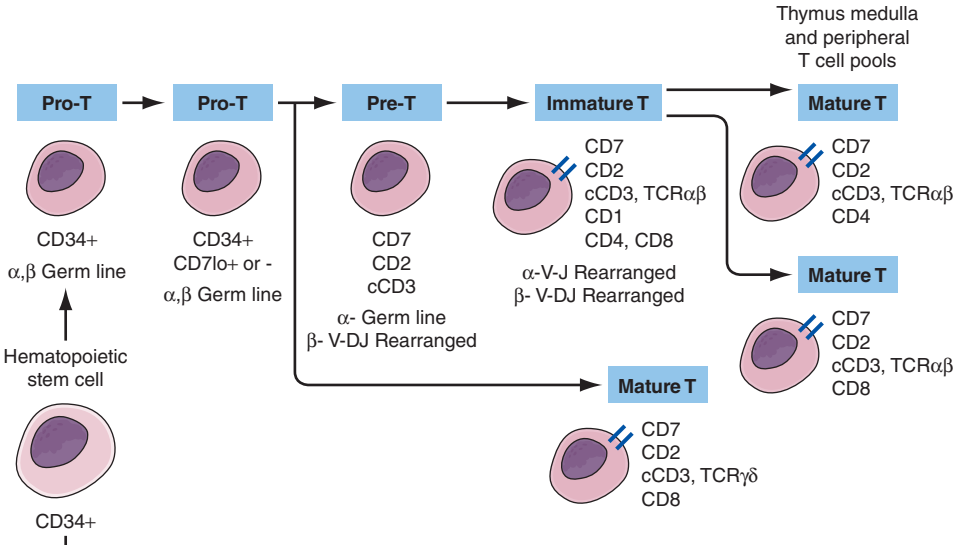


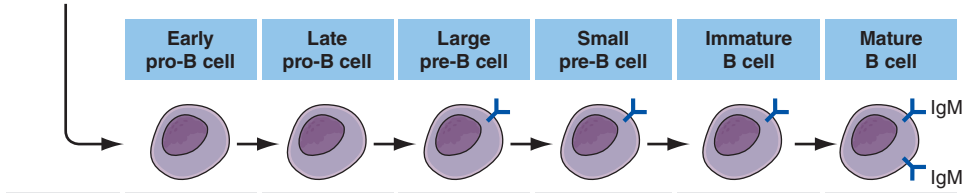


| | | | | | | |
|---|---|---|---|---|---|---|
| **High-chain genes** | DJ rearranged | VDJ rearranged | VDJ rearranged | VDJ rearranged | VDJ rearranged | VDJ rearranged |
| **Low-chain genes** | Germ line | Germ line | Germ line | VDJ rearranged | VDJ rearranged | VDJ rearranged |
| **Surface Ig** | Absent | Absent | μ H-chain at surface as part of pre-β receptor | μ H-chain in cytoplasm and at surface | IgM expressed on cell surface | IgD and IgM made from alternatively spliced H-chain transcripts |
| **Surface marker proteins** | CD34<br>CD10<br>CD19<br>CD38 | CD10<br>CD19<br>CD20<br>CD38<br>CD40 | CD19<br>CD20<br>CD38<br>CD40 | CD19<br>CD20<br>CD38<br>CD40 | CD19<br>CD20<br>CD40 | CD19<br>CD20<br>CD21<br>CD40 |

**FIGURE 372e-6 Development stages of T and B cells.** Elements of the developing T and B cell receptor for antigen are shown schematically. The classification into the various stages of B cell development is primarily defined by rearrangement of the immunoglobulin (Ig) heavy (H) and light (L) chain genes and by the absence or presence of specific surface markers. The classification of stages of T cell development is primarily defined by cell-surface marker protein expression (sCD3, surface CD3 expression; cCD3, cytoplasmic CD3 expression; TCR, T cell receptor). *(Adapted from CA Janeway et al [eds]: Immunobiology. The Immune Systemic Health and Disease, 4th ed. New York, Garland, 1999; with permission.)*

Effector memory T cells reside in nonlymphoid organs and respond rapidly to repeated pathogenic infections with cytokine production and cytotoxic functions to kill virus-infected cells. Central memory T cells home to lymphoid organs where they replenish long- and short-lived and effector memory T cells as needed.

In general, CD4+ T cells are the primary regulatory cells of T and B lymphocyte and monocyte function by the production of cytokines and by direct cell contact (Fig. 372e-2). In addition, T cells regulate erythroid cell maturation in bone marrow and, through cell contact (CD40 ligand), have an important role in activation of B cells and induction of Ig isotype switching. Considerable evidence now exists that colonization of the gut by commensal bacteria (the gut microbiome) is responsible for expansion of the peripheral CD4+ T cell compartment in normal children and adults.

Human T cells express cell-surface proteins that mark stages of intrathymic T cell maturation or identify specific functional subpopulations of mature T cells. Many of these molecules mediate or participate in important T cell functions (Table 372e-1, Fig. 372e-6).

The earliest identifiable T cell precursors in bone marrow are CD34+ pro-T cells (i.e., cells in which TCR genes are neither rearranged nor expressed). In the thymus, CD34+ T cell precursors begin cytoplasmic (c) synthesis of components of the CD3 complex of TCR-associated molecules (Fig. 372e-6). Within T cell precursors, TCR for antigen gene rearrangement yields two T cell lineages, expressing either TCR-αβ chains or TCR-γδ chains. T cells expressing the TCR-αβ chains constitute the majority of peripheral T cells in blood, lymph node, and spleen and terminally differentiate into either CD4+ or CD8+ cells. Cells expressing TCR-γδ chains circulate as a minor population in blood; their functions, although not fully understood, have been postulated to be those of immune surveillance at epithelial surfaces and cellular defenses against mycobacterial organisms and other intracellular bacteria through recognition of bacterial lipids.

In the thymus, the recognition of self-peptides on thymic epithelial cells, thymic macrophages, and DCs plays an important role in shaping the T cell repertoire to recognize foreign antigen (*positive selection*) and in eliminating highly autoreactive T cells (*negative selection*). As immature cortical thymocytes begin to express surface TCR for antigen, autoreactive thymocytes are destroyed (negative selection), thymocytes with TCRs capable of interacting with foreign antigen peptides in the context of self-MHC antigens are activated and develop