Al-Mustaqbal University College

Pharmacy Department / Second Stage

PHYSIOLOGY

L 3: Genetic Control of the Cell

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Genetic Control of Protein Synthesis, Cell Function, and Cell Reproduction

All cells of the body have ***genes*** located in their nuclei.
Genes control heredity from parents to children.
These same genes also control day-to-day function of all the body's cells.
The genes control cell function by determining which substances are synthesized within the cell, which structures, which enzymes, which chemicals.
*Each gene (a segment of deoxyribonucleic acid "DNA") → controls the formation of ribonucleic acid "RNA" (**transcription)** that spreads throughout the cell to control the formation of a specific protein (**translation)**.*
***Gene Expression:** It is the entire process, from **transcription** of the genetic code in the nucleus to **translation** of the RNA code and formation of proteins in the cell cytoplasm.*
A large number of different cellular proteins are possible to form, because there are approximately 30,000 different genes in each cell.

Term	Meaning
Genome	Whole length of DNA
Gene	A segment of DNA (short or long)
Gene expression	Transcription + translation processes
Transcription	Copying the genetic code of a gene into mRNA
Translation	Synthesis of protein according to the genetic code

Genes in the Cell Nucleus

DNA (in the nucleus) comprising numbers of genes that are attached end on end forming extremely long double-stranded helical molecules.

The basic chemical compounds involved in the formation of DNA:

(1) Phosphoric acid, (2) Deoxyribose (sugar),

(3) 4 nitrogenous bases: 2 purines (adenine "A" and guanine "G")

2 pyrimidines (thymine "T" and cytosine "C").

*The **constant** phosphoric acid and deoxyribose form the two helical strands that are the backbone of the DNA molecule.*

*The **variable** nitrogenous bases lie between the two strands and connect them.*

The first step in a DNA strand formation is the formation of sequenced ***nucleotide***

Nucleoside = [1 deoxyribose + 1 nitrogenous base]

Nucleotide = Nucleoside + 1 phosphoric acid

i.e.; Nucleotide = [1 phosphoric acid + 1 deoxyribose + 1 nitrogenous base]

*4 separate **nucleotides** are thus formed, one for each of the four bases: deoxyadenylic, deoxythymidylic, deoxyguanylic, and deoxycytidylic acids*

The second step is base pairing which loosely hold the two DNA strands together.

Base paring means that hydrogen bonds are formed between the **purine** and **pyrimidine** bases, the two respective DNA strands.

But note that base pairing is as follow:

1. Adenine (purine) bound with thymine (pyrimidine) by two hydrogen bonds. $A = T$
2. Guanine (purine) bound with cytosine (pyrimidine) by three hydrogen bonds. $G \equiv C$

Final step is that the double helical structure of DNA is compacted in the cell by association with histones (proteins), and further compacted into chromosomes.

A diploid human cell contains 46 chromosomes

The gene

The gene: is a sequence of DNA nucleotides that codes for a single polypeptide chain.

Polypeptide chain*: an ordered amino acid sequence of <100 amino acids.*

Protein: an ordered amino acid sequence of >= 100 amino acids.

Proteins have many structures and perform many function

A typical eukaryotic gene is made up of a strand of DNA that includes ***coding*** and ***noncoding*** regions - *has 5' start and 3' end.*

Coding regions are usually broken into several translated segments "exons" separated by non-translated segments "introns" - *This is unlike prokaryotes genes.*

Out of the gene there are **promoter** and **regulatory** elements

Term	Meaning	Role
Gene	A segment of single strand of DNA	Contain the codes for protein synthesis (has 5' start and 3' end regions)
Exons	Translated segments of agene	The transcribed nucleotides coded for amino acids sequence
Introns	Non-translated segments of agene	The transcribed nucleotides coded for nothing
Promoter element	Nucleotide sequence (TATA box) near the 5' start region of the gene	The site at which RNA polymerase bind and start transcription of gene
Regulatory element	DNA sequence near the 5' region or 3' regions of the gene	Include enhancer and silencer sequences to enhance or terminate transcription of gene

