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► COVER: 'Achilles' heel' by Tom Wilson, inspired by the Review on p418.



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Most readers will be familiar with the distinction between the innate and adaptive immune responses. Innate immunity forms the first line of defence against invading microorganisms and occurs rapidly, without the need for cell division or differentiation. The innate response is primarily based on the recognition of a restricted number of conserved microbial elements by germline-encoded intracellular and cell-surface host recognition receptors. By contrast, the somatically generated diversity of the cell-surface receptors on the B and T cells that are responsible for the later, adaptive immune response is such that these cells can recognize an almost infinite number of antigens.

You might be less familiar, however, with a type of immune cell that combines features of both the innate and adaptive immune systems. On page 405 of this issue, Mitchell Kronenberg and colleagues discuss these natural killer T (NKT) cells, which express both a T-cell receptor that is characteristic of adaptive immunity and the surface receptors typical of NK cells, which are involved in the innate immune response. The article focuses on invariant NKT (*i*NKT) cells, which express an invariant T-cell-receptor (TCR) α -chain. *i*NKT cells can be activated directly and indirectly: the indirect activation pathways allow these cells to respond to various bacterial, viral and parasite antigens and the direct activation pathway is involved in the response to a more restricted range of microorganisms.

Elsewhere, on page 453, Moradpour, Penin and Rice review the recent exciting progress that has been made in our understanding of the replication of hepatitis C virus, and on page 418, Bill Steinbach and colleagues discuss the prospects for harnessing the fungal calcineurin pathway to develop novel antifungals.

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