PS10-7: Proteasome storage granules and misassembled proteasome aggregates are distinct proteasome inclusions

Ofri Karmon[1], Lee Peters[1], Galit David-Kadoch[1], Zanlin Yu[2], Rotem Hazan[1], Shay Ben-Aroya[1], Michael H. Glickman[2]
[1]Bar-Ilan University, Israel; [2]Technion-Israel Institute of Technology, Israel

Cellular toxicity introduced by protein misfolding threatens cell fitness and viability. Failure to eliminate these polypeptides is associated with various aggregation diseases. In eukaryotes, the ubiquitin proteasome system (UPS) plays a vital role in protein quality control (PQC), by selectively targeting misfolded proteins for degradation. While the assembly of the proteasome can be naturally impaired by many factors, the regulatory pathways that mediate the sorting and elimination of misassembled proteasomal subunits are poorly understood. We reveal how the dysfunctional proteasome is controlled by the PQC machinery. We found that among the multilayered quality control mechanisms, UPS mediated degradation of its own misassembled subunits is the favored pathway. We also demonstrated that the Hsp42 chaperone mediates an alternative pathway, the accumulation of these subunits in cytoprotective compartments, and also distinguishes them from proteasome storage granules, proteasome aggregates that are formed upon carbon depletion. Thus, we show that proteasome homeostasis is controlled through probing the level of proteasome assembly, and the interplay between UPS mediated degradation or their sorting into distinct cellular compartments.

PS10-8: *SFP1* as an effector of prion-dependent lethality in yeast

Andrew G. Matveenko[1,2,3], Mikhail V. Belousov[1], Stanislav A. Bondarev[1], Polina B. Drozdova[1,3], Yury A. Barbitoff[1], Svetlana E. Moskalenko[1,2], Anton A. Nizhnikov[1,2], Galina A. Zhouravleva[1,3]
[1]Dept. of Genetics and Biotechnology, St Petersburg State University, St Petersburg, Russia; [2]St. Petersburg Branch, Vavilov Institute of General Genetics of the Russian Academy of Sciences, St. Petersburg, Russia; [3]Laboratory of Amyloid Biology, St. Petersburg State University, St. Petersburg, Russia

Studies of translation termination in yeast *Saccharomyces cerevisiae* are intertwined with studies of prions since at least three yeast prions ([*PSI*$^+$], [*ISP*$^+$], and [*NSI*$^+$]) are known to affect translational fidelity. [*PSI*$^+$] and [*ISP*$^+$], the respective prion forms of the release factor Sup35 and transcriptional regulator Sfp1, have antagonistic effects, *i.e.* suppression and antisuppression of nonsense mutations. Previously, we proposed a synthetic lethality test for genes that may influence properties of the translation termination factors Sup35 and Sup45. It is based on the fact that combination of most *sup45* mutations with [*PSI*$^+$] prion in diploids is fatal. During studies of Q/N-rich transcription factors we found that additional expression of *SFP1* gene enhances the synthetic lethality by strengthening the [*PSI*$^+$] phenotype, even though antisuppressor properties have been described previously for Sfp1 overexpression. Elevated expression of *SFP1* influenced both *SUP35* and *SUP45* mRNA levels, but we observed changes only in Sup35 protein level. Still we found that alteration of a putative Sfp1 binding site in the promoter of *SUP45* affects strain phenotype although very slightly. We conclude that, apart from its role in [*ISP*$^+$] formation, Sfp1 might affect nonsense suppression via regulation of transcription of both *SUP35* and *SUP45*. The research was supported by RRC MCT SPbSU. The authors acknowledge Saint-Petersburg State University for research grants 1.37.291.2015, 0.37.696.2013 and Russian Foundation of Basic Research for research grants 13-04-00645 and 14-04-31265.

PS10-9: The importance of *S. cerevisiae* Hsp31p conserved Cys138 residue for the stability and subcellular localization of this protein

Urszula Natkańska[1], Adrianna Skoneczna[2], Marek Skoneczny[1]
[1]Department of Genetics and Laboratory of Mutagenesis and DNA Repair, Warsaw, Poland; [2]Institute of Biochemistry and Biophysics, Polish Academy of Sciences, Warsaw, Poland

S. cerevisiae Hsp31p belongs to the ubiquitous DJ-1/ThiJ/PfpI superfamily of proteins. On the basis of the crystal structures determined for a number of members of this family from various organisms, including Hsp31p and human Parkinson's disease-associated DJ-1, they share many structural features, yet they do not necessarily have similar molecular function(s). One of those features is single cysteine residue residing in a cavity of the molecule and forming, together with nearby histidine and glutamic acid, the so-called catalytic triad, found in many hydrolases and transferases. The Hsp31p catalytic triad most closely resembles those found in cysteine