

# Nucleotide Excision Repair in Mammals

observed

XP  
CS  
PIB105 (photosensitivity) / TTD } many phenotypic similarities

XPB = homolog of SSL2/RAO25/

- some defects lead to TTD

- some lead to XPB

- microinjection of TFIIH into cells can rescue XPB

DNA repair (by UDS) (+ XPD + TTD)A

mutant UDS corrected by TFIIH injection

XP	XP A	-
	B	+
	C	-
	D	+
	E	-
	F	-
	G	-
	TTDA	+

\* - in vitro TFIIH corrects repair defect in XPB, XPD, TTDA  
this shows the TFIIH injection does not work  
by activating ix of genes.

- immunoprecipitation of TFIIH leads to repair defect extract  
- this can be fixed by addition of extracts from  
XPB, XPC, RPE ... but not by addition of XPB, D, TTDA

Van Gool

ERCC6 - Antibodies

- showed that Ab binds to fraction w/ TEFIF & POLC
- does not copurify w/ TEFIH, TEFIIA, TEFIF, TEFIB

RAD26

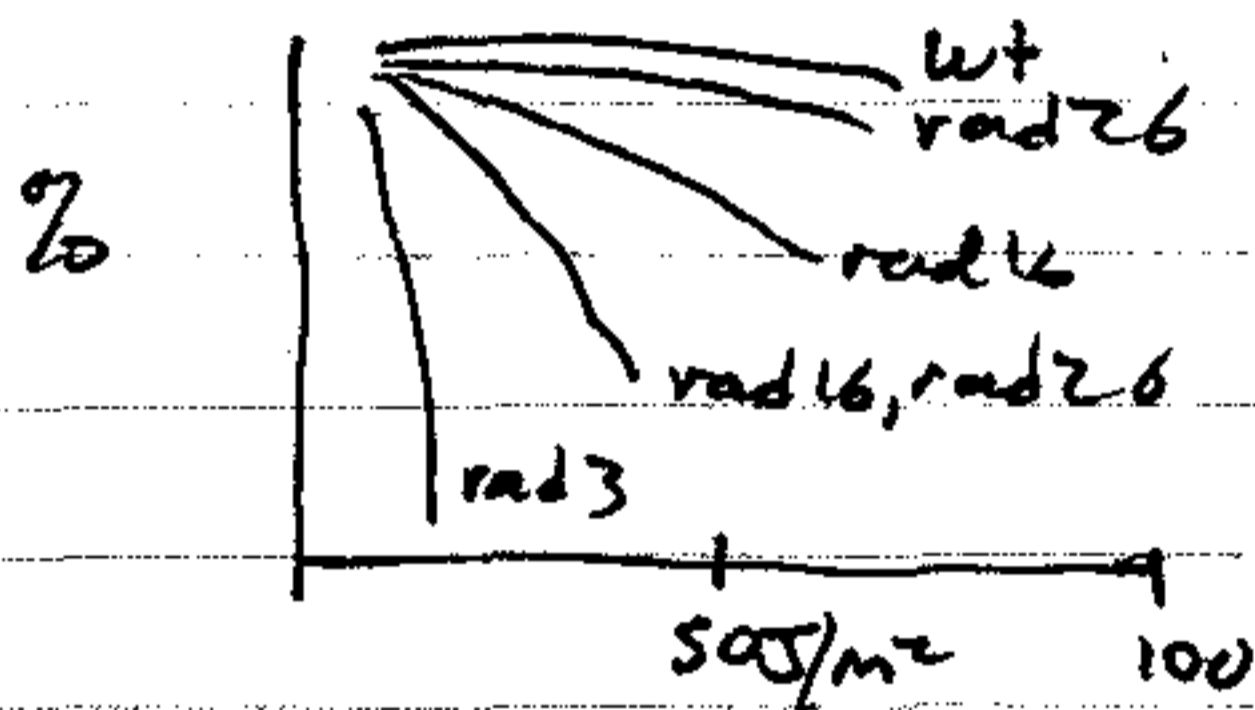
- disruption mutant

① no UV sensitivity relative to WT

- explanation - maybe background repair v. high

② defectives in TCR

RAD26/RAD7 & RAD16 Double mutants



rad16 } no repair of  
rad7 } NTS

MOUSE KO

few detectable phenotype

- UV sensitivity to exposed skin
- fibroblasts +/- are UV sens.
- RNA syn. recovery lower
- no UDS difference
- TS of P53 repair is lower

