BCHM 421/422 – 2022/2023

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Project Title: Tracking bone morphogenetic protein signaling for the manipulation of blood vessel growth

Keywords: bone morphogenetic proteins (BMPs), DNA cloning, angiogenesis, vascular biology, human cell culture

Project Background/Goals: Bone morphogenetic protein (BMP)-9 is a circulating growth factor that regulates blood vessel integrity, growth, and repair[1]. Research in the Ormiston lab examines how loss-of-function mutations in the gene encoding type II BMP receptor (*BMPR2*) can cause BMP9-induced endothelial hyperproliferation in pulmonary arterial hypertension (PAH), a disease of uncontrolled vascular overgrowth in the lungs[2]. Our ultimate goal is to develop BMP9-based therapies that target dysregulated blood vessel growth in diseases like PAH and cancer.

We have recently created a split fluorescence reporter construct[3] to monitor the kinetics of BMP9 signaling in living cells. The 421/422 student will:

- Use this split fluorescence construct to examine the impact of siRNA-mediated *BMPR2* silencing on BMP9 signaling kinetics and angiogenic growth in cultured human endothelial cells.
- Screen known regulators of BMP9 signaling, such as the Nedd4 family of ubiquitin ligases[4], to identify the factors driving altered BMP9 signaling and uncontrolled angiogenesis in the context of *BMPR2* loss.
- Create tagged clones of specific Nedd4 ligases for use in cell-based ubiquitination assays[5].

Experimental Approaches: human endothelial cell culture, fluorescence live cell microscopy, DNA cloning, siRNA silencing, qPCR, immunoblotting

References:

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