

Bankhead-Coley Cancer Research Program

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*Drug Discovery Program
H. Lee Moffitt Cancer Center & Research Institute*

*2009 Program
Bridge (1-year project)*

Project Title: Role of Id1 in NSCLC Progression and Metastasis

Project Summary: Non-small cell lung carcinoma (NSCLC) is highly correlated with smoking, and smokers constitute about 75 percent of NSCLC patients. Many tobacco-specific carcinogens present in cigarette smoke cause DNA damage, leading to the mutation of vital genes like Ras, p53, and Rb. In addition, many of these tobacco carcinogens as well as nicotine itself can promote cell proliferation and angiogenesis (growth of new blood vessels) through the nicotinic acetylcholine receptors (nAChRs). NSCLC in smokers and non-smokers are qualitatively different and have different molecular signatures. Given the fact that the primary cells of the lung that give rise to these tumors can proliferate and invade in response to signals transduced through nAChRs as well as EGFR (epidermal growth factor receptor), we hypothesize that there might be common mediators of these signals in smokers and non-smokers. We propose that Id1 protein is a common mediator of proliferation, invasion, and angiogenesis in NSCLC in smokers and non-smokers; further, both nAChRs and EGFR induce Id1 by activating Src and STAT3 proteins. Based on these observations, we plan (1) To assess whether Id1 is a common mediator of NSCLC growth in response to nicotinic receptor and EGFR signaling and (2) To evaluate the role of Id1 in nAChR-induced angiogenesis and metastasis. We believe that these studies will shed new light on the molecular mechanisms underlying the genesis of NSCLC and lead to the discovery of new drugs that combat this disease by targeting Id1.