

IN BRIEF

 AUTOIMMUNITY**GWASs can explain why the drugs don't work**

Genome-wide association studies (GWASs) have identified genetic variants associated with disease, but, as most variants only modestly affect disease risk, the overall medical relevance of GWASs has been questioned. This study explains how a better functional understanding of these variants could be medically useful. The authors found that rs1800693 — a single-nucleotide polymorphism (SNP) in the gene encoding tumour necrosis factor receptor 1 (TNFR1) — leads to the expression of an altered protein ($\Delta 6$ -TNFR1) that is secreted as a soluble TNF receptor. GWASs previously found that rs1800693 is associated with multiple sclerosis, but not with rheumatoid arthritis, psoriasis or Crohn's disease. Notably, although TNF antagonists can be an effective treatment for these latter diseases, they can exacerbate disease (or even promote disease onset) in patients with multiple sclerosis. This suggests that TNF antagonists mimic the disease-promoting effects of $\Delta 6$ -TNFR1. Therefore, if combined with proper follow-up studies, GWASs across common autoimmune diseases may help to predict the efficacy of therapies for these diseases.

ORIGINAL RESEARCH PAPER Gregory, A. P. *et al.* TNF receptor 1 genetic risk mirrors outcome of anti-TNF therapy in multiple sclerosis. *Nature* 8 Jul 2012 (doi:10.1038/nature11307)

 TUMOUR IMMUNOLOGY**T_H9 cells tackle tumours**

Purwar *et al.* report that interleukin-9 (IL-9)-producing T cells can promote immunity to melanoma. In a model of melanoma, mice with deficiencies in T helper 17 (T_H17) cell-promoting pathways showed decreased tumour growth and increased survival; this improved clinical outcome was found to be partially dependent on IL-9. In adoptive transfer experiments using different populations of tumour-specific T_H cells, mice that received T_H9 cells showed the greatest resistance to tumour growth. Treatment with exogenous IL-9 also limited tumour growth, and the antitumour effects of IL-9 were found to be dependent on mast cells. Finally, populations of IL-9-producing T cells could be identified in the skin and peripheral blood of healthy humans, but the frequencies of these cells were decreased in metastatic melanoma lesions.

ORIGINAL RESEARCH PAPER Purwar, R. *et al.* Robust tumor immunity to melanoma mediated by interleukin-9-producing T cells. *Nature Med.* 8 Jul 2012 (doi:10.1038/nm.2856)

 PARASITE IMMUNITY **$\gamma\delta$ T cells boost DC responses to malaria**

Previous studies have shown that $\gamma\delta$ T cells promote protective immunity to malaria, but the mechanisms involved were not clearly understood. This study shows that $\gamma\delta$ T cells are important for dendritic cell (DC) activation during infection with *Plasmodium berghei*, a non-lethal malarial parasite. The production of interferon- γ and expression of CD40 ligand by $\gamma\delta$ T cells enhanced co-stimulatory molecule and interleukin-12 expression by DCs, which promoted the development of protective CD4⁺ T cell responses during *P. berghei* infection. $\gamma\delta$ T cell-deficient mice died following infection with *P. berghei*; however, these mice developed protective immunity if they were administered an agonistic CD40-specific antibody after infection. It will be interesting to explore whether this therapeutic strategy could be useful in humans.

ORIGINAL RESEARCH PAPER Inoue, S. *et al.* Enhancement of dendritic cell activation via CD40 ligand-expressing $\gamma\delta$ T cells is responsible for protective immunity to *Plasmodium* parasites. *Proc. Natl Acad. Sci. USA* 9 Jul 2012 (doi:10.1073/pnas.1204480109)