James Perry
PhD Candidate

“Chemo and Radioresistance in Brain-Related Tumors”

Thursday, April 3rd
BRT 105
2:00-5:00 PM
VITA

10/19/1984 . . . . . . . . . . . . . . . . . . . . . . . . . . . . . Born – Bristol, CT

May, 2006 . . . . . . . . . . . . . . . . . . . . . . . . . . . . . B.S. Microbiology,
B.S. Cellular and Molecular Biology,
University of Maine

COMMITTEE MEMBERS

Dr. Arnab Chakravarti, MD

Dr. Balveen Kaur, PhD

Dr. Chang-Hyuk Kwon, PhD

Dr. Timothy Cripe, MD, PhD

Dr. Tim Lautenschlaeger, MD

FUTURE PLANS

Post Graduation, my plans involve searching for a post doctoral position or industry job in the greater Boston area. I will likely continue in a translational medicine setting in the field of novel therapeutics. My career plans involve eventually working in an industry position, and trying to place and emphasis on my family.
ABSTRACT

Glioblastoma and brain metastasis from breast cancer are two notoriously aggressive and difficult to treat neoplasms of the brain. Glioblastoma (GBM) is the most common adult brain tumor, affecting nearly 9,000 patients per year. Brain metastasis from breast cancer occurs in approximately 5% of patients overall, and in 10-16% of patients with metastatic disease. Median survival time for Glioblastoma patients is 15 months, while outcomes for breast cancer brain metastasis patients are also poor, with median survivals ranging from 3.4-25.3 months.

In this work, we will introduce Galectin-1 as a novel regulator of the PI3K signaling pathway. Galectin-1 expression alters radioresistance in glioma cell lines, activates PI3K signaling in vitro and in cell culture, interacts with the PI3K enzyme, and prevents pharmacological inhibition of this enzyme. This data demonstrate that Galectin-1 directly modulates PI3K signaling leading to patient relevant outcomes and leads us to believe that Galectin-1 can serve as an alternative activator of the PI3K pathway.

αVβ3 integrins have been identified to play a direct role in tumor cell growth as well as invasion and metastasis. Here, we show that
Galectin-1 may play a role in protecting glioma cells from the effects of cilengitide. Cilengitide induced detachment and apoptosis while reducing proliferation in slightly greater rates in Galectin-1 knockdown cells in an isogenic U87 cell model. This new information posits Galectin-1 as a molecule of interest as a possible predictive marker for cilengitide treatment efficacy.

The ability of cilengitide to enhance the effects of radiation was examined preclinically in breast cancer cell lines. We demonstrated that cilengitide induced cellular detachment, reduced proliferation, and induced apoptosis in our cell line panel. Combined treatment with cilengitide and radiation served to further reduce proliferation compared to either treatment alone, although clonogenic assays did not show formal radiosensitization. Following β3 integrin knockdown, radiosensitization in combination with cilengitide was observed in a previously non-responsive cell line (MDA-MB-231). These data suggest that the combination of radiation therapy and cilengitide may prove to be effective.

RECENT ABSTRACTS AND PRESENTATION

- Perry, J, Chakravarti, A, Lautenschlaeger, T. 2012. Galectin-1 reduces the efficacy of PI3K pathway inhibitors in glioblastoma cells. Poster, AACR 103rd annual meeting, Chicago, IL
- RTOG June 17-20 2010; Philadelphia, PA – Oral Presentation, Brain Tumor Translational Research Program (TRP)