase attachment, the polymerase causes **unwinding** of about two turns of the DNA helix and separation of the unwound portions of the two strands.

# Transcription details-2

- 3. As the polymerase moves along the DNA strand, it temporarily *unwinds and separates the two DNA strands at each stage* of its movement. As it moves along, it adds at each stage a new activated RNA nucleotide to the end of the newly forming RNA chain by the following steps:
  - 3a: First it causes a hydrogen bond to form between the end base of the DNA strand and the base of an RNA nucleotide in the nucleoplasm.
  - 3b: Then, one at a time, *the RNA polymerase breaks two of the three phosphate radicals away from each of these RNA nucleotides*, liberating large amounts of energy from the broken high-energy phosphate bonds; *this energy is used to cause covalent linkage of the remaining phosphate on the nucleotide with the ribose on the end of the growing RNA chain* (fig. 3-7).
  - 3c: When the RNA polymerase reaches the end of the DNA gene, it encounters a new sequence of DNA nucleotides called the *chain-terminating sequence= STOP!*; *this causes the polymerase and the newly formed RNA chain to break away from the DNA strand*. Then the polymerase can be used again and again to form still more new RNA chains (*why?, what kind of molecule is RNA polymerase?*).
  - 3d: As the new RNA strand is formed, its weak hydrogen bonds with the DNA template break away, because *the DNA has a high affinity for rebonding with its own complementary DNA strand*. Thus, the RNA chain is forced away from the DNA and is released into the nucleoplasm.

# Transcription details-3

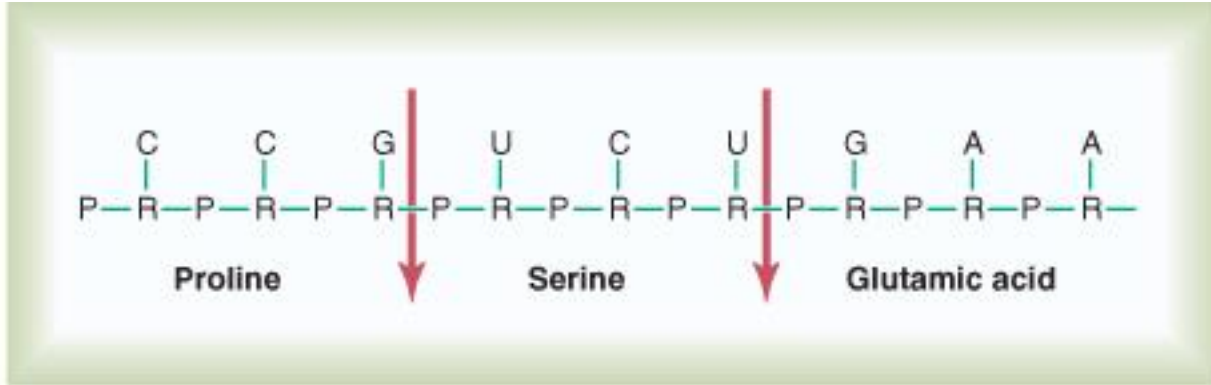
- Thus, the code that is present in the DNA strand is eventually transmitted in complementary form to the RNA chain. The ribose nucleotide bases always combine with the deoxyribose bases in the following combination:

<u>DNA base</u>	<u>RNA base</u>
• guanine	cytosine
• cytosine	guanine
• adenine	uracil
• thymine	adenine

# Three different types of RNA

- The 3 types of RNA have different functions:
- 1. Messenger RNA: carries the genetic code to the cytoplasm for controlling the type of protein formed.
- 2. Transfer RNA: transports activated amino acids to the ribosomes to be used in assembling the protein molecule.
- 3. Ribosomal RNA: along with about 75 different proteins, forms ribosomes, the physical and chemical structures on which protein molecules are actually assembled.

# RNA codons= triplet of bases



© Elsevier. Guyton & Hall: Textbook of Medical Physiology 11e - [www.studentconsult.com](http://www.studentconsult.com)

- Figure 3-8 shows a small segment of a molecule of messenger RNA. Its codons for the amino acids proline, serine, and glutamic acid are shown.

