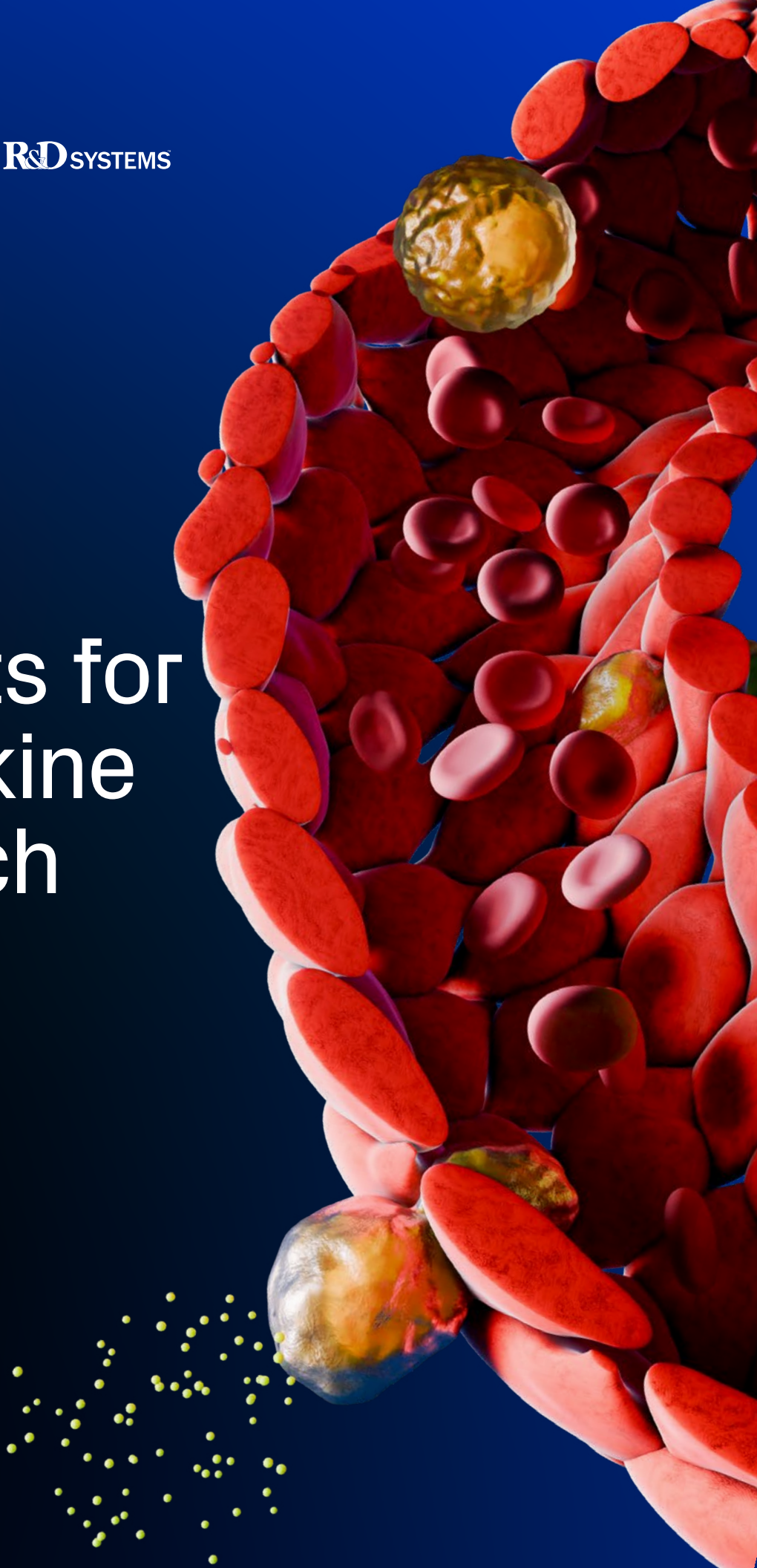


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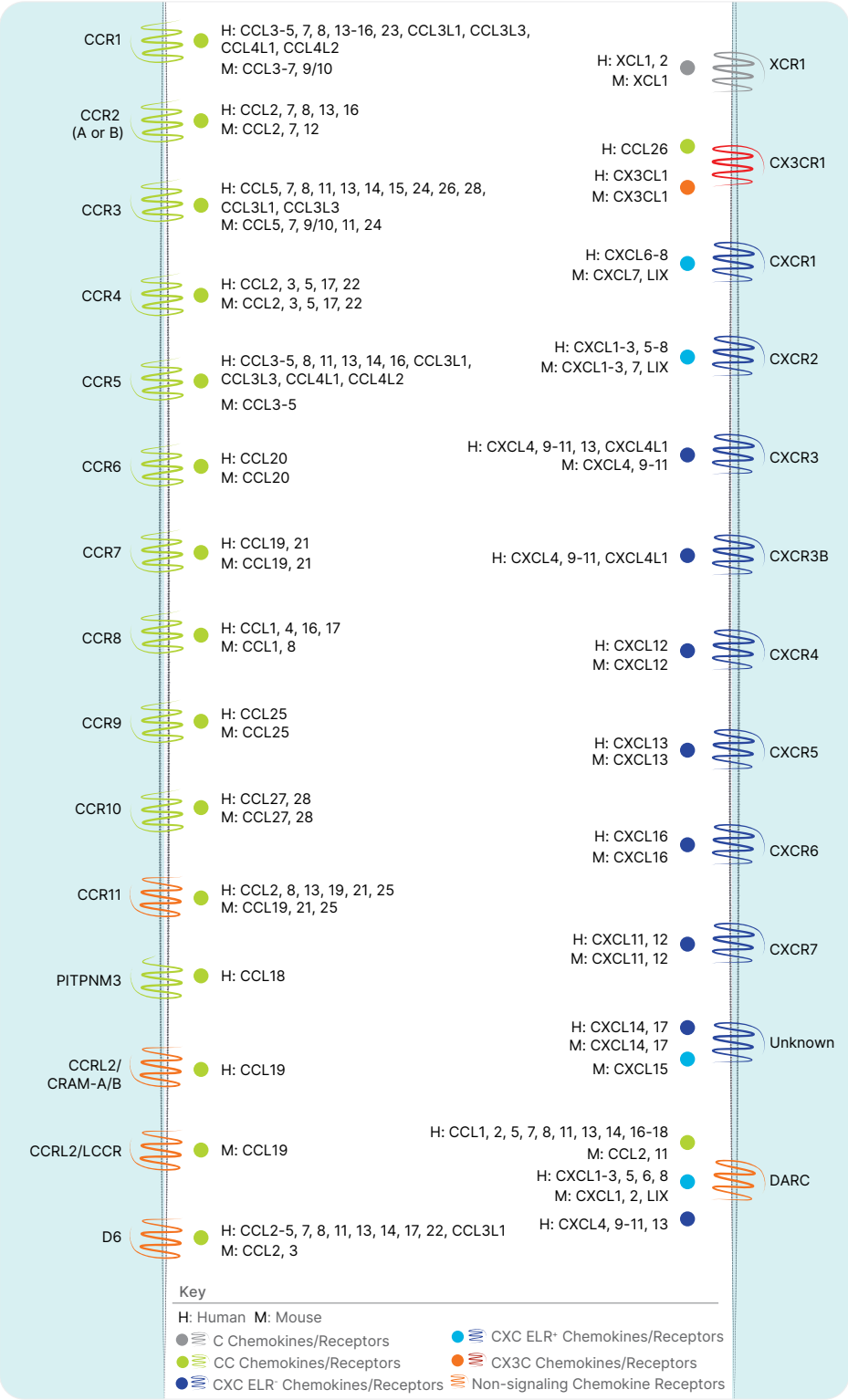
The Chemokine Family

Chemokines are small cell surface-localized or secreted chemotactic cytokines that bind to and activate specific G protein-coupled chemokine receptors. Most chemokines have at least four conserved N-terminal cysteine residues that form two intramolecular disulfide bonds. Four chemokine subfamilies (CXC, CC, C and CX3C) have been defined based upon the placement of the first two cysteine residues.^{1,2} The CXC chemokine subfamily is characterized by two cysteine residues separated by one amino acid. Within this subfamily, two CXC classes are further defined by the presence or absence of an ELR motif sequence. ELR- CXC chemokines act as chemoattractants for lymphocytes, while ELR+ CXC chemokines are chemoattractants for neutrophils. Additionally, CXC chemokines can mediate angiogenesis.³ The CC chemokine subfamily is defined by two adjacent cysteine residues. CC chemokines induce inflammatory responses via regulation of monocyte, macrophage, mast cell, and T cell migration.⁴ C chemokines are characterized by a single cysteine residue and are constitutively expressed in the thymus where they regulate T cell differentiation.⁵ The CX3C chemokine subfamily is defined by two cysteine residues separated by three amino acids. Cell surface-localized CX3CL1/ Fractalkine mediates leukocyte adhesion while soluble CX3CL1/Fractalkine is chemotactic for leukocytes.⁶ CX3CL1/Fractalkine is also a critical regulator of microglia-neuron communication during neural development.⁷

While chemokine receptors generally bind only one subfamily of chemokines, within those subfamilies, most chemokines display promiscuous receptor binding patterns.^{1,2} The redundancy of chemokine ligand-receptor binding may ensure robust signaling. In addition, promiscuous binding and non-signaling chemokine receptors offer mechanisms by which chemokine signaling can be regulated by either subtle differences in receptor signaling or differences in ligand-receptor expression patterns.⁸ Select chemokine ligands and receptors are implicated in HIV infection and persistence, while aberrant chemokine expression and signaling is associated with pathological conditions including inflammatory diseases and cancer.^{1,2,9-11}

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CXC Chemokines

CXC chemokines, also known as α chemokines, are critical regulators of normal development and immune responses. The CXC chemokine subfamily consists of nineteen ligands and seven receptors. CXC chemokines that contain an ELR motif are potent angiogenic factors, while ELR- CXC chemokines are angiostatic. Select CXC chemokines and receptors regulate hematopoietic stem cell migration. They are also involved in regulating tumor progression and are of interest as targets for therapeutic intervention.¹⁻³

