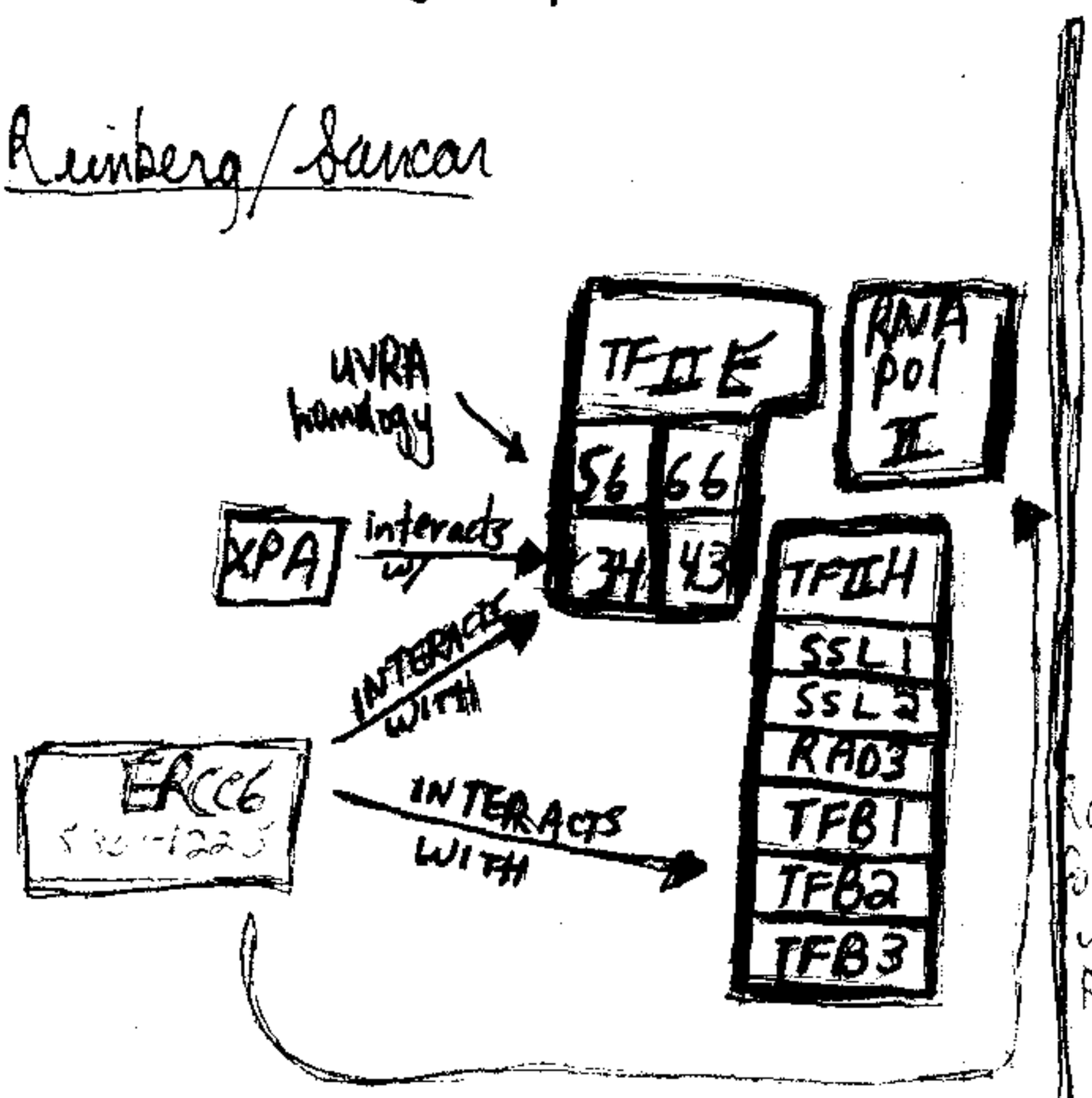
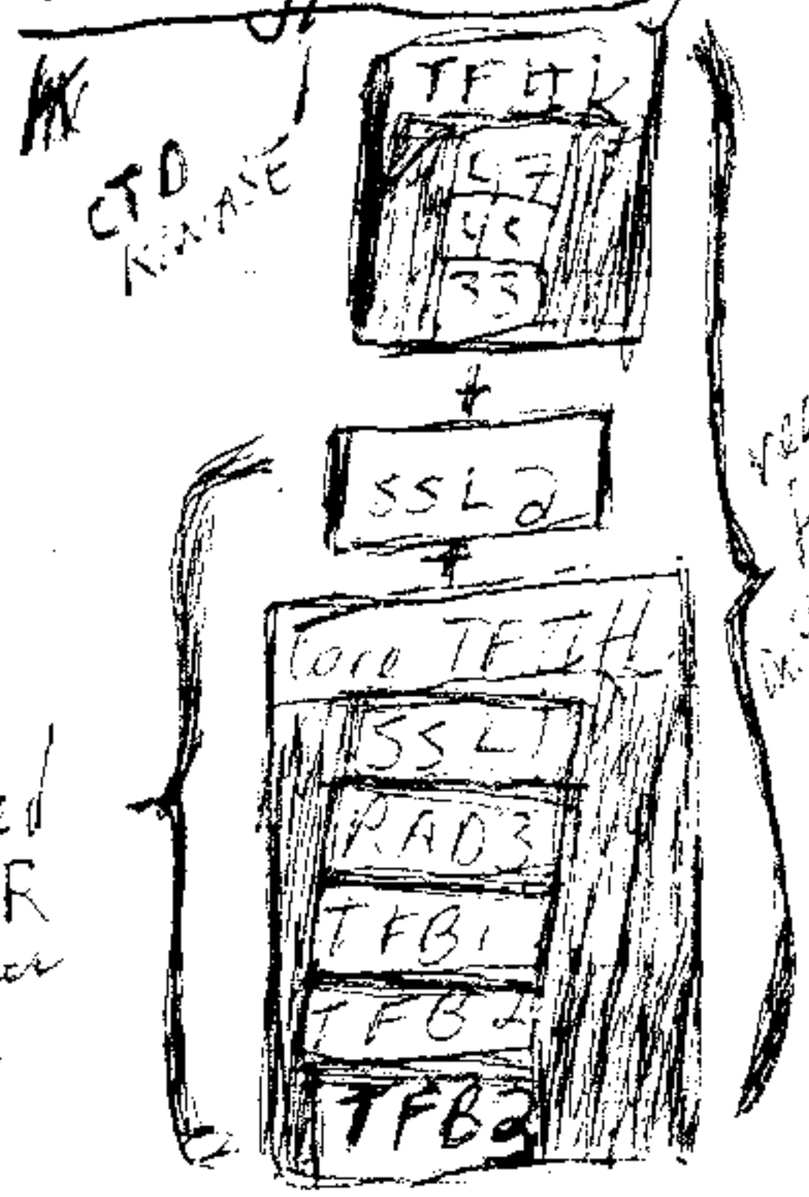
Phil - meeting report

