11. Cellula staminale

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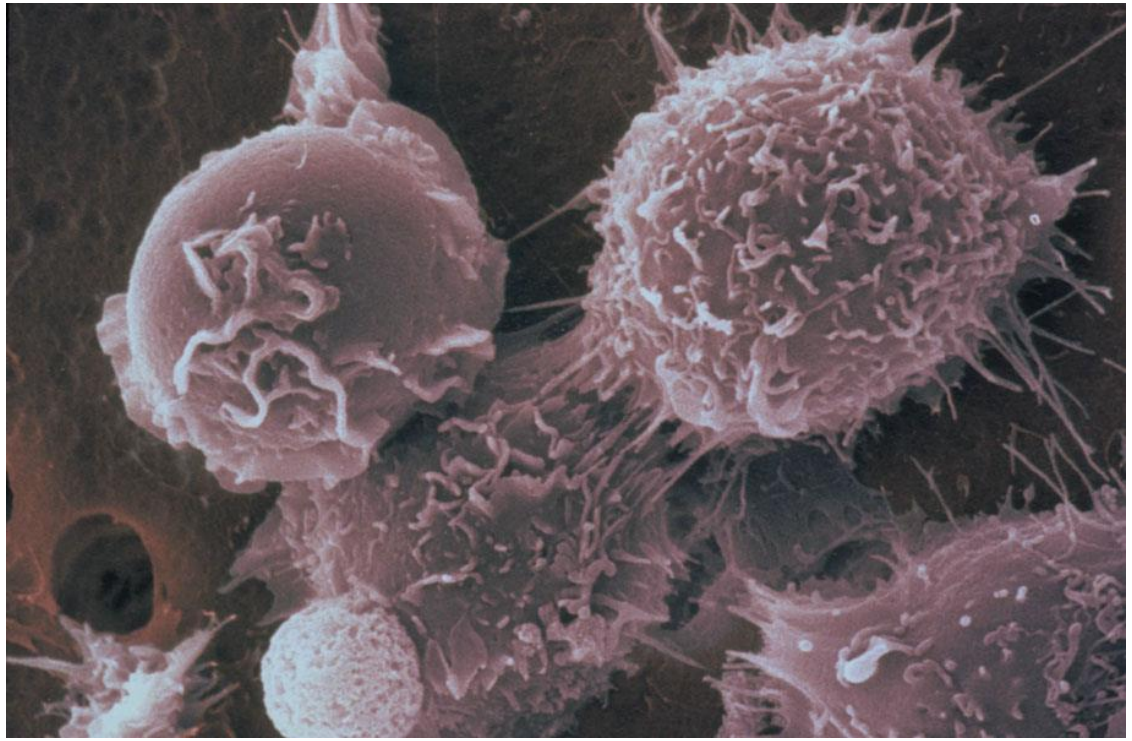
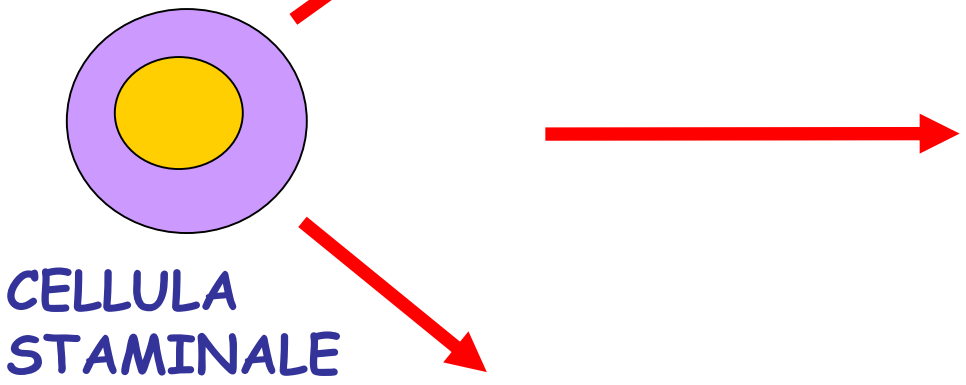
CELLULA STAMINALE



