MBG FOCUS TALK

hosted by Erik Østergaard Jensen


MBG Focus Talks in Molecular Biology

Monday February 26, 2018 at 9:15 - 10:00
Dept. of Mathematics, 1532-116 (Aud G1)

Sebastian Falk, Ph.d.

Max-Planck-Institute for Biochemistry, Martinsried, Germany

Structural and functional insights into the nuclear RNA Exosome

The nuclear exosome mediates the processing and decay of a large variety of transcripts, including rRNAs, sn(o)RNAs, tRNAs and non-coding RNAs such as CUTs and PROMPTs. The exosome is formed by a 10-subunit core complex (Exo-10) that is present in both the nuclear and cytoplasmic compartments and degrades RNAs in a processive manner. Genetic and biochemical data have shown that the exosome core associates with compartment specific cofactors. In the nucleus, Exo-10 associates with the distributive RNase Rrp6 and its interacting partner Rrp47, with the helicase Mtr4 and the small protein Mpp6. Biochemical and structural data have shed many insights on how the core complex and some of the cofactors function. The least understood cofactor is Mpp6. How Mpp6 binds and how it impacts on the activities of the nuclear exosome complex is currently unclear.

Using a combination of x-ray crystallography and biochemistry we show that Mpp6 interacts with both the exosome and the helicase Mtr4. We identified the central domain of Mpp6 as exosome binding site and solved the crystal structure of this complex at 3.2 Å resolution. The structure reveals how the conserved central domain of Mpp6 binds onto conserved surfaces of the cap protein Rrp40. We mapped the Mtr4 binding site to the conserved N-terminus of Mpp6 and using RNase protection assays, we show that Mpp6 is required to effectively channel RNA through the Mtr4 helicase into the exosome core. Thus Mpp6 functions as an adapter protein that facilitates stable integration of Mtr4 into the nuclear exosome complex for effective RNA processing.

More recently, we were able to reconstitute the complex of the 14-meric nuclear exosome together with a bona fide substrate, a maturing large ribosomal subunit (pre-60S). We used cryo-EM to visualize the nuclear exosome complex captured on a pre-60S subunit during 7S-to-5.8S rRNA processing. The structure shows how the nuclear co-factors of the exosome are sandwiched between the exosome core (Exo-10) and the remodeled 'foot' structure of the pre-60S particle, which harbors the 5.8S rRNA precursor.