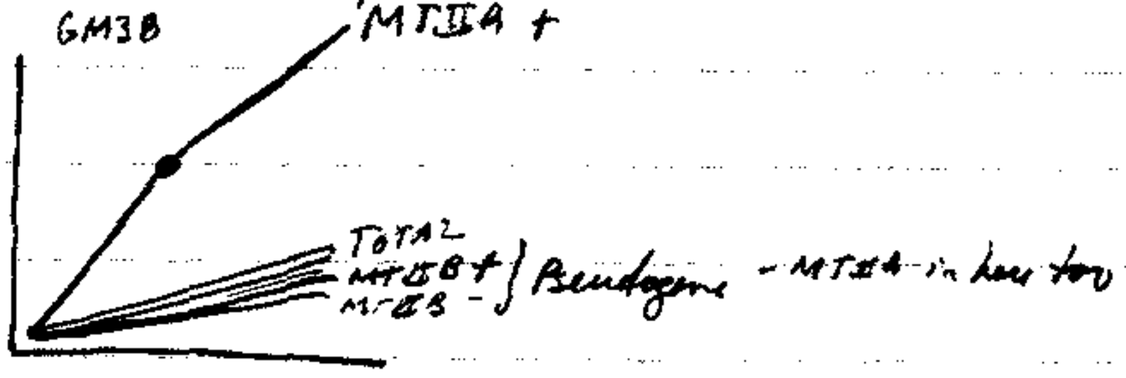
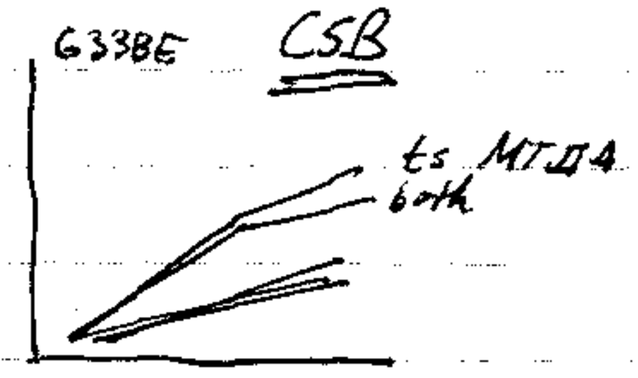
Lab Meeting - P. Cooper

Previously

Lieden & Cooper --- precipitating repair patches for ionizing radiation damage
- had been reports that CS cells were ionizing radiation sensitive

