

DNA REPAIR MECHANISMS

8 March 1996, 9 Mar 01, 10 Mar 04, 12Mar08, 13Mar09, 10 Feb 10, 12Mar10
 GMSLG 7th: p 510-519, 9th: 531-550

SUMMARY OF MUTAGENESIS:

Four ways mutations can be induced:

- 1) deamination, depurination (spontaneous or chemically)
- 2) base analogs allow mis matching
- 3) alteration, tautomerization of bases, mispairing results
- 4) Damage DNA so replication cannot proceed, SOS causes **relaxation of stringency**

DNA REPAIR: Major errors leading to mismatching/missing bases:

- depurinated sites** 5000-10000/ day in human cells (glycosidic bond unstable)
- deaminated cytosines:** by random thermal collision with H₂O 100/day
- pyrimidine dimers:** UV caused

Why Thymine in DNA, rather than uracil??

allows distinction, correction between deaminated C and T (otherwise looks like U)

Repair endonuclease: detects error, nicks backbone, DNA poly I rpc-synth.

DNA glycosidase detects deaminated, removes base, then endonuclease etc follows
 proceeds **bidirectionally** fr origin (*oriC*) at 83 min on *E coli* map

Excision-resynthesis: (p. 532) detects distortion in DNA, activates endonuclease to cut several bases away 12 base long section removed, resynthesized (pol I) and ligated

SOS bypass: (p. 538) blockage during replication is relieved by insertion of random base to continue replication. SOS proteins bind with pol III to loosen (relax) its **stringency**.

photoreactivation: (p. 532) splits photo dimers of pyrimidines, requires visible light

alkyltransferase: (p. 511) transfers alkylation products (i.e., DES, etc) to enzyme, inactivates enzyme

DNA glycosylase repair: cuts out damaged bases, leaving AP site

apurinic or apyrimidinic sites endonuclease cuts at AP sites, exonucleases nibble away, resynthesize and ligate

Mismatch repair: (p. 537) DNA pol III can edit out mismatches during replication. Depends on 6-methylation of adenine which occurs at GATC sites after polymerization. The new strand is not methylated until several minutes after polymerization, can tell old fr new strand, corrects *new* mismatched base.

Recent scanning theory: Mismatch scanning proteins mark mismatched spot and chain to be removed, chain is cleaved, etc.

Electrons are passed along properly matched bases in DNA, knocking off mismatch scanning machinery. Mismatched bases do not allow electron transmission, increases chance of early detection by scanning machinery, which triggers repair.

