HERV encoded envelope proteins – key players in autoimmunity?

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The pathogenesis of most autoimmune diseases is as yet unknown. Human endogenous retroviruses (HERV) have been discussed to play a role in autoimmune diseases of most body organs such as e.g. brain, skin, joints, muscles, bowel, endocrine glands, kidney and blood vessels. The key feature of autoimmune diseases is inflammation. When autoimmunity would be driven by HERVs, the according inflammation needs to be explained. HERV-encoded envelope proteins (env) can presumably act as strong immune stimulators (superantigens). Previously, we have demonstrated that T-cell superantigens such as Staphylococcal enterotoxin A (SEA) are capable to induce a cellular inflammatory reaction in different organs such as CNS, joints and muscles of experimental animals. The character of the inflammation induced by the same superantigen (SEA) differed from organ to organ and showed similarities with the respective autoimmune diseases known for each of the investigated organs. Induction of inflammation by the superantigen did not require adjuvant-crackup of immune tolerance, which is a necessary requirement in so-called autoimmune disease models that use conventional antigens. Beside cellular inflammatory features, many autoimmune diseases show humoral autoimmune characteristics such as oligoclonal immunoglobulin bands in multiple sclerosis cerebrospinal fluid or different types of blood serum autoantibodies in other autoimmune diseases. Previously, we have shown that B-cell superantigens such as gp120, i.e. part of the HIV-envelope, are capable to activate blood leucocytes in vitro to produce immunoglobulin in an oligoclonal manner. Antigen specificities present among these immunoglobulins were e.g. Measles, Rubella, Herpes-Zoster. When a superantigenic stimulus is taken into consideration, the diverse autoantibody specificities present in many autoimmune diseases becomes easy to understand.

Another feature of autoimmune diseases is organ degeneration. Usually organ degeneration is attributed to inflammation alone. However, degeneration may develop almost or completely without inflammation such as e.g. in primary progressive multiple sclerosis. When the dualism of HERV and HERV-superantigen driven inflammation is taken into consideration, it becomes readily understandable that HERV effects may exist by themselves, i.e. without inflammation. Thus, a HERV pathogenesis is better compatible with known features of autoimmune diseases than the so-called autoimmune models with conventional antigens.