Dissertation Defense - Jessica Roman, PhD Biosciences

November 21, 2022 1:00 - 3:00 PM

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

dstgerma@gmu.edu

Candidate: Jessica Roman

Program: PhD, Biosciences

Date: Monday November 21st, 2022

Time: 1:00 PM

Meeting Location: https://gmu.zoom.us/j/97113769934?pwd=ZWpNWjIycTJCbnNsclZaYi9NUHkxQT09

Title: New Hybrid Molecular Modalities Comprised of DNA-Origami and Interfering Peptides as Inhibitors of Protein-Protein Interactions in Mammary Cancers: The Development of Multivalent Synthetic Decoy Receptors

Committee Chair: Dr. Lance Liotta

Committee Members: Dr. Amanda Haymond Still, Dr. Remi Veneziano, Dr. Aarthi Narayanan

ABSTRACT:
Immunotherapy has been tremendously successful in treating hematological malignances and melanoma. In breast cancer, however, immunotherapy typically fails. A major factor implicated for this failure is immunosuppressive molecular crosstalk within the mammary tumor microenvironment. These transient protein-protein interactions (PPIs) provide the context of interactions between tumor cells and recruited immune cells, ultimately determining tumor fate. This makes PPIs an important therapeutic target; however, drug discovery over the years has been particularly challenging. The large surface area involved in many PPIs, in conjunction with poorly defined topology of direct contact interfaces, means that it is extremely difficult to develop therapeutics with the specificity required to target single PPIs, while minimizing interference with other PPIs. Using two innovative technologies, DNA Origami and Protein Painting, we developed a novel molecular modality of drugs that are large enough to encompass a specific PPI contact interface, interacts with multiple targets for improved binding capability, and are fully synthesized without use of a biological system. The result is a multivalent, fully synthetic decoy receptor capable of inhibiting select PPIs, based on specific hotspot residue touch points. In this work, we demonstrate a prototype of this modality against the IL-33/ST2 axis, a signaling complex heavily implicated in breast cancer disease progression.