Department of Neurology and Clinical Neuroimmunology,
RSS Grudziadz, Poland
Oddział Neurologii i Neuroimmunologii Klinicznej,
Regionalny Szpital Specjalistyczny w Grudziądzu

Department of Neurology, Medical University of Lublin, Lublin, Poland
Katedra i Klinika Neurologii, Uniwersytet Medyczny w Lublinie

MATEUSZ SPŁAWSKI, ROBERT BONEK,
MARTA TYNECKA-TUROWSKA, KONRAD REJDAK

Chemokines - general characteristics and selected aspects of immunopathogenesis of multiple sclerosis

Chemokiny - charakterystyka ogólna i wybrane aspekty imunopatogenezy stwardnienia rozsianego

Key words: proinflammatory chemokines, chemokine receptors, multiple sclerosis, immunopathogenesis

Słowa kluczowe: chemokiny prozapalne, receptory chemokinowe, stwardnienie rozsiane, immunopatogeneza

INTRODUCTION

Cytokines are a diverse group of molecules that regulates cellular processes. They have influence on growth, proliferation and stimulation of cells involved in immune response and hematopoietic cells (bone marrow stem cells).[2]

Because of its structure, there are four types of cytokines:

1. Type I cytokines (hematopoietin);
2. Type II cytokines (interferons and IL-10);
3. chemokines;
4. TNF superfamily (tumor necrosis factor).

Cytokines are characterized by pleiotropy (the ability to affect multiple cells and induce different effects) and redundancy (the ability of different cytokines to exert the same effect). They can act antagonistically (block interaction) or synergistically. Depending on the site of secretion, they may act on the same cells by which they are secreted (autocrine action), neighboring cells (paracrine action), or cells at a considerable distance, e.g. in another organ (endocrine action).[2]

PROINFLAMMATORY CHEMOKINES - GENERAL CHARACTERISTICS

Chemokines are alkaline proteins with low molecular weight (about 8 - 14 kDa). They are made of 70 - 100 amino acids (according other sources of 70 to 125 amino acids). The first chemokine was identified in 1961, that was chemokine CXCL4. We currently know about 50 different types of chemokines and about 20 chemokine receptors. Due to the physiological properties we distinguish lymphoid (constitutive or homeostatic) and proinflammatory chemokines (induced). Lymphoid chemokines include: CXCL12, CXCL13, CCL19, CCL21, CCL25, CCL27. They are involved in the circulation of lymphocytes, the movement of dendritic cells to peripheral lymphatic organs and mature thymocytes to the corresponding thymus regions. Proinflammatory chemokines appear during inflammatory reactions. Other chemokine functions of chemokine include immunomodulatory effects, chemotactic effects on blood cells, adhesion activation, stimulation or inhibition of hematopoietic cell growth.[7, 8, 11, 33, 67, 89]

In major part, chemokines contain at least four cysteines. They form two disulfide bridges - between the first and third and between the second and fourth cysteic rests. On the grounds of the mutual arrangement of cysteine residues in the NH2 region, we have four groups of chemokines: CXC (α), CC (β), C (γ) and CX3C (δ). In these formulas X is an amino acid - in CC chemokines the cysteic rests adhere to each other. In the CXC group they are separated by one amino acid, whereas in the CX3C group the cysteine groups separate the three amino acids. Among the CX3C chemokines, the molecules that comprise the three amino acid sequence of glutamic acid - leucine - arginine (ELR) can be distinguished. They attract myeloid cells, whereas chemokines without that sequence act on leukocytes [7, 8, 67, 82, 89]

In chemokines we distinguish two areas that interact with the receptors - the terminal NH2 residue present before the first cysteine and the exposed loop between the second and third cysteine residues. An exposed cysteine loop is involved in the binding of chemokine to the receptor, while the rest of the NH2 participates in further signaling to the inside of the cell [7, 8, 67, 82]

CYTOKINE RECEPTORS

The cytokine receptors can be divided into 5 groups [2]

a) Ig-like receptors;

b) class I cytokine receptors (hematopoietins);

c) class II cytokine receptors (interleukins and IL-10 family);

d) receptors for TNF superfamily molecules;

e) G protein - coupled receptors.