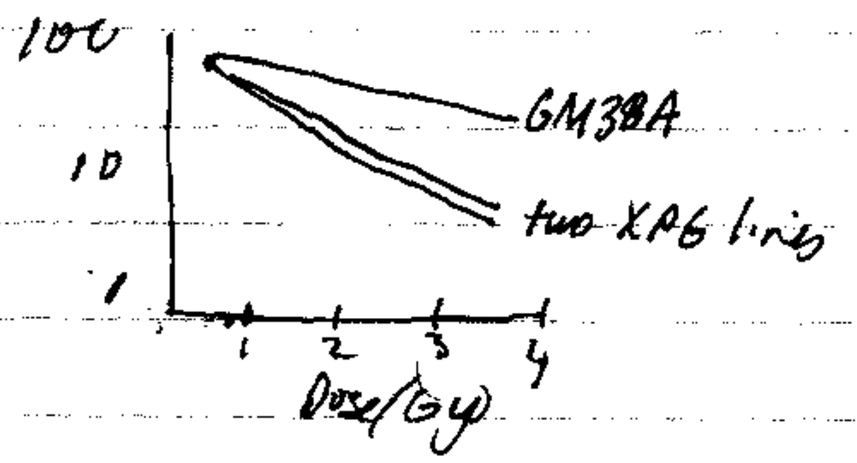


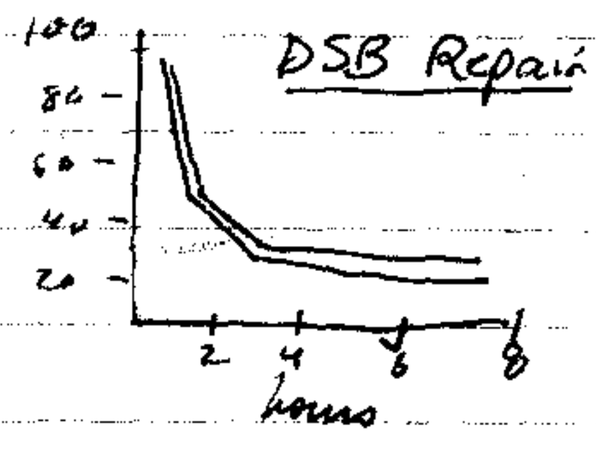


- so... don't know with this assay what is being repaired

XPG

- v. rare defect (9 patients)
- ½ have CS phenotype
- one of patients cells reported to be ionizing radiation sensitive
- v. lowly expressed (~10 copies of RNA/cell)



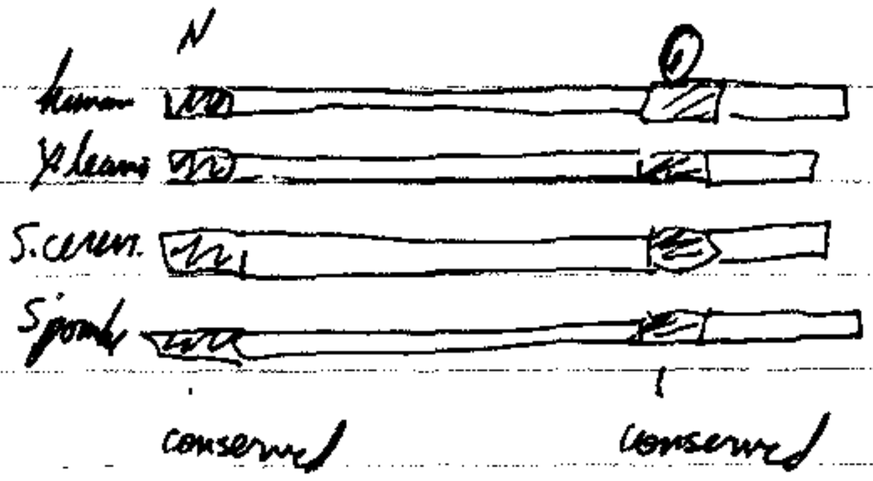


- clinical symptoms very heterogeneous

Cells	Defect	Clinical phenotype
GM38	none	
XP12LO	XP-G (defect in excision)	mild XP
XP3BR, XP2BI	XP-G (defect in excision)	severe XP; some CS
XPCS4LV, XPCS2LV	XP-G (defect in excision)	severe CS

