Chemokines and their receptors

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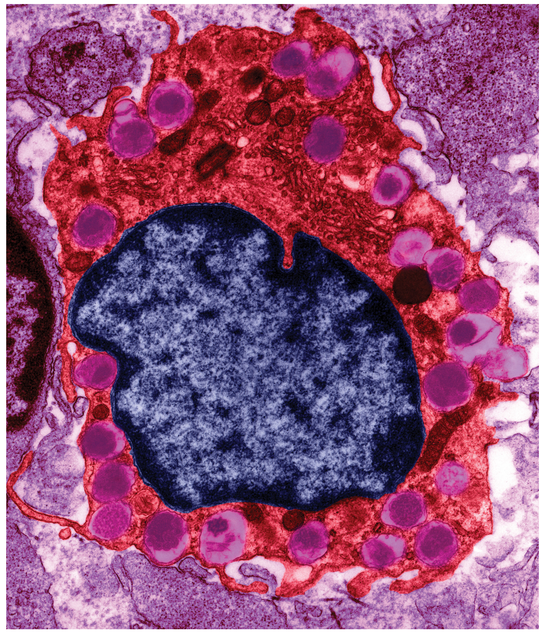
Chemokines

Chemokines are a family of small cytokines. They are classified according to shared structural characteristics such as small size (they are all approximately 8-10 kDa in size), and the presence of four cysteine residues in conserved locations that are key to forming their 3-dimensional shape. The name is derived from their ability to induce directed chemotaxis in nearby responsive cells; they are chemoattractant cytokines. Some chemokines are considered proinflammatory and can be induced during an immune response to promote cells of the immune system to a site of infection, while others are considered homeostatic and are involved in controlling the migration of cells during normal processes of tissue maintenance or development. Chemokines are found in all vertebrates, some viruses and some bacteria, but none have been described for other invertebrates. These proteins exert their biological effects by interacting with G protein-linked transmembrane receptors called chemokine receptors, that are selectively found on the surfaces of their target cells.



Alpha chemokines (CXC)

The alpha chemokine family is characterized by the separation of the first two cysteine residues in the amino acid sequence by one amino acid (C-X-C). Alpha chemokines act primarily on neutrophils as chemoattractants and activators, including neutrophil degradation, with the release of myloperoxidase and other enzymes.

Beta chemokines (CC)

Beta chemokines are secreted proteins characterized by two adjacent cysteines (C-C). This family of chemokines induce changes in intracellular calcium concentration and enzyme release in monocytes.

Gamma chemokines (C)

Gamma chemokines (C subfamily) lack two of the four invariant cysteine residues normally found in the CC and CXC chemokines and have an extended C-terminus.

Delta chemokines (CX3C)

Delta chemokines contain a unique CX3C cysteine motif (3 amino acids between the conserved cysteine residues) near the N-terminal.

Key to conjugations

Text colour	Conjugation
	FITC
	Phycoerythrin
	Biotin
	Unconjugated

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Alpha chemokines (CXC)

