Haematopoietic stem cells (HSCs) continuously replenish blood cells that are lost by attrition or trauma. They are capable of self-renewal and are currently the only adult stem-cell type routinely used in clinical settings to replace lost cells. HSCs are mostly quiescent but can be mobilized from their niche to proliferate and differentiate into lineages of the innate and adaptive immune system, as well as into red blood cells and platelets. Cell-fate decisions are initiated and maintained by specific combinations of transcription factors, the activity of which is orchestrated by extrinsic and intrinsic signals. The study of changes in regulatory networks during haematopoietic differentiation has long served as a paradigm for basic processes of cell-fate specification and its aberrations, such as those that occur in leukaemia. The easy accessibility and transplantability of normal and leukaemic haematopoietic cells has led to the discovery of cytokines, oncogenes and cancer stem cells and to some of the most celebrated successes of targeted drug design.
Haematopoietic stem cells (HSCs). Cells that are capable of reconstituting all lineages of the haematopoietic system after transplantation into lethally irradiated mice. Long-term repopulating HSCs (LT-HSCs) do this life-long and after secondary transplantations into irradiated hosts, whereas short-term repopulating HSCs (ST-HSCs) only show multilineage repopulation for a few weeks. LT- and ST-HSCs can be identified and isolated by flow cytometry on the basis of their expression of specific cell-surface antigens.

Lineage commitment
Also known as cell-fate determination; a process whereby HSCs become specialized while losing their self-renewal capacity.

Progenitor cells
Also known as precursor cells; are intermediates between HSCs and differentiated cells with restricted differentiation potential, high proliferative capacity, but little or no self-renewal capacity. They are probably equivalent to the transit amplifying cells of other adult stem-cell systems.

Myeloid cells
A term variously used to define non-lymphoid cells or cells of the monocyte–macrophage compartment (known as myelomonocytic cells).

Granulocytes
A group of cells including neutrophils, eosinophils, and basophils, but the term is often used for neutrophils only.

Stem-cell niches
Specialized microenvironments that control stem-cell dormancy and the balance between stem-cell self-renewal and differentiation.

Plasticity
The capacity of defined cell types to acquire new identities. The extent of plasticity of HSCs and haematopoietic progenitors under physiological conditions is controversial and probably quite limited. However, re-specification of cell fate can be induced by enforced transcription factor expression, cell fusion or nuclear transfer.

Self-renewal
The ability of cells to repeatedly generate at least one identical daughter cell.

Bone-marrow and/or HSC transplantation
A procedure involving injection of HSCs or bone marrow into irradiated hosts to determine the cell’s biological potential. In the clinic it is a life-saving procedure after chemotherapy or radiation therapy that destroys the haematopoietic system. Bone-marrow transplantation typically requires immunosuppression to prevent graft rejection due to tissue mismatch.

Cord-blood stem cells
These are fetal HSCs present in the umbilical cord of newborns. They are used clinically as an alternative to bone-marrow-derived HSCs. If stored frozen and thawed years later, they can be useful for regenerating the haematopoietic system of the donor, obviating the danger of tissue rejection of mismatched transplants.

Dormancy and mobilization
Although HSCs self-renew, they are mostly quiescent, dividing approximately once a month. Proliferation can be activated in response to injury or injection of cytokines, such as granulocyte colony-stimulating factor (G-CSF). G-CSF also induces the exit of HSCs from their niches and mobilization of the cells into the circulation, a procedure that is used clinically to obtain HSCs from a patient’s blood.

Cytokines and chemokines
Secreted proteins that stimulate cell growth, survival and differentiation.

Colony-forming assay
If seeded in semi-solid medium, blood-cell precursors form colonies in the presence of appropriate cytokines. This assay is widely used to define a cell’s differentiation potential and to identify biologically active molecules.

Cancer and/or leukaemia stem cells
These are self-renewing cells capable of generating leukaemia after transplantation. They can give rise to more differentiated cells comprising the bulk of the leukaemia. Cancer stem cells, first identified in acute myeloid leukaemia, are critical targets for intervention.

Lineage priming
The promiscuous expression of myeloid–erythroid lineage associated markers in HSCs.

Background reading


