Relevance of the CXCR4/CXCR7-CXCL12 axis and its effect in pathophysiological conditions.

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The impact of the C-X-C receptor (CXCR) 7 and its close co-player CXCR4 in different physiological and pathophysiological processes has been extensively investigated within the last decades. Following activation by their shared ligand C-X-C ligand (CXCL) 12, both chemokine receptors can induce various routes of cell signaling and/or scavenge CXCL12 from the extracellular environment. This contributes to organ development and maintenance of homeostasis. Alterations of the CXCR4/CXCR7-CXCL12 axis have been detected in diseases such as cancer, central nervous system and cardiac disorders, and autoimmune diseases. These alterations include changes of the expression pattern, distribution, or downstream effects. The progression of the diseases can be regulated in preclinical models by the use of various modulators suggesting that this axis serves as a promising therapeutic target. It is therefore of great interest to investigate CXCR4/CXCR7/CXCL12 modulators in clinical development, with several CXCR4 and CXCL12 modulators such as plerixafor, ulocuplumab, balixafortide, and olaptesed pegol having already reached this stage. An overview is presented of the most important diseases whose outcomes can be positively or negatively regulated by the CXCR4/CXCR7-CXCL12 axis and summarizes preclinical and clinical data of modulators of that axis. Contrary to CXCR4 and CXCL12 modulators, CXCR7 modulators have, thus far, not been extensively studied. Therefore, more (pre)clinical investigations are needed.

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