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► **COVER:** 'Pathways' by Neil Smith; inspired by the Review on p127.



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All cells of the immune system are derived from precursors in the bone marrow, the most primitive of which are haematopoietic stem cells (HSCs). A lack of suitable technology has meant that, until recently, it has been difficult to define the distinct steps and sites of early lymphocyte development from HSCs. However, recent data have begun to define the specialized niches in the bone marrow in which HSC differentiation and self-renewal are controlled, and in which B-cell development is completed.

The final steps of development to become a T cell are completed in the thymus and not, as for B cells, in the bone marrow. Although T-cell development in the thymus is one of the best-characterized systems of mammalian cellular differentiation and lineage commitment, there are still many unanswered questions: for example, which precursors travel from the bone marrow and settle in the thymus, and what are the precise molecular signals that specify cell fate and induce these precursors to become T cells?

Understanding the environmental factors and signalling pathways that determine early lymphocyte development are of great interest not only to scientists but also to clinicians, because the knowledge gained has potential clinical application for the treatment of immunodeficient individuals, such as individuals with genetic mutations that result in immunodeficiency or patients who have been administered myeloablative agents to treat haematopoietic malignancies. As a result of this widespread interest in early lymphocyte development, we have commissioned four articles addressing distinct aspects of this topic. These articles can be found in this special issue of the journal and are accompanied by a Web Focus (<http://www.nature.com/nri/focus/lymphocytedev>).

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