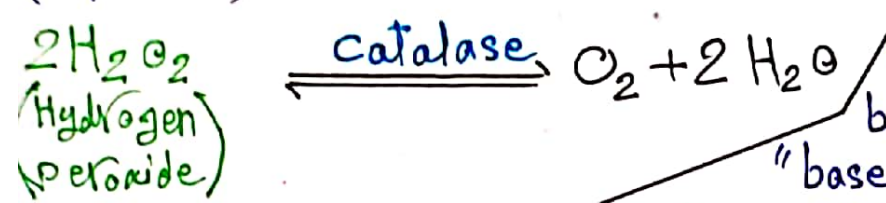
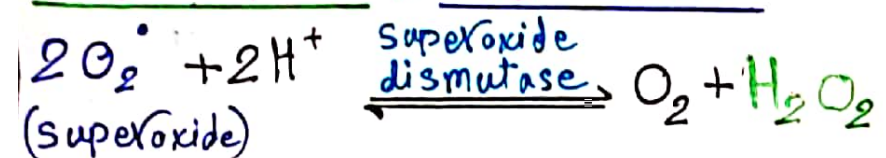


Prevention of errors before they happen

deoxygenation of reactive oxygen species & oxygen radicals



Direct reversal of damage

■ Pyrimidine dimers :-

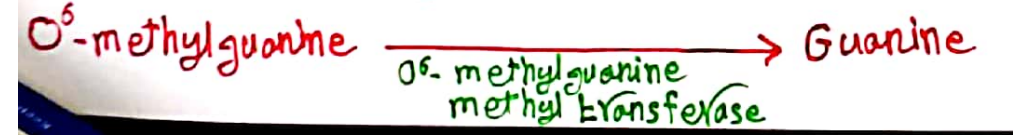
Exposure to sunlight \Rightarrow UV light hit the DNA \Rightarrow formation of a covalent interaction (50-100 reactions per second) between two adjacent pyrimidine bases "commonly between two thymines" forming structures known as cyclobutane pyrimidine dimers.

are reversed by enzymes known as photolyases (covalent interaction are removed)

■ Specific mispairing :-

Alkylating agents can transfer methyl group to guanine forming 6-methyl guanine, which pairs with thymine, after replication, you will have (AT) instead of (GC).

• Addition of large chemical \Rightarrow carcinogens.
• Repair of O⁶-methylguanine :-



Repair mechanisms

Excision repair pathways

Base excision repair

DNA glycosylases :-

They remove damaged base (don't cleave phosphodiester bonds, but instead cleave N-glycosidic "base-sugar" bonds of damaged base)

\rightarrow generating an apurinic or apyrimidinic site (both are called AP sites) and then this base can be repaired (AP site is repaired) by AP endonuclease repair pathway.

Example: uracil-DNA glycosylase, removes uracil from DNA.
 \rightarrow AP endonucleases cleave the phosphodiester bonds at AP sites
 \rightarrow The deoxyribose is removed.

"C" \leftarrow DNA pol. \leftarrow DNA replication
"U" \leftarrow DNA replication
"G" \leftarrow DNA replication
"T" \leftarrow DNA replication

Transcription coupled repair

• RNA pol. pauses (stalls) when encountering a lesion.
• TFIIH and other factors carry out the incision, excision and repair reactions.

Then, transcription can continue normally.

Nucleotide excision repair

- Include the breaking of a phosphodiester bond.
- In bacteria, the Uvr(A/B/C) protein complex does this work.
- Helicase removes the strand.
- In human cells, defect in this mechanism causes Xeroderma pigmentosum (XP).
- XP proteins have different functions including damage recognition and enzyme activities (endonuclease, helicase)
- The UV light cause cell death in xeroderma pigmentosum.

Very similar to Muts/MutL, respectively. Except: it's not post-replication repair rather it's co-replication mechanism, so as replication takes place mismatches are repaired.

• **Cockayne's syndrome**: a condition caused by mutation in a CSB protein, which recognizes that the RNA pol. is stalled due to a mutation.
• It recruits XPA, RPA and TFIIH

Mismatch repair and post-replication repair

In prokaryotes

This is mediated by the (mut) protein system.
• Original DNA strands are methylated.
• The newly synthesized strands are not methylated (takes place at the adenine)
• DNA methylation \leftarrow مethylating

In humans

Two proteins, hMSH2 and hMLH1 are very similar to Muts/MutL, respectively. The newly synthesized lagging strand could be identified by nicks at either end of okazaki fragments.
• The leading strand might be identified by its growing 3' end.
• mutation in MSH followed by MLH \rightarrow HNPCC.

Translesion DNA Synthesis

(DNA pol. synthesize DNA over the lesions).
• They have low fidelity, lack proofreading mechanism.

Recombinational repair

When double strand breaks of DNA occur \rightarrow takes place by NHEJ/HR

• BRCA 1 activates homologous recombination repair.
• BRCA 2 can recruit Rad51 to the ssDNA