Principles of Inheritance and Variation

1 INTRODUCTION

- Genetics deals with inheritance and variation of characters from parents to offsprings. Inheritance is the process by which characters are passed on from parent to progeny. Variation is the degree by which progeny differ from their parents.
- Humans knew that the causes of variation was hidden in sexual reproduction.

2 MENDEL'S LAWS OF INHERITANCE

- Gregor Mendel conducted hybridisation experiments on garden peas for seven years (1856-1863) and proposed the laws of inheritance.
- Mendel selected 14-true breeding pea plant varieties as pairs, which were similar except for one character with contrasting traits.

Contrasting traits studied by Mendel in Pea

S.No.	Characters	Contrasting Traits
1.	Stem height	Tall/Dwarf
2.	Flower colour	Violet/White
3.	Flower position	Axial/Terminal
4.	Pod shape	Inflated/Constricted
5.	Pod colour	Green/Yellow.
6.	Seed shape	Round/Wrinkled
7.	Seed colour	Yellow/Green

3 INHERITANCE OF ONE GENE

- Mendel found that F_1 always resembled either of the parents, but in F_2 (produced by selfing F_1) both traits appeared; $3/4^{th}$ showed the dominant trait and $1/4^{th}$ the recessive.
- Both traits were identical to their parental type and did not show any blending, i.e. none were of INTERMEDIATE type.
- Mendel got similar results for all traits.
- To determine the genotype of dominant trait at F_2, Mendel performed test cross.

3-A. BASED ON MONOHYBRID CROSS, MENDEL PROPOSED TWO GENERAL RULES

- **LAW OF DOMINANCE:** Explains the expression of only one parental character in F_1 of monohybrid cross and both F_2. It also explains the proportion of 3 : 1 obtained at the F_2.
- **LAW OF SEGREGATION:** The factors or alleles of a pair segregate from each other such that gametes receive only one of the two factors.

4 INCOMPLETE DOMINANCE

- F_1 did not resemble either of the parents and was in between the two. Seen in Dog flower (Snapdragon or *Antirrhinum* sp.)

  In this case:

  RR = has red flowers., rr = has white flowers.

  But Rr has pink flowers.
- Here Genotypic ratio at F_2 is like Mendelian monohybrid cross 1 : 2 : 1 but phenotypic ratio changed from 3 : 1 (to 1 : 2 : 1)

5 EXPLANATION OF CONCEPT OF DOMINANCE

In diploid organisms, there are two copies of each gene, i.e., a pair of alleles. One of them may be different, i.e., modified.

(i) The normal allele produces normal enzyme needed for transformation of substrate.

(ii) If, the modified allele produces normal/less efficient enzyme, which produces same phenotype/trait, it is dominant, but if it produces non-functional or no enzyme, the phenotype will be affected and recessive trait is seen.

'Factors' or genes are the units of inheritance. They contain information required to express a particular trait in an organism

British geneticist R.C Punnett developed a graphical representation call Punnett square to calculate possibility of all possible genotype of offsprings in a genetic cross

6 CO-DOMINANCE

- F_1 resembles both parents.
- ABO blood group in human being is controlled by Gene-I, having three alleles I^A, I^B and i. I^A and I^B produce slightly different form of sugar, while i does not produce any sugar.
- I^A and I^B are completely dominant over i, but when I^A & I^B are present together, they express their own sugars, because of Co-Dominance hence RBC have both sugars.
- There are six genotypes and four phenotypes in human ABO blood types.

7 PLEIOTROPY

A single gene can exhibit multiple phenotypic expression. It is the effect of a gene on metabolic pathways which contribute towards different phenotypes.

Example:

(a) Phenylketonuria (Single gene) → 1. Mental retardation; 2. Reduction in hair & skin pigmentation

(b) Starch Synthesis gene in pea-(B) → 1. Seed Shape **(Dominance)**; 2. Size of strach grain **(Incomplete dominance)**

	Size	Shape
BB	Large grains	Round
Bb	Intermediate sized grains	Round
bb	Small grains	Wrinkled

8 MULTIPLE ALLELES

- More than two alleles governing the same character.
- ABO blood grouping is a very good example of multiple alleles. Since in an individual only two alleles are present, multiple alleles can be found only in population studies.