Reinberg / Sancar



Kornberg / Friedberg



SSL2/XPB - active helicase needed for tx

RAD3/XPD - silent helicase needed for NER

3/15/95

Summary	TFIIK	SSLO
RAD3	p47	SSL2
TFB1	p45	
SSL1	p33	
p38		
p55		

tx ← (TFIIK) + (CORE-SSL2) + (NER PROTS) → repair
(RAD 1, 2, 4, 10, 14)

~~Is SSL2 req'd for tx?~~

- no CTD kinase activity w/o TFIIK
- Is SSL2 required?
  - ran TFIIH over column w/ SSL2 Ab.
  - reconst. assay - no tx w/o SSL2

Repairosome

2/10/90

Lab Meeting

Rose

Meeting Updates

- Gordon conferences -- Mammalian DNA Repair
  M. Smerdon -- organizer

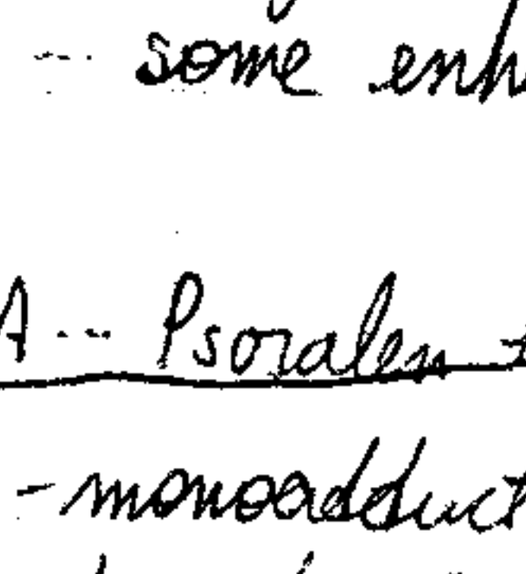
- A. Wolffe - chromatin structure
  - acetylation of histones opens up regions for tx & replication