Anne McLaren Nature 414, 129-131:2001

CELLULA STAMINALE: definizione



CELLULA STAMINALE

Self-renewal: dividendosi riproduce se stessa

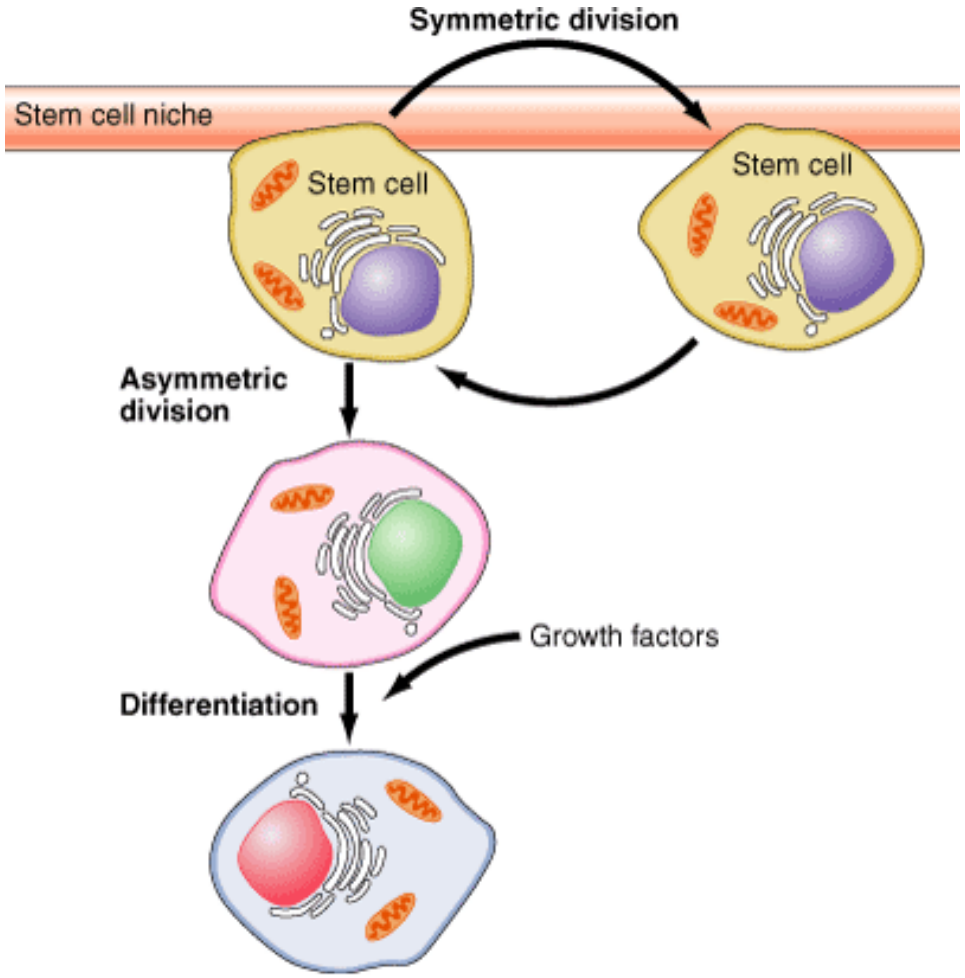
Differenziazione: dà origine a cellule più specializzate

Genera, mantiene, e rimpiazza le cellule differenziate terminali entro i loro specifici tessuti

Sviluppo e turnover cellulare fisiologico

Danno tissutale dovuto a lesioni

Cellula staminale

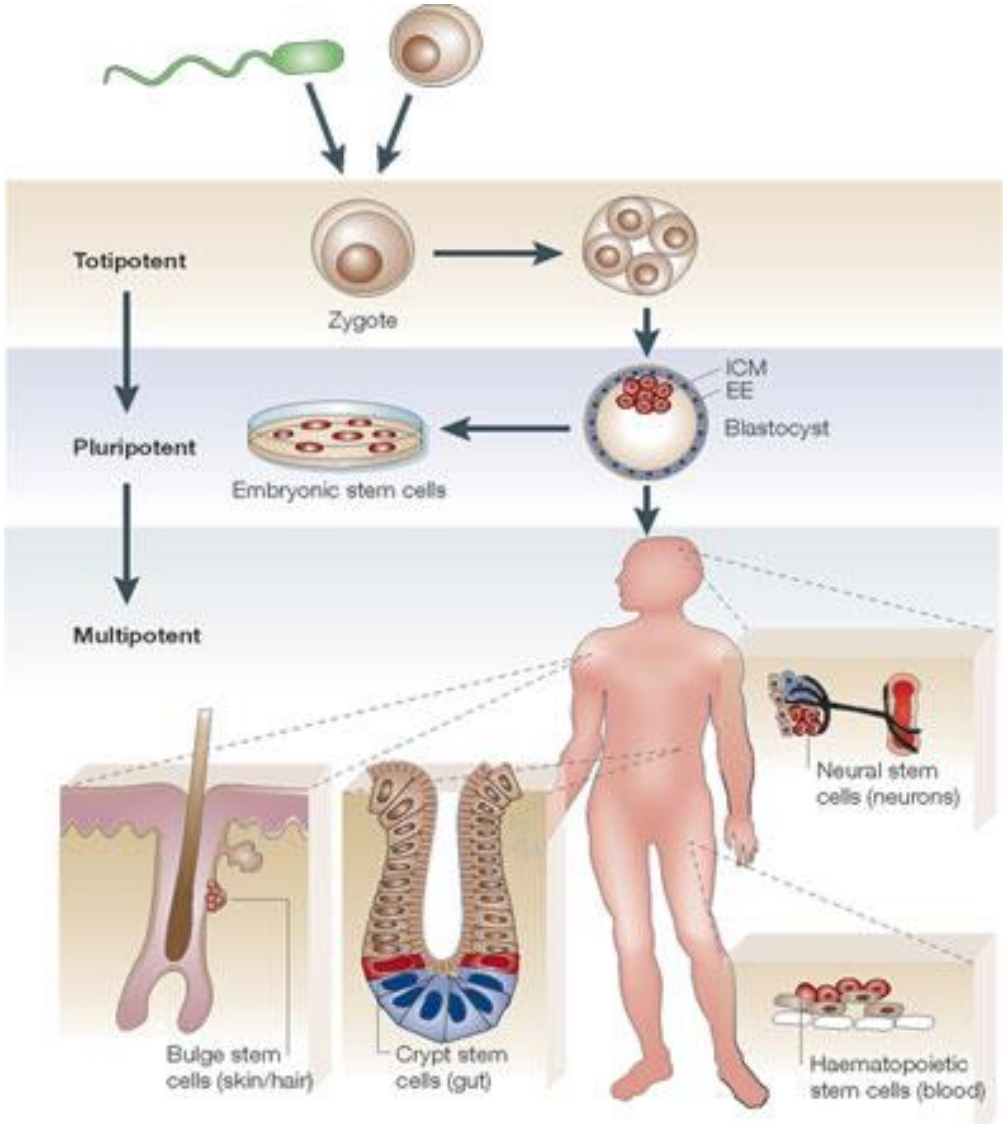


The stem-cell hierarchy

there are multiple different types of stem cells, each defined by their production ability.

