GENETICS

- Genetics is the study of **heredity** and **variations.** Its expression influences the functions of individuals at all levels.
- Evidently, this branch of biology involves the study of molecules, cells, organisms and populations as well using many different experimental approaches.
- Genetic studies have many applications in the areas of agriculture and medicine.
- For example **Gene therapy** is used to replace the defective gene with normal gene in treating some diseases.
- Knowledge of genetics plays a significant role in understanding the processes of evolution.
- **Bateson** coined the term Genetics.
- Later Francis **Galton** coined the term **Eugenics** which is the direct application of genetic knowledge for human welfare.
- Later the term **Euphenics,** that deals with the symptomatic treatment of genetic disorders was coined.
- Although inheritance of biological traits had been recognised for thousands of years, the first fruitful results were obtained only by **Gregor Johann Mendel**, who is regarded as **'the father of genetics'.**

MULTIPLE ALLELES AND BLOOD GROUPS :

- Generally a gene has two alternative forms called alleles. Sometimes a gene has three or more forms.
- **If a gene has more than two alleles, these alleles are called multiple alleles.** The condition is called **multiple allelism.**
- **Number of genotypes from multiple** alleles is given by the **expression n(n+1)/2. Where n =** no. of alleles. Multiple alleles can be best explained with ABO blood groups.

THE ABO BLOOD GROUPS :

- **Karl Landsteiner**, 1902 observed the ABO blood grouping in humanbeings.
- The phenotypes "A", "B", and "AB" are characterised by the presence of antigens on the surface of red blood cells.
- The phenotype "O" is with out antigens on the surface of RBC. These are under the control of a gene located on chromosome 9.
- The four phenotypes of blood groups identified are due to the antigens A and B**.**
- **A group of blood** has antigen "A" on the RBC and "anti B" antibody in plasma. **B group of blood** has Antigen "B" on RBC and "anti A" antibody in the plasma.
- **AB group of blood** has Antigens "A" and "B" on the RBC but no antibodies in the plasma. Antigen A and B are absent on RBC but both "anti A" and "anti B" antibodies are in the plasma in **O group of blood**.
- The ABO phenotype of any individual can be ascertained by mixing a blood sample with antiserum containing "anti-A" or "anti-B" antibodies.
- If any antigen is present on the surface of the RBC of a person that reacts with the reactive antibody, it causes clumping or agglutination of the red blood cells.
- If a clump is formed with anti-A, the blood is of A group. If the clump is formed with anti-B the blood is of B group. If the clump is formed with both anti-A and anti-B, the blood is of AB group and if no clump is produced with either of the antibodies then the blood is of O group.
- **Bernstein,** 1924 discovered that these phenotypes were inherited as the result of three alleles of a gene.
- This hypothesis was based on the studies of the blood types of many different families. I^A, I^B and I^O are the three alleles of the gene I, which represents the **isoagglutinogen** (antigen).
- The antibodies anti-A and anti-B are called **isoagglutinins.** Isoagglutinins are the antibodies of an individual of a species causing agglutination reactions in another individual of the same species.
- I^A and I^B alleles are responsible for the production of the respective antigens A and B.
- I^O allele does not produce any antigen. I^O is the recessive allele. I^A and I^B alleles are dominant to the allele I^O, but are codominant to each other ($I^A = I^B > I^O$).
- Six types are possible with 3 alleles- I^AI^A, I^AI^O, I^BI^B, I^BI^O, I^AI^B and I^OI^O.
- The phenotype of I^AI^A and I^AI^O is 'A' type of blood, the phenotype of I^BI^B and I^BI^O is 'B' type of blood, the phenotype of I^AI^B is 'AB' type of blood and the phenotype of I^OI^O is 'O' type of blood.
- "AB" phenotype is the **universal recipient** and O phenotype is the **universal donor**. Agglutination occurs due to binding of antibody and antigen. This agglutination becomes heavy whenever the binding antibodies are more in the recipient, in blood transfusions.

THE Rh ANTIGENS :

- **Landsteiner, Levine** and others (1940) discovered another antigen called **Rh antigen** (D-antigen).
- Rh factor was first detected in the RBC of Rhesus monkeys and later in man. If a blood sample reacts with "anti Rh" antibodies, it is called Rh positive.

- If it does not react, it is called Rh negative. People with this antigen are referred to as Rh-positive (relatively common) and without antigen are Rh-negative.
- Rh positive is dominant over Rh-negative. Anti D antibodies or Rh antibodies (against Rhesus antigens) are absent in the plasma in natural conditions. These antibodies are produced in Rh negative blood whenever Rh-positive blood mixes with the negative blood.
- Rh antigens and antibodies are involved in the disorder **erythroblastosis foetalis,** or **haemolytic disorder** of the **new born** (HDNB). It manifests in an Rh-positive foetus whose father is Rh-positive and mother is Rh-negative.
- The genetic consequence in this marriage is the immunological incompatibility between the mother and the growing foetus. The foetal blood passes through the ruptured placenta at birth to the Rh-negative maternal blood.
- The mother's immune system recognises the Rh antigens and gets sensitised. Sensitised immune system in the mother produces Rh antibodies and also releases **memory cells** (memory cells produce the antibodies immediately whenever exposed to Rh antigens).
- These antibodies are **IgG antibodies**, which are small in size. So **they can cross through placenta and enter the foetal blood circulation.**
- Generally the first child of this genetically incompatible marriage is unaffected because foetus is delivered by the time the mother gets sensitised and antibodies accumulate to cross through placenta of foetus.
- During the second pregnancy, these antibodies increase in concentration due to memory cells and cross through placenta to enter the blood circulation of foetus.
- The blood cells of the Rh-positive foetus are destroyed, causing HDNB. Haemolytic anaemia is the symptom in this disorder.
- In case father is heterozygous Rh-positive, only the successive Rh positive children may be affected with the disorder erythroblastosis foetalis.
- This can be prevented by injecting the Rh antibodies to the mother immediately after the delivery. The foetal RBC will be destroyed in the mother by giving the Rh- antibodies.
- Hence the sensitisation, or activation of memory cells will be prevented in the mother.
- **Ronald A. Fisher** has proposed that three closely located (linked) genes are involved in the inheritance of Rh factor.
- **Weiner** proposed the existence of eight alleles at a single Rh locus. Fisher system shows that the gene locus, with D and d alleles, is the most important for the synthesis of Rh antigens.
- The presence of at least one dominant D allele results in the Rh-positive phenotype, where as the dd genotype causes the Rh-negative blood type.

Wiener Nomenclature	Fisher-Race Nomenclature	Phenotype
R^1	CDe	Rh^+
R^2	cDE	
R^0	cDe	
R^z	CDE	
r	cde	Rh^-
r'	Cde	
r''	cdE	
r^y	CdE	

There are 36 possible genotypes in children (8 x 9/2 = 36)
Homozygous dominant genotypes are 10 (4 x 5/2 = 10)
Heterozygous dominant genotypes are 16
Number of possible genotypes for Rh^+ according to Weiner system are 26