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CTLA-4 blocks activation of arthritogenic T cells

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Keywords

CTLA-4Ig, collagen induced arthritis, gene therapy

Context

A second "costimulatory" signal is required for T cell activation; the prototype T cell costimulatory receptor is CD28. Cytotoxic T lymphocyte associated antigen (CTLA)-4 downregulates activated T cells via a soluble form (CTLA-4Ig) which blocks CD28 signalling. CTLA-4Ig delivered intravenously is being evaluated as a treatment for rheumatoid arthritis. This study examines the effects of adenovirally delivered CTLA-4Ig in the treatment of established collagen-induced arthritis (CIA).

Significant findings

The authors conclude that gene therapy with soluble CTLA-4 effectively blocks activation of arthritogenic T cells *in vivo*. Treatment CTLA-4Ig suppressed CIA in a dose-dependent manner.

Comments

This study represents a new strategy for treating CIA by focusing on the suppression of T cell activation, which appears to be effective once the disease has been established. Since previous anti-T-cell therapies for rheumatoid arthritis have been ineffective, this approach could have applications in this disease. However, gene therapy will not be an immediate option in humans as the situation could be quite different from that in animal models and immunodeficiency could be expected.

Methods

Gene transfer mediated by replication-deficient recombinant adenovirus, chimeric CTLA-4Ig fusion protein, DBA/1 mice

References

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