

## METAvivor Final Report

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Grant title: Targeting novel tumor-stroma interactions in breast cancer brain metastases

Preliminary studies revealed that PDGFR $\beta$  activity primes the brain tumor microenvironment (TME) resulting in the development of breast brain metastases in an experimental metastasis system, and increased intracranial growth that can be inhibited pharmacologically with a highly selective PDGFR inhibitor. Using human breast cancer primary tumor tissue, we were further able to demonstrate that high PDGF-B is prognostic of the development of brain metastases. Combined, these data led to the hypothesis that in a subset of breast cancer patients, tumor-derived PDGF-B drives metastatic growth at sites expressing PDGFR $\beta$ , such as in the brain. During the METAvivor funding period, we gained proficiency and utility of multiple experimental metastasis model systems (tail vein, intracardiac, intracranial), which are currently being used to confirm whether pharmacologic inhibition of PDGFR is an effective treatment for established brain metastases. We have also successfully acquired FFPE tumor tissue from eight patients with breast cancer that metastasized to the brain. For each patient, we obtained tissue from both the primary tumor and associated brain metastasis culminating in 16 patient samples total. We then used laser capture microdissection to isolate tissue from each sample's tumor "epithelium" and "stroma". The cDNA libraries of these 32 samples have been successfully generated and the RNA-sequencing and downstream analysis are ongoing. These sequencing results should reveal novel pathways involved in breast cancer associated ligand-receptor crosstalk with the ultimate goal of identifying targetable players to treat women with metastatic disease.