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Tamoxifen as a modulator of CXCL12-CXCR4-CXCR7 chemokine axis: A breast cancer and glioblastoma view

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Abstract

The chemokine stromal cell-derived-factor 1 (SDF)-1/CXCL12 acts by binding to its receptors, the CXC-4 chemokine receptor (CXCR4) and the CXC-7 chemokine receptor (CXCR7). The binding of CXCL12 to its receptors results in downstream signaling that leads to cell survival, proliferation and migration of tumor cells. CXCL12 and CXCR4 are highly expressed in breast cancer (BC) and glioblastoma (GBM) compared to normal cells. High expression of this chemokine axis correlates with increased therapy resistance and grade, tumor spread and poorer prognosis in these tumors. Tamoxifen (TMX) is a selective estrogen receptor modulator (SERM) that inhibits the expression of estrogen-regulated genes, including growth and angiogenic factors secreted by tumor cells. Additionally, TMX targets several proteins, such as protein kinase C (PKC), phospholipase C (PLC), P-glycoprotein (PgP), phosphatidylinositol-3-kinase (PI3K) and ion channels. This drug showed promising antitumor activity against both BC and GBM cells. In this review, we discuss the role of the CXCL12-CXCR4-CXCR7 chemokine axis in BC and GBM tumor biology and propose TMX as a potential modulator of this axis in these tumors. TMX modulates the CXCL12-CXCR4-CXCR7 axis in BC, however, there are no studies on this in GBM. We propose that studying this axis in GBM cells/patients treated with TMX might be beneficial for these patients. TMX inhibits important signaling pathways in these tumors and the activation of this chemokine axis is associated with increased therapy resistance.

Keywords: Breast cancer; CXCL12-CXCR4-CXCR7; Chemokine; Glioblastoma; Tamoxifen.