BIOCHEMISTRY- BP203T

UNIT: 4 NUCLEIC ACID METABOLISM AND GENETIC INFORMATION TRANSFER

CLASS:5

TOPIC: ORGANIZATION OF MAMMALIAN GENOME

The **organization of the mammalian genome** is highly structured and complex, reflecting the need to tightly regulate gene expression, replication, and repair. Here is an overview of its main features:

1. DNA Sequence and Chromosomes

- The mammalian genome is composed of **double-stranded DNA** packaged into **linear chromosomes**.
- Humans have **23 pairs of chromosomes** (46 total), while other mammals have different numbers (e.g., mice have 20 pairs).
- Each chromosome contains **coding** (genes) and **non-coding** sequences (regulatory elements, repetitive elements, etc.).

2. Genes and Gene Structure

- **Protein-coding genes** make up about **1-2%** of the genome.
- Genes include:
    - **Exons** (coding sequences)
    - **Introns** (non-coding regions between exons)
    - **Promoters** and **enhancers** (regulatory DNA sequences)

- Many genes undergo **alternative splicing**, producing multiple protein variants from a single gene.

3. Non-Coding DNA

- A large portion of the genome is non-coding but **functionally important**.
- Includes:
    - **Regulatory elements** (enhancers, silencers, insulators)
    - **Non-coding RNAs** (e.g., microRNAs, lncRNAs)
    - **Repetitive elements** (transposons, satellite DNA)

4. Chromatin Structure

- DNA is wrapped around **histone proteins**, forming **nucleosomes** — the basic unit of chromatin.
- Chromatin exists in two forms:
    - **Euchromatin** – loosely packed, transcriptionally active
    - **Heterochromatin** – tightly packed, transcriptionally silent
- Chromatin structure is dynamic and regulated by **histone modifications**, **DNA methylation**, and **chromatin remodeling complexes**.

5. Higher-Order Genome Organization

- Chromatin is further organized into:
    - **Topologically Associating Domains (TADs)** – regions of the genome that interact more frequently with themselves than with other regions.
    - **Chromosome territories** – distinct regions in the nucleus occupied by individual chromosomes.
    - **Loops** between enhancers and promoters facilitate gene regulation.

6. Mitochondrial Genome

- Mammals also have a small **mitochondrial genome** (~16.5 kb in humans), inherited maternally.
- Encodes 37 genes, mostly related to oxidative phosphorylation.

The **organization of the mammalian genome** in the context of **nucleic acid metabolism** and **genetic information transfer** reflects how DNA is structured, maintained, and expressed to ensure accurate flow of genetic information from DNA to RNA to protein. Here is a breakdown aligned with the **central dogma of molecular biology** and **nucleic acid processes**:

1. DNA Organization and Replication (Nucleic Acid Metabolism)

A. Chromatin and Nucleosomes

- **DNA is wrapped around histone proteins** forming nucleosomes → compacts DNA and regulates accessibility for transcription, replication, and repair.
- Chromatin can be:
    - **Euchromatin**: accessible, gene-rich, actively transcribed
    - **Heterochromatin**: compact, gene-poor, silenced

B. Replication Origins

- **Replication begins at multiple origins** along each chromosome.
- **Replication forks** progress bidirectionally.
- Controlled by:
    - **Origin recognition complexes (ORC)**
    - **DNA polymerases**
    - **Helicases, primases, ligases**, etc.

C. DNA Repair and Maintenance

- Mechanisms include:
    - **Base excision repair**
    - **Nucleotide excision repair**

- **Mismatch repair**
- **Double-strand break repair (HR and NHEJ)**

- Ensures genomic stability and faithful inheritance.

2. Transcription and RNA Processing (Genetic Information Transfer)

A. Gene Structure

- Includes **promoters**, **enhancers**, **exons**, **introns**, and **terminators**.
- **Transcription factors** and **RNA polymerase II** initiate mRNA synthesis at promoter sites.

B. Transcription

- Occurs in the **nucleus**.
- mRNA is transcribed from the **template DNA strand**.
- Controlled by:
  - **Enhancers/silencers**
  - **Transcription factors**
  - **Epigenetic marks** (e.g., DNA methylation)

C. RNA Processing

- **Primary transcript (pre-mRNA)** undergoes:
  - **5' capping**
  - **Splicing** (removal of introns)
  - **3' polyadenylation**
- Processed mRNA is exported to the cytoplasm for translation.

3. Translation and Protein Synthesis

A. mRNA Translation

- Occurs on **ribosomes** in the **cytoplasm**.
- **mRNA codons** are read to assemble amino acids into proteins using:

- **tRNA** (transfer RNA)
- **rRNA** (ribosomal RNA)
- **Initiation, elongation, and termination factors**

B. Post-Translational Modifications

- Proteins may undergo **folding, cleavage, phosphorylation, glycosylation**, etc., for full functionality.

4. Regulatory RNAs and Non-Coding Elements

- **miRNAs, siRNAs**: regulate mRNA stability and translation.
- **lncRNAs**: regulate chromatin structure, transcription, and splicing.
- **snRNAs, snoRNAs**: involved in splicing and ribosome biogenesis.
- These elements form an additional layer of control in gene expression.

5. Epigenetic and Structural Genome Features

A. DNA Methylation

- Suppresses gene expression, often in promoter CpG islands.

B. Histone Modifications

- Acetylation, methylation, phosphorylation affect chromatin state and transcription.

C. 3D Genome Architecture

- **TADs** and **chromatin loops** facilitate spatial regulation of gene expression.
- Enhancer-promoter contacts are essential for tissue-specific gene expression.

6. Genome in Cell Cycle and Inheritance

- During **mitosis**, chromatin condenses into visible chromosomes for segregation.
- During **meiosis**, homologous recombination increases genetic diversity.

Summary Table

Process	Key Molecules Involved	Location
DNA Replication	DNA polymerases, helicases, ligase	Nucleus
Transcription	RNA polymerase II, transcription factors	Nucleus
RNA Processing	Spliceosome, capping enzymes	Nucleus
Translation	Ribosomes, tRNA, mRNA	Cytoplasm
Epigenetic Regulation	DNMTs, histone modifiers	Nucleus
RNA-mediated Regulation	miRNA, siRNA, lncRNA	Nucleus/Cytoplasm