Chemokine	Alternative names	Role/expression	AbID	Main receptors
CXCL1	GRO-α / MGSAα (MIP2α/KC)	Inducible neutrophil chemoattractant factor. Detected in mammary fibroblasts, mammary epithelial cells, endothelial cells, activated monocytes, macrophages and neutrophils.	ab9905 ab17678	CXCR2 (IL8RB)
CXCL2	GRO-β / MGSAβ (MIP2β/KC)	Promotes neutrophil and basophil chemotaxis and degranulation.	ab9950 ab25903	CXCR2 (IL8RB)
CXCL3	GROγ / MGSAγ (MIP2γ/KC)	Induces chemotactic activity in neutrophils. May play a role in inflammation and affects endothelial cells in an autocrine fashion.	ab9843	CXCR2 (IL8RB)
CXCL4	PF-4	Released from alpha granules of activated platelets, binds to heparin. Neutralizes heparin like molecules on the endothelial surface of blood vessels, thereby inhibiting local antithrombin III activity and promoting coagulation. Strong chemoattractant for neutrophils and fibroblasts. Probably has a role in inflammation and wound repair.	ab9561 ab49735	CXCR3 beta isoform (CD183b)
CXCL5	ENA-78	Expressed by fibroblasts. Induced by bacterial lipopolysaccharides. Chemoattractant for neutrophils and involved in their activation. Produced concomitantly with CXCL8 in response to stimulation with IL1 or TNF alpha.	ab9802 ab17694	CXCR2 (IL8RB)
CXCL6	GCP-2	Neutrophil recruitment to inflammatory sites.	ab9923	CXCR2 (IL8RB) CXCR1 (IL8RA)
CXCL7	NAP-2	Potent chemoattractant and activator of neutrophils. Stimulates various cellular processes including DNA synthesis, mitosis, glycolysis, intracellular cAMP accumulation, prostaglandin E2 secretion and synthesis of hyaluronic acid and sulfated glycosaminoglycan. Also stimulates formation and secretion of plasminogen activator by synovial cells.	ab9554 ab17520	CXCR2 (IL8RB)
CXCL8	IL8	Major mediator of inflammatory response, secreted by several cell types in response to inflammatory stimulus. A chemoattractant and also a potent angiogenic factor. Attracts neutrophils, basophils, and T-cells (but not monocytes). Strongly suggested role in the regulation of angiogenic activity in cancer and in idiopathic pulmonary fibrosis. Also causes neutrophil recruitment to inflammatory sites.	ab10769 ab14040 ab56320 ab27369	CXCR2 (IL8RB) CXCR1 (IL8RA) DARC
CXCL9	MIG	Produced by stimulated monocytes, macrophages and endothelial cells. Selectively chemoattracts Th1 lymphocytes and also exerts other activities including inhibition of tumor growth, angiogenesis and inhibition of colony formation of hematopoietic progenitors. Human CXCL9 is active on murine cells.	ab9720 ab17703	CXCR3 beta isoform (CD183b)
CXCL10	IP-10	Chemoattractant for CD4+ T cells and inhibits early normal and leukemic hematopoietic progenitor proliferation. Produced by a wide variety of cell types ranging from neutrophils to hepatocytes, endothelial cells and keratinocytes. Involved in a variety of inflammatory pathologies such as HIV encephalitis, cutaneous T cell lymphoma and chronic hepatitis. Strongly suggested in the regulation of angiogenic activity in cancer.	ab9938 ab8399	CXCR3 beta isoform (CD183b)
CXCL11	I-TAC	Chemoattractant for interleukin-activated T cells but not unstimulated T cells, neutrophils or monocytes. Induces calcium release in activated T cells. It may play an important role in CNS diseases which involve T cell recruitment and in skin immune responses. Expressed at high levels in peripheral blood leukocytes, pancreas and liver astrocytes and at moderate levels in thymus, spleen and lung. Induced by IFN gamma and IFN beta.	ab9955 ab26946	CXCR3 beta isoform (CD183b)
CXCL12	SDF-1α/β	A strong chemoattractant for lymphocytes. Binding to its receptor inhibits HIV1 entry. During embryogenesis, CXCL12 directs migration of hematopoietic cells from fetal liver to bone marrow and the formation of large blood vessels. In adulthood it plays an important role in angiogenesis by recruiting endothelial progenitor cells. A very important factor in carcinogenesis and the neovascularisation linked to tumor progression.	ab9797 ab18919	CXCR4
CXCL13	BCA-1	Strongly expressed in the follicles of the spleen, lymph nodes, and Peyer's patches. Preferentially promotes the migration of B lymphocytes (compared to T cells and macrophages), apparently by stimulating calcium influx into, and chemotaxis of, cells expressing Burkitt's lymphoma receptor 1 (BLR1). It may therefore function in the homing of B lymphocytes to follicles.	ab33178 ab9975	CXCR5
CXCL14	BRAK (breast and kidney-expressed chemokine) / Bolekine	Constitutively expressed at the mRNA level in certain normal tissues but absent from many established tumor cell lines / cancers. A chemoattractant for monocytes and can activate these cells in the presence of an inflammatory mediator prostaglandin-E2. Also a potent chemoattractant and activator of dendritic cells. It is implicated in homing of these cells and can stimulate the migration of activated NK cells. Also inhibits angiogenesis, possibly as a result of its ability to block endothelial cell chemotaxis.	ab46010 ab46008	Unknown
CXCL15	Lungkine	Recruits neutrophils during lung inflammation. It is abundant in epithelial cells of the murine lung, and can also be found in other mucosal and endocrine organs and to a lesser extent in certain fetal tissues. No human homolog has been identified and a specific cell surface receptor has not yet been found.	CXCL15 protein (ab49907)	unknown
CXCL16	Small inducible cytokine B6	Acts as a scavenger receptor on macrophages, which specifically binds to oxidized low density lipoprotein, suggesting that it may be involved in pathophysiologies such as atherogenesis. Produced by dendritic cells found in the T cell zones of lymphoid organs and by cells found in the red pulp of the spleen. In response to the inflammatory cytokines IFN gamma and TNF alpha. Expressed as a cell surface bound molecule or a soluble chemokine. Chemoattractant for several subsets of T cells and natural killer T cells.	ab27222 ab27222	CXCR6