Chemokines interact on individual cells with receptors that are bounded to the G protein. Chemokine receptors overlap the cell membrane seven times (7 transmembrane domains), and their intermembrane domain is similar to rhodopsin. They are built from 340 to 370 amino acids [2, 7, 8, 61, 67, 82]

Chemokine receptor activation is complicated and involves several phases. These receptors are included in the group of receptors linked to G proteins. In the first phase, the ligand binds to the N-terminal receptor portion, what brings the change in its conformation and enables binding the ligand to the activation domain. Then the signal runs through the βγ protein G subunits, what runs to activation of phospholipase C (PLC) and phosphatidyl-3-OH-inositol kinase (PI3Kγ), that activates protein kinase B. As a result, secondary transmitters are created - inositol 1,4,5- triphosphate (responsible for calcium ions), diacylglycerol (responsible for activation of protein kinase C). Besides, on the cell surface, there may be Duffy (DARC) and D6 receptors, which has no signaling significance. Their task is probably to regulate the concentration of chemokines [42, 67, 82, 83]

THE ROLE OF CHEMOKINES

Chemokines and their receptors are involved in the patomechanism of many diseases. It has been shown that CCL3, CCL4 and CCL5 chemokines inhibit HIV infection, whereas CCR5 and CXCR4 receptors (along with the CD4 molecule) facilitate the entry of HIV into the cell. The CXCR4 receptor (along with CCR7) is also involved in the tumor spreading process. CCL2, CCL4, CXCL8 and CXCL10 chemokines participate in the formation of inflammatory infiltrates in rheumatoid arthritis, whereas, elevated levels of CCL3, CCL4, CCL5, CXCL10 and CXCL11 have been reported in multiple sclerosis. Among chemokines produced constitutively in central nervous system (CNS), the presence of CX3CL1 (fractalkine) and CXCL12 (SDF-1, stromal-cell-derived factor) have been reported. In the pathogenesis of allergic diseases, chemotactic effects on eosinophils have been reported for exemple in case of CCL2, CCL3, CCL5, CCL11. The presence of CCL2 has been reported in atheromatous plaques, whereas the V64I polymorphism within the CCR2 polypeptide chain is associated with heart disease [12, 15, 18, 21, 54, 69, 72, 82, 84]

CHARACTERISTICS OF SELECTED PROINFLAMMATORY CHEMOKINES

Characteristics of selected proinflammatory chemokines: CXCL1/GRO-α, CXCL9/MIG, CXCL11/I-TAC, CX3CL1/Fractalkine, CCL2/MCP-1, CCL5/RANTES, CCL7/MCP-3, CCL17/TARC, CXCL13/BCA-1, CCL3/MIP1-α, CCL4/MIP1-β, CCL8/MCP-2, CCL19/ELC, CCL21/SLC, CXCL8/IL-8, CXCL10/IP-10, CXCL12/SDF-1:

- CXCL1/GRO-α, is a small cytokine belonging to the CXC group. With people, it is encoded by the CXCL1 gene, which is located on chromosome 4. CXCL1 is produced by melanoma cells and has mitogenic properties. It affects neutrophils, monocytes, macrophages and epithelial cells. It participates in the development of the spinal cord by inhibiting the migration of oligodendrocytes. In addition, it is involved in the processes of angiogenesis, arterogenesis, inflammation and wound healing or cancer. It works on the CXCR2 receptor. Studies on mice have

shown that CXCL1 reduces the severity of multiple sclerosis symptoms and has neuroprotective effects. In cerebrospinal fluid and blood of patients with multiple sclerosis, elevated concentrations of CXCL1 chemokine has been found.[1, 16, 26, 27, 51, 71, 74, 79]

- CXCL9/MIG, is a cytokine belonging to the CXCL group. It is also known as monokine induced by gamma interferon (MIG), a T cell, which is induced by INF-γ. It is closely related to CXCL10 and CXCL11 chemokines. It is encoded by the CXCL9 gene, which is located on chromosome 4 (locus 4q21.1, next to the CXCL10 and CXCL11 genes). It works on T cells and NK cells by the CXCR3 receptor (similarly to CXCL10 and CXCL11 chemokines). It is distributed by MMP-8 (in two places) and MMP-9 (in three positions). CXCL9 cytokine has shown to be an important biomarker for the development of heart failure and left ventricular dysfunction, what may suggest a correlation between the level of this chemokine and the aforementioned conditions. There was also an elevated level in cerebrospinal fluid in patients with relapsing-remiting multiple sclerosis (RRMS) and expression in the central nervous system.[1, 4, 36, 49, 71, 81]