Term	Definition	Example
Totipotency	Ability to form the embryo and trophoblast of the placenta	Fertilised oocyte or zygote
Pluripotency	Ability to differentiate into almost all cells of the three germ layers	Embryonic stem cells
Multipotency	Ability to differentiate into a limited range of cell lineages appropriate to the location	Adult, somatic, or tissue-based stem cells
Unipotency	Ability to generate one cell type	Type II pneumocyte

The stem-cell hierarchy



The **totipotent zygote** formed by the fusion of egg and sperm divides to form the inner cell mass (ICM) and the extra-embryonic (EE) tissue of the blastocyst.

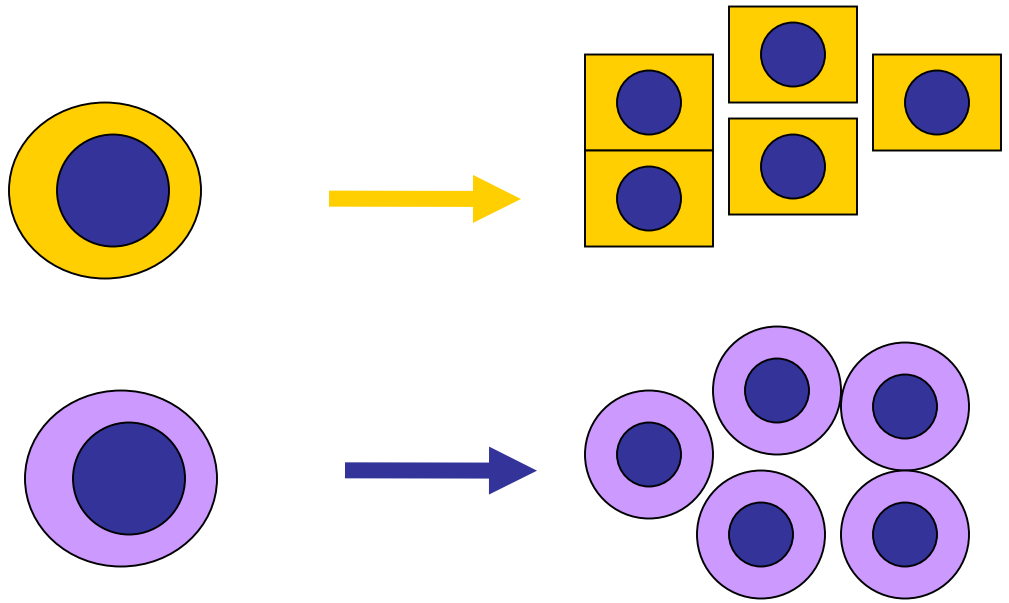
During the development of the embryo, the **pluripotent stem cells** in the ICM become increasingly restricted in their lineage potential and generate tissue-specific, **multipotent stem cells**

Eckfeldt CE et al, Nat Rev Molecular Cell Biology 6;726-737:2005.

Human stem cells: heterogeneity

- Embryonic stem cells
- Adult stem cells intrinsic to various tissues
  - Hemopoietic stem cells
  - Mesenchimal stem cells
  - Neural stem cells
  - Hepatic stem cells
  - Pancreatic stem cells
  - Stem cells of the skin (Keratinocytes)
  - Epitelial stem cells of the lung
  - Stem cells of the intestinal epithelium
  - Endothelial stem cells
  - Skeletal muscle stem cells
  - Cardiac stem cells
  - Etc.

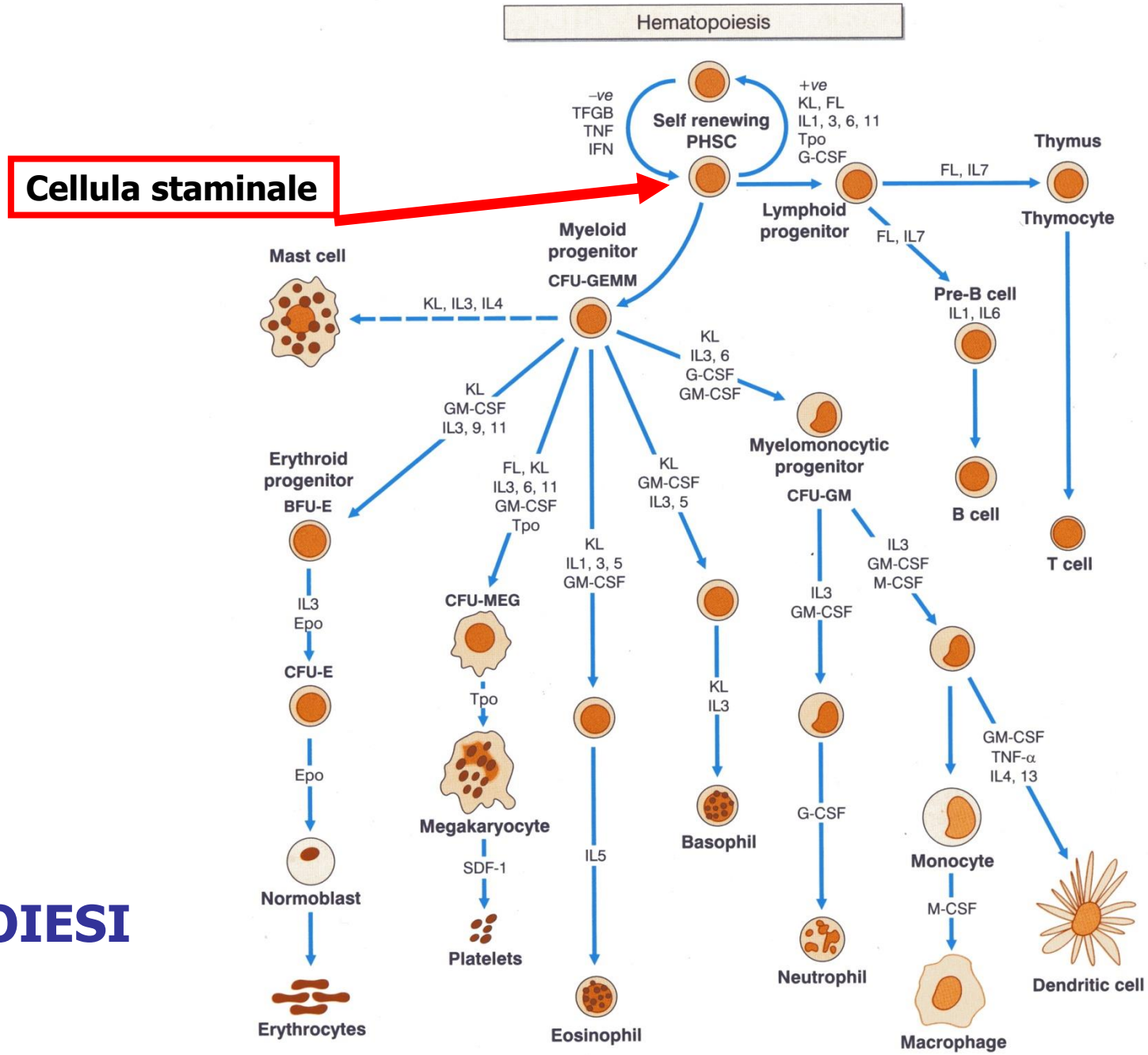
Models for differentiation of adult stem cells into solid-organ-specific cells