Beta chemokines (CC)

Chemokine	Alternative names	Role/expression	AbID	Main receptors
CCL1	1-309 (TCA-3), Scya1	Glycoprotein secreted by activated T cells. Attracts monocytes, NK cells, and immature B cells and dendritic cells by interacting with a cell surface chemokine receptor CCR8.		CCR8
CCL2	MCP-1 / MCAF(JE)	Chemoattractant for monocytes and basophils but not neutrophils or eosinophils. Augments monocyte anti-tumor activity. CCL2 is implicated in the pathogenesis of diseases characterized by monocytic infiltrates like psoriasis, rheumatoid arthritis and atherosclerosis. It may be involved in the recruitment of monocytes into the arterial wall during the disease process of atherosclerosis.	ab7202 ab21554 ab17424	CCR2 CCR11 DARC
CCL3	MIP-1a / LD78α	Expressed primarily in T cells, B cells, and monocytes after antigen or mitogen stimulation. Adhesive effects on lymphocytes. CCL3 can inhibit the proliferation of hematopoietic stem cells.	ab9673 ab62137	CCR1 CCR5

Beta chemokines (CC) (Continued)

Chemokine	Alternative names	Role/expression	AbID	Main receptors
CCL3L1	LD78β gene duplication	Closely related to CCL3. Its receptor CCR5 is a co-receptor for HIV; binding of CCL3L1 to CCR5 inhibits HIV entry, and CCL3L1 has been shown to exhibit potent activity in HIV suppression assays.	ab36129	CCR5 Chemokine binding protein 2
CCL4	LAG-1 gene duplication, MIP-1β	Chemoattractant and adhesive effects on lymphocytes, preferentially attracting CD4+ T cells.	ab9675 ab10384	CCR1 CCR5
CCL5	RANTES	Chemoattractant for monocytes, memory T helper cells and eosinophils. It causes the release of histamine from basophils and activates eosinophils. One of the major HIV suppressive factors produced by CD8+ T cells.	ab9679 ab11455	CCR1 CCR3 CCR4 CCR5 DARC
CCL6	(C-10 / MRP-2)	Chemoattractant only expressed in rodents. In mice, expressed in cells from neutrophil and macrophage lineages, and can be induced under conditions suitable for myeloid cell differentiation. CCL6 is highly expressed in bone marrow cultures that have been stimulated with the cytokine GM-CSF and can be induced in the mouse lung by IL13. In activated T cell lines, expression of CCL6 is greatly reduced.	ab10351 ab33835	CCR1 CCR2 CCR3
CCL7	MCP-3	Secreted chemokine which attracts macrophages during inflammation and metastasis. The protein is an in vivo substrate of matrix metalloproteinase 2, an enzyme which degrades components of the extracellular matrix.	ab9681 ab12732	CCR1 CCR2 CCR3
CCL8	MCP-2	Chemoattractant for monocytes, lymphocytes, basophils and eosinophils. Important to inflammatory host responses and is found in the highest concentration in the small intestine and peripheral blood cells.	ab10392 ab39627	CCR1 CCR2 CCR5 CCR11
CCL9/10	MIP-1γ MRP-2	Mediates hepatobiliary excretion of numerous organic anions and may function as a cellular cisplatin transporter, with highest expression in liver. CCL9/10 is a member of the MRP family of multidrug resistance related proteins, and its overexpression has been observed in a subset of cisplatin resistant cell lines. Defects in CCL9/10 are the cause of Dubin-Johnson syndrome.	ab3373	CCR1
CCL11	Eotaxin	Regulates the recruitment and activation of inflammatory leukocytes, particularly eosinophils. May play a fundamental role in the development of allergic responses.	ab8018 ab25904	CCR3
CCL12	MCP-5	A strong chemoattractant for human monocytes and murine peritoneal macrophages. Exhibits only a weak response on mouse eosinophils at high concentrations and is not active on mouse neutrophils.	ab18938 ab9737	CCR2
CCL13	MCP-4	Similar to CCL7. Powerful eosinophil chemoattractant. Induces chemotaxis of monocytes and T lymphocytes.	ab9558 ab17551	CCR1 CCR2 CCR3 CCR11
CCL14	HCC-1	Produced as a precursor which is processed to generate a mature active protein exhibiting 46% amino acid homology to CCL3 and CCL4. Expressed in various tissues including spleen, bone marrow, liver, muscle and gut.	ab14528 ab55752	CCR1
