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HIV interaction with target cell: the relevance of CCR8 chemokine receptor as coreceptor for HIV-1 and HIV-2

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The human immunodeficiency virus (HIV) replication cycle begins by sequential interactions between viral envelope glycoproteins and cellular receptors that ultimately lead to viral envelope and cell membrane fusion. The cellular receptors involved in these initial events are the CD4 molecule and a member of seven-transmembrane, G-protein-coupled, receptors (GPCRs) family, referred as coreceptor.

The majority of the information regarding coreceptors usage by HIV strains derives almost exclusively from studies using HIV-1 isolates. However, we and others have provided evidences that HIV-2 interaction with cellular receptors is remarkably different. HIV-2 isolates able to infect cells in the absence of CD4, the promiscuous use of chemokine receptors as coreceptors and the non-usage of either CCR5 or CXCR4 are notorious examples of the heterogeneous mechanisms by which HIV-2 interacts with target cells.

In this report we focused on the contribution of CCR8 as alternative coreceptor in HIV-1 and HIV-2 infection, using primary isolates obtained from patients at different disease stages.

We find that this coreceptor was efficiently used by 15 out of 61 HIV-2 isolates tested (24,6%). More surprisingly, however, was the frequency with which CCR8 was used by HIV-1 isolates: 54,8% (17/31) of the strains tested was able to infect CCR8-expressing cells. Our results also reveal that CXCR4 usage, either alone or together with CCR5 and/or CCR8, was more frequently observed in HIV-1 than in HIV-2 (83.9% and 44.3% for HIV-1 and HIV-2 isolates, respectively). Directly related to this is the finding that the exclusive use of CCR5 (R5 biotype) is significantly more common in HIV-2 isolates than in HIV-1 (50.8% and 6.5%, respectively).

Taken together the more frequent acquisition of CXCR4 and/or CCR8 usage observed in HIV-1 isolates and the more frequent preservation of R5 biotype by HIV-2, may be related with the slower disease progression generally observed in HIV-2 infected patients.

Keywords: HIV, CCR8, Chemokine receptor, Pathogenesis