LAY ABSTRACT

Metastatic breast cancer (MBC), characterized by the spread of cancer cells from the breast to other parts of the body such as the brain, remains the leading cause of breast cancer-related deaths. This type of cancer is particularly challenging to treat due to its aggressive nature and resistance to conventional therapies. Triple-negative breast cancer (TNBC), a subtype of MBC, does not respond to hormone therapies or drugs that target HER2, leaving patients with limited treatment options. Our research has identified Polo-like kinase 1 (Plk1), an enzyme crucial for promoting cell growth and division, as a potential new target for therapy. Plk1 is highly active in aggressive breast cancer cells but not in normal breast cells. In our studies, the drug BI2536, which inhibits Plk1, successfully induced cancer cell death and prevented the spread of these cells to the brain.

Moreover, our research shows that combining BI2536 with another drug, erastin, which induces a form of cell death known as ferroptosis, significantly reduces the viability of metastatic breast cancer cells. This combination is particularly effective against aggressive cancer cells while sparing normal cells. Our proposed study aims to further investigate how these drugs work together to suppress the migration and invasion of cancer cells, both in the lab and in animal models. By understanding the mechanisms behind these effects, we hope to develop new, more effective treatment strategies for metastatic breast cancer. This research holds the promise of providing new hope and better outcomes for patients battling this devastating disease.