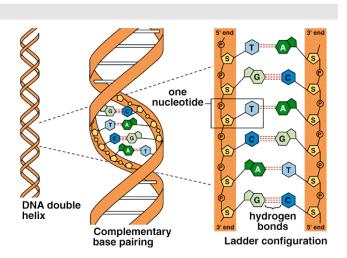
# DNA and Protein Synthesis - "Life is a Three Letter Word!" - CHAPTER NOTES

## What is DNA?

- DNA is the control molecule of life. DNA has three major functions:
- 1. <u>DNA CONTROLS CELLULAR ACTIVITIES</u>, including reproduction.
- DNA <u>carries a CODE</u>. Genetic <u>instructions</u> are encoded in the <u>sequence of bases</u> strung together in DNA.
- DNA from male and DNA from female together become the genetic information of offspring in sexual reproduction.
- RNA molecules function in the processes by which those DNA instructions are used in building the <u>proteins</u> on which all forms of life are based.
- 2. **DNA MAKES EXACT COPIES OF ITSELF** to pass onto other cells.



• DNA does this through a process called "replication."

# 3. DNA UNDERGOES MUTATIONS

- <u>mutations</u> and <u>recombinations</u> in the structure and number of DNA molecules are the source of life's diversity.
- <u>Evolution</u>, in essence, proceeds from the level of DNA. Different combinations of DNA sequences due to
  mutations and sexual reproduction explain the existence of all the different species that have lived on this Earth.

# Furthermore...

- DNA is the source of the <u>unity of life</u>
- Life most likely began as a nucleic acid. (recall that there are TWO Types of Nucleic acids: DNA & RNA).
- The first form of life on this planet is thought by many biologists to be a self-replicating strand of RNA.

#### A BRIEF HISTORY OF DNA RESEARCH (no, this is not on the test!)

- DNA was first isolated by the Swiss biochemist Johann Friedrich **Miescher** in **1869**. Because DNA molecules are acidic and are found in the nucleus, Miescher called them nucleic acids. Over 80 years passed, however, before scientists understood that DNA contains the information for carrying out the activities of the cell. How this information is coded or passed from cell to cell was unknown. To break the code, scientists first had to determine the structure of DNA..
- During the 1950's, a fierce competition to determine the three dimensional structure of DNA took place. The race was won in 1953 by
  <u>James Watson</u>, an American biologist, and <u>Francis Crick</u>, a British physicist. Working together at Cambridge University in England,
  Watson and Crick solved the puzzle using scale modes of nucleotides. Their success depended a great extent on evidence collected by
  other biologists, especially X-ray data from British biochemists Roslind Franklin and Maurice Wilkins.
- In 1958, the mechanism for DNA replication was determined by **Meselson** and **Stahl**. In the **GENETIC CODE** of **3 DNA nucleotides for 1 amino acid** was worked out by Crick and his coworkers.

#### Important Dates in early DNA research:

Date	Discovery
1869	Nucleic Acids identified
1928	Transfer of genetic material between bacteria observed (Frederick Griffith)
1944	DNA carries genetic code (Oswald Avery and coworkers)
1950	Protein chains sometimes helical; DNA structure similar (Linus Pauling)
1951	X-ray data for DNA structure produced (Franklin, Wilkins)
1951	Nitrogen base ratio related to genetic code (Chargaff)
1953	DNA double helix discovered (James Watson, Francis Crick)
1958	Mechanism for DNA replication determined (Matthew Meselson, Franklin Stahl)
1961	3 DNA nucleotide code for 1 amino acid (Crick and coworkers)

