1. Introduction to Gene Editing

Nobel Prize in Chemistry 2020

- **Recipients**: Emmanuelle Charpentier and Jennifer A. Doudna
- **Achievement**: Development of CRISPR-Cas9, a precise gene-editing technology
- **Applications**:
    - Treatment of genetic diseases
    - Cancer therapy
    - Development of pest- and disease-resistant crops
- **Significance**: CRISPR-Cas9 allows targeted modifications in DNA, revolutionizing genetic research and therapy.

Key Question

- **Doubt**: How can genes, which are invisible, be edited?
- **Answer**: Advances in understanding DNA and gene structure enable precise manipulation using technologies like CRISPR-Cas9.

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2. DNA: Location and Structure

Location of DNA

- **Found in**: Nucleus of eukaryotic cells, within chromosomes
- **Chromosomal Composition**:
    - DNA
    - Histone proteins
- **Structure**:
    - DNA wraps around histone octamers to form **nucleosomes**.
    - Nucleosomes coil to form **chromosomes**.
    - Chromosomes consist of **chromatids** connected by a **centromere**.

Table 1: Components of Chromosomes

Component	Description
DNA	Genetic material carrying hereditary information
Histone Proteins	Form octamers; DNA wraps around them
Nucleosome	DNA wound around histone octamer
Chromatid	One of two identical parts of a chromosome
Centromere	Region connecting chromatids

Discovery of DNA Structure

- **Key Scientists**:
  - **James Watson and Francis Crick**: Proposed the double helix model in 1953
  - **Rosalind Franklin**: Provided critical X-ray diffraction data ("Photo 51")
  - **Maurice Wilkins**: Contributed to X-ray studies
- **Nobel Prize**: Awarded to Watson, Crick, and Wilkins in 1962
- **Rosalind Franklin's Contribution**: Her work was pivotal but unrecognized during her lifetime (died in 1958).

Structure of DNA

- **Model**: Double helix
- **Components**:
  - **Strands**: Two antiparallel strands made of sugar-phosphate backbone
  - **Rungs**: Nitrogenous base pairs connected by hydrogen bonds
- **Nitrogenous Bases**:
  - Adenine (A) pairs with Thymine (T)
  - Guanine (G) pairs with Cytosine (C)
- **Nucleotide**: Basic unit of DNA, consisting of:
  - Sugar (deoxyribose)
  - Phosphate group
  - Nitrogenous base

Table 2: Worksheet 1.1 - Structure of DNA

Question	Answer
Number of strands in DNA	Two (double helix)
Molecules used to make strands	Deoxyribose sugar, phosphate groups
Molecules used to make rungs	Nitrogenous bases (A, T, G, C)
Different types of nitrogen bases	Adenine, Thymine, Guanine, Cytosine
Formation of rungs	Hydrogen bonds between complementary bases (A-T, G-C)
Mode of nitrogen base pairing	Complementary: A pairs with T, G pairs with C
Molecules in a nucleotide	Deoxyribose sugar, phosphate group, nitrogenous base

Size of DNA

- **Length**:
  - Single chromosome: ~5 cm
  - 46 chromosomes in a human cell: ~2 m
  - All cells in a human body: ~67 billion miles
- **Implication**: DNA is highly compacted within the nucleus.

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3. Chromosomes

Composition

- **Primary Components**: DNA and histone proteins
- **Structure**:
  - **Histone Octamer**: Eight histone proteins
  - **Nucleosome**: DNA wound around histone octamer
  - **Chromosome Formation**: Coiling of nucleosomes
  - **Chromatids**: Two identical parts of a chromosome, joined by a centromere

Human Chromosomes

- **Total Number**: 46 (23 pairs)
- **Types**:
  - **Somatic Chromosomes**: 22 pairs, control physical characteristics
  - **Sex Chromosomes**: 1 pair (XX in females, XY in males)

- **Homologous Chromosomes**: One chromosome from each parent, forming a pair
- **Sex Determination**:
    - **X Chromosome**: Larger, carries more genes
    - **Y Chromosome**: Smaller, contains SRY gene (triggers testis development)

