Thesis Defense Announcement
To: The George Mason University Community

Candidate: Sreehari Girish Kumar
Program: MS in Biology

Date: June 14, 2022

Time: 1:00 PM Eastern Time

Zoom Link: https://gmu.zoom.us/j/92194593829?pwd=akU2WXNVUGNERkdmR0xMVmNVWVppdz09

Title: **A Proteomic Profile of Imidacloprid and its Active Metabolites Desnitro-Imidacloprid and Imidacloprid-Olefin in Human Neural Cells**

Committee Chair: Dr. Nadine Kabbani
Committee Members: Dr. Karl Fryxell, Dr. James L. Olds

All are invited to attend the defense.

ABSTRACT:
Neonicotinoids are a popular class of pesticides around the world and have been shown to bind both insect and mammalian nicotinic acetylcholine receptors (nAChRs). Imidacloprid (IMI), is amongst the most commonly used neonicotinoids in agriculture and domestic applications with strong neurotoxic effects in many organisms. However, the potential for neurotoxicity in its two main metabolites desnitro-imidacloprid (DN-IMI) and imidacloprid-olefin (IMI-olefin), are not yet clear despite evidence that they can bind with high affinity to the mammalian nAChR. In this study, we used Lund Human Mesencephalic (LUHMES) cells, as a human cell line model for dopaminergic neurodegeneration to test the effects of IMI and its metabolites. Cells were treated with 50μM IMI, DN-IMI, and IMI-olefin for 48 hours, and then examined for proteomic changes using liquid-chromatography electrospray ionization mass spectrometry (LC-ESI MS/MS). Bioinformatic analysis using Gene Ontology (GO) and enrichment analysis was performed using Kyoto Encyclopedia of Genes and Genomes (KEGG), Reactome, and WikiPathways databases. Our results provide novel insight into convergent as well as differential molecular modifications by IMI, DN-IMI, and IMI-olefin in neural cells. These studies aim to begin to explore pathways of neonicotinoid neurotoxicity leading to neurodisease in exposed individuals.