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Comprehensive overview of biophysical studies of lipoprotein stability

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Lipoproteins are nanoparticles comprised of proteins and lipids that provide vehicles for transport of fat and cholesterol in circulation. High levels of certain lipoproteins increase the risk of heart disease. Each lipoprotein is a non-covalent assembly of several proteins and several hundred lipids. The major challenge in the biophysical analysis of lipoproteins arises from their heterogeneity in size (7-100 nm), density (1.06-1.22 g/L), and protein and lipid composition. Moreover, lipoproteins are highly dynamic assemblies undergoing continuous remodeling via various enzymatic and non-enzymatic reactions. This provides a major challenge for detailed structural studies of lipoproteins. To overcome this challenge, we designed an integrated biophysical approach by combining far- and near-UV circular dichroism (CD) spectroscopy, turbidity, differential scanning calorimetry (DSC), fluorescence spectroscopy, transmission electron microscopy (EM), size-exclusion chromatography (SEC) and other methods to analyze the structure and remodeling of all major lipoprotein classes. This integrated approach was used to study thermal denaturation of human low- and high-density lipoproteins (LDL and HDL, or bad and good cholesterol). The results clearly showed that lipoprotein stability is controlled by kinetics barriers. Interestingly, heat-induced remodeling of all lipoproteins involves partial protein unfolding/dissociation and lipoprotein fusion and rupture. These structural transitions mimic key aspects of in-vivo lipoprotein remodeling. These and other emerging approaches will allow one to study structural, dynamic and functional properties of larger more challenging systems. Ultimately, such integrated approaches are hoped to bridge the gap between the biophysical studies of isolated macromolecules or their complexes, and the complexity of cellular systems.

Biography

Shobini Jayaraman has completed her PhD from Indian Institute of Technology, Madras, India and Postdoctoral studies from Weizmann Institute of Science, Israel. She was the recipient of Sir Charles Clore fellowship at Weizmann Institute of Science. Currently, she is a Senior Research Scientist at Boston University School of Medicine. She serves as the liaison for academic and industrial contract research services at Boston University. She has published more than 25 papers in reputed journals. Her recent publication in *JBC* has been chosen as paper of the month in May-2014 by International Atherosclerosis Society.

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