

James & Esther King Biomedical Research Program

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*Molecular Oncology
H. Lee Moffitt Cancer Center & Research Institute*

*2010 Program
New Investigator Research
(3-year project)*

Project Title: Determine Clinic Pathological Significance of Alteration of NGB and Regulation by AKT2 in Lung Cancer

Project Summary: Lung cancer is the leading cause of cancer-related death in the world. The risk of developing lung cancer is directly related to smoking because patients eventually resist chemotherapeutic drugs and radiotherapy. Therefore, there is a need to understand the molecular mechanism of this resistance. Activation of the AKT (one of the oncogenic protein families that plays an important role in cell signaling for tumor development) pathway by tobacco components increases lung epithelial cell proliferation and survival, and inhibits apoptosis (programmed cell death) in response to DNA damage. Similarly to AKT, mTOR regulates cellular processes critical to tumorigenesis such as cell growth, proliferation, and metabolism, and many cancers are characterized by aberrant activation of mTOR, including lung cancer. Recently, we identified a tumor suppressor protein, NGB, which is associated with AKT and mTOR and is frequently altered in various human tumors including lung cancer. Overexpression of NGB significantly reduced lung cancer cell growth, proliferation, and metastasis. Therefore, compelling evidence may be implicating NGB as a bona fide tumor suppressor. However, this hypothesis has not yet been tested in vivo. We plan to address this question using a novel mouse model with NGB loss of function. This study will provide important insights to the research community to guide potential strategies to inhibit cancer progression.