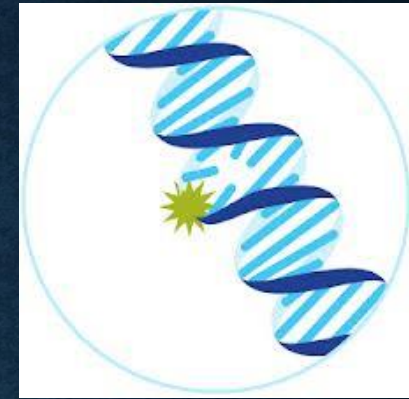


Block 2

DNA DAMAGE AND REPAIR



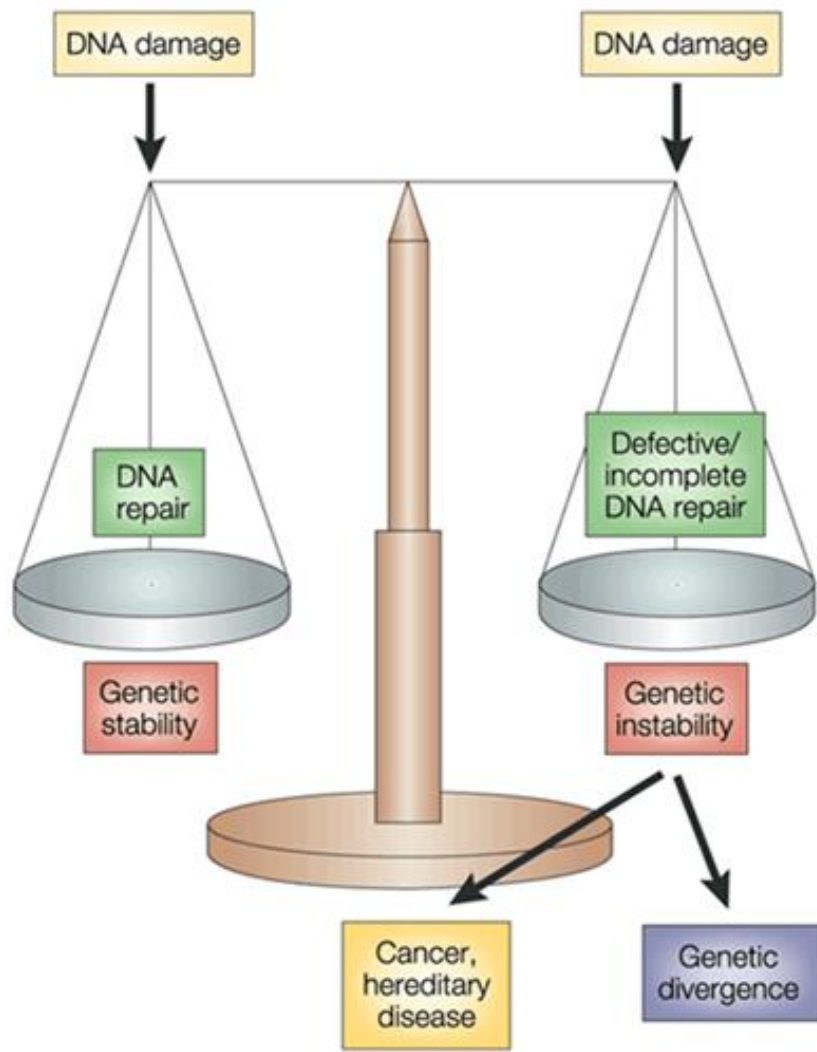
Arya Adiningrat

Department of Oral Biology and Biomedical Sciences

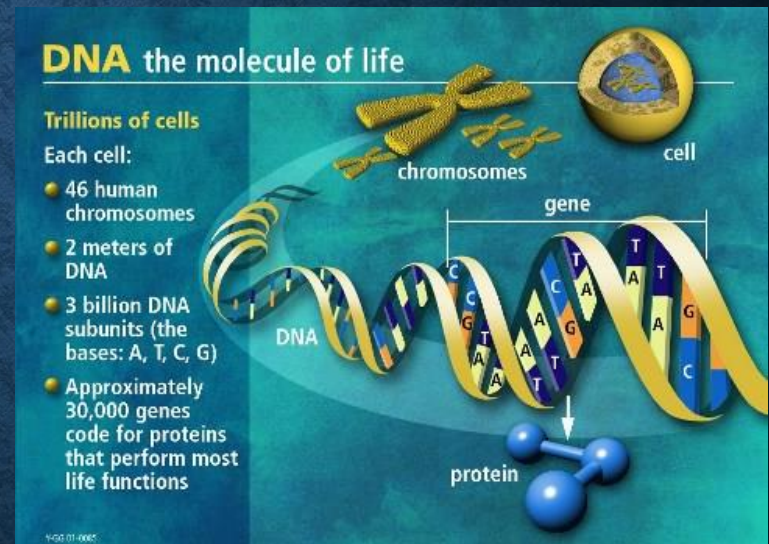
Dental School of Medicine and Health Sciences Faculty

Universitas Muhammadiyah Yogyakarta





The role of DNA as a repository genetic information depends in part on its inherent stability. The chemical transformations that do occur are generally very slow in the absence of an enzyme catalyst. However, that even very slow reactions that alter DNA structure can be physiologically significant. The processes such as carcinogenesis and aging may be intimately linked to slowly accumulating, irreversible alterations of DNA.



