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► **COVER:** 'Damage and Repair' by Neil Smith, inspired by the Review on p261.



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**T** helper 1 ( $T_H1$ ) and  $T_H2$  cells as we know them today — which is as  $CD4^+$  T-cell subsets producing distinct cytokines (interferon- $\gamma$  and interleukin-4 (IL-4), respectively) — were first described in 1986 in *The Journal of Immunology* by Mosmann *et al.* Since then, our knowledge of T-cell biology has increased enormously, and many more distinct  $CD4^+$  T-cell subsets have been identified, including  $T_H3$  cells, which are characterized by their production of transforming growth factor- $\beta$  (TGF $\beta$ ), and  $CD4^+CD25^+$  regulatory T cells, which can produce IL-10 and TGF $\beta$  (although whether these cytokines are required for their suppressive function remains controversial). Recent studies have reported the existence of a population of  $CD4^+$  T cells that produces the pro-inflammatory cytokine IL-17. In the Opinion article on page 329, Chen Dong discusses the evidence supporting the suggestion that IL-17-producing  $CD4^+$  T cells are a unique  $T_H$ -cell lineage that is distinct from the  $T_H1$ - and  $T_H2$ -cell lineages in terms of the cytokines that are produced by these cells and the transcription factors that mediate their development.

One of the reasons for the huge interest in IL-17-producing  $T_H$  cells is that IL-17 has been shown to have a pro-inflammatory function in several animal models of autoimmunity, and its expression has been associated with several inflammatory diseases in humans, including rheumatoid arthritis. However, before IL-17-producing  $T_H$  cells can be considered as potential therapeutic targets, we need to learn more about their biology. And, as indicated in a Research Highlight on page 260 — which describes a recent paper in *Immunity* that reports a role for TGF $\beta$  in regulating the development of IL-17-producing  $T_H$  cells — we might be in for some surprises!

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on acid-free paper