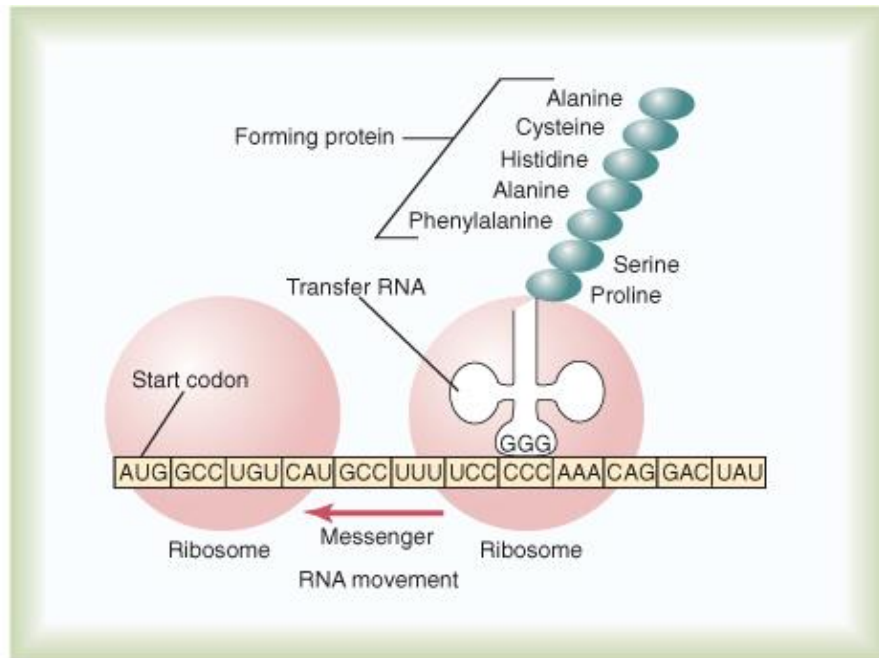
RNA codons for the different amino acids.

Table 3-1 (Book) gives the RNA codons for the 20 different amino acids found in protein molecules. Note that most of the amino acids are represented by more than one codon; also, one codon represents the signal “start” and three codons represent “stop”.

# Transfer RNA- the anticodons

- Another type of RNA that plays an essential role in protein synthesis is called transfer RNA (tRNA), because it transfers amino acid molecules to protein molecules as the protein is being synthesized. Each type of tRNA combines specifically with 1 of 20 amino acids that are to be incorporated into proteins.
- The tRNA then acts as a carrier to transport its specific type of amino acid to the ribosomes, where protein molecules are forming. In the ribosomes, each specific type of tRNA recognizes a particular codon on the messenger RNA (mRNA), and thereby delivers the appropriate amino acid to the appropriate place in the chain of the newly forming protein molecule

# tRNA-2



© Elsevier. Guyton & Hall: Textbook of Medical Physiology 11e - [www.studentconsult.com](http://www.studentconsult.com)

- Because the function of tRNA is to cause attachment of a specific amino acid to a forming protein chain, it is essential that each type of tRNA also have specificity for a particular codon in the mRNA (fidelity of translation). The specific code in the tRNA that allows it to recognize a specific codon is again a triplet of nucleotide bases and is called an anticodon. This is located approximately in the middle of the tRNA molecule (at the bottom of the cloverleaf configuration show in fig. 3-9).

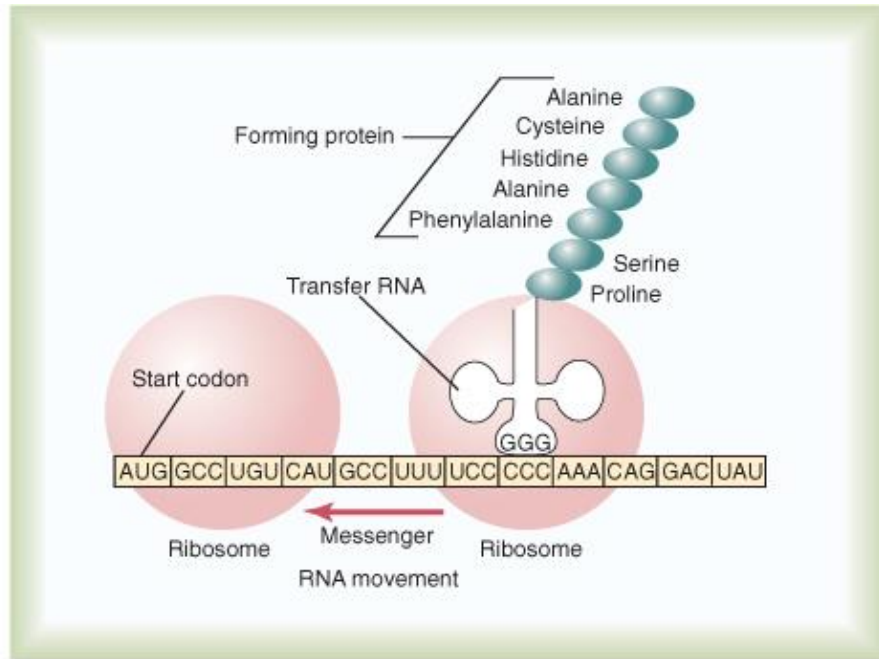
During formation of the protein molecule, the anticodon bases combine loosely by hydrogen bonding with the codon bases of the mRNA. In this way, the respective amino acids are lined up one after another along the mRNA chain, thus establishing the appropriate sequence of amino acids in the newly forming protein molecule.