Heating and extreme of pH

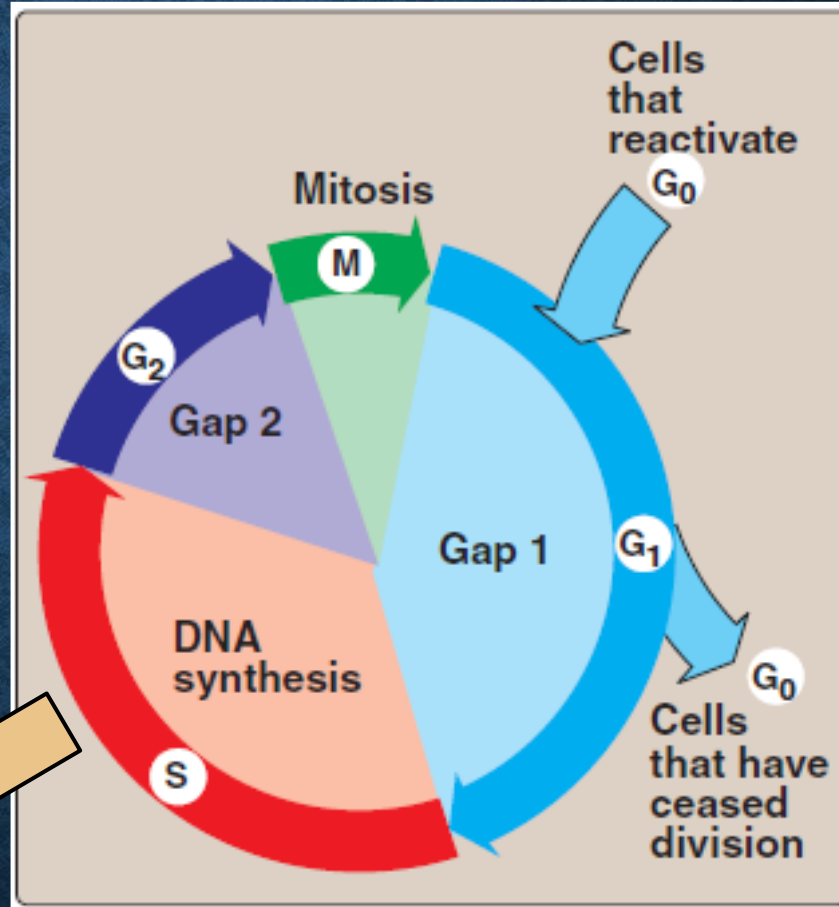
→ May denature the double helix structure of DNA

- By disrupting the hydrogen bond between paired bases
- Lead to the unwinding the helix

→ If not completely separated → rapid one step process of renaturation (After temperature and pH return)

