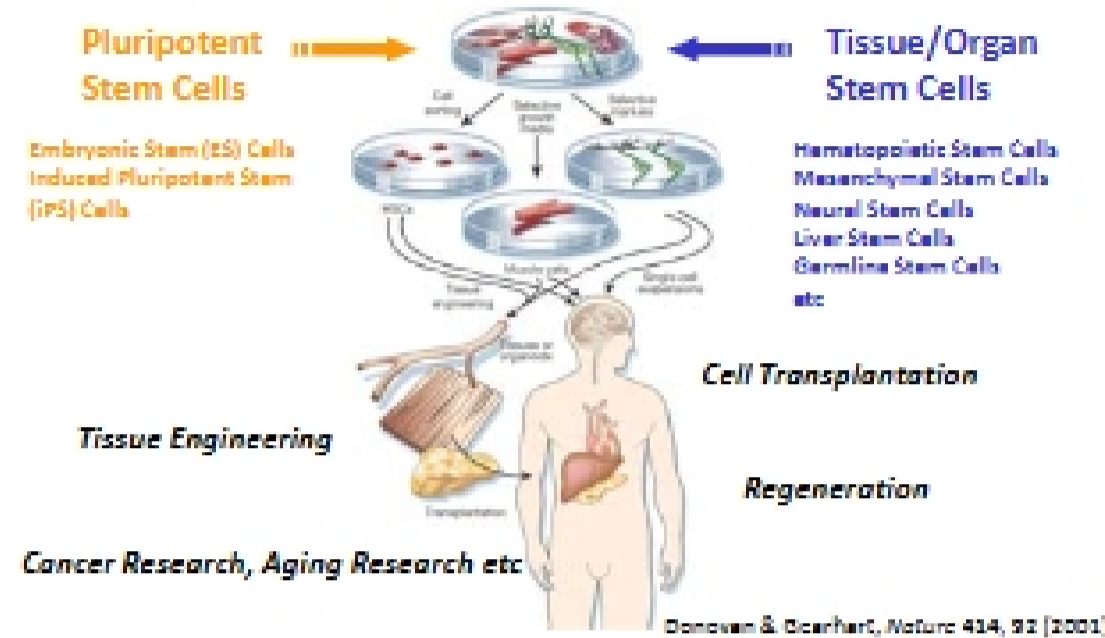


Stem Cells and Regenerative Medicine

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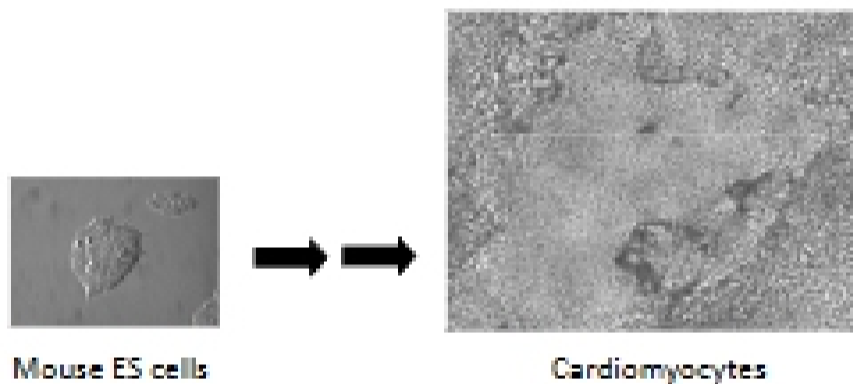
Program in Stem Cell and Regenerative Medicine
<http://stemcell.ufl.edu/>

Stem Cells in Biomedical Research



ES Cell-Derived Cardiomyocytes

ES cells can differentiate *in vitro* into functional cardiac myocytes



The Mouse With A Human Ear On Its Back

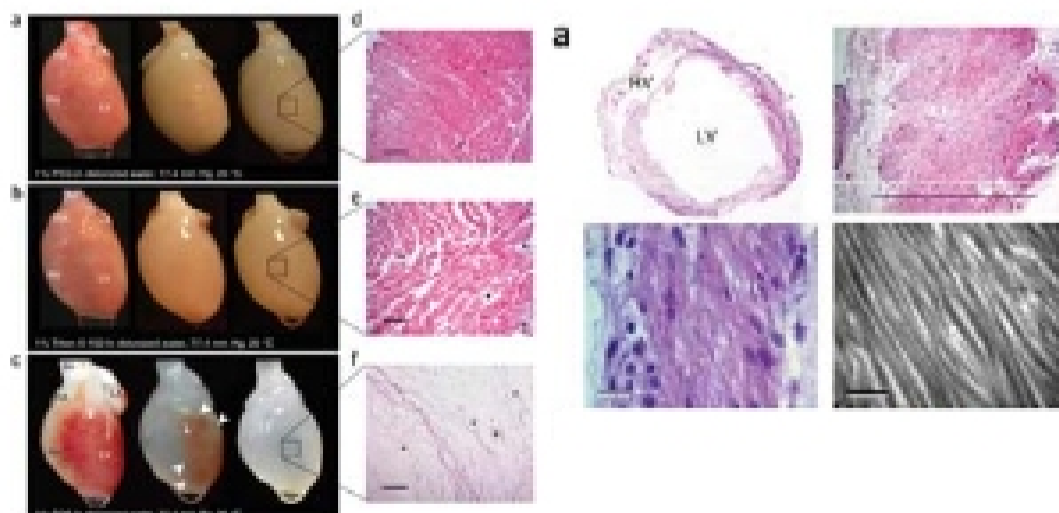
By implantation of ear-like scaffolding of porous, biodegradable polyester fabric + human cartilage cells



C. Vacanti and R. Langer (1995)

Heart Engineering

Ott et al (2008) Nat Med 14, 213



Kidney Engineering

Ross et al (2009) J Am Soc Nephrol 20, 2338



Lecture Agenda

11/27/2008 (Tue)

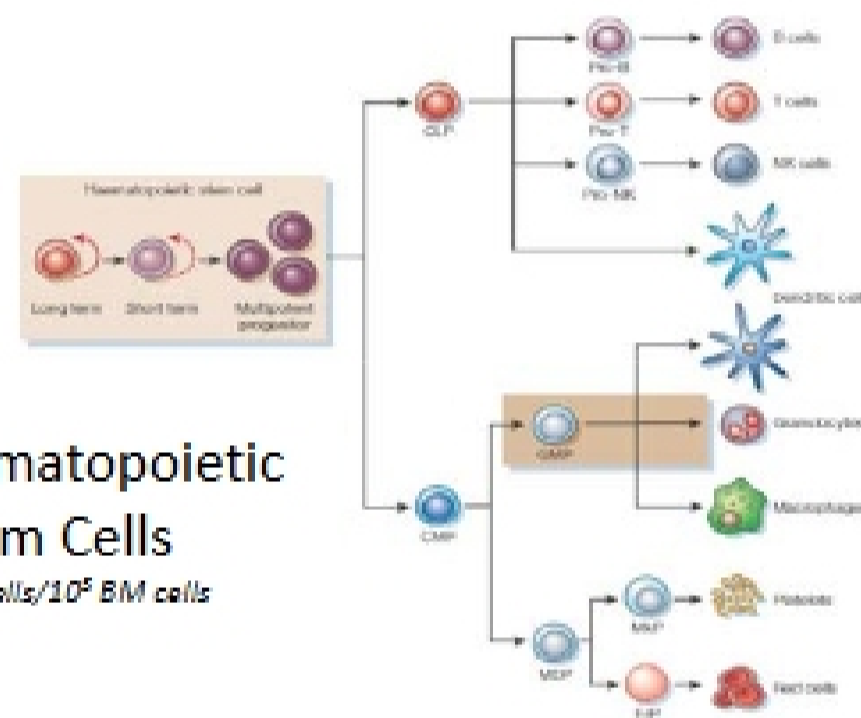
1. Stem Cells in Homeostasis
2. Regeneration Research in Other Organisms
3. Embryonic Stem Cells and induced Pluripotent Stem Cells

1. Stem Cells in Homeostasis

- Why do we need stem cells?
- How do we define stem cells?
- Where do stem cells reside?
- How do stem cells differentiate?