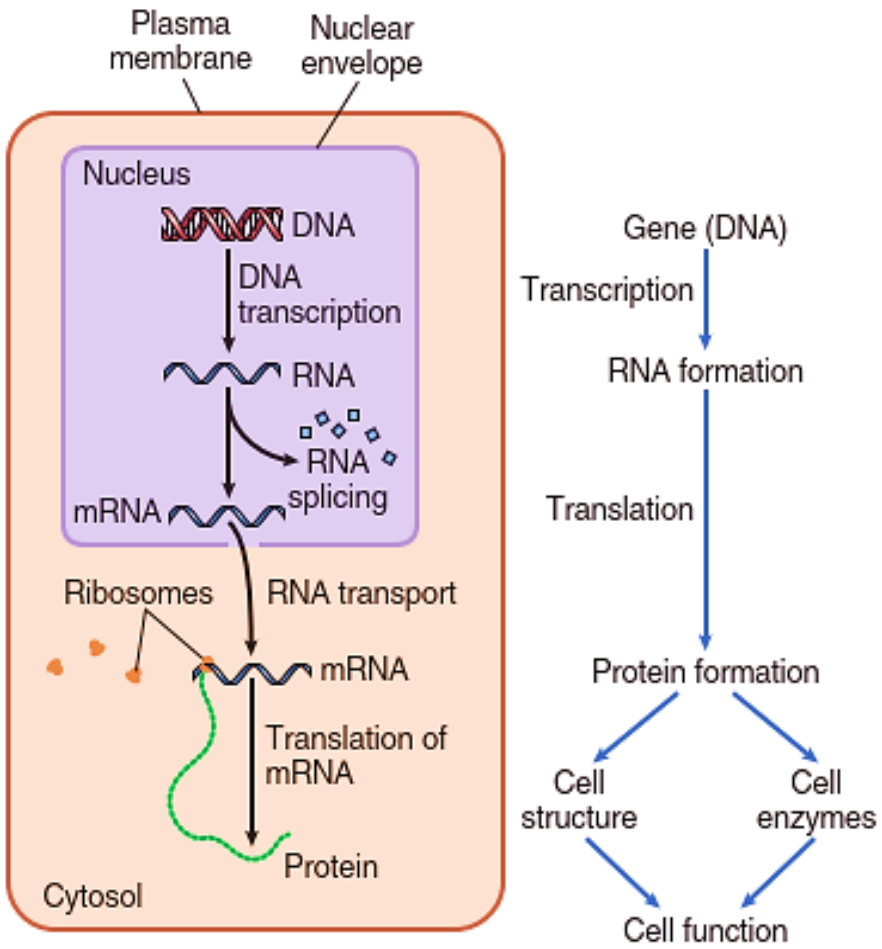


Figure 3-1. The general schema by which genes control cell function. mRNA, messenger RNA.

