Activating the Molecule of Mass Destruction

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Proteasomes are 700 kDa complexes of 28 protein subunits that are assembled in a barrel-like architecture. They are abundant in the cytosol and nucleus of eukaryotic cells, where they degrade numerous protein substrates in order to perform housekeeping and regulatory functions. The proteolytic active sites are sequestered inside the hollow proteasome structure, thereby protecting inappropriate substrates from degradation. Proteasomes are activated in vivo by activators that bind to the end rings of alpha subunits. The best known of these is the 19S activator, which mediates degradation of polyubiquitylated substrates. Two other activators, 11S and Blm10/PA200, stimulate hydrolysis of small peptide substrates. Structural and biochemical data will be presented on the interaction of an 11S activator with proteasome, and the mechanism of opening the entrance port into the proteasome interior will be discussed. Preliminary studies on the Blm10 activator will also be presented.

Keywords: proteins structure, proteasome, macromolecular structures