

LECTURE #4: PROTEIN TURNOVER AND PROTEIN PROCESSING

1. Sensing defective proteins
 - A. Bacteria
 - C-terminal transpeptidation in bacteria (tag machinery: SsrA/tmRNA, SmpB, SspB; degradation machinery: ClpA/ClpP, ClpX/ClpP, HslU/HslV)
 - B. Eukaryotes
 - The N-end rule
 - Regulated removal of proteins
 - Unfolded protein response and ERAD
2. Ubiquitin and other ubiquitin-related proteins: versatile protein tags
 - Ubiquitin
 - SUMO-1/sentrin/Smt3
 - Rub1/Nedd8
 - Apg12 in Autophagy
3. Ubiquitinylation of eukaryotic proteins requires an enzyme cascade
 - E1 (ubiquitin activating enzyme)
 - E2 (ubiquitin conjugating enzymes)
 - E3 (ubiquitin ligases)
 - HECT domain-containing proteins
 - RING domain-containing proteins
 - > SCF (Skp1, Cdc53/cullin-1, F-box protein) complex
 - > Anaphase-promoting complex (APC) or cyclosome
 - > VHL complex (cullin-2/elongin B/C)
 - U box-containing proteins
 - E4 (ubiquitin chain assembly factors)
4. Proteasomes
 - Structure
 - Function
 - Regulation
5. Other irreversible proteolytic modifications of proteins
 - Hormone precursor processing
 - C-terminal maturation and conjugation to membrane anchors
 - GPI (“PIG tails”)
 - Cholesteroylation of Hedgehog family members
 - Spatzle processing by Easter
 - Notch signalling
 - Activation of *Cubitus interruptus*
 - Activation of SRE-BP
6. Intramolecular self-cleavage (intein excision and protein splicing)