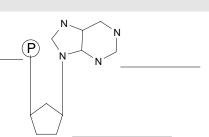
## The Structure of Nucleic Acids

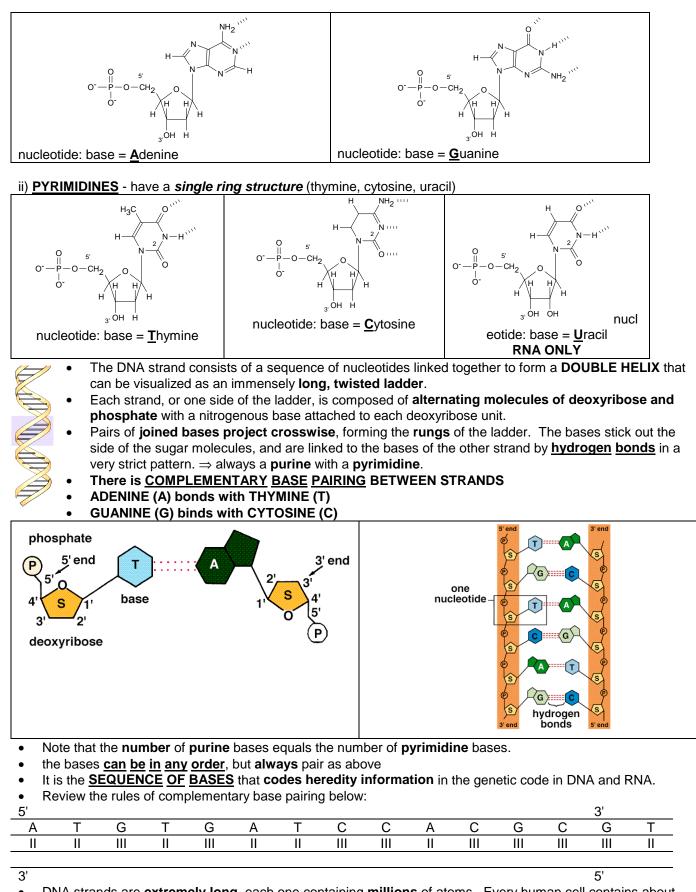
- DNA & RNA are POLYMERS of NUCLEOTIDES
- Each nucleotide is composed of:
  - 1. a **pentose** (5 carbon) **SUGAR**
  - 2. a PHOSPHATE group
  - 3. a nitrogenous BASE

### there are two types of bases:

i) **<u>PURINES</u>** - have a *double ring structure* (adenine &

guanine)

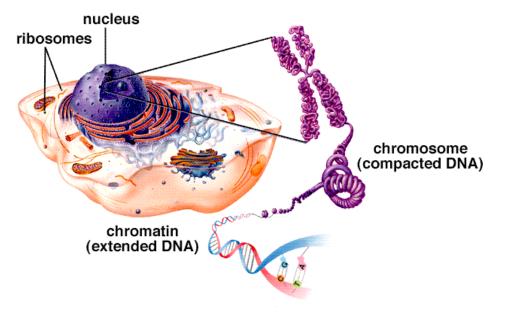




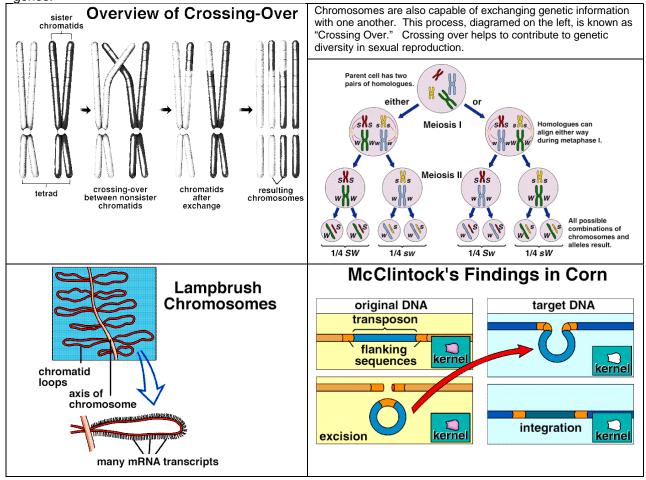
• DNA strands are **extremely long**, each one containing **millions** of atoms. Every human cell contains about one meter of these twisted strands. (this amounts to about **4 billion pairs** of bases).

# GENES AND CHROMOSOMES

- <u>GENES</u> are the units of inheritance that control particular characteristics or capabilities of an organism. Genes are located on the chromosomes of the cell nucleus and consist of segments of DNA molecules.
- A gene consists of a sequence of about **1000 DNA base-pairs** (though there is considerable variation in this length). About **175,000** genes compose the DNA molecule of a single human chromosome. The genes act in pairs that dictate **traits**.



- Genes control cellular chemical reactions, by directing the formation of enzymes.
- Genes always occur in **pairs**. Half of each person's genes come from the mother and half from the father. Most ordinary characteristics like height and eye color are determined by <u>combinations</u> of several different genes.



**REPLICATION - DNA making identical copies of itself** 

- Inherent in DNA's structure is a mechanism for reproducing itself. Before a cell can divide, all of the DNA must be duplicated.
- This duplication process is called **REPLICATION.**
- each strand of DNA can be viewed as a **template**: like a potter's mold. it can produce a "reverse image" copy of itself (a **complementary** copy). Each new strand of DNA produced has a sequence of bases exactly complementary to the template strand.

