Department of Molecular and Cellular Biology

Graduate Seminar MCB*6500

Friday, March 16, 2018 in SSC 1511 @ 12 noon

presented by:

Sydney Pascetta

(Advisor: J. Uniacke)

"Cadherin-22 signaling as a modulator of cellular adhesion and migration in hypoxic breast cancer cells"

Cell-cell adhesion is facilitated by adherens junctions in epithelial and endothelial tissues. These contacts enable cells to collectively proliferate and migrate in processes such as embryonic development, wound healing, and cancer progression. Hypoxia is connected to all these processes, but arises in tumors through oncogene-driven proliferation of cancer cells in the absence of efficient vasculature and is strongly connected to metastasis leading to patient mortality. Many solid tumors display collective invasion in which cells invade cohesively as a multicellular unit, but how this is coordinated in hypoxic cells is largely unexplored. Cadherins are a superfamily of transmembrane proteins that mediate cell-cell adhesion. Our lab has identified cadherin-22 as a hypoxia-induced cell-cell adhesion protein that promotes glioblastoma and breast cancer cell-cell adhesion and invasion. Furthermore, cadherin-22 colocalizes with tumor hypoxia and correlates with low patient survival in glioma and invasive ductal breast carcinoma patient tumor specimens. Here, I propose to investigate the signaling mechanisms utilized by cadherin-22 to develop its potential as a therapeutic target against breast cancer metastasis. I will begin by investigating β-catenin, which has a putative binding site in the cadherin-22 cytoplasmic domain. β-catenin is stabilized by the Wnt signaling pathway where it translocates to the nucleus to promote cell migration. I hypothesize that hypoxic induction of cadherin-22 sequesters active β-catenin to favor cell-cell adhesion. I will test this by generating cadherin-22 mutants, performing protein-protein interactions, performing *in vitro* cell adhesion and migration assays, and measuring β-catenin nuclear activity via immunofluorescences and qRT-PCR.