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GENETICS OF MULTIPLE SCLEROSIS RELATED TO CCSVI

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Multiple sclerosis (MS) is a complex disorder probably resulting from interaction between environmental and genetic predisposing factors, still uncharacterised. A known association between HLA region on 6p21.32 and MS exists. Recently, a picture of chronic cerebrospinal venous insufficiency (CCSVI) in consequence of stenosing venous malformation of the main extra-cranial outflow routes (VM) has been described in patients affected with MS, introducing an additional phenotype with possible pathogenic meaning in MS.

In order to explore the presence of copy number variations (CNVs) within the HLADRA locus we designed a custom CGH array fully covering the 7 Mb of the HLADRA locus region, (6,899,999bp; chr6:29,900,001-36,800,000). Genomic DNA of the 15 patients with CCSVI/VM and MS was hybridised in double.

In total patients showed 322 CNVs of which 225 extragenic and 97 intragenic. We identified 234 known polymorphic CNVs in the 15 patients. The majority of these CNVs are in non-coding or extragenic regions. The overall number of CNVs is correlated with the number of extracranial VM with a trend toward significance ($r=0.52$, $r2=0.27$, $p=0.0545$). The contribution to the correlation is due to the extragenic CNVs, being significantly correlated to the number of stenosing VM ($r=0.53$, $r2=0.28$, $p<0.05$), whereas the intragenic CNVs did not result significantly associated to the VM phenotype.