In vitro Characterization of HER2 Positive Breast Cancer Brain Metastases

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Background Breast cancer, the most common cancer in women results in 40,000 deaths annually. Different breast cancer subsets are defined based on the expression of specific receptors: estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2). Brain metastases are estimated to occur in 30-55% of patients with ER-, PR-, HER2+ disease. Trastuzumab and Pertuzumab target the HER2 receptor pathway but are not effective against breast cancer brain metastases, perhaps due to the blood brain barrier. The goal of this project was to conduct an in vitro characterization of three of the ER-, PR-, HER2+ breast cancer brain metastases. Methods Cell proliferation and migration assays were performed after treatment with trastuzumab and a combination of trastuzumab and pertuzumab. Immunohistochemistry of ER, PR, and HER2 receptor status were investigated. Comparative genomic hybridization compared genomic DNA from the original patient's metastatic brain tumor and its subsequent cell lines. Results Immunohistochemistry showed ER-, PR-, and HER2+ staining in the patient tumors. MTT cell proliferation assays and migration assays also revealed no significant differences with the treatment of trastuzumab or the combination. Comparative genomic hybridization arrays revealed similar gene copy number changes per cell in the following genes: HER2, PIK3CA, SOX2, MDM4, FOXL2, CARD11. Conclusion The cell lines derived from ER-, PR-, HER2+ breast cancer brain metastases did not demonstrate any response in cell proliferation or migration following in vitro treatment of HER2 targeting agents, suggesting that inadequate drug penetration in the brain does not fully account for its failure in treating breast cancer brain metastases.

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