DEOXYRIBONUCLEIC ACID

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By the end of lecture we will able to know: (basic chemistry of genetic)

- Chemical structure of DNA
- CHARGAFF’S RULE
- FORMs OF DNA
- Biomedical importance
NUCLEIC ACID

• Nitrogenous non-protein substances made up of polymeric macromolecules called NUCLEOTIDES.
Two types of nucleic acid present in living organisms

1. DNA - Deoxyribonucleic acid
2. RNA - Ribonucleic acid
DEOXYRIBONUCLEIC ACID

KEEP CALM AND ACTIVATE PRIOR KNOWLEDGE
Every living thing is made of cells.**

Most plant and animal cells have a nucleus.** The nucleus tells the cell what to do.

Inside the nucleus are chromosomes.**

Chromosomes are made of long strands of tightly coiled DNA. (If you stretched out the DNA from a human cell, it would be about six feet long!)
AMAZING DNA FACTS

• DNA from a single human cell extends in a single thread for almost 2 meters long!!!

• It contains information equal to some 600,000 printed pages of 500 words each!!!
  (a library of about 1,000 books)
Every living thing has **DNA**. That means that you have something in common with a zebra, a tree, a mushroom and a beetle!!!!
DEOXYRIBONUCLEIC ACID

- DNA is the molecular basis of inheritance
- DNA is a polymer of deoxyribonucleotides.
- It is found in chromosomes, mitochondria and chloroplast.
- The nuclear DNA is bounded to basic proteins called histone.
- DNA is present in every nucleated cell and carries genetic information.
DNA is Coiled Around Histone Proteins

- DNA is wrapped around nuclear proteins called Histones
- This forms a complex called a Nucleosome
- Histones are H1, H2A, H2B, H3, H4
DNA is Further Packaged
CHEMICAL STRUCTURE

DNA consist of three components

1. Nitrogenous base
   a. purine
   b. pyrimadine
      DNA = adenine, cytosine, guanine, thymine.

2. Pentose sugar
   D-2-deoxyribose

3. Phosphate group

DNA is made up of repeating molecules called NUCLEOTIDES
DNA Nucleotide

Phosphate Group

Nitrogenous base (A, G, C, or T)

Sugar (deoxyribose)
Nucleic Acid Structure
Polymerization

Phosphodiesterase

(PPi)
Nucleic Acid Structure
Polymerization

Sugar Phosphate “backbone”

Nucleotide
Nucleic Acid Structure
Polymerization

Sugar Phosphate
“backbone”

Bases

5’ TAG-CAC 3’
Watson & Crick proposed...

• DNA had specific pairing between the nitrogen bases:
  - ADENINE – THYMINE
  - CYTOSINE - GUANINE

• DNA was made of 2 long stands of nucleotides arranged in a specific way called the “Complementary Rule”
Nitrogenous Bases

• **PURINES**
  1. Adenine (A)
  2. Guanine (G)

• **PYRIMIDINES**
  3. Thymine (T)
  4. Cytosine (C)
In fact, the DNA usually consists of a double strand of nucleotides.

The sugar-phosphate chains are on the outside and the strands are held together by chemical Bonds (Hydrogen bonds) between the bases.
DNA Double Helix

- "Rungs of ladder"
- Nitrogenous Base (A, T, G or C)
- "Legs of ladder"
- Phosphate & Sugar Backbone
Chargaff’s Rule (1940)

The molar equivalence b/w the purines and pyrimidines bases of DNA

- **Adenine** must pair with **Thymine**
- **Guanine** must pair with **Cytosine**
- Their amounts in a given DNA molecule will be **the same**.
CHARGAFF’S RULE

• The purines to pyrimidines ratio in DNA = 1
  i.e. \( A + G = T + C \) or \( \frac{A + G}{T + C} = 1 \)

