Deciphering the Role of Cytokine-Induced Glutamate Dynamics in Breast Cancer Brain Metastasis

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Metastasis is a critical stage in cancer progression, where tumor cells spread from their original site to distant organs, often leading to dire consequences. Our research delves into the intricacies of the "extravasation" process, wherein tumor cells exit the bloodstream to infiltrate the parenchyma of target organs. In particular, we try to understand the proclivity of breast cancer cells to form metastases within the brain. Our data indicate that "brain-seeking" cells possess the ability to disrupt the integrity of the blood-brain barrier by releasing a suite of inflammatory cytokines. This indication adds a layer of complexity to the already acknowledged correlation between cytokine activity and metastasis formation. Our data indicate that specific metabolic alterations are induced by cancer-released cytokines on brain resident cells like astrocytes, notably the accumulation and subsequent release of glutamate within the brain. This glutamate enhances the migratory and invasive capabilities of tumor cells that are predisposed to targeting the brain. We finally demonstrated that inhibiting pathways used by metastatic cells, particularly those involving glutamate and cytokines, could prevent brain metastases. Our research provides new insights into the tumor ecosystem in breast cancer and identifies novel therapeutic targets for brain metastases, paving the way for innovative treatment strategies to improve outcomes for patients at risk of brain metastasis.