# Ribosomal RNA

- The third type of RNA in the cell is ribosomal RNA: it constitutes about 60% of the ribosome. The remainder of the ribosome is protein, containing about 75 types of proteins that are both structural proteins and enzymes needed in the manufacture of protein molecules.
- Formation of ribosomes in the nucleolus.
- As the ribosomal RNA forms, it collects in the nucleolus, a specialized structure lying adjacent to the chromosomes. When large amounts of ribosomal RNA are being synthesized in cell manufacturing large amounts of protein, the nucleolus is a large structure, whereas in cells that synthesize little protein, the nucleolus may not even be seen.
- --Proteins are formed in the cytoplasm of the cell, but not in the cell nucleus, because the nucleus does not contain mature ribosomes.

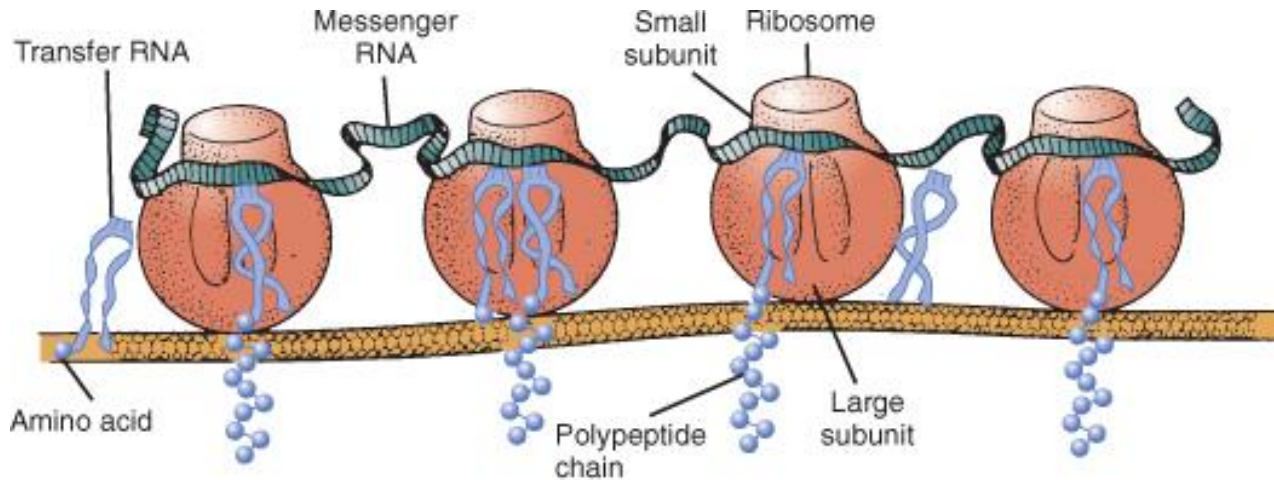
# Formation of proteins on the ribosomes- the process of *translation*



© Elsevier. Guyton & Hall: Textbook of Medical Physiology 11e - [www.studentconsult.com](http://www.studentconsult.com)

- When a molecule of mRNA comes in contact with a ribosome, it travels through the ribosome, beginning at a predetermined end of the RNA molecule specified by an appropriate sequence of RNA bases called the chain-initiating codon.
- Then, as shown in fig. 3-9, while the mRNA travels through the ribosome, a protein molecule is formed- a process called translation. Thus the ribosome reads the codons of the mRNA in much the same way that a tape is read as it passes through the playback head of a tape recorder.
- Then, when a stop or chain-terminating codon slips past the ribosome, the end of a protein molecule is signaled and the protein molecule is freed into the cytoplasm

