Adalimumab suppresses markers of structural damage in ankylosing spondylitis

Therapy with anti-tumor necrosis factor agents improves the symptoms of ankylosing spondylitis (AS); however, evaluation of these agents' disease-modifying capability in placebo-controlled trials is hampered by limitations of the modified Stoke AS Spinal Score, which, despite its 'gold standard' status, has poor capacity to detect radiographic progression. A recent randomized, placebo-controlled study investigated the effects of adalimumab on biomarkers thought to be predictive of structural damage in patients with AS.

Patients with long-standing active AS received 40 mg of adalimumab ($n = 38$) or placebo ($n = 44$) every other week for 24 weeks. Adalimumab treatment significantly decreased concentrations of serum matrix metalloproteinase 3 and urinary C-telopeptide fragment of type II collagen; however, it had no effect on N-telopeptide of type I collagen, a serum biomarker of bone resorption, reinforcing findings from a previous study of infliximab. Interestingly, a strong correlation was noted between C-telopeptide fragment of type II collagen and C-reactive protein levels, suggesting that adalimumab reduces cartilage turnover via amelioration of inflammation. A significant, but weaker, correlation between matrix metalloproteinase 3 and C-reactive protein might be explained by the limited number of patients with peripheral joint involvement. A notable lack of correlation between biomarker levels and MRI findings suggests that they measure separate aspects of disease progression.

The capacity of adalimumab to suppress biomarkers associated with AS progression and the absence of correlation with MRI findings suggests that future studies should measure both outcome parameters.

Original article Maksymowych WP *et al.* (2008) Beneficial effects of adalimumab on biomarkers reflecting structural damage in patients with ankylosing spondylitis. *J Rheumatol* **35:** 2030–2037

Oral vaccine protects against disease in a mouse model of RA

A *Salmonella* vector expressing colonization factor Ag I (CFA/I), which was developed as a diarrhea vaccine, has previously been shown to have anti-inflammatory properties. A study by Kochetkova *et al.* has now demonstrated that the vaccine provides protection from collagen-induced arthritis (CIA), a mouse model of rheumatoid arthritis (RA), by altering the function of type-II-collagen-specific $CD4^+$ T cells.

The development of CIA was suppressed in DBA/1 mice that were orally immunized with *Salmonella*–CFA/I, compared with those that received vector-only or phosphate-buffered saline (control groups), as demonstrated by marked reductions in cartilage degeneration and proinflammatory cytokine production following challenge with type II collagen. Analysis of T cells purified from the lymph nodes of protected mice showed reduced proliferation of type-II-collagen-specific $CD4^+$ T cells and increased production of regulatory cytokines, including interleukin (IL)-4 and TGF-β. Notably, neutralization of IL-10, TGF-β or IL-4 by monoclonal antibodies compromised the protective effect of *Salmonella*–CFA/I administration, highlighting the important role of these cytokines in the suppression of CIA. Adoptive transfer experiments after CIA induction showed that both $CD4^+CD25^-$ and $CD4^+CD25^+$ T-cell subsets confer protection and suppress production of IL-17, IL-27 and tumor necrosis factor, but the effect is optimal with total $CD4^+$ T cells.

The results of this study show that *Salmonella*–CFA/I vaccine has the therapeutic potential to suppress the development of CIA in susceptible mice.

Original article Kochetkova I *et al.* (2008) Vaccination without autoantigen protects against collagen II-induced arthritis via immune deviation and regulatory T cells. *J Immunol* **181:** 2741–2752

$IgG4^+$ multi-organ lymphoproliferative syndrome: a new clinical entity?

Mikulicz's disease, the clinical syndrome of swollen lacrimal and salivary glands with marked mononuclear cell infiltration, has long been considered a manifestation of Sjögren's syndrome (SS). Researchers in Japan now propose that this is in fact a distinct clinical entity, $IgG4^+$ multi-organ lymphoproliferative syndrome (MOLPS), based on diagnostic