

Mark Hoffstrader - Ubiquitin - Degradation

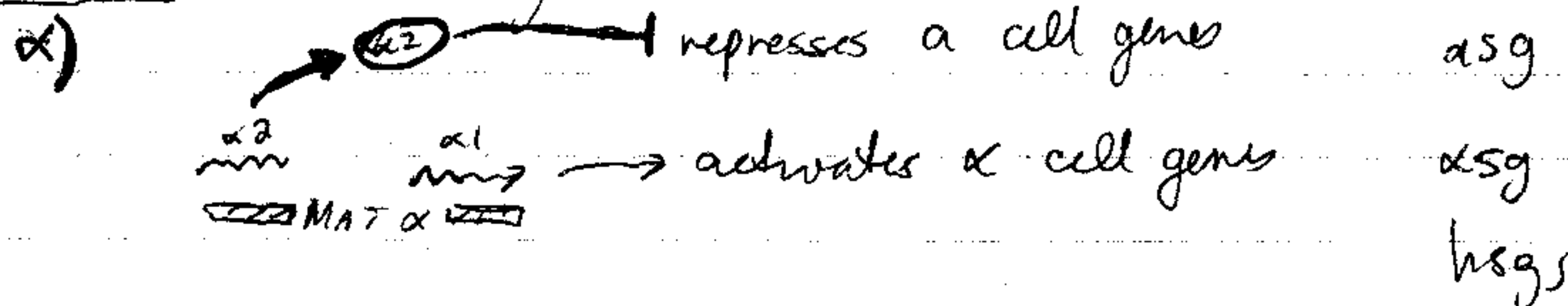
Protein Degradation

- majority is energy-dependent (trypsin is NOT)
- highly regulated (e.g. cyclins in cell cycle)
- highly specific (e.g. cyclin vs. histone)

Functions

- sanitation
- surveillance (e.g., don't want trypsin in cytoplasm)
- regulatory

MAT $\alpha 2$ - model for degradation



a) makes ~~oil~~ protein; expresses asg's
hsgs

α/α $\alpha 2$ represses asgs

$\alpha 1$ $\alpha 2$ represses hsgs (haploid spec. genes)

$\alpha 2$

- half life of ~ 1'
- no accum. of obvious intermediates
- contains degradation signals

ubiquitin
ubiquitin?