- CXCL11/I-TAC, is a CXC chemokine. With people, it is encoded by the CXCL11 gene, located on chromosome 4 (locus 4q21.1). Expression of this gene is strongly induced by INF-γ and INF-β, but weakly by INF-α. It affects the CXCR3 chemokine receptor, demonstrating a higher affinity for this receptor than cytokines CXCL9 and CXCL10. High level of CXCL11 is found in peripheral blood leukocytes, pancreas and liver. Moderate level in the thymus, spleen and lung, and the lowest expression in the small intestine, placenta and prostate. Similarly to CXCL9 and CXCL10, it is a biomarker of heart failure and left ventricular systolic dysfunction. No elevated blood or central nervous system (CNS) platelets have been demonstrated in patients with multiple sclerosis. CXCL11 may appear in cerebro-spinal fluid.[3, 4, 13, 56, 71, 73]

- CX3CL1/Fractalkine is a large cytokine belonging to the CX3C chemokine group. It is made of 373 amino acids - the N-terminal extracellular segment forms a 76-amino acid chemokine portion containing the CX3C fragment, followed by a 241 amino acid mucosal stalk, and the 19-amino acid transmembrane portion and the 37-amino acid C- final. The Fractalkine coding gene is located on chromosome 16 (16q13). In contrast to the majority of chemokines, it is produced within vascular endothelial cells and nerve cells. Its presence has also been demonstrated in certain organs such as the brain, heart, kidneys, adrenals, lungs and liver. CX3CL1 expansion in the central nervous system is greater than in the other mentioned organs. It acts on monocytes, T cells, NK cells and microglial cells via the CX3CR1 receptor. The CXCR1 receptor has also shown on the surface of neutrophils, mast cells, platelets, smooth muscle cells, and dendritic cells. Increased CX3CL1 concentration and increased expression of CX3CR1 receptor have been found in the pathogenesis of atherosclerosis, coronary heart disease, isolated pulmonary hypertension, renal disease (diabetic nephropathy, membrane nephropathy, focal and segmental glomerulosclerosis and glomerulosclerosis,

glomerular mesangial-renal neoplasia, and others), rheumatoid diseases (RA), allergic reactions, hepatitis C and HIV. It has been shown a high level of the CX3CL1/Fractalkine in the cerebrospinal fluid and blood of patients with relapsing-remiting multiple sclerosis (RRMS).[1, 6, 22, 48, 50, 59, 63, 64, 66, 71, 75, 80, 88]

- CCL2/MCP-1, is a small chemokine belonging to the CC group. It is also called the monocyte chemoattractant protein 1 (MCP-1). Its mass is 11,025 kDa (according to other sources about 13 kDa). The CCL2 protein gene is encoded on chromosome 17 (17q12). The CCL2 precursor contains a signal peptide of 23 amino acids, whereas mature CCL2 is composed of 76 amino acids. CCL2 cytokine acts on monocytes, T and B lymphocytes, dendritic cells and NK cells via CCR1, CCR2 and CCR4 receptors. CCL2 concentration is higher in Caucasians. Cytokine CCL2 is involved in the pathogenesis of many diseases, including psoriasis, rheumatoid arthritis, atherosclerosis, glomerulonephritis. It is also involved in the neuroleptic and neurodegenerative processes of the central nervous system (CNS). Increased expression of CCL2 has been reported in patients with epilepsy, cerebrovascular disease, Alzheimer's disease, autoimmune encephalomyelitis and post-traumatic brain injury. In patients with multiple sclerosis, CCL2 level in the cerebrospinal fluid and blood levels is lower.[1, 19, 23, 24, 30, 34, 44, 57, 71, 87]

- CCL5 / RANTES, is a small cytokine from the chemokine CC group, which molecular weight is about 8 kDa. The gene encoding the CCL5 protein is on chromosome 17 (17q12). It works on monocytes, eosinophils, dendritic cells and T cells. With the help of IL-2 and INF-γ it induces proliferation and activation of NK cells. It works by chemokine receptors CCR1, CCR3 and CCR5. It also activates the G-protein-coupled receptor-GPR75. RANTES has been reported in more than 100 disease. Together with related chemokines (MIP-1α and MIP-1β) it was identified as a natural inhibitory factor for HIV activity, secreted by activated CD8 + T cells and other immune cells. In recent years it is possible to synthesize RANTES protein in vivo by Lactobacillus jensen bacteria. Increased level of CCL5 in blood and cerebrospinal fluid and central nervous system (CNS) expression in patients with multiple sclerosis have been reported.[1, 12, 17, 31, 70, 71, 78]

