MULTIPLE SCLEROSIS

Gene–vitamin D interactions likely to influence pathogenesis and risk of relapse in multiple sclerosis

Variants in genes implicated in the vitamin D pathway modify the relationship between levels of the circulating vitamin D metabolite 25(OH)D and risk of relapse in patients with multiple sclerosis (MS), new research shows. Moreover, several single nucleotide polymorphisms (SNPs) are associated with the risk of relapse or with 25(OH)D levels. “This is the first time that it has been shown that particular genotypes modify an association between a biomarker and MS relapse,” explains Ingrid van der Mei, lead investigator of the study, which was conducted in Australia.

Previous work indicated that high levels of 25(OH)D are associated with a reduced rate of relapse in patients with MS. 25(OH)D levels potentially influence regulatory T-cell function—thought to be important in MS pathogenesis. “However, we know that an interplay between genes and environmental factors causes MS

and modifies its progression,” explains van der Mei.

The investigators conducted a longitudinal study of 141 patients with relapsing–remitting MS over ~2.3 years. The patients’ serum 25(OH)D levels were measured every 6 months, and their genotypes were examined. 276 SNPs in 21 genes related to vitamin D metabolism and vitamin D receptor factor complex formation were analysed.

“...particular genotypes modify an association between a biomarker and MS relapse...”

Notably, the researchers found that two intronic SNPs (rs908742 in *PRKCZ* and rs3783785 in *PRKCH*) modified the risk of relapse, and that two further SNPs (rs1993116 in *CYP2R1* and rs7404928 in *PRKCB*) were associated with low levels of 25(OH)D. Furthermore, the investigators

reported a cumulative effect of the risk genotypes on 25(OH)D levels and risk of relapse in these patients. The protein kinase C family of genes influence T-cell activation and are associated with several neurological diseases. The researchers hypothesize that altered T-cell function might underlie the autoimmune T-cell response thought to drive MS.

More high-quality longitudinal studies are now needed. “It is critical, in the first instance, that these findings are replicated in other clinical cohorts of MS patients,” asserts van der Mei, while noting that trials of vitamin D supplementation in patients with MS are already underway.

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