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TABLE // 01

CXC Chemokine Receptors

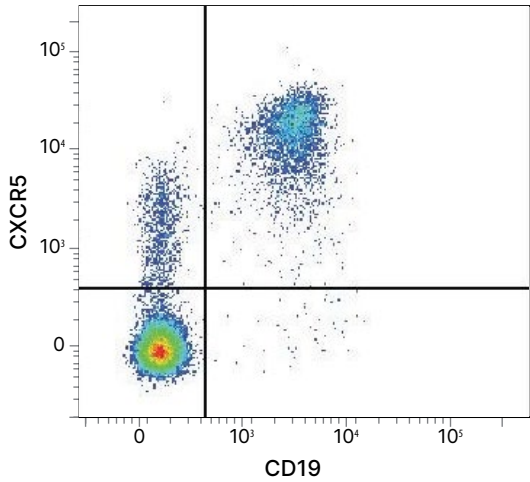
Molecule	Antibodies	Tocris Small Molecule Agonists & Antagonists
CXCR1/ IL-8 RA	H (B/N, FC, IHC) M (FC)	
CXCR2/ IL-8 RB	H (B/N, FC, IHC) M (B/N, FC, IHC) R (FC)	✓
CXCR3	H (B/N, FC, IHC) M (FC) R (FC)	
CXCR4	H (B/N, FC, IHC) M (B/N, FC, ICC, IHC) F (FC, ICC)	✓
CXCR5	H (B/N, FC, ICC, IHC) M (FC, ICC)	
CXCR6	H (FC) M (FC)	
CXCR7/ RDC-1	H (FC,IHC) M (FC,WB)	✓
DARC	H (FC, ICC) M (FC, IHC, WB) R (FC, IHC, WB)	

SPECIES KEY

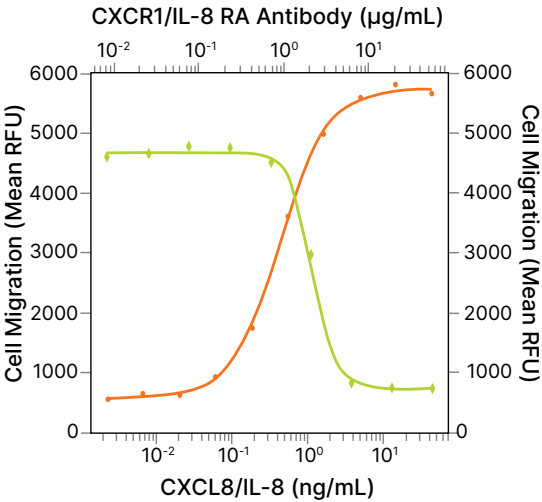
H Human, M Mouse, R Rat, B Bovine, Ca Canine, CR Cotton Rat, F Feline, P Porcine, RM Rhesus Macaque, V Viral

APPLICATION KEY

B/N Blocking/Neutralization, E ELISA (Cap. or Det.), FC Flow Cytometry, ICC Immunocytochemistry, IHC Immunohistochemistry, IP Immunoprecipitation, WB Western Blot



Detection of CXCR5 in CD19+ Human PBMCs by Flow Cytometry. Human peripheral blood mononuclear cells (PBMCs) were stained with a Fluorescein-conjugated Mouse Anti-Human CD19 Monoclonal Antibody (Catalog # FAB4867F) and an APC-conjugated Mouse Anti-Human CXCR5 Monoclonal Antibody (Catalog # FAB190A).



Chemotaxis Induced by CXCL8/IL-8 and Neutralization using a Human CXCR1/IL-8 RA Antibody. Recombinant Human CXCL8/IL-8 (Catalog # 208-IL) chemoattracts the BaF3 mouse pro-B cell line transfected with human CXCR1/IL-8 RA in a dose-dependent manner (orange line). The amount of cells that migrated through to the lower chemotaxis chamber was measured by Resazurin (Catalog # AR002). Chemotaxis elicited by 1 ng/mL Recombinant Human CXCL8/IL-8 was neutralized by increasing concentrations of Human CXCR1/IL-8 RA Monoclonal Antibody (Catalog # MAB330; green line).



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TABLE // 02

CXC Chemokines

Molecule	Recombinant & Natural Proteins	Antibodies	ELISAs
CXCL1/2/3/GRO	CR	H (B/N, FC, WB) CR (B/N, WB)	
CXCL1/GRO α /KC/CINC-1	H M R	H (B/N, E, FC, WB) M (B/N, E, WB) R (B/N, IHC, WB)	H M R
CXCL2/GRO β /MIP-2/CINC-3	H M R CR	H (B/N, FC, WB) M (B/N, E, ICC, IHC, WB) R (B/N, E, WB)	H M R
CXCL3/GRO γ /CINC-2/DCIP-1	H M R	H (B/N, FC, WB) M (B/N, WB) R (B/N, E, WB)	R
CXCL4/PF4	H M R	H (E, FC, WB) M (E, WB)	H M
CXCL5/ENA-70	H		
CXCL5/ENA-74	H		
CXCL5/ENA-78	H	H (B/N, E, FC, IHC, WB)	H
CXCL6/GCP-2	H	H (B/N, E, WB)	H
CXCL7/NAP-2	H	H (B/N, E, WB)	H
CXCL7/Thymus Chemokine-1	M R	M (B/N, E, IHC, WB) R (B/N, E, IHC, WB)	M
CXCL8/IL-8	H P Ca F	H (B/N, E, FC, ICC, IHC, WB) P (B/N, E, WB) Ca (B/N, E, ICC, WB) F (B/N, E, ICC, WB)	H P Ca F
CXCL9/MIG	H M	H (B/N, E, FC, ICC, WB) M (B/N, E, WB)	H M
CXCL10/IP-10/CRG-2	H M CR	H (B/N, E, FC, ICC, WB) M (B/N, E, IHC, WB) CR (B/N, WB)	H M
CXCL11/I-TAC	H M	H (B/N, E, WB) M (B/N, E, WB)	H M
CXCL12/SDF-1	H M F RM	H (B/N, E, FC, ICC, IHC, WB) M (B/N, E, FC, ICC, IHC, WB)	H M
CXCL12/SDF-1 α	H M F RM		M
CXCL12/SDF-1 β	H F	H (B/N, E, WB)	
CXCL12/SDF-1 γ	H		
CXCL13/BLC/BCA-1	H M	H (B/N, E, FC, IHC, WB) M (B/N, E, IHC, WB)	H M
CXCL14/BRAK	H M	H (E, WB) M (WB)	H
CXCL15/Lungkine	M	M (E, WB)	M
CXCL16	H M	H (B/N, E, FC, IHC, WB) M (B/N, E, FC, WB)	H M
CXCL17/VCC-1	H M	H (FC, ICC, WB) M (WB)	
LIX	M R	M (B/N, E, WB) R (B/N, E, WB)	M