Distinct stem cells differentiate each into its own organ-specific cells

EMOPOIESI

Cellula staminale

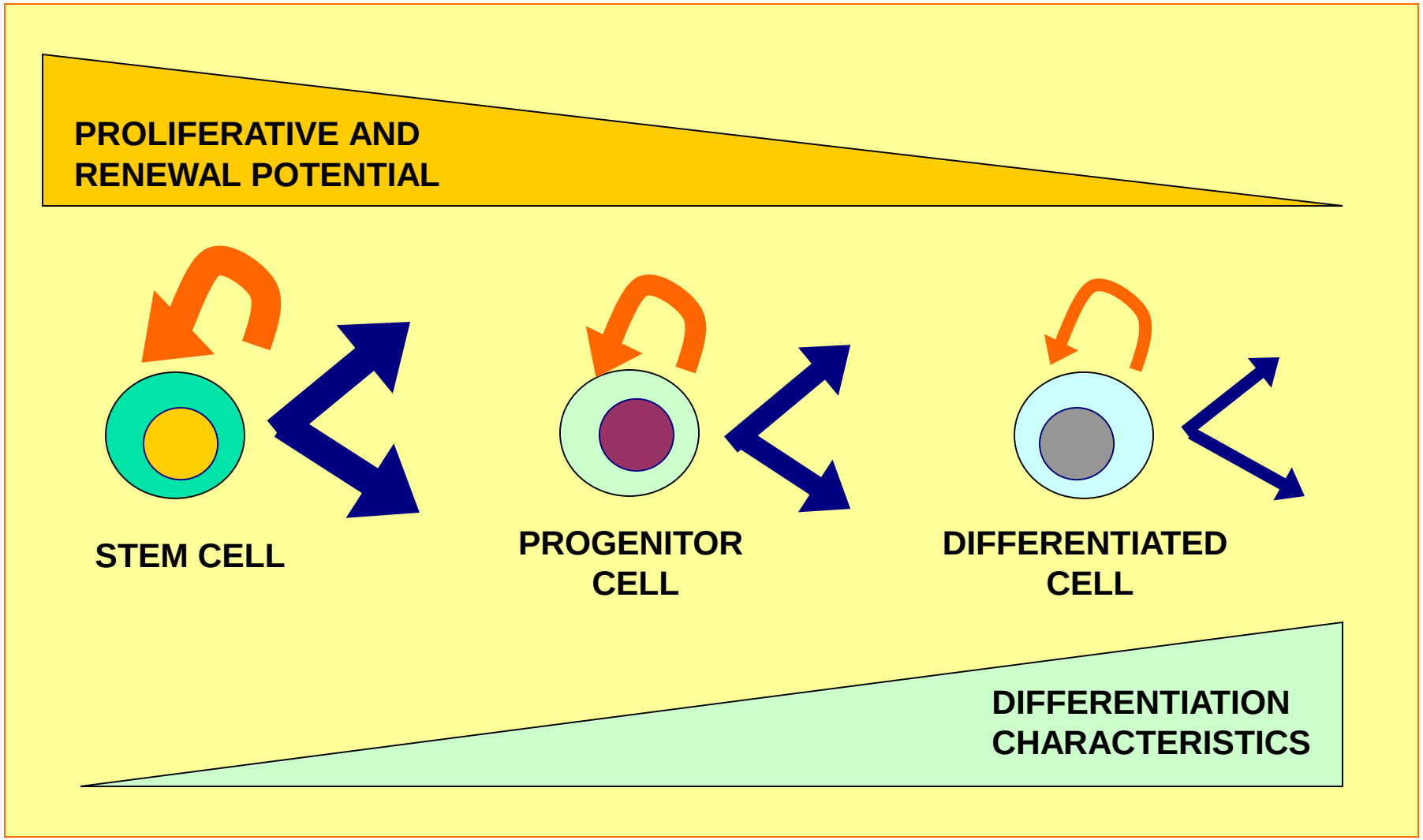


The cellular compartment model

- The compartment model has given rise to terms that are generally applied to cells of hematopoietic origin.

  - **Stem cells** are those that are multipotent and self-renewing.
  - **Progenitor cells** have limited ability to self–renew and are likely to be unipotential or of very limited multipotential.
  - **Precursor cells** are restricted to a single lineage, such as neutrophil precursors, and are the immediate precursors of the mature cells found in the blood.
  - **The mature cells** are generally short-lived and reprogrammed to be highly responsive to cytokines, while the stem cells are long-lived, cytokine-resistant and generally quiescent.

