REGIONAL CENTRE FOR BIOTECHNOLOGY
Seminar series

Tails of EIF1A Promotes Ribosomal Scanning and AUG Selection: Unveiling Tale of Tails

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Translation initiation in bacteria and eukaryotes locates authentic start codon in ribosomal P-site. Against bacterial translation initiation that relies on base pairing between Shine-Delgarno (SD) sequence on mRNA and anti-SD sequence of 16S rRNA, eukaryotes employ "scanning" to recognize the start codon. eIF1A is the eukaryotic ortholog of bacterial initiation factor 1(IF1), but contains an additional helical domain and long unstructured N- and C-terminal tails (NTT and CTT). We discovered scanning enhancer (SE) in the CTT of eIF1A that promotes recruitment of the eIF2·GTP·$tRNA_i^{Met}$ ternary complex (TC), and also suppresses initiation at non-AUG codons. SE deletion is lethal and partial SE mutation produces strong defects in TC recruitment and elevated non-AUG initiation. Remarkably, defects conferred by SE mutant are suppressed by mutations in NTT or helical domain, dubbed as scanning inhibitors (SIs), of eIF1A. Our *in vivo* and *in vitro* results indicate that SE and SI elements regulate start codon selection through opposing effects on TC binding. We envision that SE promotes TC binding to the scanning-conducive "open" conformation of the ribosome in a manner that prevents base-pairing between initiator and P-site triplets, and SI promotes transition to a scanning-arrested "closed" conformation is promoted by perfect codon-anticodon pairing at AUG.