Thesis Defense - John R. Hamre III, PhD, Bioinformatics and Computational Biology
July 06, 2021 4:30 - 6:00 PM
VIEW EVENT
All are invited to attend the defense. For more information please contact Graduate Coordinator at kharrism@gmu.edu.

Candidate: John R. Hamre III

Program: PhD, Bioinformatics and Computational Biology

Date: Tuesday, July 6, 2021

Time: 4:30 PM

Place: https://gmu.zoom.us/j/98625567331?pwd=QnlmQ0UyOHFNM0t2aUw3UTdlZ05CQT09

Title: THE PROTEIN BACKBONE PHI AND PSI ANGLES DEFINE A UNIVERSAL FEATURE SET FOR MACHINE LEARNING PREDICTION OF THE PHENOTYPIC EFFECTS OF GENETIC VARIANTS
Committee Chair: Dr. M. Saleet Jafri

Committee Members: Dr. Dimitri Klimov, Dr. Amarda Shehu

ABSTRACT:

Mutagenic pathogenesis and acquired drug resistance are leading obstacles in disease management and current therapies. Molecular dynamics simulations are now technically robust enough to elucidate the data whereby these irregularities can be quantified. We have implemented these simulations to develop multiple methods to predict if a specified variant will have a pathogenic effect, cause drug resistance, or be a suitable therapeutic candidate using a multiplexed machine learning approach. Further, we were able to predict the severity of the disease that each variant caused owing to Euclidean distance calculations of the phi and psi angles. These studies have successfully predicted variant pathogenicity with 90% accuracy or greater without the use of overtraining by applying separation of variance and utilizing the specified importance that machine learning affords. In the amyloid beta peptide, the age of onset of the disease was correlated to the Euclidean distance values, and in calmodulin a correlation of the distances to the experimental data for RyR open probability and severe heart arrhythmias was established. In BCL-2, Euclidean distances were correlated to binding pocket structural features and Venetclax drug resistance. Lastly, methyltransferase activity was correlated to peptide structures that occur at the nsp10/nsp16 coronavirus interface and new peptide drug analogs were proposed for future antiviral research.