7 Summary

The etiopathogenesis of most autoimmune diseases (AIDs) is not yet understood. The clinical pictures of retrovirus infected animals and the presence of cross-reactive antibodies against retroviral antigens, which are detectable in serum samples from AID patients, suggest a role of retroviruses in the etiology of such diseases. A considerable part of the human genome consists of human endogenous retrovirus (HERV) sequences, and several studies implied that expression of normally quiescent HERV sequences might be involved in AID development. However, so far no virus or HERV expression could be linked clearly to the etiopathogenesis of one of the AIDs studied in this work (MS, scleroderma, SLE, spondylitis ankylosans).

In order to clarify the conflicting results which were obtained with different methods and materials in various laboratories over time, highly sensitive methods were needed. In this study, the differential display was modified as a retrovirus generic screening tool for cell culture material. The Mg^{2+} based reverse transcriptase (RT) activity assay was optimized and Mn^{2+} was introduced as second cation. In order to determine the potential effect of HERV expression, a panel of quantitative RT real-time PCRs was established. The sensitivity, reliability, and suitability of the assays for cell culture supernatants and plasma was demonstrated. Samples from children and adolescents with early onset MS (EOMS), or affected by active MS at the time of sampling and from adults with MS were analyzed in comparison to those from healthy individuals, from children and adolescents affected by neurological diseases and from adults affected by non-MS autoimmune diseases (scleroderma, SLE, spondylitis ankylosans).

Plasma samples from scleroderma, SLE, and spondylitis patients were analyzed for RT activity. None of the patients showed elevated RT activity in comparison to healthy controls. Thus, it seems to be unlikely that exogenous retroviruses are involved as infectious agents in the etiopathogenesis of the AIDs examined. The expression patterns for three different HERV sequences showed significant differences for groups of healthy controls compared to diseased individuals, and for children and adolescents in comparison to adults. The different groups of children and adolescents showed no significant differences in the HERV expression patterns when compared to age-matched controls, except for young male MS patients with active MS at the time of sampling. Significantly higher expression of the three HERV sequences was detected for male children/adolescents with active MS in comparison to healthy and age-matched males. In contrast to other studies, no elevated expression of any of the tested HERV sequences was detected for MS patients. Spondylitis ankylosans patients showed significantly lower expression of MSRV and HERV-W, while SLE patients showed significantly higher expression of HERV-W when compared to healthy controls. Different expression levels were detected for healthy children/adolescents in comparison to healthy controls for two of three HERV sequences (HERV-H and MSRV). These findings suggest that HERV expression may vary with age.