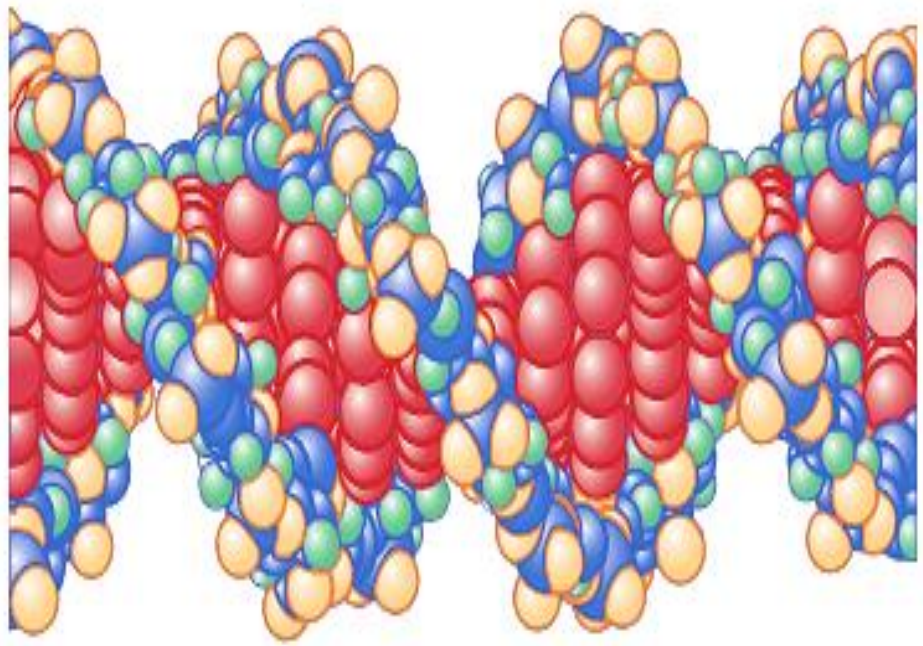
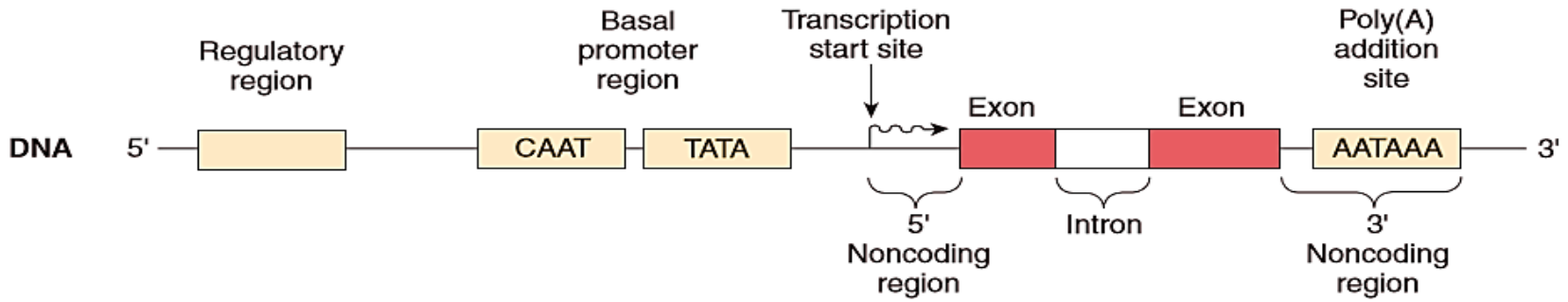


Figure 3-2. The helical, double-stranded structure of the gene. The outside strands are composed of phosphoric acid and the sugar deoxyribose. The internal molecules connecting the two strands of the helix are purine and pyrimidine bases, which determine the "code" of the gene.



Ribonucleic Acids (RNA):

The strands of the DNA double helix:

Replicate themselves to form new strands.

Serve as templates by lining up complementary bases for the formation in the nucleus of ribonucleic acids (RNA).

RNA differs from DNA in that:

It is single-stranded

Has uracil in place of thymine.

Its sugar moiety is ribose rather than 2'-deoxyribose.

The code that is present in the DNA strand is eventually transmitted in complementary form to the RNA chain.

