CXC chemokine receptor 4 (CXCR4) blockade in cancer treatment

Review | Published: 11 March 2023

Volume 149, pages 7945–7968, (2023) Cite this article

Shunshun Bao, Mohammad Darvishi, Ali H Amin, Maysoon T. Al-Haideri, Indrajit Patra, Khadisha Kashikova, Irfan Ahmad, Fahad Alsaikhan, Zahraa Haleem Al-qaim, Moaed E. Al-Gazally, Bahman Abedi Kiasari ✉, Bahareh Tavakoli-Far ✉, Akmal A. Sidikov, Yasser Fakri Mustafa & Reza Akhavan-Sigari

Abstract

CXC chemokine receptor type 4 (CXCR4) is a member of the G protein-coupled receptors (GPCRs) superfamily and is specific for CXC chemokine ligand 12 (CXCL12, also known as SDF-1), which makes CXCL12/CXCR4 axis. CXCR4 interacts with its ligand, triggering downstream signaling pathways that influence cell proliferation chemotaxis, migration, and gene expression. The interaction also regulates physiological processes, including hematopoiesis, organogenesis, and tissue repair. Multiple evidence revealed that CXCL12/CXCR4 axis is implicated in several pathways involved in carcinogenesis and plays a key role in tumor growth, survival, angiogenesis, metastasis, and therapeutic resistance. Several CXCR4-targeting compounds have been discovered and used for preclinical and clinical cancer therapy, most of which have shown promising anti-tumor activity. In this review, we summarized the physiological signaling of the CXCL12/CXCR4 axis and described the role of this axis in tumor progression, and focused on the potential therapeutic options and strategies to block CXCR4.