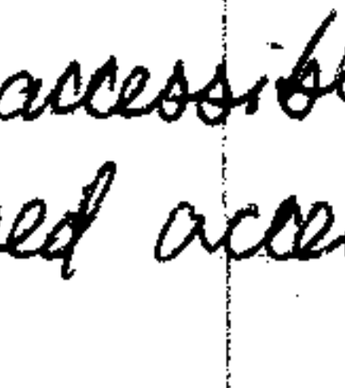
M Bradbury

CPDs -- only ~50% accessible
-- some enhanced access

PUVA -- Psoralen + UVA
- monoadduct is much more mutagenic per toxicity than crosslinks

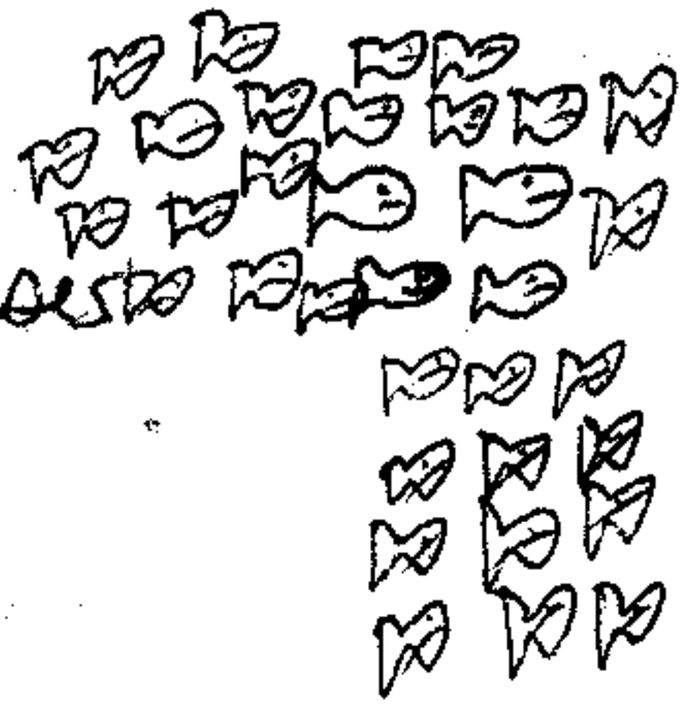
MATS





John Essigman

HUBF --- bind cis-plat adducts & binds cruciform
--- tx. factor hijacking



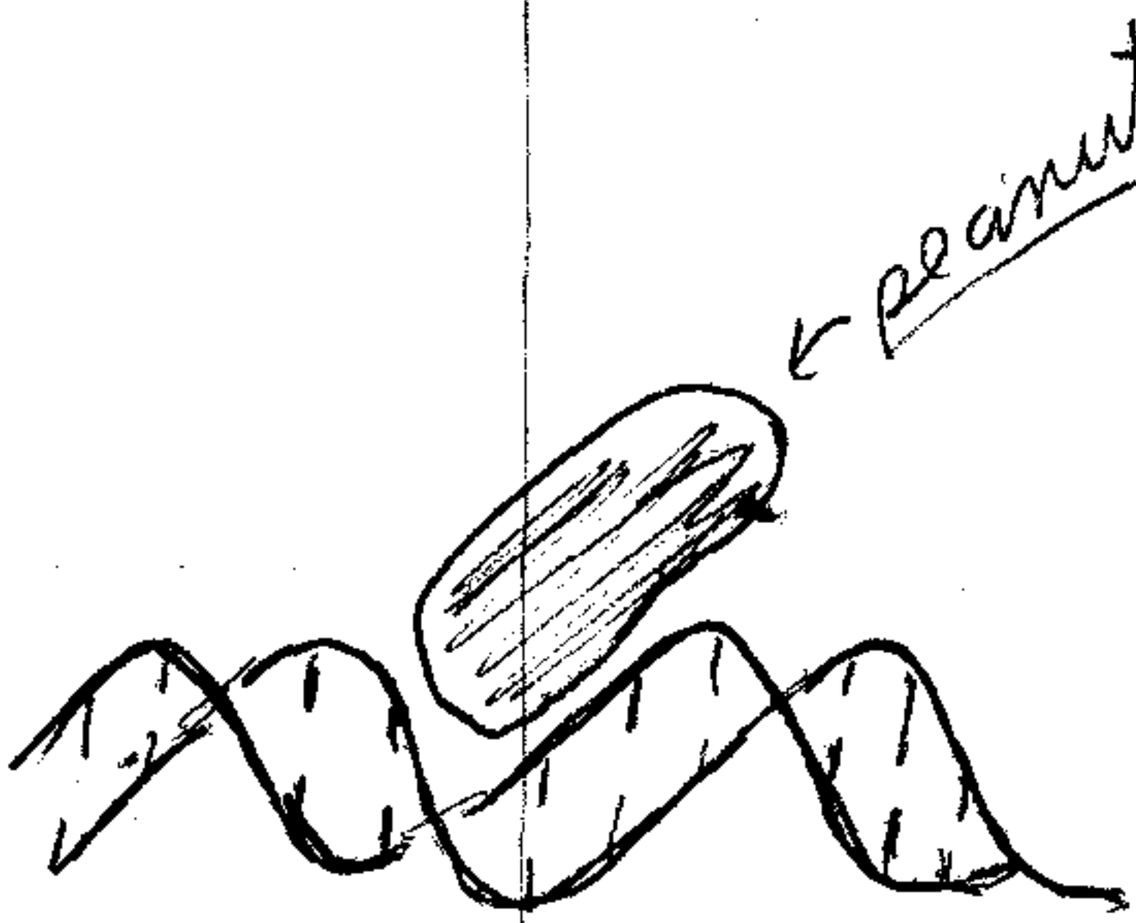
M. McLeod

