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INTEGRATIVE ANALYSIS OF CXCR4/CXCL12 AXIS GENE EXPRESSION ALTERATIONS IN BREAST CANCER AND ITS PROGNOSTIC RELEVANCE.

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Abstract

Cancer metastasis is the major delimiting factor in the failure of therapeutic strategies currently practised and epithelial-mesenchymal transition (EMT) has been observed to be one of the key regulators of metastasis as it confers the invasive phenotype. Chemokines have been shown to be directly involved in mediating the metastatic ability of cancer cells, particularly CXCR4 chemokine receptor. The purpose of the present study was to explore the expression levels of CXCR4/CXCL12 axis in different subtypes of breast cancer using dataset analysis. The mRNA expression levels and genomic alterations of CXCR4 and CXCL12 in different cancers were analyzed via the Oncomine and cBioPortal. In addition, co-expression analysis, mutations and clinical survival relevance has been analysed in various datasets. Results of our analysis suggest a significant association of CXCR4/CXCL12 axis in breast cancer and as a potential prognostic biomarker.

Keywords: CXCR4, breast cancer, invasion, survival, co-expression, dataset.

Introduction

Cancer remains one of the most devastating diseases in the world. Reduced survival rate of cancer is mainly due to metastasis, relapse and lack of effective therapies (1). Increasing evidence indicates that tumor microenvironment interactions have a crucial role in tumor initiation and progression (2). Numerous studies indicates that the inflammatory environment provided by the chemokines regulates the interaction between tumor cells and stromal cells to create a permissive microenvironment for tumor progression and invasion. In particular, the chemokine receptor 4 (CXCR4) and its ligand (CXCL12) are two important factors in the cross-talking between cancer cells and their microenvironment regulating diverse processes in cancer including EMT, invasion, angiogenesis and metastasis (3).

Levels of CXCR4 have been found to increase significantly in cancer cells which enable the tumor cells to acquire resistance to current therapies. Directed metastasis and migration of cancer cells towards target organs is mediated by the CXCR4/CXCL12 pathway (4). Studies on leukemia and solid tumors substantiate that CXCR4 signaling events prominently contribute to chemoresistance. Henceforth, targeting the CXCR4/CXCL12 signaling pathway with antagonists has significantly blocked the spreading of tumor cells and development of metastasis in a variety of solid cancers (5).