Chem 412 Seminar
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Proteasomes: "When Death Comes aKnock'n

Proteins are involved in nearly every facet of a living cell,s normal growth an development, consequently, their levels must be closely maintained for a cell to remain healthy. Many human diseases arise as a result of poorly regulated levels of specific proteins. Both the rate of synthesis and degradation influence the maintenance of correct protein levels. Over the past several decades much has been learned about the control of protein synthesis, however, much less is know about protein degradation, particularly the degradation taking place within cells. The Proteasome/Ubquitin system is believed to be responsible for 80 to 90 % of the protein degradation that takes place within a living cell. It is only in the last decade that the important cellular role that this large macmolelcular system plays has been appreciated. And only more recently that insights into the structure and function of this system has been gained. The Proteasome/Ubiquitin system has been implicated in numerous diseases including neurodegenerative diseases, cystic fibrosis and cancer. The seminar will review what is known about the structure and function of proteasomes and will relate the potential role that proteasome play in some well-known human diseases.

- D. Voges, P. Zwickl, and W. Baumeister, "The 26S Proteasome: A Molecular Machine Designed for Controlled Proteolysis." *Annu. Rev. Biochem.* (1999) **68**: 1015-1068.

- A. Goldberg, S. Elledge and J.W. Harper, "The Cellular Chamber of Doom," *Scientific American* (2001) **284:** 68-73.

- A. Schwartz and A. Ciechanover, "The Ubiquitin-Proteasome Pathway and Pathogenesis of Human Diseases," *Annu. Rev. Med.* (1999) **50**: 57-74.

- Y. Lam *et al.*, "Inhibition of the Ubiquitin-Proteasome System in Alzheimer's Disease." *Proc. Nat. Acad. Sci. USA* (2000) **97**: 9902-9906.

- M. Gentzsh and J. Riordan, "Localization of Sequences within the C-Terminal Domain of the Cystic Fibrosis Transmembrane Conductance Regulator Which Impact Maturation and Stability." *J. Biol. Chem.* (2001) **276**: 1291-1298.