Student name: Adrika Chaudhuri

Student number: 22MS044

DNA Repair

1. Errors that remain undetected by DNA polymerase are repaired by **post replication mismatch repair system**.
2. Their failure to detect mismatches elevate mutation rate by **10-1000x**.

Mismatch Repair Pathway

Enzymes involved: MutS, MutH, MutL, DNA pol I.

What do they do?

- MutS embraces the mismatched bp and induces a kink
- MutS recruits the MutH and MutL enzymes
- MutS hydrolyses ATP
- MutH (endonuclease) cuts the mismatched DNA
- Exconuclease removes the excised DNA
- DNA pol I fills in the gap.

Why does the exonuclease go beyond the mismatched DNA pair and also remove healthy pairs?

Ans: Probably to make enough space for the DNA pol 1 to sit on it.

How does it know which strand to cut?

Ans: The GATC strand in the parental sequences have methylated A residues due to *E.coli* enzyme Dammethylase. Since daughter strands are new, such epigenetic controls have not yet been exerted on them. The repair system uses this to differentiate between old and new DNA.

Base Excision Repair

Repairs: **Single base damage** due to depurination, alkylation, oxidation and deamination

DNA glycosylases

DNA glycosylases recognize and remove damaged bases in DNA and are thus essential for maintaining genomic integrity, and they also function in other important processes including transcriptional regulation and somatic hypermutation to generate antibody diversity.

BER Pathway

Mechanism:

1. DNA glycosylase recognises the damaged base and cleaves it from the backbone.
2. An AP endonuclease cleaves the phosphodiester backbone near the damaged site
3. DNA polymerase removes it with its 5′–3′ exonuclease activity and fills the site up from the free 3′OH site.
4. The nick remaining is sealed by DNA ligase.

What are the products of UV radiation on thymines?

1. Cyclobutane thymine dimers
2. 6-4 photoproduct

Note: UV radiation also causes kink in sugar phosphate backbone by drawing A-T's closer together.

Nucleotide Excision Repair

In prokaryotes, DNA lesions of 13-18 nucleotides, containing the damaged DNA, are created by enzymes and removed.
In eukaryotes, such lesions are 22-28 bp long.

Photolyases

Photolyases, are active mainly on the skin, and require visible light to function. They reverse the damage caused by UV radiation exposure.
Even in the absence of photoreactivating light, photolyase plays an advantageous role in the cell by stimulating the repair of damaged DNA. This "dark function" is due to the stimulation of the nucleotide excision repair pathway by photolyase. As a general rule, the more a lesion distorts the DNA structure, the more efficiently it is recognized and removed by the excision nuclease system. Cyclobutane pyrimidine dimers cause only modest distortions of the DNA helix compared to (6-4) photoproducts and are repaired at a much lower rate in the absence of photolyase. Photolyase, presumably by binding the damage and flipping the dimer out of the helix, increases distortion of the DNA and accelerates the rate-limiting damage recognition step of the excision repair complex.