# Sequence of Events in Replication:

- **UNZIPPING:** the DNA double 1. helix **unwinds**, and the two strands of DNA separate; hydrogen bonds between the bases break
- 2. COMPLEMENTARY BASE PAIRING: new nucleotides move in to pair up with bases of each template strand of DNA. These new nucleotides are always floating around within the nucleoplasm. ADJACENT 3.
- NUCLEOTIDES BOND: sugar-phosphate bonds form between adjacent nucleotides of the new strand to complete the molecule. The new molecule winds into a double helix.
- each new strand of DNA produced contains one "old" strand (the template) and one new strand. This is known as "SEMI-CONSERVATIVE" replication. Since half of the original molecule is conseved in each of the new molecules, this ensures that there will be

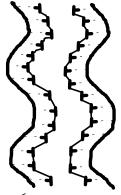
#### very, very accurate replication of the parent molecule.

- this process proceeds by the action of several very specific enzymes (e.g. DNA Polymerases, gyrase, helicase)
- DNA Replication backbones are shown in dark color.) nucleotides are parental strands. replication. Each double helix is strand (light).

Region of parental DNA helix. (Both

Region of replication (simplified). Parental DNA helix is unwound and unzipped. New pairing with those in

Region of completed composed of an old parental strand (dark) and a new daughter

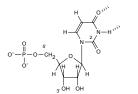




product of replication by on DNA molecule is two complete double-stranded DNA molecules, each with one

new strand and one original stand that **acted as a template** for replication.

RNA: RIBONUCLEIC ACID: how DNA communicates its message.



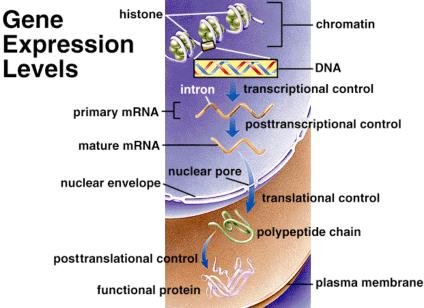
- RNA is the genetic material of some viruses and is necessary in all organisms for protein synthesis to occur. RNA could have been the "original" nucleic acid when life first arose on Earth some 3.8 billion years ago.
- Like DNA, all RNA molecules have a similar chemical organization, consisting of nucleotides.
- Like DNA, each RNA nucleotide is also composed of three subunits:

Uracil

a 5-carbon sugar called <u>RIBOSE</u>.
 a **PHOSPHATE group** that is

attached to one end of the sugar molecule

- 3. one of several different **nitrogenous <u>BASES</u>** linked to the opposite end of the ribose.
- There is <u>one base that is different</u> from DNA -- the base <u>URACIL</u> is used instead of <u>thymine</u>.(G, A, C, are otherwise the same as for DNA)
- RNA is <u>SINGLE-STRANDED</u>, unlike DNA which is double stranded. RNA, therefore, is **not** a double helix.
- <u>RNA is produced from DNA</u> by a process called <u>TRANSCRIPTION</u>. The steps of transcription are as follows:
- A specific section of <u>DNA unwinds</u>, exposing a set of bases
- Along one strand of DNA (called the "sense" strand), complementary RNA bases are brought in. In RNA, <u>Uracil binds to the Adenine on DNA</u>. As in DNA, cytosine binds to guanine. The other strand of the DNA molecule (the "missense" strand), isn't read in eukaryotic cells.
- 3. Adjacent RNA nucleotides form sugar-phosphate bonds.
- 4. The **<u>RNA</u> strand is <u>released</u>** from DNA (RNA is a single-stranded nucleic acid).
- 5. The **DNA** molecule **rewinds**, and returns to its normal double helix form.
- 6. Once produced, the mRNA strand is often *processed* (certain sections called <u>introns</u> are cut out, a "Poly-A" tail is added to the 3' end, and a "cap" is added to the 5' end).
- RNA can then **leave the nucleus** and go into the **cytoplasm**.
- The enzyme involved in transcription is known as RNA polymerase.
- This process occurs in the **nucleus** (and, in particular, **dark coloured spots** in the nucleus called <u>nucleoli</u> (singular = **nucleolus**)



This mRNA transcript is ready to move into the cytoplasm.

Transcription is going on here—the nucleotides of mRNA are joined by the enzyme RNA polymerase in an order complementary to a strand of DNA.

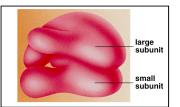
One portion of DNA—a particular gene or genes—is transcribed at one time.

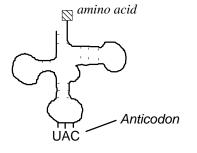
G	Α	С	Α	Α	С	Т	G	G	Α	Т	С	G	А	С	DNA
															•
															mRNA

• There are <u>3 types of RNA</u>, each with different functions.

### rRNA, tRNA, and mRNA - The agents of Protein Synthesis

 RNA that is involved in protein synthesis belongs to one of three distinct types: <u>ribosomal RNA</u> (rRNA), <u>transfer RNA</u> (tRNA), and <u>messenger RNA</u> (mRNA).