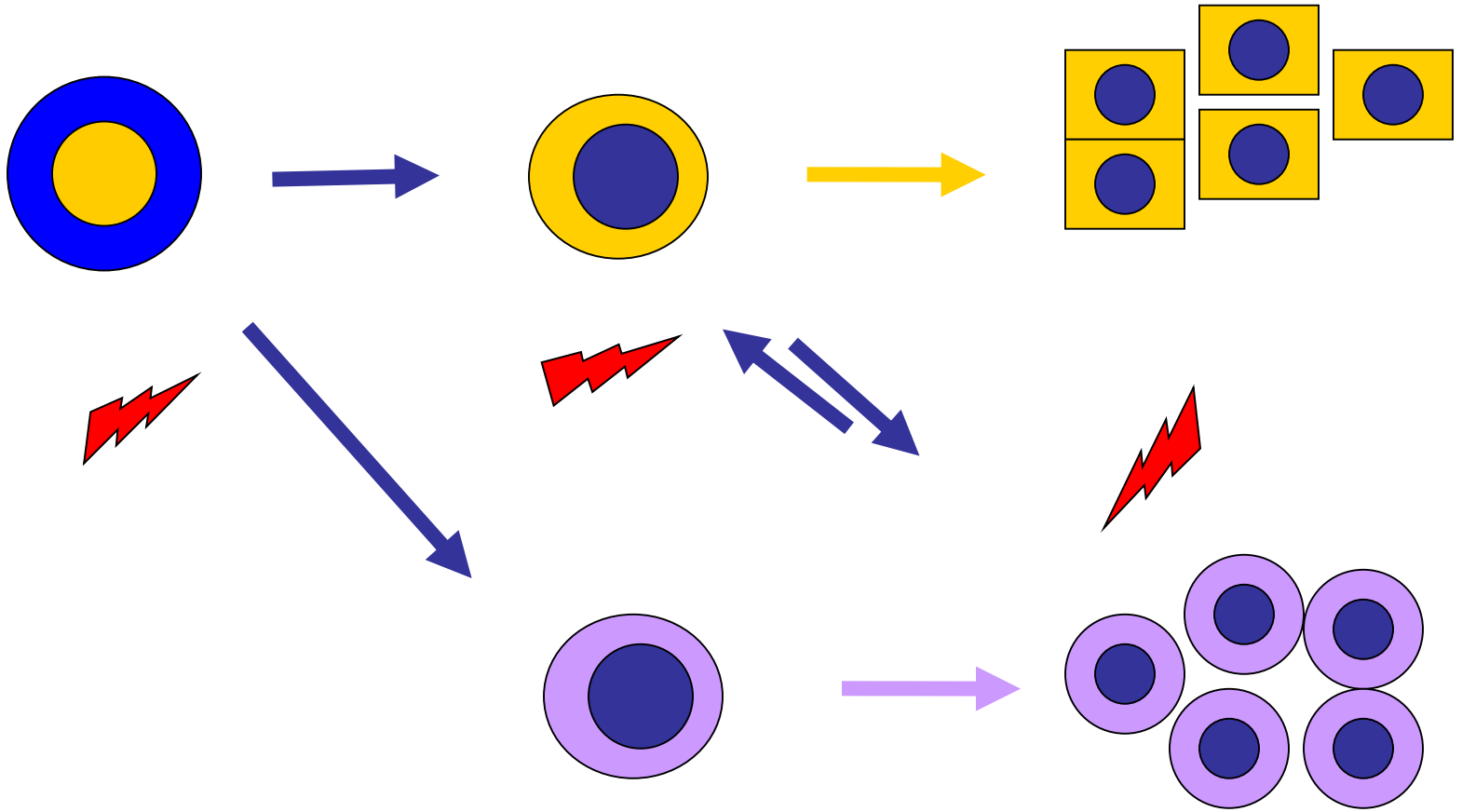
Stem cell renewal and differentiation



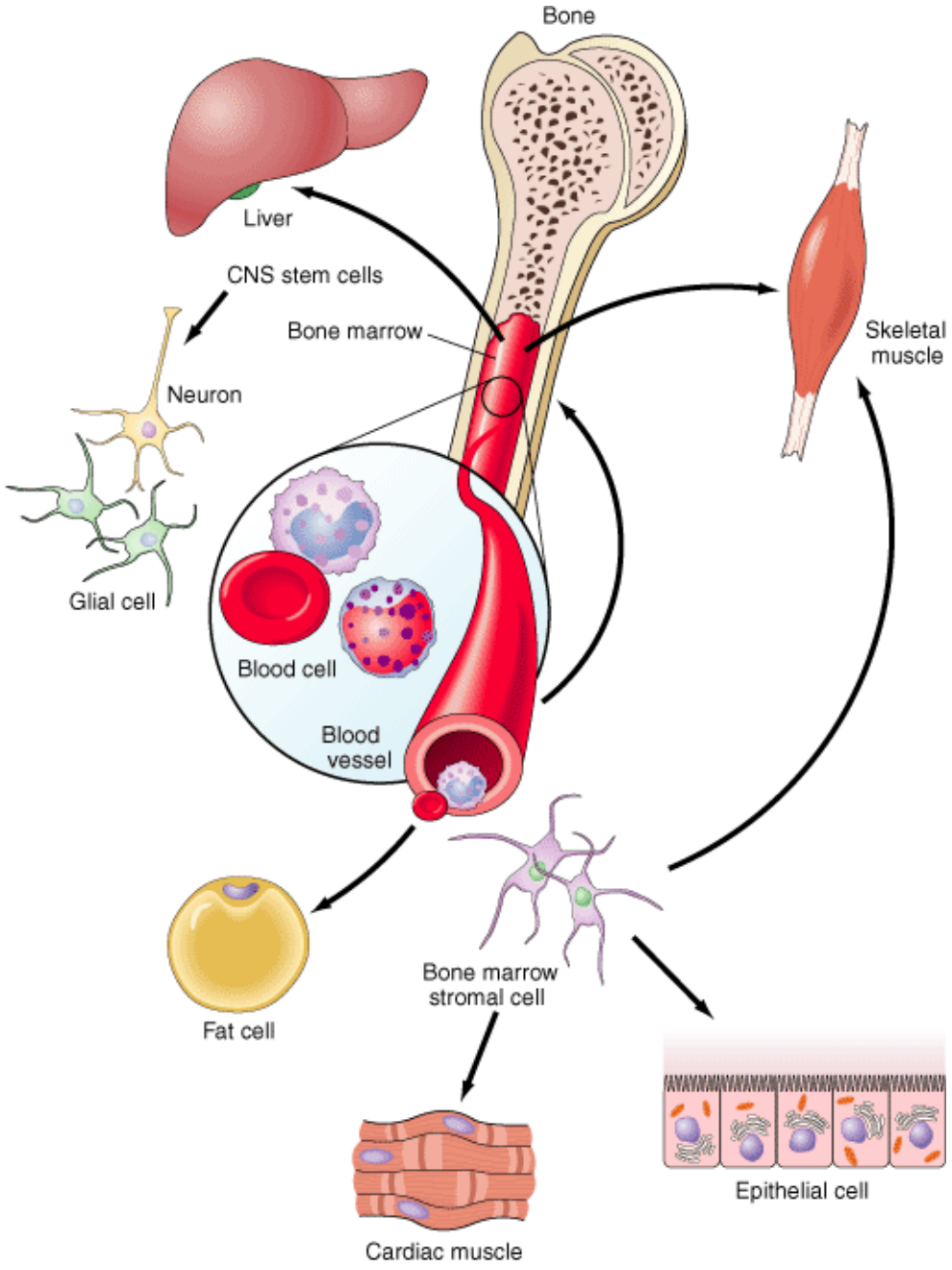
Plasticità delle cellule staminali

- Capacità delle cellule staminali di uno specifico tessuto od organo
  1. di acquisire caratteristiche fenotipiche e funzionali di un differente tessuto od organo
  2. di crossare in alcuni casi verso linee somatiche di diversa derivazione embrionale