# Polyribosomes



© Elsevier. Guyton & Hall: Textbook of Medical Physiology 11e - [www.studentconsult.com](http://www.studentconsult.com)

- A single mRNA molecule can form protein molecules in several ribosomes at the same time because the initial end of the RNA strand can pass to a successive ribosome as it leaves the first, as shown in figs. 3-9 and 3-10.
- The protein molecules are in different stages of development in each ribosome. As a result, clusters of ribosomes frequently occur, 3 to 10 ribosomes being attached to a single mRNA at the same time. These clusters are called polyribosomes
- Many ribosomes attach to the ER.
- Note in fig. 3-10 newly forming polypeptide (protein) chains passing through the ER membrane into the endoplasmic matrix. It should be noted that except in glandular cells in which large amounts of protein-containing secretory vesicles are formed, *most proteins synthesized by the ribosomes are released directly into the cytosol* instead of into the ER = **targeting of the protein product**.

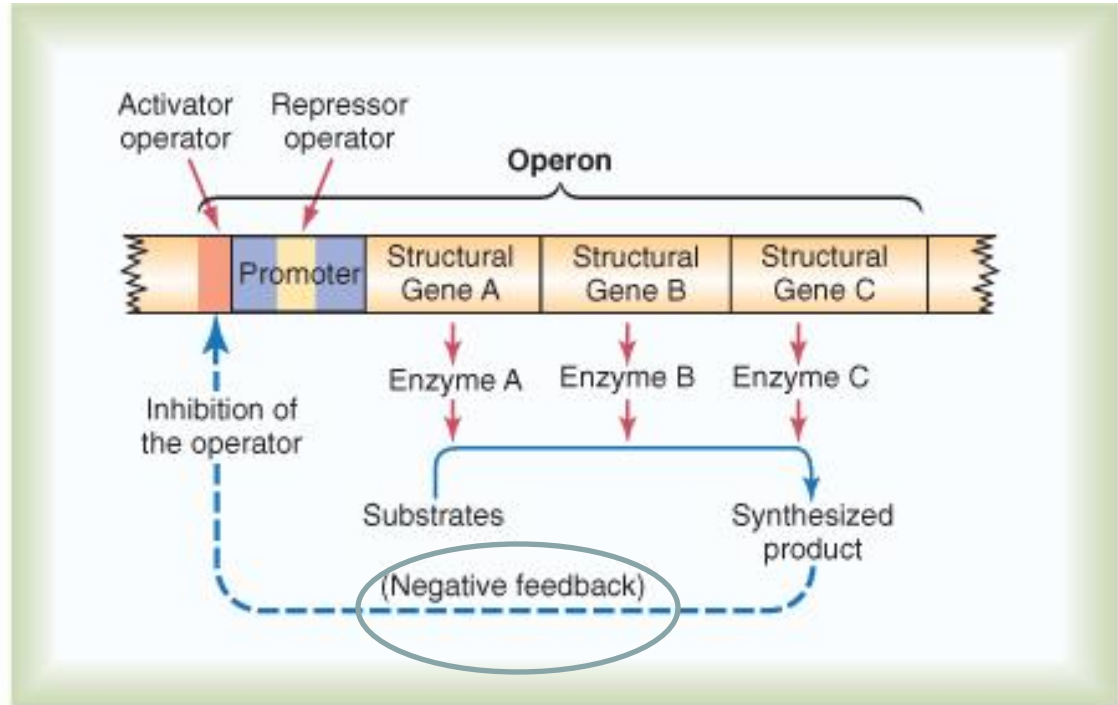
# Chemical steps in protein synthesis

- A total of 4 high-energy bonds are used for each amino acid added to the protein chain in protein synthesis, making this process one of the most energy-consuming processes of the cell.
- -the amino acids in the protein chain are linked via a *peptide linkage*.