→ If completely separated → two steps renaturation occur

Cyclins and Cdk

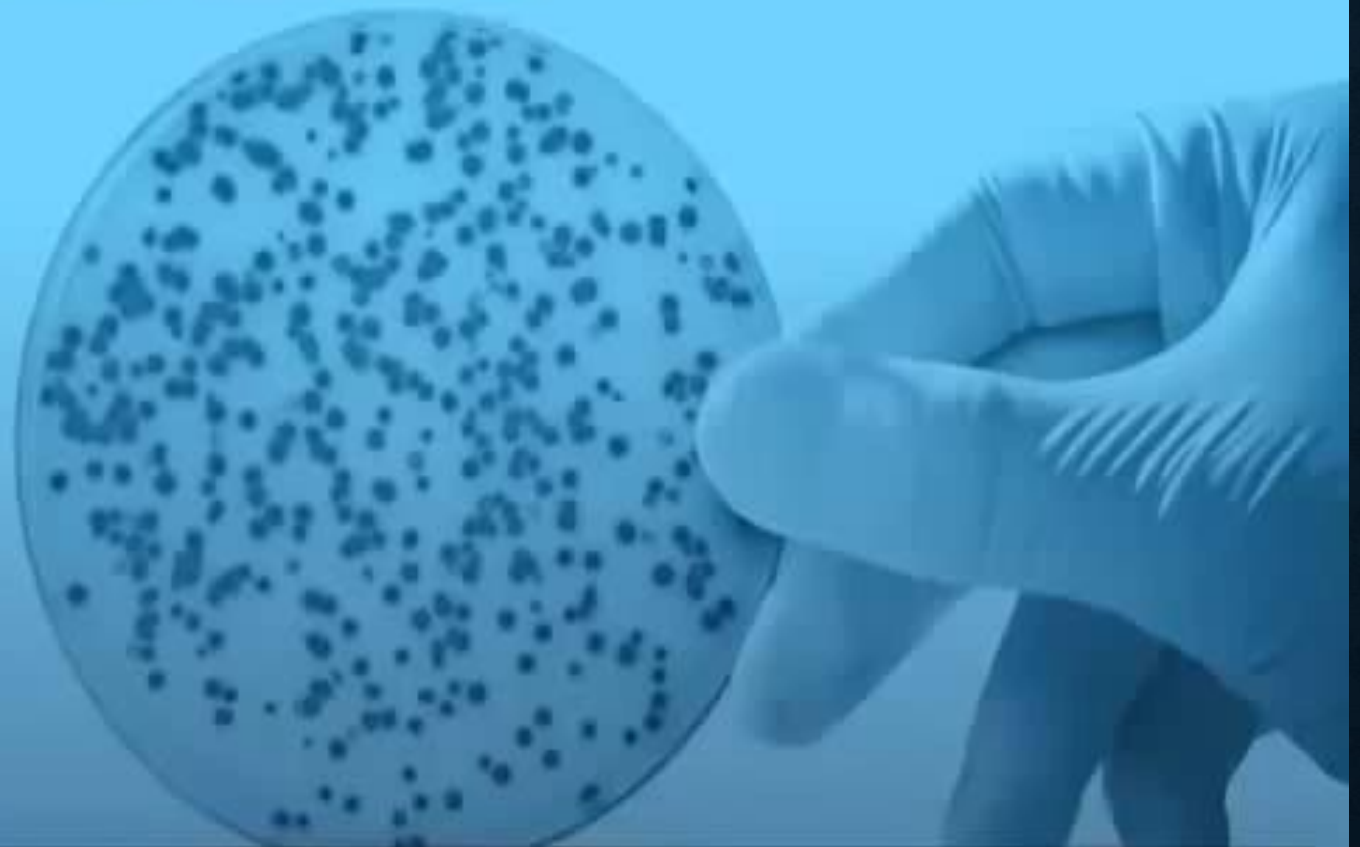


DNA replication

Eukaryotic cell cycle

DNA REPLICATION

SYNTHESIZING IDENTICAL GENETIC MATERIAL



IMC

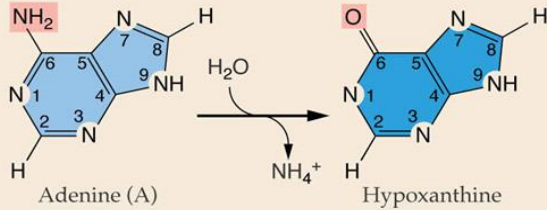
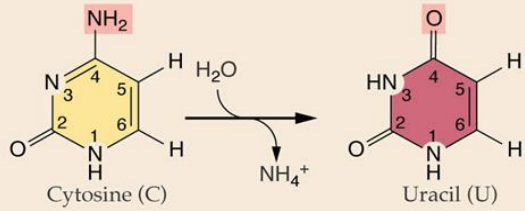
Cells, like these prokaryotic *E. coli* cells, replicate themselves quickly and efficiently. Part of the process of asexual

DNA damage

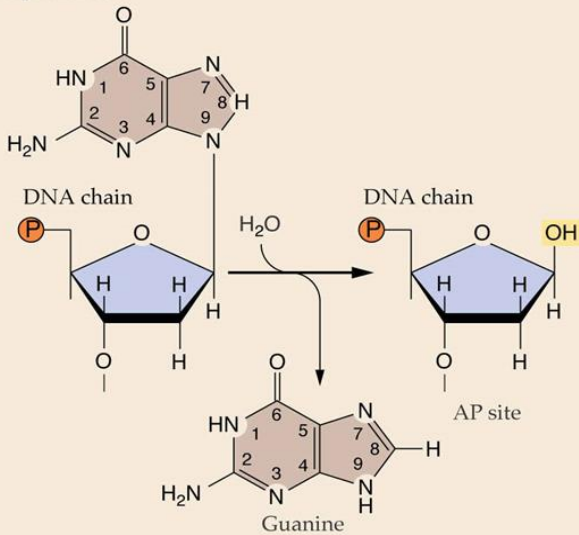
1. Deamination: (C → U and A → hypoxanthine)
2. Depurination: purine base (A or G) lost
3. T-T and T-C dimers: bases become cross-linked, T-T more prominent, caused by UV light (UV-C (<280 nm) and UV-B (280-320 nm))
4. Alkylation: an alkyl group (e.g., CH₃) gets added to bases; chemical induced; some harmless, some cause mutations by mispairing during replication or stop polymerase all together
5. Oxidative damage: guanine oxidizes to 8-oxo-guanine, also cause SS and DS breaks, very important for organelles
6. Replication errors: wrong (or modified) nucleotide inserted
7. Double-strand breaks (DSB): induced by ionizing radiation, transposons, topoisomerases, homing endonucleases, mechanical stress on chromosomes, or a single-strand nick in a single-stranded region (e.g., during replication and transcription)

