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OX40/OX40L in RA

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Keywords

Collagen arthritis, costimulation, immunotherapy, OX40, OX40L, RA

Context

OX40, a tumor necrosis factor receptor (TNFR) family member on activated T cells, binds OX40L, a TNF family member on B cells, dendritic cells and endothelium. Their interaction provides T- and B-cell costimulation with T-cell activation and B-cell antibody production. Endothelial adhesion of activated T-cells and activation of dendritic cells may also result. This study investigated their role in inflammatory arthritis.

Significant findings

OX40L monoclonal antibody abrogated murine collagen-induced arthritis (CIA) when administered for 4 days from boosting immunisation but not if administered 7 days later. Serum IgG2a anti-collagen titres were specifically reduced; *in vitro*, T-cell proliferation in response to collagen was maintained, but a-interferon production was inhibited.

Rheumatoid arthritis synovial fluid T cells but not peripheral blood T cells expressed OX40, and OX40L was present on synovial sublining cells.

The authors conclude that OX40/OX40L interaction is not necessary for T-cell activation but enhances Th1 responses. The therapeutic effect of blockade may represent a reduced Th1 response, but also perhaps reduced migration of activated T cells to the joint.

Comments

This work suggests a potential target for RA immunotherapy but additional arthritis models need to be studied, as does the effect of blockade of OX40/OX40L in human synovial cultures or in SCID mice

bearing human synovial tissue. Additional mechanistic studies are needed to assess effects on lymphocyte migration, as well as actions on synovial antigen presenting cells and B cells, and modulation of synovial cytokine production. General immunosuppressive effects of therapy also require investigation. It is premature to recommend *in vivo* human studies, but a costimulatory interaction that modulates T-cell responses suggests an attractive therapeutic target. It is important to remember, however, that Th2 responses can also be damaging.

Methods

Collagen arthritis, blocking studies, proliferation assays, anti-collagen titres, immunohistochemistry

References

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