# Control of gene function and biochemical activity in cells

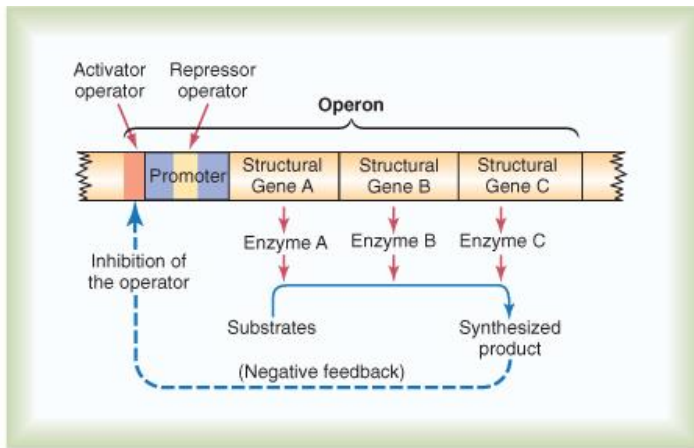
- The degree of activation of respective genes must be controlled. (why?)
- there are basically two methods by which the biochemical activities in the cell are controlled.
- One of these is genetic regulation and the other is enzyme regulation

# Genetic regulation



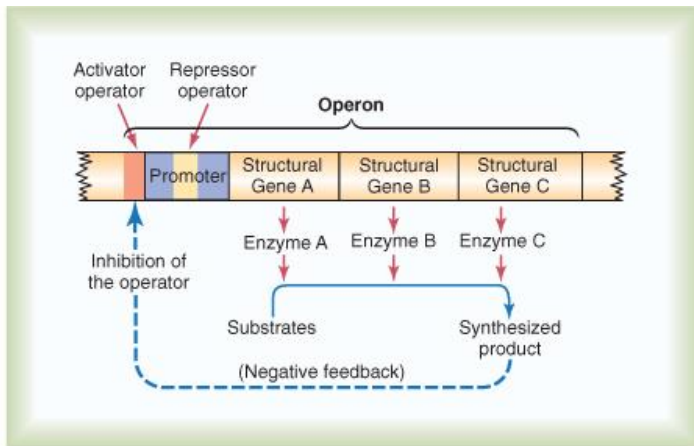
- The operon of the cell and its control of biochemical synthesis- function of the promoter.
- Synthesis of a cellular biochemical product usually requires a series of reactions, and each of these reactions is catalyzed by a special protein enzyme. Formation of all the enzymes needed for the synthetic process often is controlled by a sequence of genes located one after another on the same chromosomal DNA strand. This area of the DNA is called an *operon*, and the genes responsible for forming the respective enzymes are called structural genes.
- In fig. 3-12 three respective structural genes are shown in an operon, and it is demonstrated that they control the formation of three respective enzymes that in turn cause synthesis of a specific intracellular product – **and note the negative feedback (more later).....**
- Note in the figure the segment on the DNA called the *promoter*. This is a group of nucleotides that has specific affinity for RNA polymerase, as already discussed. This polymerase must bind with this promoter before it can begin traveling along the DNA strand to synthesize RNA. Therefore, *the promoter is an essential element for activating the operon.*

# Control of the operon by a repressor protein



- Also note in figure 3-12 an additional band of nucleotides lying in the middle of the promoter. This area is called a **repressor** because a regulatory protein can bind here and prevent attachment of RNA polymerase to the promoter, thereby blocking transcription of the genes of this operon. Such a negative regulatory protein is called a **repressor protein**.
- The operon can also be controlled by activator proteins, as shown in fig. 3-12

# Negative feedback control of the operon



- Finally, note that in fig. 3-12 that the presence of a critical amount of a synthesized product in the cell can cause *negative feedback inhibition* of the operon that is responsible for its synthesis.
- In this way, once the required synthesized product has become abundant enough for proper cell function, the operon becomes dormant.
- Conversely, when the synthesized product becomes degraded in the cell and its concentration decreases, the operon once again becomes active. In this way the concentration of the product is regulated.



# Control of intracellular function by enzyme regulation

- Some cell activities are controlled by intracellular inhibitors or activators that act directly on specific intracellular enzymes.
- Enzyme inhibition.
- Some chemical substances formed in the cell have direct feedback effects in inhibiting the specific enzyme systems that synthesize them.
- Almost always the synthesized product acts on the first enzyme in a sequence, rather than on the subsequent enzymes, usually binding directly with the enzyme and causing an allosteric conformational change that inactivates it. *By binding to the first enzyme, this prevents buildup of intermediary products that are not used.*
- Enzyme inhibition is another example of negative feedback control.
- Enzyme activation.
- Enzymes that are normally inactive often can be activated when needed. Example from book: restoration of depleted ATP.

