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Human Endogenous retrovirus type W family encodes a pro-inflammatory envelope protein expressed in multiple sclerosis brain lesions and is likely to comprise unfixed proviral copies in the human population

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Human endogenous retroviruses (HERV) are complex and heterogeneous multicopy families of genetic elements which represent about 8 % of the human genome. HERV copies can retain transcriptional activity but complete and functional provirus have not been identified so far.

Retrovirus-like particles with reverse transcriptase (RT) activity were shown in macrophage cultures from patients with multiple sclerosis (MS). PCR extension to all retroviral genes in purified particles with specific buoyant density and reverse transcriptase activity was achieved and unravelled the previously unknown HERV-W family. As many unfixed HERVs (Marchi et al. J.Virol. 2014), the corresponding provirus has not already been isolated. Nonetheless, HERV-W env, gag and pol-encoded proteins are detected in all active MS brain lesions analysed to date, whereas HERV-W envelope displays potent neuro-inflammatory pathogenicity.

We have now identified cultured cells expressing all HERV-W gag-pol-env encoded proteins detected with specific monoclonal and polyclonal antibodies by WB analysis, along with RT activity in supernatants. Polyproteins, cleaved capsid and RT bands are seen for gag and pol, as full-length glycosylated monomer and multimers for env, indicating that HERV-W copies with complete orfs for gag, pol and/or env exist in human cells but are not described in the existing databases.

We should therefore seek for still undescribed and unfixed HERV-W copies in DNA. Analysing their distribution in the human populations as in patients with diseases for which HERV-W proteins and RNA levels are associated with etiopathogeny or lesions, could clarify the involvement of HERV-W elements in several chronic inflammatory diseases.

Biography

Herve Perron has completed his PhD in 1991 (Virology) and HDR (Professor Thesis; Biology) in 2000 from the Faculty of Medicine, Joseph Fourier University, Grenoble-France. He isolated and characterized a novel retroviral element from Multiple Sclerosis (MSRV), itself defining a novel family of human endogenous elements (HERV-W). He reviewed about a hundred manuscripts for more than 40 scientific and medical journals and is author in about 70 peer-reviewed publications. He is presently Chief Scientific Officer of Geneuro SA, Geneva-Switzerland. Geneuro develops innovative humanized antibody treatments for Multiple Sclerosis and for other diseases involving HERV-W as psychoses associating neuroinflammation.

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