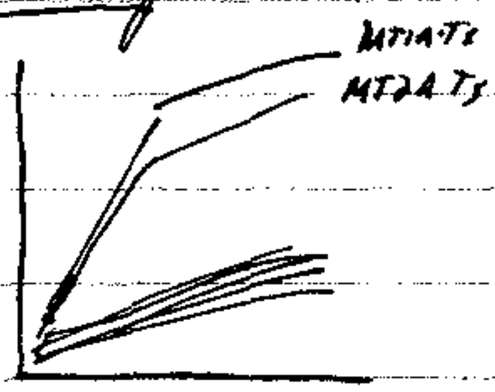
mutations in different XPGs

XP125LO -- ① pt. mutation

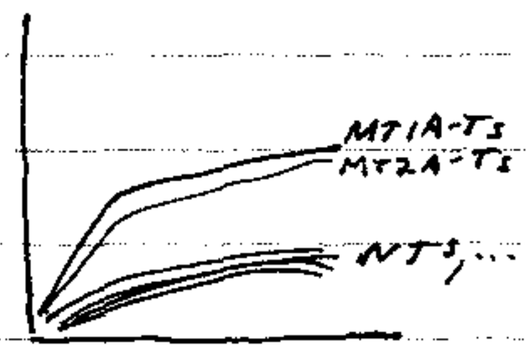


Repair synthesis is defective after X-rays

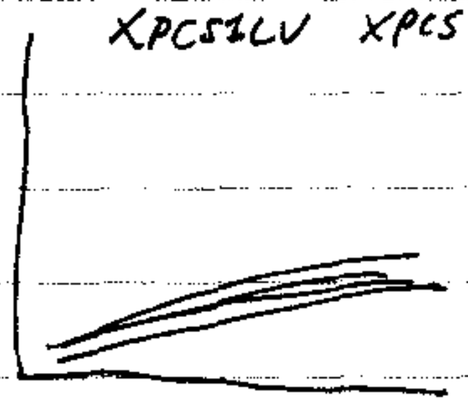
ICR for X-rays



Intermediate XPG's

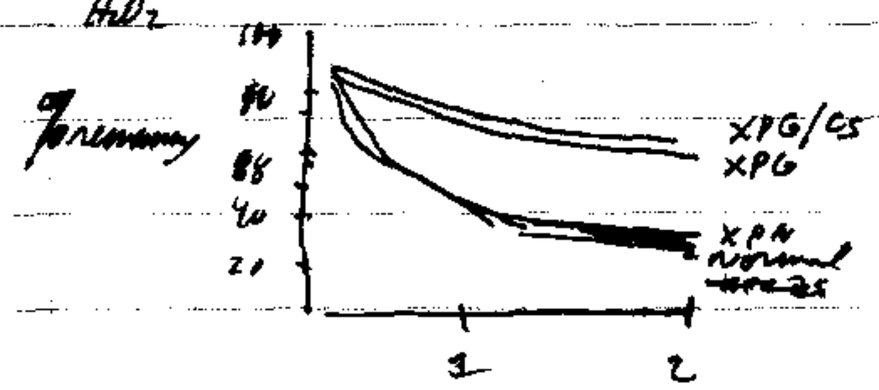


XPCS1LV XPCS2LV

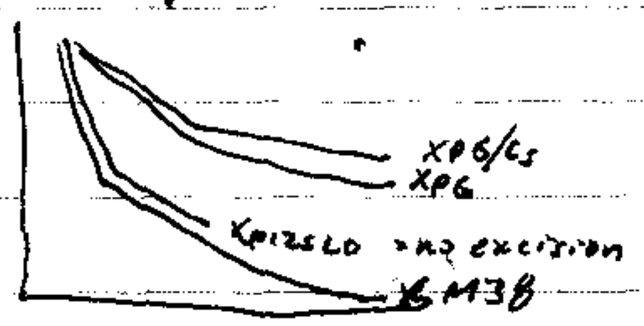


So--what damage is not being TCR'd

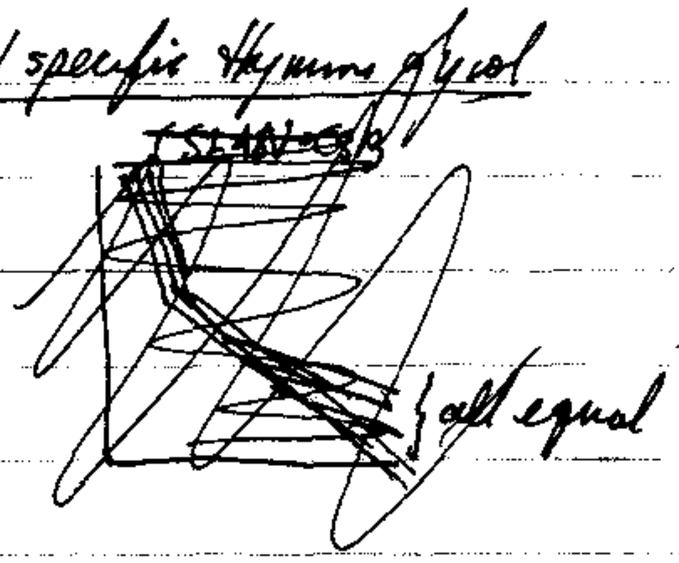
Thymine glycol removal

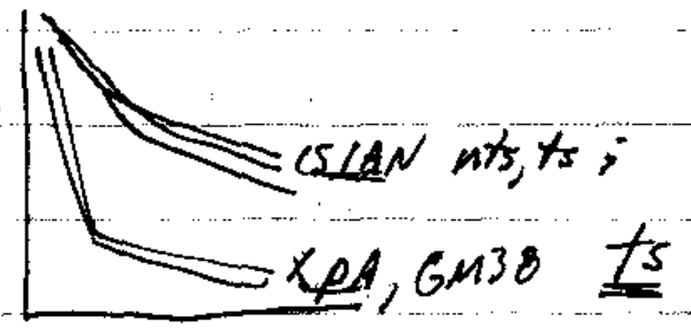


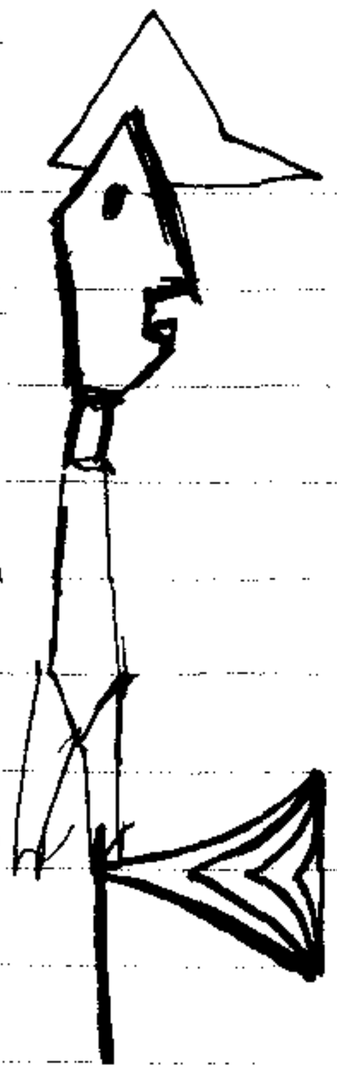
X-rays