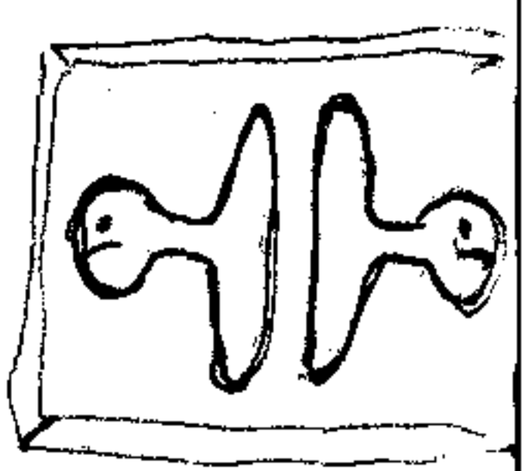
BPDE -- run of G's binding increases

L. Fritz

- mammalian rRNA gene repair
- separate machin from actin rDNA
- no diff. in repair of diff. fractions MOUSE

- bleomycin repair in human
- v. high in DHFR & rRNA





TCR

- ~~PCR~~, Mellon
  1. in LoVo (MSH2⁻)
     - defective in txcr in DHFR
  2. MLH1⁻
     - same thing
  3. MLH1⁻ w/ chrom. complementation
     - TXCR⁺

