Subject: Botany (M)
Paper: CC7
Semester: 3rd

Remark: Add relevant diagram with the content of this lecture note.

DNA repair: DNA molecules (replicating and non replicating) are susceptible to chemical alteration and damages which leads to gene mutation. The sources of damage may be categorized into- exogenous or environmental agents (UV rays, genotoxic compounds), endogenous or byproducts of normal cellular processs (reactive oxygen species which are generated in normal aerobic respiration), spontaneous or induced chemical process (deamination).

Repair Mechanisms: Damaged DNA may be repaired in vivo.

1. **Base and nucleotide excision repair**: There are 2 types of excision repair system- Basic excision repair (BER) and Nucleotide excision repair (NER) Former is involved in correcting the minor alterations of nitrogenous bases which are caused by spontaneous hydrolysis or chemical agent. The first step of BER involves recognition of the altered base by DNA Glycosylase which cuts the glycosidic bond between the base and the sugar and create an apyramidinic site. Such sugar moiety is then recognised by an enzyme AP endonuclease which makes a cut in the sugar backbone of the AP site. The distortion form in the DNA helix is recognized by the excision repair system. Further it is activated to make ultimate correction of the error. On the other hand DNA lesion that distort the regular helix is repaired by NER pathway. The source of such changes is exogenous mainly. Products of *uvr* family of genes are involved in recognizing and excision of the lesions in the DNA. Specific number of nucleotides are excised out around the both ends of the lesion. The repair is completed by DNA polymerase I and DNA ligase. The normal strand opposite the lesson act as template for the replication resulting in repair. The excision repair process consists of the following 3 basic steps and usually known as cut and paste system. The error present on one of the two strands of the helix is first recognised and enzymatically cleaved out by a nuclease which is known as excision. It ultimately forms a gap on one strand in the helix. After that DNA polymerase fills the gap by inserting deoxyribonucleotides complementary to those on the intact strength. Finally, DNA ligase seals the final nick and close the gap. This type of repair system has been conserved throughout the evolution and found in prokaryotic and eukaryotic organism. It is light independent repair system and repair damage caused by both exogenous and endogenous agent. It is relatively a simple system of locating, excising and repairing the damage. An autosomal recessive trait in human known as Xeroderma pigmentation is due to the inability to repair thymine dimerisation induced by UV light.
2. **Photoreactivation**: UV ray induced mutation generate pyrimidine dimers. Albert Kelner showed that in E. *coli* DNA damage could be partially reversed through the exposure of irradiated cells to the blue light range of visible spectrum for brief period of time. This process is temperature dependent and enzymatic in nature. Photoreactivation enzyme

(PER) can be isolated from extracts of *E. coli* cells which cleaves the bonds between thymine dimers and reverse the effect of UV damage. But the enzyme cannot be detected in humans and other eukaryotes.

3. **Proofreading and mismatch repair:** The common type of error in DNA is made during replication when an incorrect nucleotide is inserted by DNA polymerase. DNA polymerase III control its own synthesis by proofreading each step during synthesis. When an incorrect nucleotide is inserted the enzyme complex recognizes the error and act as an exonuclease which cuts the incorrect nucleotide and then replace it. Those errors that remain after proofreading, rely on another mechanism called mismatch repair. The alteration or mismatch at first detected and then the incorrect nucleotides must be removed and finally the replacement with the correct nucleotide must occur. But a problem exist with the correction of a mismatch when compared to excision repair in which lesions signals its repair. In case of mismatch repair, the non complementary pair of nucleotide is recognized. In *E. coli* and some other bacteria this process is based on DNA methylation An enzyme adenine methylase recognize the DNA sequence (5 ---GATC----3) as a substrate and after recognition methyl group is added to each of the adenine residues. This type of modification is stable throughout the cell cycle. After further round of replication the newly synthesized strands become temporarily unmethylated. The repair enzyme recognizes the mismatch and binds to the un methylated strand. An endonuclease protein create a nick either in 5'or 3' end to the mismatch on the unmethylated strand. The nicked strand is degraded and replaced and mismatch is excised.
4. **SOS repair system and post replication repair**: Another repair pathway is called the SOS repair system which responds to damaged DNA. SOS repair system may or may not involve rec A. A lesion is encountered during DNA synthesis that interfere with further synthesis of DNA. recA gene controls the translation of a enzyme that aids in homologous single strands of DNA to reform double helices. recB and recC genes produce subunits of an enzyme with exonuclease activity. recBC exonuclease or DNA polymerase V in *E. coli* respond to the crisis and allow replication to continue. They are referred to as translational polymerase. Post replication repair was discovered in an excision defective strain of *E. coli* .This system responds after damage DNA has escaped repair and failed to be completely replicated. When DNA with a lesion (pyrimidine dimers) is being replicated DNA polymerase stops at the damaged site and then skips over it. Thus a gap is formed along the newly synthesized strand. the RecA protein directs recombinational exchange and the gap is filled by the insertion of a segment initially present on the undamaged complementary strand. Gap created on the donor strand can be filled by repair synthesis as replication proceeds. This repair system is also known as homologous recombination repair. rec system consists of three genes. Post replicative repair seem less efficient than excision repair. Repair of the lesions may result in transition, transversion, additions, and deletions.