Tales of poly(A) tails: Mechanistic insights into the mRNA poly(A) tail machinery

Almost every eukaryotic mRNA has a poly(A) tail which is added by a 1 MDa multi-protein complex called Cleavage and Polyadenylation Factor (CPF/CPSF). There are four different enzymes in CPF (nuclease, polymerase and two protein phosphatases) but it is not understood how these are co-ordinated to define mRNA 3'-ends and regulate transcription. In addition, it is not clear what makes the poly(A) RNA sequence unique. We use a combination of structural biology (cryo-EM, X-ray crystallography, NMR) and biochemical reconstitution to address these questions and to gain mechanistic insight.