

## **Multiple Sclerosis: a complex disease with complex genetics**

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Multiple sclerosis (MS) is a chronic inflammatory autoimmune disorder of the central nervous system that leads to disability. MS is characterized by relapses (unpredictable attacks) and progressiveness (neurologic decline). MS is considered as a typical common complex disease where several environmental factors (e.g. infection, sunlight, smoking and diet) influence pathogenesis in a genetically susceptible individual to cause the disease. Until recently, only HLA region was steadily reported as a genetic susceptibility factor for MS. Worldwide extensive linkage studies in multiple families failed to uncover pathogenic mutations. In the era of candidate gene association studies a huge amount of data was published (free access to the [www.msgene.org](http://www.msgene.org)) albeit results remaining contradictory for the majority of the genes. In 2007, after the introduction of genome-wide genetic association studies (GWAS) for large scale association studies, the first two susceptibility genes (*IL2RA* and *IL7RA*) along with the confirmation of HLA-DRA locus were reported. Since then, many GWAS and meta-analyses were published and currently there are 110 established MS risk variants at 103 discrete loci in human genome (most of them in immune response pathway). Research in MS genetics is currently driven by the new generation sequencing technology (exome and whole-genome sequencing) and first results have been published pointing probably to the first gene (*CYP27B1*) that may cause rare familial MS. Despite progress in unraveling the genetics factors that underlie MS pathogenesis, the link for environment-gene interactions is still mainly unknown. Dysregulation of *N*-glycosylation provides probably the first link to this interaction.