

James & Esther King Biomedical Research Program

Zheng, Hong

Molecular Oncology

H. Lee Moffitt Cancer Center & Research Institute

2010 Program

Postdoctoral Research Fellowship

(3-year project)

Project Title: Regulation of SirT1 Activity by Extra-cellular pH in Lung Cancer

Project Summary: Tobacco is one of the strongest cancer-causing agents. Tobacco use is associated with a number of different cancers, including lung cancer, chronic lung diseases, and other diseases. According to recent research, tobacco smoke maintains an acidic systemic environment that may facilitate the development of lung cancer. Previous studies have shown that lung cancer cells overexpress SirT1, but its role or mechanism of pathogenesis is unknown. SirT1 is an important regulator of energy metabolism and stress resistance while DBC1 (a gene) has emerged as a novel regulator of SirT1 and a potential signaling mediator in the SirT1 pathway. This study addresses the regulation of SirT1 activity by extra-cellular pH in lung cancer. We plan to characterize the structure of acidosis- (abnormally high acidity) induced DBC1 fragment and to identify how it is generated, testing the significance of DBC1S production on SirT1 activity and tumor cell response to chemotherapy. As a result, we will be able to determine how SirT1 contributes to tumor progression and treatment resistance, and whether SirT1 inhibitor can be used in the treatment of lung cancer.