

BAY-3153: A Chemical Probe for CCR1

Version 1.0 (24th March 2021)

Web link for more details: <https://www.sgc-ffm.uni-frankfurt.de/#!specificprobeoverview/BAY-3153>

Overview

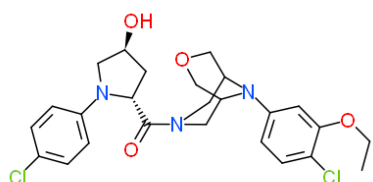
[CCR1](#) is a receptor for C-C type chemokines and a member of the rhodopsin-like subfamily of GPCRs. It is highly expressed by monocytes/macrophages, T-cells and dendritic cells and essential for adhesion and transendothelial diapedesis of leukocytes, leukocyte differentiation and proliferation, T-cell activation and Th-1/Th-2 polarization. CCR1 deletion or inhibition reduces macrophage numbers leading to reduced fibrosis and improving kidney morphology.

Summary

Chemical Probe Name	BAY-3153
Negative control compound	BAY-173
Target(s) (synonyms)	CCR1 (C-C motif chemokine receptor 1, SCYAR1, CMKBR1)
Recommended cell assay concentration	Use at concentration up to 100 nM for BAY-3153 and BAY-173; BAY-3153 has a low solubility but a high permeability (stable for 4 hours); use with negative control for best interpretation of data.
Suitability for <i>in vivo</i> use and recommended dose	BAY-3153 is well suited to perform <i>in vivo</i> studies. It was tested in rats with 10 mg/kg and resulted in a reduction of infiltrating macrophages after renal ischemia/reperfusion injury (I/RI).
Publications	None at time of writing
Orthogonal chemical probes	BI 639667
<i>In vitro</i> assay(s) used to characterise	Biochemical CCR1 assay (Ca ²⁺ -flux)
Cellular assay(s) for target-engagement	

Chemical Probe & Negative Control Structures and Use

BAY-3153 Chemical Probe



SMILES:

CCOC1=CC=C(C=C1)N1C2CN(CC1COC2)C([C@H]1C[C@@H](CN1c1ccc(cc1)[Cl])O)=O

InChIKey: LZSPYTNRPEZBK-OXYJHPMESA-N

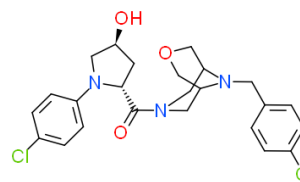
Molecular weight: 505.2

Storage: As a dry powder or as DMSO stock solutions (10 mM) at -20 °C.

DMSO stocks beyond 3-6 months or 2 freeze/thaw cycles should be tested for activity before use

Dissolution: Soluble in DMSO up to 10 mM; use only 1 freeze/thaw cycle per aliquot

BAY-173 *Negative Control*



SMILES:

C1[C@@H](CN(C2CCC(CC2)[Cl]))[C@H]1C(N1CC2COCC(C1)N2Cc1ccc(cc1)[Cl])=O

InChIKey: DONGAXKBPGSGCS-ZSTXGWISA-N

Molecular weight: 475.1

Storage: As a dry powder or as DMSO stock solutions (10 mM) at -20 °C.

DMSO stocks beyond 3-6 months or 2 freeze/thaw cycles should be tested for activity before use

Dissolution: Soluble in DMSO up to 10 mM; use only 1 freeze/thaw cycle per aliquot

Chemical Probe Profile

In vitro Potency & Selectivity:

BAY-3153 shows potent activity in a biochemical CCR1 assay (Ca²⁺-flux) (IC₅₀ = 3 nM (human) / 11 nM (rat) / 81 nM (mice)) whereas BAY-173 has 400-fold less *in vitro* potency (IC₅₀ = 1200 nM (human), 8500 nM (mice)). BAY-3153 is inactive on hCCR3; IC₅₀ > 30 μM for human CCR2, CCR4, CCR5, CCR6, CCR7, CCR8, CCR9, CCR10, CXCR1, CXCR2, CXCR3, CXCR4 and CXCR5. The closest off-target in a GPCR scan (45 at 10 μM) is TMEM97 (K_i = 1476.05 nM).

Potency in Cells and Cellular Target Engagement:

BAY-3153 shows *in vivo* efficacy on infiltrating macrophages in experimental renal ischemia/reperfusion model in mice.