Table 3: Types of Human Chromosomes

Chromosome Type	Number	Function
Somatic	22 pairs	Control physical characteristics
Sex	1 pair (XX/XY)	Determine sex and related traits

Chromosomal Variations

- **Normal Constitutions**:
    - Female: 44 + XX
    - Male: 44 + XY
- **Variant Constitutions**:
    - **Turner Syndrome (44 + X0)**: Single X chromosome, female with underdeveloped sexual characteristics
    - **Triple-X Syndrome (44 + XXX)**: Three X chromosomes, female
    - **Klinefelter Syndrome (44 + XXY)**: Two X and one Y, male with some female traits
    - **XYY Syndrome (44 + XYY)**: One X and two Y, male

Table 4: Chromosomal Variations

Condition	Genetic Constitution	Characteristics
Turner Syndrome	44 + X0	Underdeveloped female sexual characteristics
Triple-X Syndrome	44 + XXX	Female, often asymptomatic
Klinefelter Syndrome	44 + XXY	Male with female traits
XYY Syndrome	44 + XYY	Male, often taller, minimal effects

Why Chromosomes Appear in Pairs?

- **Reason**: One chromosome is inherited from each parent, ensuring genetic diversity and stability.

Chromosome Numbers in Organisms

- **Examples**:
  - Human: 46
  - Dog: 78
  - Cat: 38
  - Rice: 24
- **Activity**: Create a table of chromosome numbers for local organisms.

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4. Genes

Definition

- **Gene**: Specific sequence of nucleotides in DNA that codes for a protein
- **Function**: Provides instructions for:
  - Formation of characteristic features
  - Regulation of metabolic activities

Location

- Genes are located on chromosomes within the DNA.

Role in Sex Determination

- **Y Chromosome**: Contains the SRY gene, critical for male development.

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5. Protein Synthesis

Overview

- **Purpose**: Genes direct the synthesis of proteins, which determine traits and metabolic functions.
- **Stages**:
  - **Transcription**: Occurs in the nucleus
  - **Translation**: Occurs in the cytoplasm

Transcription

- **Process**:
  - A gene's nucleotide sequence is copied to form **mRNA** (messenger RNA).
  - Enzymes facilitate the process.
- **Outcome**: mRNA carries genetic instructions from DNA to ribosomes.

Translation

- **Process**:
  - **tRNA** (transfer RNA) brings specific amino acids to the ribosome based on mRNA codons.
  - **rRNA** (ribosomal RNA) in ribosomes links amino acids to form proteins.
- **Outcome**: Protein is synthesized according to mRNA instructions.

Table 5: Stages of Protein Synthesis

Stage	Location	Key Molecules	Process Description
Transcription	Nucleus	DNA, mRNA	mRNA is formed from DNA template
Translation	Cytoplasm	mRNA, tRNA, rRNA	Amino acids are linked to form proteins

Types of RNA

- **mRNA**: Carries genetic code from DNA to ribosomes
- **tRNA**: Transfers specific amino acids to ribosomes
- **rRNA**: Component of ribosomes, facilitates protein assembly

Table 6: Types of RNA

RNA Type	Function
mRNA	Carries genetic instructions for protein synthesis
tRNA	Transfers amino acids to ribosomes
rRNA	Forms part of ribosomes, aids in protein assembly

Flow Chart of Protein Synthesis

1. **Transcription**:
   - DNA unwinds
   - mRNA is synthesized
2. **mRNA Transport**:

- mRNA moves from nucleus to cytoplasm

3. **Translation**:
    - mRNA binds to ribosome
    - tRNA delivers amino acids
    - rRNA links amino acids to form protein

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6. Heredity and Variation

Definitions

- **Heredity**: Transmission of characteristics from parents to offspring
- **Variation**: Differences in traits between offspring and parents
- **Cause**: Genes inherited from parents

