

DEPARTMENT OF CANCER BIOLOGY  
COLLEGE OF MEDICINE

SUMMER RESEARCH OPPORTUNITIES FOR UNDERGRADUATE WOMEN

APPLICATION DEADLINE: 03/01/2018

**PROJECT TITLE: CRISPR-Cas9 based strategies to selectively alter PRPS isoform expression**

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**Project Description**

This research project will investigate the distinct roles of two isoforms of a key rate-limiting enzyme of nucleotide biosynthesis, phosphoribosyl pyrophosphate synthetase (PRPS). Mutations in PRPS1 are the cause of several inherited disorders, and overexpression of PRPS2 contributes to several cancers. Our lab has found that - as opposed to working separately - strikingly, we observe that both isozymes associate tightly as part of a complex. This led us to hypothesize that alterations in the expression of individual isoforms are responsible for "fine-tuning" the metabolic output of the PRPS enzyme in cells. This proposed WISE study will employ emerging CRISPR-Cas9-based technologies to selectively alter the levels of individual isozymes and determine the consequences on nucleotide production and cell proliferation and survival. Specifically, the student will use several strategies including traditional CRISPR-Cas9-based genome editing, enzyme-dead Cas9-based CRISPRi to suppress expression, and enzyme-dead Cas9-based CRISPRa to stimulate expression of PRPS1/2 isoforms. Initially, we will focus our efforts in MYC-driven lymphoma cell culture models (Burkitt's lymphoma) which we know rely on high levels of PRPS2 to sustain proliferation and survival. Upon completion of the study, we will learn the therapeutic "threshold" of PRPS isoform expression necessary to impede tumor growth and we will test for the first time the effect of PRPS1 modulation on lymphomagenesis.