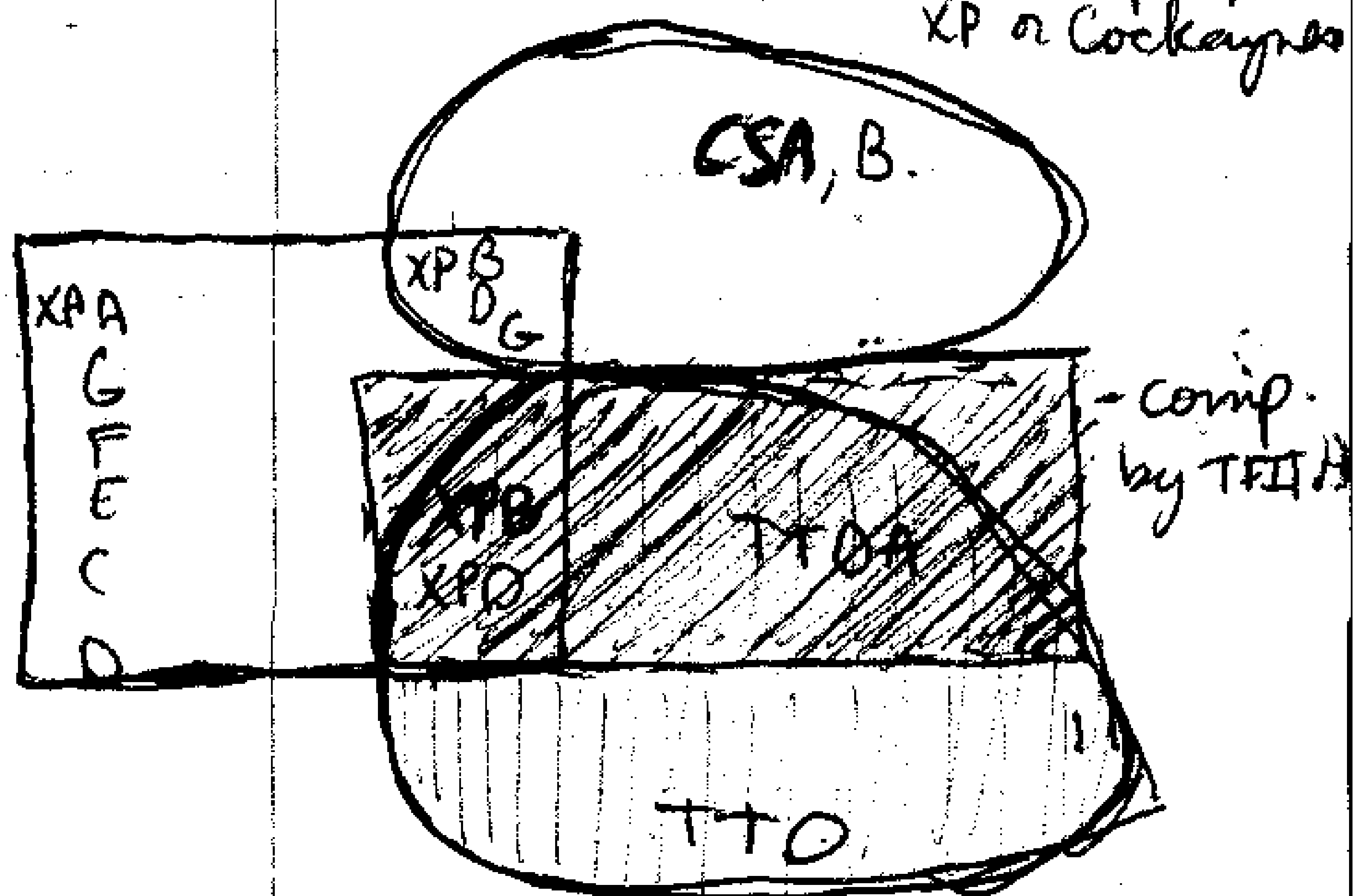
Pfeifer - fine structure
- many sites of hotspots are @ CpG
  - 245 } methylated
    248 }
  - some methylated sites not hotspots
  - all methylated CpGs which are also DNAse I resistant they are slow spots for repair
  - methylation reduces 6-4s

J. Hoeijmakers

① tx problems
- PIBIDS
- haywire
- shiver mouse

[illegible]

TFIIH components
- TTDA
  - defective in NER
  - complemented by TFIIH injection
  - no overlap w/ XP or Cockaynes



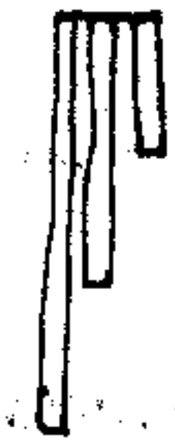
ERCC1
XPA
XPC
XPG
XPF
CSB

} DO NOT INTERACT w/ TFIIH

S. Wilson
- pol B .. mutants mice (double mutant cell line)
  - defective in BER
  - sensitive to MMS (double mutant mice dead).

