Bio 301
10·16·91

Phil Hanawalt : Ce DNA repair

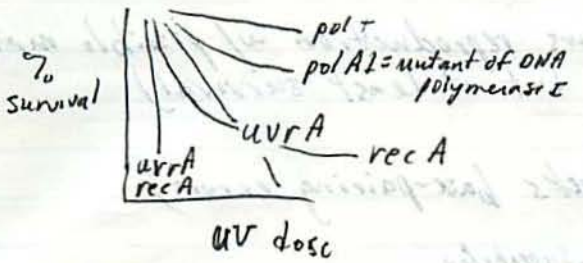
environment → DNA damage → repair
→ death
→ change, transformation...

How do you know repair is occurring?

①

- regular light induces "repair" : PHOTOREACTIVATION
  the link between pyrimidines is broken

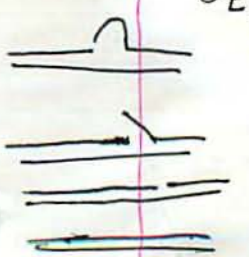
② mutants defective in repair



- recA important in SOS + recombination

in uvrA recA ... cannot survive one pyrimidine dimer

③ EXCISION REPAIR ... of dimers, bulges...
(3+ E.coli genes needed / 8+ human genes needed)



ⓐ incision (endonuclease recognizes distortion)
- must recognize damage vs. structure
ⓑ repair replication
ⓒ excision
ⓓ rejoining w/ polynucl. ligase

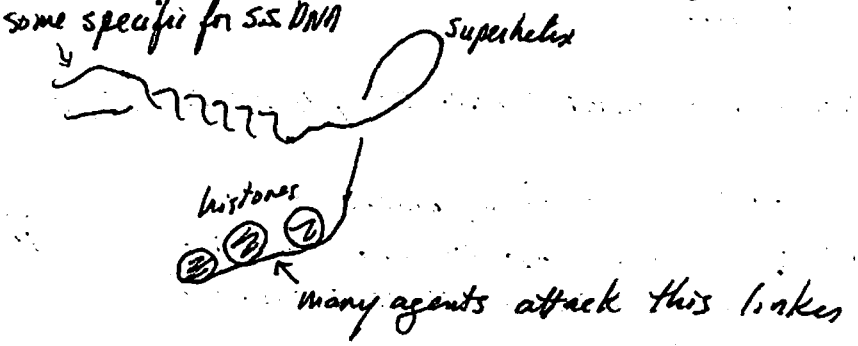
Xerodoma pigmentosa -- v.v. sensitive to UV light
① defect in 1st stem leads to cancer
② many complementation groups

Cockaynes
Cockayne syndrome
① v. sensitive to light
but no cancer

Types of change
① strand breaks
② C → U by deamination (repaired by enzyme that recognizes U in DNA)
③ base loss (purines)
④ modification CH_3 added to guanine O_6 CH_3
ALKYLTRANSFERASE - suicide enzyme recognizes & removes this & then destroyed
⑤ bulky adducts
cisplatin does this
⑥ protein crosslinking
⑦ interstrand linkage
⑧ pyrimidine dimers - intrastrand

Types of repair
① Direct
② Excision
③ Replication (allows reproduction w/ possible mutation but at least survival)
④ Post-replication repair
⑤ Mismatch repair (checks base-pairing errors)

Differences based on structure



Differences betw. f(x) regions of DNA:

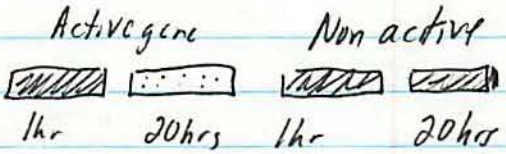
① transcription areas
② non-transcribed areas (e.g. near centromeres : ∆ DNA)
③ replication origin
④ front of replication forks

These areas may have different rates/types of DNA repair.

Humans & mice v.v. similar in response to DAMAGE
but humans repair much much more damage.

... Caused by selective repair of active genes
... Determined by

cells → damage → isolate DNA → digest → cut w/ enzyme that targets damaged sites
(wait 20 hrs)



∴ ACTIVE GENES REPAIRED MORE EFFICENTLY

TRANSCRIBED STRAND REPAIRED MORE THAN NON-TRANSCRIBED STRAND
- model: blocked transcription unit leads to repair

Xerodoma pigmentosa
- limited domain repair
- cancer increase

Cockaynes syndrome
- defective repair of expressed genes
- no cancer increase

∴ DAMAGE IN NON-TRANSCRIBED REGIONS ⇒ CANCER

How do terminally differentiated cells deal?
e.g. neurons don't repair much
but repair specifically