Chemokine receptors (version 2019.4) in the IUPHAR/BPS Guide to Pharmacology Database

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Abstract

Chemokine receptors (nomenclature as agreed by the NC-IUPHAR Subcommittee on Chemokine Receptors [417, 416, 31]) comprise a large subfamily of 7TM proteins that bind one or more chemokines, a large family of small cytokines typically possessing chemotactic activity for leukocytes. Additional hematopoietic and non-hematopoietic roles have been identified for many chemokines in the areas of embryonic development, immune cell proliferation, activation and death, viral infection, and as antibiotics, among others. Chemokine receptors can be divided by function into two main groups: G protein-coupled chemokine receptors, which mediate leukocyte trafficking, and "Atypical chemokine receptors", which may signal through non-G protein-coupled mechanisms and act as chemokine scavengers to downregulate inflammation or shape chemokine...
Chemokines in turn can be divided by structure into four subclasses by the number and arrangement of conserved cysteines. CC (also known as β-chemokines; \( n = 28 \)), CXC (also known as α-chemokines; \( n = 17 \)) and CX3C \( (n = 1) \) chemokines all have four conserved cysteines, with zero, one and three amino acids separating the first two cysteines respectively. C chemokines \( (n = 2) \) have only the second and fourth cysteines found in other chemokines. Chemokines can also be classified by function into homeostatic and inflammatory subgroups. Most chemokine receptors are able to bind multiple high-affinity chemokine ligands, but the ligands for a given receptor are almost always restricted to the same structural subclass. Most chemokines bind to more than one receptor subtype. Receptors for inflammatory chemokines are typically highly promiscuous with regard to ligand specificity, and may lack a selective endogenous ligand. G protein-coupled chemokine receptors are named according to the class of chemokines bound, whereas ACKR is the root acronym for atypical chemokine receptors \[32\]. There can be substantial cross-species differences in the sequences of both chemokines and chemokine receptors, and in the pharmacology and biology of chemokine receptors. Endogenous and microbial non-chemokine ligands have also been identified for chemokine receptors. Many chemokine receptors function as HIV co-receptors, but CCR5 is the only one demonstrated to play an essential role in HIV/AIDS pathogenesis. The tables include both standard chemokine receptor names \[657\] and aliases.

**Contents**

This is a citation summary for Chemokine receptors in the Guide to Pharmacology database (GtoPdb). It exists purely as an adjunct to the database to facilitate the recognition of citations to and from the database by citation analyzers. Readers will almost certainly want to visit the relevant sections of the database which are given here under database links.

GtoPdb is an expert-driven guide to pharmacological targets and the substances that act on them. GtoPdb is a reference work which is most usefully represented as an on-line database. As in any publication this work should be appropriately cited, and the papers it cites should also be recognized. This document provides a citation for the relevant parts of the database, and also provides a reference list for the research cited by those parts.

Please note that the database version for the citations given in GtoPdb are to the most recent preceding version in which the family or its subfamilies and targets were substantially changed. The links below are to the current version. If you need to consult the cited version, rather than the most recent version, please contact the GtoPdb curators.

**Database links**

Chemokine receptors
http://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=14
Introduction to Chemokine receptors
http://www.guidetopharmacology.org/GRAC/FamilyIntroductionForward?familyId=14

Receptors

CCR1
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=58
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CCR4
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=61
CCR5
References


52. Ben-Baruch A, Grimm M, Bengali K, Evans GA, Chertov O, Wang JM, Howard OM, Mukaida N,
Matsushima K and Oppenheim JJ. (1997) The differential ability of IL-8 and neutrophil-activating peptide-2 to induce attenuation of chemotaxis is mediated by their divergent capabilities to phosphorylate CXCR2 (IL-8 receptor B). *J. Immunol.* **158**: 5927-33 [PMID:9190946]


61. Blednov YA, Bergeson SE, Walker D, Ferreira VM, Kuziel WA and Harris RA. (2005) Perturbation of...


78. Brumme ZL, Dong WW, Chan KJ, Hogg RS, Montaner JS, O'Shaughnessy MV and Harrigan PR. (2003) Influence of polymorphisms within the CX3CR1 and MDR-1 genes on initial antiretroviral therapy response. AIDS 17: 201-8 [PMID:12545080]


97. Castellucci L, Jamieson SE, Miller EN, Menezes E, Oliveira J, Magalhães A, Guimarães LH, Lessa M, de Jesus AR and Carvalho EM et al. (2010) CXCR1 and SLC11A1 polymorphisms affect susceptibility to


142. CytoDyn. PRO 140


used by simian and human immunodeficiency viruses. Nature 388: 296-300 [PMID:9230441]


Prevention of crescentic glomerulonephritis by immunoneutralization of the fractalkine receptor CX3CR1 rapid communication. *Kidney Int.* **56**: 612-20 [PMID:10432400]


Fox JC, Nakayama T, Tyler RC, Sander TL, Yoshie O and Volkman BF. (2015) Structural and agonist properties of XCL2, the other member of the C-chemokine subfamily. *Cytokine* **71**: 302-11 [PMID:25497737]


BLR1, directs B cell migration to defined lymphoid organs and specific anatomic compartments of the spleen. *Cell* 87: 1037-47 [PMID:8978608]


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ligand of the constitutively recycling atypical human chemokine receptor CRAM-B. *Immunology* **129**: 536-46 [PMID:20002784]


357. Liu FY, Safdar J, Li ZN, Fang QG, Zhang X, Xu ZF and Sun CF. (2014) CCR7 regulates cell migration and invasion through MAPKs in metastatic squamous cell carcinoma of head and neck. *Int. J. Oncol.* **45**: 2502-10 [PMID:25270024]


408. Murakami T, Cardones AR, Finkelstein SE, Restifo NP, Klaunberg BA, Nestle FO, Castillo SS, Dennis PA


504. Sato N, Ahuja SK, Quinones M, Kostecki V, Reddick RL, Melby PC, Kuziel WA and Ahuja SS. (2000) CC chemokine receptor (CCR)2 is required for langerhans cell migration and localization of T helper cell type 1 (Th1)-inducing dendritic cells. Absence of CCR2 shifts the Leishmania major-resistant phenotype to a susceptible state dominated by Th2 cytokines, β cell outgrowth, and sustained neutrophilic inflammation. *J. Exp. Med.* **192**: 205-18 [PMID:10899907]


Smith MW, Dean M, Carrington M, Winkler C, Huttley GA, Lomb DA, Goedert JJ, O'Brien TR, Jacobson LP and Kaslow R et al. (1997) Contrasting genetic influence of CCR2 and CCR5 variants on HIV-1 infection and disease progression. *Hemophilia Growth and Development Study (HGDS), Multicenter AIDS Cohort Study (MACS), Multicenter Hemophilia Cohort Study (MHCS), San Francisco City Cohort (SFCC), ALIVE Study. Science** **277**: 959-65  


Speterslage J, Frank S, Heneweer C, Egberts J, Schniewind B, Buchholz M, Bergmann F, Giese N,


Coincidence of elevated Lp(a) and MCP-1 -2518 G/G genotype in CAD patients. *Atherosclerosis* **158**: 233-9 [PMID:11500196]


564. Traynor TR, Kuziel WA, Toews GB and Huffnagle GB. (2000) CCR2 expression determines T1 versus T2
polarization during pulmonary Cryptococcus neoformans infection. *J. Immunol.* **164**: 2021-7


PMID:20660125


Expression cloning of the STRL33/BONZO/TYMSTR ligand reveals elements of CC, CXC, and CX3C chemokines. *J. Immunol.* **166**: 5145-54 [PMID:11290797]