SPECIES KEY

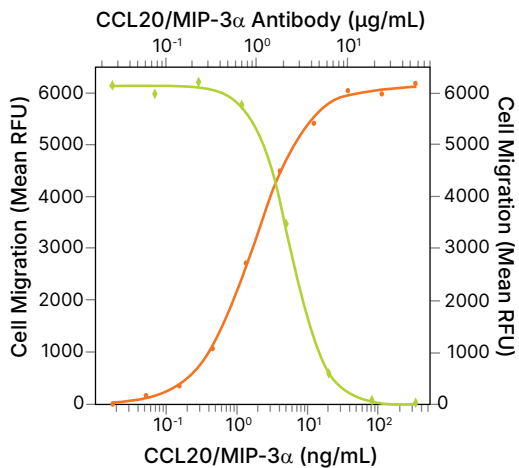
H Human, M Mouse, R Rat, B Bovine, Ca Canine, CR Cotton Rat, F Feline, P Porcine, RM Rhesus Macaque, V Viral

APPLICATION KEY

B/N Blocking/Neutralization, E ELISA (Cap. or Det.), FC Flow Cytometry, ICC Immunocytochemistry, IHC Immunohistochemistry, IP Immunoprecipitation, WB Western Blot

CC Chemokines

CC chemokines, also known as β chemokines, are critical mediators of the inflammatory response. The CC subfamily contains thirty-four ligands and eleven receptors. Many of these are implicated in chronic inflammatory diseases including rheumatoid arthritis, atherosclerosis, and metabolic syndrome.¹ CC chemokines also regulate the recruitment of leukocytes to the tumor microenvironment, particularly tumor-associated macrophages and myeloid-derived suppressor cells.²



Chemotaxis Induced by CCL20/MIP-3 α and Neutralization using a Human CCL20/MIP-3 α Antibody. Recombinant Human CCL20/MIP-3 α (Catalog # 360-MP) chemoattracts the BaF3 mouse pro-B cell line transfected with human CCR6 in a dose-dependent manner (orange line). The amount of cells that migrated through to the lower chemotaxis chamber was measured by Resazurin (Catalog # AR002). Chemotaxis elicited by 10 ng/mL Recombinant Human CCL20/MIP-3 α is neutralized by increasing concentrations of Human CCL20/MIP-3 α Monoclonal Antibody (Catalog # MAB360; green line).

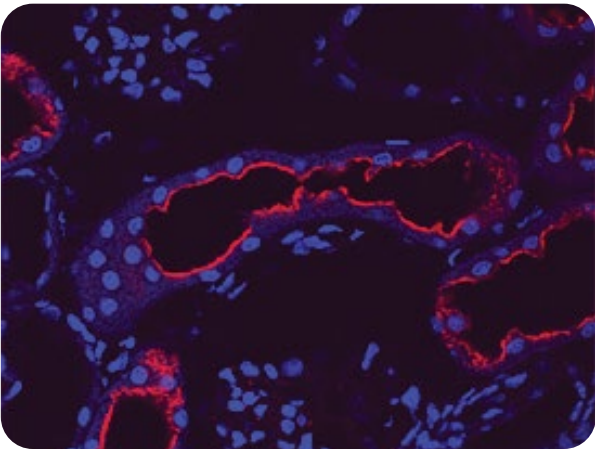
TABLE // 03

CC Chemokines

Molecule	Recombinant & Natural Proteins	Antibodies	ELISAs
CCL1/I-309/TCA-3	H M	H (B/N, E, WB) M (B/N, E, WB)	H M
CCL2/JE/MCP-1	H M R Ca	H (B/N, E, FC, IHC, WB) M (B/N, E, FC, WB) Ca (B/N, E, ICC, WB) CR (WB)	H M R Ca
CCL3/MIP-1 α	H M R CR	H (B/N, E, FC, ICC, IHC, WB) M (B/N, E, FC, ICC, IHC, WB) R (B/N, IHC, WB) Ca (WB) CR (B/N, WB)	H M
CCL3L1/MIP-1 α Isoform LD78 β	H		
CCL4/MIP-1 β	H M R Ca CR	H (B/N, E, FC, ICC, IHC, WB) M (B/N, IHC, WB) R (B/N, WB) Ca (ICC, WB) CR (B/N, WB)	H M

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Detection of CCL3/MIP-1 α in Rat Kidney. Perfusion-fixed frozen sections of rat kidney were stained for CCL3/MIP-1 α expression using a Mouse Anti-Rat CCL3/MIP-1 α Monoclonal Antibody (Catalog # MAB66251). The tissue was stained using the NorthernLights™ 557-conjugated Donkey Anti-Mouse IgG Secondary Antibody (Catalog # NL007; red) and counterstained with DAPI (blue). Specific staining was localized to the plasma membranes of epithelial cells in convoluted tubules.