Spontaneous

Deamination

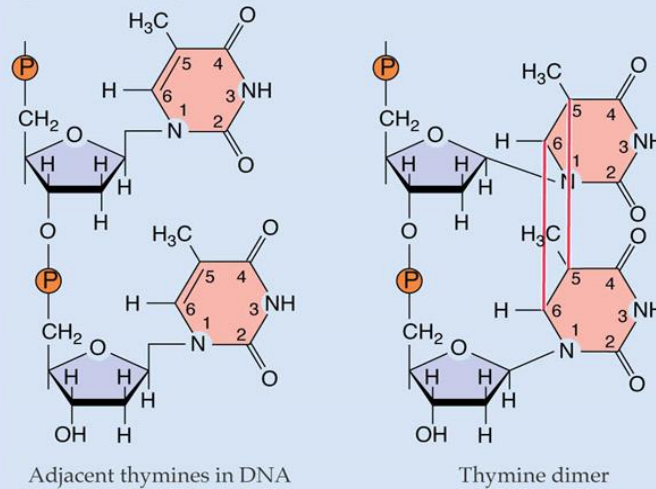


Depurination

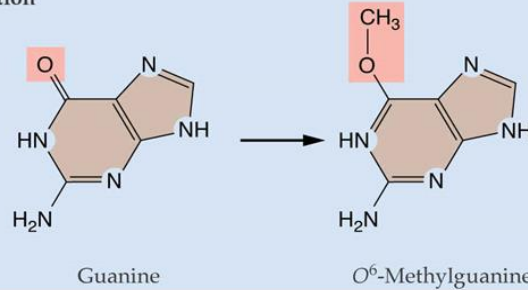


Induced

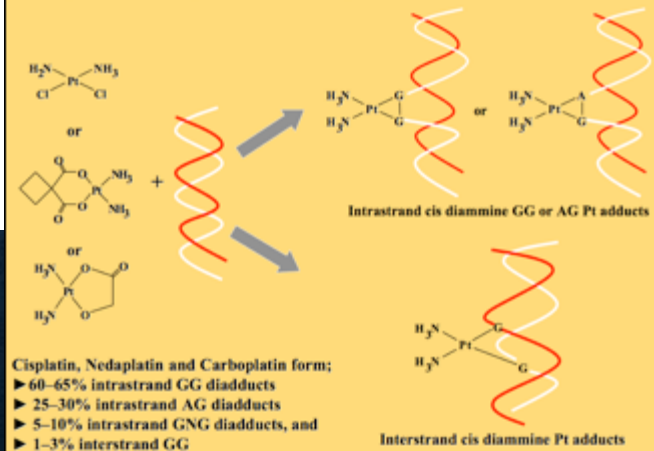
Exposure to UV light



Alkylation



Cisplatin, Carboplatin and Nedaplatin and their adducts in DNA



DNA damage and repair

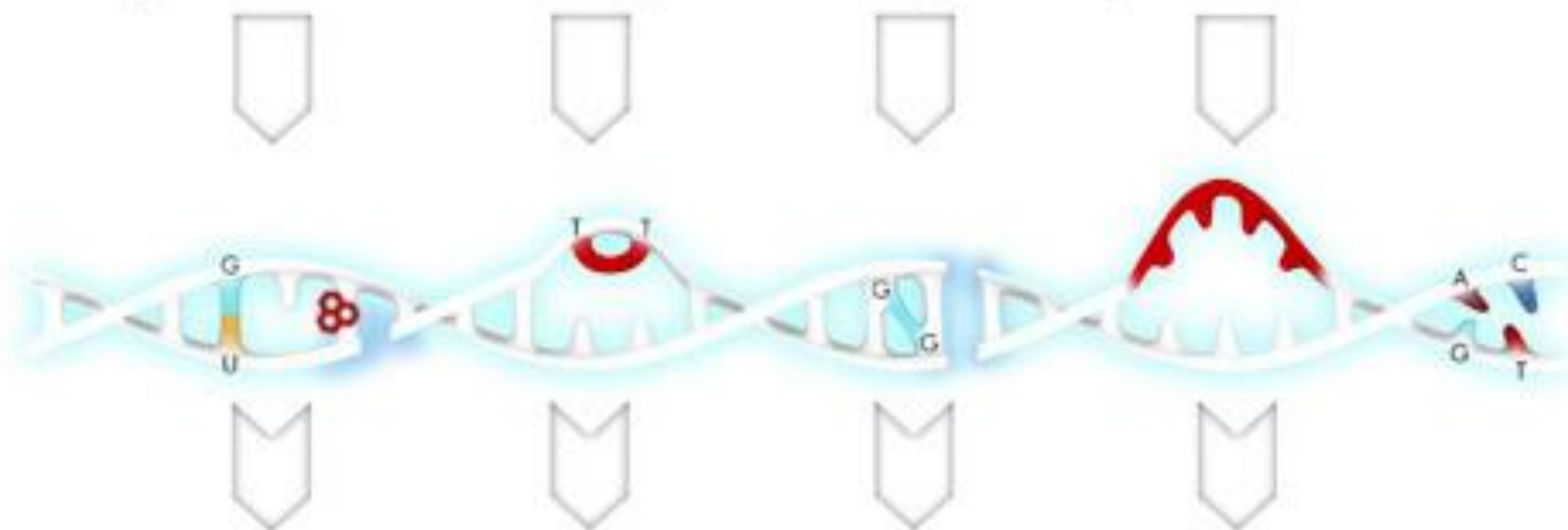
Damaging agents

X-rays
alkylating agents
hydrolysis
O₂ radicals

UV irradiation
chemical mutagens

X-rays
anti-tumor agent

replication errors



abnormal bases
base adducts
single-strand break
abasic site

bulky adducts
thymidine dimers

double-strand break
interstrand crosslink

A-G mismatch
T-C mismatch
base insertion
base deletion

Repair processes

base-excision
repair (BER)

