EXPERIMENTAL ARTHRITIS

Inducing tolerance with CD40 siRNA

Silencing expression of CD40 using small interfering RNA (siRNA) can inhibit the development of disease in the collagen-induced arthritis (CIA) mouse model, by temporarily inducing tolerance rather than autoimmunity, according to a paper published in *Arthritis Research & Therapy*.

“Onset of disease was delayed in mice receiving CD40 siRNA ... and the severity of disease in these animals was reduced”

“There has been promising evidence that interruption of the CD40-CD154 interaction may be effective for modulating autoimmunity, but developing practical approaches to this blockade has proved difficult,” explains Robert Inman, one of the lead researchers on this study.

Here, siRNA targeting CD40 or control siRNA was systemically administered to DBA mice using a hydrodynamic method (injection into the tail vein) either before

or after antigen challenge with type II collagen (CII). Onset of disease was delayed in mice that received CD40 siRNA rather than control siRNA prior to antigen challenge, and the severity of disease in these animals was reduced. Protective effects of CD40 siRNA were also seen when the siRNA was administered after CII administration.

“Amelioration of arthritis was associated with suppression of T_H1 cytokine and autoantibody formation, as well as upregulation of T regulatory cells,” explains Inman. “Using this approach, we demonstrated antigen-specific immune modulation and inhibition of joint inflammation in the CIA mouse model,” Inman adds. “These findings support the feasibility of transient gene-silencing as a possible therapeutic approach in autoimmune diseases.”

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Original article Zheng, X. *et al.* RNAi-mediated CD40-CD154 interruption promotes tolerance in autoimmune arthritis. *Arthritis Res. Ther.* **12**, R13 (2010)