Molecule	Recombinant & Natural Proteins	Antibodies	ELISAs
CCL4L1/LAG-1	H		
CCL5/RANTES	H M Ca CR F	H (B/N, E, FC, ICC, IHC, WB) M (B/N, E, ICC, WB) Ca (B/N, ICC) CR (B/N, WB) F (B/N, E, WB)	H M R Ca
CCL6/C10	M	M (B/N, E, FC, WB)	M
CCL7/MCP-3/MARC	H M	H (B/N, E, FC, WB) M (B/N, WB)	H
CCL8/MCP-2	H	H (B/N, E, WB) M (WB)	H M
CCL9/10/MIP-1 γ	M	M (B/N, E, WB)	M
CCL11/Eotaxin	H M	H (B/N, E, FC, IHC, WB) M (B/N, E, IHC, WB)	H M
CCL12/MCP-5	M	M (B/N, E, WB)	M
CCL13/MCP-4	H	H (B/N, FC, WB)	H
CCL14/HCC-1/HCC-3		H (B/N, E, WB)	
CCL14a/HCC-1		H (B/N, E, WB)	H
CCL14b/HCC-3		H (B/N, E, WB)	
CCL15/MIP-1 δ	H	H (B/N, E, WB)	H
CCL16/HCC-4	H	H (B/N, E)	H
CCL17/TARC	H M	H (B/N, E, FC, IHC, WB) M (B/N, E, WB)	H M
CCL18/PARC	H	H (E, FC, WB)	H
CCL19/MIP-3 β	H M R	H (B/N, E, FC, WB) M (B/N, E, ICC, WB)	H M
CCL20/MIP-3 α	H M R	H (B/N, E, ICC, IHC, WB) M (B/N, E, WB)	H M R
CCL21/6Ckine	H M R	H (B/N, E, ICC, WB) M (B/N, E, FC, IHC, WB)	H M
CCL22/MDC	H M	H (B/N, E, FC, WB) M (B/N, E, WB)	H M
CCL23/Ck β 8-1	H	H (B/N, E, WB)	
CCL23/MPIF-1	H	H (B/N, E, WB)	H
CCL24/Eotaxin-2/MPIF-2	H M	H (B/N, E, IHC, WB) M (B/N, E, WB)	H M
CCL25/TECK	H M	H (B/N, E, WB) M (B/N, E, IHC, WB)	H M
CCL26/Eotaxin-3	H	H (B/N, E, IHC, WB)	H
CCL26-like/Eotaxin-3-like		R (WB)	
CCL27/CTACK	H M R	H (B/N, E, IHC, WB) M (B/N, E, IHC, WB)	H M
CCL28	H M	H (B/N, E, WB) M (B/N, E, WB)	H M

SPECIES KEY
H Human, M Mouse, R Rat, B Bovine, Ca Canine, CR Cotton Rat, F Feline, P Porcine, RM Rhesus Macaque, V Viral
APPLICATION KEY
B/N Blocking/Neutralization, E ELISA (Cap. or Det.), FC Flow Cytometry, ICC Immunocytochemistry, IHC Immunohistochemistry, IP Immunoprecipitation, WB Western Blot

TABLE // 04

CC Chemokine Receptors

Molecule	Antibodies	Tocris Small Molecule Antagonists
CCR1	H (FC) M (FC, WB)	✓
CCR2	H (FC, IHC) M (FC, ICC)	✓
CCR3	H (B/N, FC, IHC) M (FC)	✓
CCR4	H (FC) M (WB) R (FC)	✓
CCR5	H (B/N, FC, ICC, IHC, IP, WB) M (FC, WB) R (FC)	✓
CCR6	H (FC, IHC) M (FC, IHC) R (FC)	
CCR7	H (B/N, FC, ICC, IHC) M (B/N, FC, ICC)	
CCR8	H (B/N, FC) M (FC, WB) R (FC, WB)	
CCR9	H (FC, ICC, IHC) M (FC) R (FC)	
CCR10	H (FC) M (FC) R (FC)	✓
CCR11	H (FC)	
CCRL2/CRAM-A/B	H (FC)	
CCRL2/LCCR	M (FC, ICC)	
D6	H (FC)	

TABLE // 05

CC Chemokine-related Molecules

Molecule	Recombinant & Natural Proteins	Antibodies
CCI	V	V (B/N, WB)
MCK-2		V (WB)
MCV-type II Chemokine-like Protein	V	V (B/N, WB)
MIP-I	V	V (B/N, WB)
MIP-II	V	V (WB)
MIP-III		V (WB)
TAFA1/FAM19A1	H	H (B/N, IHC, WB)
TAFA2/FAM19A2	H	H (B/N, IHC, WB)
TAFA3/FAM19A3		H (FC, WB)
TAFA4/FAM19A4	H	H (FC, WB)
TAFA5/FAM19A5	H	H (IHC, WB) M (WB) R (WB)

C Chemokines

C chemokines, also known as γ chemokines, mediate homing and leukocyte maturation within lymphoid tissues. This subfamily consists of two ligands, XCL1 and XCL2, which both bind to XCR1. The XCR1 receptor is expressed on a unique subset of dendritic cells (DCs) that cross-presents antigens to T cells.¹⁻³ The specificity of XCR1 expression on cross-presenting DCs makes it an attractive target for antigen delivery by DC-targeted cancer vaccines.^{1,4}

