Thesis Defense - Chamodya T. Ruhunusiri, MS Biology

Apr 14, 2021, 2:30 - 4:30 PM
VIEW EVENT
All are invited to attend the defense. For more information please contact Graduate Coordinator at kharrism@gmu.edu.

Candidate: Chamodya T. Ruhunusiri
Program: Biology, M.S.

Date: April 14, 2021
Time: 2:00 PM

Place: https://gmu.zoom.us/j/93724511155?pwd=bXdhN0d1N1FSaHBLenNoaDliSkFsdz09

Title: Cell Death Mechanisms and Response to Immune Checkpoint Inhibitors in Lung Cancer

Committee Chair: Dr. Mariaelena Pierobon

Committee Members: Dr. Ancha Baranova, Dr. Ylenia Chiari

ABSTRACT:

Lung cancer is the leading cause of cancer-related deaths worldwide. Developing more effective treatment options for this group of patients remains a main priority in oncology. Immunosurveillance, or the ability of immune cells to identify and eliminate cancerous cells, is a key mechanism for controlling cancer growth and progression. However, cancer cells can escape immunosurveillance through different mechanisms. For example, expression of the programmed death-1 ligand (PD-L1) on tumor cells and its interaction with the programmed death-1 receptor (PD-1) has an inhibitory effect on the activation of T-cells and affects their ability to eliminate malignant cells. Thus, the PD-L1/PD-1 axis has become a therapeutic target in cancer, and monoclonal antibodies targeting PD-L1 and PD-1 have been approved by the FDA as treatment options for lung cancer patients. However, predicting response to this treatment remains a challenge in oncology.

Since programmed cell death mechanisms are highly intertwined with immune activation, we hypothesize that tumor-associated immunogenic (Necroptosis and Pyroptosis) and non-immunogenic (Apoptosis and Autophagy) cell death mechanisms may affect response to agents targeting the PD-L1/PD-1 axis differently. To explore this hypothesis, we have used 57 lung cancer specimens collected from patients treated with a PD-L1 or PD-1 inhibitor. Tumor cells were isolated from the surrounding cells using Laser Capture Microdissection (LCM). To investigate programmed cell death mechanisms associated with response to anti-PD-L1/PD-1 treatment, we used the Reverse Phase Protein Microarray (RPPA) and measured the expression and activation of 37 proteins involved in immunogenic and non-

immunogenic cell death pathways. This work advances our understanding on the molecular events that modulate the expression of immune checkpoints on tumor cells and response to treatments targeting the PD-L1/PD-1 axis.