9 INHERITANCE OF TWO GENES

- Mendel also worked and crossed pea plants that differed into two characters and got a phenotypic ratio of 9 : 3 : 3 : 1 and genotype ratio of 1 : 2 : 2 : 4 : 1 : 2 : 1 : 2 : 1.
- Based on these DIHYBRID CROSSES Mendel proposed the:

LAW OF INDEPENDENT ASSORTMENT

The law states that when two pairs of traits are combined in a hybrid, segregation of one pair of characters is independent of the other pair of characters.

10 CHROMOSOMAL THEORY OF INHERITANCE

- **Walter Sutton & Theodore Boveri** noted that the behaviour of chromosomes was parallel to behaviour of genes and they used chromosome movement to explain Mendel's Laws.
- Sutton united the knowledge of chromosomal segregation with Mendelian principles and called it chromosomal theory of inheritance.
- Experimental verification was done by T.H. Morgan, who worked with fruit flies *Drosophila melanogaster*.

11 *DROSOPHILA MELANOGASTER* WERE SUITABLE FOR GENETIC STUDIES

- They could be grown on simple synthetic medium in laboratory.
- They complete their life cycle in about two weeks.
- A single mating could produce a large number of progeny flies
- There is a clear differentiation of sexes.
- Also, it has many types of hereditary variations that can be seen with low power microscopes.

12 LINKAGE AND RECOMBINATION

- Morgan carried out several dihybrid crosses in *Drosophila* to study genes that were sex-linked, similar to the dihybrid crosses of Mendel in peas.
- But the F_2 ratios deviated significantly from 9 : 3 : 3 : 1 (expected when the two genes are independent).
- When two genes in a dihybrid cross were situated on the same chromosome, the proportion of **parental gene combinations** were much higher than **non-parental type.** Morgan attributes it to physical association or linkage of two genes and used term recombination to describe non-parental gene combinations.
- Some genes were very-tightly linked **(Showed very low recombinations)**, while others were loosely linked **(Showed higher recombinations).**
- Morgan's student Alfred Sturtevant used frequency of recombination between genes on same chromosome as a measure of distance between genes and mapped their position on chromosomes.

  Today GENETIC MAPS are extensively used as a starting point in sequencing whole genomes as done in case of Human Genome Project.

13 POLYGENIC INHERITANCE

- Traits controlled by three or more genes are polygenic traits. It also takes into account influence of environment.
- The phenotype reflects the contribution of each allele, i.e., the effect of each allele is ADDITIVE.

  E.g., Human Skin Colour
- AABBCC has darkest skin colour; aabbcc has lightest and AaBbCc intermediate colour. Other example is height in Humans.

14 SEX-DETERMINATION

GENETIC/CHROMOSOMAL BASIS

- Initial clue came from Insects. The X-body of Henking was in fact x-chromosome

TYPES

(a) XO-Type = Male heterogamety
  e.g. = Grasshopper

(b) XY-Type = Male heterogamety
  e.g. = Insects, Man

(c) ZW-Type = Female heterogamety
  e.g. = Birds

SEX-DETERMINATION IN HUMANS

- Genetic make-up of SPERM determines sex of the child and in each pregnancy there is always 50% probability of a male or female child.
- It is unfortunate that in our society females are blamed for giving birth to female children.

SEX-DETERMINATION IN HONEY BEE

- Haplo-diploid sex-determination
- Unfertilised egg develops as male (drone) i.e. haploid; queen & worker bees (females) are diploid.

15 MUTATION

- Results in alteration of DNA sequences and consequently results in changes in the genotype and the phenotype of an organism.
- Loss (deletions) or gain (insertion/duplication) of a segment of DNA result in chromosome alteration.
- Alteration in chromosomes result in abnormalities or aberrations. Chromosomal aberrations are commonly observed in cancer cells.
- Mutations also arise due to change in a single base pair of DNA, known as point mutation; eg: Sickle-cell anemia.
- Deletions and insertions of base pairs of DNA causes frame-shift mutations.
- Chemical and physical factors that induce mutations are called mutagens.