Types of RNA

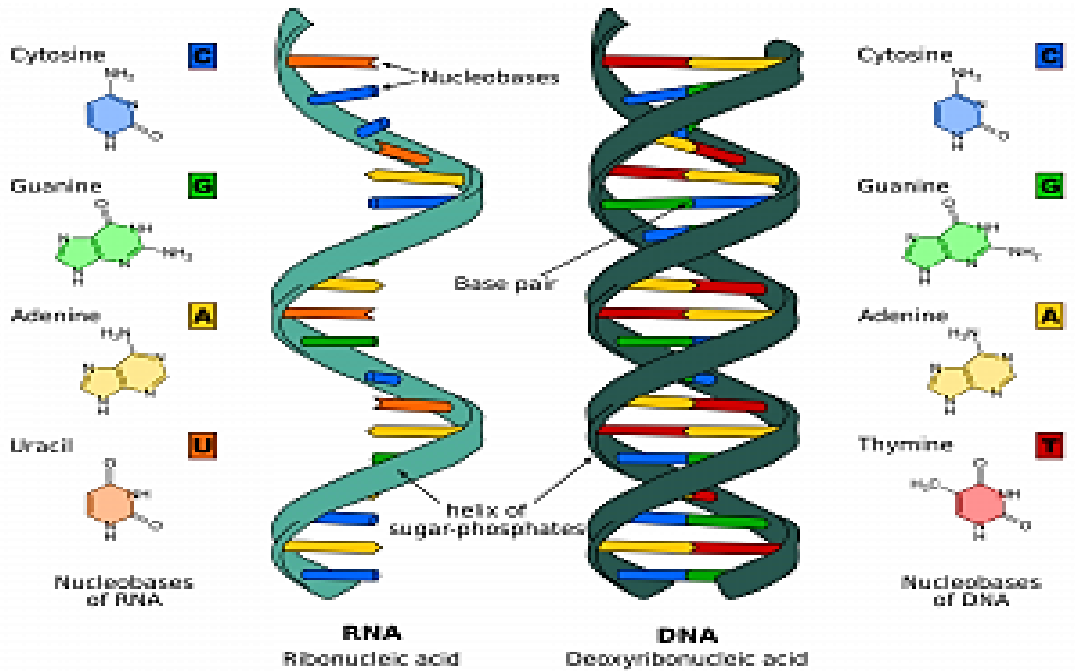
Each type of RNA plays an independent and entirely different role in protein formation:
1. Messenger RNA (**mRNA**): carries the **genetic code** to the cytoplasm for controlling the type of protein formed.
2. Transfer RNA (**tRNA**): transports activated amino acids to the ribosomes to be used in assembling the protein molecule.
3. 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. The ribosome is the physical structure in the cytoplasm on which protein molecules are actually synthesized.

4. MicroRNA (miRNA): single stranded RNA molecules of 21 to 23 nucleotides that can regulate gene transcription and translation. They believed to play an important role in the normal regulation of cell function, and alterations in miRNA function have been associated with diseases such as cancer and heart disease.

mRNA - The codons: *Long, single RNA strands that are suspended in the cytoplasm.*

Composed of several 100s to several 1000s RNA nucleotides in unpaired (single) strands.
They contain codons that are exactly complementary to the code triplets of the DNA genes.

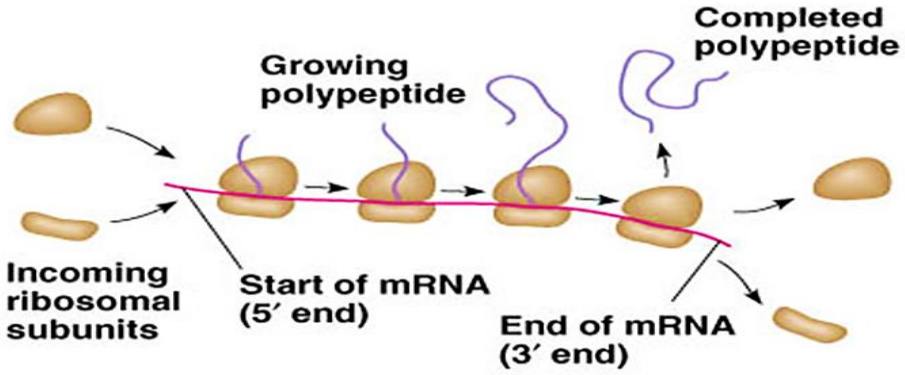
	DNA	RNA
Sugar	Deoxyribose	Ribose
Bases	Adenine, guanine, cytosine, thymine	Adenine, guanine, cytosine, uracil
Structure	Double stranded helix	Single stranded helix



