The chemokine receptor CXCR4 belongs to the large superfamily of G-protein-coupled receptors, and is directly involved in a number of biological processes including organogenesis, hematopoiesis, and immunity. Recent evidence shows the role of CXCR4 in a variety of diseases including cancer and WHIM syndrome. Expression of CXCR4 in cancer metastasis appears to be due to dysregulation of the receptor leading to enhanced signaling. CXCR4 was also found to be a prognostic marker in various types of cancer including leukemia and breast cancer. These observations reveal that CXCR4 is an important molecule involved in several aspects of cancer progression. The SDF-1-CXCR4 axis is also involved in normal stem cell homing. Cancer stem cells also express CXCR4 suggesting that the SDF-1-CXCR4 axis directs their trafficking/metastasis to organs that highly express SDF-1 such as the lymph nodes, lungs, liver, and bones and the regulation of CXCR4 and how dysregulation contributes to disease progression.