PEPTIDE MODULATES SLE GENE EXPRESSION

The tolerogenic peptide hCDR1 modulates *in vivo* the expression of genes implicated in the pathogenesis of systemic lupus erythematosus (SLE), according to research led by Edna Mozes. The immunomodulatory effects of hCDR1 therapy in the peripheral blood mononuclear cells of patients with mild-to-moderate SLE are consistent with those observed in several mouse models of the disease.

The synthetic peptide, designed by Mozes and colleagues to be specific to SLE, is based on the complementarity-determining region (CDR) 1 of a human monoclonal anti-DNA antibody. Studies in animal models have shown that the clinical improvements induced by hCDR1 in mice are attributable to the generation of FOXP3⁺CD4⁺CD25⁺ regulatory T cells, the upregulation of transforming growth factor- β (TGF- β) and the suppression of pathogenic cytokines. The results of the current double-blind study show that treatment with hCDR1 also modulates gene expression *in vivo* in patients with SLE.

In blood samples from the five patients who received active treatment, gene expression of the proinflammatory cytokines interleukin (IL)-1 β , tumor necrosis factor, interferon γ and IL-10, the B-lymphocyte stimulator (BLyS), and the proapoptotic molecules caspase-3 and caspase-8 were downregulated after 24 consecutive weekly injections of hCDR1. Gene expression of FOXP3 and TGF- β was upregulated over the same period. By contrast, no significant effects on gene expression were observed in the four patients who received placebo injections. Clinical improvements were observed in patients treated with hCDR1 but not in the placebo group.

The results of this small study should be interpreted with caution, but suggest that correction of dysregulated gene expression by hCDR1 could hold promise as a specific treatment for SLE.

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