Dissertation Defense - Ngoc Bao Vuong, PhD Biosciences

November 11, 2022 2:00 - 4:00 PM

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

Candidate: Gifty Mensah
Program: PhD, Biosciences
Date: Friday November 11th, 2022
Time: 2:00 PM

Meeting Location: IABR Conference Room 1004
Title: Biomarkers for Predicting Cancer in Women with Suspicious Mammograms
Committee Chair: Dr. Alessandra Luchini
Committee Members: Dr. Virginia Espina, Dr. Mariaelena Pierobon, Dr. Barney Bishop, Dr. Lance Liotta

ABSTRACT:

Breast cancer is the second most common cancer in women in the U.S. Mammography screening, despite being the most common method in breast cancer diagnosis, suffers from high false-positive findings. This results in women having a false-positive recall undergoing a pathologic biopsy for a suspicious lesion on mammography, which causes unwarranted stress, anxiety, and increases in health care expenses. In this study, we aim to identify panels of biomarkers from three different biofluids that correlate with a positive follow-up biopsy to increase the specificity and sensitivity of suspicious mammograms. We developed a sensitive mass spectrometry pipeline using nanotechnology to achieve panels of low-abundance protein markers for breast cancer at early-stage development. The proteomic results identified three panels of markers from plasma, serum, and saliva with ROC AUC > 0.8 that distinguish early-stage cancer patients from non-cancer individuals with suspicious mammograms. Most candidate biomarkers found in our work are associated with various molecular functions including cell differentiation, migration and metastasis, calcium metabolism, cell checkpoints, and cell-mediated immunity. Many of the biomarkers are related to breast cancer signaling pathways including JAK-STAT, Akt/Raf, and MAPK4/MAPK6 in various breast cancer subtypes. The potential outcome of the host biomarker panel is a much higher diagnostic specificity and sensitivity in mammography screening in women with suspicious mammograms.

Calcium transport through calcium effluxes/channels is important in regulating breast cancer proliferation at the early stage. The breast duct intraductal lumen is a non-sterile environment and the microbiome in the breast has been shown to include bacteria that enhance the formation of mineral deposits, including calcium salts. To understand the actual functional role of the microbial ecosystem in breast cancer, we characterized the proteome of the microbiome in three biofluid types of patients with breast cancer as compared with non-cancer patients. We identified microbiome that encode enzymes that regulate various types of calcium salts such as calcium phosphate, calcium carbonate and calcium oxalate. Lactobacillus rhamnosus was one of the few species that showed a higher abundance in the case versus control. To functionally validate a relationship between microbiome and breast cancer calcium handling, we developed a 3D co-culture model to evaluate the influence of L. rhamnosus derived-extracellular vesicles (EVs) on calcium deposition in breast cancer cells. Our results showed calcium deposition and mRNA expression of calcium channels acted in a dose-dependent manner in breast cancer spheroids when exposed to different environmental calcium levels and bacterial EVs. We propose that L. rhamnosus-derived EVs influence calcium regulation and mineral deposition in the hypoxic breast cancer milieu. The influence of microbiome on calcium deposition in breast cancer can impact cancer research, potentially leading to the establishment of new markers for early cancer detection and preventive or therapeutic interventions.