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Hypoxic Environments Regulate CXCR4 Expression and Drive Collective Cell Migration

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Approximately 90% of the deaths related to breast cancer are caused by metastatic dissemination of the disease. Furthermore, once a tumor has reached the metastatic stage there is only a 22% chance of 5-year overall survival for the patient. Accumulated evidence has demonstrated that exchange of information between tumor cells and its extracellular matrix environment, such as hypoxia, contributes to cancer metastasis. CXCR4, a G-protein coupled receptor that activates intracellular signaling pathways controlling cell shape, migration and proliferation, is hypothesized to contribute to tumor cell migration away from the primary site. The objective of this project was to investigate the role of hypoxia to regulate CXCR4 expression and drive cell migration. Using a 3D hydrogel system to mimic features of the tumor microenvironment, studies reveal hypoxia leads to up-regulated CXCR4 expression. Furthermore, CXCR4 knockdown via shRNA resulted in decreased CXCR4 expression that did not change under hypoxia. Findings from this study indicate a potential role for CXCR4 signaling that is regulated by hypoxia. These findings are significant as they begin to provide insight regarding escape mechanisms cancer cells use to metastasize to distant tissue.