Subject: FW: Z-reg Thesis Gadziala
Date: Thursday, July 18, 2024 at 9:08:07 AM Eastern Daylight Time
From: SSB Faculty List on behalf of Diane St. Germain
To: SSB-FACULTY-LIST-L@LISTSERV.GMU.EDU

Thesis Defense Announcement
To: The George Mason Community

Candidate: Matthew Gadziala
Program: M.S. in Biology
Date: Monday August 5, 2024
Time: 5:00 PM Eastern Time (US and Canada)

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Committee Chair: Dr. Ali Andalibi
Committee Members: Dr. Ancha Baranova, Dr. Lance Liotta

Title: "Mechanisms of Hymecromone (4-Mu)-Induced Suppression of Meningioma Cells"

Abstract:

Neurofibromatosis type 2 (NF2) is a heritable neoplasia syndrome that affects 1 in 25,000 people with a high penetrance of nearly 100% in most people. Currently few effective treatment plans exist that reduce schwannoma growth and slow the onset of subsequent hearing loss and other audiovestibular comorbidities. The NF2 gene is a tumor suppressor gene that encodes for Merlin (moesinezrin-radixin-like protein), which is a vital intracellular protein that relays and coordinates a plethora of signaling pathways concerning extracellular

and intracellular cues. When phosphorylated, this protein is inactive and has been shown to allow proliferation and reduce tumor suppressive functions.

Hymecromone, 4- methylumbelliferone (4-MU), is a possible therapeutic option that targets tumor growth by inhibiting hyaluronan, or hyaluronic acid (HA) synthesis. HA is a vital extracellular and pericellular component that has been implicated to facilitate proper tumor growth and proliferation in most cell types by binding to the receptors cluster differtiation-44 (CD44) and receptor for hyaluronan-mediated motility (RHAMM). 4-MU has been shown to significantly inhibit HA production and ultimately reduce the metastatic potential of the cancer cell. Here, 4-MU is shown to have a dose-dependent modulation of Merlin phosphorylation and hyaluronan synthase 2 (HAS2) levels in the meningioma cell line, IOMM-LEE. Additionally, 4-MU was found to mitigate the cancer cell's overall response to carbonyl cyanide m-chlorophenylhydrazone (CCCP), a potent mitochondrial uncoupler, by reducing P-Akt, PTEN Induced Kinase 1 (PINK1), and HAS2 levels in a dose-dependent manner.

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