- CCL7/MCP-3, is a small chemokine, previously known as a monocyte-chemotactic protein 3 (MCP3). It belongs to the group of chemokines CC. It works on T and B lymphocytes, monocytes, NK cells, eosinophils, dendritic cells via CCR1, CCR2, CCR3 and CCR5 receptors. It can be produced by tumor cells and macrophages. The gene coding for the CCL7 protein is located on chromosome 17 (17q12). It works with MMP2. It has shown an expression within patients with multiple sclerosis. However, elevated level of CCL7 in the blood and cerebrospinal fluid in these patients hasn't been observed.[1, 43, 52, 53, 71]

- CCL17/TARC, is a small cytokine that belongs to the CC family of chemokines. It is specific for T lymphocytes, which act on the CCR4 receptor. The CCL17 protein encoding gene is located on chromosome 16 (16q21), similar to the genes for CCL22 and CX3CL1. In patients with multiple sclerosis an increased level of CCL17 in cerebrospinal fluid and decreased blood levels has been found. There is no expression in the central nervous system (CNS).[1, 71]

- CXCL13/BCA-1, is a CXC chemokine. It works on T and B lymphocytes, monocytes and dendritic cells via the CXCR5 receptor. It has shown its increase expression in lymph nodes, liver, spleen and intestines. The gene encoding the CXCL13 protein is located on chromosome 4 (4q21.1). Patients with multiple sclerosis have elevated CXCL13 level both in the blood and in the cerebrospinal fluid and high expression in the central nervous system (CNS). The usefulness of CXCL13 in cerebrospinal fluid (elevated levels) has been demonstrated in acute phase of neuroboreliosis.[1, 32, 37, 71]

- Chemokine CCL3 is also known as macrophage inflammatory protein 1-alpha (MIP1-alpha). CCL3 is a cytokine belonging to the CC chemokine family and in humans is encoded by the CCL3 gene, located on chromosome 17 (17q12). Polymorphisms at this locus may be associated with both resistance and susceptibility to infection by human immunodeficiency virus type 1. It works on monocytes, neutrophils, eosinophils, T lymphocytes and B lymhocytes via CCR1, CCR4 and CCR5 receptors. CCL3 is involved in the acute inflammatory state and causes a monophasic fever - the fever induced by MIP-1 is not inhibited by the cyclooxygenase inhibitors. Generalized expression of CCL3 in the bone marrow, liver and other organs has been demonstrated. Patients with multiple sclerosis have elevated CCL3 level in the blood and expression in the central nervous system (CNS).[1, 14, 45, 71, 85]

- CCL4 is also known as macrophage inflammatory protein-1β (MIP1-β). It is a small cytokine that belongs to the CC family of chemokines and is encoded by CCL4 gene, located on chromosome 17 (17q12). CCL4 work on CD8+ lymhocytes via CCR5 receptor. It is a major HIV-suppressive factor produced by CD8+ T lymphocytes. It has been shown that CCL4 interacts with CCL3. High expression of CCL4 in the bone marrow and liver has been detected. There is an expression in the central nervous system (CNS) in patients with multiple sclerosis. CCL4 was not detected in blood and in the cerebrospinal fluid.[1, 12, 25, 71]

- CCL8/MCP-2, is a small cytokine belongs to the CC family of chemokines. The gene for CCL8 is located on chromosome 17 (17q11.2). CCL8 precursor protein is made up of 109 amino acids, while mature CCL8 contains 79 amino acids. It works by CCR1, CCR2, CCR3 and CCR5 receptors on monocytes , eosinophils, T lymphocytes and dendric cells. This chemokine may contribute to tumor-associated leukocyte infiltration and to the antiviral state against HIV infection. Broad expression in small intestine, fat and 22 other tissues. CCL8 expression in central nervous system (CNS) has been demonstrated in patients with multiple

sclerosis. MCP-2 was not detected in blood and in the cerebrospinal fluid [1, 71, 76, 77]

- CCL19 is a small cytokine belonging to the CC chemokine family. It is also known as EBI1 ligand chemokine (ELC) and macrophage inflammatory protein-3-beta (MIP3-beta). CCL19 is encoded on p-arm of chromosome 9. CCL19 is expressed in thymus and lymph nodes (high level), in trachea and colon (moderate level) and in stomach, small intestine, lung, kidney and spleen (low level). It works on T and B lymphocytes via CCR7 receptor. Patients with multiple sclerosis have elevated CCL19 level in the blood. There is no expression in central nervous system and no high level of CCL19 in cerebrospinal fluid.[1, 62, 71, 86]