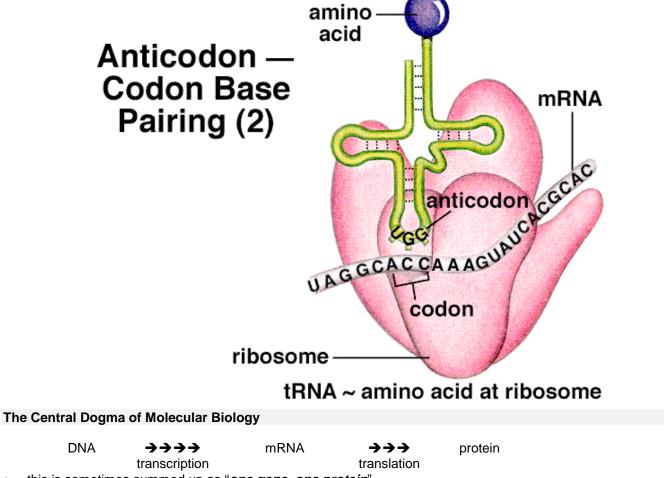




**<u>RIBOSOMAL RNA</u>** (rRNA) - **becomes a <u>structural part of</u>** <u>**ribosomes**</u> and serves as a genetic **link** between mRNA and tRNA. Ribosomal RNA is associated with protein, forming bodies called **ribosomes**. Ribosomes are the <u>sites</u> <u>of protein synthesis</u>.

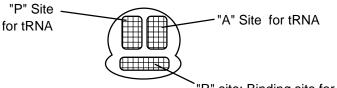


- Ribosomal RNA varies in size and is the *most plentiful* RNA. It **constitutes 85% to 90%** of total cellular RNA.
- <u>TRANSFER RNA</u> (tRNA) is used to <u>deliver amino acids</u> from the <u>cytoplasm</u> to the <u>ribosome</u>. There is a different tRNA for each amino acid. The function of each type of tRNA is to bring its specific amino acid to a ribosome.
- The tRNA molecules consist of about 80 nucleotides and are structured in a cloverleaf pattern. They constitute about 5% of the cell's total RNA.
- <u>MESSENGER RNA</u> (mRNA) <u>carries</u> the <u>genetic</u> <u>code</u> contained in the sequence of bases in the cell's DNA from the nucleus to the Ribosome.
- mRNA: acts as a "go-between" for DNA in the nucleus and the ribosomes in the cytoplasm.
- mRNA constitutes 5% to 10% of the cell's RNA.



• this is sometimes summed up as "one gene, one protein"

- mRNA, once produced, leaves the nucleus through pores in the nuclear envelope, and enters the cytoplasm. This is where <u>TRANSLATION</u> occurs.
- Translation is the process that changes the RNA message into the actual protein. It occurs at the surface of the RIBOSOME.
- The <u>order of the bases in DNA</u>, and then subsequently <u>mRNA</u>, <u>determines the</u> <u>amino acid sequence of the protein</u> being made.

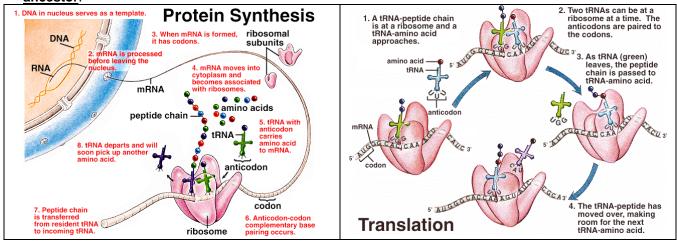


"R" site: Binding site for mRNA

- Each amino acids is coded for by 3 bases (this is known as a TRIPLET CODE)
- There are 20 different amino acids, but only 4 different bases in DNA/RNA.
- Each three-letter unit of mRNA is called a <u>CODON</u>.
- There are 4<sup>3</sup> (= 64) codons possible --> therefore there are easily enough codons to code for all the necessary amino acids.
- In fact, the same amino acid is often specified by more than one codon. However (and this is very important), the reverse is never true: that is, any one codon only specifies ONE amino acid -- there is no vagueness in the code (e.g. CCU will *always* produce proline).
- The code also contains "<u>punctuation</u>." It tells when to <u>start</u> reading the gene for a particular protein and when to <u>stop</u>.
- Each codon corresponds to an **amino acid**, or a "**start**" or "**stop**" synthesis signal. And *here it is*, the most important chart in all of Biology: the <u>GENETIC CODE</u>!

