HIV type 1 glycoprotein 120 inhibits human B cell chemotaxis to CXC chemokine ligand (CXCL) 12, CC chemokine ligand (CCL)20, and CCL21.

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Abstract:

We analyzed the modulation of human B cell chemotaxis by the gp120 proteins of various HIV-1 strains. X4 and X4/R5 gp120 inhibited B cell chemotaxis toward CXCL12, CCL20, and CCL21 by 40-50%, whereas R5 gp120 decreased inhibition by 20%. This gp120-induced inhibition was strictly dependent on CXCR4 or CCR5 and lipid rafts but not on CD4 or V(H)3-expressing BCR. Inhibition did not impair the expression or ligand-induced internalization of CCR6 and CCR7. Our data suggest that gp120/CXCR4 and gp120/CCR5 interactions lead to the cross-desensitization of CCR6 and CCR7 because gp120 does not bind CCR6 and CCR7. Unlike CXCL12, gp120 did not induce the activation of phospholipase Cbeta3 and PI3K downstream from CXCR4, whereas p38 MAPK activation was observed. Similar results were obtained if gp120-treated cells were triggered by CCL21 and CCL20. Our results are consistent with a blockade restricted to signaling pathways using phosphatidylinositol-4,5-bisphosphate as a substrate. X4 and X4/R5 gp120 induced the cleavage of CD62 ligand by a mechanism dependent on matrix metalloproteinase 1 and 3, CD4, CXCR4, Galpha(i), and p38 MAPK, whereas R5 gp120 did not. X4 and X4/R5 gp120 also induced the relocalization of cytoplasmic CD95 to the membrane and a 23% increase in CD95-mediated apoptosis. No such effects were observed with R5 gp120. The gp120-induced decrease in B cell chemotaxis and CD62 ligand expression, and increase in CD95-mediated B cell apoptosis probably have major deleterious effects on B cell responsiveness during HIV infection and in vaccination trials.

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