Strand specific thymine glycol







∴ Glycosylase Tx coupled repair is not dependent on XPA
but it is dependent on XPG

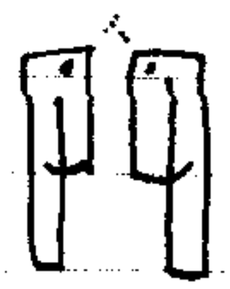
what else happens to the strand w/ Tx block?

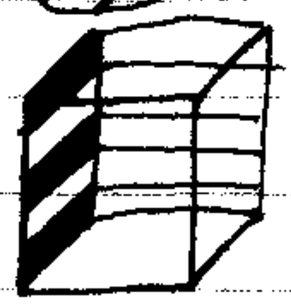
Normal TCR is dependent on XPG but
not on its excision activity.

MODEL

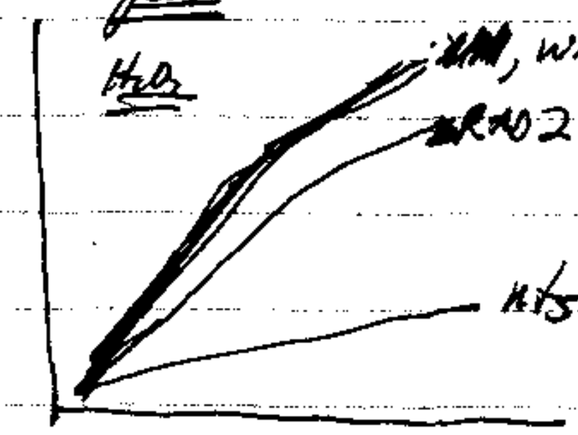
- maybe need to remove stalled tx. complex to
get repair at any lesion

Matsumoto & Kogenhagen
two types of UVR repair
© short patch
© long patch - PCNA dependent





Yeast
H₂O₂



H₂O₂ -- but no survival change