Sheet no.**1**

Molecular biology

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Black color:doctor's explanation, Navy color:slides,blue color:extra information, red color:Dr. Khaldoun's notes, highlighted sentence:modified, purple color: book's note.

-Topics:

1- General description of molecular biology

2- Introduction to nucleic acids

3- DNA-Hereditary (hereditary: the sum of all biological processes by which particular characteristics are transmitted from parents to their offspring)

4- Watson-Crick Model

5- Central Dogma

1- General description of molecular biology

Q: What is the molecular biology?

A: ***The knowledge of the structure, function, transmission of genes and the understanding of interactions among both genes, between genes and the environment.***

-we will study the structure of DNA and RNA as genetic material. DNA organization and its replication, mutation and repair in both prokaryotes and eukaryotes will be covered, , transcription of information from DNA to RNA, and then to proteins as well as gene expression will also be discussed, the course will cover some molecular biology techniques.

Q: Why molecular biology is important in medicine?

A: ***Molecular biology is one of the most rapidly advancing fields in medicine and is now integral to all aspects of biomedical sciences such as pharmacology, biochemistry, microbiology and pathology. because of that you have to understand molecular biology.***

- Every physician who practices in the 21st century will require a basic knowledge of the principles of molecular biology and their application to a wide variety of clinical problems. *(Doctor didn't give this part much importance)*

-The practice of modern medicine includes recognition of the role of genetic factors in health and disease. **(By understanding molecular biology)**

-We should know and understand many aspects of molecular biology, such as:

1. What genes are and how they are organized.
2. How genes are arranged in chromosomes and how chromosomes replicate.
3. The nature of mutations and how they are repaired, and how they contribute to human variability and disease.
4. What genes do: the flow of genetic information from DNA to RNA to protein.
5. How gene expression is controlled.
6. The significance of the Human Genome Project to medicine.

2- Introduction to nucleic acids

-We have 20 different amino acids, and by linking to each other in different sequences will do a variable proteins that we need, the same thing for nucleic acids.

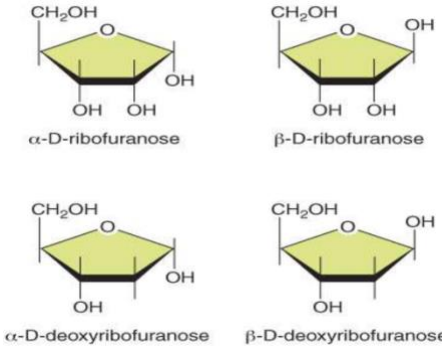
*We consider a nitrogen base as base because it is proton acceptor (chemistry 101).

*We consider a nucleic acid as an acid because of the presence of the negatively charged on phosphate group.

-There are two types of nucleic acid:

1- DNA contains the sugar Deoxyribose.

2-RNA contains the sugar Ribose



-Alpha means that hydroxyl groups at the same direction.

-Beta means that hydroxyl groups at the opposite direction.

-Remember, we can't use cis and trans terms here, why?

Cis and trans are only used if there are two substituted.

Deoxyribose= Ribose – oxygen atom at C2

Ribose is pentose, aldose, furanose.

*Back to biology 101:

1-pentose means the sugar is composed from 5 carbon atoms.

2-aldose means that the C=O at the end of carbon skeleton.

3-furanose is composed by the reaction between hydroxyl group at C1 and hydroxyl group at C4 to form close cycle of sugar.As simply, furanose is a five-membered ring system consisting of four carbon atoms and one oxygen atom.

Each carbon in the ring can tell us information about itself.
Carbon 1': will bind to the nitrogenous base.
Carbon 2': differentiates between the sugars ribose and deoxyribose through the presence or the absence of the hydroxyl group OH- on it.
Carbon 3': we will attach the next nucleotide to it.
Carbon 4': attaches to the carbon located outside the ring(5'C).
Carbon 5': attaches to the phosphate group.

-All sugars in nucleic acids are found in the form of furanose and not in the form of an open straight chain of pentose.

-The sugar in nucleic acids could be ribose or deoxyribose.

-NOW, what about D in the name of sugar? (In the image above)

D sugar means that the hydroxyl group at the carbon before the last (C4) is to the right in the open chain.

L sugar means that the hydroxyl group at the carbon before the last (C4) is to the left in the open chain.

