Course Objectives:

- To understand basic principles and techniques of genetics
- To consider alterations in the genetic material
- To consider how genes can be transferred from one organism to another

**Mutation:**
Mutation is a hereditary change in base sequence of that genome. It may be good or bad. It can be brought about by genetic recombination.

**Difference between mutation and genetic recombination**
Mutation brings about a small amount of genetic change while genetic recombination creates much larger changes.

**Similarities in mutation and genetic recombination.**
Both fuel the evolutionary process
Mutation produces mutants.

**Mutant:** is a strain of any cell or virus carrying a change in nucleotide sequence and is definitely different from its parent in **genotype**(nucleotide sequence of the genome). Genotype is represented by three small letters and a capital letter e.g. hisC. Mutants may differ from parents **phenotypically** (observable properties of the mutant). Phenotype of an organism is designated by a capital letter followed by two lower case letters with either a plus or minus superscript

**Wild strain:** The strain isolated from nature

**Isolation of Mutants:** Some mutants are selectable while others are non selectable

**Selectable mutants:** These are strains that grow and outgrow and replace the parent e.g. an antibiotic resistant mutant and can be selected under appropriate environmental conditions

**Selection:** This is a tool allowing the isolation of a single mutant from a population containing millions and billions of parental organisms

**Non-selectable mutants:** These are usually obtained through screening process e.g. colour loss in a pigmented organism

**Isolation of mutants:** This is done by replica plating by growing organisms on agar plate lacking a particular nutrient that will be required by the mutant. Such a mutant is called **auxotroph.**
**Prototrophs:** These are the original parents from which the mutants are derived

**Penicillin-selection method:** This is a method used to isolate mutants such as auxotrophs which will not be affected by penicillin.

**Types of mutation**

Two broad types of mutation

- 1. Induced mutations
- 2. Spontaneous mutations: can be caused by exposure to natural radiation and by oxygen radicals and errors in the pairing of bases during DNA replication. The following are mutations due to alterations in base pairs.
- Point mutation: Mutations that are caused by base pair substitutions in the DNA or by loss or gain of a single base pair
- Silent mutation: Mutation that does not affect the phenotype of the cell.
- Missense mutation: Mutation due to change in the ensuing polypeptide as a result of informational “sense” (precise sequence of amino acids)
- Nonsense mutations: Mutation that produces a stop codon that results in premature termination of translation leading to incomplete polypeptide that almost certainly not be functional
- Transitions: Mutations in which one purine base (A or G) is substituted for another purine or one pyrimidine base (C or T) is substituted for another pyrimidine
- Transversions: Point mutations in which a purine base is substituted for a pyrimidine base or vice versa

**Mutagenesis:** Brought about by a variety of chemical, physical and biological agents that increase the mutation rate and therefore said to induce mutations. These agents are called mutagens.

**Examples of chemical and physical mutagens and mode of action**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Action</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Base analogs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-Bromouracil</td>
<td>Incorporated like T, faulty pairing with G</td>
<td>AT------GC</td>
</tr>
<tr>
<td>2-Aminopurine</td>
<td>Incorporated like A, faulty pairing with C</td>
<td>AT------GC</td>
</tr>
<tr>
<td><strong>Chemicals reacting with DNA</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nitrous acid (HNO₂)</td>
<td>Deaminates A &amp; C</td>
<td>AT------GC &amp; GC---AT</td>
</tr>
<tr>
<td>Hydroxylamine (NH₂OH)</td>
<td>Reacts with C</td>
<td>GC-----AT</td>
</tr>
<tr>
<td>-----------------------</td>
<td>--------------</td>
<td>-----------</td>
</tr>
<tr>
<td><strong>Alkylation agents</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethyl methane sulfonate</td>
<td>Puts methyl on G, faulty pairing with T</td>
<td>GC-----AT</td>
</tr>
<tr>
<td>Mitomycin, nitrogen mustards, nitrosoguanidine</td>
<td>Cross links DNA strands, faulty region excised by DNase</td>
<td>Both point mutations &amp; deletions</td>
</tr>
<tr>
<td><strong>Intercalating dyes</strong></td>
<td>Inserts between 2 base pairs</td>
<td>Microinsertions &amp; microdeletions</td>
</tr>
<tr>
<td>Acridine, ethidium bromide</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Radiation</strong></td>
<td>Pyrimidine dimer formation</td>
<td>Repair may lead to error or deletion</td>
</tr>
<tr>
<td>Ultraviolet</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ionizing radiation e.g. x-rays</td>
<td>Free-radical attack on DNA, breaking chain</td>
<td>Repair may lead to error or deletion</td>
</tr>
</tbody>
</table>

**Transfer of genetic information in bacteria**

1. Transformation: Free DNA released from one cell is taken up by another cell
2. Transduction: DNA transfer is mediated by virus. Two types of transduction:
   a. Generalized transduction in which any gene on the donor chromosome can be transferred to the recipient e.g. *Salmonella enterica* with phage P22; *E. coli* and phage P1
   b. Specialized transduction allows extremely efficient transfer but is selective and transfer only a small region of the bacterial chromosome e.g. galactose genes were transduced by the temperate phage lambda of *E. coli*
3. Conjugation: DNA transfer involves cell-cell contact and a conjugative plasmid in the donor cell

F Plasmids: F means fertility and plasmids are circular DNA molecule of 99,159 bp. It contains genes that regulate DNA replication and contains transposable elements that allow the plasmid to integrate into the host chromosome.