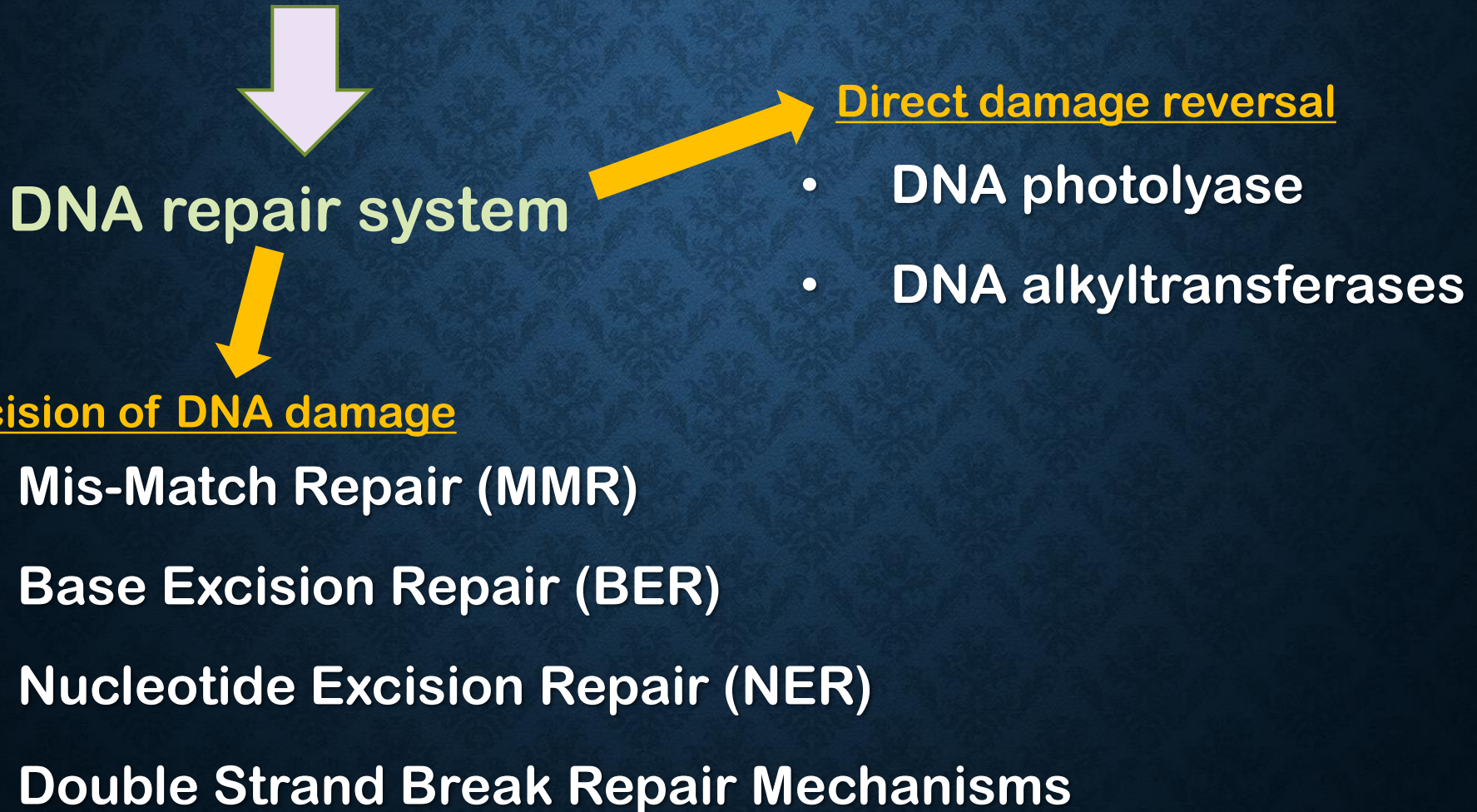
nucleotide-excision
repair (NER)

recombination
repair (HR, EJ)

