

Project 3

**Talin-1: A Metastasis Suppressor
in Lung Cancer.**

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Sydney Whiteheart, Ph.D. co- Mentor

**No human subjects or human subject materials involved
in this project.**

No Vertebrate animals will be used in this project.

DESCRIPTION: State the application's broad, long-term objectives and specific aims, making reference to the health relatedness of the project. Describe concisely the research design and methods for achieving these goals. Avoid summaries of past accomplishments and the use of the first person. This abstract is meant to serve as a succinct and accurate description of the proposed work when separated from the application. If the application is funded, this description, as is, will become public information. Therefore, do not include proprietary/confidential information. **DO NOT EXCEED THE SPACE PROVIDED.**

Lung cancer is a multifactorial disease caused by a cascade of genetic events, including changes in cell cycle checkpoint and progression, cell proliferation, and chromosome stability, which leads to the development of a primary carcinoma. After establishment of the primary tumor, changes in normal cell adhesion and motility subsequently allow these tumor cells to escape from the original tumor, migrate to secondary sites, and grow anew. The acquisition of this capacity in the primary tumor frequently results in clinically incurable disease, and these secondary tumors, or metastases, are a significant contributor to mortality and morbidity in lung cancer patients. Several genetic lesions on chromosome 9 at position 9p21 have been associated with lung cancer. Among these is the focal adhesion protein **Talin-1**, which is involved in cell adhesion and motility. Talin-1 levels are decreased in certain lung cancer cells.

The **HYPOTHESIS** to be evaluated is that dysregulation of Talin-1 leads to altered cell adhesion leading to anchorage-independent growth of cells in the primary tumor. Acquisition of this phenotype then increases the invasiveness of these cells and results in the development of metastatic lung cancer.

SPECIFIC AIMS. This hypothesis will be addressed by **(1)** determining the molecular basis for the Talin-1 deficiency at the gene, mRNA, and protein levels in lung cancer cells; **(2)** determining the role of Talin-1 in lung cancer cell adhesion, migration, and invasion, with particular emphasis on the behavior of lung cancer cells in three-dimensional culture matrices that mimic the cellular environment *in vivo*; and **(3)** extending these studies to a broad panel of lung cancer cell lines representing each histological class of lung cancer so that previously unknown general features of metastatic lung cancer will be identified.

SIGNIFICANCE. These studies will provide insight into the molecular and cellular mechanisms of lung cancer progression and determine whether Talin-1 is a suppressor of metastasis in lung cancer. These studies will also lead to the development of new prognostic indicators and therapeutic strategies for treatment of metastatic lung cancer.

PERFORMANCE SITE(S) (*organization, city, state*)
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KEY PERSONNEL. See instructions. Use continuation pages as needed to provide the required information in the format shown below. Start with Principal Investigator. List all other key personnel in alphabetical order, last name first.

Name	Organization	Role on Project
McCann, Richard O.	University of Kentucky	Principal Investigator
Foster, Stanley	University of Kentucky	Research Technician
Kelly-Senetar, Melissa	University of Kentucky	PhD Student
Wurth, Mark A.	University of Kentucky	MD-PhD Student

Disclosure Permission Statement. Applicable to SBIR/STTR Only. See instructions. Yes No