Subject: Dissertation Defense - Thomas Philipson, PhD Biosciences
Date: Friday, July 11, 2025 at 11:20:12 AM Eastern Daylight Time
From: SSB Faculty List on behalf of Diane St. Germain
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Dissertation Defense Announcement
To: The George Mason University Community

Candidate: Thomas Raymond Philipson

Program: PhD in Biosciences

Date: Wednesday July 23, 2025

Time: 10:00 AM Eastern Time (US and Canada)

Location: In person**,** Life Science Engineering Bldg. #4402, Science & Tech Campus
And via Zoom
Join Zoom Meeting
https://gmu.zoom.us/j/97817346037?pwd=mYsuGcAK8DFIZsyhEKLFqORldDNrJd.1

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Committee Chair: Dr. Lance Liotta

Committee members: Dr. Alessandra Luchini, Dr. Jeffrey Moran, Dr. Virginia Espina

Title: The Pink1/Puma Axis: A Novel Survival Mechanism in Platinum Resistant Ovarian Cancer

Abstract:

Platinum-resistant ovarian cancer (PROC) is a major clinical challenge. Over 80% of patients relapse following first line chemotherapy. Previous studies targeting DNA repair mechanisms

and ABC channel mediated drug export have failed to overcome platinum resistance. Our central hypothesis is that ovarian cancer cells may evade apoptosis through export of key apoptotic proteins via secretory mitophagy (SM), the process of exporting mitochondrial components in the form of extracellular vesicles (EVs). Our experimental evidence suggests SM is a novel pro-survival mechanism of PROC. Herein we investigate the clinical relevance of this hypothesis using in vitro and in vivo clinical ovarian biospecimen proteomic profiling. Reverse phase protein array analysis of ovarian cancer cell lines shows strong correlation between PINK1, the initiator of SM, with key apoptotic regulators including p53, PUMA, cytochrome-c, BAX, and BCL2. EV characterization revealed elevated levels of apoptotic markers in PROC. We extended our investigation into human clinical specimens by collecting ovarian tumor interstitial fluid EVs. Computational modeling of tumor microenvironment fluid dynamics demonstrates dense EV accumulation in ovarian tumors. The patient interstitial fluid EVs have a strong correlation between PINK1 and key apoptotic proteins. This evidence supports our hypothesis that SM is a pro-survival mechanism in ovarian cancer. Tumor interstitial fluid EVs may be a novel diagnostic tool for assessing platinum resistance prior to treatment. These discoveries provide the basis to sensitize ovarian cancer to platinum therapy though blockade of pro-apoptotic protein export.

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