SFB 960-/BZR – Kolloquium

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H 53

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Structure of the nuclear exosome captured on a maturing pre-ribosome

The RNA exosome is an evolutionary conserved macromolecular machine that degrades a large variety of RNAs from their 3' end. The exosome is formed by 10 core subunits (Exo-10) and is present in both the nucleus and the cytoplasm. Exosome-mediated RNA degradation leads to the elimination of nuclear and cytoplasmic transcripts in turnover and quality control pathways, and to the partial trimming of RNA precursors in nuclear biogenesis pathways. How the exosome combines versatility and specificity to either eliminate or precisely process RNAs is not well understood. One level of regulation is achieved through the interaction with cofactors. In the nucleus Exo-10 associates with four cofactors, which are conserved from yeast to human. These include the heterodimeric ribonuclease Rrp6/Rrp47, the helicase Mtr4 and the adapter protein Mpp6, which facilitates recruitment of Mtr4 into the exosome complex. Biochemical and structural data have shed many insights on how the core complex and some of the cofactors function. However, it is unclear how the helicase Mtr4 works together with the exosome to remodel physiological ribonucleoprotein particles (RNP) and to target them for degradation.

We have now proceeded to study how the nuclear exosome core complex recognizes bona fide RNP substrates. Therefore, we reconstituted the complex of the 14-meric nuclear exosome together with a maturing large ribosomal subunit (pre-60S). We then used cryo-EM to visualize the nuclear exosome complex captured on a pre-60S subunit during the 7S-to-5.8S rRNA processing reaction. The structure shows how the nuclear cofactors of the exosome are sandwiched between the exosome core and the remodeled ‘foot' structure of the pre-60S particle, harboring the 5.8S rRNA precursor. Furthermore, it elucidates the architecture of the nuclear RNA exosome itself, and reveals how the helicase Mtr4 assists in the degradation of structured RNAs.

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