NANYANG TECHNOLOGICAL UNIVERSITY SINGAPORE

School of Biological Sciences
College of Science

Seminar Announcement

Mechanism of beta-chaperone activity of Lipocalin type Prostaglandin D synthase

Date: 11 May 2018

Time: 4 p.m.

Venue: Classroom 1, SBS

Speaker:

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The conformational change in amyloid β peptides from their soluble monomeric forms to insoluble aggregates is believed to be the central pathogenesis associated with Alzheimer's disease (AD). Molecular chaperones are the protein machineries which primarily aid in folding and assembly of newly synthesized polypeptides and the refolding of misfolded or damaged proteins. We investigated one such protein called Lipocalin type Prostaglandin D synthase (L-PGDS), the second most abundant protein in the cerebrospinal fluid, which is found to have chaperone activity for amyloid β peptides with implications in Alzheimer's Disease. Few studies have shown that molecular chaperones exhibit protective role in neurodegenerative disorders by inhibiting the aggregation of aggregation-prone proteins. L-PGDS exhibits its protective role as a chaperone by binding to the monomeric peptide and inhibiting the aggregation of Aβ40 and Aβ (25-35) in Thioflavin T assay. Interaction of L-PGDS with monomeric Aβ40 was monitored by solution NMR, Small Angle X-ray scattering, Transmission Electron Microscopy, ITC, ESR followed by MD-based hybrid structure reconstruction.

The protective role of molecular chaperones also include the ability to disaggregate the larger aggregates. In this context, we used L-PGDS to show the dismantling of preformed fibrils of Aβ40 and Aβ (25-35) through Thioflavin T assay. This process is directly visualized in a number of TEM images. We have used L-PGDS to dissolve protein aggregates collected from the brain tissue of Alzheimer's disease patients. In SDS-PAGE, the aggregates treated with L-PGDS showed more bands compared to the samples treated with Formic acid and Hexafluoroisopropanol thus indicating that the L-PGDS is able to extract out some proteins from the insoluble aggregates more efficiently. Given the protective role of molecular chaperones against pathogenic protein aggregates in neurodegenerative diseases, they are logical targets for drug development to modulate aggregation and clearance of these toxic aggregates. Indeed, pharmaceutical induction of molecular chaperones has been demonstrated to effectively inhibit the formation of pathogenic aggregates in disease models. In this line, we propose L-PGDS as a possible agent for protecting the amyloid β monomers and disaggregation of amyloid aggregates in Alzheimer's disease.