# Summary:

- There are two principal methods by which cells control proper proportions and proper quantities of different cellular constituents: 1) the mechanism of genetic regulation and 2) the mechanism of enzyme regulation. Both genes and enzymes can be either activated or inactivated.
- These regulatory mechanisms are most often functioning as feedback control systems that continually monitor the cell's biochemical composition and make corrections as needed, but on occasion, substances from outside the cell (especially hormones), also control the intracellular biochemical reactions by activating or inactivating one or more of the intracellular control systems.

# The DNA-Genetic system also controls cell reproduction

- Life cycle of the cell
- The life cycle of the cell is the period from cell reproduction to the next cell reproduction. When mammalian cells are not inhibited and are reproducing as rapidly as they can, this life cycle may be as little as 10 to 30 hours. It is terminated by a series of distinct physical events called mitosis that cause division of the cell into two new daughter cells (don't worry about the stages of cell reproduction).
- The actual stage of mitosis lasts for only about 30 minutes, so that more than 95 percent of the life cycle of even rapidly reproducing cells is represented by the interval between mitosis, called interphase.
- Except in special conditions of rapid cellular reproduction, inhibitory factors almost always slow or stop the uninhibited life cycle of the cell. Therefore, different cells of the body actually have life cycle periods that vary from as little as 10 hours for highly stimulated bone marrow cells to an entire lifetime of the human body for most nerve cells.

# Cell reproduction begins with replication of DNA

- The principal enzymes for replicating DNA are a complex of multiple enzymes called *DNA polymerase*, which is comparable to RNA polymerase.
- It attaches to and moves along the DNA template strand while another enzyme, *DNA ligase*, causes bonding of successive DNA nucleotides one to another, using high-energy phosphate bonds to energize these attachments.

# DNA repair, DNA proofreading and mutation

- During the hour or so between DNA replication and the beginning of mitosis, there is a period of very active repair and proofreading of the DNA strands. That is, wherever inappropriate DNA nucleotides have been matched up with the nucleotides of the original template strand, special enzymes cut out the defective areas and replace these with appropriate complementary nucleotides. This is achieved by the same DNA polymerases and DNA ligases that are used in replication. This repair process is referred to as DNA proofreading.
- Because of repair and proofreading, the transcription process rarely makes a mistake. But when a mistake is made, this is called a *mutation*. The mutation causes formation of some abnormal protein in the cell rather than a needed protein, often leading to abnormal cellular function and sometimes even cell death.
- Given that there are 25,000 or more genes in the human genome and that the period from one human generation to another is about 30 years, one would expect as many as 10 or more mutations in the passage of the genome from parent to child.
- As a further protection, however, each human genome is represented by two separate sets of chromosomes with almost identical genes. Therefore, one functional gene of each pair is almost always available to the child despite mutations

# Chromosomes and their replication

- The DNA helixes of the nucleus are packaged in chromosomes. The human cell contains 46 chromosomes arranged in 23 pairs. Most of the genes in the two chromosomes of each pair are identical or almost identical to each other, although occasionally this is not the case.
- In addition to DNA in the chromosome, there is a large amount of protein in the chromosome, composed mainly of many small molecules of electropositively charged histones.
- The histones are organized into cores. Small segments of each DNA helix are coiled sequentially around one core after another.
- The histone cores play an important role in the regulation of DNA activity because *as long as the DNA is packaged tightly, it cannot function as a template for either the formation of RNA or the replication of new DNA.*

# Cell mitosis

- The actual process by which the cell splits into two new cells is called mitosis.
- *(don't worry about the different stages).*
- Control of cell growth and cell reproduction
- Certain cells grow and reproduce all the time, such as the blood-forming cells of the bone marrow, germinal layers of the skin, and epithelium of the gut.
- Many other cells, however, such smooth muscle cells, may not reproduce for many years. A few cells, such as the neurons and most striated muscle cells, do not reproduce during the entire life of a person, except during the original period of fetal life.

