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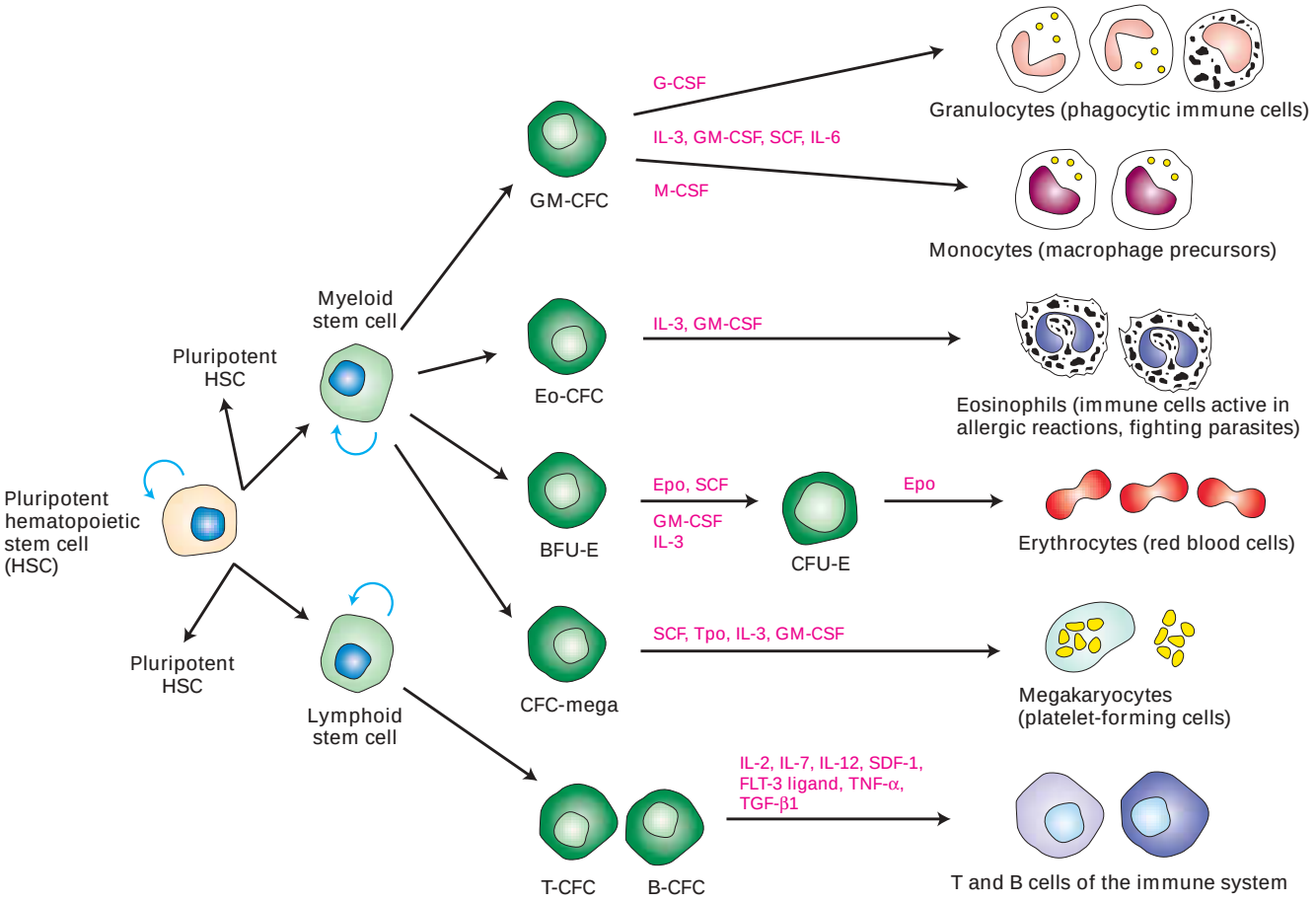
Skin also contains dendritic epidermal T cells, an immune-system cell that produces a certain form of the T-cell receptor (see Table 14-1). When dendritic epidermal T cells are genetically modified so they do not produce T-cell receptors, wound healing is slow and less complete than in normal skin. Normal healing is restored by addition of keratinocyte growth factor. The current hypothesis is that when dendritic epidermal T cells recognize antigens on cells in damaged tissue, they respond by producing stimulating proteins, such as keratinocyte growth factor, that promote keratinocyte growth and wound healing. Many other signals also control the growth of skin cells, including Wnt/β-catenin, Hedgehog, calcium, transforming growth factor α (TGFα), and TGFβ. Discovering how all these signals work together to control growth and stimulate healing is a substantial challenge that will advance our understanding of diseases such as psoriasis and skin cancer and perhaps pave the way for effective treatments. ▮

Another continuously replenished tissue is the blood, whose stem cells are located in the bone marrow in adult animals. The various types of blood cells all derive from a single type of *pluripotent hematopoietic stem cell*, which gives rise to the more-restricted myeloid and lymphoid stem cells (Figure 22-5). The frequency of hematopoietic stem cells is about 1 cell per 10^4 bone marrow cells, even lower than the frequency of intes-



▲ FIGURE 22-5 **Formation of differentiated blood cells from hematopoietic stem cells in the bone marrow.** Pluripotent stem cells may divide symmetrically to self-renew (curved arrow) or divide asymmetrically to form a myeloid or lymphoid stem cell (light green) and a daughter cell that is pluripotent like the parental cell. Although these stem cells are capable of self-renewal, they are committed to one of the two major hematopoietic lineages. Depending on the types and amounts of cytokines present, the myeloid and lymphoid stem cells generate different types of precursor cells (dark green), which are incapable of self-renewal. Precursor cells are detected by their ability to form colonies containing the differentiated cell types shown at right, measured as "colony-forming cells (CFCs)." The colonies are detected on the spleen of animals that have had their own cells eliminated and the precursor cells introduced. Further cytokine-induced proliferation, commitment, and differentiation of the precursor cells give rise to the various types of blood cells. Some of the cytokines that support this process are indicated (red labels). GM = granulocyte-macrophage; Eo = eosinophil; E = erythrocyte; mega = megakaryocyte; T = T-cell; B = B-cell; CFU = colony-forming unit; CSF = colony-stimulating factor; IL = interleukin; SCF = stem cell factor; Epo = erythropoietin; Tpo = thrombopoietin; TNF = tumor necrosis factor; TGF = transforming growth factor; SDF = stromal cell–derived factor; FLT-3 ligand = ligand for fms-like tyrosine kinase receptor 3. [Adapted from M. Socolovsky et al., 1998, *Proc. Nat'l. Acad. Sci. USA* **95**:6573.]