Department of Biological Sciences

JOB TALK (SKYPE)

Speaker: Dr. Neha Jain, PhD
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Date/Time: Thursday, 10th May, 2018 at 04:00 pm
Venue: L-2, LHC

Jumping the Barrier: Interactions Between Human and Bacterial Amyloidogenic Proteins

The hallmark of neurodegenerative disorders such as Parkinson's and Alzheimer's is the presence of highly stable ordered cross-β-sheet aggregates of proteins called 'amyloid'. Recent years have witnessed the emergence of a new class of amyloids designated as 'functional amyloids' where the amyloid fold is not deleterious to the cell, but is instead harnessed to perform diverse functions. Functional amyloids are produced by all cell types from microbes to human beings. A majority of the microbial amyloids play roles in surface adhesion (biofilm formation) and structural integrity and thus provide a fitness advantage. Often, these microbial amyloids play a key role in the progression of human diseases. Although *in vitro* studies have provided information on the structural and sequence determinants that control amyloid formation, not much is known about how these intrinsic properties are influenced by other proteins and factors present in the immediate environment.

My research aims at understanding the molecular basis of the interactions between human and bacterial amyloids. One of the best-studied functional amyloids are curli fibers produced by many Gram-negative bacteria. The major curli subunit, CsgA (**c**urli **s**pecific **g**ene A), is assembled into β-sheet rich amyloid fibres on the cell-surface and contributes to biofilm formation. The first part of my talk will be focused on how bacterial amyloids influence aggregation of human amyloids. Our studies have showed that bacterial curli amyloids can modulate amyloid assembly of human α-synuclein, a protein involved in progression of Parkinson's disease (PD). This study will contribute towards understanding the role of gut microbiota in the onset of PD. In the second part of my talk, I will discuss the role of human amyloidogenic protein, transthyretin, in inhibiting bacterial amyloids and amyloid-dependent biofilm formation. Our findings suggest that transthyretin can potentially act as an ATP-independent chaperone that can be used to enhance treatment or prophylaxis of infections characterized by prominent biofilm formation.

Our work reveals a conformational relationship across the biological kingdom between the classes of proteins that may yield insight into the protein-protein interactions that are responsible for human disorders. In addition, these studies will provide deeper molecular insights into the impact of human microbiome and its association with complexity of pathological mechanisms of amyloid diseases.