# Cell Mitosis-2

- Experiments have shown at least three ways in which growth can be controlled. First, growth is often controlled by growth factors that come from other parts of the body. Some of these circulate in the blood, others originate in adjacent tissues.
- Second, most normal cells stop growing when they have run out of space for growth (contact inhibition).
- Third, cells grown in tissue culture often stop growing when minute amounts of their own secretions are allowed to collect in the culture medium. This too, could provide a means for negative feedback control of growth (draw diagram on board).



# Cell differentiation

- A special characteristic of cell growth and cell division is cell differentiation, which refers to changes in physical and functional properties of cells as they proliferate in the embryo to form the different bodily structures and organs
- Can a cell proliferate and differentiate at the same time?

# Apoptosis- programmed cell death

- The 100 trillion cells of the body are members of a highly organized community in which the total numbers of cells is regulated not only by controlling the rate of cell division but also by *controlling the rate of cell death*.
- When cells are no longer needed or become a threat to the organism, they undergo a suicidal programmed cell death or apoptosis.
- This process involves a specific proteolytic cascade that causes the cell to shrink and condense, to disassemble its cytoskeleton, and to alter its cell surface so that a neighboring phagocytic cell, such as a macrophage, can attach to the cell membrane and digest the cell.

# Apoptosis-2

- In contrast to programmed death, cells that die as a result of an acute injury usually swell and burst due to loss of cell membrane integrity, a process called *cell necrosis*.
- Necrotic cells may spill their contents, causing inflammation and injury to neighboring cells.
- Apoptosis, however, is an orderly cell death that results in disassembly and phagocytosis of the cell before any leakage of its contents occurs, and neighboring cells usually remain healthy.

# Apoptosis-3

- Apoptosis is initiated by activation of a family of proteases called caspases. These are enzymes that are synthesized and stored in the cell as inactive procaspases.
- The mechanisms of activation of caspases are complex, but once activated, the enzymes cleave and activate other procaspases, triggering a cascade that rapidly breaks down proteins within the cell.
- The cell thus dismantles itself, and its remains are rapidly digested by neighboring phagocytic cells.

# Apoptosis-4

- A tremendous amount of apoptosis occurs in tissues that are being remodeled during development. Even in adult humans, billions of cells die each hour in tissues such as the intestine and bone marrow and are replaced by new cells.
- Programmed cell death, however, is precisely balanced with the formation of new cells in health adults. Otherwise, the body's tissues would grow or shrink inappropriately.
- Recent studies suggest that abnormalities of apoptosis may play a key role in neurodegenerative diseases such as Alzheimer's disease, as well as in cancer and autoimmune disorders.
- Some drugs that have been used successfully for chemotherapy appear to induce apoptosis in cancer cells

# Cancer

- Cancer is caused in all or almost all instances by mutation or by some other abnormal activation of cellular genes that control cell growth and cell mitosis. The abnormal genes are called oncogenes. As many as 100 different oncogenes have been discovered.
- Also present in all cells are antioncogenes, which suppress the activation of specific oncogenes. Therefore, loss of or inactivation of antioncogenes can allow activation of oncogenes that lead to cancer.

# Cancer-2

- Only a minute fraction of the cells that mutate in the body ever lead to cancer.
- There are several reasons for this:
- 1) most mutated cells have less survival capability than normal cells and simply die.
- 2) only a few of the mutated cells that do survive become cancerous, because even most mutated cells still have normal feedback controls that prevent excessive growth.
- 3) cells that are potentially cancerous are often destroyed by the body's immune system before they grow into a cancer.
- 4) usually several different activated oncogenes are required simultaneously to cause a cancer.

# Cancer-3

- Chance alone is all that is required for mutations to take place. However, the probability of mutations can be increased many fold when a person is exposed to certain chemical, physical, or biological factors including the following:
  - 1) ionizing radiation;
  - 2) chemical substances- these are called *carcinogens*;
  - 3) Physical irritants;
  - 4) hereditary tendencies;
  - 5) viruses



# Invasive characteristic of the cancer cell

- The major differences between the cancer cell and the normal cell are the following:
- 1) the cancer cell does not respect usual cellular growth limits;
- 2) cancer cells are often far less adherent to one another than are normal cells, so they can spread throughout the body;
- 3) some cancers also produce *angiogenic factors* that cause many new blood vessels to grow into the cancer, thus supplying the nutrients required for cancer growth.
- Why do cancer cells kill? In most cases the answer is relatively simple- they out-compete normal cells for the nutrients needed to keep the body going.

# End!