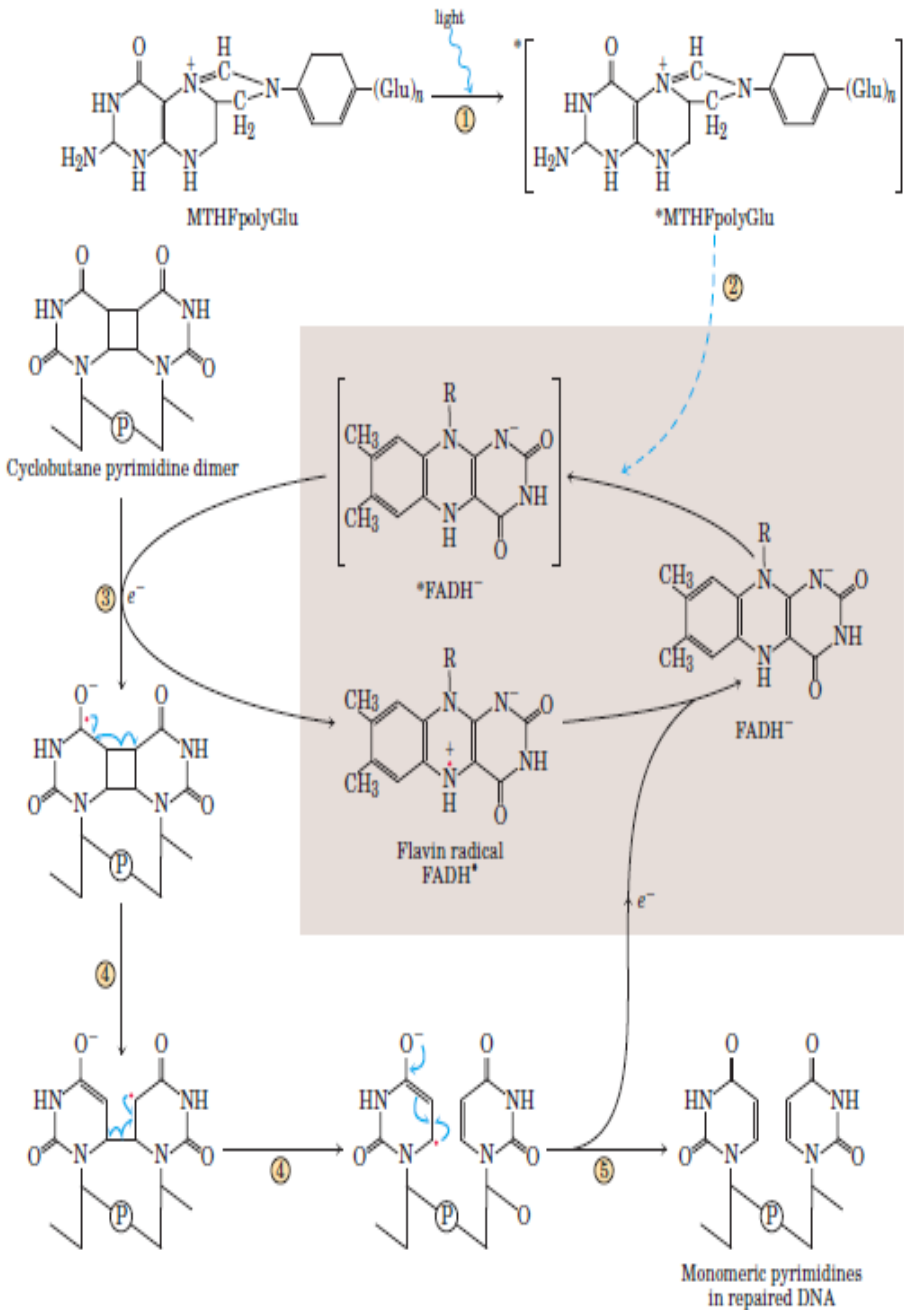
mismatch repair

Damaged protein and RNA molecules can be quickly replaced by using information encoded in the DNA...

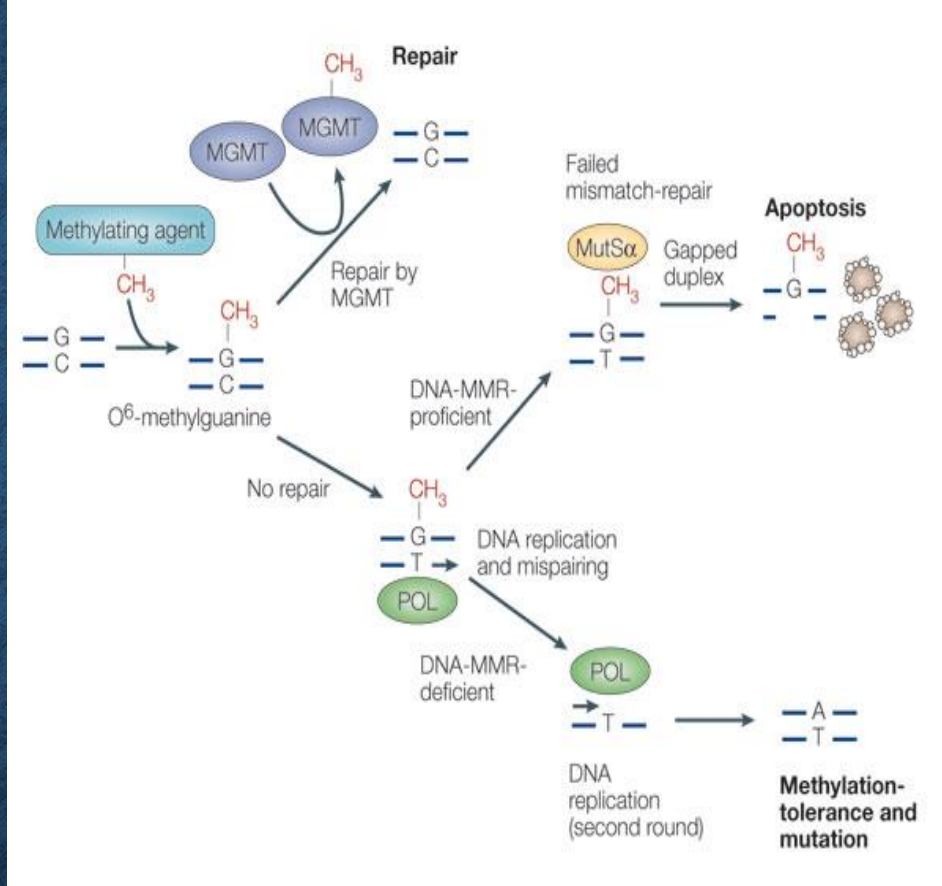
However, the DNA themselves are **irreplaceable**.



