



POSTER PRESENTATION

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# Expression and activation of human endogenous retroviruses of the W family in blood cells and astrocytes: implications for the pathogenesis of multiple sclerosis

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## Background

Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system, with demyelination and gliosis. Proposed pathogenic co-factors triggering MS pathogenesis are the Epstein Barr virus (EBV), and two elements of the W family of human endogenous retroviruses (HERV-W): MSR<sub>V</sub>, that forms free virions, and syncytin-1, the ERVWE1env protein; both retroelements have neuropathogenic properties. In the past we studied MSR<sub>V</sub> in MS patients in various temporal and clinical stages; in all cases, striking parallels between MS behaviour and MSR<sub>V</sub>/HERV-W presence/load were found. By simultaneous detection of MSR<sub>V</sub> and HHV-6, we found a direct correlation between MS and MSR<sub>V</sub> presence/load, but not for HHV-6. MS brains over-express MSR<sub>V</sub>env and syncytin-1 transcripts, with respect to controls, while EBV presence was not detected.

## Materials and methods

Since late EBV seroconversion is a strong risk factor for MS development, we performed *in vitro* experiments on PBMC from MS patients and MSR<sub>V</sub><sup>+</sup> volunteers, as well as on U87-MG astrogloma cells, that were studied as such or were exposed to EBV or to recombinant EBV glycoprotein350 (EBVgp350), or to proinflamma-

tory cytokines. The levels of MSR<sub>V</sub>env and syncytin-1 mRNAs were evaluated by discriminatory real time RT-PCR assays. Flow cytometry was used to evaluate the HERV-Wenv protein on the plasmamembrane, as well the PBMC subsets.

## Results

Basal expression of MSR<sub>V</sub>env and syncytin-1 occurs in astrocytes and in NK, B and monocyte cells, but not in T cells. This uneven expression is amplified in naive MS patients. Astrocyte infection by EBV and exposure to EBVgp350 stimulate the expression of HERV-W/MSR<sub>V</sub>/syncytin-1, with requirement of the NF- $\kappa$ B pathway. In EBVgp350-treated PBMC, MSR<sub>V</sub>env and syncytin-1 are activated in B cells and monocytes, but not in T cells, nor in the highly expressing NK cells. The latter cells, but not the T cells, are activated by proinflammatory cytokines.

## Conclusions

The study demonstrates that there are interactions among the above proposed MS-cofactors. *In vivo*, a pathogenic outcome would depend on activation in abnormal situations/tissues, as it may occur in delayed EBV infection, or in the presence of particular host genetic backgrounds, or both.

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