REGIONAL CENTRE FOR BIOTECHNOLOGY
Seminar series

Polyglutamine amyloids: aggregation mechanism and cytotoxicity

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Monday, 26th, August, 2013
11:00 AM
Seminar Room

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Abstract

Polyglutamine (polyQ) amyloid formation has been implicated playing an important role in nine neurodegenerative diseases including Huntington's disease (HD). A clear mechanistic understanding of the process of polyglutamine aggregation is essential to better understand their potential roles in disease, and to better devise practical approaches for therapeutics. Our laboratory focuses on understanding the aggregation mechanism of polyQ amyloids and elucidating their cellular activities relevant to Huntington's disease. We find that the size of the critical nucleus for polyQ aggregation is repeat length dependent. Biophysical studies show that beta-hairpin formation may be both a critical step in the nucleation of amyloid formation and a core feature of the resulting fibrils. These studies have also explored a new polyQ aggregation inhibitor based on one of our beta-hairpin frameworks. This work also reveals that seeding and cytotoxicity of polyQ amyloid are both independent of amino acid chirality. The results obtained provide hope for improved understanding of polyglutamine amyloid growth, with implications for discovering new disease mechanism and therapeutics.

In addition to my current research work I will also discuss briefly about my future research plan on "Deciphering protein assemblies for therapeutics and biomaterial app lications".