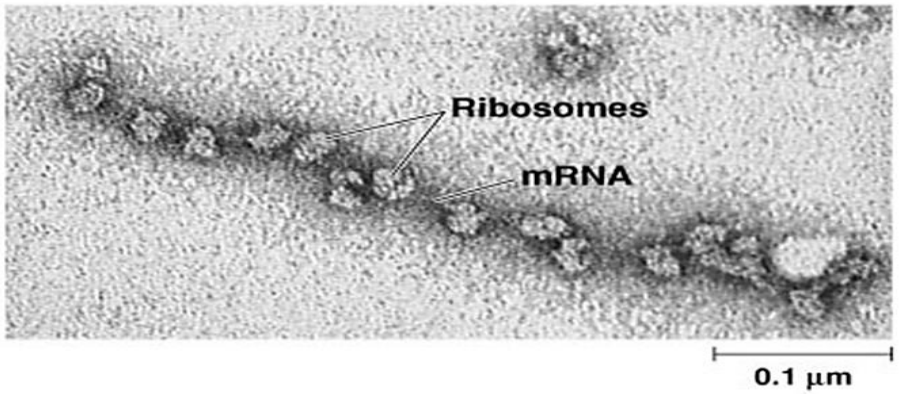
Protein Synthesis and Secretion

In order for a gene to be expressed, it first must be used as a guide, or template, in the production of a complementary strand of messenger RNA. This mRNA is then itself used as a guide to produce a particular type of protein whose sequence of amino acids is determined by the sequence of base triplets (codons) in the mRNA.

When mRNA enters the cytoplasm, it attaches to ribosomes, which appear in the electron microscope as numerous small particles. The mRNA passes through a number of ribosomes to form a "string-of-pearls" structure called a *polyribosome* (or *polysome,* for short), as shown in figure



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



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

The association of mRNA with ribosomes is needed for the process of **genetic translation**, the production of specific proteins according to the code contained in the mRNA base sequence. Each mRNA molecule contains several hundred or more nucleotides, arranged in the sequence determined by complementary base pairing with DNA during transcription (RNA synthesis). Every three bases, or base triplet, is a code word—called a codon—for a specific amino acid. As mRNA moves through the ribosome, the sequence of codons is translated into a sequence of specific amino acids within a growing polypeptide chain.

Control of Gene Function and Biochemical Activity in Cells:

Genes control both the physical and the chemical functions of the cells.

Each cell has powerful internal feedback control mechanisms that keep the various functional operations of the cell in step with one another.

There are basically two methods by which the biochemical activities in the cell are controlled. One of these is ***genetic regulation**, in which the degree of activation of the genes themselves is controlled, and the other is ***enzyme regulation**, in which the activity levels of already formed enzymes in the cell are controlled.

Genetic Regulation

Formation of all the enzymes needed for the synthetic process often is controlled by a sequence of genes located one after the other on the same chromosomal DNA strand. This area of the DNA strand is called an **operon,** and the genes responsible for forming the respective enzymes are called **structural genes**. In the DNA strand there is segment called the **promoter**. This is a group of nucleotides that has specific affinity for RNA polymerase. The 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 Intracellular Function by Enzyme Regulation

In addition to control of cell function by genetic regulation, some cell activities are controlled by intracellular inhibitors or activators that act directly on specific intracellular enzymes. Thus, enzyme regulation represents a second category of mechanisms by which cellular biochemical functions can be controlled.

PROTEINS

Proteins are made up of large numbers of amino acids linked into chains by peptide bonds joining the amino group of one amino acid to the carboxyl group of the next.
In addition, some proteins contain carbohydrates (glycoproteins) and lipids (lipoproteins)

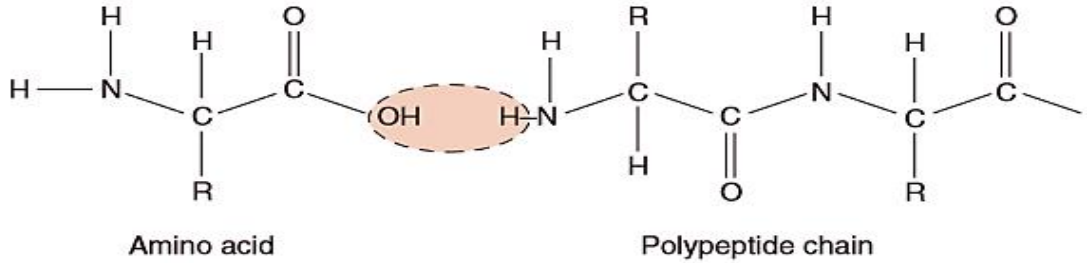
Peptide: amino acid chain containing 2-10 amino acid residues.
Polypeptide: amino acid chain containing more than 10 but fewer than 100 amino acid residues.
Protein: amino acid chain containing 100 or more amino acid residues. ▪

