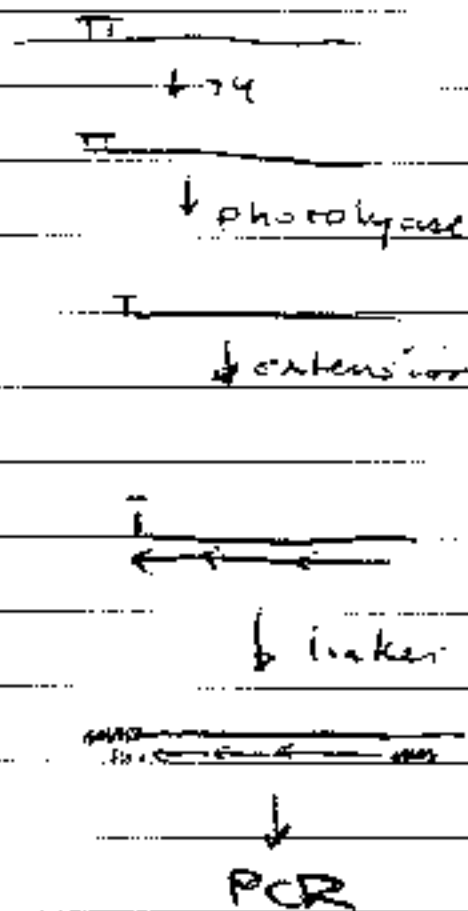


- show lesions in NTS are most of the mutations
- mutations are at evolutionarily conserved regions
- non KP patients show no strand bias

Tornalutti & Pfeifer



P53

w/strand variation in repair rates

TS

TTN → CCN →

CC → TT

CCN → TTN = Pro → Phe
Leu

ACC → ATT = Thr → Ile

TCC → TTT = Ser → Phe

GCC → GGT = Ala → Val

C → T

Dave Crowley - P53 Mutations

Evans et al Cancer Res 53: 5377-81. 1993

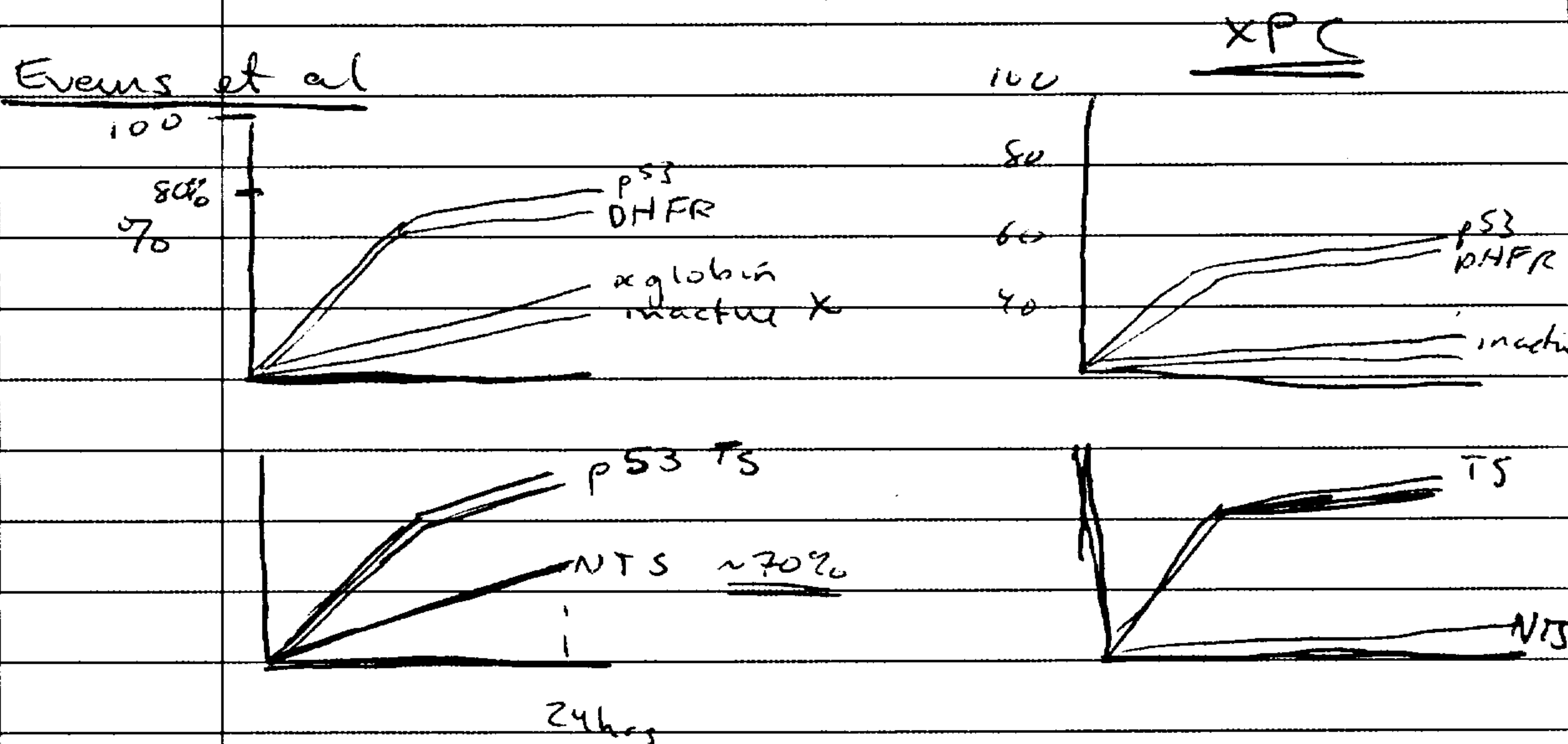
Dumaz et al PNAS 90:10529-533. 1993

Tornaletti + Pfeifer. Science 263:1436-38. 1994

XPA ... no excision repair

XPC ... repair only in active genes

XPU ... no repair deficiency but XP phenotype



→ predict strand bias in mutation

Dumaz et al - Mutation spectrum

- XP tumor cells → extract DNA/RNA → RT-PCR
 ↓ ↑
 SSCP sequence

- 17/43 tumors have point mutations

- all mutations at dipyrimidines 8370 CC
 1790 TT/CT/TC

- why more CC? ... because A rule limits mutations at TT sites?