Oral Contributions

[MS6] Macromolecular Assemblies
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[MS6-01] Structure of The RNA-bound Eukaryotic Exosome Complex.
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RNA degradation serves a multitude of functions in all domains of life. RNA decay modulates the abundance of transcripts and is the ultimate step in quality control pathways that detect and eliminate defective RNAs. The main cellular machinery responsible for degrading RNAs in the 3'-to-5' direction is the RNA exosome complex. The exosome is conserved in all eukaryotes studied to date. Related complexes are also present in bacteria and archaea, highlighting the importance of this ancient molecular machine. The archaeal exosome has a barrel-like architecture formed by 9 polypeptides and containing 3 phosphorolytic RNase activities. RNA substrates reach the active sites by threading through the central channel of the barrel. The eukaryotic exosome contains a minimum of 10 different proteins with a molecular mass of 400 kDa (Exo-10). The 9-subunit core of the eukaryotic exosome (Exo-9) shares a similar architecture with prokaryotic complexes, but is catalytically inert. The RNase activity of Exo- 10 is hydrolytic and provided by the tenth subunit, Rrp44. We show via a combination of biochemical and X-ray structural studies at 2.8Å that RNA substrates reach the exoribonuclease site of yeast Exo-10 by threading through the 9-subunit barrel structure, reminiscent of the prokaryotic complexes [1,2]. Although the catalytic function of the exosome core has been lost during evolution, the substrate recruitment and binding properties have been conserved from prokaryotes to eukaryotes [1,3].

[1] Makino D. L., Baumgärtner M, and Conti E. (2013). Crystal structure of an 11-subunit eukaryotic exosome complex bound to RNA. Nature, 495, 70-75.
[2] Bonneau F., Basquin J., Ebert J., Lorentzen E., and Conti E. (2009). The yeast exosome functions as a macromolecular cage to channel RNA substrates for degradation. Cell, 139, 547-559.
[3] Lorentzen E., Basquin J. and Conti E. (2008). Structural organization of the RNA degrading exosome. Curr. Op. Struct. Biol. 18, 709-713.

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