T CELLS: FRIENDS AND FOES

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Although the late 19th century witnessed several groundbreaking discoveries that laid the foundation of modern immunology, including the identification of "germs" as the cause of infectious disease (by Robert Koch and Louis Pasteur) and the first descriptions of phagocytosis (by Élie Metchnikoff) (Smith, 2015; Cohn, 2017), it was not until the mid-1960s that the essential role of lymphocytes in adaptive immunity was established, owing to the pioneering work of Jim Gowans (Gowans and et al., 1962). Since then, an extensive experimental effort unveiled not only the remarkable phenotypic and functional diversity of lymphocytes but also their implication in a vast array of physiological and pathological processes (Smith and et al., 2017; Ebbo and et al., 2017; Rawlings and et al., 2017; Qi, 2016; Bjorkstrom and et al., 2016). $CD19^+$ lymphocytes expressing the so-called B-cell receptor (BCR, a monomeric transmembrane variant of a type M immunoglobulin) are commonly referred to as "B cells," reflecting their main anatomical site of maturation (the ***b***one marrow, in humans, and the ***b***ursa of Fabricius in birds). Similarly, $CD3^+$ lymphocytes expressing the so-called T-cell receptor (TCR), in any of its variants, are generally dubbed "T cells" or "T lymphocytes," with direct reference to the ***t***hymus (Murphy and Weaver, 2016). Both B and T cells employ their exclusive receptors for reacting to antigenic entities as they proliferate to establish an adaptive immune response. However, while activated B cells differentiate into plasma cells that secrete mature immunoglobulins (de facto, soluble variants of the BCR), the expansion of T cells is not accompanied by TCR secretion (Murphy and Weaver, 2016). Moreover, while the BCR can recognize both particulate and soluble antigens, most TCRs recognize only small peptides presented in the context of MHC molecules. That said, a small percentage (approx. 2%) of

human T cells expresses a poorly diverse set of TCRs composed of γ and δ chains that recognize specific antigens irrespective of MHC presentation, de facto operating as an innate immune effector (Nielsen and et al., 2017; Mondragon and et al., 2016). Of note, the entire combinatorial diversity of the BCR and TCR repertoires in a single individual is (at least theoretically) capable to provide protection against virtually all possible antigenic challenges (Murphy and Weaver, 2016; Rudqvist and et al., 2018).

The cellular and molecular biology of T cells has major pathophysiological relevance. On the one hand, mature T cells are quintessential for the control of infections, not only as they can directly eliminate cells bearing intracellular pathogens—function performed by $CD8^+$ cytotoxic T lymphocytes (CTLs) (Tscharke and et al., 2015; Voskoboinik and et al., 2015)—but also as they secrete a large panel of cytokines that support innate and humoral immunity against extracellular pathogens—a function performed by both $CD4^+$ helper T (T_H) cells and $CD8^+$ CTLs (Bevan, 2004; Crotty, 2015; Gasteiger and Rudensky, 2014). Moreover, T cells have a major role in both natural and therapy-driven anticancer immunosurveillance (Kroemer and et al., 2015; Shankaran and et al., 2001). Thus, T cells are potent weapons that control organismal homeostasis and can (at least potentially) be harnessed for therapeutic purposes. Accordingly, when T cells are the target of viral infections, such as in the case of HIV-1, the profound immunosuppressive state that ensues T-cell depletion may have catastrophic consequences (in the absence of adequate clinical management) (Barouch and Deeks, 2014; Walker and Yu, 2013). On the other hand, T cells underlie the pathogenesis of various conditions including most (if not all) autoimmune disorders, graft rejection, and some hematological tumors (e.g., cutaneous T-cell lymphoma) (Espinosa and et al., 2016; Chong and Perkins, 2014; Suarez-Fueyo and et al., 2017; Petrelli and van Wijk, 2016; Tripodo and et al., 2009). Thus, in some clinical settings, the deregulated activity or proliferation of T cells constitutes a prominent therapeutic target.

In *The biology of T cells* (a thematic issue of the successful *International Review of Cell and Molecular Biology* series), world-leading experts in the field offer an overview of the major molecular and cellular aspects of T-cell biology and their links to human pathophysiology. Each of the chapters of *The biology of T cells* focuses on one specific facet of the

development, phenotype, function, study, or pathophysiological relevance of T lymphocytes. The book (which consists of two parts, part A and part B) is equally addressed to expert investigators, who may wish to expand their knowledge on the biology of T cells, and to newcomers to this exciting and rapidly expanding area of research.

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