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Hosted by A/P Adam Yuan

mRNA processing, degradation and quality control in eukaryotes



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Eukaryotic mRNA precursors (pre-mRNAs), produced by Pol II transcription, must undergo extensive maturational processing, including 5'-end capping, splicing and 3'-end cleavage and polyadenylation. Turnover of mature mRNAs is mediated by exoribonucleases that function in the 5'→3' or 3'→5' direction (as well as other enzymes), which are important for the degradation of defective mRNAs as well (mRNA quality control). A nuclear 5'→3' exoribonuclease (XRN) also couples pre-mRNA 3'-end processing and Pol II transcription termination.

The presentation will cover our recent structural and functional studies on the large protein complex that is involved in pre-mRNA 3'-end processing, as well as the XRN. For example, we discovered that the Pol II C-terminal domain (CTD) phosphatase Ssu72 requires the cis configuration of the pSer5-Pro6 peptide bond, the first time that a protein phosphatase has been shown to recognize the cis peptide in its active site.

Unexpectedly, our structure of the protein partner (Rai1) that stimulates the nuclear XRN (also known as Rat1) led to the discovery of a novel quality control mechanism for mRNA 5'-end capping. The effects of this new 5'-end capping surveillance mechanism on mRNA stability, splicing and 3'-end processing in yeast and in mammalian cells will also be described.