Faculty of Biology Paper of the Month: April 2014

Awarded to Graduate Student Nurit Livant Levanon

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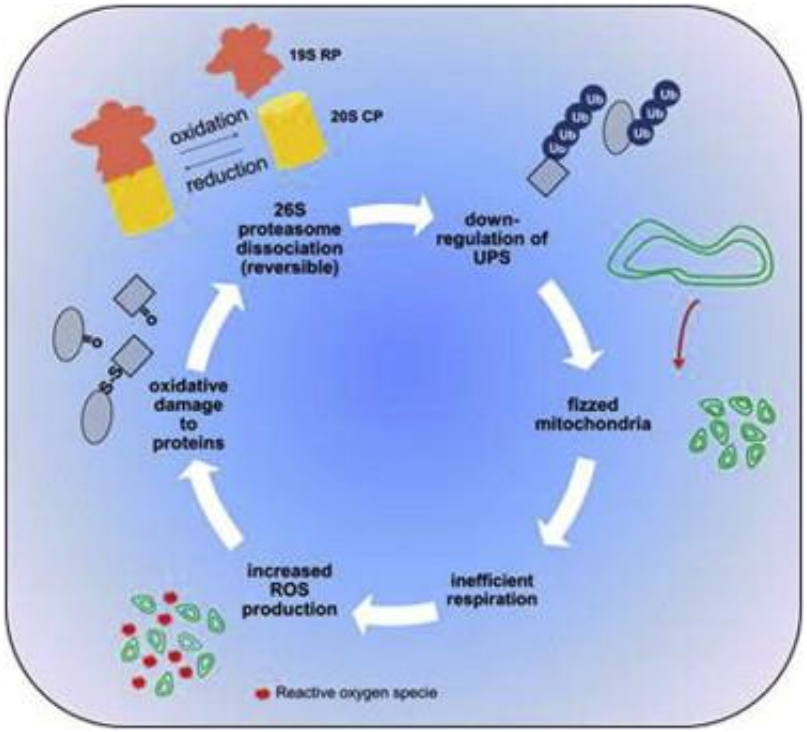

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Reversible 26S Proteasome Disassembly upon Mitochondrial Stress

Nurit Livnat-Levanon,[1] Éva Kevei,[2] Oded Kleifeld,[1,3] Daria Krutauz,[1] Alexandra Segref,[2] Teresa Rinaldi,[4] Zoi Erpapazoglou,[5] Mickael Cohen,[5] Noa Reis,[1] Thorsten Hoppe,[2] and Michael H. Glickman[1,*]
[1]Department of Biology, Technion-Israel Institute of Technology, Haifa 32000, Israel
[2]Institute for Genetics, University of Cologne, Cologne 50674, Germany
[3]Department of Biochemistry and Molecular Biology, Faculty of Health Sciences, Monash University, Melbourne, VIC 3800, Australia
[4]Department of Biology and Biotechnology, University of Rome "La Sapienza," Rome 00185, Italy
[5]Centre National de la Recherche Scientifique, UMR8226, IBPC, and Sorbonne Universités, UPMC, UMR8226, LBMCE, 75005 Paris, France
*Correspondence: glickman@tx.technion.ac.il
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Summary
In eukaryotic cells, proteasomes exist primarily as 26S holoenzymes, the most efficient configuration for ubiquitinated protein degradation. Here, we show that acute oxidative stress caused by environmental insults or mitochondrial defects results in rapid disassembly of 26S proteasomes into intact 20S core and 19S regulatory particles. Consequently, polyubiquitinated substrates accumulate, mitochondrial networks fragment, and cellular reactive oxygen species (ROS) levels increase. Oxidation of cysteine residues is sufficient to induce proteasome disassembly, and spontaneous reassembly from existing components is observed both in vivo and in vitro upon reduction. Ubiquitin-dependent substrate turnover also resumes after treatment with antioxidants. Reversible attenuation of 26S proteasome activity induced by acute mitochondrial or oxidative stress may be a short-term response distinct from adaptation to long-term ROS exposure or changes during aging.