The RNA exosome complex: the Dr Jekyll and Mr Hyde of RNA degradation

All RNAs in eukaryotic cells are eventually degraded. The RNA exosome is a conserved macromolecular machine that degrades a vast number and variety of RNAs. Exosome-mediated RNA degradation leads to the complete elimination of nuclear and cytoplasmic transcripts in turnover and quality control pathways, and to the partial trimming of RNA precursors in nuclear processing pathways. How the exosome combines specificity and versatility to either eliminate or process RNAs has been a long-standing question.

Over the years, our group has used biochemical and structural approaches to understand how the exosome core complex channels RNA substrates for degradation and how it associates with its nuclear and cytoplasmic cofactors. Visualizing how the exosome cofactors interact with pre-ribosomes in the nucleus and with mature ribosomes in the cytoplasm has provided insights into the mechanisms with which different exosome-ribosome assemblies underpin opposite outcomes of RNA degradation: a constructive function of the nuclear exosome in the maturation of the large ribosomal subunit and a destructive function of the cytoplasmic exosome in the destruction of ribosome-bound mRNAs. Ongoing work is uncovering the unanticipated levels of regulation intrinsic to this multi-purpose degradation machinery.

Host: Patrick Cramer