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► **COVER:** 'The right hat for the job' by Simon Bradbrook, inspired by this month's Focus on CD4+ T-cell diversity.


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Writing in *Nature Immunology* in June 2006, Robert Coffman — who together with Timothy Mossman was one of the founding fathers of the T_H1–T_H2-cell hypothesis — expressed his expectation that ultimately "the understanding of immune regulation will exceed the ability of the original T_H1–T_H2 hypothesis to adequately organize and explain it."

In April 1986 in the *Journal of Immunology*, Coffman and Mossman were the first to show at a clonal level that $CD4^+$ T cells could be divided into two subsets on the basis of cytokine production. However, they cautioned that their research "raises the question of the total diversity of T cell phenotypes. [...] it is quite possible that other T cell types exist *in vivo*." Indeed, since 2006, we have recognized T_H17 cells as a third T-cell lineage, and T follicular helper cells might also be a distinct T-cell subset. Two studies in the December 2008 issue of *Nature Immunology* show that T_H2 cells can be reprogrammed by TGFβ to become a new functional subset that produces IL-9 and IL-10. Together, these studies support the idea that $CD4^+$ T cells have more functional plasticity than previously appreciated, an idea that is explored in the accompanying Poster, produced with support from UCB.

Nevertheless, the importance of the T_H1–T_H2-cell classification and the research that it inspired cannot be underestimated. Studying the regulation of T_H1- versus T_H2-cell differentiation led to renewed interest in innate immunity and the role of Toll-like receptors in matching the type of adaptive response to the immune challenge. The reciprocal relationship between T_H1 and T_H2 cells indirectly inspired research into the inhibitory properties of T cells, which led to characterization of the previously elusive concept of regulatory T cells. The contents of this Focus issue, sponsored by Schering-Plough, and modern immunology in general, owe a lot to the ideas of Coffman and Mossman.

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