Endozigous retroviruses in genomes of species

Biochemical forms of pHERV-W Env antigen (transfected cells with reference plasmids)

Result:
- No specific signal was obtained in cell extracts transfected with plasmids expressing GFP or SYN
- GN_mAb_Env01 and GN_mAb_Env04 specifically detected pHERV-W Env monomeric and oligomeric

Methods:
- Transfected samples with reference plasmids: HEK-293T cells were transfected with expression plasmids, using pCMV-GFP (control protein), pCMV-HIV-Env (Env isolate; GenBank no. AF313501.1) or pCMV-SIVp (plaque synctin-1, a "physiologically adapted" copy; GenBank no. KF072526.1)
- Brain samples: Snap-frozen microcryostome brain samples were obtained from the Brain Bank of Pathology, VU University Medical Center, Amsterdam, NLD. 5 from active MS lesions, 4 from MS normal appearing white matter (NAWM) and 5 from non-MS Controls

Conclusions:
- pHERV-W Env was identified as monomer and oligomer in reference transfected cell extracts. In the soluble fraction from MS lesions or sera, a unique large peak of hexamer was detected around 360-400 kDa. This was absent in MS NAWM and control extracts, suggesting that pHERV-W Env is highly expressed in MS lesions and in the brain of patients with MS. However, in cases where hexamers disappeared after deglycosylation, like in transfected cells, in the MS stage samples or sera, the N-linked glycans were labeled in all conditions, whereas the C-terminus hydrophobic region became detectable after deglycosylation only. A suitable structural organization is proposed here as the best possible soluble form.
- Given previously described effects of the pHERV-W Env antigen, this soluble hexameric form now raises the question about its relationship with the soluble demyelinating and cytotoxic factor (300kDa) described in MS (H. Lassmann Exp Neurol 2014; Lisak et al., 2017).
- If antigenically related, this soluble demyelinating factor should also be targeted by anti-pHERV-W Env neutralizing antibody (GN9AC1), currently in clinical development in MS.