Subject: Dissertation Defense - Dalal Baljoon, PHD Biosciences
Date: Friday, November 8, 2024 at 11:55:09 AM Eastern Standard Time
From: SSB Faculty List on behalf of Diane St. Germain
To: SSB-FACULTY-LIST-L@LISTSERV.GMU.EDU

Dissertation Defense Announcement
To: The George Mason University Community

Candidate: Dalal Baljoon

Program: PhD in Biosciences

Date: Wednesday, November 20, 2024

Time: 11:00 a.m. EST

Location: Conference Room 1004,
Institute for Advanced Biomedical Research (IABR)
10920 George Mason Cir, Manassas, VA 20109

Committee Chair: Dr. Alessandra Luchini

Committee members: Dr. Lance Liotta, Dr. Barney Bishop, Dr. Paul Russo

Title: Proteomic Approaches to Characterize a Novel Biomaterial for *In-Situ* Delivery Of Biologic Drug in Cancer Immunotherapy

Abstract:
Triple-negative breast cancer (TNBC) is a particularly aggressive subtype of breast cancer with limited treatment options and a poor prognosis due to its lack of estrogen, progesterone, and HER2 receptors, which renders it unresponsive to conventional hormone therapies. Although recent advances in immunotherapy have proven effective for certain cancer types, therapy resistance continues to be a major challenge in TNBC.
This study explores the hypothesis that a suture thread can be loaded with immunotherapy drugs and used to stitch the tumor directly, enabling sustained slow release within the tumor tissue, facilitating immune cell recruitment, and exerting potent anti-tumor activity. To enhance the immune response within the tumor microenvironment, we investigated a combination of the immune checkpoint inhibitor anti-PD-L1 monoclonal antibody and the immune cell-recruiting chemokine CXCL9. We assessed the drug release kinetics and confirmed the functional activity of the released drugs using in vitro molecular and cellular assays. The efficacy of this strategy was demonstrated in a syngeneic murine model of TNBC, with mouse tissue analyzed through immunohistochemistry and cytology

techniques. An innovative approach involving the analysis of extracellular vesicles (EVs) in the interstitial fluid fraction of the tissue was used to assess the therapy's impact on the tumor microenvironment. Stitching the mouse mammary tumors with the drug loaded thread induced an increase in immune cell infiltration and tumor necrosis. Analysis of the interstitial fluid EVs provided further evidence that the treatment is effective in inducing stress responses, inhibiting tumor cell survival, proliferation, and progression, and facilitating immune cell recruitment.

The findings presented in this dissertation support the potential of a neoadjuvant therapeutic strategy involving drug-loaded suture threads for tumor treatment. Further molecular, cellular, and preclinical studies are warranted.

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