CCL15	HCC-2 / LKN-1 / MIP-1δ / MIP-5	Induces changes in intracellular calcium concentration in monocytes. CCL15 is thought to act through the CCR1 receptor but also binds to CCR3.	ab14531 ab17707	CCR1 CCR3
CCL16	HCC-4 / LEC	Chemoattractant for lymphocytes and monocytes but not for neutrophils. It also shows a potent myelosuppressive activity and suppresses proliferation of myeloid progenitor cells. Its expression is upregulated by IL10.	ab626 ab17439	CCR1
CCL17	TARC (ABCD-2)	Chemoattractant for T lymphocytes but not monocytes or granulocytes. CCL17 binds to chemokine receptors CCR4 and CCR8. This chemokine plays important roles in T cell development in the thymus as well as in trafficking and activation of mature T cells.	ab9816 ab30975	CCR4 DARC
CCL18	MIP-4 / DC-CK1 / PARC / AMAC-1	A chemoattractant for lymphocytes but not monocytes or granulocytes. Specifically, it attracts naive T cells, CD4+ and CD8+ T cells and thus may play a role in both humoral and cell-mediated immunity. Some evidence suggests that CCL18 may also be involved in B cell migration into lymph nodes. Expressed at high levels in lung, lymph nodes, placenta, and bone marrow.	ab9849 ab12749	unknown
CCL19	MIP-3β / ELC / Exodus 3	Constitutively expressed in various lymphoid tissues. The level of expression can be strongly up-regulated by inflammatory signals or down-regulated by the anti-inflammatory cytokine IL10. Attracts cultured human lymphcytes, dendritic cells, human T and hematopoietic progenitor cells.	ab9351 ab9831	CCR7
CCL20	MIP-3a / LARC/ Exodus 1	Chemoattractant that attracts lymphocytes and neutrophils, but not monocytes. CCL20 inhibits proliferation of myeloid progenitors in colony formation assays. It may be involved in formation and function of the mucosal lymphoid tissues by attracting lymphocytes and dendritic cells towards epithelial cells.	ab9349 ab9829	CCR6
CCL21	6Ckine / SLC / Exodus 2	Research indicates that CCL21 influences lymphocyte homing to secondary lymphoid organs, integrin-mediated lymphocyte adhesion, and may act via the EBI1 ligand chemokine (ELC) receptor, CCR7. Chemoattractant for thymocytes and activated T cells. CCL21 is a known receptor for small inducible cytokine A19 (another member of the cytokine family).	ab10364 ab10350	CCR7
CCL22	MDC / STCP-1 / (ABCD-1)	Chemoattractant for natural killer cells, chronically activated T lymphocytes, monocytes and dendritic cells. It has no chemoattractant activity for eosinophils, neutrophils or resting T lymphocytes. May play a role in the trafficking of activated T lymphocytes to inflammatory sites and other aspects of their physiology.	ab53002 ab10379	CCR4
CCL23	MPIF-1 / MIP-3 / CKβ-8	Chemoattractant for monocytes, resting T-lymphocytes and neutrophils. Inhibits proliferation of myeloid progenitor cells and is highly expressed in adult lung, liver, skeletal muscle and pancreas. There are moderate levels of CCL23 in fetal liver, adult bone marrow and placenta.	ab9929 ab62138	CCR1
CCL24	MPIF-2 / Eotaxin-2	Like CCL11, activates and attracts eosinophils and basophils. CCL24 mRNA is weakly expressed in activated monocytes and T lymphocytes. Inhibits colony formation in myeloid progenitor cells.	ab10370 ab62306	CCR3
CCL25	TECK	Chemoattractant for dendritic cells, thymocytes and activated macrophages, but is inactive on peripheral blood lymphocytes and neutrophils.	ab2164 ab2164	CCR9
CCL26	Eotaxin-3	Expressed by several tissues including heart, lung and ovary and in endothelial cells that have been stimulated with the cytokine IL4. Chemoattractant for eosinophils and basophils.		CCR3
CCL27	CTAK / ILC (ESkine)	Attracts skin-associated memory T-lymphocytes. CCL27 may play a role in mediating homing of lymphocytes to cutaneous sites.	ab36771	CCR3, CCR2, CCR10
CCL28	MEC	Chemoattractant for resting CD4 or CD8 T cells and eosinophils. It induces calcium mobilization in a dose-dependent manner and may play a role in the physiology of extracutaneous epithelial tissues, including diverse mucosal organs.	ab36692 ab37326	CCR10, CCR3

