

James & Esther King Biomedical Research Program

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*2006 Program
New Investigator (3-year project)*

Project Title: The Mode of Action of the Antitumor Agent Apratoxin A

Project Summary: The long-term objectives of the research include the discovery of potential new drug targets for anticancer therapy and the assessment of the therapeutic potential of the recently discovered antitumor agent, apratoxin A. Currently approved anticancer drugs are directed against only a small number of targets and most of the drugs are derived from natural products. Both facts emphasize the need to discover new targets and justify the exploration of natural products for drug discovery. This project will comprehensively investigate the mechanism of action of the marine natural product apratoxin A, which displays potent cytotoxicity against various cancer cell lines. Apratoxin A may target a key player in cancer cell growth that is distinct from other current targets for anticancer therapy. The identification of apratoxin A's target is a prerequisite for the potential development of apratoxin-based therapeutics and may lead to the discovery and validation of a new therapeutic target. Preliminary data shows that apratoxin A ultimately inhibits the activation of a protein called STAT3 that is critical for cancer cell growth. However, the cause of this desirable effect is unknown and is the subject of the proposed investigation. The impact of apratoxin A on other signaling pathways critical for survival of cancer cells will be assessed using classical approaches, as well as, modern tools of the post-genomic era. Hypotheses derived from genomic and proteomic screens will be tested.