Stem cell plasticity

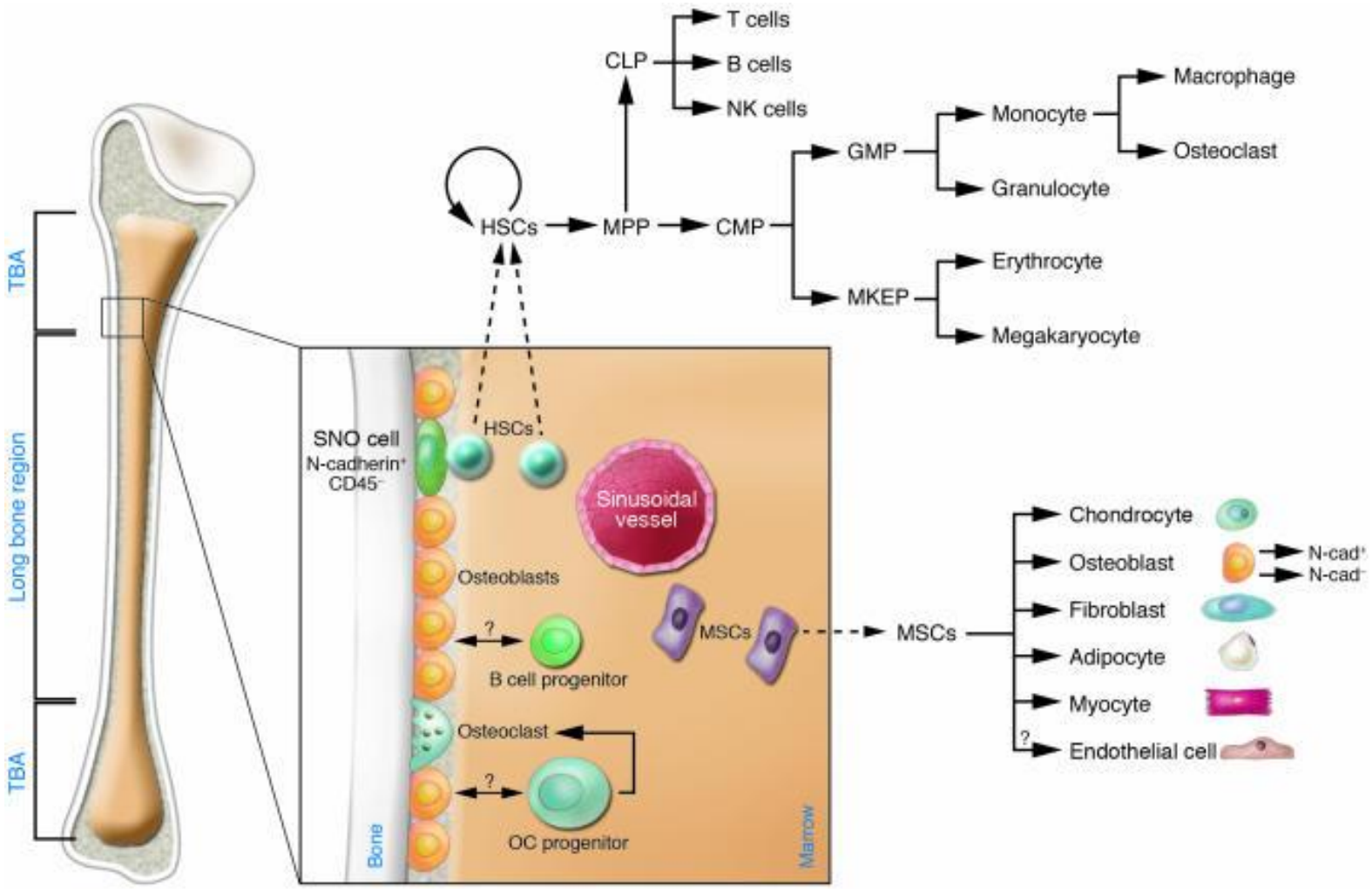


Plasticity of adult stem cells



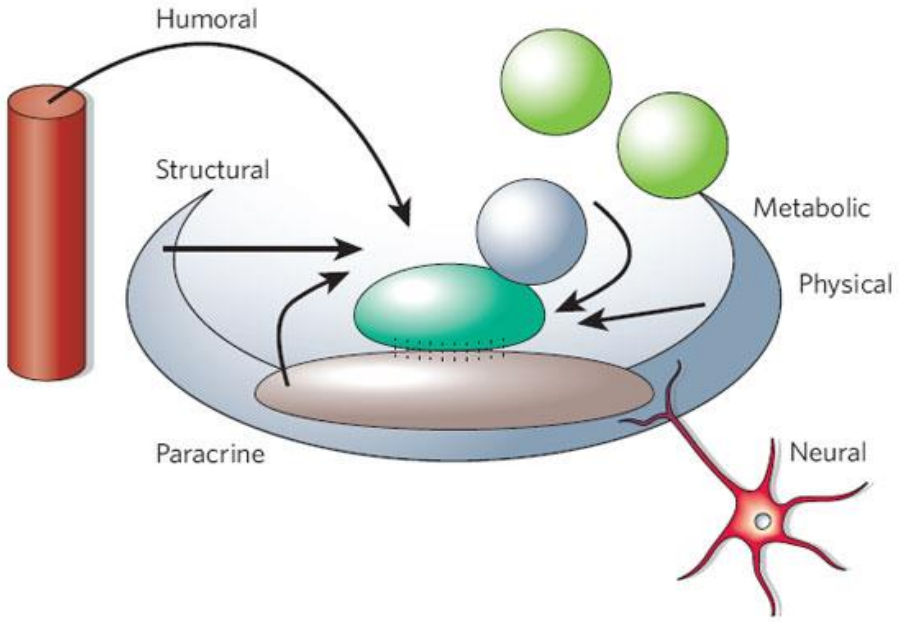
Stem cell niche