L and D are isomer

-REMEMBER, nucleic acid is polynucleotide chain like a polypeptide chain.

-Sugar is one of the components of the building blocks of nucleic acid.

very important

- Nucleotide is composed of three components:

1) Sugar (now you are familiar with sugar)

2) Nitrogen base

3) Phosphate group

-We have two types of nitrogen bases, one is small, its nitrogen base is called PYRIMIDINE (Thymine and cytosine, six-membraned ring) and other one is big, and its nitrogen base is called PURINE (Adenine and Guanine, six-membraned ring and it is fused to five-membraned ring).

-There are three types of pyrimidine in DNA or in RNA:

In DNA: Thymine and Cytosine.

In RNA: Uracil (which replaces Thymine) and Cytosine.

-Note: SOMETIMES there is Uracil in DNA when cytosine in our genome is converted to uracil.As a result, mutations will be happened, diseases will be produced UNLESS this is repaired.

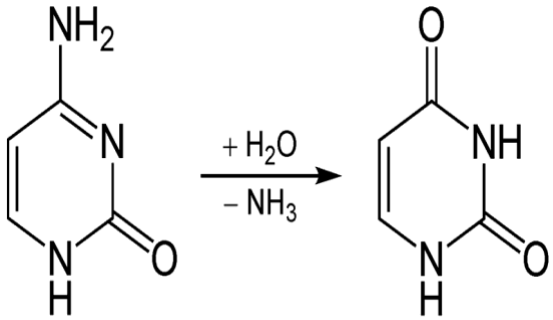
What is the mechanism that produces uracil from cytosine? By deamination which is happened spontaneously sometimes.

[No need to memorize the chemical structures if A, T, C, G, U, but you have to be able to differentiate them from each other]

-Just a hint to differentiate them from each other.

1)T—> 1 ring, methyl group, 2 ketone groups, no amino group.

2)C—>1 ring, no methyl group, 1 ketone group, 1 amino group.

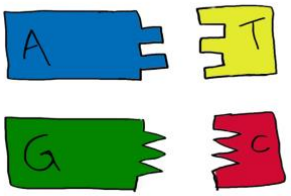


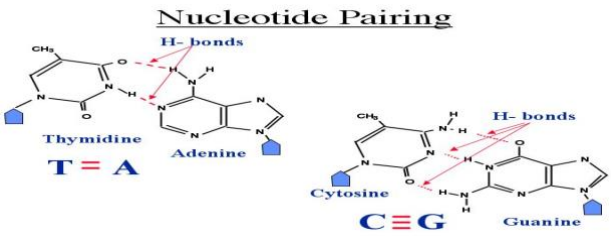
Cytosine Uracil

-If you remove amino group from cytosine, you get uracil.

3)A—>2 rings, amino group, NO ketone group.

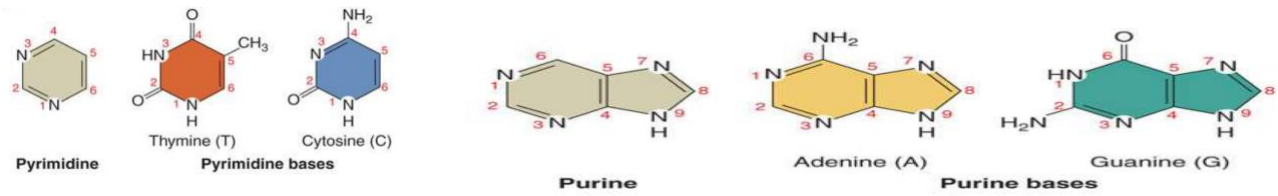
4)G—>2 rings, amino group, ketone group.





-C base paired with G (3 hydrogen bonds)

-A base paired with T (2 hydrogen bonds)



A nucleoside is a purine or a pyrimidine with a pentose, which is either ribose or deoxyribose.

-**The numbering of nitrogen bases**:

-Nitrogen bases numbering without primes (without primes 3',5' NOT prime numbers like 2,3,5,7,11).

-Why all that?

-To differentiate the atoms of sugar from the atoms of the nitrogen bases; because when we study the nucleotide metabolism, we will be able to know the sources of these atoms, and what are the molecules that are responsible to participate in the synthesizing of purine and pyrimidine ((later on biochemistry)).

-Nucleoside forming by attachment between nitrogen base and sugar by a **N-glycosidic bond** which is a **covalent bond**.

