Department of Molecular and Cellular Biology
Graduate Seminar MCB*7500

Friday, May 27, 2022 @12:45 p.m.

presented by:

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(Advisor: Dr. Shaun Sanders)

“Palmitoylation as a regulator of localization and function of endoplasmic reticulum chaperones in glioblastoma multiforme.”

The Hsp70 GRP78 (HSPA5) and Hsp90 GRP94 (HSP90B1), normally reside in the endoplasmic reticulum. However, with strong induction of the unfolded protein response (UPR), a fraction of them localizes to and anchors at the cell surface. There, they enhance signaling pathways related to cell proliferation and stemness, for example PI3K/AKT and SRC/STAT3. Cell surface expression of GRP78 and GRP94 is particularly prominent in cancers, including glioblastoma multiforme (GBM), a highly aggressive and deadly brain cancer. Conversely, targeting cell surface (cs) GRP78 with antibodies or silencing GRP78 expression attenuates cancer cell proliferation. The mechanisms of ER chaperone trafficking and anchoring at the cell surface are unclear. The addition of long-chain fatty acids to proteins, a process known as palmitoylation, modulates interactions of soluble proteins with lipid membranes. Thus, we hypothesize that palmitoylation of GRP78 and GRP94 anchors them at the cell surface to enhance GBM proliferation. First, using various palmitoylation assays in U-87 GBM cell line I will confirm palmitoylation of both proteins in the presence and absence of ER stress, establish which palmitoyl acyl transferase enzymes (PATs) palmitoylate them, and determine the subcellular localization of palmitoylation. Then, I will investigate how palmitoylation contributes to GRP78 and GRP94 cell surface localization using microscopy and biochemical assays in U-87 cells. Additionally, I will examine if palmitoylation may regulate chaperone functions of GRP78 and GRP94. Finally, by using a cerebral organoid model I will determine if reducing palmitoylation of these chaperones could be a potential therapeutic target for decreasing proliferation of GBM.