SUMMARY

Human herpesvirus 6 (HHV-6) and human immunodeficiency virus type 1 (HIV-1) may interact during transplacental transmission of HIV-1. The placental syncytiotrophoblast (ST) layer serves as the first line of defence of the foetus against viruses. Patterns of replication of HHV-6 variant A (HHV-6A) and HIV-1 were analyzed in singly and dually infected human term ST cells cultured *in vitro*. HHV-6A replication was restricted at the level of early gene products in singly infected ST cells, whereas no viral protein expression was found in cells infected with HIV-1 alone. Coinfection of ST cells with HHV-6A and HIV-1 resulted in production of infectious HIV-1. In contrast, no enhancement of HHV-6A expression was observed in cell cultures infected with both viruses. Uninfected ST cells were found to express CXCR4 and CCR3 but not CD4 and CCR5 receptors. Infection of ST with HHV-6A did not induce CD4 expression and had no influence on chemokine receptor expression. Activation of HIV-1 from latency in coinfected cells was mediated by the immediate early A and B gene products of HHV-6A. Open reading frames U86 and U89 of the A region were able to activate HIV-1 replication in a synergistic manner. The data suggest that in vivo double infection of ST cells with HHV-6A and HIV-1 could contribute to the transplacental transmission of HIV-1 but not HHV-6A.

HHV-6 frequently reactivates in HIV-1 infected patients, and is thought to be a cofactor in AIDS progression. Macrophages are targets and reservoirs of HIV-1 and HHV-6, hence, they have an important role in the dissemination and the pathogenesis of these viruses. The effects of HHV-6A on replication of R5 variants of HIV-1 in macrophages was examined. For this purpose, HIV-1 replication was investigated in macrophages infected with HIV-1 alone or along with HHV-6A. Our results demonstrated that HHV-6A significantly suppressed HIV-1 replication in coinfected cultures. HHV-6A infection resulted in increased secretion of RANTES and IL-8. Experiments with exogenous RANTES and IL-8 revealed that these chemokines also significantly suppressed HIV-1 replication in infected macrophages. RANTES is able to induce desensitization and internalization of CCR5, the chemokine coreceptor of R5 variants. In addition, IL-8 receptor activation results in cross-desensitization and cross-internalization of CCR5. We found that CCR5 sensitivity and expression level is diminished in HHV-6A infected macrophage cultures compared with uninfected cells. Taken together, our results indicate that HHV-6A infection decreases the susceptibility of macrophages to R5 variants of HIV-1 in which the HHV-6A induced RANTES and IL-8 may have importance.