Chapter 5: Molecular Basis of Inheritance

Comprehensive Study Notes

Class 12 Biology - NCERT Based

EXAM SPRINT - Complete Coverage for NEET and Board Examinations

Introduction

The molecular basis of inheritance deals with the chemical nature of genetic material and the mechanisms by which genetic information is stored, replicated, and transmitted from one generation to the next. DNA (deoxyribonucleic acid) serves as the genetic material in most organisms, while RNA (ribonucleic acid) functions primarily as a messenger and adapter molecule.

5.1 The DNA

5.1.1 Structure of Polynucleotide Chain

Basic Components:

- **Nitrogenous Base:** Purines (Adenine, Guanine) and Pyrimidines (Cytosine, Thymine in DNA; Uracil in RNA)
- **Pentose Sugar:** Deoxyribose in DNA, Ribose in RNA
- **Phosphate Group:** Links nucleotides together

Linkages:

- **N-glycosidic linkage:** Base to sugar (1'C of sugar)
- **Phosphoester linkage:** Phosphate to sugar (5'C of sugar)
- **3'-5' phosphodiester linkage:** Between nucleotides

Chain Structure:

- 5'-end: Free phosphate group
- 3'-end: Free -OH group
- Backbone: Sugar-phosphate
- Bases: Project from backbone

5.1.2 Double Helix Model (Watson-Crick, 1953)

Key Features:

1. **Two polynucleotide chains** with sugar-phosphate backbone
2. **Anti-parallel polarity:** 5'→3' and 3'→5'
3. **Base pairing:** A=T (2 H-bonds), G≡C (3 H-bonds)
4. **Right-handed helix:** Pitch = 3.4 nm, 10 bp per turn
5. **Distance between bp:** 0.34 nm
6. **Complementary strands:** Enable replication

Central Dogma: DNA → RNA → Protein

5.1.3 Packaging of DNA Helix

DNA Length Calculations:

- Human genome: 3.3×10^9 bp × 0.34 nm = 2.2 meters
- E. coli: 4.6×10^6 bp = 1.36 mm

Prokaryotic Organization:

- **Nucleoid:** DNA-protein complex
- **Proteins:** Positively charged, organize DNA in loops

Eukaryotic Organization:

- **Histones:** Basic proteins (lysine, arginine rich)
- **Histone octamer:** 8 histone molecules
- **Nucleosome:** 200 bp DNA wrapped around histone octamer
- **Chromatin:** "Beads-on-string" structure
- **Euchromatin:** Loosely packed, transcriptionally active
- **Heterochromatin:** Densely packed, transcriptionally inactive

5.2 The Search for Genetic Material

5.2.1 Transforming Principle (Griffith's Experiment, 1928)

Setup: Streptococcus pneumoniae

- **S strain:** Smooth, virulent (polysaccharide coat)
- **R strain:** Rough, non-virulent (no coat)

Key Observations:

- Live S strain: Mice die
- Live R strain: Mice survive
- Heat-killed S strain: Mice survive
- Heat-killed S + Live R: Mice die, live S recovered

Conclusion: "Transforming principle" transferred from dead S to live R

5.2.2 Biochemical Characterization (Avery, MacLeod, McCarty, 1944)

Experimental Approach:

- Purified biochemicals from heat-killed S cells
- Tested transformation ability
- Used specific enzymes: Proteases, RNases, DNases

Results:

- Proteases: No effect on transformation
- RNases: No effect on transformation
- DNases: Inhibited transformation

Conclusion: DNA is the transforming principle

5.2.3 Hershey-Chase Experiment (1952)

Experimental Design:

- Bacteriophages infecting E. coli
- Radioactive labeling:
  - ^{32}P: Labels DNA (phosphorus in DNA, not protein)
  - ^{35}S: Labels protein (sulfur in protein, not DNA)

Procedure:

1. Grow viruses in radioactive medium
2. Allow infection of bacteria
3. Remove viral coats by blending
4. Centrifuge to separate virus from bacteria