  E.g UV radiations can cause mutations in organisms

16 GENETIC DISORDERS

PEDIGREE ANALYSIS

- Controlled crosses are not possible in case of human beings. Study of family history about inheritance of a particular trait provides an alternative. Such analysis in several generations of a family is called pedigree-analysis.

SYMBOLS USED IN THE HUMAN PEDIGREE ANALYSIS	
	Male
	female
	sex unspecified
	affected indviduals
	mating
	mating between relatives (consanguineous mating)
	parents above and children below
	parents with male child affected with diseases
5	five unaffected offspring

MENDELIAN DISORDERS

- Mainly determined by alteration or mutation in a single gene.
- It may be dominant or recessive. Autosomal or Sex-linked.

Examples:

(1) **Colour-blindness**
- Sex-linked recessive.
- Due to defect in either red or green cone of eye due to mutation in certain genes present on X-Chromosome
- **8% of males & only about 0.4% of females affected.**

(2) **Haemophilia**
- X-linked recessive
- A single protein that is part of cascade of proteins involved in blood clotting is affected.

(3) **Sickle-Cell anaemia**
- Autosome linked recessive
- Controlled by single pair of allele Hb^A and Hb^S.

(4) **Phenylketonuria**
- Inborn error in metabolism. Autosomal recessive. Affected individual lack enzyme which converts phenylalanine to tyrosine. Results in mental retardation.

(5) **Thalassemia**
- Autosomal recessive, could be due to mutation or deletion.
- **α-thalassemia:** Controlled by two closely linked genes HBA1 and HBA2 on Chr-16.
- **β-Thalassemia:** controlled by single gene HBB on Chr-11.

CHROMOSOMAL DISORDERS

- Caused due to absence or excess or abnormal arrangement of one or more chromosomes.
- Failure of segregation of chromatids during cell-division cycle resulting in gain or loss of a chromosome(s), is called ANEUPLOIDY.
- Failure of Cytokinesis after telophase stage of cell division results in an increase in a whole set of chromosomes in an organism, this is called POLYPLOIDY, **often seen in plants**.
- TRISOMY or MONOSOMY leads to very serious consequences in the individual.

Common examples of chromosomal disorders.

(I) **Down's Syndrome:** Trisomy of 21; was first described by Langdon Down (1866).

Symptoms:
i) Short Statured
ii) Small round head.
iii) Furrowed tongue
iv) Partially open mouth.
v) Palm is broad with palm crease
vi) Physical, psychomotor & mental development is retarded.

(ii) **Klinefelter's Syndrome:** Karyotype = 47 xxy, overall masculine development, however GYNAECOMASTIA is also expressed. Such individuals are sterile.

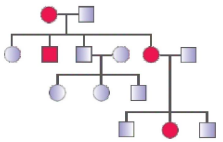
(iii) **Turner's Syndrome:** Due to absence of one of the X-chromosomes, i.e., 45 with XO. Such females are sterile as ovaries are rudimentary besides lack of other secondary sexual characters.

Pedigree analysis of

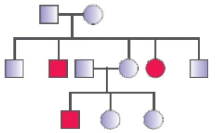
(a) Autosomal dominant trait (e.g., Myotonic dystrophy)

(b) Autosomal recessive trait (e.g., sickle-cell anaemia)

(a)



(b)



- T.H. Morgan found that in *Drosophila* the genes for yellow body and white eye were very tightly linked and showed only 1.3% recombination, while white eye and miniature wing showed 37.2% recombination.
- In Honeybee, males produce sperms by mitosis, they do not have father and thus cannot have sons, but have grand-fathers and can have grandsons.
- Cystic fibrosis is autosomal recessive disorder.
- Chromosomal disorders can be easily studied by the analysis of KARYOTYPES.
- Inheritable mutations can be studied by generating a pedigree of a family.
- The family pedigree of Queen Victoria shows a number of haemophilic descendents as she was a carrier of the disease.
- Thalassemia differs from sickle-cell anaemia in that the former is a quantitative problem of synthesising too few globin molecules while the latter is a qualitative problem of synthesising an incorrectly functioning globin.