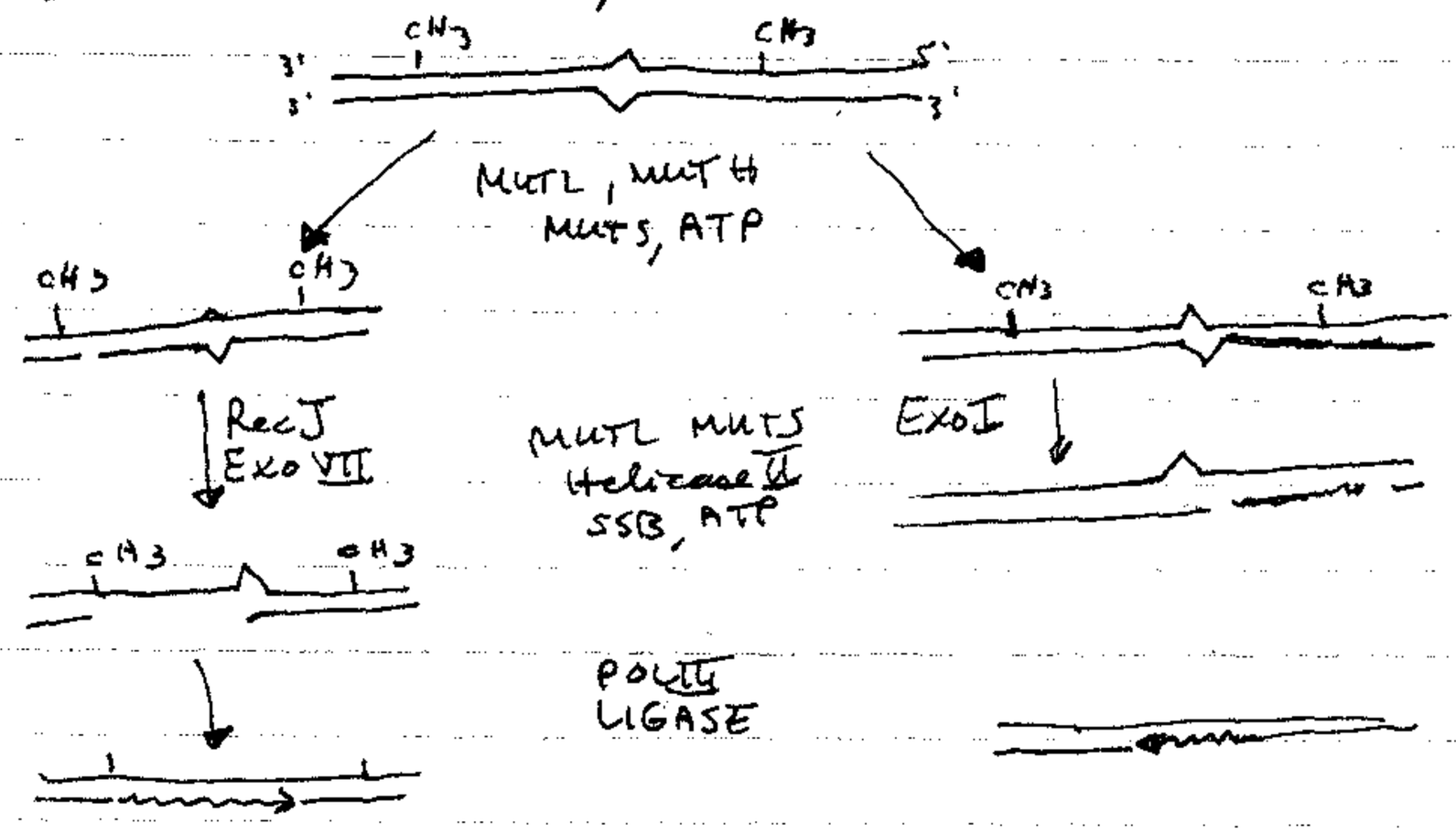
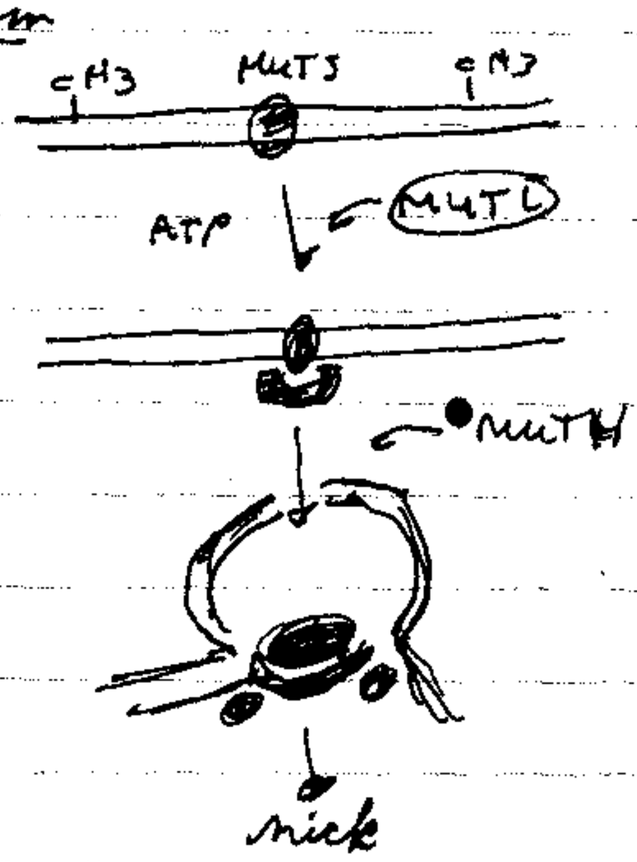
5/18/95

PModrich : Mrs. Match Repair & Genetic Instability

Methyl Directed Mismatch Repair



Mechanism

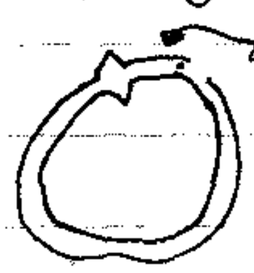


How know which exonuclease to load?

- thinks helicase II travels along DNA to open up
- can monitor SS nature of DNA using KMnO4 which O2 thymine in SS.

HUMAN SYSTEM

⊙ get strand specificity with nicks (using extracts)



⊗ RER+ = replication error prone
- most of these lines are deficient in mismatch repair
- most defects are biochemically recessive
- most are defective in base-base & gaps
- all are blocked prior to incision

2 IN-VITRO Biochemical Complementation Groups

① = MLH1 + PMS2

hMUTSα = ② = hMSH2 + p160 (= same sz as GTBP) ✓
= another MUTS homolog
= binds to mismatches

H6 = MLH1 defect : no mismatch repair

LoVo = ΔMSH2 : no mismatch repair

defectives in p160 { MT1 = ? / can be complemented defect only in base-base mismatch
HCT15 = ? / w/ hMUTSα : " " " " " "

LIKE recJ exo VII

One colon cancer line is selectively defective in mismatch repair ONLY when nick is on one side

HAVE IDENTIFIED TWO CELL LINES THAT ARE RER+
BUT HAVE APPARENTLY NORMAL MISMATCH