ubiquitin?
ubiquitin
ubiquitin

ubiquitin
ubiquitin
ubiquitin
ubiquitin
ubiquitin

Degradation Signals

- C-termini = DEG2
- N-termini = DEG1

Selected cells deficient in degradation of B-gal-DEG1-fusion

- checked degradation of $\alpha 2$ also
- DOA (deg of $\alpha 2$) = ~~no~~

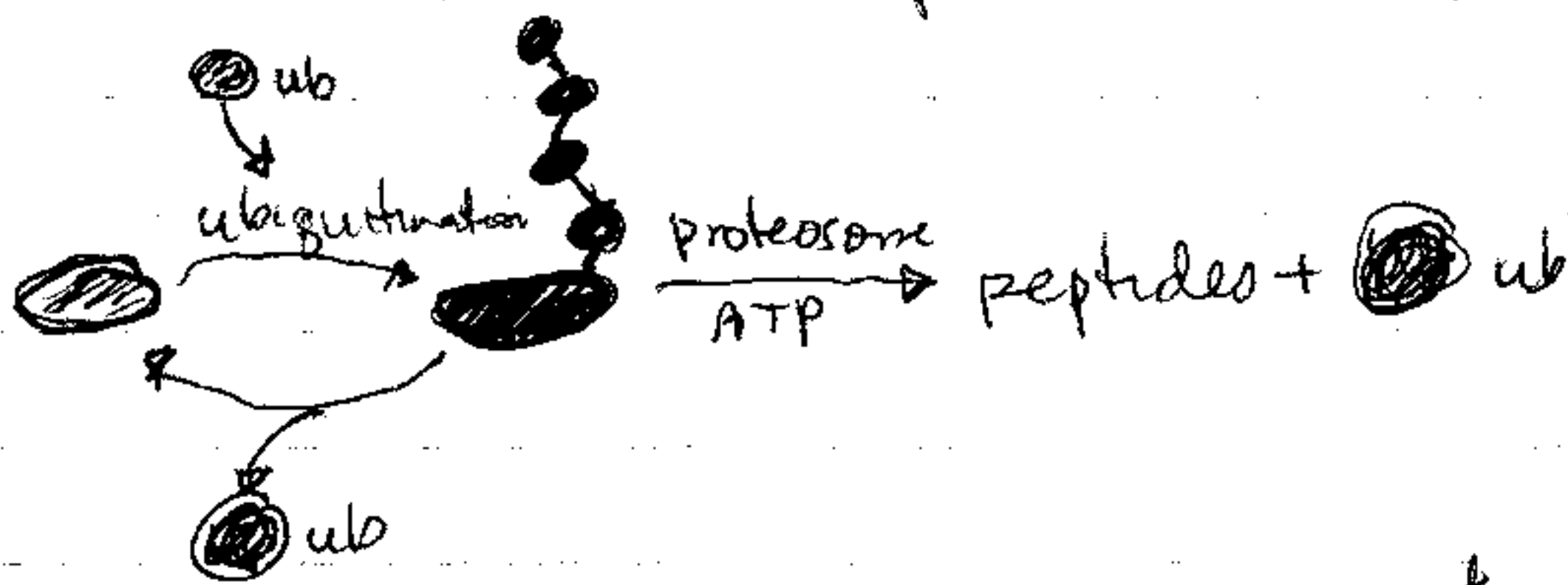
DOA1 =

DOA2 = Ubc6

DOA3 = Prg1/Pre2 = proteasome subunit

DOA4 = deubiquitinating enzyme

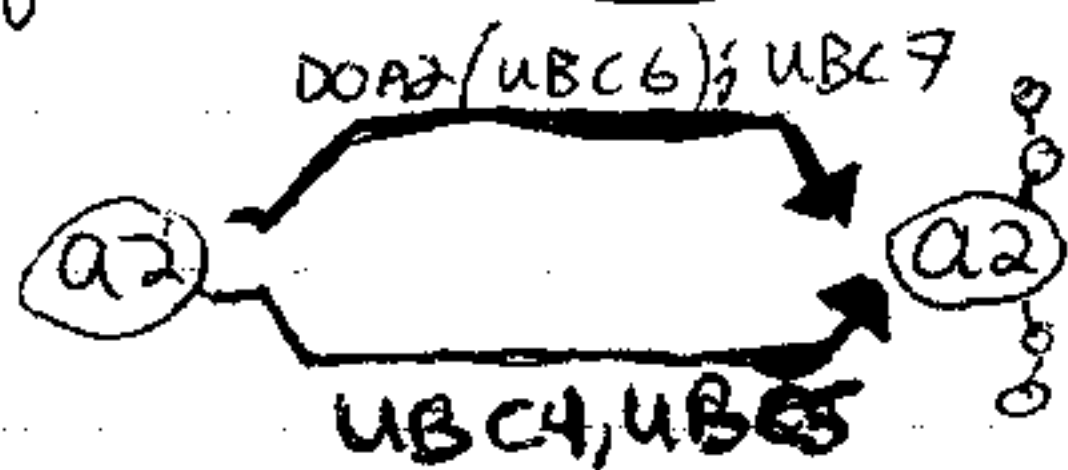
DOA5 = Pup2 = proteasome subunit



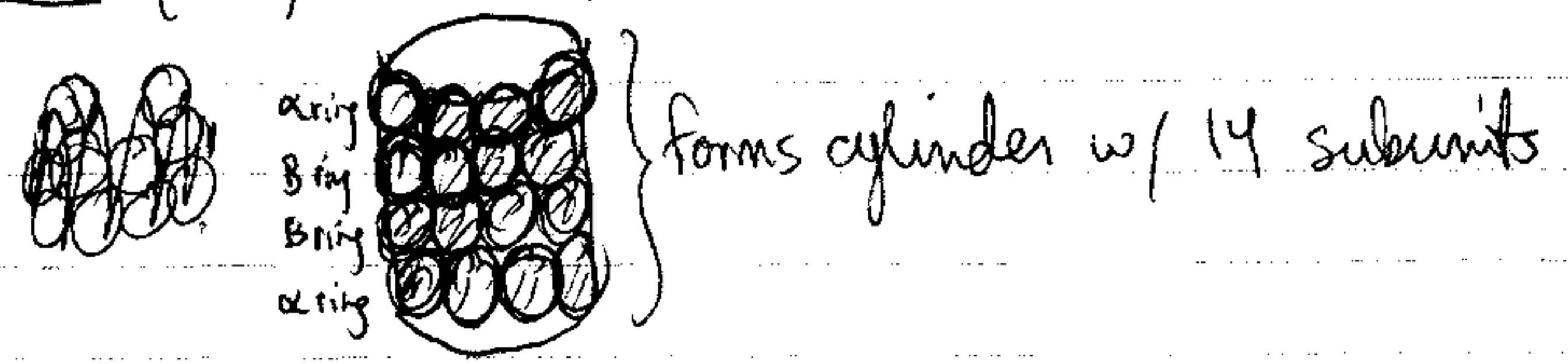
- multiple UBCs
- one proteasome
- o some prot. targeted by diff. UBCs

Ubiquitination of $\alpha 2$

UBC6 & 7 interact

