

Pharmacy Student Summer Research Fellowship Proposal for 2021

FACULTY INFORMATION:

NAME: Nukhet Aykin-Burns, PhD

DEPARTMENT: Pharmaceutical Sciences, Division of Radiation Health

LOCATION: BioMed II – room # 441A-2

PROJECT INFORMATION:

TITLE: Role of IDH2 in mitochondrial metabolism following radiation

LOCATION OF THE PROJECT: BioMed II – rooms # 438-2 and 435-2

BRIEF DESCRIPTION OF THE PROJECT: Radiation induced liver disease (RILD) is the major limitation to use of radiotherapy in hepatocellular carcinomas (HCC). Therefore it is vital to determine mechanisms how ionizing radiation leads to RILD in order to design better HCC therapies with minimal side effects in normal tissues. IDH2 is a mitochondrial NADP⁺-dependent enzyme that supports regeneration of reduced glutathione (GSH) or reduced thioredoxin by providing NADPH to enzymes Glutathione Reductase or Thioredoxin Reductase. We proposed that IDH2 deficiency following radiation exposure exacerbates injury to the normal liver cells and contributes to RILD. With the help of UAMS Genetic Models Core a number of single guide RNAs (sgRNAs) targeted to IDH2 were designed and introduced, along with Cas9, into normal liver epithelial Clone 9 cells. The screening of the cells confirmed the bi-allelic deletion in 8 clones and the loss of IDH2 protein at different levels (40-100% loss) was determined using western blot analysis in these cells. In this project we will characterize the metabolic changes (mitochondrial) in these cells in the absence and presence of radiation exposure.

STUDENT'S RESPONSIBILITIES-DUTIES IN THE PROPOSED PROJECT:

- 1- To measure mitochondrial ETC proteins by Western Blotting in cells
- 2- To measure redox enzyme activities in cells
- 3- To determine mitochondrial metabolism using substrate utilization assays in cells
- 4- To determine mitochondrial bioenergetics in cells

ESTIMATED TIME FOR PROJECT COMPLETION: 10 weeks

DOES THE WORK INVOLVE ANIMAL RESEARCH? NO

ORAL/POSTER PRESENTATION OPPORTUNITY @: Annual National Meeting of Radiation Research Society, UAMS Student Research Day, Redox Biology Meetings

MANUSCRIPT SUBMISSION: Possible journal names for this work to be submitted: Radiation Research, Free Radical Biology and Medicine