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Research Progress of Chemokine CXCL13/CXCR5 in Tumor

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Abstract

Chemokine receptor is a kind of to participate in the chemotaxis of neutrophils, mononuclear macrophages and macrophage inflammatory chemokines immune cell migration of directional growth of malignant cells, its chemotactic function by corresponding factor receptor mediated, not only in the inflammatory reaction and allergic reaction plays an important role, at the same time to participate in the directional growth and metastasis of malignant tumor. Among them, chemokine CXCL13 and its receptor CXCR5 are abnormally widely expressed in a variety of malignant tumors and are closely related to the treatment progress of a variety of tumors.

Keywords

CXCR5; CXCL13; Chemokine; Review.

1. Introduction

Chemokines are small molecular polypeptides with molecular weight (MR) 8-10 [1]. Chemokines are a class of tumor cell growth factors or ligands capable of chemotactic inhibition and can selectively attract and activate different cell types [2]. Chemokines are conducive to tumor growth and progression. The destruction of chemokine signals mainly affects various functions of tumor genesis and development [3]. Elevated expression of different chemokine ligands and receptors has been reported in many tumors [4], therefore, abnormal activation of underlying signaling effects has been shown to affect the most typical processes of cancer. The chemokine (CX-C motiv) ligand 13 (CXCL13) and its homologous receptor CXCR5 (i.e., the CXCL13/CXCR5 axis) represent an emerging example of this disrupted chemokine ligand/ receptor pair axis, with abnormal activation mostly in the pro-cancer direction.

2. Overview of main structure and functions of CXCL13/CXCR5

CXCL13 is a cell chemokine, which can not only attract a large number of B-type lymphocytes, but also promote the cell migration of T lymphocytes and macrophages [6-7]. It plays an important role in regulating the blood infiltration of inflammatory lymphocytes, promoting the maturation of lymphocytes and stably improving the blood environment in the body. CXCL13 is secreted by follicular dendritic cells (FDC), which are found in secondary lymphatic tissues, lymph nodes and serum follicles. Saeki et al. [8] believed that DC in the skin acted directly with B cells in the B-cell band and regulated CXCL13 to promote its differentiation and maturation. Dendritic tumor cells (DCs) are also potent professional tumor antigens and can provide host cells. The CXCL13/CXCR5 interaction promotes B cells to regulate T cell immune response. In response to infection, antigen-carrying DC and CT4+T cells can up-regulate CXCR5 [9]. In prostate cancer and breast cancer, CXCR5 expression mediated by inhibiting chemotactic growth can help to inhibit tumor chemotactic growth and prevent invasion. Analysis of the molecular and signaling events regulated by CXCL13,

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and how this chemokine dynamically controls the interaction between tumor cells and tumor microenvironment, is key to the identification of new tumor therapeutic effectors and therapeutic targets.

3. The main role of CXCR5/CXCL13 signal in different malignancies and studies

3.1 CXCR5/CXCL13 are associated with breast cancer

Chen et al. [10] have confirmed that there is a certain correlation between the expression of CXCL13 tumor signal receptor in breast cancer patients and the clinical prognosis and pathological response characteristics of patients with adverse malignant tumors. CXCL13 has a medium-high expression in breast cancer patients, and is closely associated with a variety of adverse clinical prognosis tumor factors such as lymph node tumor cell receptor metastasis and negative expression of estrogen-transfer-positive cell receptor signal. Muller et al. [11] found that CXCL13 expression was present in breast cancer and was associated with metastasis. In addition, CXCL13 overexpression was associated with adverse prognostic factors for breast cancer. Studies have shown that the expression level of p53 suppressor gene and CXCR5 chemokine receptor in breast cancer cell lines is negatively correlated. P53 leads to an increase in CXCR5 mRNA and protein levels. Biswas et al. [13] confirmed that the gene expressions of CXCL13 and CXCR5 were significantly related to the induction of breast cancer cell metastasis. Microarray analysis showed that CXCL13 was significantly overexpressed in breast cancer specimens [14].

