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► **COVER:** 'Hide and seek' by Simon Bradbrook, inspired by the Review on p911.



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The immune system is dynamic, continually changing to accommodate the needs of the body during infections, injury or stress. A multitude of regulatory mechanisms underlie these continuous changes, from factors that influence the initial stages of immune-cell development to the pathways that fine-tune the phenotype and functional responses of effector cells. On [page 948](#), Pärt Peterson and colleagues discuss recent research on AIRE (autoimmune regulator), which has a crucial role in shaping the repertoire of developing T cells. In addition, two articles in this issue take a look at heterogenous immune-cell subsets — dermal dendritic cells ([page 935](#)) and macrophages ([page 958](#)) — that have unique and essential roles in the immune system. The phenotype and function of the cells that make up each of these populations can vary depending on the location or disease context in which they are found.

Despite the dynamic and flexible nature of the immune system, problems still occur. As discussed by Gökhan Hotamisligil and Ebru Erbay on [page 923](#), the dysregulation of the pathways that link immunity and metabolism can give rise to diseases such as type 2 diabetes and atherosclerosis. In addition, pathogens have evolved to subvert various mechanisms of host immune defence. On [page 911](#), Andrew Bowie and Leonie Unterholzner discuss how viruses resist immune clearance by evading detection through host pattern-recognition receptor pathways.

Immune-mediated diseases and tumours can arise when environmental or intrinsic factors overwhelm the body's ability to maintain healthy immune homeostasis. Promising research suggests that it is possible to treat such diseases and re-establish immune homeostasis using various approaches. However, as discussed by Rachel Caspi on [page 970](#), recapitulating the body's natural balance through therapy is not a simple matter.

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