Cytomegalovirus-encoded gamma-chemokine vXCL1 selectively activates XCR1 expressed on CD4- dendritic cells

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Dendritic cells (DC) expressing the chemokine receptor XCR1 are specialized in antigen cross-presentation to control infections with intracellular pathogens such as viruses. XCR1+ DC are attracted by XCL1, a gamma-chemokine secreted by activated CD8+ T cells and Natural Killer cells. Cytomegalovirus (CMV) is the only virus to encode a viral XCL1 analogue (vXCL1) that competes for XCR1 binding with the endogenous chemokine. Both vXCL1 encoded by rat CMV (RCMV) and rat XCL1 (rXCL1) bind to and induce chemotaxis in exclusively XCR1+ CD4- rat DC. Interestingly, rXCL1 binds to XCR1 of rats and humans, whereas vXCL1 functions as a selective agonist for rat XCR1 emphasizing host specificity of the virus. Moreover, constitutive internalization of XCR1 was observed after transfection of HEK293A cells as well as on splenic XCR1+ CD4- DC. After transfection, XCR1 internalization was enhanced after binding of vXCL1 and rXCL1 with vXCL1 being a stronger agonist and was shown to be independent of beta-arrestin 1 or 2. In this study, we show that both vXCL1 homologues act as selective agonists and thus have the same function as endogenous rXCL1. In addition, we demonstrate that XCR1 is internalized after ligand binding that impairs chemotactic activity of rXCL1 and thus XCR1+ DC function.

Keywords : cytomegalovirus, viral XCL1 analogue, XCR1, dendritic cells, internalization
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