Columbia | Special Seminar
The Cantor Series in Biophysics: "Double Header"

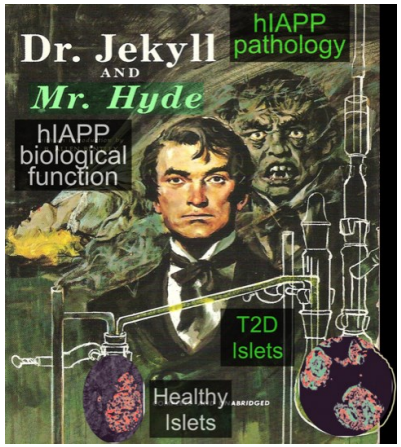
Monday, March 26, 2018 at 1:00pm at The New York Structural Biology Center at 89 Convent Avenue

Protein aggregation investigated by NMR spectroscopy
(at 1:00pm)

Presented by Bernd Reif
Technische Universität München, Department Chemie, Garching, Germany, Helmholtz-Zentrum München, Institut für Strukturbiologie, Neuherberg, Germany

Many (>25) diseases are associated with deposition of insoluble protein aggregates in different kinds of tissue. On the other hand, proteins involved in bacterial biofilm formation and hormone storage, as well as proteins contributing to formation membraneless cellular organelles take over important functions in living organisms.

The talk will focus on the structural charaterization of aggregates formed by the Alzheimer's disease Aβ peptide, the type 2 diabetes peptide hIAPP and aggregates formed by immunoglobulin light chain proteins implicated in AL-amyloidosis. We show how small molecules such as the green tea compound epigallocatechin-gallate (EGCG) and Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) interact with amyloid aggregates. Results on the interaction between misfolding proteins and molecular chaperones such as the small heat shock protein (sHSP) αB-crystallin (aB) are presented. We show that MAS solid-state NMR techniques are applicable for the structural characterization of large soluble protein complexes, in case the tumbling correlation time exceeds the rotor period, using αB crystallin (600 kDa), the 20S proteasome core particle in complex with its 11S activator (1.1 MDa), and 50S ribosomal complexes as examples.



References

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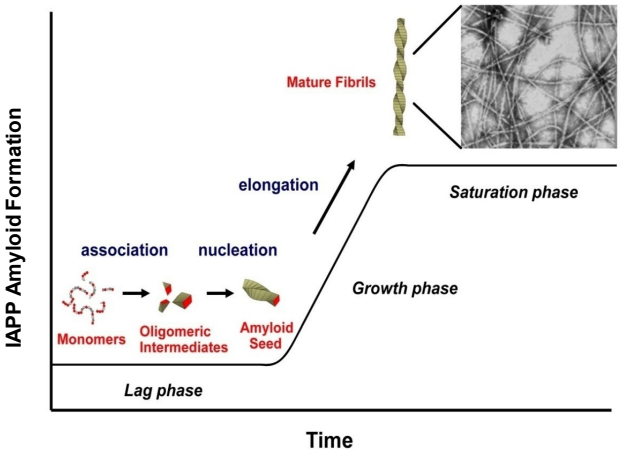
The Molecular Basis of Amyloid Induced Cell Death
(at 2:00pm)

Presented by Daniel Raleigh
The Laufer Center for Quantitative Biology, Stony Brook University, The Institute of Structural and Molecular Biology, University College London

Amyloid formation, the pathological aggregation of normally soluble proteins to form b-sheet rich structure, plays a central role in more than 25 different human pathologies, but the molecular basis of cell death and the detailed mechanism of amyloid formation are still unknown. We focus on islet amyloid formation in type-2 diabetes. The hormone islet amyloid polypeptide plays a role in glucose homeostasis, but aggregates to form islet amyloid in type-2 diabetes. Islet amyloid formation contributes to β-cell dysfunction and death in the disease and to the failure of islet transplants. Concurrent time resolved biophysical measurements and cell viability assays have identified the toxic species formed during islet amyloid formation. Real time multi-dimensional infrared spectroscopy, studies with novel fluorescent probes and more conventional methods have defined the pathway of self-assembly and the nature of the toxic species. The methods developed during our studies of islet amyloid formation are broadly applicable to a wide range of protein deposition disorders. Biochemical studies combined with collaborative studies of intact islets and transgenic mice have defined a new receptor based mechanism of amyloidosis induced cell death.



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