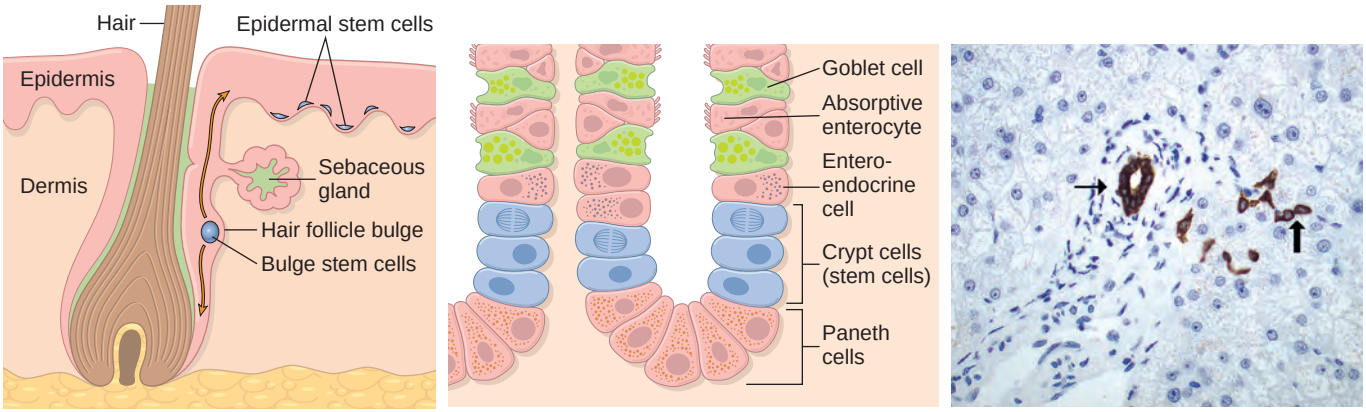


**Figure 1-21** Stem cell niches in various tissues. **A,** Skin stem cells are located in the bulge area of the hair follicle, in sebaceous glands, and in the lower layer of the epidermis. **B,** Small intestine stem cells are located near the base of the crypt, above Paneth cells. **C,** Liver stem cells (*oval cells*) are located in the canals of Hering (*thick arrow*), structures that connect bile ductules (*thin arrow*) to parenchymal hepatocytes. Bile duct cells and canals of Hering are stained here with an immunohistochemical stain for cytokeratin 7. (**C,** Courtesy Tania Roskams, MD, University of Leuven, Belgium).

after chemotherapy (e.g., for leukemia), or to provide normal precursors to correct various blood cell defects (e.g., sickle cell disease, Chapter 14).

Besides hematopoietic stem cells, the bone marrow (and notably, other tissues such as fat) also contains a population of *mesenchymal stem cells*. These are multipotent cells that can differentiate into a variety of stromal cells including chondrocytes (cartilage), osteocytes (bone), adipocytes (fat), and myocytes (muscle). Because these cells can be expanded to large numbers, and can also generate a locally immunosuppressive microenvironment (thus potentially evading rejection), they may represent a ready means of manufacturing the stromal cellular scaffolding for tissue regeneration.

### *Regenerative Medicine*

**The ability to identify, isolate, expand, and transplant stem cells has given birth to the new field of regenerative medicine.** Theoretically, the differentiated progeny of ES or adult stem cells can be used to repopulate damaged tissues, or to construct entire organs for replacement. In particular, there is considerable excitement about the therapeutic opportunities for restoring damaged tissues that have low intrinsic regenerative capacity, such as myocardium after a myocardial infarct or neurons after a stroke. Unfortunately, despite an improving ability to purify and expand stem cell populations, much of the initial enthusiasm has been tempered by difficulties encountered in introducing and *functionally integrating* the replacement cells into sites of damage.

Another potential problem is the immunogenecity of most stem cells; although mesenchymal stem cells may be weakly immunogenic, most other adult stem cells, as well as ES cells (from fertilized blastocysts), express histocompatibility (HLA) molecules of the sperm and egg donors that provoke immunologic rejection by the host (Chapter 6). Hence, considerable effort has been expended to generate cells that are totipotential like ES cells but are derived from the patient into whom they will be implanted. To accomplish this, a handful of genes have been identified whose products can—remarkably—reprogram somatic cells to achieve the "stem-ness" of ES cells. When such genes are introduced into fully differentiated cells (e.g., fibroblasts), *induced pluripotent stem cells (iPS cells)* are generated (Fig. 1-22). Since these cells are derived from the patient, their differentiated progeny (e.g., insulin-secreting β-cells in a patient with diabetes) can be engrafted without eliciting a rejection reaction. Another exciting recent development is genomic editing, a process using a nuclease

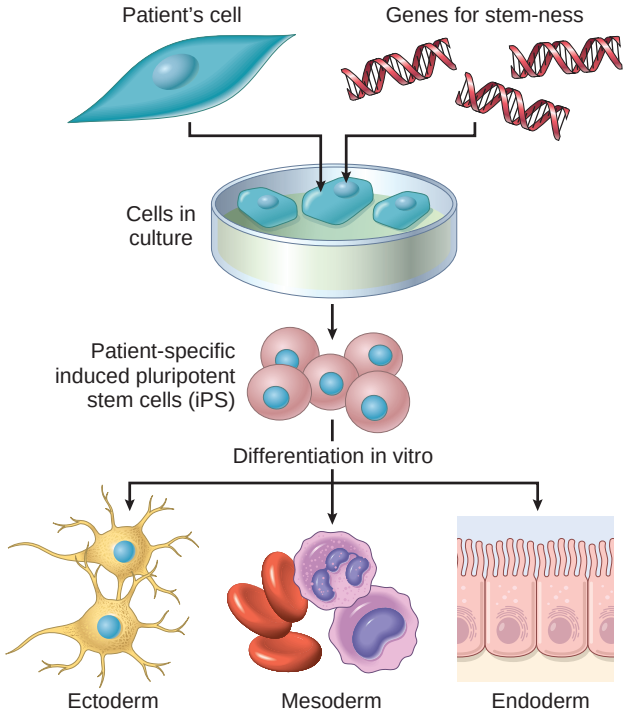


**Figure 1-22** The production of induced pluripotent stem cells (iPS cells). Genes that confer stem cell properties are introduced into a patient's differentiated cells, giving rise to stem cells that can be induced to differentiate into various lineages. (Modified from Hochedlinger K, Jaenisch R: Nuclear transplantation, embryonic stem cells, and the potential for cell therapy. N Engl J Med 349:275-286, 2003.)