- CCL21/SLC, is a small cytokine belongs to the CC family of chemokines. The gene for CCL21 is located on chromosome 9 (9p13.3). It is also known as secondary lymphoid-tissue chemokine (SLC). CCL21 has six conserved cysteine residues instead of the four cysteines typical to chemokines. It works on T lymphocytes, activated B lymphocytes, dendric cells and natural killers cells (NK cells). CCL21 elicits its effects by binding to a cell surface chemokine receptor known as CCR7. CCL21 is expressed in lymph node, splen, appendix and thyroid. There is no expression in central nervous system (CNS). Patients with multiple sclerosis have elevated CCL21 level in the blood.[1, 29, 47, 71]

- CXCL8, also known as interleukin 8 (IL-8), is a member of the CXC chemokine familly. This chemokine is produced by macrophages, epithelial cells, airway smooth muscle cells and endothelial cells. In humans, the CXCL8 protein is encoded by the CXCL8 gene located on q-arm of chromosome 4 (4q13.3). The interleukin 8 precursor protein is composed of 99 amino acids, while the active form contains 72 amino acids. Many receptors on the surface membrane can bind the CXCL8 receptor, most commonly the CXCR1 and CXCR2 receptors. It works on neutrophils and monocytes. IL-8 is an important mediator of the immune reaction in the innate immune system response. It induces chemotaxis in target cells, migration toward the site of infection and phagocytosis. Interleukin 8 is involved in the pathogenesis of psoriasis, colorectal cancer and cystic fibrosis. CXCL8 was shown to be associated with obesity. This chemokine is also a potent angiogenic factor. Patients with multiple sclerosis have elevated CXCL8 level both in the blood and in the cerebrospinal fluid and expression in the central nervous system (CNS).[1, 9, 10, 28, 46, 58, 68, 71]

- CXCL10 is a CXC chemokine. It is also known as Interferon gamma-induced protein 10 (IP-10) or small-inducible cytokine B10. Its mass is 8,7 kDa. The CXCL10 protein gene is encoded on the long arm of the chromosome 4 (4q21.1). CXCL10 is secreted by monocytes, endothelial cells and fibroblasts. CXCL10 cytokine (similar to CXCL9 and CXCL11) has shown to be an important biomarker for the development of heart failure and left ventricular dysfunction. It works on t lymphocytes and natural killers cells (NK cells) via CXCR3 receptor.

CXCL10 has broad expression in appendix, lymph node and 14 other tissues. IP-10 level is an important index in the assessment of treatment in patients with chronic hepatitis C and HIV. Patients with multiple sclerosis have elevated CXCL10 level both in the blood and in the cerebrospinal fluid and high expression in the central nervous system (CNS).[1, 3, 4, 5, 20, 35, 39, 40, 49, 60, 71]

- CXCL12/SDF-1 is a cytokine belonging to CXC group. Another name is the stromal cell-derived factor 1. It is encoded by CXCL12 gene located on chromosome 10 (10q11.21). CXCL12 plays a role in many diverse cellular functions, including embryogenesis, immune surveillance, inflammation response, tissue homeostasis, and tumor growth and metastasis. Mutations in this gene are associated with resistance to human immunodeficiency virus type 1 infections. CXCL12 is expressed in many tissues, including brain, heart, thymus, kidney, lung, liver, spleen and bone marrow. It works on monocytes, plasma cells, T lymphocytes, B lymphocytes and dendric cells via CXCR4 receptor. CXCL12 plays a role in neuroinflammation by attracting leukocytes across the blood brain barrier. CXCL12 may have a beneficial effect in patients with Alzheimer's disease. Patients with multiple sclerosis have high level of CXCL12 in blood and high expression in central nervous system (CNS).[1, 38, 55, 65, 71]

CHEMOKINES IN MULTIPLE SCLEROSIS

Table 1[1, 71]

Chemokine	Receptor	Target cells	Level in CSF	Level in blood	Expression in CNS
CCL2/MCP-1	CCR1, CCR2	T lympocytes, B lymphocytes, monocytes, dendritic cells, NK cells	↓	↓	+
CCL3/MIP1-α	CCR1, CCR4, CCR5	Monocytes, neutrophils, eosinophils, T lymphocytes, B lymphocytes	↑		+
CCL4/MIP1-β	CCR5	CD8+ lymphocytes			+
CCL5/RANTES	CCR1, CCR3, CCR5	Monocytes, eosinophils, T lymphocytes, dendritic cells	↑	↑	+
CCL7/MCP-3	CCR1, CCR2, CCR3,CCR5	Monocytes, eosinophils, T lymphocytes, B lymphocytes, NK cells, dendritic cells			+
CCL8/MCP-2	CCR1, CCR2, CCR3,CCR5	Monocytes, eosinophils, T lymphocytes, dendritic cells			+
CCL17/TARC	CCR4	T lymphocytes	↑	↓	
CCL19/ELC	CCR7	T lymphocytes, B lymphocytes	↑		
CCL21/SLC	CCR7	T lymphocytes, activated	↑		