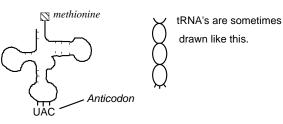
AAU	ASPARAGINE	CAU	HISTIDINE	GAU	ASPARTIC ACID	UAU	TYROSINE
AAC		CAC		GAC		UAC	
AAA	LYSINE	CAA	GLUTAMINE	GAA	GLUTAMIC ACID	UAA	STOP
AAG		CAG		GAG		UAG	STOP
ACU	THREONINE	CCU	PROLINE	GCU	ALANINE	UCU	SERINE
ACC		CCC		GCC		UCC	
ACA		CCA		GCA		UCA	
ACG		CCG		GCG		UCG	
AGU	SERINE	CGU	ARGININE	GGU	GLYCINE	UGU	CYSTEINE
AGC		CGC		GGC		UGC	
AGA	ARGININE	CGA		GGA		UGA	STOP
AGG		CGG		GGG		UGG	TRYPTOPHAN
AUU	ISOLEUCINE	CUU	LEUCINE	GUU	VALINE	UUU	PHENYLALANINE
AUC		CUC		GUC		UUC	
AUA		CUA		GUA		UUA	LEUCINE
AUG	METHIONINE	CUG		GUG		UUG	
	*START						

 The genetic code is <u>universal</u>: the <u>same codons</u> stand for the <u>same amino acids</u> in all living things (well, almost all living things). This "Biochemical Unity" suggests that all living things have a <u>common evolutionary</u> ancestor.



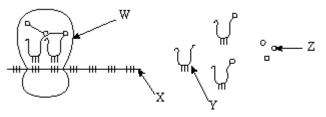
- The steps in TRANSLATION: can be divided into 3 subprocesses:
- 1. **INITIATION:** the mRNA, with its **START CODON (AUG)** attaches to the "R" site of the ribosome.
- a. The AUG codon always initiates translation and codes for the amino acid methionine.

- b. <u>tRNA</u> binds to the <u>start codon</u> of mRNA. The tRNA has a binding site of 3 bases called an <u>ANTICODON</u> that is <u>complementary</u> to the mRNA codon. Therefore, the codon of mRNA of AUG is "read" by a tRNA that has a UAC anticodon. The tRNA that has this anticodon carries, at it's tail, the amino acid methionine.
- c. This methionyl-tRNA is in the <u>P</u> site of the ribosome. The <u>A</u> site next to it is available to the tRNA bearing the next amino acid.
- There is a specific tRNA for each mRNA codon that codes for an amino acid.



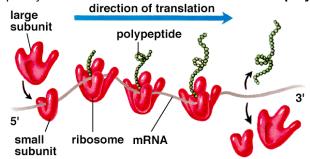
tRNA with Methionine

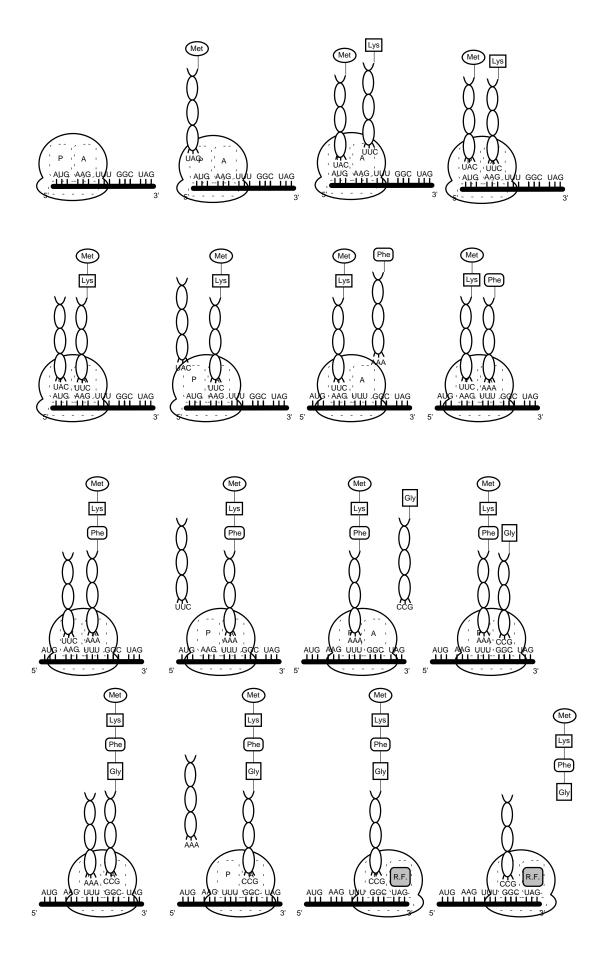
- 2. <u>ELONGATION</u>: more amino acids are added and connected together to form a polypeptide, as specified by the mRNA sequence.
- a. an incoming amino-acyl-tRNA (lets call this AA<sub>2</sub>-tRNA<sub>2</sub>) recognizes the codon in the A site and binds there.
- b. a peptide bond is formed between the new amino acid and the growing polypeptide chain.
- c. the amino acid is removed from tRNA<sub>1</sub> (bond breaks between aa<sub>1</sub> and tRNA<sub>1</sub>)
- d. the tRNA<sub>1</sub> that was in the P site is released, and the tRNA in the A site is translocated to the P site.
- e. the <u>ribosome moves over one codon</u> along the mRNA (to the right in our diagram, or more specifically in the 5' ----> 3' direction.)
- f. This movement shifts the tRNA<sub>2</sub> (which is attached to the growing amino acid chain) to the P site.
- g. tRNA<sub>3</sub> with aa<sub>3</sub> can now move into A site and bind with the next codon on mRNA.
- h. **THIS PROCESS** <u>**REPEATS**</u>, and the CHAIN <u>**ELONGATES**</u> as long as there are new codons to read on the mRNA.
- 3. <u>**TERMINATION**</u>: The process above repeats until a special codon, called a **STOP CODON**, is reached. There are 3 Stop codons: <u>**UAA**</u>, **<u><b>UAG**</u>, **<u><b>UGA**</u>.
- a. the stop codons do not code for amino acids but instead act as signals to stop translation.
- b. a protein called <u>release factor</u> binds directly to the stop codon in the A site. The release factor causes a water molecule to be added to the end of the polypeptide chain, and the chain then separates from the last tRNA.
- c. <u>the protein is now complete</u>. The mRNA is now usually broken down, and the ribosome splits into its large and small subunits.
- d. the new protein is sent for **final processing** into the **endoplasmic reticulum** and **golgi apparatus**.



