Congratulations to Our Pilot Grant Program Winners!

The Department of Radiation Oncology announced the selection of the 2017 pilot proposal submitted by Dr. Eileen Connolly and Dr. Peter Grabham in a statement issued by Dr. Tom Hei, Professor and Vice-Chair yesterday. The main goal of the pilot grant program is to award innovative project that would generate preliminary data leading to the development of an NIH R01 or similar grant. While there were several great proposals, the review panel recommended the Connolly/Grabham project entitled “The role of Notch in regulating the response of tumor vasculature to high dose radiation” for the one year award. Their proposal is to explore the role the Notch signaling pathway plays within the tumor microenvironment (TME) in relation to increased anti-tumor immune response after stereotactic body radiotherapy (SBRT) is used to administer high dose radiation. Please see below for the full abstract and links to both Dr. Connolly’s and Dr. Grabham’s websites for more on their work.

ABSTRACT: Stereotactic body radiotherapy (SBRT); which allows for selective delivery of high dose radiation (HDRT) to tumors while sparing normal tissue, is increasingly being utilized in the clinic. Despite this, the radiobiological mechanism by which HDRT affects the tumor vasculature and tumor microenvironment (TME) is not fully understood. HDRT has been found to induce endothelial cell (EC) apoptosis, but little is known about its effect on the vascular mural cells/pericytes of tumor vasculature. Pericytes promote stabilization and maturation of the vasculature through interaction with and support of ECs, and the Notch pathway largely facilitates this interaction. HDRT has also been increasingly recognized to have a modulatory affect on the immune response within the TME and there is increased excitement about the possibility of activating anti-tumor immunity with SBRT. Notch signaling is not only important for angiogenesis but is also implicated in immune cell response to vascular inflammation what role this might have on TME response to HDRT is unknown. We therefore hypothesize that Notch signaling in the tumor vasculature regulates the response to HDRT and plays an integral part in vessel repair and TME response. To elucidate the role of Notch signaling in the tumor vasculature’s response to HDRT, we propose in vitro experiments employing human capillary tissue models of vasculogenesis
subjected to HDRT and selective Notch inhibition. From these experiments we will establish the role of Notch in micro-vessels damage and longer-term repair. We also propose in vivo experiments using a Notch reporter mouse to visualize Notch signaling within the TME as well as determine relationship of Notch signaling to vascular response to HDRT in vivo. Data obtained from this proposal will serve as preliminary data for future R01 application to define the role of Notch signaling in the vascular response to HDRT and what role this plays in the global TME response.