Tata Institute of Fundamental Research
Survey No. 36/P, Gopanpally Village, Serilingampally, Ranga Reddy Dist., Hyderabad – 500 046

Internal Seminar

Investigating the interplay between metabolism and alternative splicing: intron retention

Srishti Priya

TIFR, Hyderabad

Eukaryotic genomes have accumulated introns over the course of evolution with intron abundance correlating with complexity. Especially, in mammals, introns harboring weak or alternatively spliced splice sites are abundant in terms of number as well as diversity of identities, but their function, significance and splicing regulation largely remain unknown. Intron retention at weak splice sites are both causally and consequentially associated with aging and diseases but also occurs under dietary restriction and aids survival under nutritional stress. Furthermore, homeostatic control of intron retention have been shown to be candidate specific as well as global which have been speculated to be associated with burst expression. In addition to modulating gene expression via nonsense-mediated decay pathway, intron retention can therefore also act as a gating mechanism for gene expression which becomes extremely relevant in physiological oscillatory changes in gene expression dictated by fed-fast cycles and circadian rhythms. While intron retention is phenomenologically linked with aging and dietary restriction, the molecular mechanisms that lead to long-term cumulative loss of splicing fidelity or short-term dynamic physiological changes that affect splicing and intron retention are not explored.

SON, a nuclear speckle protein and a splicing adaptor, is known to increase the splicing efficiency at weak splice sites. Based on acetylome data of knockout mice of SIRT1, an NAD-dependent deacetylase and a “master regulator” of metabolism, we hypothesize that SON activity is regulated by post-translational modifications brought about by SIRT1. We aim to unravel the interplay of splicing and metabolism, both dependent and independent of SON, focusing on intron retention. In this talk I will present my literature survey of the field and pose the open questions.

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10:00 AM

Auditorium, TIFR-H