Public Abstract

Rationale: Our lab has found that a class of small molecular inhibitors, the cyclosporines, inhibit activation of breast cancer cells by growth factors. Furthermore, we have found that non-immunosuppressive cyclosporines, such as NIM811, when tested in mouse models of breast cancer have the capacity to block micrometastatic "seeds" of breast cancer from becoming macrometastatic tumors. Given that micrometastatic seeding of breast cancer is thought to occur early in the clinical course of those destined to have Stage IV breast cancer, cyclosporines could "treat breast cancer metastasis to improve outcome", a stated goal of Metavivor.

Goal: To test our hypothesis that non-immunosuppressive cyclosporines can inhibit the progression of micro- to macro-metastatic breast cancer in cutting edge models of breast cancer metastasis and examine how these agents alter signaling, gene expression, and the microenvironment within the metastatic niche. These studies will provide necessary additional data to translate these findings into clinical trials of these agents.

Anticipated clinical applications and interim outcomes: Our preliminary data indicate that non-immunosuppressive cyclosporines can prevent the progression of micro- to macro-metastatic disease. Since the vast majority of breast cancer deaths are due to the macrometastatic disease progression, cyclosporines could be of significant benefit treating high-risk patients. The pre-clinical data obtained by the studies outlined here will facilitate the translation of these agents into clinical trials.