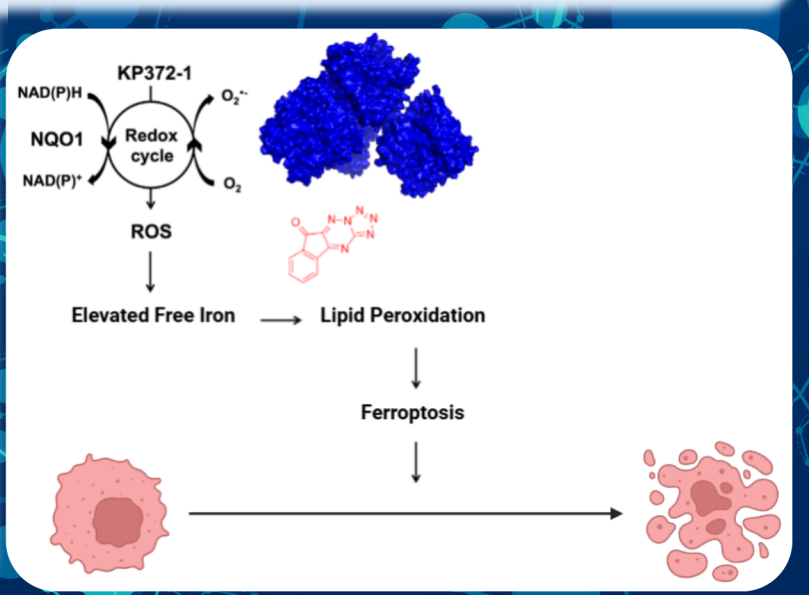
CHEMISTRY DEPARTMENT SEMINAR

Targeting Pancreatic Cancer by Combining NQO1 Vulnerabilities with Iron Imbalance

Samuel Dick

Department of Chemistry, New Mexico Tech

Pancreatic cancer is known for extreme lethality and resistance to therapeutic approaches. The overall goal of this research proposal is to determine the biochemical and biological implication of NAD(P)H Quinone Oxidoreductase 1 (NQO1) hyperactivation and elevated labile iron pool (LIP) on pancreatic cancer, and determine the ramification of enhanced ROS generation and iron imbalance as an approach to overcome resistance. Many pancreatic cell lines show an overexpression of NQO1. NQO1 is a detoxification enzyme that detoxifies quinone substrates to hydroquinone via a two electron reduction, generating reactive oxygen species (ROS). NQO1 can be hyperactivated using redox-cycling substrates leading to an increased level of ROS generation. Iron in cells can react with ROS using Fenton chemistry, leading to lipid peroxidation. Lipid peroxidation is the major trigger for ferroptosis: an iron-dependent non-apoptotic cell death pathway. We hypothesize that iron imbalance with NQO1-hyperactivation enhances pancreatic cancer specific cell death.



February 06th @2 pm – Lopez 106