A Yasui - N. Cresson

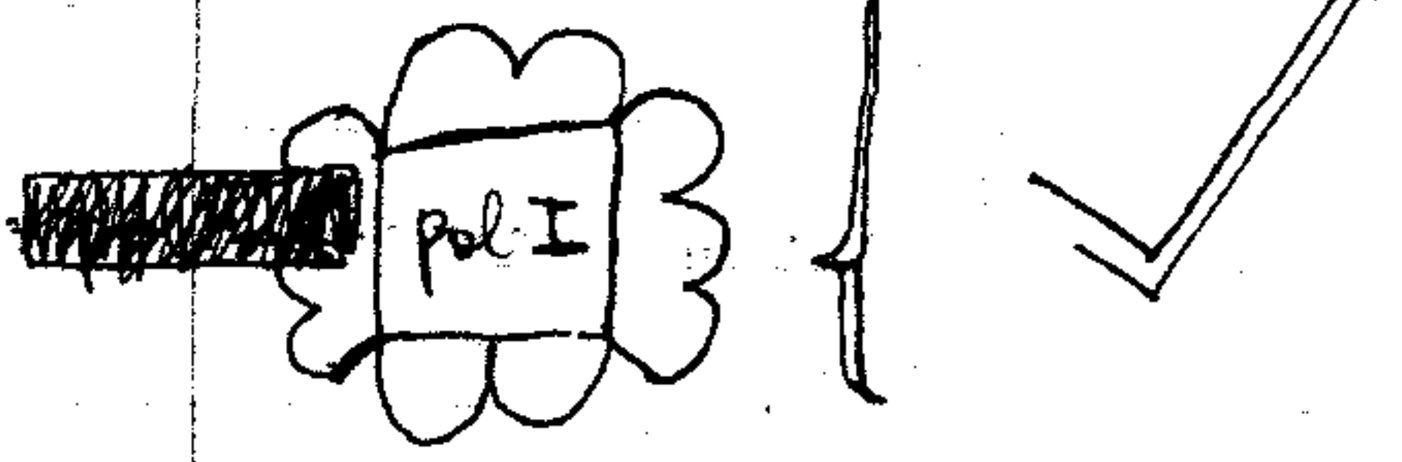
- [redacted] enzymes cut at 6-4's, CPDs



- MUS18
- like S. pombe (Bowman--)