• In DNA molecule, the glycosidic bonds between sugar and bases are not directly opposite each other hence two grooves of unequal width are formed around the double helix. The edge of the helix >180 degree, it is called the major groove and when it is <180 degree, it is called minor groove.
BASE-PAIRINGS

H-bonds

G

C

T

A
DNA double Helix

1. Rt handed in B-DNA and A-DNA and Lt handed in Z –DNA.
2. Consists of two polydeoxynucleotide strands twisted around each other on a common axis.
3. Two axis are antiparallel i.e one runs in 3' to 5', and other 5' to 3' direction.
4. Diameter of helix is 20 Å.
5. Each turn (pitch) is 34 Å.
6. hydrophilic backbone of deoxyribose phosphate towards periphery of molecule and hydrophobic bases are inside.
7. Two strands are not identical but complementary to each other due to base pairing.
8. Two strands held together by H-bonds. 
   \[ A = T \quad \text{and} \quad C \equiv G. \]
9. The complementary base pairing proves Chargaff’s rule.
10. The double helix has wide major and narrow minor grove.
11. The genetic information on template or sense strand and the other as antisense.
The sequence of bases in DNA forms the **Genetic Code**

A group of three bases (**a triplet**) controls the production of a particular amino acid in the cytoplasm of the cell.

The different amino acids and the order in which they are joined up determines the sort of protein being produced.
The proteins build the cell structures.

They also make enzymes.

The DNA controls which enzymes are made and the enzymes determine what reactions take place.

The structures and reactions in the cell determine what sort of a cell it is and what its function is.

So DNA exerts its control through the enzymes.
STRUCTURE OF DNA

PRIMARY STRUCTURE

• Chromosomal DNA consists of a very long DNA molecules (M wt $1.6 \times 10^6$ to $2 \times 10^{10}$)
• Each DNA molecule is a polymer of about $10^{10}$ deoxyribonucleotides.
• DNA has following 4 different forms of deoxyribonucleotides.
MONOMERIC UNITS OF DNA

a. Adenine deoxyribonucleotides\([dA]\)
b. Thymine deoxyribonucleotides\([dT]\)
c. Guanine deoxyribonucleotides\([dG]\)
d. Cytocine deoxyribonucleotides\([dC]\)
• Each nucleotide is linked to the neighbouring nucleotide through 3´,5´-phosphodiester bond.
• The DNA stand that bears a free 5´-phosphate group without phosphodiester linkage is called 5´-end, the opposite end bears a free 3´-OH or 3´-phosphate group is called the 3´-end.
• The primary structure of DNA is the number and sequence of different deoxyribo-nucleotides in its strands joined together by phosphodiester linkage.
1) Phosphodiester bonds
5’ and 3’ links to pentose sugar

2) N-glycosidic bonds
Links nitrogenous base to C1’ pentose in beta configuration
5' - 3' polarity

Phosphodiester bonds

5' end

3' end

3'-hydroxyl

5'-phosphate
SECONDRY STRUCTURE

• It is double stranded helix formed by the two polydeoxyribonucleotides strands coiled around a central axis.
• The helix is right/left handed.
• The strands are antiparallel to each others.
• Sugar + phosphate = back bone of helix. (hydrophilic).
• The aromatic hydrophobic rings of bases, located in the interior of the helix are perpendicular to the long axis of the helix.
• Adenine of one DNA strand bound to Thymine of other DNA strand by double H=H bound.
• Guanine of one DNA strand bound to Cytosine of other DNA strand by triple H \equiv \ H bound.
Nucleic Acid Structure
“Base Pairing”
DNA Double Helix

[Diagram showing the structure of a DNA double helix with labeled nucleotides and sugar-phosphate backbones.]

