Abstract for the category: MS and related disorders (16)

Title:

Transactivation of endogenous retroviruses by the Epstein-Barr virus - pathophysiologically relevant key mechanism of multiple sclerosis?

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Introduction:

In Europe, more than 90% of all people are positive for Epstein-Barr virus (EBV) before the age of 30. Even without apparent immunodeficiency, EBV is involved in the pathogenesis of neoplasias, e.g. Hodgkin's and Burkitt's lymphomas. An association of EBV with the pathogenesis of multiple sclerosis (MS) is suggested. Interestingly, EBV seems to be able to transactivate so-called human endogenous retroviruses (HERV). If these integrated virus copies have intact open reading frames, their proteins could possibly contribute to auto-inflammatory and degenerative processes that are observed in the pathogenesis of autoimmune diseases such as MS. The hypothesized mechanism is shown (see figure attached).

Methods:

The expression of EBV and HERV sequences in EBV-immortalized lymphoblastoid cell lines of healthy donors (coLCL) and MS patients (MSLCL) was investigated by quantitative *real-time* PCR. In addition, we analyzed overall expression pattern in coLCL and MSLCL by DNA microarrays.

Results:

The expression of EBV nuclear antigen 2 (*EBNA2*) was higher in MSLCL than coLCL. In MSLCL, a stronger correlation of *EBNA2* and the lytic EBV life cycle transcripts of *EBNA1* with HERV-K, -H and -W transcripts was observed. Furthermore, DNA microarray analyses showed higher transcript amounts of a known MS risk locus (*HLA-DRB5*, Chr. 6p21.3) in the MSLCL.

Conclusion:

The study supports the hypothesis of an EBV-mediated transactivation of HERV in the pathogenesis of MS. The stronger correlation of HERV and EBV transcripts in MSLCL suggests that EBV lytic and latent programs may be regulated differently in B cells of MS patients and healthy controls.