Pharmacy Student Summer Research Fellowship Proposal for 2020

FACULTY INFORMATION:

NAME: Peter A. Crooks
DEPARTMENT: Pharmaceutical Sciences, College of Pharmacy

LOCATION: Biomed-2, Room #112-2

PROJECT INFORMATION:

TITLE: ROLE OF A SIGNALING MOLECULE, HYDROGEN SULFIDE, RELEASED BY NOVEL THIADIAZOLIDINONES (TDZD) DERIVATIVES AS ANTI-AGING TREATMENTS

LOCATION OF THE PROJECT: UAMS, Biomed-2, Room #112-2

BRIEF DESCRIPTION OF THE PROJECT:

Hydrogen sulfide (H_2S) is a gasotransmitter acting as an endogenous modulator that plays significant physio-pathological roles in several biological systems. H_2S is mainly derived from two pyridoxal-5-O-phosphate (PLP)-dependent enzymes, cystathionine-b-synthase (CBS) and cystathionine-g-lyase (CSE), or from a third PLP-independent pathway that combines the actions of 3-mercaptopyruvate sulfurtransferase (3-MST) and cysteine aminotransferase (CAT). Inorganic sources of H_2S, such as NaHS, and relatively selective inhibitors of either CBS or CSE have been used for evaluating the physio-pathological involvement of the H_2S pathway in the regulation of several biological functions. In the current research field one of the emerging areas is the development of drugs containing hydrogen sulfide (H_2S) releasing moieties that could be used as therapeutic agents or linked to known drugs to afford novel synergistic codrugs. Recent preclinical studies on neurologic diseases have demonstrated that the administration of H_2S at physiological or pharmacological levels attenuates brain injury. We speculate that release of H_2S, if it involves reaction of an endogenous molecule containing a cysteine residue, may explain how thiadiazolidinone (TDZD) analogs exert their anti-aging activity at the cellular level.

STUDENT'S RESPONSIBILITIES-DUTIES IN THE PROPOSED PROJECT:

Preparation and characterization of novel TDZD conjugates. Characterization of these novel TDZD conjugates will involve NMR, HPLC/MS and IR spectral analysis. Students will then test these conjugates in cellular screening assays as protein aggregation inhibitors.

ESTIMATED TIME FOR PROJECT COMPLETION: 8 to10 weeks

DOES THE WORK INVOLVE ANIMAL RESEARCH? No

ORAL/POSTER PRESENTATION OPPORTUNITY: Yes

MANUSCRIPT SUBMISSION: Possible peer-reviewed journals this work will be submitted to:

Journal of Medicinal Chemistry, European Journal of Medicinal Chemistry, Bio-organic and Medicinal Chemistry.