

Gene name: **CCR2**    Previous HGNC Symbols for CCR2 Gene: CMKBR2

**External Ids for CCR2 Gene:** HGNC: [1603](#)    NCBI Gene: [729230](#)    Ensembl: [ENSG00000121807](#)  
OMIM®: [601267](#)    UniProtKB/Swiss-Prot: [P41597](#)

**NCBI Gene Summary:** The protein encoded by this gene is a receptor for monocyte chemoattractant protein-1, a chemokine which specifically mediates monocyte chemotaxis. Monocyte chemoattractant protein-1 is involved in monocyte infiltration in inflammatory diseases such as rheumatoid arthritis as well as in the inflammatory response against tumors. The encoded protein mediates agonist-dependent calcium mobilization and inhibition of adenylyl cyclase. This protein can also be a coreceptor with CD4 for HIV-1 infection. This gene is located in the chemokine receptor gene cluster region of chromosome 3.

**GeneCards Summary:** CCR2 (C-C Motif Chemokine Receptor 2) is a Protein Coding gene. Diseases associated with CCR2 include [Polycystic Lung Disease](#) and [Human Immunodeficiency Virus Type 1](#). Among its related pathways are [Class A/1 \(Rhodopsin-like receptors\)](#) and [GPCR downstream signalling](#). Gene Ontology (GO) annotations related to this gene include *G protein-coupled receptor activity* and *chemokine receptor activity*. An important paralog of this gene is [CCR5](#).

**UniProtKB/Swiss-Prot Summary:** Key functional receptor for CCL2 but can also bind CCL7, and CCL12 (PubMed:[23408426](#), [38157855](#), [8048929](#), [8146186](#)). Also transduces signaling mediated by CCL13 (PubMed:[38157855](#)). Its binding with CCL2 on monocytes and macrophages mediates chemotaxis and migration induction through the activation of the PI3K cascade, the small G protein Rac and lamellipodium protrusion (PubMed:[38157855](#)). Also acts as a receptor for the beta-defensin DEFB106A/DEFB106B (PubMed:[23938203](#)). Regulates the expression of T-cell inflammatory cytokines and T-cell differentiation, promoting the differentiation of T-cells into T-helper 17 cells (Th17) during inflammation (By similarity). Facilitates the export of mature thymocytes by enhancing directional movement of thymocytes to sphingosine-1-phosphate stimulation and up-regulation of S1P1R expression; signals through the JAK-STAT pathway to regulate FOXO1 activity leading to an increased expression of S1P1R (By similarity). Plays an important role in mediating peripheral nerve injury-induced neuropathic pain (By similarity). Increases NMDA-mediated synaptic transmission in both dopamine D1 and D2 receptor-containing neurons, which may be caused by MAPK/ERK-dependent phosphorylation of GRIN2B/NMDAR2B (By similarity). Mediates the recruitment of macrophages and monocytes to the injury site following brain injury (By similarity). ( [CCR2\\_HUMAN,P41597](#) )

**Cellular localization:** mainly nucleus, plasma membrane.

**Full Name:** C-C Motif Chemokine Receptor 2

**Protein Type:** G protein-coupled receptor (GPCR)

**Main Ligands:** Primarily binds CCL2 (MCP-1), but also CCL7, CCL8, CCL13



## Biological Function

CCR2 is a chemokine receptor expressed on:

- **Monocytes (especially inflammatory monocytes)**
- **Macrophages**

- T cells
- Dendritic cells
- Basophils

## Key Functions:

Chemotaxis: Recruits immune cells to sites of inflammation or infection.

Monocyte mobilization: Critical for moving monocytes from bone marrow into circulation and to tissues.

Vascular inflammation: Involved in leukocyte-endothelial interactions.

Tissue remodeling: Participates in wound healing, fibrosis, and angiogenesis

## CCR2 in Sepsis

CCR2 plays a major role in the **innate immune response** to infection and sepsis pathophysiology.

### During Early Sepsis:

- CCL2–CCR2 axis drives recruitment of inflammatory monocytes to:
  - Infected tissues (e.g., lungs in pneumonia)
  - Circulation (via bone marrow mobilization)
- Enhances cytokine release, including IL-6, IL-1 $\beta$ , and TNF- $\alpha$
- Contributes to organ damage via excessive immune cell infiltration

### During Later/Resolution Phase:

- CCR2+ monocytes contribute to tissue repair, phagocytosis, and anti-inflammatory signaling

## Experimental Evidence

### Animal Models:

- CCR2 knockout mice show:
  - Reduced leukocyte infiltration into infected organs
  - Protection from septic shock, depending on infection severity
  - Delayed clearance of pathogens, in some cases (impaired host defense)

### Protein Studies:

- Serum CCL2 levels correlate with sepsis severity, and indirectly reflect CCR2 activity.



## Clinical Relevance

### Diagnostic:

- Upregulated in early-stage sepsis on circulating monocytes
- CCL2/CCR2 axis is used as a marker of monocyte-driven inflammation

### Prognostic:

- High CCR2 expression linked to:
  - Worse outcomes in sepsis (when overexpressed)
  - Increased risk of acute respiratory distress syndrome (ARDS)



### Therapeutic Target:

- CCR2 antagonists are under investigation (e.g., for COVID-19 inflammation, cancer, atherosclerosis).
- May modulate immune cell infiltration in severe infection, including sepsis.



## Pathways Involving CCR2

Chemokine signaling (hsa04062): Major receptor for MCP-1/CCL2.

Cytokine-cytokine receptor interaction: Initiates downstream pro-inflammatory cascades.

Leukocyte transendothelial migration: Promotes monocyte extravasation.

Sepsis inflammatory modules: Upstream regulator in immune cell recruitment.



## Supporting Literature

Doi: 10.1164/rccm.201003-0416OC .

Doi: 10.1002/JLB.4MR0820-049RR

Doi: 10.1016/j.jamcollsurg.2015.07.083

## KEGG:

