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2001 Program
Investigator Initiated (2-year project)

Project Title: Preclinical studies on angiogenic therapy for the treatment of vascular disease.

Project Summary: This project sought to construct rAAV expressing constitutive and hypoxia regulated VEGF and analyze angiogenesis and neovascularization in rat ischemic hindlimb and myocardial ischemia models.

Project Successes: Substantial progress was made on all aims as originally proposed. The first preclinical trial ever to use a hypoxia regulated AAV vector for the treatment of peripheral artery disease and myocardial ischemia was undertaken. Research confirmed that new vessels produced using temporary transfer vectors including adenovirus produce only short-term and temporary relief from ischemia, and most of the neo-vessels disintegrate 4-6 weeks after treatment. This suggests that all current procedures used to promote vessel growth in ischemic tissues (including the 25 clinical trials currently ongoing) are flawed and are unlikely to generate sustained improvement in any of the patients. Numerous tissue samples were accumulated requiring histological and immunochemical techniques.

Progress was made such that the research team was ready to initiate clinical trials using this new technology before the final installment of funds from the program was withdrawn. Delays were encountered as staffing to implement the histological analyses of the tissue samples was jeopardized. As the clinical market includes peripheral artery disease (annual cost of approximately \$5 billion) and coronary artery disease (annual cost exceeds \$100 billion), a timely clinical trial of this technology in the state of Florida would have been a major financial as well as a political boost for the state.

Publications from BRP funded research in Peer Reviewed Journals:

Webster KA. Therapeutic angiogenesis: a complex problem requiring a sophisticated approach. *Cardiovasc Toxicol.* 2003;3(3):283-298.

New grants based in part on BRP-funded work:

National Heart, Lung, and Blood Institute

Title: Regulated therapeutic angiogenesis: for ischemic disease

Project Period: 2003 – 2007

Award amount: \$1,500,000