The exosome – ribosome connection: coupling the RNA degradation and translation machineries

To date, biochemical and structural studies on the macromolecular complexes that synthesize or degrade eukaryotic RNAs and proteins have investigated these machines individually to understand how they execute different steps in the gene expression process. Although the individual complexes catalyze their reactions independently of each other in vitro, increasing evidence suggests that they function in a highly coordinated manner in vivo. The molecular basis for how these macromolecular machines are linked and coordinated is largely unknown. Over the years, we have used biochemical and structural approaches to understand the molecular mechanisms of the RNA exosome, a conserved RNA-degrading machine that mediates the processing and decay of a wide variety of transcripts. The exosome has indeed destructive functions, for example in the degradation of ribosome-bound mRNAs in the cytoplasm, but has also constructive functions in the maturation of structured RNAs in the nucleus. One of the best-studied pathways is the exosome-mediated maturation of the large ribosomal subunit, in particular the processing of the 5.8S rRNA that precedes the export of the pre-60S to the cytoplasm. Using a combination of X-ray crystallography and cryo-EM approaches, we have captured a yeast nuclear exosome holo-complex as it processes a late pre-60S ribosomal particle. Besides providing a snapshot of how the nuclear exosome couples its helicase and ribonuclease activities and how the pre-60S is remodeled before export, the structure shows how these two distinct machineries can work together in a transient fashion as a single structural and functional unit.

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The lecture will be followed by a chalk-board session for PhD students