

November 28, 2022 10:00 AM - 12:00 PM

All are invited to attend the defense. For more information please contact Graduate Coordinator at

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**Candidate:** Kianoush Jeiran

**Program:** PhD, Biosciences

**Date:** Monday November 11th, 2022

**Time:** 10:00 AM

**Meeting Location:** <https://gmu.zoom.us/j/92465559801?pwd=Z2cxNnNqSjAxdzV6MlV1WHdFVXFqQT09>

**Title:** Apolipoprotein-B100 Structural Model and Assembly by Computational Modeling, Cross-Linking, and Electron Microscopy

**Committee Chair:** Dr. Ancha Baranova

**Committee Members:** [Dr. Alessandra Luchini](#), [Dr. Fatah Kashanchi](#), [Dr. Alan Remaley](#)

**ABSTRACT:**

Lipoproteins are particles consisting of lipids and amphipathic proteins that carry various components in the bloodstream. ApolipoproteinB-100 (ApoB-100) is a member of large lipid transfer protein superfamily and the largest of all apolipoproteins. Despite developing new modeling algorithms and expanding structural databases, there is no complete structural model for apoB-100 that includes all of its domains and how they interact with each other. Therefore, we have developed a novel method based on the “divide and conquer” algorithm, using PSIPRED software, by breaking apoB-100 into 11 domains. Models of each domain were prepared using I-TASSER, MODELLER, RoseTTAFold, Phyre2, and DEMO. Subsequently, we used disuccinimidyl sulfoxide (DSSO), a mass spec cleavable cross-linker, and disulfide bonds to validate each model by the experimental data. We obtained 65 unique DSSO cross-links, of which 87.5% were within a 26 Å size limit in the final model. We also evaluated the positions of cysteine residues involved in the eight known disulfide bonds in apoB-100, and each pair was measured within the expected 5.6 Å constraint. Finally, multiple domains were merged by applying constraints based on detected long-range DSSO cross-links to generate five subunits and subsequently merged the subunits to achieve an uninterrupted architecture for apoB-100 around the lipid particle. Moreover, the dynamics of apoB-100 during particle size transitions was examined by comparing very low density lipoprotein (VLDL) and low density lipoprotein (LDL) computational models and using experimental cross-linking data.