(maybe assoc. only happens w/ UV irradiation)

mm

3/30/95

# Mechanism of TCR in mammalian cells - Anika

## Adenosine Deaminase (ADA) gene

- b-y repair
- XPC cell lines -- repair b-y's only in TS

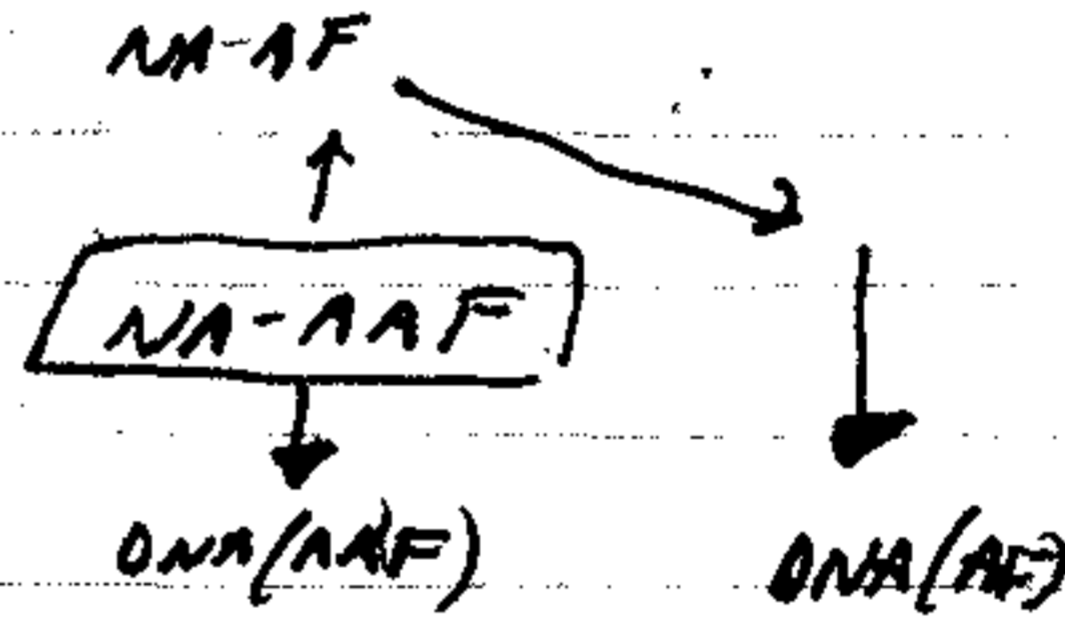
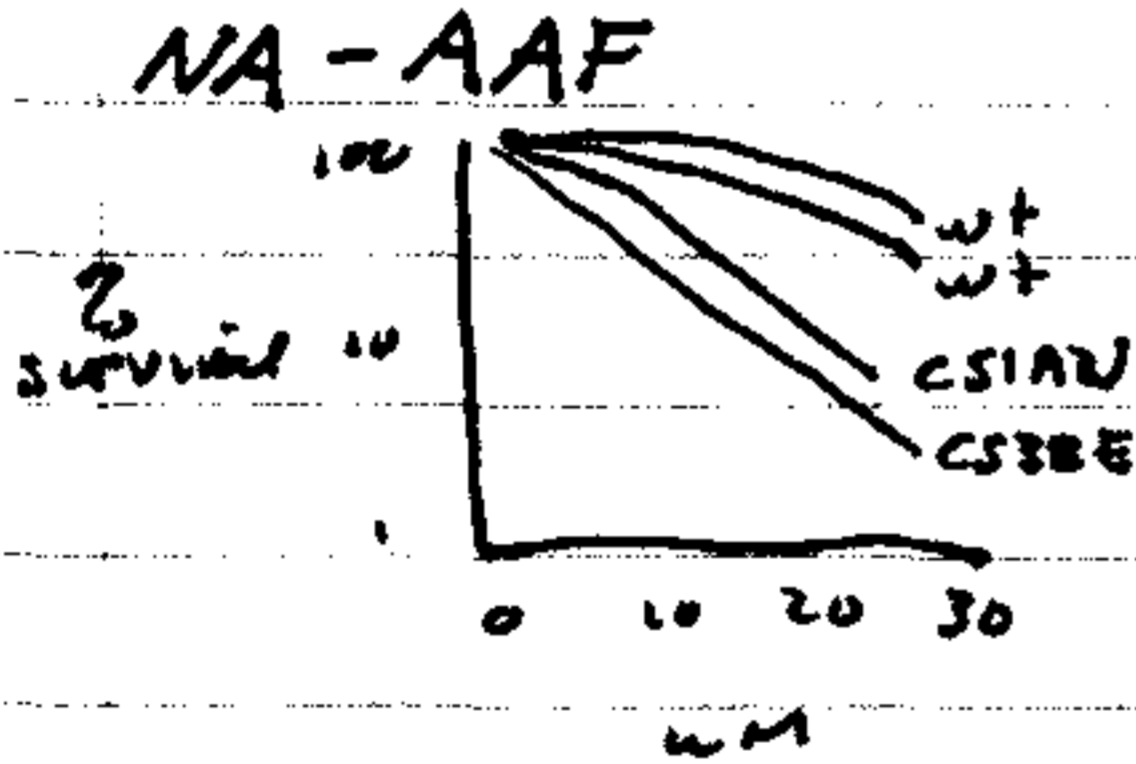
Some evidence that TCR is dose dependent  
 - at higher doses... transcription inhibited / less TCR  
 - & more dimers

## CSF

Late appearance of TCR coincides w/ RNA synthesis recovery.

