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HHV-6A infection induces the expression of HERV-W in human cells

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ABSTRACT

Several studies have associated herpesvirus infections with human endogenous retroviruses (HERV), suggesting they could synergistically participate in the establishment of autoimmune diseases like multiple sclerosis (MS). Among the HERV-W family, the envelope protein (ENV) from the multiple sclerosis-associated retroviral element (MSRV) was shown to exhibit strong pro-inflammatory properties via TLR-4 signaling. We have analyzed here the interaction between HHV-6A and HERV-W-ENV. We infected the HSB-2 T-lymphocytes, U87 glioblastoma and SH-S5SY neuroblastoma cell lines with HHV-6A (GS). The mRNA expression of ENV from different HERVs (syncytin-1, MSRV and HERV-K18) was quantified by quantitative RT-PCR and shown the HERV-W-ENV over-expression in HHV-6A infected cells. These results were confirmed by immunofluorescence. We then analyzed the HHV-6A receptor (CD46) involvement in HERV-W activation (HERV-W-ENV/GAG), using different ligands of CD46 including UV-inactivated HHV-6A, measles virus and anti-CD46 antibody. Our results reveal that HHV-6A can increase the expression of ENV from the HERV-W family, confirming the previous data demonstrating HHV-6A-induced expression of K18 ENV. Furthermore, preliminary results of CD46 stimulation have shown that, contrary to anti-CD46 Ab, the inactivated HHV-6A and measles virus don't induced HERV-W-ENV/GAG expression in U87 cells. This result suggested that the engagement of CD46 using HHV-6A and measles binding site was not involved in HERV-W activation mechanism. Finally, our results have shown a fast reactivation of HERV-W elements after HHV-6A infection, including MSRV-ENV, which is known to induce MS by inflammatory responses through TLR4. Therefore, they expand the specter of HHV-6 effects in the modulation of the immune response and

support the hypothesis that cross-talks between HHV-6A and HERV may contribute to inflammatory diseases and participate to MS etiology.