Chemokine	Receptor	Target cells	Level in CSF	Level in blood	Expression in CNS
		B lymphocytes dendritic cells, NK cells			
CXCL1/GRO-α	CXCR2	Monocytes, neutrophils			+
CXCL8/IL-8	CXCR1, CXCR2	Monocytes, neutrophils	↑	↑	+
CXCL9/MIG	CXCR3	T lymphocytes, NK cells	↑		+
CXCL10/IP-10	CXCR3	T lymphocytes, NK cells	↑	↑	+
CXCL11/I-TAC	CXCR3	T lymphocytes, NK cells		+/-	
CXCL12/SDF-1	CXCR4	Monocytes, plasma cells, T lymphocytes, B lymphocytes, dendritic cells	↑		+
CXCL13/BCA-1	CXCR5	T lymphocytes, B lymphocytes, monocytes, dendritic cells	↑		+
CX3CL1/Fractalkine	CX3CR1	Monocytes, lymphocytes, NK cells, glial cells	↑	↑	

CONCLUSIONS

It has been shown that chemokines and their receptors play an important role in the pathogenesis and course of multiple sclerosis. They are one of the main factors responsible for the migration of inflammatory cells into the central nervous system (CNS). It has been shown that patients with relapse have an increased expression of CXCR3 on CD4 + T lymphocytes and decreased expression of CCR5. Current research may suggest that the use of chemokine inhibitors may have a significant impact on the inhibition of the development of multiple sclerosis. This may open new possibilities in the treatment of multiple sclerosis [8, 41].

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ABSTRACT

Chemokines are low-molecular proteins from the cytokine group secreted by immune cells. Chemokines regulate many cellular processes. We distinguish between lymphoid and proinflammatory chemokines. Due to the construction, chemokines were divided into four groups. Chemokines and their receptors have been shown to play an important role in the development and course of multiple sclerosis. The aim of this article was to present the general characteristics of chemokines and their impact on development and imunopathogenesis of multiple sclerosis. This article has been written on the basis of PubMed articles and other resources. Chemokines and their receptors play an important role in many cellular processes. Their significance in the pathogenesis of multiple sclerosis has also been demonstrated. Conducting further studies on chemokines and their inhibitors may open new possibilities in the treatment of multiple sclerosis. Multiple sclerosis (MS) is a chronic, inflammatory, autoimmune disease of the central nervous system (CNS) with complex etiology. Understanding of the immunopathogenesis and the role of chemokines in this process may be helpful in the development of new methods of treatment of multiple sclerosis.

STRESZCZENIE

Chemokiny to niskocząsteczkowe białka z grupy cytokin, które są wydzielane przez komórki odpornościowe. Chemokiny regulują wiele procesów komórkowych. Wyróżniamy chemokiny limfoidalne i prozapalne. Ze względu na budowę chemokiny zostały podzielone na cztery grupy. Wykazano, że chemokiny i ich receptory odgrywają ważną rolę w rozwoju i przebiegu stwardnienia rozsianego. Celem artykułu było omówienie ogólnej charakterystyki chemokin i ich wpływu na rozwój i immunopatogenezę stwardnienia rozsianego. Artykuł ten został napisany w oparciu o źródła zaczerpnięte z bazy PubMed oraz innych źródeł. Chemokiny i ich receptory odgrywają ważną role w wielu procesach komórkowych. Wykazano także ich znaczenie w patogenezie stwardnienia rozsianego. Prowadzenie dalszych badań nad chemokinami i ich inhibitorami może otworzyć nowe możliwości w leczeniu stwardnienia rozsianego.Stwardnienie rozsiane (MS) to przewlekła, zapalna, autoimmunologiczna choroba ośrodkowego układu nerwowego (OUN) o złożonej etiologii. Zrozumienie immunopatogenezy i roli chemokin w tym procesie może być pomocne w opracowaniu nowych metod leczenia stwardnienia rozsianego.

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