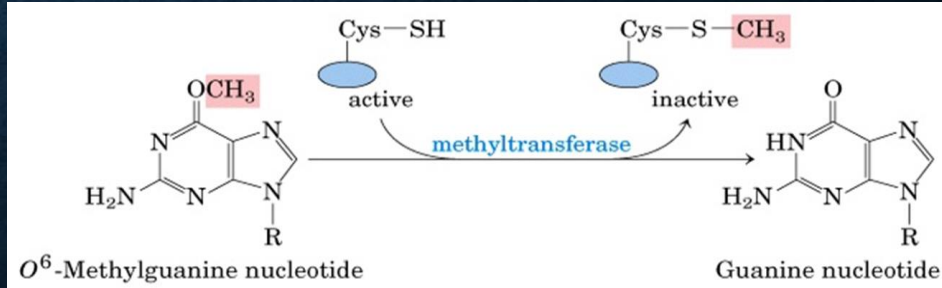
Photolyase



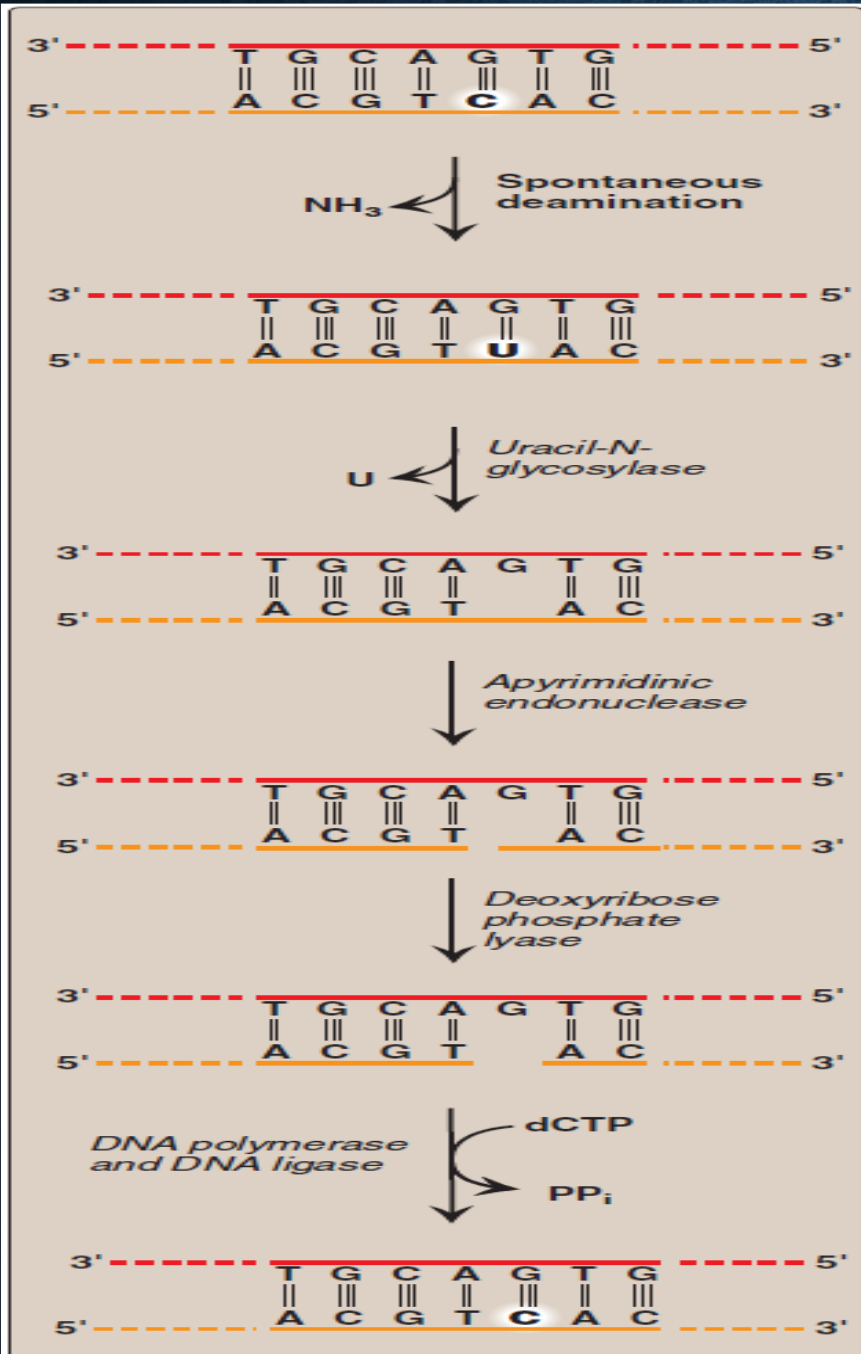
Alkyltransferases



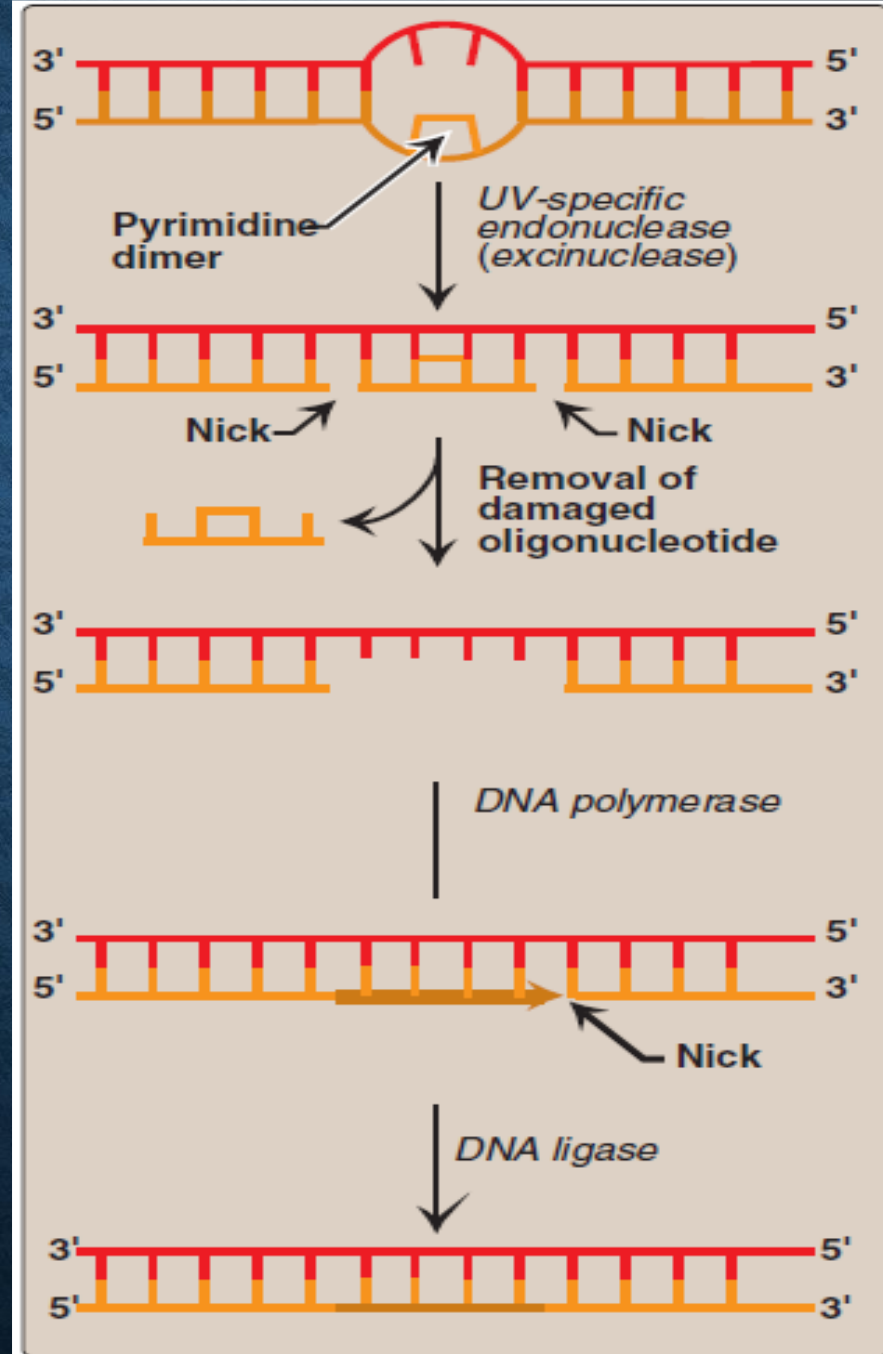
Copyright © 2005 Nature Publishing Group
Nature Reviews | Cancer