Please Label these Parts

• Often, many ribosomes will <u>simultaneously</u> transcribe the same mRNA. In this way, many copies of the same protein can be made quickly. These clusters of ribosomes are called **polysomes**.





# **GENETIC MUTATIONS**

- During the molecular maneuvering that occurs with DNA replication, if nucleotides are <u>lost, rearranged, or</u> <u>paired in error</u>, the resulting change in instruction of the genetic code could lead to a protein that does not function properly when the DNA's code is translated.
- A MUTATION is a change in an organism resulting from a chemical change in the structure of a gene.
- Although mutations have occurred throughout history, it wasn't until 1927 that Herman Muller, an American geneticist, developed the first experiments to study how and why they occurred. Genetic mutations can be caused by both internal and external factors. Any factor that can cause a mutation is called a <u>MUTAGEN</u> (e.g. Dioxins, benzene, UV light, asbestos, DDT, cigarette smoke, x-rays etc. etc.)
- Change will first be reflected in the **RNA** copy, then in the enzyme or other protein that the RNA codes for, and finally in the appearance of new traits in the living organism.
- There are two main categories of mutations: <u>GENE MUTATIONS</u> (<u>affect only one gene</u>), and <u>CHROMOSOMAL MUTATIONS</u> (<u>affect many genes</u> because they affect entire chromosomes or parts of chromosomes).
- A mutation occurs because of the <u>alteration in one or more base pairs</u> of the DNA molecule, garbling the existing genetic code. Sometimes the pattern of normal base pairing is altered, causing the substitution of one base pair for another. Sometimes the pairing capacity of a specific base is changed, producing abnormal base pairing. Sometimes an extra base is <u>added</u>, sometimes a base is <u>deleted</u>. Mutations where bases are added or deleted are called frameshift mutations.
- It takes only a single different pair of bases to produce a different or imperfect organism.

• Consider an analogy of a "mutation" to a sentence in English.

### EXAMPLE OF THE EFFECT OF A MUTATION:

ORIGINAL MESSAGE:	THE	BI <b>G</b>	DOG	BIT	TED	AND	RAN	OFF
DELETION/FRAME SHIFT:	THE	BID	OGB	ITT	EDA	NDR	ANO	$\mathbf{FF}$

• Try it for yourself: Here is a section of DNA before a mutation.

DNA	Т	Α	С	G	G	G	С	Т	С	Т	Α	G	С	G	А	G	А	Т	Α	Т	Т
mRNA	Α	U	G	С	С	С	G	А	G	А	U	С	G	С	U	С	U	А	U	А	Α
a.a. Methionine			Р	rolin	е	Gl	ut. ac	cid	lso	leuci	ine	Α	lanin	е	L	eucir	ne		Stop		

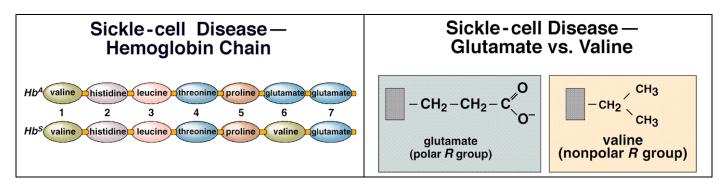
• Here the same section is after **one extra base** (a G in the third codon) has been **added** to the original sequence.