## Compare AAF w/ UV

LEON M.



## tx. cells w/ NA-AAF

JUST LIKE  
w/ UV

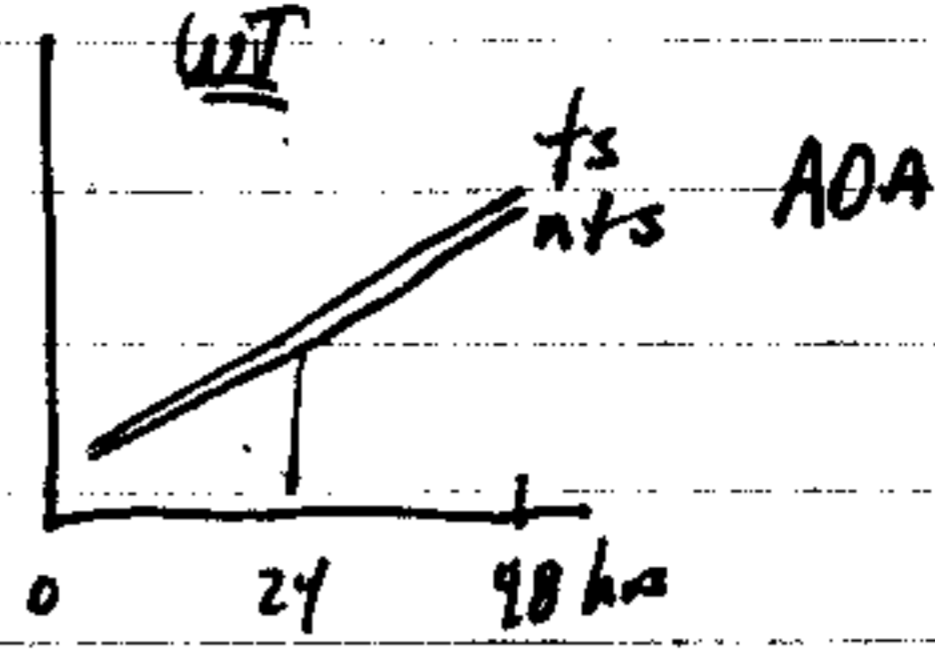
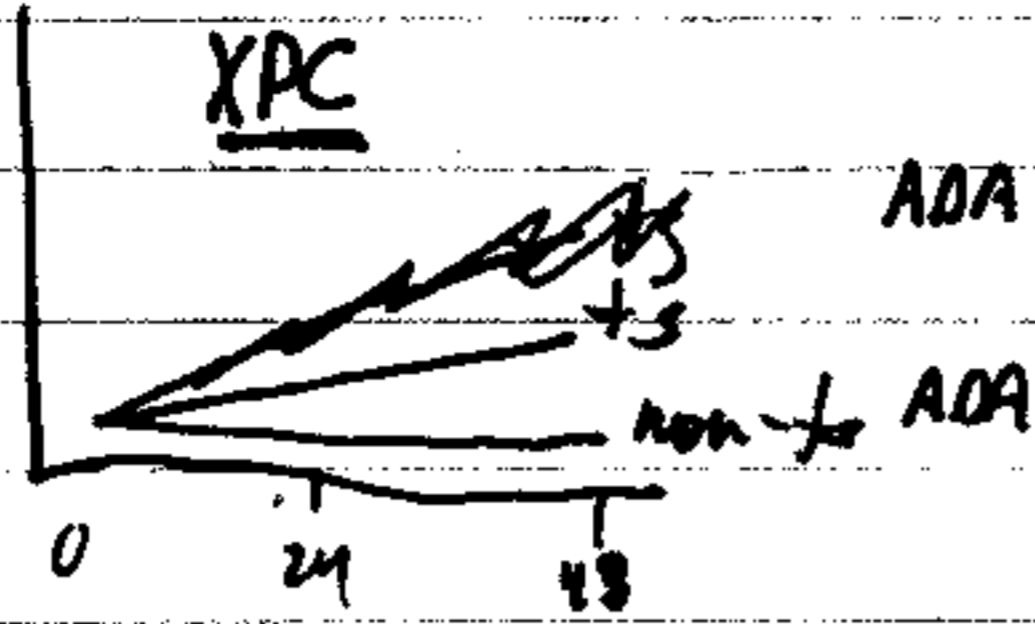
- only detect AF adducts
- RNA synthesis inhibited in WT, XPC, CS cells
- RNA syn. recovery only in WT, XPC
- not much diff. betw. WT & CS in DNA repair replication

## measure AAF/AF w/ UVRABC

- tx. region more actively repaired than non tx
- overall repair relatively slow



To repair



MODEL

- need tx. to have TCP
- but do you need TCP to recover tx.



← so ... want to irradiate/damage before ~~or~~ during transcription)

- ① ts inhibit tx
- ② then do damage
- ③ then study TCP