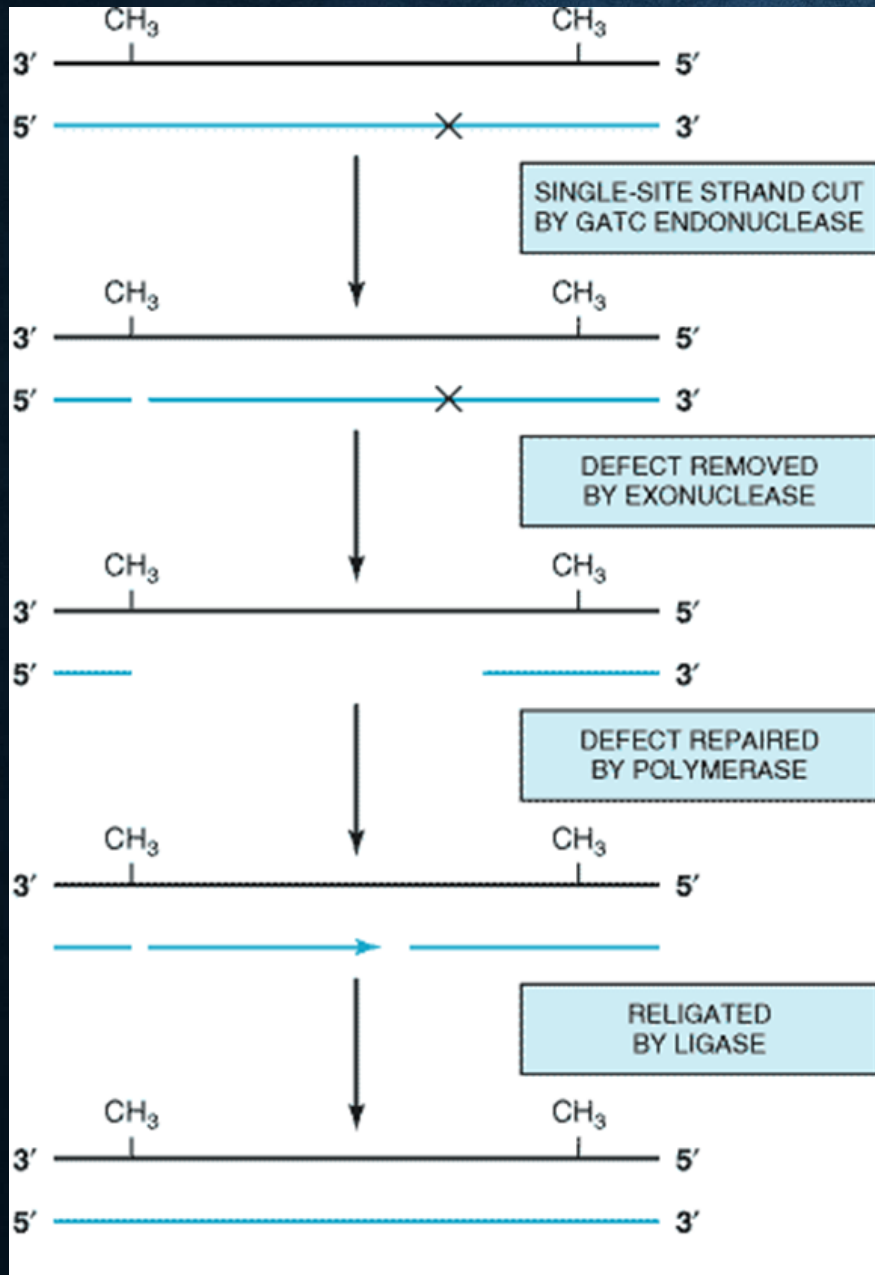
Base-Excision Repair (BER)



Nucleotide-Excision Repair (NER)



Mis-Match Repair (MMR)



DNA recombination

