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Journal club

DIVISION OF LABOUR BY CD4$^+$ T HELPER CELLS

It is now well accepted that CD4$^+$ T cells come in different flavours, including: T helper 1 (T_H1) cells that produce interferon-γ (IFNγ) and are involved in responses to intracellular pathogens; T_H2 cells that produce interleukin-4 (IL-4), IL-5 and IL-13, and respond to helminth infections; and T_H17 cells that produce IL-17A and IL-17F, and deal with extracellular pathogens. This division of labour has led to specific CD4$^+$ T cell subsets being associated with specific diseases (autoimmunity for T_H1 and T_H17 cells, and allergic responses for T_H2 cells). However, ~30 years ago, this level of complexity was only beginning to be appreciated, as documented in a landmark study by Robert Coffman and colleagues (Mossmann *et al.*, 1986).

Beginning in the late 1970s, initial studies in mice had suggested that there were subsets of L3T4$^+$Lyt2$^-$ (CD4$^+$CD8$^-$) T cells with different activities (Tada *et al.*, 1978; and Kim *et al.*, 1985). These groups, as well as others, showed that there were T cell populations that provided different forms of help in antibody responses. These studies suggested that there was diversity within the CD4$^+$ T cell pool, but the underlying mechanisms remained obscure.

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This changed in 1986, when Mossmann *et al.* used T cell clones to show that there were two distinct subsets of T helper cells. Using the nomenclature of Tada *et al.*, they referred to these subsets as T_H1 cells (producing IFNγ, IL-2 and lymphotoxin) and T_H2 cells (producing BSF1 and TCGF2 (now both known as IL-4), and MCGF2 (now both known as IL-5)). The T_H2 cell clones could also induce the expression of Ia antigens on B cells and enhance IgG1 and IgE synthesis. Importantly, IFNγ was capable of inhibiting both of these T_H2 cell activities, which showed that the subsets cross-regulated each other.

The remarkable aspect of this work was that it was carried out at a time before enzyme-linked immunosorbent assays, cytokine-specific antibodies, intracellular flow cytometry and quantitative PCR. The T helper cell clones were characterized using bioassays for the activities they produced. This work pioneered subsequent analysis of CD4$^+$ T cell differentiation and represented a paradigm shift in how immune responses are assessed and studied.

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ORIGINAL ARTICLE Mossmann, T. R. *et al.* Two types of murine helper T cell clone. I. Definition according to profiles of lymphokine activities and secreted proteins. *J. Immunol.* **136**, 2348–2357 (1986)
FURTHER READING Tada, T. *et al.* Two distinct types of helper T cells involved in the secondary antibody response: independent and synergistic effects of Ia$^-$ and Ia$^+$ helper T cells. *J. Exp. Med.* **147**, 446–458 (1978) | Kim, K. J. *et al.* Distinct functional phenotypes of cloned Ia-restricted helper T cells. *J. Exp. Med.* **162**, 188–201 (1985)