Ackert Hall, Room 120
Wednesday, October 29, 2025
4:00 P.M.

Coffee and Cookies
Chalmers Hall, Room 168
3:45 P.M.

Biochemistry & Molecular Biophysics Seminar

The Lipoprotein Structural Landscape: Insights from Humans and Insects

Dr. Zachary Berndsen

Department of Biochemistry
University of Missouri

Lipoproteins are complex macromolecular nanoparticles that transport lipids through the circulatory system. They consist of a phospholipid monolayer containing free cholesterol and apolipoproteins surrounding a hydrophobic core of acylglycerols and esterified cholesterol. Apolipoprotein B100 (apoB) in vertebrates and apolipophorin-II/I (apoLp-II/I) in insects share a common ancestral origin and function as the non-exchangeable structural scaffolds of low-density lipoprotein (LDL) and lipophorin (Lp), respectively. These large amphipathic proteins direct lipoprotein assembly, maintain particle integrity, and mediate receptor interactions.

In vertebrates, apoB-containing lipoproteins are secreted as very-low-density lipoproteins (VLDL) that undergo a one-way catabolism into cholesterol-ester–rich LDL, which are cleared from circulation via receptor-mediated endocytosis. In contrast, insect Lp functions as a reusable lipid shuttle, cycling between lipid-poor high-density (HDLp) and lipid-rich low-density (LDLp) forms through reversible lipid exchange. These processes requires extensive conformational changes to preserve particle stability across wide range of particle sizes and lipid loads.

Here, we present cryo-electron microscopy (cryo-EM) structures of human apoB from LDL, both unbound and in complex with the LDL receptor, as well as structures of insect apoLp-II/I from multiple HDLp and LDLp subtypes. These structures reveal coordinated conformational transitions underlying lipid loading and unloading, receptor engagement, and lipid packaging. Despite substantial evolutionary divergence, key structural and functional features are conserved, highlighting how shared molecular architecture has been adapted to distinct physiological roles across species.