

**Invitation to M.Tech. Thesis Defense of Shivansh Verma: August 21, 2023 (Monday): 03:30 PM - 04.30 PM IST**

In Partial Fulfillment of the Requirements for the Degree of

**M.Tech. CB**

**Shivansh Verma (MT21230)**

Will defend his thesis

**Title: “Analysis of Gene Expression and Structural Variations in Common Genes Across Populations: Implications for Cardiovascular Disease and Reverse Cholesterol Pathway”**

IIIT-D Faculty and Students are invited

**Date: August 21, 2023 (Monday)
Time:** **03:30 PM - 04.30 PM IST
Online over Google meet (**[**https://meet.google.com/acu-wsnr-mnt**](https://meet.google.com/acu-wsnr-mnt)**)**

**Examiner: Internal:   Tarini Ghosh**

**~~External~~/Internal: Jaspreet Kaur Dhanjal**

**Advisor: Arjun Ray**

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**Abstract**

Cardiovascular disease (CVD) remains a significant global health challenge, influenced by a complex interplay of genetic and environmental factors. Dysregulated lipid metabolism, a key contributor to CVD, disrupts cholesterol balance and triggers atherosclerotic plaque formation. Understanding how genetics affect lipid balance is crucial for innovative treatments.This study focuses on lipid metabolism, vital for heart health, and its genetic influencers.We combine insights from three independent studies, each uncovering genetic links to lipid metabolism. By merging these findings, we aim for a comprehensive understanding of the genetic landscape. \\

Initially, we identify important genes from each study and then connect them across diverse populations. These genes hold the key to understanding the genetic basis of CVD.Our research delves into how genetic variations impact protein-ligand interactions in terms of binding energy related to lipid metabolism, using virtual screening. We use a method called molecular docking with Autodock Vina, assessing binding energies among 54,162 compounds. To understand the significance of binding energy differences, we use a statistical test (Kolmogorov-Smirnov or K-S test), revealing significant variations in binding energies for specific genes. A significance level (p-value) of 0.05 guides our findings.

Our analysis uncovers intriguing insights, highlighting specific genetic variations that cause significant changes in binding energy. These variations can greatly affect crucial protein-ligand interactions, influencing the function of these proteins. For instance, variants like THOC5 V579I, NPC1 R1266Q, NPC1 M642I, NPC1 I858V, NPC1 H215R, ABCA1 V825I, ABCA1 R219K, and ABCA1 K1587R display noticeable differences in binding energies. In contrast, variants like THOC5 V525I, MECR F96L, ENPP2 S493P, and CBR4 L70M show minimal changes, implying less impact on binding energy hence protein-ligand interactions.

Our study advances our understanding of how genetic variations impact dynamic protein-ligand interactions in terms of binding affinity. These variations could affect protein function, influencing lipid metabolism and heart health. Notably, we identify genetic variants associated with significant changes in binding energies, potentially altering protein-ligand interactions linked to lipid metabolism. These findings extend to lipid balance and the Reverse Cholesterol Transport pathway, both essential for heart health.The study's importance lies in its innovative approach to studying how genetic variants impact lipid metabolism at the molecular level. By combining virtual screening and statistical analysis, we identify genetic variations that potentially affect protein binding energies, offering insights into treating lipid-related disorders and CVD.