**Presenter**: Zachary Smith

**Authors**: ZACHARY SMITH, McKayla Ford, Christina Davidson, Paula Vertino

**Title: Regulation of Transcription by Histone Demethylase KDM5B in Breast Cancer**

**Abstract**

The H3K4me3 demethylase KDM5B is overexpressed in a wide array of cancers and promotes tumor growth in cancer cell lines and mouse models. This has motivated the development of KDM5 inhibitors as anticancer agents. Treating breast cancer cells with these inhibitors slows their growth and increases their sensitivity to endocrine therapy. H3K4me3, the histone post translational modification that KDM5B removes, is present at the promoters of nearly all actively transcribed genes. Broader H3K4me3 domains at promoters are associated with higher expression and decreased transcriptional pausing. Therefore, one way in which KDM5B may promote tumor growth is through narrowing H3K4me3 domains at the promoters of certain genes. H3K4me3 domains at tumor suppressor promoters are also narrower in tumors than in normal tissues, which may cause a decrease their expression that promotes tumor growth. We hypothesize that overexpression of KDM5B in cancer promotes tumor growth by influencing RNA polymerase pause control to cause dysregulation of gene expression. To test this, KDM5B knockdown MCF7 breast cancer cell lines were created using stably expressed shRNAs targeting KDM5B. Cut and Tag is being used to profile KDM5B and H3K4me3 localization across the genome and Pro-Seq will be used to map transcription elongation in these cell lines. These data will provide greater insight into the protumorigenic role of KDM5B in breast and other cancers.