five different *TNF*-promoter polymorphisms. Only –238A showed a statistically significant association with disease ($P = 0.01$) in both populations. The meta-analysis suggested that individuals with this variant had an approximately doubled risk of developing psoriatic arthritis (odds ratio 2.29, 95% CI 1.48–3.55).

The inconsistent results of earlier studies might have been caused by inadequate sample numbers, ethnic differences between populations, and small effect sizes of *TNF* polymorphisms, say the authors. They caution, however, that the association between –238A and psoriatic arthritis should be confirmed by large-scale studies.

Original article Rahman P *et al.* (2006) TNFα polymorphisms and risk of psoriatic arthritis. *Ann Rheum Dis* **65:** 919–923

Strong evidence that anti-PDGFR antibodies cause scleroderma

A rigorous, international study published in the *New England Journal of Medicine* has demonstrated the presence of IgG autoantibodies that stimulate the fibroblast receptor for platelet-derived growth factor (PDGFR-stimulatory antibodies) in sera from patients with systemic sclerosis (scleroderma).

The authors performed a series of experiments that confirmed that these antibodies recognized and activated native PDGFR on fibroblasts. *In vitro,* purified PDGFR-stimulatory antibodies triggered pathways that resulted in the intracellular generation of reactive oxygen species and upregulation of type I collagen gene expression, as well as conversion of human primary fibroblasts to an active, myofibroblast phenotype. Baroni *et al*. suggest that these effects could account for the oxidative stress and fibrosis that are the cellular and systemic hallmarks, respectively, of systemic sclerosis.

Sera from 46 white patients (38 women) with systemic sclerosis, who had not taken immunosuppressive medication in the previous 6 weeks, were compared with sera from 20 control individuals (matched for age, sex and ethnicity), as well as with sera from 54 individuals with a range of autoimmune conditions. All of the patients with systemic sclerosis, and none of the other individuals, were positive for PDGFR-stimulatory antibodies.

The authors noted that PDGFR-stimulatory antibodies did not completely replicate the effects of PDGF: they hypothesize that these autoantibodies generate a more persistent stimulus than PDGF does. Direct proof of the causative role of these antibodies in systemic sclerosis, however, awaits *in vivo* studies in large, ethnically diverse populations of patients.

Original article Baroni SS *et al.* (2006) Stimulatory autoantibodies to the PDGF receptor in systemic sclerosis. *N Engl J Med* **354:** 2667–2676

RA therapy with infliximab and adalimumab linked with infection and malignancy

A systematic review and meta-analysis has concluded that patients with rheumatoid arthritis (RA) treated with the anti-tumor necrosis factor (TNF) antibodies infliximab or adalimumab have an increased risk of serious infections, and a dose-dependent increased risk of malignancies. There has previously been uncertainty over the extent to which anti-TNF agents are associated with serious infection and malignancy, mainly because of difficulty with the interpretation of sparse data from trials that were not adequately powered to detect these rare adverse events.

The meta-analysis included placebo-controlled studies of patients diagnosed with RA according to American College of Rheumatology criteria, who were randomly allocated to receive infliximab or adalimumab for ≥12 weeks. Nine trials, comprising 3,493 patients treated with an anti-TNF antibody and 1,512 patients who received placebo, were analyzed. Published data from the trials was supplemented with information from the trial sponsors and principal investigators.

There were 29 malignancies in anti-TNF-treated patients, and 3 malignancies in placebo-treated patients. Malignancies were most common in patients treated with high doses of an anti-TNF antibody. Infections occurred in 126 anti-TNF-treated patients, and in 26 placebo-treated patients.

There were some limitations to this systematic review, including scarcity of event data, and heterogeneity between trials. The authors conclude that patients' risk of adverse