Dr Jekyll and Mr Hyde:
the exosome complex in RNA processing and decay

Elena Conti

Max Planck Institute of Biochemistry, Munich, Germany (conti@biochem.mpg.de)

RNA degradation serves a multitude of functions in all domains of life. In eukaryotic cells, complete degradation of RNAs in constitutive and quality-control decay pathways modulates the abundance of transcripts and eliminates defective RNAs. In addition, partial degradation of precursor transcripts plays an important role in the processing and maturation of structured RNAs. The exosome is a multisubunit complex that degrades RNAs from their 3' end in both decay and processing pathways. How the same machinery can carry out both functions has been a long-standing question in the RNA field.

The eukaryotic exosome contains a core of 10 different proteins with a molecular mass of 400 kDa (Exo-10). Using biochemical and structural studies, we have shown that nine subunits are catalytically inert but form a cylindrical structure that binds RNA substrates and threads them to the only catalytically active subunit in the complex, Rrp44. In vivo data suggest that this core-dependent route to Rrp44 is used by the majority of RNAs, but that a core-independent route to the exoribonuclease also exists and is used by a subset of nuclear RNAs.

While the exosome core is ubiquitous, the auxiliary factors it associates with are specific for the nuclear and cytoplasmic functions of the complex. In the nucleus, Exo-10 associates with different cofactors to form a holo-complex. We have now determined the structure of a 500 kDa yeast exosome complex comprising Exo-10 and two nuclear cofactors: the 3'-5' distributive exoribonuclease Rrp6 and its obligate binding partner and regulator Rrp47 (Exo-12). The structural data allow us to visualize core-dependent and core-independent paths of RNA substrates in Exo-12 and suggest the mechanism with which the exosome switches from processive degradation to trimming during the maturation of 5.8S rRNA.