- P: Phosphate group
- O: Oxygen atom
- G: Adenine (A) base
- C: Guanine (G) base
- T: Thymine (T) base
- A: Adenine (A) base
Nucleic Acid Structure
The double helix

Minor Groove

Major Groove
• The antiparallel strands of DNA are not identical, but are complementary.
• This means that they are positioned to align complementary base pairs: C with G, and A with T.
• So you can predict the sequence of one strand given the sequence of its complement.
• Useful for information storage and transfer!
FORMs OF DNA

- DNA exist in several conformations depending upon the bases, composition, chemical and physiological conditions and structure. The double helical structure of DNA exists in at least 6 different forms A-E and Z, among those following are important:
  - 1. B- DNA.
  - 2. A- DNA.
  - 3. Z- DNA.
Essential features of B-DNA

- Right twisting
- Double stranded helix
- Anti-parallel
- Bases on the inside (Perpendicular to axis)
- Uniform diameter (~20Å)
- **Major** and **minor** groove
- Complementary base pairing
B-DNA

- Right-handed helix
- Intermediate
- Planes of the base pairs nearly perpendicular to the helix axis
- Tiny central axis
- Wide + deep major groove
- Narrow + deep minor groove
GEOMETRY OF B-DNA

- B-DNA IS BIOLOGICALLY THE MOST COMMON
- BASE THICKNESS
  - AROMATIC RINGS WITH 3.4 Å THICKNESS
  - IDEAL B-DNA HAS 10 BASE PAIRS PER TURN
- MINOR GROOVE IS NARROW
- MAJOR GROOVE IS WIDE
DNA conformations

**A-DNA**

- Right-handed helix
- Widest
- Planes of the base pairs inclined to the helix axis
- 6A hole along helix axis
- Narrow + deep major groove
- Wide + shallow minor groove
- 11.6 BP PER TURN
DNA conformations

**Z-DNA**

- Left-handed helix
- Narrowest
- Planes of the base pairs nearly perpendicular to the helix axis
- No internal spaces
- No major groove
- Narrow + deep minor groove
## DNA conformations

<table>
<thead>
<tr>
<th></th>
<th>A- DNA</th>
<th>B-DNA</th>
<th>Z-DNA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Helix</strong></td>
<td>Right-handed</td>
<td>Right-handed</td>
<td>Left-handed</td>
</tr>
<tr>
<td><strong>Width</strong></td>
<td>Widest</td>
<td>Intermediate</td>
<td>Narrowest</td>
</tr>
<tr>
<td><strong>Planes of bases</strong></td>
<td>planes of the base pairs inclined to the helix axis</td>
<td>planes of the base pairs nearly perpendicular to the helix axis</td>
<td>planes of the base pairs nearly perpendicular to the helix axis</td>
</tr>
<tr>
<td><strong>Central axis</strong></td>
<td>6A hole along helix axis</td>
<td>tiny central axis</td>
<td>no internal spaces</td>
</tr>
<tr>
<td><strong>Major groove</strong></td>
<td>Narrow and deep</td>
<td>Wide and deep</td>
<td>No major groove</td>
</tr>
<tr>
<td><strong>Minor groove</strong></td>
<td>Wide and shallow</td>
<td>Narrow and deep</td>
<td>Narrow and deep</td>
</tr>
</tbody>
</table>
A form
B form
Z form

28 Å
You can tell people apart by their fingerprints...

Because everyone’s fingerprints are different!
DNA is like a fingerprint because everyone's is a little different!

How does the police look at DNA to figure out who committed a crime?
The DNA gets cut up by special scissors!!!
The scissors can only cut the same colour!
All of the cut up pieces of DNA are different sizes.
A special machine sorts the DNA by size. (Little pieces are fast, so they move faster to the bottom.)
We are **ALL** a little bit different!

Miss Hiba’s DNA

Sara’s DNA
Our DNA has different sizes of pieces so it makes a different pattern when it’s all cut up.

Miss Hiba’ DNA

Sara’s DNA
This is what it really looks like!!!
ANY QUESTION
• CHATTERJEA BIOCHEMISTRY
• LIPPINCOTT BIOCHEMISTRY
• HARPERS BIOCHEMISTRY
• SATYANARAYANA BIOCHEMISTRY
• INTERNET

Thank you