

## Bankhead-Coley Cancer Research Program

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*Translational Research Institute  
The Scripps Research Institute*

*2010 Program  
New Investigator Research  
(3-year project)*

**Project Title:** Inhibition of the Transport of Glutamine, Essential Amino Acids, and Lactate as a Multi-targeted Strategy for Cancer Chemotherapy

**Project Summary:** Cancer drugs often target unique properties of tumor cells. For example, cancers tend to grow rapidly, demand a large blood supply, and spread quickly. Tumor cells need high levels of nutrients to fuel their growth. Cancer researchers have long studied the ways by which tumors meet their high-energy demands, but only recently have they described techniques to find drugs that work by disrupting energy input. Many nutrients enter cells using proteins called transporters. Glutamine, an important amino acid, enters cells by a transporter. Glutamine is also a fuel for other transporters, including one that delivers essential amino acids. Tumors also use transporters to rid themselves of wastes, including lactate, which they must pump out or else they become acidic. We have recently found that a substance that blocks lactate transport halts growth and even kills human lymphoma cells. A wide range of cancer types have very high levels of the transporters for glutamine, essential amino acids, and lactate. We wish to find the first drug that blocks them. We have made experimental substances that disrupt two transporters at once and found that they kill lymphoma cells. Such drugs may be broadly effective, having two modes of action that both target properties shared by tumor cells. Importantly, they may prove useful against tumors resistant to all available drugs, such as lymphomas and breast, brain, colon, skin, lung, and prostate cancers.