Bankhead-Coley Cancer Research Program

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2006 Program
Bridge - New Investigator
(2-year project)

Project Title: Mechanisms of MMP-Induced Malignancy in Breast Cells

Project Summary: The structure and form of the body is defined by dense networks of proteins known as the extracellular matrix. At early stages of cancer development, the growth of tumors is constrained by the extracellular matrix. Cancers become much more dangerous when they begin to synthesize matrix metalloproteinases (MMPs), specialized enzymes that break down the extracellular matrix, as this allows the tumors to metastasize, spreading throughout the body. Because of this critical role of MMPs in cancer progression, considerable research effort has been invested to identify inhibitors of MMPs that could be used as anticancer therapeutics. However, MMPs also function in many normal physiological processes, including wound healing and development of new blood vessels, and the MMP inhibitors that were tested for anticancer activity were more detrimental than positive. What is needed is a better understanding of the tumor-specific activities of MMPs so that more effective therapeutics can be designed. This research team has recently identified specific pathways induced by MMPs in tumors that stimulate invasion and metastasis. In this grant, specific experiments are designed to elucidate these pathways so as to reveal potential points of therapeutic intervention. The team has already learned that induction of tumorigenic behaviors by MMPs requires the production of reactive oxygen species, highly activated molecules that damage tissues and compromise the structure of the extracellular matrix. These reactive oxygen species have already been extensively studied for their role in aging; the team's studies provide a new insight into their role in tumor development as well. In this grant, experiments are designed to identify how MMPs act upon cells to induce the production of reactive oxygen species and also to determine how the reactive oxygen species stimulate aggressive cellular behaviors. The research team believes that identifying the points of convergence between MMPs and reactive oxygen species will lead to novel and much more effective therapies that target metastasis, the most dangerous aspect of tumor behavior.