**Tata Institute of Fundamental Research**
Survey No. 36/P, Gopanpally Village, Serilingampally, Ranga Reddy Dist., Hyderabad - 500107

# Internal Webinar

## Functional analysis of regulatory mechanisms of UPF1 and its role in the Staufen-mediated mRNA decay pathway

## Manjeera Gowravaram

### Heinrich Heine Universität Düsseldorf

The RNA helicase UPF1 has been implicated in several mRNA degradation pathways, whose catalytic activity was shown to be crucial for remodelling mRNPs to facilitate mRNA decay. In mammals, UPF1 has two isoforms as a result of alternative splicing. Using structural and biochemical assays, I have characterised the longer isoform of UPF1 (UPF11) and compared its catalytic activities with respect to the shorter isoform, UPF12. A structural element (termed as regulatory loop) was identified that adopts different conformations between the two isoforms, and as a result, mediates differential effects on its catalytic activities. These results point towards a mode of regulation of UPF1 that is critical for modulating its enzymatic activity in cell.

UPF1 and the mammalian Staufen proteins (Stau1 and Stau2) mediate degradation of mRNA containing complex secondary structures in their 3'-untranslated region (UTR) through a pathway known as Staufen-mediated decay (SMD). Using biochemical assays, I show the recruitment and activation of UPF1 in the SMD pathway. Additionally, I also demonstrate the involvement of UPF2, a known activator of UPF1 in SMD for the first time. The study elucidates the molecular mechanisms of SMD and points towards extensive cross-talk between UPF1- mediated mRNA decay pathways in cells.

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***2:30 PM***