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

Internal Webinar

Transthyretin protein: Towards amyloid structure determination

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Transthyretin (TTR) is a transporter protein of thyroxine (T4 thyroid hormone) and retinol binding protein in the bloodstream, cerebrospinal fluid and is also expressed in the retina. Transthyretin is a highly amyloidogenic protein forming amyloid deposits in the heart and brain tissue, as well as in other organs in the severe or advanced cases of the disease. Deposits of wild type TTR (wtTTR) aggregates are seen in the cases of systemic senile amyloidosis, whereas familial amyloidosis polyneuropathy and familial amyloidosis cardiomyopathies show deposition of mutant variants of TTR. Structurally, transthyretin is a β-rich protein that exists as a homotetramer in its native conformation. Transthyretin amyloid has been generated by acid precipitation (pH 4.3) for over 3 decades with very little high resolution structural information. The lack of high resolution structures have been due to both biochemical and methodological limitations. Without the high resolution structure of physiologically relevant fibrils, development of drugs and therapeutic intervention for the treatment of amyloidosis are hindered. Furthermore, a clear understanding of the mechanisms of fibrillation are missing. In my talk, I will talk about the work we have done in the past one year to optimise the expression, purification and fibril forming conditions of TTR so as to obtain good quality fibrils which can subsequently be structurally characterized utilising solid-state NMR.

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11:30 AM