3.2 CXCR5 / CXCL13 and lung cancer

Singh et al. [15] used flow cytometry to find that the expression level of CXCR5 was significantly increased in non-lung cancer cell lines compared with small cell lung cancer cell lines. Cao Baosen compared lung cancer tissue with normal lung tissue, and the results showed that with the increase of clinical stage and tumor volume, the expressions of CXCR5 and CXCL13 tended to increase, while the cell migration induced by CXCL13 showed that the non-lung cancer cell line with small cell lung cancer cell line had strong cell migration ability. It is confirmed that the CXCR5-CXCL13 biological axis influences the progression of lung cancer, CXCR5 and CXCL13 can be used as biomarkers for lung cancer, and targeting the CXCR5-CXCL13 biological axis may be a feasible strategy to contribute to the treatment of lung cancer.

3.3 CXCR5 / CXCL13 and bowel cancer

In colorectal cancer, CXCL13/ CXCR5 signaling neural axis promotes normal pathogenesis, migration and immune invasion of colon tumor epithelial cells through the MMPI3K/Akt neural pathway and endocrine hormone MMP-13 [16-17]. Similarly, a recent study by Zheng et al. [18] also found that CXCL13/ CXCR5-mediated PI3K/Akt pathway activation was associated with enhanced tumor progression. Liu YK et al. [19] also found that CXCR5/CXCL13 had a certain genetic association with malignant lymph node cell transfer factor used in nodular rectal cancer. Xing et al. [20] found that the number of CXCR5+CD8+T cells significantly increased in colorectal cancer tumor tissues. Meijer et al. [21] reported that macrophages can directly induce the formation of colon cancer cell line CT26 expressing CXCR5 in some mice either in vivo or in vitro.CXCLL3 is mainly widely distributed in mouse liver, lymph nodes and other human tissues, and liver lymph nodes and mouse liver are one of the main sources and target cell organs of cell metastasis in the treatment of colorectal cancer. These results suggest that the CXCR5/ CXCLL3 biological axis has been playing an extremely important and pivotal role in the treatment of NCRC metastasis.

3.4 CXCR5/CXCL13 and prostate cancer

In a mouse model of early prostate cancer, knockout of the tumor suppressor gene kinase PTEN and the transitional expression of oncosuppressor protein kinase Cε can effectively promote the development of early prostate cancer in mice. NF-κB specificity, synergism, and up-regulation of CXCL13 expression in benign prostate cancer [22]. CXCL13 is mediated by signaling in its JNK

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pathway and it is mediated by signaling in this pathway to inhibit the normal growth and proliferation of tumor epithelial cells in malignant prostate cancer. The excitable pattern of proteins in hormone-resistant cells is ultimately attributable to the interaction of CXCL13 and its receptor CXCR5. CXCL13 can promote the amplification of cellular signal cascades and even regulate the invasion and growth of advanced prostate cancer cells.

3.5 CXCR5/CXCL13 and other tumors

Studies [23] found that CXCL13 levels in serum of patients with hepatitis B infection-related liver cancer increased and increased with the decrease of differentiation degree of liver cancer, indicating that CXCL13 is closely associated with liver disease. Ding et al. [24] found abnormal expression of CXCL13 in patients with gastric cancer, suggesting that CD40+ marrow derived suppressor cells could regulate its expression. In addition, Cha et al. [25] studied the apoptotic mechanism of diffuse large B lymphocyte peripheral lymphoma cells and found that the apoptosis of peripheral lymphocyte CXCR5+CD4+T cells may directly promote the proliferation and proliferation of lymphocyte cells by indirectly inhibiting the massive apoptosis of large lymphoma malignant cells. The main role of CXCR5+CD4+T tumor cells is to promote tumor differentiation by blocking and reducing the sources of the secretions of tumor cytokine IL-1 and cell enhancer IL-10, suggesting that the CXCR5 signaling induction pathway has always played an important role in promoting the development and differentiation of tumor cells.

4. Looking forward

At present, clinical studies on CXCR5/CXCL13 biological cell axis are extensive, and they have been applied continuously in the clinical prevention, diagnosis and drug therapy of malignant tumors. So far, most of the clinical experiments show that the main function of CXCR5 / CXCL13 information mediated axis while involved in mediating cancer early transfer of normal cells, but its function mediated basic mechanisms of many diseases in tumor cells to normal transfer is not yet clear, believe in the near future, with the deepening of the tumor medical research and modern medical information technology constantly With progress, its important role in a variety of cancer centers will become increasingly clear. Therefore, the in-depth analysis of chemokines and their corresponding chemokine receptors can also provide a new technical means for promoting the clinical treatment and development of new neoplastic granulocyte autoimmune diseases.

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