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## Mutagenesis and Types of DNA Repair

### Mutagenesis

#### Definition

- Process by which the genetic information of an organism is changed in a stable manner, leading to a Mutation [1] (<http://http://en.wikipedia.org/wiki/Mutation>).
- Spontaneously/result of exposure to mutagens/ experimentally
- Can lead to cancer and various heritable diseases, but it is also the driving force of evolution

#### Classification:

- by cause: spontaneous / induced
- by effect on structure: small-scale / large-scale
- by impact on protein sequence: frameshift, missense, nonsense, neutral, silent

### DNA Repair

#### Definition

- Major defence against environmental damage to cells
- Present in all organisms
- Involved in processes that minimize cell killing, mutations, replication errors, persistence of DNA damage

#### Types

1. Direct Reversal
2. Base Excision Repair
3. Nucleotide Excision Repair
4. Mismatch Repair

#### 1. Direct reversal

- Does not require a template
- Specific to the type of damage incurred
- Does not involve breakage of phosphodiester backbone

#### Types:

- Thymidine dimers
- Methylation of guanine bases
- Methylation of cytosine and adenine bases

#### 2. Base Excision Repair (BER)

Removal of the incorrect base by DNA N-glycosylase (create AP site), then AP endonuclease removes the AP site and neighboring nucleotides. The strand is extended by a DNA polymerase I and DNA ligase.

#### 3. Nucleotide Excision Repair (NER)

Proteins are responsible for removing damaged nucleotides. The gap is then filled by DNA polymerase I and DNA ligase.

Error in NER leads to Precanceroses (Xeroderma pigmentosum).

NER differs from BER in:

- Different enzymes
- Nucleotide is removed along with many other adjacent nucleotides (NER removes a large "patch" around the damage)
- NER can only recognize lesions that distort the DNA helix
- BER is limited by the fact that the number of glycosylases that can recognize damage and initiate repair is limited

#### 4. Mismatch Repair

Deals with correcting mismatches of the normal bases (Watson-Crick base pairing). The faulty strand is nicked at the nearest GATC base sequence. Enzymes in this process are involved in both base-excision repair and nucleotide-excision repair.

Error leads to Hereditary non polyposis colon cancer.