D. Bogenhagen

- → Xenopus extracts
- → 5s RNA gene
- → tx. blocks



P53 mutants

- survival lower

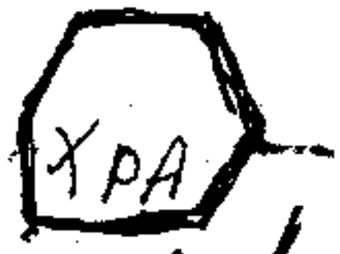
B. Stillman

- ~~NOT~~!
- PCNA not DNA binding -- just donut
- RFC --- opens up PCNA donut

Hoeijmakers - mouse mutants

ERCC1 KO -

- smaller
- can delete 100 nt from N. Term
- can delete
- cannot delete Cterm



- mutants normal phenotype but no NER

- ERCC3 mutant
  - homozygotes die as embryos
- ERCC6
  - no TCR

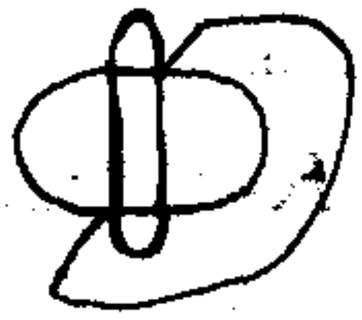
BAD- Cold Spring Harbor

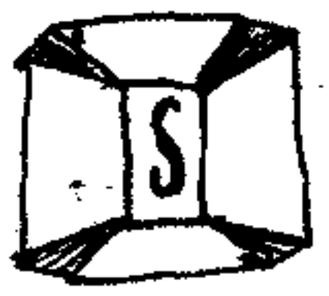
Vogelstein

HNPCC tumors -- from 90% of the patients -- microsat. instability

-HMSH2
-HPMS1
-HPMS2

4 Causes of microsat. instability
① defect in mismatch repair
② repair/replication
③ clonal variation
④ art. facts





suggests some may be due to polT

T. Petes

- 33 bp GT expands
- 51 bp GT contracts

} seems to think DNA slippage is more likely

one AT base pair in the middle stabilizes hairpin

Methyltransferase

mgt⁻ = sensitive to O-6-meG
mgt⁻ msh⁻ = resistant to O-6-meG

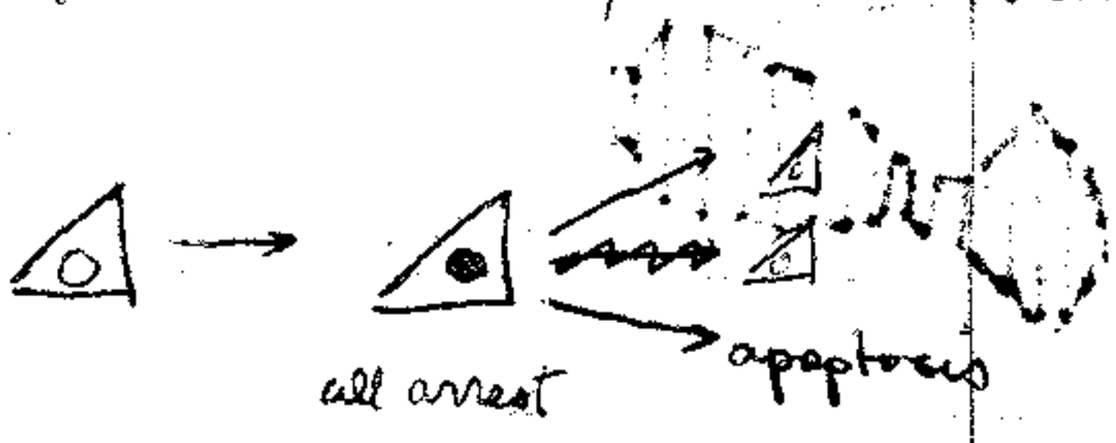
3/10/95

Lab Meeting

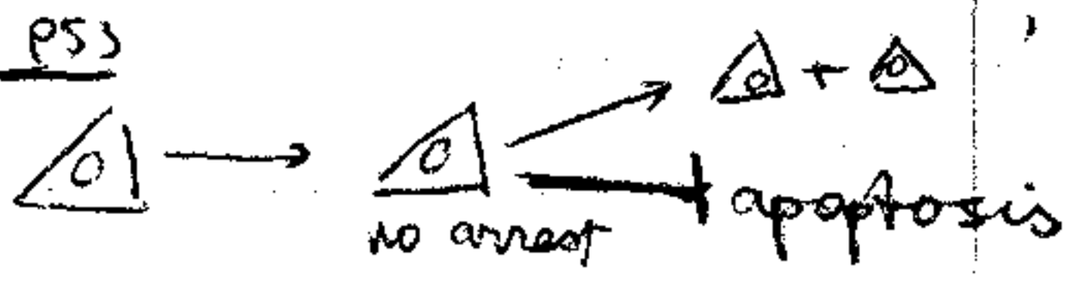
JIM FJORD

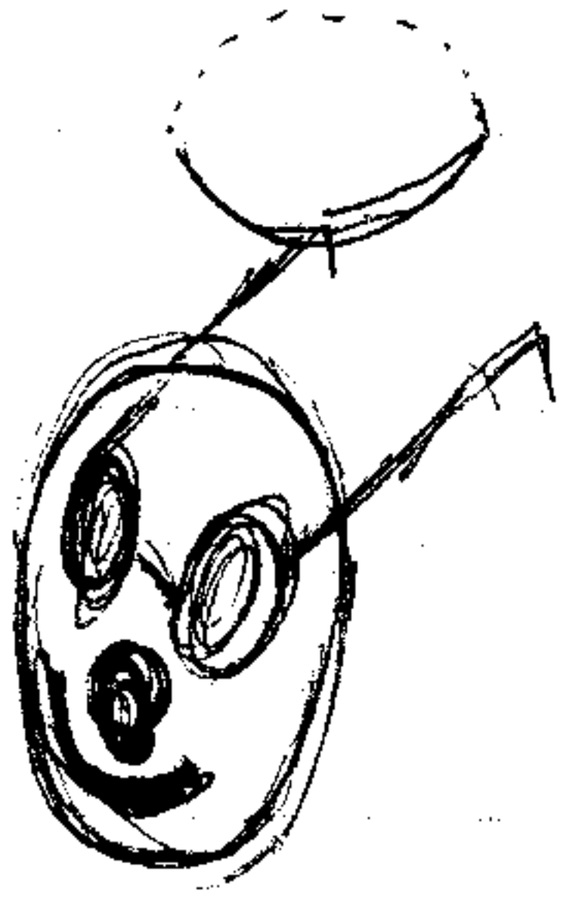
REPAIR & UV SENSITIVITY IN P53 MUTANTS

wT P53



mutant P53





LI-FRAUMENI SYNDROME

- mutants in P53 more resistant to UV
- mutants (-/∅) lower repair of CPD's
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ELISA ASSAY