No Apparent Higher Frequency of Copy Number Alterations of the HERV-W_Xq22.3 Locus Region in Patients with Multiple Sclerosis

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Abstract

Approximately 8% of the human genome are of retroviral origin. Human endogenous retroviruses (HERVs) derive from germ-line colonizations by distinct exogenous retroviruses that occurred millions of years ago. Few HERVs still encode retroviral proteins and HERV proteins have been involved in human physiology and pathology, including a pathophysiological role of multi-copy HERV-W, specifically HERV-W Envelope (Env) protein in Multiple Sclerosis (MS). The precise genetic origin of pathophysiologically relevant HERV-W Env protein remains unclear. A HERV-W Env-encoding locus (ERVW-1) encodes a full-length Env (Syncytin-1) that is involved in formation of the placental syncytiotrophoblast layer. Our own previous findings imply that, rather than ERVW-1, a HERV-W locus located in human chromosome Xq22.3 (HERV-W_Xq22.3) might be of relevance in MS. HERV-W_Xq22.3 lacks most of the proviral 5' portions, yet harbours a 542 aa env ORF interrupted only by a stop mutation at codon 39, the next downstream start located at codon 68. HERV-W_Xq22.3 Env is detected by HERV-W Env-specific antibodies. Mouse mAb GN-mAB_03 (3B2H4), employed for immunohistochemical detection of HERV-W Env in MS lesions, recognizes HERV-W_Xq22.3 Env, but not Syncytin-1, thus the protein detected by GN-mAB_03 in MS lesions might originate from HERV-W_Xq22.3. HERV-W_Xq22.3 locates within a genome region with copy number variations (CNVs). HERV-W_Xq22.3 within a CNV region is expected to alter the "normal", sex-specific number of HERV-W_Xq22.3 copies, potentially affecting expression levels of HERV-W_Xq22.3 accordingly. We studied a conceivable association of the copy number of the HERV-W_Xq22.3 locus region with MS by measuring copy numbers of the HERV-W_Xq22.3 locus region in gDNA from patients with MS compared to healthy controls. We did not detect significantly different copy numbers of the HERV-W_Xq22.3 locus region between those groups. Our results provide further insight into how the HERV-W_Xq22.3 locus may (not) be involved in the development of MS.

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Keywords: human endogenous retrovirus, HERV, multiple sclerosis