al and Lenz et al[5]). Despite spectacular advances since the introduction of rituximab, many patients with advanced disease and a high Follicular Lymphoma International Prognostic Index (FLIPI) score have disease recurrences.[6] For such patients, the continued study of autologous transplantation, possibly in combination with rituximab for in vivo purging, remains an important area of investigation. ■

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● ● ● CHEMOKINES, CYTOKINES, AND INTERLEUKINS

Comment on Liu et al, page 2531

Thymus colonization: a shared responsibility

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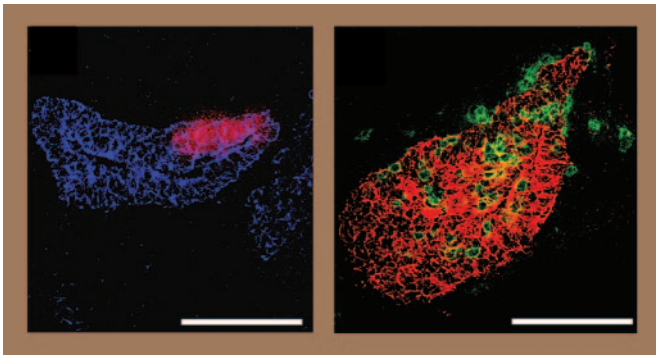
Chemokine production by thymic epithelial cells has been implicated in the recruitment of T-cell progenitors to the thymus. Here, Liu and colleagues show cooperation between the thymus and the parathyroid in chemokine-mediated thymus colonization.

In this issue of *Blood*, Liu and colleagues have analyzed the mechanisms that regulate the recruitment of lymphoid precursors to the thymus. This a is a critical step in the production of T cells, as although the thymus provides a specialized microenvironment that supports the development of lymphoid precursors, these cells are produced in extrathymic tissues and have to undergo a migratory journey culminating in thymus seeding. The mechanisms regulating thymus colonization are not clear, and it is likely that progenitors enter the thymus in different ways during development. For example, in the embryo, lymphoid precursors can enter prior to thymus vascularization, whereas at later stages, cells enter the thymus via the circulation.[1,2]



Chemokine expression and fetal thymus colonization: a role for the parathyroid. See the complete figure in the article beginning on page 2531.

Liu et al analyzed the first wave of progenitors to colonize the prevascularized thymus rudiment, which is notable in that these progenitors are able to generate a specialized subset of epidermal γδ T cells that regulate immune responses in the skin.[3] By carefully analyzing progenitor recruitment in embryos deficient in particular chemokine receptors, the authors show that the attraction of lymphoid precursors to the prevascular thymus anlagen depends upon their expression of CCR9 and CCR7. In contrast, following thymus vascularization, CCR7/CCR9 double-deficient precursors are able to enter the thymic microenvironment, a finding that directly demonstrates temporally regulated mechanisms of thymus seeding.

As these findings suggested a role for the ligands of these receptors, CCL25 (for CCR9) and CCL19/21 (for CCR7), in early thymus colonization, the authors went on to analyze chemokine expression in the early thymic anlagen. Perhaps surprisingly, immunohistochemical analysis demonstrated anatomic compartmentalization of chemokine expression within the third pharyngeal pouch (see figure). Thus, while CCL25 was detected at 2 sites, the ventral-posterior domain that gives rise to the thymus and the dorsal-anterior domain that forms the parathyroid, CCL21 expression was detected only in the parathyroid region (see figure). Moreover, at embryonic day 11.5, the initial attraction of lymphoid progenitors in FoxN1-deficient nude mice, which lack thymic production of CCL25, occurred normally. Collectively, these findings identify CCR9 and CCR7 as key chemokine receptors regulating recruitment of progenitors to the prevascular thymic anlagen and demonstrate a previously unrecognized synergy between the parathyroid and the thymus in chemokine-mediated recruitment of lymphoid progenitors. ■

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