SPECIAL SEMINAR

MONDAY 18/03/19, 12:00 AM

Building 211, room 112

SPEAKER:

Prof. Olga Gursky
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TOPIC:

Amyloid formation by lipid binding proteins: Prediction versus experiment

Apolipoproteins transport lipids in circulation in the form of lipoprotein nanoparticles (aka Good and Bad Cholesterol) that are central to cardiovascular health. Apolipoproteins can transiently dissociate from the lipid surface in a labile free form that can misfold and cause amyloid disease. Misfolding of apoAs, apoCs and serum amyloid A (SAA) causes systemic amyloidoses, while apoE4 is a critical risk factor in Alzheimer's disease and a ubiquitous constituent of amyloid plaques. To explain why apolipoproteins are over-represented in amyloid diseases, we used sequence-based bioinformatics approaches to assess amyloid-forming potential of human apolipoproteins and to identify “hot spots” segments that are likely to initiate β-aggregation. Mapping such segments on the available x-ray crystal or NMR structures of apolipoproteins helped explain why some of them readily form amyloid while others do not. Surprisingly, our analysis shows that the rank order of the amino acid sequence propensity to form amyloid (apoB>apoA-II>apoC-II≥apoA-I, apoC-III, SAA, apoC-I>apoA-IV, apoA-V, apoE) does not correlate with the proteins' involvement in amyloid disease. Rather, it correlates directly with the strength of the protein-lipid association, which increases with increasing protein hydrophobicity. Therefore, the lipid surface-binding function and the amyloid-forming propensity are both rooted in apolipoproteins' hydrophobicity, suggesting that functional constraints make it difficult to completely eliminate pathogenic apolipoprotein misfolding. We propose that apolipoproteins have evolved protective mechanisms against misfolding,

such as the sequestration of the amyloidogenic segments via the native protein-lipid and protein-protein interactions involving amphipathic α-helices and β-sheets.

Hosting: Prof. Shai Rahimipour

For more info: http://www.bumc.bu.edu/phys-biophys/people/faculty/gursky/