**Lay Summary**

“c-Met mediated microglia polarization promotes brain metastasis by generating an immune suppressive microenvironment” manuscript under preparation.

We are going to submit a R01 grant using the preliminary data generated from this grant in the next June cycle 2024.

**Summary of important findings**  
 1. Activation of c-Met pathway promotes TGFb expression through p-38 signaling.

2. TGFb promotes M2 polarization of microglia.

3. TGFb treated microglia suppress CD8 T cell activation.

4. Targeting c-Met by PTER enhances anti-PD-1 efficacy in treating brain metastasis in vivo.

Immunotherapy has become a stand of care for many cancers including breast cancer. However, treating patients with brain metastasis is still challenging largely due to the poor delivery efficiency of antibody and unique immune microenvironment. Our findings about how TGFb secreted from brain metastatic cells reprogram the microglia cell to become immunosuppressive is translation and highly clinical relevant. Our preclinical data showed synergistic anti-tumor effect of PTER and anti-PD-1 in treating brain metastasis may provide novel therapeutic approach for breast cancer patients with brain metastasis.