Historical Context

- **Gregor Mendel**: Father of genetics
    - Conducted experiments on pea plants (Pisum sativum)
    - Formulated **Laws of Inheritance**
- **Key Events**:
    - Born: 1822, Czech Republic
    - Studied at University of Vienna (1851–1853)
    - Conducted experiments (1856–1863)
    - Published findings (1866)
    - Findings rediscovered in 1900 by Hugo de Vries, Carl Correns, and Erich von Tschermak

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7. Mendel's Experiments

Monohybrid Cross

- **Definition**: Cross involving one pair of contrasting traits (e.g., height: tall vs. dwarf)
- **Example**:
    - **Parental (P) Generation**: Tall (TT) × Dwarf (tt)
    - **F1 Generation**: All tall (Tt)
    - **F2 Generation**: Tall (TT, Tt) and dwarf (tt) in 3:1 ratio

- **Key Concepts**:
  - **Dominant Trait**: Expressed in F1 (e.g., tall)
  - **Recessive Trait**: Hidden in F1, reappears in F2 (e.g., dwarf)
  - **Alleles**: Different forms of a gene (T for tall, t for dwarf)
  - **Genotype**: Genetic constitution (e.g., TT, Tt, tt)
  - **Phenotype**: Observable trait (e.g., tall, dwarf)

Table 7: Monohybrid Cross Results

Generation	Genotype Ratio	Phenotype Ratio
F1	100% Tt	100% Tall
F2	1 TT : 2 Tt : 1 tt	3 Tall : 1 Dwarf

Mendel's Postulates (Monohybrid Cross)

1. **Two Factors**: Each trait is controlled by two alleles.
2. **Dominance**: One trait (dominant) is expressed in F1; the other (recessive) is hidden.
3. **Segregation**: Alleles separate during gamete formation.
4. **3:1 Ratio**: Dominant to recessive traits in F2.

Why No Intermediate Height?

- **Reason**: Complete dominance; the tall allele (T) fully masks the dwarf allele (t).

Dihybrid Cross

- **Definition**: Cross involving two pairs of contrasting traits (e.g., height and seed shape)
- **Example**:
  - **Parental Generation**: Tall, round (TTRR) × Dwarf, wrinkled (ttrr)
  - **F1 Generation**: All tall, round (TtRr)
  - **F2 Generation**: 9 tall/round : 3 tall/wrinkled : 3 dwarf/round : 1 dwarf/wrinkled
- **Key Concept**: **Independent Assortment** – Genes for different traits segregate independently.

Table 8: Dihybrid Cross Results

Generation	Phenotype Ratio (F2)
F1	100% Tall, round (TtRr)
F2	9 Tall/round : 3 Tall/wrinkled : 3 Dwarf/round : 1 Dwarf/wrinkled

Mendel's Postulate (Dihybrid Cross)

- **Independent Assortment**: Alleles of different genes assort independently during gamete formation.

Why New Traits in F2?

- **Reason**: Recombination of alleles due to independent assortment creates new trait combinations.

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8. Non-Mendelian Inheritance

Overview

- Mendel's laws do not explain all inheritance patterns.
- **Non-Mendelian Inheritance**: Deviates from Mendel's principles due to complex gene interactions.

Types of Non-Mendelian Inheritance

1. **Incomplete Dominance**:
    - **Definition**: Neither allele is fully dominant; results in an intermediate phenotype
    - **Example**: Red (RR) × White (WW) four o'clock plants → Pink (RW) flowers
2. **Co-dominance**:
    - **Definition**: Both alleles are expressed simultaneously
    - **Example**: Roan coat in cattle (red and white hairs)
3. **Multiple Allelism**:
    - **Definition**: A gene has more than two alleles
    - **Example**: ABO blood groups (IA, IB, i alleles)
4. **Polygenic Inheritance**:
    - **Definition**: Multiple genes control a single trait
    - **Example**: Skin color (varies due to melanin production)