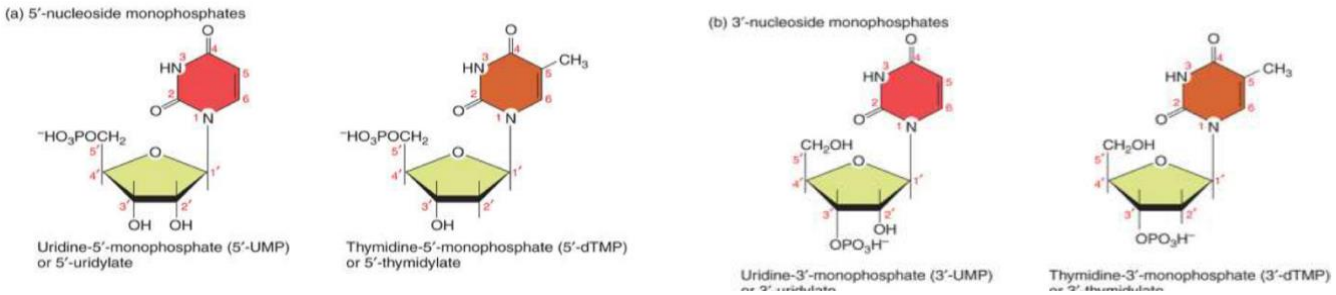
-In pyrimidine N1 attaches to 1'C **BUT** in purine N9 attaches to 1'C **-remember the numbering system of nitrogen bases-.**

-What is the difference between uracil and uridine (to name but a few)**?**

-Uracil is a nitrogen base but uridine is a nucleoside.

-What about the bonds between two nucleosides in different chains? They are hydrogen bonds **NOT** N-glycosidic bonds **(The bonds form between NITROGEN BASES not sugar)** (Not necessary to identify or memorize the site between two nucleosides, and where hydrogen bonds are formed, we will take it when we talk about double helical structure).

-What is the difference between the structures in the image above and the structures in the image below?



The difference is the phosphate group, which is the third component of nucleic acids, when the phosphate group is attached, the structure now is called a nucleoside monophosphate (if one phosphate group is attached), if two phosphate groups are attached the structure is a nucleoside diphosphate, and so on.

If the nucleoside attaches to a phosphate group, the structure is called a nucleotide, regardless the number of phosphate group.

***JUST FOR INCLUSIVELY, the table below is in the book, but doctor doesn't mention that in the lecture.**

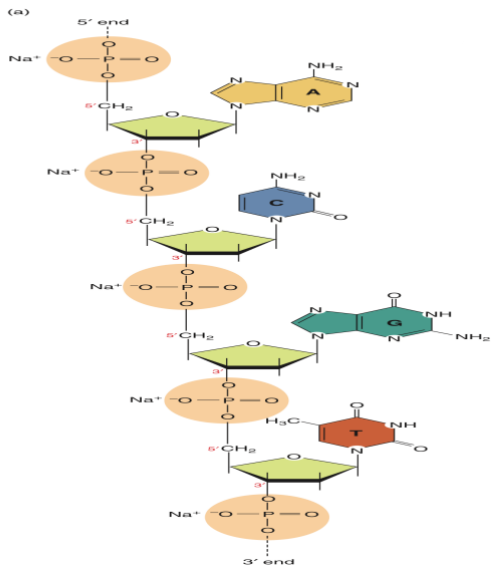
TABLE 1.1 Bases, Nucleosides, and Nucleotides

Base	Sugar	Nucleoside	5′-Mononucleotide
Uracil (U)	ribose	uridine	Uridine-5′-monophosphate or 5′-uridylate (5′-UMP)
Cytosine (C)	ribose	cytidine	Cytidine-5′-monophosphate or 5′-cytidylate (5′-CMP)
Adenine (A)	ribose	adenosine	Adenosine-5′-monophosphate or 5′-adenylate (5′-AMP)
Guanine (G)	ribose	guanosine	Guanosine-5′-monophosphate or 5′-guanylate (5′-GMP)
Thymine (T)	deoxyribose	deoxythymidine[1]	Deoxythymidine-5′-monophosphate or 5′-deoxythymidylate (5′-dTMP)[1]
Cytosine (C)	deoxyribose	deoxycytidine	Deoxycytidine-5′-monophosphate or 5′-deoxycytidylate (5′-dCMP)
Adenine (A)	deoxyribose	deoxyadenosine	Deoxyadenosine-5′-monophosphate or 5′-deoxyadenylate (5′-dAMP)
Guanine (G)	deoxyribose	deoxyguanosine	Deoxyguanosine-5′-monophosphate or 5′-deoxyguanylate (5′-dGMP)