TABLE // 06

C Chemokine & Receptor

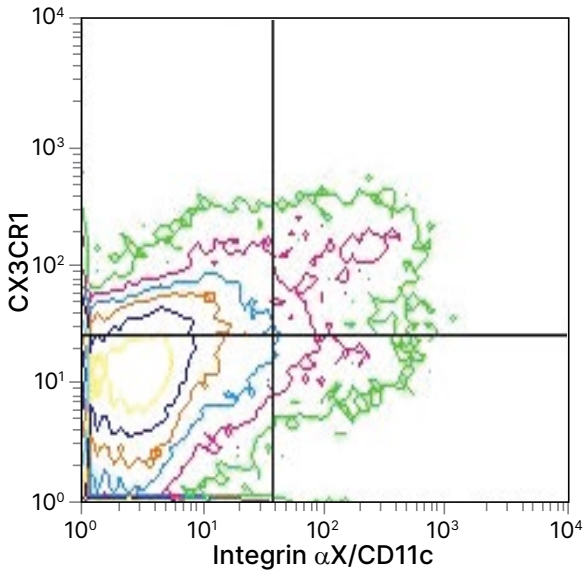
Molecule	Recombinant & Natural Proteins	Antibodies	ELISAs
XCL1/Lymphotactin	H	H (B/N, E, WB) M (B/N, E, IHC, WB)	H M
XCR1		H (FC, ICC, WB)	

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CX3C Chemokines

The CX3C chemokine subfamily, also known as the δ subfamily, regulates leukocyte homing and adhesion. There is only one CX3C chemokine ligand, CX3CL1/Fractalkine, which binds to CX3CR1. CX3CL1/Fractalkine mediates an inflammatory response and appears to play a significant role in inflammatory disorders including atherosclerosis, allergen-induced asthma, and neuro-inflammation.¹⁻⁴



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Detection of CX3CR1 and Integrin αX/CD11c on Mouse Splenocytes by Flow Cytometry. Mouse splenocytes were stained with an APC-conjugated Goat Anti-Mouse CX3CR1 Antigen Affinity-purified Polyclonal Antibody (Catalog # FAB5825A) and a PE-conjugated anti-mouse Integrin αX/CD11c antibody.

TABLE // 07

CX3C Chemokine & Receptor

Molecule	Recombinant & Natural Proteins	Antibodies	ELISAs
CX3CL1/Fractalkine	H M R	H (B/N, E, FC, IHC, WB) M (B/N, E, FC, WB) R (B/N, E, IHC, WB)	H M R
CX3CR1		H (FC, WB) M (FC, WB)	

TABLE // 08

Other Chemotactic Molecules

Molecule	Recombinant & Natural Proteins	Antibodies	ELISAs
Chemerin	H M	H (E, FC, WB) M (B/N, E, FC, WB)	H M
ChemR23		H (FC) M (FC)	



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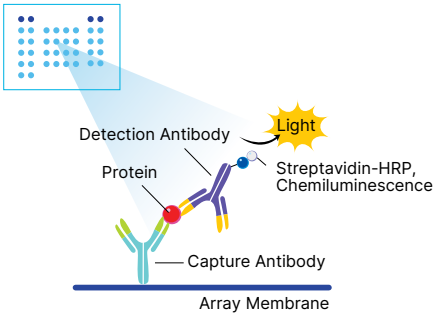


TABLE // 09

Proteome Profiler Antibody Arrays

Proteome Profiler Antibody Arrays
Human Chemokine Antibody Array (Catalog # ARY017) Contains 4 membranes – each spotted in duplicate with 31 different chemokine antibodies
CCL1/I-309, CCL2/MCP-1, CCL3/CCL4 (MIP-1α/MIP-1β), CCL5/RANTES, CCL7/MCP-3, CCL14/HCC-1/HCC-3, CCL15/MIP-1δ/LKN-1, CCL17/TARC, CCL18/PARC, CCL19/MIP-3b, CCL20/MIP-3α, CCL21/6Ckine, CCL22/MDC, CCL26/Eotaxin-3, CCL28, CX3CL1/Fractalkine, CXCL1/GROα, CXCL4/PF4, CXCL5/ENA-78, CXCL7/NAP-2, CXCL8/IL-8, CXCL9/MIG, CXCL10/IP-10, CXCL11/I-TAC, CXCL12/SDF-1, CXCL16, CXCL17/VCC-1, XCL1/Lymphotactin, Chemerin, IL-16, Midkine
Mouse Chemokine Antibody Array (Catalog # ARY020) Contains 4 membranes – each spotted in duplicate with 25 different chemokine antibodies
CCL2/JE/MCP-1, CCL3/CCL4 (MIP-1α/MIP-1β), CCL5/RANTES, CCL6/C10, CCL8/MCP-2, CCL9/10/MIP-1γ, CCL11/Eotaxin, CCL12/MCP-5, CCL21/6Ckine, CCL22/MDC, CCL27/CTACK, CCL28, CX3CL1/Fractalkine, CXCL1/KC, CXCL2/MIP-2, CXCL9/MIG, CXCL10/IP-10/CRG-2, CXCL11/I-TAC, CXCL12/SDF-1, CXCL13/BLC/BCA-1, CXCL16, Chemerin, Complement Component C5/C5a, IL-16, LIX