Hematopoiesis of bone cells and marrow stromal cells



J Clin Invest. 116:1195–1201;2006

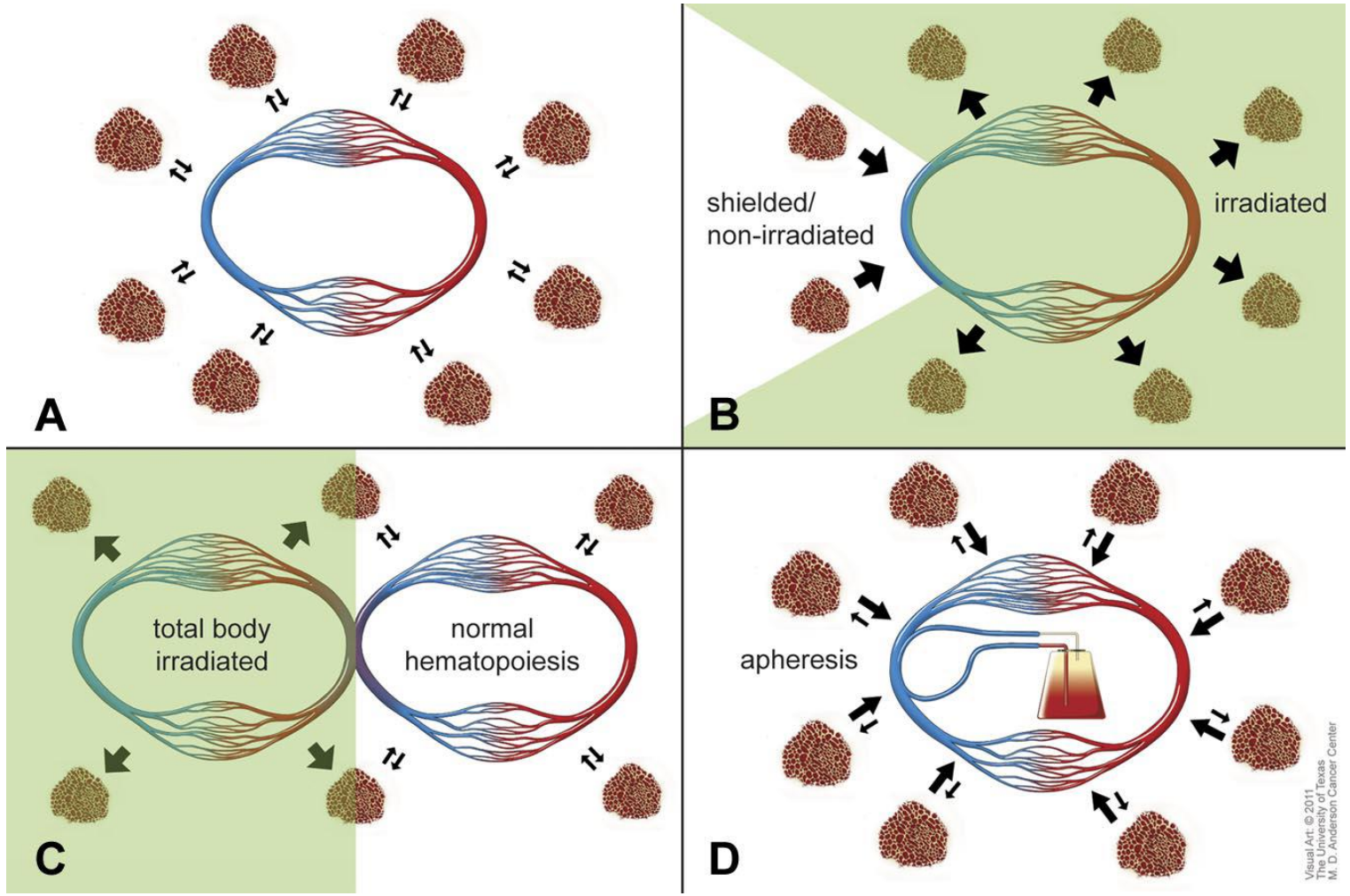
Inputs feeding back on stem-cell function in the niche



