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Project Title
Leveraging Quiescence to Overcome Resistance to Standard of Care Chemotherapy in Triple-negative Breast Cancer

Type of Cancer
Triple-negative Breast Cancer

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Area of Research

Breast cancer is the most common non-skin cancer in the United States and the second leading cause of cancer-related death among women. However, it has been clear for two decades that breast cancer is not one disease, but several diseases, each with its own distinct clinical trajectories and prognosis. Triple-negative breast cancer (TNBC), lacking expression of the estrogen and progesterone receptors and with amplification of HER2/Neu, is an aggressive tumor type that disproportionately affects younger and Black women and carries the worst prognosis of all breast cancer subtypes. Some progress in treatment of TNBC has been made over the past few years, increasing the number of targeted therapies from zero to three; however, two of these treatments are only available to a minority of TNBC patients, dictated by either the presence of a genetic mutation (PARP inhibitors), or by certain tumor characteristics (immunotherapy). The third targeted therapy (sacituzumab-govitecan) is available to all TNBC patients, but only as second-line therapy and after the development of metastatic disease, which, as of today, remains a death sentence. First-line treatment for all TNBC patients consists of the same cytotoxic chemotherapies that have been used for decades which, despite great effort, we have been largely unable to improve upon, both in terms of achieving better survival outcomes or decreased burden of side effects. There is still much work to be done. Historically, cancer researchers have focused on developing therapeutics geared toward rapidly dividing cells, since cancer cells need to escape the normal controls on cell division and divide millions of times to form a tumor. However, recent data has demonstrated that the cells within a tumor that are not actively dividing or dividing very slowly—so-called quiescent cells—may be particularly problematic. Quiescent cells will evade cytotoxic chemotherapies relying on active cell division for efficacy. Recent evidence suggests that quiescent cells that survive chemotherapy and then resume dividing when chemotherapy is withdrawn behave more aggressively and are more resistant to future therapies. I propose that learning what leads tumor cells to stop dividing and enter quiescence, how quiescent cells are changed by surviving chemotherapy, and, ultimately, how to kill quiescent tumor cells, will unveil new and needed treatment strategies for TNBC.

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