• Here the same section is after two bases have been switched from the original sequence.

mRNA a.a.	A Mo	U thion	G	<u>G</u>	C Llanin	C	G Gli	A ut. A	G	A	U leuci	<u>С</u>	G	C Ianin	<u>C</u>	C	U eucir	A	U	A Stop	A
DNA	Т	А	С	<u>C</u>	G	G	С	Т	С	Т	А	G	С	G	G	G	А	Τ	А	Т	Т

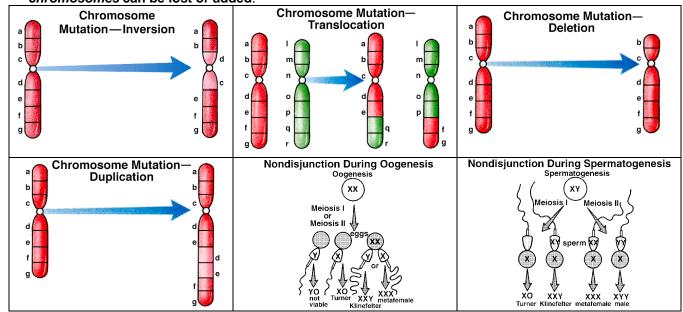
Notice the different effects that different "point" mutations can have!

- If there is a change in the DNA that causes a change in the significant part of the mRNA codon(s), a different amino acid will be translated, and a different protein will be made. Usually random changes are <u>HARMFUL</u> (frequently mutations are lethal). About one time in million, the change might actually improve the protein (this is called a <u>BENEFICIAL MUTATION</u>. Beneficial mutations, while infrequent, drive the <u>evolution</u> of species!
- Occasionally, a mutations will be "<u>neutral</u>" that is it will have no effect on the protein produced (as in the case
  of the second mutation in the second example above), or it will change an amino acid on a non-vital part of the
  protein.
- Gene mutations can cause <u>GENETIC DISORDERS</u>. For example, with the disease of <u>SICKLE</u> <u>CELL ANEMIA</u>, the normal round-shaped red blood cells are intermingled with some having a <u>sickle</u> shape. The sickle cells block the veins and arteries. As fewer and fewer normal red blood cells are able to pass through the congested blood vessels, the tissue and cells become starved for oxygen and other nutrients. This disease occurs when one amino acids present in the hemoglobin (the molecule of red blood cells responsible for oxygen and carbon dioxide transport) is misplaced because of an error in the messenger RNA which was made by a piece of DNA with <u>one</u> of its base pairs out of arrangement.



So, there are two main types of mutations:

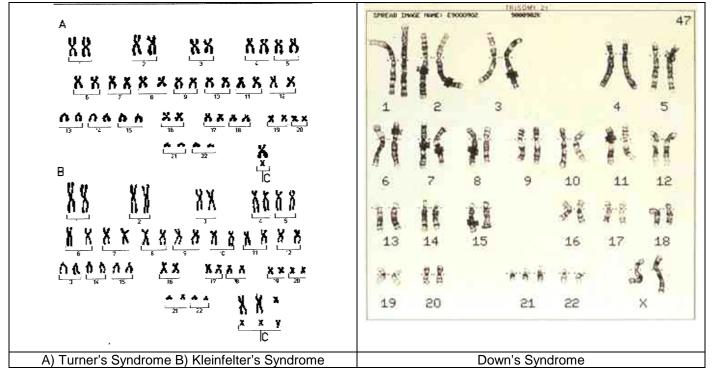
- 1. <u>GENE</u> Mutations: affect only a single gene. May be caused by a change (e.g. substitution, deletions, additions) in a single nucleotide. The effect on the individual depends on the gene's role. The sickle-cell anemia is a good example of a genetic disorder caused by a gene mutation.
- 2. <u>CHROMOSOMAL</u> Mutations: occur after chromosomes are broken (e.g. due to exposure to radiation, addictive drugs, pesticides) and reform abnormally. Pieces of chromosomes can be lost, added, or whole chromosomes can be lost or added.

