

PUBLIC/LAY ABSTRACT

RATIONALE

As treatments for breast cancer improve and patients live longer, breast-to-brain metastasis is becoming more common and can severely affect quality of life, daily function, and survival. 10–15% of women with metastatic breast cancer develop brain metastases—however, rates as high as 30% (HER2+) and 50% (triple-negative) are observed. Brain metastases can develop years after initial breast cancer diagnosis, meaning tumor cells must adapt traits over time to survive and grow in the brain’s unique environment.

Our team has discovered two important patterns (“signatures”) in brain metastases:

1. **Brain mimic signature:** tumor cells adopt brain-like gene features.
2. **Brain adaptation signature:** brain cells near the tumor adopt tumor-like gene features.

These changes may drive tumor growth and affect how the disease responds to treatment. However, we still do not know exactly which cells in the brain metastases environment are most involved, how these changes happen, or how they relate to patient outcomes. Filling these gaps could lead to new ways to monitor the disease and new strategies to slow or stop the growth of established brain metastases.

GOALS

1. Learn how breast cancer cells and brain cells interact to help tumors survive and grow in the brain.
2. Understand how the brain mimicry and adaptation signatures contribute to disease progression.
3. Determine whether these signatures can be monitored through cerebrospinal fluid (CSF), a body fluid that bathes the brain and spinal cord.
4. Identify biological pathways linked to these signatures that could be targeted in future studies.

INTERIM OUTCOMES

1. Create detailed spatial maps of brain metastases and surrounding brain tissue showing which cells are involved in mimicry and adaptation, and how they are arranged.
2. Link brain mimicry and adaptation patterns to clinical outcomes such as survival, recurrence, and treatment response.
3. Show whether CSF can be used to detect and track these patterns over time.
4. Generate a list of key genes and pathways to guide future treatment development.

CLINICAL APPLICATIONS/IMPACT

Most breast cancer research focuses on the cancer cell itself, but brain metastases are shaped by a complex “ecosystem” of cancer cells and surrounding brain cells. By studying both, we can uncover the biological “conversations” that help tumors grow in the brain.

This will be the first study to link brain mimicry and adaptation signatures to real patient outcomes and to test whether they can be monitored using CSF. Results could lead to:

- Better tools to predict which patients are at higher risk of brain metastasis progression.
- New ways to monitor treatment response and detect early signs of recurrence.
- Future therapies that disrupt harmful tumor–brain interactions.

By focusing on patients who already have brain metastases—a group often excluded from clinical trials—this work addresses a major unmet need and aims to improve both quality of life and survival.