

A3 Regulation of proteasome complexes

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Proteasomes play a major role in nonlysosomal proteolysis and also in the processing of proteins for presentation by the MHC class I pathway. In animal cells they exist in several distinct molecular forms which contribute to the different functions. 26S proteasomes contain the core 20S proteasome together with two 19S regulatory complexes. Alternatively, PA28 complexes can bind to the ends of the 20S proteasome to form PA28-proteasome complexes and PA28-proteasome-19S hybrid complexes have also been described. Immunoproteasome subunits occur in 26S proteasomes as well as in PA28-proteasome complexes. There are differences in the subcellular distribution of the different forms of proteasomes. The γ -interferon inducible PA28 subunits are predominantly located in the cytoplasm, while 19S regulatory complexes of 26S proteasomes are present in the nucleus as well as in the cytoplasm. Immunoproteasomes are greatly enriched at the endoplasmic reticulum (ER) where they may facilitate the generation of peptides for transport into the lumen of the ER. Several subunits of proteasomes are phosphorylated including alpha subunits C8 and C9. Treatment with gamma-interferon decreased the level of phosphorylation of proteasomes and we have found that phosphorylation of C8 is essential for the stability of 26S proteasomes.