CXC Chemokine ligand 12 (CXCL12) mediates multiple myeloma cell line (RPMI 8226) chemotxis via PLC□3, PI3K/AKT, RhoA, NFkB and ERK1/2

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Abstract:

In multiple myeloma (MM) blood-borne malignant plasma cells home to bone marrow (BM), where they accumulate in close contact with stromal cells. Nevertheless, the mechanisms responsible for MM cell chemotaxis are still poorly defined. In the present study we explored the mechanisms involved in the chemotaxis of RPMI 8226 cell line, RPMI 8226 cell line was found to express CCR3, CCR5, CCR9, CXCR3 and CXCR4, but these cells were migrated only towards CXCL12 (the ligand for CXCR4). To clarify the signaling pathways involved in the regulation of MM cell chemotaxis, we therefore analyzed the effect of various inhibitors targeting intracellular effectors proteins on the CXCL12-mediated RPMI 8226 chemotaxis using flow cytometry and western blot analysis. Using flow cytometry, we observed that the chemotaxis of RPMI 8226 cell to CXCL12 was completely abrogated by adding AMD (CXCR4 antagonist), PTX (G-protein coupled receptor inhibitor) and U73122 (phospholipase C beta; PLC□ inhibitor), moreover, CXCL12-mediated RPMI 8226 chemotaxis was partially inhibited by 1 □M wortmannin (WM, Class II PI3K inhibitor)), SH5 (AKT inhibitor), Y27632 (Rho-A inhibitor), SN50 (IkB□ inhibitor), PD98059 (ERK1/2 MAPK inhibitor) and Na3VO4 (phosphatase inhibitor). These results were further confirmed by using western blot analysis where we observed that triggering of CXCR4 by CXCL12 resulted in the activation of PLC□3, PI3K/AKT, RhoA, I□B□ and ERK1/2. In conclusion, our results revealed that PLC□3, PI3K/AKT, RhoA, IKB□ and ERK1/2 are crucial effectors for CXCL12- mediating MM cell chemotaxis.

Keywords:

Multiple myeloma cell, chemokine, chemotaxis, flow cytometry, western blot.

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