[1]Deoxythymidine and deoxythymidine-5′-monophosphate are also called thymidine and thymidine-5′-monophosphate, respectively. When thymine is attached to ribose, the nucleoside is called ribothymidine and the nucleotide is called ribothymidylate. This nomenclature convention follows from the fact that thymine is most frequently attached to deoxyribose.

-Now you have to know that nucleic acids are polynucleotide chains (later on, we will take how nucleotides link to each other).

- DNA is a linear chain of deoxyribonucleotides (e.g:dAMP,dTMP,dCMP)



-DNA and RNA are polynucleotide chains, but in RNA instead of T, it has U.

Segment of a polydeoxyribonucleotide. ((this structure is extended structure as a sodium salt))-the image above-.

-At 3’ end there is hydroxyl group.

-At 5’ end there is phosphate group.

- All DNA and RNA chains have a 5’ and 3’ terminus.

- Phosphodiester bond joins neighboring nucleosides (two nucleosides are contributed, between two molecules of sugar NOT nitrogen bases).

- Phosphodiester is formed between 3’C of the first nucleotide and 5’C of the second nucleotide.

-First nucleotide in all polynucleotides doesn’t possess phosphodiester, but it has a phosphate group at 5’.

-last nucleotide has a hydroxyl group at 3’.

3- DNA-Hereditary:

Scientists want to know what is the chemical nature of the hereditary material, is it a protein? RNA? polysaccharide? DNA?

Fred Griffith started to investigate what is the chemical nature of the hereditary material of eukaryotics and prokaryotics ,in 1928 there was a sudden breakthrough of pneumonia caused by [S(streptococcus). pneumoniae bacteria]

Fred Griffith studied the bacteria, he found that this bacterium has two colonies on their culture:

- **S (smooth) bacteria – lethal.**
- **Mutant R (rough) bacteria – non-lethal.**

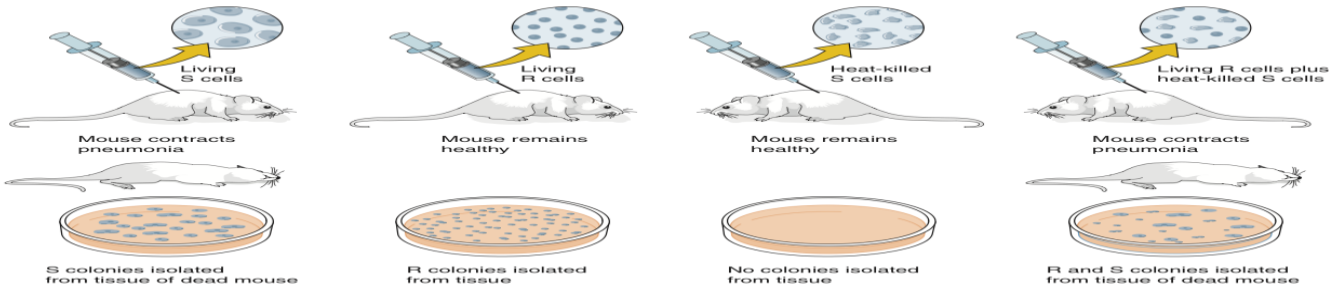


FIGURE 1.11 Griffith's experiment demonstrating bacterial transformation. A mouse dies from pneumonia if injected with the virulent S (smooth) strain of *Streptococcus pneumoniae*. However, the mouse remains healthy if injected with either the nonvirulent R (rough) strain or the heat-killed S strain. R cells in the presence of heat-killed S cells are transformed into the virulent S strain, killing the mouse.

-he treated the S bacteria by heating,the result is heat killed S bacteria which is non-lethal.

***When we say this bacterium (the singular form of the "bacteria") is lethal or pathogenic, we are talking about phenotype.**

***Phenotype: the set of observable characteristics of an individual resulting from the interaction of its genotype.**

-The Chemical Nature of the Transforming Principle:

- 1944 - Avery, Mcleod and McCarty

-When heat killed S bacteria and R bacteria are mixed the result is LETHAL, why? Because the genetic material is changed when heat killed S bacteria penetrated R bacteria, this changing in genetic material is called transformation.