Gamma chemokines (C)

Chemokine	Alternative names	Role/expression	AbID	Main receptors
XCL1	Lymphotactin	Expression is restricted to activated CD8+ T cells and other class I MHC restricted T cells (absent in CD4+ T cells). Produced by lymphocytes and acts on both lymphocytes and NK cells, indicating a possible messenger role in T cell chemoattraction. No activity is exerted on monocytes or neutrophils. It has recently been shown that XCL1 is a key regulator of lymphocyte motility and adhesion during acute allograft rejection.	ab51795 ab9955	XCR1
XCL2	SCM-1b	Predominantly expressed in activated T cells. Also found at low levels in unstimulated cells. Induces chemotaxis of cells expressing the chemokine receptor XCR1.		XCR1

Delta chemokines (CX3C)

Chemokine	Alternative names	Role/expression	AbID	Main receptors
CX3CL1	Fractalkine (neurotactine)	Leukocyte chemoattractant expressed in various tissues including brain, heart, lung, kidney, skeletal muscle and testis. Up-regulated in endothelial cells and microglia by inflammatory signals. It's receptor, CX3CR1, a specific receptor for CX3CL1, mediates both leukocyte migration and adhesion.	ab25088 ab17514	CX3R1

Alpha chemokine receptors

Receptor	Alternative names	Role/expression	AbID
CXCR1	IL8RA	Expressed on neutrophils.	ab13018 ab38989 ab38991 ab8042
CXCR2	IL8RB	Expressed on neutrophils.	ab14935 ab38998 ab39007 ab8042
CXCR3 beta isoform	CD183b	Predominantly expressed on T lymphocytes, and also on other lymphocytes (some B cells and NK cells).	ab10402
CXCR4		Highly expressed in brain, heart, white blood cells, vascular endothelial cells and umbilical cord endothelial cells.	ab2074 ab1671
CXCR5		Specifically expressed in Burkitt's lymphoma and lymphatic tissues, such as follicles in lymph nodes as well as in spleen.	ab12965 ab19017

