

Bankhead-Coley Cancer Research Program

Liao, Daiqing

*Anatomy and Cell Biology
University of Florida*

*2009 Program
Bridge (1-year project)*

Project Title: Mechanism of Antagonizing Mdm2 and Mdm4 by Adenovirus Type 12 E1B 55-kda Protein

Project Summary: The p53 gene is one of the most frequently mutated genes in cancers. In tumors that do not carry p53 mutations, it is inactivated by oncogenes (genes that contribute to the production of a cancer) called Mdm2 and Mdm4 that are implicated in cancer etiology and progression. The consequence of disabled p53 is transformation of normal cells, leading to malignant tumors. In addition, functional p53 is critical for the beneficial responses of anticancer chemotherapies and radiotherapies. Thus, lack of functional p53 also contributes to therapeutic resistance. Therefore, restoration of functional p53 pathway is a focal point of anticancer drug discovery. We have been studying the interaction between p53 and the E1B 55-kDa protein (E1B) from adenovirus, a harmless virus that is widely used in gene therapy. We found that E1B interacts with Mdm2 and Mdm4 and promotes their degradation. This mechanism is expected to stabilize p53 and increase its anticancer activities. Our objective is to evaluate the effects of E1B in restricting proliferation of breast cancer cells with known genetic status of p53 and on tumor regression using a mouse cancer model. The outcome may guide future clinical applications for treating patients based on precise knowledge of molecular abnormalities of specific patients. Our immediate goal is to establish feasibility of this innovative anticancer strategy to attract long-term federal funding for this project in Florida.