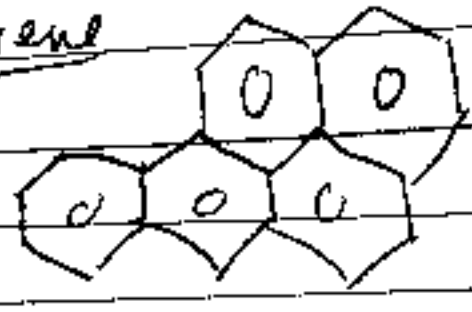
Dave Shikiana

Behavior of Tx at Benzpyrene

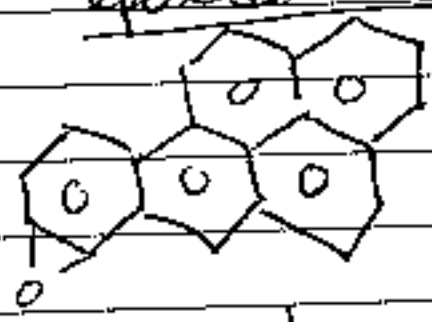
Polycyclic aromatic hydrocarbons

Benzpyrene



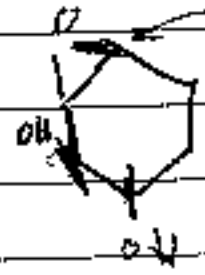
↓ P450

epoxide added



↓ epoxide hydrotase

↓ another epoxide



- reacts w/ bases at this position
- usually N2 guanine
- some N6 adenine

N^2-BPDE-dG into oligo

+ - trans
- - trans
+ - cis
- - cis

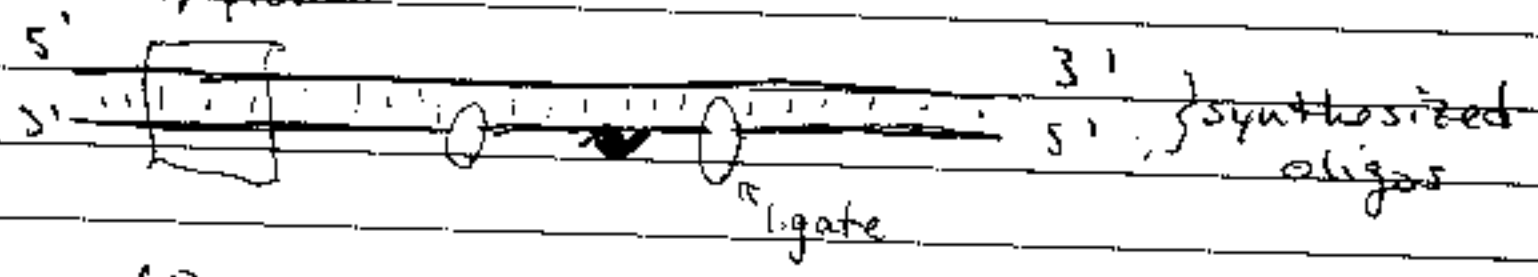
mutagenesis - higher in runs of G's ... point mutations ... usually G → A

*

3' - C C A T C G C T A C C - 5'

+ trans ... G* is correctly base paired
... BPDE points towards 5'
... in minor groove
... most important biologically

I7 RNA polymerase
promoters well defined
readily available



RESULTS

① all 4 enantiomers ... RNA pol. impeded

inhibition ② + trans > - trans > + cis >> - cis

③ most truncation is at damage

④ - cis stops -3 to damage

⑤ no detectible misincorporation of RNA around damage

RNA pol III

RNA

↓

..... polyA

↓ rev tx.

- - - - - -

↓ DNA pol

↓ RFLP

DS cont

CCATCNCTACC

↓

CCATCGCTACCaaa
CCATCCCTACCaaa
CCATCACTACCaaa
CCATCTCTACCaaa

} diff. RFLP

GENE SPECIFIC REPAIR OF ALKYLATION DAMAGE

3-Me-Ad
- seems to impair RNA synthesis
- in DHFR ... no bias in repair of tx strand

Longer chain alkylating agent
- base excision repair not as good
- nucleotide excision repair takes over

glycosylases { 3-Me-Ad I ... v. specifically removes 3-MeAd
3-Me-Ad II ... not as specific

O-6-Me-G ...

ethyl-phospho-triesters
- can cleave w/ v. high [OH]
- can be repaired by E. coli