Inflammatory response of endothelial cells to HERV.W Envelope

Patrice N Marche

The envelope protein of an MS-associated retrovirus activates brain endothelium. MSRV (multiple sclerosis associated retroviral element) was initially isolated from patients with MS and belongs to the HERV.W family which is integrated in the human germline. The envelope protein (Env-ms) can be expressed in macrophages in active plaques in the brain, and in the plasma of most MS patients. Env-ms displays pro-inflammatory properties for several types of immune cells expressing TLR4, a pattern recognition receptor of innate immunity. In the present study, the aim was to analyze the effects of Env-ms on the blood-brain barrier (BBB) at a molecular and functional level. For this, we used the HCMEC/D3 brain endothelial cell line, to model the blood–brain barrier (BBB), which expresses TLR4. We demonstrate that Env-ms is able to stimulate several inflammatory parameters : 1) overexpression of ICAM-1, a major mediator of leukocyte adhesion to endothelial cells, 2) production of the pro-inflammatory cytokines IL-6 and IL-8, 3) increase of the adhesion and the transmigration of activated immune cells through a monolayer of endothelial cells. Silencing TLR4 expression and antibodies specific to Env reduce Env-ms effects on endothelial cells. These findings support the hypothesis that Env-ms triggers activation of endothelial cells at the BBB and immune cells elsewhere (monocytes, dendritic cells, B lymphocytes…) through TLR4 pathway together, thus contributing to the immune infiltration associated to the pathogenesis of MS.

Duperray et al, International Immunology, published online Open access: http://intimm.oxfordjournals.org/content/early/2015/05/26/intimm.dxv025.full.pdf+html