Department of Molecular and Cellular Biology

Graduate Seminar MCB*6500

Friday, February 12, 2021 @12 p.m.

presented by:

Marguerite Clarke

(Advisor: Dr. Marc Coppolino)

"Investigating the role of CD63 in the β1 integrin mediated regulation of MT1-MMP"

Breast cancer is an incredibly common strain of cancer that has a 90% survival rate, but if the cancer metastasizes to other parts of the body, the survival rate drops to 20%. Understanding the mechanisms that allow cancer to metastasize is essential in order to find therapeutic targets to prevent it. β1 integrin is commonly studied for its role in cancer cell adhesion and increased invasion. It triggers a cascade that promotes invadopodia formation, degradative enzyme recruitment, and ultimately, invasion. Membrane Type 1-matrix Metalloproteinase (MT1-MMP) is one of these degradative enzymes that is highly destructive and high levels correlate with metastatic cancer. β1 integrin has been established as a key regulator of MT1-MMP and enhances the efficiency of invasion through a fairly well characterized pathway. In contrast to this, the mechanism that targets MT1-MMP for lysosomal degradation remains largely unexplored. I hypothesis that β1 integrin plays a role in the regulation of this process as well, through the tetraspanin protein CD63. CD63 is commonly found in lysosomal membranes, is able to interact with both MT1-MMP and β1 integrin, and its overexpression correlates to decreased levels of MT1-MMP. I will use co-immunoprecipitation, immunocytochemistry, and overexpression and knockdown of CD63, to elucidate the role of CD63 in the regulation and degradation of MT1-MMP. With a greater understanding of how MT1-MMP is regulated, therapeutic targets for metastatic cancer may be established.