Results:

- ^{32}P-labeled DNA: Found in bacteria

- ^{35}S-labeled protein: Remained in viral coats

Conclusion: DNA is the genetic material

5.2.4 Properties of Genetic Material

Requirements:

1. **Replication ability:** Generate copies
2. **Structural stability:** Resist changes
3. **Mutation capacity:** Allow evolution
4. **Expression ability:** Code for traits

DNA vs RNA Comparison:

Property	DNA	RNA
Stability	More stable (no 2'-OH)	Less stable (2'-OH reactive)
Structure	Double-stranded	Usually single-stranded
Mutation rate	Lower	Higher
Expression	Needs RNA intermediate	Direct protein synthesis

Conclusion: DNA better for storage, RNA better for transmission

5.3 RNA World

Key Concepts:

- RNA was the first genetic material
- RNA acts as both genetic material and catalyst
- DNA evolved from RNA for greater stability
- Life processes evolved around RNA

5.4 Replication

5.4.1 Semiconservative Model

Watson-Crick Prediction: Each new DNA molecule has one parental and one newly synthesized strand

5.4.2 Meselson-Stahl Experiment (1958)

Experimental Design:

1. Grow E. coli in ^{15}N medium (heavy nitrogen)
2. Transfer to ^{14}N medium (light nitrogen)
3. Extract DNA at different time intervals
4. Analyze by CsCl density gradient centrifugation

Results:

- Generation 0: All heavy DNA
- Generation 1: All hybrid DNA (intermediate density)
- Generation 2: 50% hybrid, 50% light DNA

Conclusion: DNA replication is semiconservative

5.4.3 Replication Machinery

Key Enzymes:

- **DNA-dependent DNA polymerase:** Main replication enzyme
- **DNA ligase:** Joins DNA fragments
- **Helicase:** Unwinds DNA helix

- **Primase:** Synthesizes RNA primers

Replication Process:

- **Origin of replication:** Specific starting point
- **Replication fork:** Y-shaped structure
- **Leading strand:** Continuous synthesis (5'→3')
- **Lagging strand:** Discontinuous synthesis (Okazaki fragments)
- **Rate:** ~2000 bp/second in E. coli

5.5 Transcription

5.5.1 Basic Process

Definition: Copying genetic information from DNA to RNA

Key Differences from Replication:

- Only one DNA strand used as template
- Only specific segments transcribed
- Uses RNA polymerase
- A pairs with U (not T)

5.5.2 Transcription Unit

Components:

1. **Promoter:** 5'-end, RNA polymerase binding site
2. **Structural gene:** Coding sequence
3. **Terminator:** 3'-end, transcription stop signal

Strand Terminology:

- **Template strand (3'→5'):** Used for RNA synthesis
- **Coding strand (5'→3'):** Same sequence as RNA (except T for U)

5.5.3 Gene Structure

Prokaryotes:

- **Monocistronic:** Single gene per transcript
- **Polycistronic:** Multiple genes per transcript (operons)

Eukaryotes:

- **Split genes:** Interrupted coding sequences
- **Exons:** Expressed sequences (in mature RNA)
- **Introns:** Intervening sequences (removed during processing)

5.5.4 RNA Types and Processing

RNA Types:

- **mRNA:** Messenger RNA (carries genetic code)
- **tRNA:** Transfer RNA (adapter molecule)
- **rRNA:** Ribosomal RNA (structural/catalytic)

Prokaryotic Transcription:

- Single RNA polymerase for all RNA types
- No processing required
- Transcription-translation coupling possible

Eukaryotic Transcription:

- **RNA Pol I:** rRNA (28S, 18S, 5.8S)
- **RNA Pol II:** mRNA precursor (hnRNA)
- **RNA Pol III:** tRNA, 5S rRNA, snRNA

RNA Processing (Eukaryotes):

