A biologic marker of disease severity in Multiple Sclerosis; the search for the Holy Grail in a Hellenic cohort

Theodoros Kyriakides

Background: Multiple sclerosis (MS) is characterized by a remarkable heterogeneity in disability progression but there is a lack of biological markers that can be used to prognosticate on an individual patient basis. There is convincing evidence that genetic variants may contribute to accrual of disability. Genes involved in innate and adaptive immunity have been implicated but molecules involved in leukocyte trafficking to the CNS also appear appealing. Methods: In total, 389 MS cases and 336 controls were recruited from three MS centres in Cyprus and Greece. We genotyped 147 tagging SNPs in 9 genes (P-selectin, integrins ITGA4, ITGB1 and ITGB7, adhesion molecules ICAM1, VCAM1 and MADCAM-1, Fibronectin 1 and Osteopontin) involved in lymphocyte adhesion processes and trafficking to the central nervous system. Severity was measured by the multiple sclerosis severity score (MSSS).Results: A significant association was detected between rs6721763 of ITGA4 gene and susceptibility to MS as well as with disease severity as measured with MSSS (p=1.46E-5). Conclusion: The current provides evidence that variants encoding adhesion molecules, responsible for lymphocyte trafficking and activation impact on MS clinical severity. These findings may have implications for prognosis, treatment options and in the selection of potential therapeutic targets