New Jersey State Commission on Cancer Research
LAY ABSTRACT OF RESEARCH PROJECT

NAME OF PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR: **Debabrata Banerjee**

Project Title: **Bone marrow derived MSCs for therapy of liver mets of CRC**

Description: **The project aims to develop therapeutic strategies based on the ability of gene modified bone marrow derived mesenchymal stromal cells to migrate to the tumor/tumor vasculature environment and deliver gene products that may inhibit tumor growth in combination with other therapeutic modalities.**

Metastasis of colorectal cancer (CRC) to the liver continues to be a major cause of death. Approximately 50,000 patients in the US and many more world wide, develop liver metastases (mets) at some point in the course of the disease. Although some of these patients are candidates for surgical removal of the mets, two thirds will recur either in the liver or at other sites after surgery.This grant proposal is a collaborative research project addressing this important health problem. It focuses on developing necessary reagents, methods and tools for novel biologic therapy approaches that take advantage of the observation that bone marrow derived mesenchymal stromal cells (MSCs) can migrate to tumor stroma and the new blood vessels surrounding the tumor mass. This project requires the active participation of the two laboratories to accomplish its goals as they have complementary expertise viz. experimental therapeutics (D.Banerjee) and stromal/endothelial cell biology (J.Glod) The experimental plan outlined in the present proposal has been designed based on preliminary work wherein a liver metastases model of colorectal cancer in nude rats has been generated. Further, targeting of tumor stroma with MSCs labeled with green fluorescent protein (GFP, this allows one to follow these cells once they are injected into the animal using fluorescence imaging) has been shown. Biologic peptides that target a transcription factor (E2F-1) often elevated in metastatic colon cancer have been generated and shown to be cytotoxic to colon carcinoma cells in culture. The hypothesis to be tested in this proposal is that gene marked marrow stromal cells can migrate to tumor stromal environment and hence can be used to deliver cytotoxic biologic therapy to the immediate tumor microenvironment. The study aims to develop a novel therapeutic strategy that is likely to increase our success in delivering cytotxic therapy to the tumor microenvironment. With the easy avalilability of bone marrow derived mesenchymal stromal cells from individuals, the relative ease of gene modification of these cells with cytotxic biologics in culture and reinjection of these cells to cancer patients the knowledge gained from the proposed studies will have immediate therapeutic impact on tumor therapy. The same principle can be applied to the treatment of other solid tumor types. Moreover, this therapeutic modality can be easily added on to standard chemotherapy. **According to statistics available from the American Cancer Society and the NJ Department of Health and Senior services New Jersey ranks 1st in the incidence of male Colorectal Cancer and ranks 4th in the incidence of female Colorectal Cancer. Thus, the results of the proposed project will likely have significant impact on the health of New Jersey residents.**