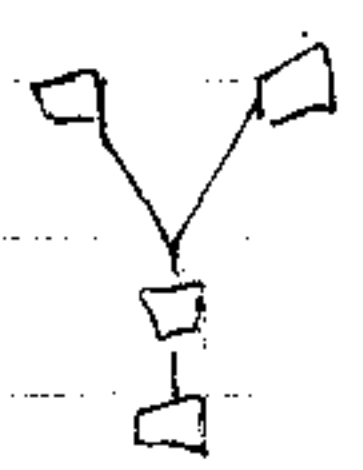


Proteasome (20S) = 700 kDa



DOA3 = processed subunit

Crystal of Proteasom

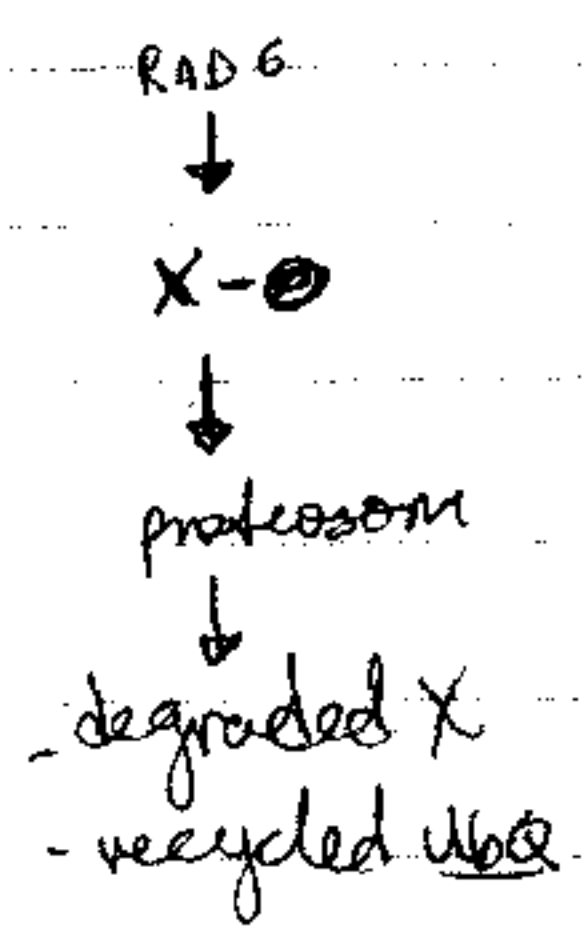


DOA4 = deubiquitination enzyme

~~UBP~~ UV & ray sensitive

- similar to UBPS (1-3) = ubiquitin specific processing protein
- DOA4 has similar motif to these
- in mutants ubiquitin chains attached to small peptides accumulate. maybe involved in recycling ubiquitin

RAD6 = UBE1



UBPs

- UBP1
- UBP2
- UBP3 = overexpression suppresses *ssl1, ssl2* ts phenotype
- ⋮
- UBP16

DOA4 = most sim. to *trc-2* = oncogene
 = also similar to *Unp* = over-expression is tumorigenic
DUB1 = involved in cell cycle arrest (B1)
 gene X =