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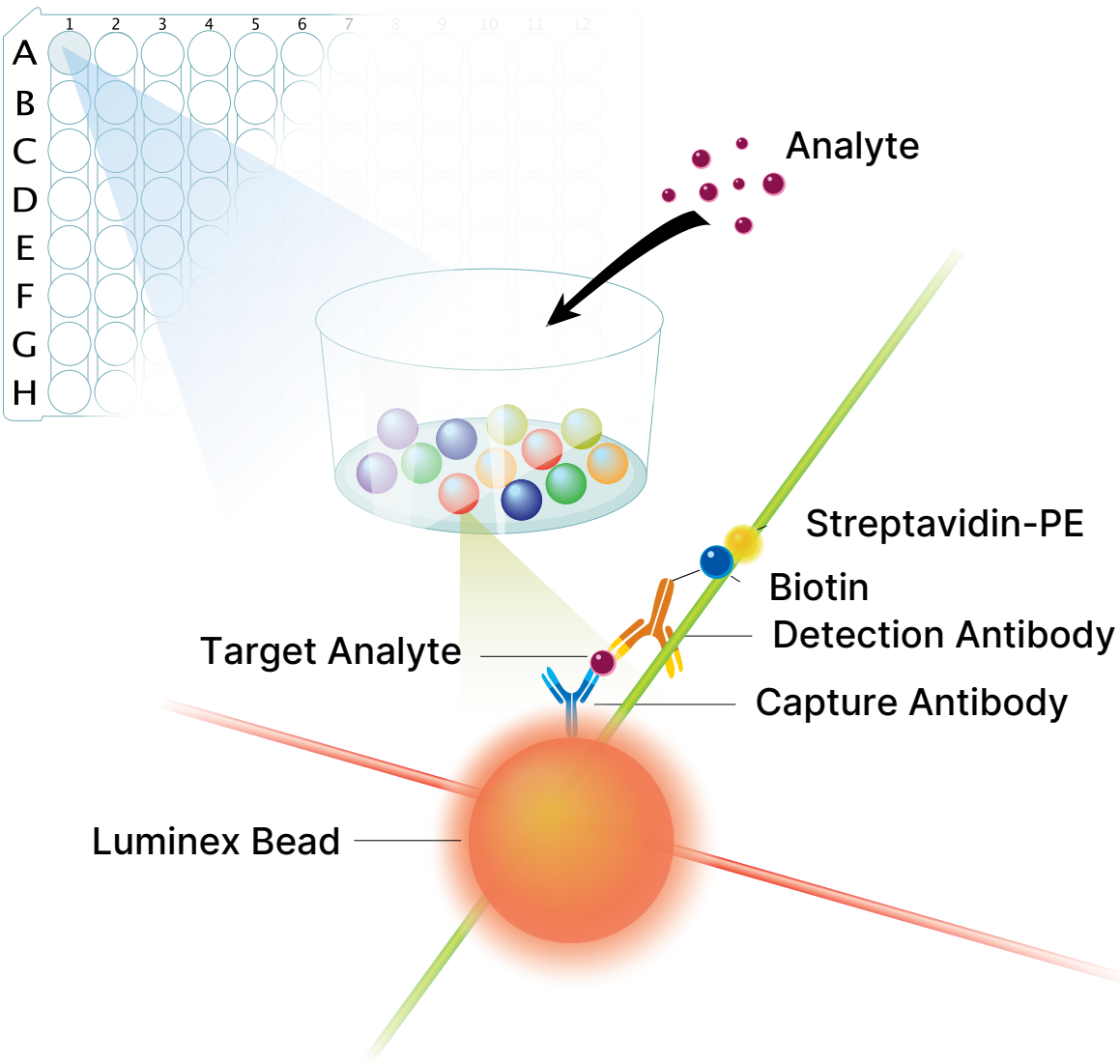
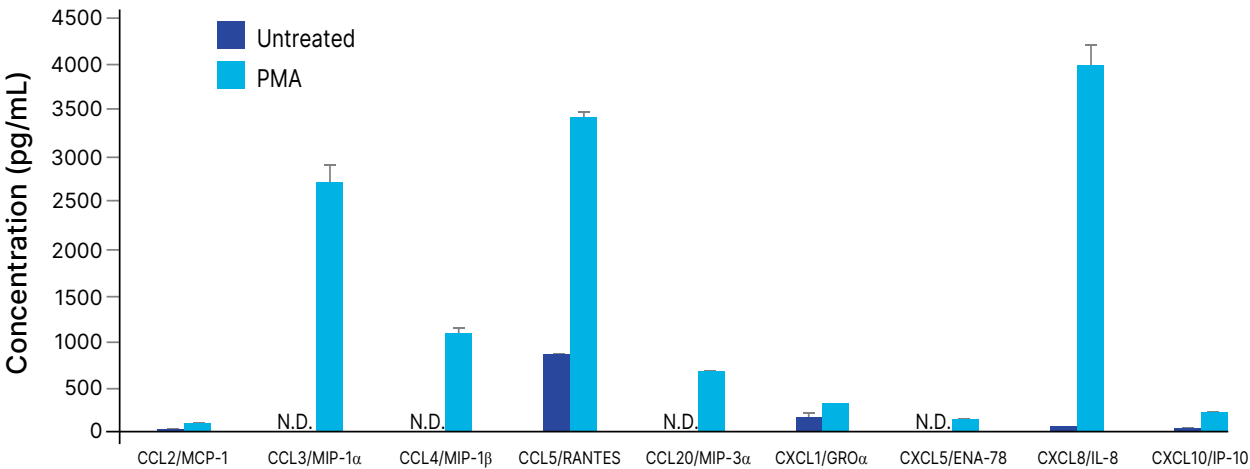