1. **Splicing:** Remove introns, join exons
2. **5' Capping:** Add methyl guanosine triphosphate
3. **3' Tailing:** Add poly-A tail (200-300 adenines)

5.6 Genetic Code

5.6.1 Code Properties

Basic Features:

- **Triplet code:** 3 nucleotides = 1 amino acid
- **64 codons:** 61 code for amino acids, 3 stop codons
- **Degenerate:** Multiple codons for same amino acid
- **Non-overlapping:** Read in continuous fashion
- **Universal:** Same code in most organisms
- **Commaless:** No punctuation between codons

Special Codons:

- **Start codon:** AUG (Methionine)
- **Stop codons:** UAA, UAG, UGA

5.6.2 Genetic Code Table

First Base	Second Base				Third Base
	U	C	A	G	
U	Phe, Phe, Leu, Leu	Ser, Ser, Ser, Ser	Tyr, Tyr, Stop, Stop	Cys, Cys, Stop, Trp	U, C, A, G
C	Leu, Leu, Leu, Leu	Pro, Pro, Pro, Pro	His, His, Gln, Gln	Arg, Arg, Arg, Arg	U, C, A, G
A	Ile, Ile, Ile, Met	Thr, Thr, Thr, Thr	Asn, Asn, Lys, Lys	Ser, Ser, Arg, Arg	U, C, A, G
G	Val, Val, Val, Val	Ala, Ala, Ala, Ala	Asp, Asp, Glu, Glu	Gly, Gly, Gly, Gly	U, C, A, G

5.6.3 Mutations and Genetic Code

Point Mutations:

- **Silent:** No amino acid change (degeneracy)
- **Missense:** Different amino acid (e.g., sickle cell anemia: Glu→Val)
- **Nonsense:** Stop codon introduced

Frameshift Mutations:

- **Insertion/Deletion:** Changes reading frame
- Effect depends on number of nucleotides:
  - 1 or 2: Frameshift (drastic effect)
  - 3 or multiples: In-frame (less severe)

5.6.4 tRNA - The Adapter Molecule

Structure:

- Cloverleaf secondary structure
- L-shaped tertiary structure

- ~75-95 nucleotides long

Functional Sites:

- **Anticodon loop:** Complementary to mRNA codon
- **Amino acid acceptor end:** 3'-CCA end
- **Variable loop:** Determines amino acid specificity

Function:

- Specific tRNA for each amino acid
- **Aminoacylation:** Charging tRNA with amino acid (requires ATP)
- **Wobble pairing:** Third position flexibility

5.7 Translation

5.7.1 Process Overview

Definition: Synthesis of proteins from mRNA template

Key Components:

- **mRNA:** Template with codons
- **tRNA:** Adapter molecules with anticodons
- **Ribosomes:** Protein synthesis machinery
- **Amino acids:** Building blocks of proteins

5.7.2 Ribosome Structure

Components:

- **Small subunit:** mRNA binding, codon recognition

- **Large subunit:** Peptide bond formation
- **Two sites:** A-site (aminoacyl), P-site (peptidyl)
- **Ribozyme activity:** 23S rRNA catalyzes peptide bond formation

5.7.3 Translation Process

Initiation:

- Ribosome binds to mRNA at start codon (AUG)
- Initiator tRNA (fMet-tRNA) binds
- Formation of initiation complex

Elongation:

- Charged tRNA binds to A-site
- Peptide bond formation
- Ribosome moves to next codon (translocation)
- Continues until stop codon

Termination:

- Stop codon reached (UAA, UAG, UGA)
- Release factors bind
- Polypeptide released from ribosome

Energy Requirements:

- 2 ATP for amino acid activation
- 1 GTP for tRNA binding
- 1 GTP for translocation

5.8 Regulation of Gene Expression

5.8.1 Levels of Regulation

Eukaryotic Regulation:

1. **Transcriptional:** Primary control point
2. **Processing:** Splicing regulation
3. **Transport:** Nuclear to cytoplasmic
4. **Translational:** Ribosome level

