

LAY ABSTRACT

Breast cancer is the most common malignant disease that affects Western women. While the primary tumors often can be cured by surgery and adjuvant therapy, metastases that arise from these primary tumors can go undetected for long periods of time, are highly resistant to therapy, and are the reason for more than 90% of breast cancer mortality. Thus, the ability to effectively treat breast cancer is largely dependent on the capacity to treat recurrent metastatic disease. A major cause for breast cancer recurrence in a metastatic form is the ability of breast cancer cells to become inactive and survive in the human body often for years after primary tumor remission. Our goal is to identify targetable vulnerabilities of inactive breast cancer cells with the goal of eliminating them before they are able to reactivate to form metastases after long periods of inactivity. Metabolic pathways provide the foundation necessary to support the tumorigenic process. Alterations in metabolic pathways and metabolic output are particularly important during the metastatic cascade, when cancer cells are most vulnerable. Importantly, these metabolic adaptations come at a cost to the cancer cells and often translate into metabolic liabilities that can be exploited to treat cancer. Here, we propose that the metabolic adaptations that are required to allow for metastatic breast cancer cells to stay inactive for long periods of time make them susceptible to the induction of a specific type of cell death. Together, this work has the potential to unveil new therapeutic targets for inactive breast cancer cells and thereby lead to the development of targeted therapies that can effectively prevent recurrent metastatic disease in breast cancer patients.