

Public/Lay Abstract:

Metastatic breast cancer arises when cancer cells spread from the breast to other organs, making the disease incurable for most patients. Patients with multiple metastatic lesions have a worse prognosis than those with a single lesion. Although the primary tumor and initial metastases can be treated, cancer often continues to spread because tumor cells can escape from existing metastases and travel through the bloodstream to form new tumors elsewhere, a process known as re-dissemination or metastasis-to-metastasis seeding. This ongoing spread complicates disease management and leads to poorer outcomes.

Our prior research has shown that tumor leave primary tumors through specialized structures in tumor blood vessels called TMEM (tumor microenvironment of metastasis) doorways. We found that some chemotherapy drugs, like paclitaxel, which are intended to eliminate cancer cells, may unintentionally make it easier for tumor cells to escape from metastatic lesions through TMEM doorways. Our work has also shown that TMEM doorways also exist in metastatic lesions, raising the concern that current chemotherapy approaches might be contributing to further cancer spread among patients already burdened by metastases, but also raising the possibility that drugs shown to inhibit dissemination through TMEM doorways may also inhibit re-dissemination. The impact of drugs on re-dissemination has not been previously studied predominantly due to a lack of technologies to directly and quantitatively measure this process.

Our project aims to address this gap by developing advanced techniques using fluorescent labeling, microfluidics, tissue clearing, and imaging to precisely track and count cancer cells as they leave metastatic lesions. With these tools, we will test how standard chemotherapies such as paclitaxel, and experimental drugs that block TMEM doorways, alone or in combination, influence re-dissemination. Understanding these effects will allow us to develop treatment strategies that not only destroy cancer cells but also prevent new metastases from forming.

The ultimate goal of this work is to offer new options for patients with metastatic breast cancer, focusing on both eliminating existing tumors and preventing further spread. This research could reduce the number of metastatic sites, preserve organ function, extend survival, and enhance quality of life. Patient advocates are actively involved to ensure the work remains patient-centered and quickly delivers benefits for those living with metastatic breast cancer.