Genetics Day Poster Submission

Presenter: Zachary Smith

Category: Graduate Student

Authors: ZACHARY SMITH, McKayla Ford, Christina Davidson, Ching-Hua Shih, Paula Vertino

Title: REGULATION OF TRANSCRIPTION BY HISTONE DEMETHYLASE KDM5B IN BREAST CANCER

Abstract: KDM5B is a histone demethylase that removes the second and third methyl groups from histone H3 lysine 4. In human breast cancers, KDM5B is often overexpressed and high KDM5B expression is correlated with decreased survival. KDM5B's tumor promoting capabilities have motivated the development of KDM5 inhibitors. These inhibitors decrease the growth rate of certain breast cancer cells and sensitize them to treatment with the DNA demethylating agent decitabine. Despite this, treatment with KDM5 inhibitor does not decrease the growth rate of some breast cancer cells. Gaining a better understanding of how KDM5B regulates gene expression could aid determining how to use KDM5 inhibitors in cancer treatment. KDM5B loss or treatment with KDM5 inhibitors increases the width of H3K4me3 domains at promoters in breast cancer cells and treating breast cancer cells with a combination of decitabine and KDM5 inhibitor causes an even larger increase. At certain gene promoters the width of H3K4me3 domains is narrower cancer cells than in normal tissues and there is decreased expression of these genes in the cancer cells. We hypothesize that KDM5B regulates tumorigenesis by narrowing promoter H3K4me3 domains at certain genes to decrease expression. To investigate KDM5B's role in breast cancer I knocked down KDM5B in MCF7 breast cancer cells. I will use KDM5B, H3K4me3, and H3K4me1 CUT&Tag and precision nuclear run-on sequencing (PRO-Seq) in the knockdown cells with and without decitabine treatment to gain new insight into how KDM5B regulates gene expression in breast cancer.