-R cells are transformed because the transforming factor or principle (heat killed S bacteria) changed the genetic constituent to cause pneumonia, but scientists didn't know the chemical structure of the transforming factor, it may be protein ,RNA, polysaccharide or DNA.

-Come here to know what is the chemical structure of the transforming factor:

1) Proteins. It can't be,why? Because when you treat it by heat or proteolytic enzyme, protein will denature and it will lose its function, then by injecting the mouse, it will die. [NO]

2)RNA. It can't be,why? Because when you proceed a treatment by RNase , RNA will get destroyed, then injects the mouse,it will die. [NO]

3)polysaccharide. It can't be,why? Because when you treat the sample by adding analysis to digest polysaccharide, then injects the mouse,it will die. [NO]

4) DNA is the genetic material, if the heat killed S bacteria is killed by DNase then injects in the mouse,the mouse will not get the pneumonia. Because of that,they conclude that DNA is the genetic material. [YES]

-To sum up:

- **Purified polysaccharides from S cells did not transform R cells.**
- **Transforming Principle not destroyed by proteolytic enzymes or Rnase.**
- **DNase inactivated the Transforming Principle • DNA is the Transforming Factor.**

- Chargaff's Rules:

-He studied a lot of DNA samples from different species, from humans, animals, etc.

He found:

- **Double stranded DNA has equimolar adenine and thymine concentrations as well as equimolar guanine and cytosine concentrations.**
- **DNA composition varies from one genus to another.**

———————————————————————————

4- Watson-Crick Model

In 1953 **,Rosalind Franklin was walking on the X-ray crystallography for DNA structure ,and she built a model of DNA as a double strands, she combined data from Griffith and Chargaff and her data and concluded that the DNA is a double stranded molecule, and she went to a conference, watson and crick attended that conference, and they published their model in a paper composed of one page In British scientific weekly nature.**

-To sum up:

Rosalind Franklin and Maurice Wilkins Generated X-ray diffraction patterns that lead to the solution of DNA's structure.

Watson and Crick built a model consistent with X-ray diffraction data.

– Double helix

– Adenine pairs with Thymine

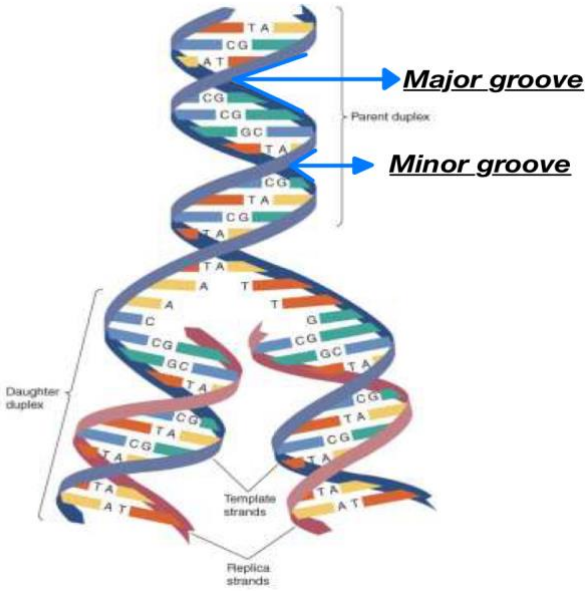
– Guanine pairs with Cytosine

– Held together by Hydrogen Bonds

-Key Features:

- **2 DNA strands twist about each other to form a double helix.**
- **Phosphate and sugar groups form backbone on the outside.**

- **Base pairs stack inside the helix**
- **Helix diameter of 2.0 nm.**
- **Adenine - Thymine base pairs – 2 hydrogen bonds.**
- **Guanine – Cytosine base pairs – 3 hydrogen bonds.**
- **Antiparallel strands – One strand 3’ to 5’ – Other strand 5’ to 3’.**
- **Sequence is always written by convention from 5’ to 3’.**
- **Major groove and Minor groove wind about outer face.**
- **Each strand serves as the template for the synthesis of the complimentary strand.**



The Nobel Prize in Physiology or Medicine in 1962 was awarded to James Watson, Francis Crick and Maurice Wilkins for their discovery of the molecular structure of DNA, which helped solve one of the most important of all biological riddles.

