

Bankhead-Coley Cancer Research Program

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*Radiation Oncology
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*2008 Program
Bridge (1-year project)*

Project Title: Enhancing Radiation Therapy: Vascular Targeting Agents

Project Summary: Cancer growth and its ability to spread are critically dependent on its supportive blood vessel network. Consequently, there has been a great deal of interest in cancer research in developing new anticancer agents that are designed to specifically damage and destroy the tumor vasculature. For the past 10 years, our laboratory has been involved in evaluating such so-called vascular disrupting agents (VDAs) using a variety of mouse and human tumor cells grown in tissue culture or mice. We have shown that these agents have the ability not only to severely damage tumors when used on their own but also to markedly increase the antitumor effects of chemotherapy or radiation therapy when used in combination with these traditional anticancer treatments. Based on preclinical studies such as our own, several of the lead VDAs have now entered clinical evaluations in cancer patients. Early indications from those trials are very encouraging, but the patient studies have also raised several questions. For example, it has become increasingly clear that further information regarding the optimization of dose scheduling and drug delivery is needed. The goal of our studies is to use human kidney cancer models grown in mice to examine several VDA treatment scheduling and dosing strategies in order to determine how to maximize VDA antitumor activity. Our preliminary findings indicate that such an approach is not only feasible but can be highly effective. These current preclinical investigations are allowing us to develop a rational choice of treatment schedules that will provide guidelines/suggestions for future clinical VDA initiatives in cancer.