- Elements of the environment that participate in regulating the system of a SC in its tissue state include
  1. the constraints of the architectural space,
  2. physical engagement of the cell membrane with tethering molecules on neighbouring cells or surfaces,
  3. signalling interactions at the interface of stem cells and niche or descendent cells,
  4. paracrine and endocrine signals from local or distant sources,
  5. neural input and
  6. metabolic products of tissue activity

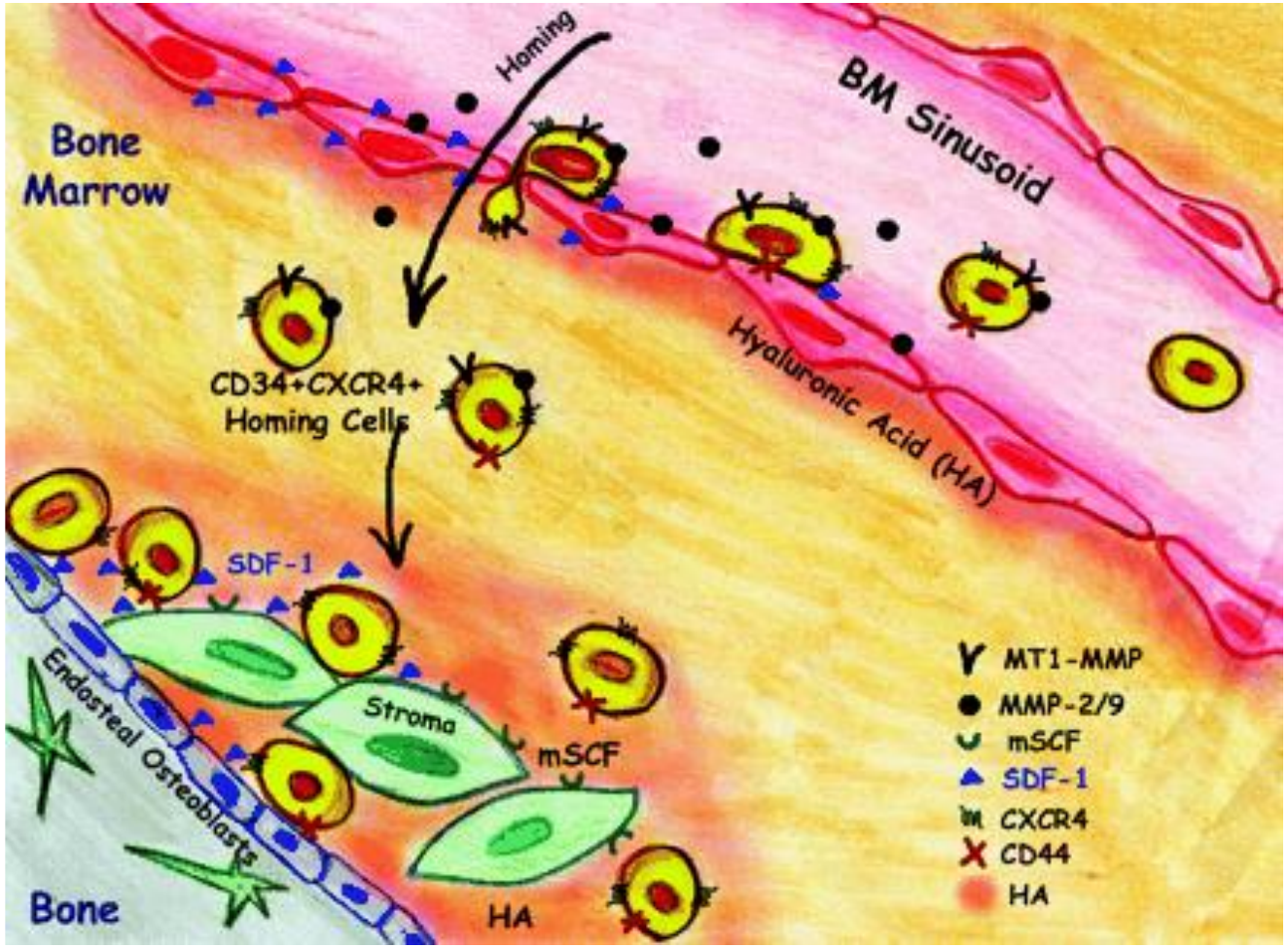
David T. Scadden, Nature 2006;441, 1075-79

Stem cell migration between BM and PB.



Blood. 2011;117(24):6411-6416

Stem cell homing to the endosteum



stromal cell-derived factor 1 (**SDF1**)

Trafficking of primitive hematopoietic cells

- Trafficking of HSCs can be divided into the components of homing, retention and engraftment.
  - **Homing** describes the tendency of cells to arrive at a particular environment,
  - **Retention** is their ability to remain in such an environment after arrival.
  - **Engraftment** reflects the ability of cells to divide and form functional progeny in a given microenvironment.