Prokaryotic Regulation:

- Primarily transcriptional control
- Coupled transcription-translation

5.8.2 Operon Model

Definition: Group of genes under common regulatory control

Components:

- **Structural genes:** Code for proteins
- **Promoter:** RNA polymerase binding site
- **Operator:** Regulatory protein binding site
- **Regulatory gene:** Codes for regulatory protein

5.8.3 lac Operon (Jacob-Monod Model)

Structure:

- **Regulatory gene (i):** Codes for repressor

- **Structural genes:**
  - **z gene:** β-galactosidase (lactose hydrolysis)
  - **y gene:** Permease (lactose transport)
  - **a gene:** Transacetylase

Regulation:

- **Without lactose:** Repressor binds operator, blocks transcription
- **With lactose:** Lactose (inducer) binds repressor, inactivates it
- **Result:** RNA polymerase can transcribe genes

Key Concepts:

- **Negative regulation:** Repressor inhibits transcription
- **Inducible system:** Induced by substrate presence
- **Glucose effect:** Catabolite repression (beyond scope)

5.9 Human Genome Project

5.9.1 Project Overview

Timeline: 1990-2003 (13 years) **Scale:** 3 billion base pairs, estimated $9 billion cost **International effort:** USA, UK, Japan, France, Germany, China

5.9.2 Goals

1. Identify all human genes (~20,000-25,000)
2. Sequence 3 billion chemical base pairs
3. Store information in databases
4. Improve data analysis tools

5. Transfer technology to industry
6. Address ethical, legal, social issues (ELSI)

5.9.3 Methodology

Approaches:

1. **EST approach:** Expressed Sequence Tags
2. **Shotgun sequencing:** Random fragments, sequence annotation

Process:

1. DNA isolation and fragmentation
2. Cloning in vectors (BAC, YAC)
3. Automated sequencing (Sanger method)
4. Computer-based sequence assembly
5. Annotation and mapping

5.9.4 Salient Features

Key Findings:

- 3,164.7 million base pairs
- ~30,000 genes (much lower than expected)
- Average gene: 3,000 bases
- Largest gene: Dystrophin (2.4 million bases)
- 99.9% similarity between humans
- <2% codes for proteins
- Large portion is repetitive sequences

- 1.4 million SNPs identified

Chromosome Statistics:

- Most genes: Chromosome 1 (2,968)
- Fewest genes: Y chromosome (231)

5.9.5 Applications and Impact

Medical Applications:

- Disease gene identification
- Personalized medicine
- Drug development
- Gene therapy

Research Impact:

- Comparative genomics
- Systems biology approach
- High-throughput technologies
- Bioinformatics development

5.10 DNA Fingerprinting

5.10.1 Principle

Basis: Polymorphism in repetitive DNA sequences

- 99.9% human DNA similarity
- 0.1% difference = 3 million base pairs
- Individual-specific patterns

5.10.2 Repetitive DNA

Types:

- **Satellite DNA:** Separated during density gradient centrifugation
- **Microsatellites:** Short tandem repeats
- **Minisatellites:** Variable Number Tandem Repeats (VNTR)

Characteristics:

- High degree of polymorphism
- Inherited from parents
- Same in all tissues of individual
- Different between individuals (except identical twins)

5.10.3 Technique (Alec Jeffreys)

Traditional Method:

1. DNA isolation
2. Restriction enzyme digestion
3. Gel electrophoresis
4. Southern blotting
5. Hybridization with VNTR probe
6. Autoradiography

Modern Improvements:

- PCR amplification (single cell sufficient)
- Multiple probe systems

- Automated analysis

5.10.4 Applications

Forensic Science:

- Crime scene analysis
- Victim identification
- Paternity testing

Other Applications:

- Population genetics
- Biodiversity studies
- Evolutionary studies
- Plant and animal breeding