Beta chemokine receptors

Receptor	Alternative names	Role/expression	AbID
CCR1		Expressed on peripheral blood lymphocytes and monocytes. There is some suggestion that this chemokine receptor is restricted to memory T-cells within the lymphocyte pool. This receptor is also designated cluster of differentiation marker CD191	ab1681 ab13240
CCR2	CD192	Expressed on the surface of monocytes, activated memory T cells, B cells and basophils in humans, and also in peritoneal macrophages in mice. It is a receptor for several monocyte chemoattractant proteins (CCL2, CCL7, CCL13) which specifically mediate monocyte chemotaxis.	ab32144 ab1668
CCR3		Receptor for CCL11 and CCL24. Expressed in blood, brain, lung, bone marrow, kidney, liver, lymph node, placenta, skin, spleen, thymus, thyroid and uterus. Within these tissues, CCR3 is expressed in specific cell types, including eosinophils, basophils, Th2 cells, CD34+ hematopoietic progenitors, keratinocytes and mast cells. The agonists for CXCR3 (CXCL9, CXCL10, CXCL11) act as antagonists for CCR3 by competing for the binding of CCL11 / CCL24 to CCR3. CCR3 is thought to play a key role in allergic diseases and is a co-receptor for HIV 1 and 2.	ab1667 ab32512
CCR4		CCR4 is preferentially expressed on Th2-type cells. In contrast to other chemokine receptors, the expression of CCR4 and CCR8 is transiently increased following TCR and CD28 engagement. Activated Th1 cells up-regulate CCR4 expression and functional responsiveness to thymus- and activation-regulated chemokine.	ab1669 ab59550
CCR5		Expressed on several cell types including peripheral blood-derived dendritic cells, CD34+ hematopoietic progenitor cells and certain activated / memory Th1 lymphocytes. Major co-receptor implicated in susceptibility to HIV-1 infection and disease.	ab1673 ab32048
CCR6		Preferentially expressed by immature dendritic cells and memory T cells where it may regulate the migration and recruitment of dendritic and T cells during inflammatory and immunological responses. Important for B lineage maturation and antigen driven B cell differentiation.	ab1659 ab13168
CCR7		Expressed in lymphoid tissues and in activated B and T lymphocytes, and has been shown to control the migration of memory T cells to inflamed tissues, stimulate dendritic cell maturation and is thought to be a mediator of EBV effects on B lymphocytes. The chemokine CCL19 has been reported to be a specific ligand of this receptor.	ab1657 ab25790
CCR8		This receptor is preferentially expressed in the thymus. Studies of this receptor and its ligands suggest a role in the regulation of monocyte chemotaxis and thymic cell apoptosis. CCR8 may contribute to the proper positioning of activated T cells within the antigenic challenge sites and specialized areas of lymphoid tissues. CCR8 expression has been reported in spleen and thymus, natural killer cells, monocytes and T cells, and at lower levels in peripheral blood leukocytes.	ab1663 ab32399
CCR9		Expressed in a range of tissues and hematopoietic cells. Functions in chemokine-driven recirculation of leukocytes and possible chemokine effects on the development and growth of vascular tumors. This receptor appears to bind the majority of beta-chemokine family members but specific function remains unknown. The differential expression of CCR9 by T lymphocytes of the small intestine and colon suggests a role in the functional specialization of immune responses in different segments of the gastrointestinal tract.	ab1662 ab38567
CCR10		Receptor for the skin-associated chemokine CCL27 as well as the novel chemokine CCL28. Associated with Th2 lymphocytes, found predominantly in the thymus. In humans,Some expression can be found in the brain, spleen, lymph node and monocytes at the nucleotide level.	ab3904 ab30718
CCR11		Specifically binds the monocyte chemoattractant protein family of chemokines, including CCL13, CCL8, and CCL2. Also binds CCL11.	ab1660 ab32564

Delta chemokine receptors

Receptor	Alternative names	Role/expression	AbID
CX3CR1		Expressed in a variety of human tissues and cell lines where it mediates leukocyte migration and adhesion. Receptor for the novel transmembrane molecule CX3CL1, and is a co-receptor for HIV-1 and HIV-2 envelope fusion and virus infection, which can be inhibited by binding of CX3CL1. Also implicated in tumor metastasis.	ab8021 ab7200

Other chemokine receptors

Receptor	Alternative names	Role/expression	AbID
DARC		A non-specific receptor for many chemokines such as CXCL8, CXCL1, CCL5, CCL2 and CCL17. It is also the receptor for the human malaria parasites Plasmodium vivax and Plasmodium knowlesi. It is also responsible for the Duffy blood group system.	ab40821 ab58965

Image: Transmission electron micrograph of a mast cell. Courtesy of the Biomedical Imaging Unit, University of Southampton, UK