Table 9: Non-Mendelian Inheritance Types

Type	Description	Example
Incomplete Dominance	Intermediate phenotype	Pink flowers in four o'clock plants
Co-dominance	Both alleles expressed	Roan coat in cattle
Multiple Allelism	More than two alleles	ABO blood groups
Polygenic Inheritance	Multiple genes control one trait	Skin color

ABO Blood Group

- **Alleles**: IA, IB, i
- **Genotypes and Phenotypes**:
  - IAIA, IAi: Type A
  - IBIB, IBi: Type B
  - IAIB: Type AB (co-dominance)
  - ii: Type O
- **Mechanism**: IA and IB are co-dominant; i is recessive.

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9. Genetic Processes for Variation

Crossing Over

- **Definition**: Exchange of genetic material between homologous chromosomes during meiosis
- **Process**:
  - Homologous chromosomes pair up
  - **Chiasma**: Point of contact where chromatids break and exchange segments
- **Outcome**: Recombination of alleles, leading to new trait combinations
- **Phase**: Prophase I of meiosis

Mutation

- **Definition**: Sudden, heritable change in genetic constitution
- **Types**:
  - Point mutations
  - Chromosomal mutations
- **Impact**: Can introduce new traits or cause genetic disorders

Table 10: Genetic Processes for Variation

Process	Description	Outcome
Crossing Over	Exchange of segments between chromosomes	New allele combinations
Mutation	Sudden change in genetic material	New traits or disorders

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10. Skin Color Variation

- **Primary Pigment**: Melanin
- **Factors Influencing**:
  - **Genetic**: Multiple genes control melanin production
  - **Environmental**: Sunlight, diet, vitamin D
  - **Geographical**: Ancestral adaptations to sunlight intensity
- **Significance**: Skin color is one aspect of human genetic diversity.

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11. Career Opportunities in Genetics

- **Branches**:
  - Molecular genetics
  - Population genetics
  - Medical genetics
  - Cytogenetics
  - Behavioral genetics
  - Genomics
- **Educational Pathways**:
  - Graduate programs: Biotechnology, microbiology, bioinformatics
  - Postgraduate: Genetic counseling, medical genetics, forensic science
  - Ph.D.: Research in pharmaceuticals, agriculture
- **Opportunities**: Healthcare, research, education, industry

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12. Let Us Assess (Key Questions)

1. **DNA vs. RNA Building Blocks**:
   - **Similarities**: Both have nucleotides with sugar, phosphate, and nitrogenous bases
   - **Differences**:
     - DNA: Deoxyribose sugar, thymine (T)
     - RNA: Ribose sugar, uracil (U)
2. **Dominance Types**:
   - Correct option: **c) i - Co-dominance, ii - Incomplete dominance, iii - Dominance**

3. **Genes Contributed by Sexual Reproduction**:
    - **Answer**: b) Half of their genes (one allele from each parent)
4. **Dihybrid Cross**:
    - **F2 Ratio**: 9:3:3:1
    - **New Traits**: Yes, due to independent assortment
    - **Non-independent Assortment**: Alters ratio due to linked genes
5. **Dominance Types Comparison**:
    - **Dominance**: One allele masks the other
    - **Co-dominance**: Both alleles expressed
    - **Incomplete Dominance**: Intermediate phenotype
6. **Phenotypic Ratios**:
    - **Monohybrid**: 3:1 (one trait)
    - **Dihybrid**: 9:3:3:1 (two traits, independent assortment)
    - **Indication**: Traits inherit independently
7. **Two Alleles per Gene**:
    - **Reason**: Diploid organisms inherit one allele from each parent
8. **Role of RNA**:
    - **Reason**: DNA remains in nucleus; RNA (mRNA, tRNA, rRNA) facilitates protein synthesis in cytoplasm
9. **ABO Blood Group**:
    - **Co-dominance**: IA and IB expressed in AB type
    - **Multiple Allelism**: Three alleles determine blood type
10. **Ova and Sex Chromosomes**:
    - **Reason**: Females (XX) produce ova with only X chromosomes