NEET-Specific Important Points

High-Yield Topics for NEET

1. **DNA Structure and Replication**
   - Chargaff's rules
   - Semiconservative replication
   - Meselson-Stahl experiment
2. **Central Dogma**
   - DNA → RNA → Protein flow
   - Transcription and translation processes
3. **Genetic Code**
   - Codon table usage

- Start and stop codons
- Mutation effects

4. **Gene Regulation**
   - lac operon mechanism
   - Positive vs negative regulation
5. **Human Genome Project**
   - Key statistics and findings
   - Applications in medicine

Common NEET Question Patterns

Conceptual Questions:

- DNA vs RNA differences
- Prokaryotic vs eukaryotic gene expression
- Mutation types and effects
- Operon regulation

Numerical Problems:

- DNA length calculations
- Codon-amino acid conversions
- Chargaff's rule applications

Experimental Analysis:

- Griffith's transformation
- Hershey-Chase experiment

- Meselson-Stahl results

Memory Aids and Mnemonics

DNA Bases: "All Teachers Give Classes"

- **A**denine, **T**hymine, **G**uanine, **C**ytosine

RNA Processing: "Cats Sit Peacefully"

- **C**apping, **S**plicing, **P**olyadenylation

Central Dogma: "Don't Read Phones"

- **D**NA → **R**NA → **P**rotein

lac Operon: "In Zygomatic Area"

- **i** gene, **z** gene, **y** gene, **a** gene

Practice Questions for NEET

Multiple Choice Questions:

1. Which experiment proved that DNA is the genetic material? a) Griffith's experiment b) Avery-MacLeod-McCarty experiment c) Hershey-Chase experiment d) Meselson-Stahl experiment
2. The genetic code is: a) Overlapping and comma-less b) Non-overlapping and comma-less c) Overlapping with punctuation d) Non-overlapping with punctuation
3. In lac operon, the inducer molecule is: a) Glucose b) Lactose c) β-galactosidase d) Repressor protein

Short Answer Questions:

1. Explain the significance of complementary base pairing in DNA replication.

2. What is the role of tRNA in protein synthesis?
3. Describe the regulation of lac operon in absence of lactose.

Long Answer Questions:

1. Describe the Hershey-Chase experiment and its significance.
2. Explain the process of transcription in eukaryotes.
3. Discuss the applications of Human Genome Project.

Summary Tables

DNA vs RNA Comparison:

Feature	DNA	RNA
Sugar	Deoxyribose	Ribose
Bases	A, T, G, C	A, U, G, C
Structure	Double-stranded	Usually single-stranded
Function	Genetic material	Messenger, adapter
Stability	More stable	Less stable
Location	Nucleus	Nucleus, cytoplasm

Types of RNA:

RNA Type	Function	Location
mRNA	Carries genetic code	Nucleus → Cytoplasm
tRNA	Adapter molecule	Cytoplasm
rRNA	Ribosome component	Ribosome
hnRNA	mRNA precursor	Nucleus
snRNA	Splicing	Nucleus

Genetic Code Properties:

Property	Description
Triplet	3 bases = 1 amino acid
Degenerate	Multiple codons for same amino acid
Universal	Same in most organisms
Non-overlapping	No shared bases between codons
Comma-less	No punctuation
Unambiguous	Each codon specifies only one amino acid

EXAM SPRINT - Master Molecular Biology

Key Success Strategy: Focus on understanding the flow of genetic information, experimental evidence for key discoveries, and regulatory mechanisms. Practice codon table usage and numerical problems involving DNA calculations.

High-Priority Topics:

1. Experimental evidence for DNA as genetic material
2. DNA replication mechanism and evidence
3. Transcription and translation processes

4. Genetic code and its properties
5. Gene regulation (lac operon)
6. Human Genome Project findings

Regular Practice Areas:

- Codon-amino acid conversions
- DNA-RNA sequence problems
- Experimental design questions
- Application-based questions

Source: NCERT Biology Class 12, Chapter 5 - Comprehensive coverage for NEET and Board examination preparation