-Rosalind is the real discoverer of DNA structure.

The double strands are complementary, it is a very important structural feature; because that explains DNA replication and DNA transcription.

-How dose it explains DNA replication?

-Each strand will be used as a template for synthesizing a new strand, the daughter strand will resemble the parent strand.

-Why it is important in DNA transcription?

-Because the RNA strand is complementary to the parent.

-The two double strands molecules are twisted to each other, it is found by experiment of using X-ray crystallography.

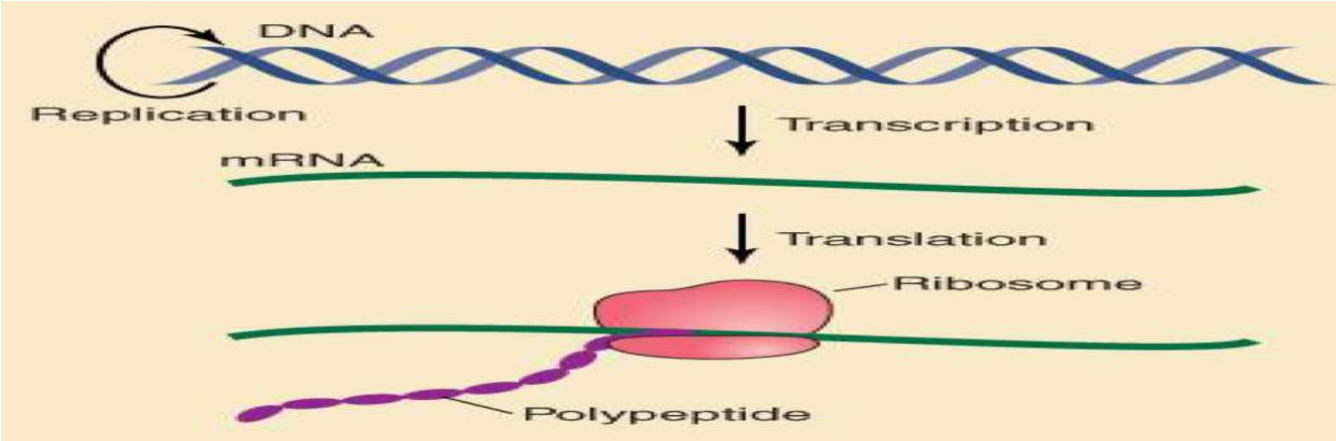
- The crystallized structure of the DNA shows us that the DNA structure is a double helix, while being in this state, the double helical structure makes two gaps, a large and a small one, the large one is called the major groove and the small one is called the minor groove, this is an important feature in this model because the transcription factors and the regulatory protiens will come and bind at the major groove (not sure if it's the major or the minor one) so that they could sneak in, read the hydrogen bonding in that specific region, read the sequence of nucleotides, help the protein bind specifically in its site into the DNA sequence and affect the expression of that gene that constitutes these sequences.

-To sum up, cells have specific proteins to bind at specific gene.

Because of this feature, genes are expressed differently despite of having the same DNA structure; because cells have different and selective proteins.

5- Central Dogma

-Central Dogma is how genetic information flows from DNA to protein.



Genetic information flows from:

– DNA to DNA (Replication)

– DNA to RNA (Transcription)

– RNA to polypeptide (Translation)

—BEST WISHES—

—END—

-Test your knowledge:

Q1) Which one of these statements about nitrogenous bases is TRUE?

A. Adenine and thymine are purines.

B.cytosine and guanine are pyrimidines.

C. guanine is a purine and Adenine is a pyrimidine.

D. Adenine is a purine, uracil is a pyrimidine.

Q2)

A.

B.

C.

D.

E.

Q3) The glycosidic bond that exists in nucleosides is between

explanation below

A. 3' carbon of sugar and N9 of adenine.

B. 1' carbon of sugar and N1 of guanine.

C. 5' carbon of sugar and N1 of cytosine.

D. 1' carbon of sugar and N9 of guanine.

E. 5' carbon of sugar and N1 of thymine

Q4) RNA molecules contain an additional oxygen atom compared to DNA molecules located on which carbon atom of the pentose sugar:

A.1.

B.2.

C.3.

D.4.

E.5.

