

Bankhead-Coley Cancer Research Program

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Bridge (1-year project)*

Project Title: Therapeutic Potential of IL-15 Plasmid Delivery to Tumors Using Electroporation

Project Summary: The long-range goal of this research program is to develop effective and safer gene-based therapies for cancer and other diseases. Metastatic melanoma is a devastating disease due to the lack of an effective treatment. The survival for patients with advanced melanoma is very poor; therefore, it is critical to develop new approaches or enhance existing therapies for melanoma. Current regimens for the treatment of this disease in advanced stages are only modestly effective at best. Systemic infusions of recombinant cytokines have been evaluated in melanoma but can be toxic because of the high doses needed, and in most cases they are not very effective. One way to attenuate the toxicity is to replace the high-dose systemic treatments with local gene therapy for one or more of these molecules either directly into the tumor cells or in close proximity to the tumor. Preclinical data from this group and from other investigators suggests that local delivery with high efficiency of plasmids encoding for cytokines with electroporation can be very effective in terms of causing regressions and complete disappearance of established tumors. The major focus of this study is the use of electrically mediated nonviral gene delivery for immunotherapy of solid tumors using the cytokine IL-15. The objectives to be accomplished during this project are as follows:

1. Establish expression patterns of IL-15 plasmid in both tumor and blood after delivery to three different tissues.
2. Determine expression levels obtained following multiple treatments.
3. Determine the response rate when treating established tumors using the treatment schedule established in the first two objectives.

Successful completion of this project will be an important step toward establishing the potential role of delivering a plasmid encoding for IL-15 delivered by electroporation as a therapy for melanoma. The study is designed to obtain a more complete characterization of this delivery approach and an understanding of how the expression pattern impacts regression. This information will be of critical importance to assess the potential of this approach for the treatment of malignancies.