**Lay Summary of important findings and potential clinical impact:** Our results highlight the importance of immune cells in breast tumor progression, particularly in driving cancer cells invasion and colonization of metastatic sites. Our findings show that Pleiotrophin (PTN), a unique and previously under-studied cytokine, contributes to inflammation within the tumor microenvironment. PTN appears to be particularly efficient in recruiting neutrophils, which have been reported to cause immune suppression. We have also identified a subset of PTN-positive cancer cells that are enriched in metastatic lesions. Uncovering the function of PTN in these unique cancer cells might have a major impact in the clinical setting. Corroborating our results in mouse model, we found PTN expression tends to go up in the serum of breast cancer patients as the disease progresses. Furthermore, stage IV breast cancer patients that have lower PTN expression have a highly significant survival advantage (median survival 78.27 months) over patients expressing high levels of PTN (median survival 27.5 months).

Completion of this project will help push PTN and its receptors as new therapeutic targets that can be investigated in the clinic for treatment of advanced breast cancer.