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Structure function analysis of Methionine aminopeptidases and species specific inhibitor discovery

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In nature almost all proteins from bacteria to humans, are synthesized with methionine as the starting amino acid coded by AUG. However, about 60-70 % of all the matured proteins lack this initiator methionine. Between the protein synthesis and the maturation processes, this amino acid is removed by the enzyme, methionine aminopeptidases (MetAP). Any alteration in this process is detrimental to the living cell. Based on this observation, MetAPs are regarded as good drug targets. However, the challenge in design of inhibitors specific against species based enzyme is high structural and sequence similarity in the active site. Surprisingly, only one amino acid (a cysteine) is conserved in the S1 pocket where the substrate methionine side chain binds. Using the structural biology, bioinformatics, molecular biology, biochemistry and proteomics approach, we have determined the role of this single amino acid in the substrate recognition for this class of enzymes. Further, we have developed species specific inhibitors. Results from this multi-tool approach to understand the protein function and design of specific inhibitors will be elaborated in the meeting.

Biography

Anthony Addlagatta obtained his bachelor's degree with specialization in industrial chemistry from Osmania University, Hyderabad, Masters and the Ph.D. degrees in Chemistry from the School of Chemistry, University of Hyderabad. He worked as a Senior Scientist at the Pacific Northwest National Laboratory, USA before joining Indian Institute of Chemical Technology (IICT) in the Centre for Chemical Biology.

His current research focus is on the human health and biotechnology. His technical expertise include bioinformatics, protein engineering, molecular, structural, cellular and computational biology, structure based drug discovery, medicinal chemistry and biotechnology.