

## James & Esther King Biomedical Research Program

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*Drug Discovery Program*

*H. Lee Moffitt Cancer Center & Research Institute*

*2008 Program*

*New Investigator (3-year project)*

**Project Title:** Functional Role of Bif-1 in the Regulation of Autophagy and Lung Tumorigenesis

**Project Summary:** Non-small cell lung cancer (NSCLC) accounts for nearly 80 percent of lung cancer cases. The incidence of NSCLC is strongly correlated with smoking and exposure to tobacco products. Although numerous efforts have improved the treatment of NSCLC, the five-year survival rate remains quite low at approximately 15 percent. Thus, identifying better targets for drug development to treat and cure lung cancer patients is urgently required.

Autophagy is a process for the degradation of intracellular components within membrane-enclosed structures. This process prevents cells from accumulating oncogenic stresses, such as unfolded proteins and damaged organelles. Moreover, the induction of autophagy can promote cell death even in apoptosis-impaired cells, suggesting that the activation of autophagy could be a new strategy for the treatment of cancer. Bif-1 is a member of the endophilin protein family that is involved in intracellular membrane dynamics. Loss of this protein inhibits autophagy induction and enhances spontaneous cancer incidence. This highlights Bif-1 not only as a regulator of autophagy, but also as a tumor suppressor. This grant aims to elucidate the molecular mechanism underlying Bif-1-mediated autophagy and to investigate the potential benefit of inducing autophagy as treatment for tobacco-induced lung cancer. The knowledge obtained through this grant may lead to the development of new drugs with the goal of improving the survival of lung cancer patients.