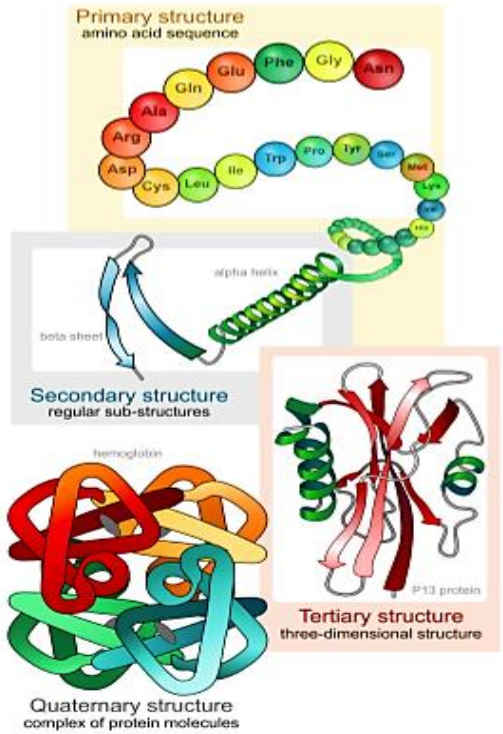
The order of the amino acids in the peptide chains is called the **primary structure** of a protein.
The chains are **twisted** and folded in complex ways, and the term **secondary structure** of a protein (refers to the spatial arrangement produced by the twisting and folding).
The **tertiary structure** of a protein is the arrangement of the twisted chains into layers, crystals, or fibers.
Many protein molecules are made of several proteins, or subunits (e.g., hemoglobin), and the term **quaternary structure** is used to refer to the arrangement of the subunits into a functional structure.

Table 3-1 RNA Codons for Amino Acids and for Start and Stop

Amino Acid	RNA Codons					
Alanine	GCU	GCC	GCA	GCG		
Arginine	CGU	CGC	CGA	CGG	AGA	AGG
Asparagine	AAU	AAC				
Aspartic acid	GAU	GAC				
Cysteine	UGU	UGC				
Glutamic acid	GAA	GAG				
Glutamine	CAA	CAG				
Glycine	GGU	GGC	GGA	GGG		
Histidine	CAU	CAC				
Isoleucine	AUU	AUC	AUA			
Leucine	CUU	CUC	CUA	CUG	UUA	UUG
Lysine	AAA	AAG				
Methionine	AUG					
Phenylalanine	UUU	UUC				
Proline	CCU	CCC	CCA	CCG		
Serine	UCU	UCC	UCA	UCG	AGC	AGU
Threonine	ACU	ACC	ACA	ACG		
Tryptophan	UGG					
Tyrosine	UAU	UAC				
Valine	GUU	GUC	GUA	GUG		
Start (CI)	AUG					
Stop (CT)	UAA	UAG	UGA			

CI, chain-initiating; CT, chain-terminating.





Cell Mitosis

The actual process by which the cell splits into two new cells is called mitosis. Once each chromosome has been replicated to form the two chromatids, in many cells, mitosis follows automatically within 1 or 2 hours.

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.

Apoptosis—Programmed 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.

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.

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.** Also present in all cells are **anti-oncogenes**, which suppress the activation of specific oncogenes. Therefore, loss of or inactivation of anti-oncogenes can allow activation of oncogenes that lead to cancer.

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; the reason for this is that these cells presumably do not require all the same growth factors that are necessary to cause growth of normal cells.

(2) Cancer cells often are far less adhesive to one another than are normal cells. Therefore, they have a tendency to wander through the tissues, to enter the blood stream, and to be transported all through the body, where they form numerous new cancerous growths.

(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.


Thank you.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