ANSWER: 1:D|2: |3:D|4:B

Q5) A template of DNA is 5-ATCGGCTACAATGTA-3; what is the complimentary DNA sequence?

A. 5'UACAUUGUAGCCGAU3'.

B. 5'TAGCCGATGTTACAT3'.

C. 5'TACATTGTAGCCGAT3'.

D. 5'TACAAAGTAGCCGAT3'.

E. 5'ATCGGCTACAATGTA3'

Q6) One strand of a DNA segment contains 33 A, 25 G, 12 T, and 41 C. how many each base is found in the original double- stranded DNA molecule? (explanation below)

A. A-46, G-50, C-50, T-46.

B. A 66, G 53, C-53, 7-66.

C. A-45, G-66, C-66 T-45.

D. A-66, G-24, C-24 T-66.

E. A-45, G-50, C50, T-45

Q7) Complementarity is a feature of DNA that indicates the following:

A. Bases are almost perpendicular to the side chains.

B. DNA is anti-parallel.

C. A minor groove is opposite to a major groove.

D. DNA is helical.

E. Number of (A+G) = number of (T+C)

Q8) Each nucleoside is attached to the other nucleoside by: (modified)

A. ionic bonds.

B. phosphodiester bonds.

C. hydrogen bonds.

D. glycosidic linkages.

E. disulfide bridges.

ANSWER: 5:C|6:C|7:E|8:B

Q9) major and minor grooves in DNA structures are formed because of:(explanation below)

A. the anti-parallel nature of the two strands of DNA.

B. DNA packing by histones.

C. the pattern of hydrogen bonding between nucleotides.

D. DNA is not perfectly helical.

E. the bending capability of DNA.

Q10) Nitrogenous bases are attached to each other by:

A. hydrogen bonds.

B. ionic bonds.

C. glycosidic linkages.

D. phosphodiester bonds.

E. disulfide bridges.

Q11)What is the maximum number of phosphate groups that can be attached to pentose sugars in nucleotides?

A. 1

B. 2

C. 3

D.4

E. there is no specific max number.

Q12) Nitrogenous bases are attached to sugar molecules by:

A. hydrogen bonds

B. ionic bonds

C. glycosidic linkages

D. disulfide bridges

E. phosphodiester bonds

ANSWER: 9:C|10:A|11:C|12:C|

- Explanations:

Q6: The number of adenine (A) bases in a DNA molecule is always equal to the number of thymine (T) bases, and the number of guanine (G) bases is always equal to the number of cytosine (C) bases.
Therefore, the complementary strand to the given DNA segment would have:

- 33 T (equal to the number of A)
- 25 C (equal to the number of G)

- 12 A (equal to the number of T)
- 41 G (equal to the number of C)

So, the total number of each base in the original double-stranded DNA molecule would be:

- A: 33 + 12 = 45
- T: 12 + 33 = 45
- G: 25 + 41 = 66
- C: 41 + 25 = 66

Therefore, the correct answer is option C: A-45, G-66, C-66, T-45.

Q9:

The major and minor grooves in DNA structures are formed because of the pattern of hydrogen bonding between nucleotides.

The DNA double helix is formed by two strands of nucleotides held together by hydrogen bonds between complementary base pairs: adenine (A) and thymine (T), and guanine (G) and cytosine (C). The base pairs are arranged in a way that the distance between the two strands is not uniform, leading to the formation of major and minor grooves.

The major groove is formed by the wider separation of the two DNA strands, and it provides a site for specific protein binding and recognition. The minor groove is formed by the closer proximity of the two DNA strands and is also involved in protein binding.

Therefore, the correct answer is C: the pattern of hydrogen bonding between nucleotides.

V2:

Page 3: I just added a note mentioned in Dr.khaldoun's lecture.

Page 4: I just added a note mentioned in Dr.khaldoun's lecture.

Page 6: To differentiate the atoms of sugar from the atoms of nitrogen bases NOT *nucleic acids*.

Page 7: I just added a table.

Page 8: started NOT starts.

Page 9: Slide 3: I just added a note mentioned in Dr.khaldoun's lecture.

Q9: the correct answer is C.

Q9: two not tow (spelling mistake).

I just removed Q2 because it depends on the information that was mentioned last year by Dr.Mamoun JUST TO MORE BENEFIT I ADDED THIS QUESTION, BUT I HAVE TO REMOVE IT, SORRY.