TITLE:

Combined targeting of Src and Met signaling pathways to impair cancer metastasis.

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RESEARCH PROJECT DESCRIPTION (brief overview of background, hypothesis, methods, role of medical student, funding and relevant publications -- SHOULD NOT EXCEED ~ 250 WORDS)

Metastasis is the major cause of therapeutic failure and high mortality in cancer patients. Src and Met are two key oncoproteins but their inhibitors alone have little meaningful clinical activity in metastatic cancer patients when used alone because of complex intracellular signaling pathways that are redundant, compensatory and cross-reactive in cancer cells. Therefore we hypothesize that combination of two types of inhibitors will yield greater effects than either agent alone on impairing tumor cell dissemination. Cell function assays (such as migration and invasion) and molecular signaling pathways (such as Western blotting and immunofluorescence staining) associated with metastasis will be determined. The candidate student will join the research studies aforementioned completely or partially. The long-term goal of this project is to develop combination treatment strategies that may ultimately provide clinical benefit and improve survival of cancer patients.

1. Dai Y, Siemann DW. BMS-777607, a small-molecule met kinase inhibitor, suppresses hepatocyte growth factor-stimulated prostate cancer metastatic phenotype in vitro. Mol Cancer Ther. 2010 Jun;9(6):1554-61. Epub 2010 Jun 1. PubMed PMID: 20515943.

2. Dai Y, Bae K, Pampo C, Siemann DW. Impact of the small molecule Met inhibitor BMS-777607 on the metastatic process in a rodent tumor model with constitutive c-Met activation. Clin Exp Metastasis. 2012 Mar;29(3):253-61. PubMed PMID: 22286523.

3. Dai Y, Shi W, Molnar N & Siemann DW. Impact of tumor hypoxia, Src, and Met signaling in the dissemination of tumor cells (Chapter 7). In: Fatatis A (ed) Signaling Pathways and Molecular Mediators in Metastasis, 1st edn. Springer, NY, USA 2012, ISBN 978-94-007-2557-7.