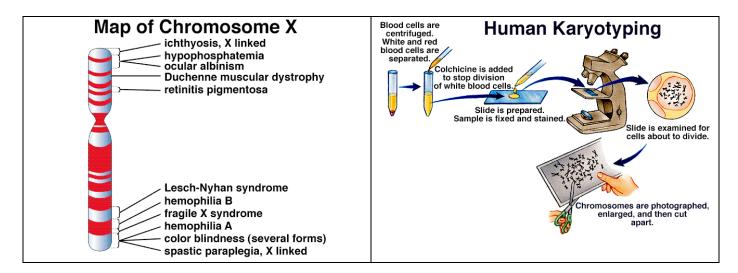


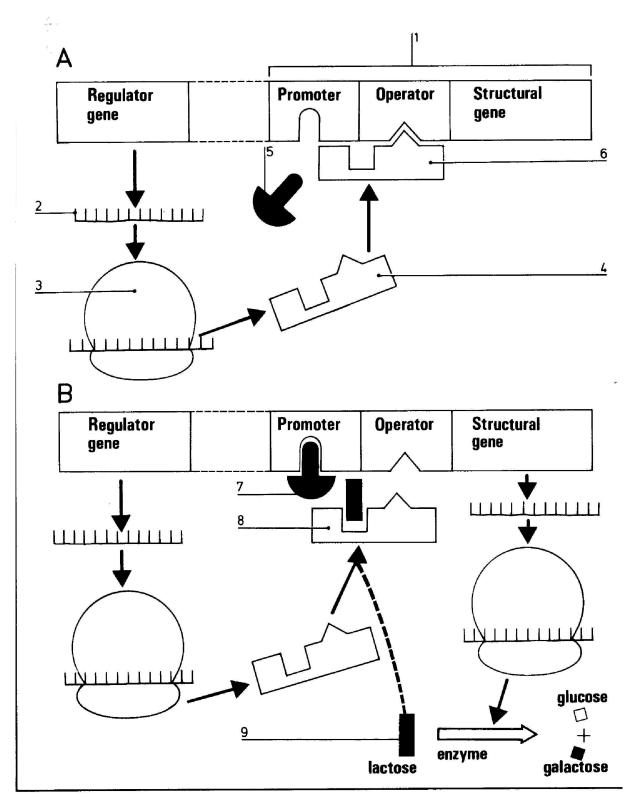
# **Genetic Disorders**

- since changes in DNA can directly affect protein synthesis, this in turn can drastically affect metabolism and body structure/function).
- For example, consider **PKU** (<u>phenylketonuria</u>): Caused by defect in the **enzyme** that converts **phenylalanine** to **tyrosine** (in PKU, tyrosine gets converted phenylpyruvic acid). This acid can build up and cause severe nervous system damage/mental retardation.
- **ALBINISM**: if the **enzyme** that converts **tyrosine** to **melanin** is defective, albinism occurs. These subjects will have no skin or hair pigment, and hence appear almost pure white.
- Most <u>birth defects</u> result from a chromosomal abnormality. The abnormality most frequently appears during meiosis when the egg and sperm cells are formed.
- One of the most common disorders is <u>DOWN'S</u> <u>SYNDROME</u>, or trisomy 21. It occurs in 1,000 out of every 100,000 births. (The chances of having a child with Down's syndrome, or *mongolism*, increases with the mother's age).
- There is **one chance in 60** that the children of a woman over the age of 40 will be affected. For women under 40 there is **one chance in 800**. Such children are born with an **extra chromosome #21** (47 chromosomes instead of the normal 46).
- During the formation of the egg, both number 21 chromosomes end up in the same egg cell.
- When the egg is fertilized by the sperm cell with its single number 21 chromosome, it produces a child with three number 21 chromosomes per cell.

- Other *trisomies* (having three chromosomes instead of the normal pair of chromosomes) which produce severe mental handicap are *trisomy 18* (*Edward's syndrome*) and *trisomy 13* (*Patau's syndrome*).
- <u>TURNER'S SYNDROME</u> is an example of an even rarer chromosomal abnormality. This condition is caused by the **absence of a second X or of the Y sex chromosome**. The result is a female child who is short and infertile.
- Some abnormalities are caused by the presence of an extra sex chromosome. The most common is
   KLEINFELTER'S SYNDROME, which occurs in about 1 out of every 700 males born. These babies have
   three sex chromosomes, two X chromosomes and one Y. They generally grow tall with long limbs and
   generally have IQ's that are significantly below those of their siblings. Spermatogenisis may be reduced or
   absent.







Gene induction –  $\beta$  galactosidase in *Escherichia coli* 

- A Operon repressed (structural gene switched off) B Operon derepressed (structural gene switched on)
- 1 Operon
- 2 mRNA
- 3 Ribosome
- 4 Active repressor
- 5 RNA polymerase

- 6 Repressor bound to operator blocking RNA polymerase binding site
- 7 RNA polymerase bound to promoter
- 8 Repressor inactivated by inducer
- 9 Inducer (lactose)