

James & Esther King Biomedical Research Program

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*Biology
Torrey Pines Institute for Molecular Studies*

*2011 Program
New Investigator Research
(3-year project)*

Project Title: Inhibitors of ADAM Proteases for Lung Cancer Therapy and Research

Project Summary: The connection between tobacco use and lung cancer is well established. Non-small cell lung cancer (NSCLC) is the leading cause of death from cancer in both men and women in the United States. A family of enzymes (proteases) called ADAM are known to be involved in cancer cell proliferation. We are proposing to discover selective inhibitors of specific members of the ADAM protease family that can be used in lung cancer research and therapy. Most of the ADAM inhibitors developed to date bind the active site zinc, resulting in off-target toxicity. We hypothesize that non-zinc-binding inhibitors that bind a secondary binding site (exosite) will selectively inhibit specific ADAM proteases and will slow or stop the progression of lung cancer. There are currently no publicly available selective inhibitors of ADAM proteases. The overall aim of this project is to develop substrates that will interact with exosites of ADAM proteases thus facilitating the discovery of selective exosite inhibitors of specific members of the ADAM protease family via screening of potential drug candidates. The successful completion of the aims of this grant will have the following impact on long-term goals of the James and Esther King Biomedical Research Program: (1) it will contribute towards a discovery of treatment for lung cancer, and (2) it will expand the knowledge of biomedical and translational researchers working in the field of lung cancer.