TABLE // 10

Chemokine Luminex Screening and Performance Assays

Chemokine Luminex Screening and Performance Assay Analytes
Human Luminex Screening Assay Analytes
CCL2/MCP-1, CCL3/MIP-1α, CCL4/MIP-1β, CCL5/RANTES, CCL8/MCP-2, CCL13/MCP-4, CCL17/TARC, CCL20/MIP-3α, CXCL1/GROα, CXCL4/PF4, CXCL5/ENA-78, CXCL8/IL-8, CXCL9/MIG, CXCL10/IP-10, CXCL11/I-TAC, CXCL13/BLC/BCA-1
Mouse Luminex Screening Assay Analytes
CCL2/JE, CCL3/MIP-1α, CCL4/MIP-1β, CCL5/RANTES, CCL20/MIP-3α, CXCL1/KC, CXCL2/MIP-2, CXCL10/IP-10/CRG-2, CXCL12/SDF-1α, LIX
Human Cytokine Panel A Luminex Performance Assay Analytes*
CCL2/MCP-1, CCL3/MIP-1α, CCL4/MIP-1β, CCL5/RANTES, CXCL5/ENA-78, CXCL8/IL-8, FGF basic, G-CSF, GM-CSF, IFN-γ, IL-1α/IL-1F1, IL-1β/IL-1F2, IL-1ra/IL-1F3, IL-2, IL-4, IL-5, IL-6, IL-10, IL-17, TNF-α, Thrombopoietin/Tpo, VEGF
Mouse Cytokine Panel Luminex Performance Assay Analytes
CCL2/JE/MCP-1, CXCL1/KC, CXCL2/MIP-2, GM-CSF, IFN-γ, IL-1β/IL-1F2, IL-2, IL-4, IL-5, IL-6, IL-10, IL-12, p70, IL-13, IL-17, TNF-α, VEGF

*Analytes in this panel are available in both the polystyrene and magnetic bead formats.



Detection of Multiple Chemokines in Cell Culture Supernates Using the Human Luminex Screening Assay. The human THP-1 monocytic leukemia cell line was treated with phorbol 12-myristate 13-acetate (PMA) for 24 hours. Cell culture supernates were collected from untreated and treated cells and the levels of multiple chemokines were simultaneously determined using the Human Luminex Discovery Assay (Catalog # LXSAHM). Of the 16 chemokines tested, 9 gave measurable values in each of the PMA-stimulated samples. The average values and standard deviations for the detectable analytes are shown. N.D. Not Detected.

Luminex® is a registered trademark of Luminex Corporation.

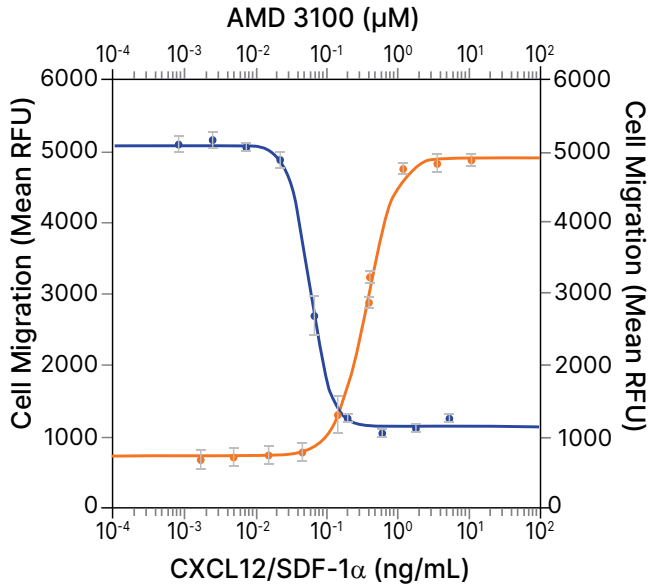


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Small Molecule Agonists & Antagonists

Chemokine receptor activity can be studied *in vivo* and *in vitro* using biochemical and peptide agonists and antagonists which modulate their activity. Chemokine receptors are G protein-coupled receptors (GPCRs) that are highly targetable, and a variety of potent and selective agonists and antagonists have been developed to facilitate chemokine research. Chemokine receptor products available from Tocris Bioscience are listed on the following page.



CXCL12/SDF-1α-induced Chemotaxis Is Antagonized by AMD 3100 Octahydrochloride. Increasing concentrations of Recombinant Human/ Feline/Rhesus Macaque CXCL12/SDF-1α (Catalog # 350-NS) were used to stimulate chemotaxis of the BaF3 mouse pro-B cell line transfected with human CXCR4. Cells that migrated to the lower compartment of a chemotaxis chamber were measured using the redox sensitive dye, Resazurin (Catalog # AR002; orange line). The effect induced by 1 ng/mL Recombinant Human/Feline/Rhesus Macaque CXCL12/SDF-1α was antagonized with increasing concentrations of the highly selective CXCR4 inhibitor, AMD 3100 octahydrochloride (Catalog # 3299; blue line).



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TABLE // 11

Chemokine Receptor Agonists & Antagonists

Chemokine Receptor Agonists		
Receptor	Product Name	Catalog #
CXCR7	TC 14012	4300
Chemokine Receptor Antagonists		
CCR1	BX 471	3496
	BX 513 hydrochloride	2769
	J 113863	2595
	UCB 35625	2757
CCR2	BMS CCR2 22	3129
	INCB 3284 dimesylate	4306
	RS 504393	2517
CCR2B	RS 102895 hydrochloride	2089
CCR3	SB 297006	4213
	SB 328437	3650
	UCB 35625	2757
CCR4	C 021 dihydrochloride	3581
CCR5	Maraviroc	3756
CXCR2	SB 225002	2725
	SB 265610	2724
CXCR4	AMD 3100 octahydrochloride	3299
	AMD 3465 hexahydrobromide	4179
	IT1t dihydrochloride	4596
	TC 14012	4300

Notes

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