SUMMER 2020 - SC INBRE / EPSCOR RET PROJECT DESCRIPTION FORM

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Research Subject Area	DNA repair and cancer/ neurodegeneration

A. Briefly describe overall research program at your laboratory.

Cancer chemotherapy and DNA repair

Although DNA is the essential carrier of genetic information, its chemical structure is surprisingly susceptible to modification, which can cause mutations that can lead to diseases including cancer and neurodegeneration. Fortunately, cells have robust surveillance systems that recognize and remove DNA damage, and thus maintain genomic integrity. There is also an irony about the connection between DNA damage and cancer. DNA damage causes the disease, it is used to treat the disease (many chemotherapeutic drugs and radiation therapy kill cancer cells by damaging DNA), and it is also responsible for the toxicities of the therapies (also kill normally dividing non-cancer cells). My lab has focused on how DNA repair pathways intersect and interact in response to environmental and chemotherapeutic DNA damage.

The specific project focuses how DNA repair influences cell death in cancer cells caused by cancer chemotherapy. DNA repair defects can cause cancer by promoting the genome instability that drives subsequent cellular changes that cause unregulated proliferation, resistance to death, and evasion of immune system detection. However, DNA repair defects also provide a susceptibility (Achilles' heel) to killing caused by chemotherapeutic DNA damaging agents. We explore how specific DNA repair defects in tumors cause sensitivity to specific chemotherapeutic drugs. The long-term goal is to provide the best advice possible on which exact drugs should be used for tumors in each individual.
One of our recent publications in this area was highlighted by the editor of the journal *Environmental and Molecular Mutagenesis*. https://www.emgs-us.org/p/bl/et/blogid=0&blogaid=443&source=6

B. Briefly describe specific project(s) for your teacher

The projects use standard and advanced techniques of molecular biology and mammalian cell culture. The cancer chemotherapy project also brings in elements of pharmacology (drug mechanism of action), while the second project brings an understanding of the biochemical basis of selected vitamin utilization. In brief, the projects will "knock out" and introduce DNA repair genes in cancer cells. The knockouts will be performed using the recently developed "gene editing" technology called CRISPR-Cas9. This will be used to disrupt DNA repair genes in non-cancer and cancer cells. DNA repair genes can also be re-introduced to test specific functions. Cell growth in the absence and presence

of anti-cancer agents will be measured, along with defined markers of DNA damage and repair to follow the time course of repair.

C. Will any other people (post docs, grad students, undergraduate students, colleagues, etc.) be involved directly with your teacher?

I will be heavily involved in all aspects of the project including general lab training. There are two graduate students in my lab who will also help with training in specific techniques as needed by the project goals.

D. Will you require any advanced reading/preparation for the teacher? If yes, please briefly describe.

Yes, there will be some selected background reading of a few chapters from college biochemistry and genetics textbooks, followed by a few primary literature publications, and other internet resources.