You are not exactly the same as you were yesterday!

- Turnover of blood cells
 - Half-life of RBCs, ~120 days
 - Losing RBCs at a rate of 2 millions per second
 - Half-life of Neutrophils, 4~7 hrs
 - Losing WBCs at a rate of 1 million per second
- Turnover of whole body
 - Losing ~1 trillion cells per day (?)

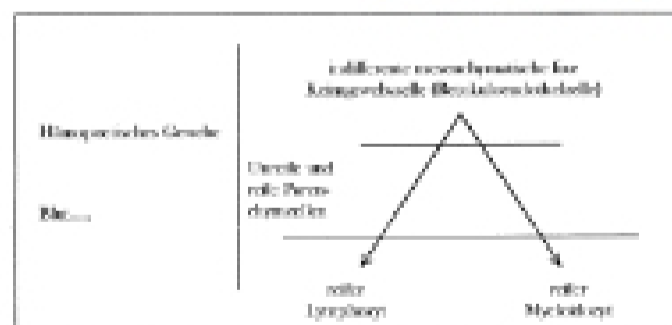


Hematopoietic Stem Cells

$3 \sim 4 \text{ cells} / 10^5 \text{ BM cells}$

"gemeinsame Stammzelle"

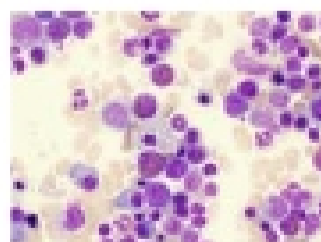
(common stem cell)



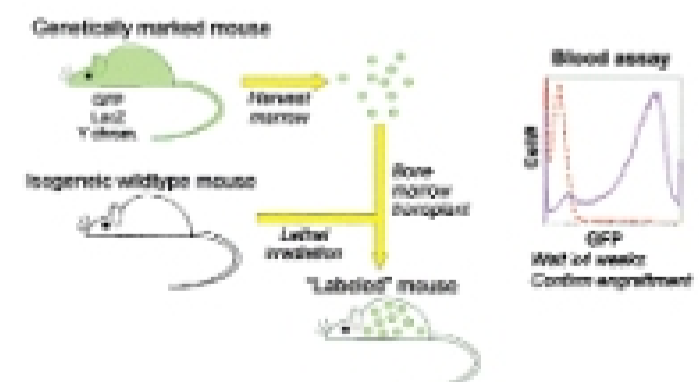
The concept of a common undifferentiated mesenchymal precursor cell for all blood lineages and endothelium, the "retikuloendotheliale" From *Acta Haematologica* 21, p. 91 (1917).

Postulated the existence of an undifferentiated stem cell giving rise to the plethora of blood cells solely based on morphological observations.

Artur Pappenheim (1870-1916)

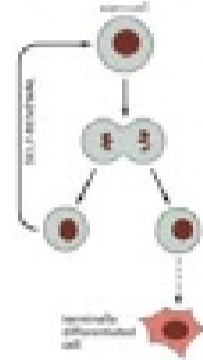


- Colony Forming Unit (Till & McCulloch, 1961)
 - Traced hematopoietic repopulation capacity to clonogenic cells.
- Bone Marrow Transplantation (1951~1956)
 - Corroborated the existence of the hematopoietic stem cells in the BM by showing hematopoietic recovery from transplanted BM after irradiation damage.

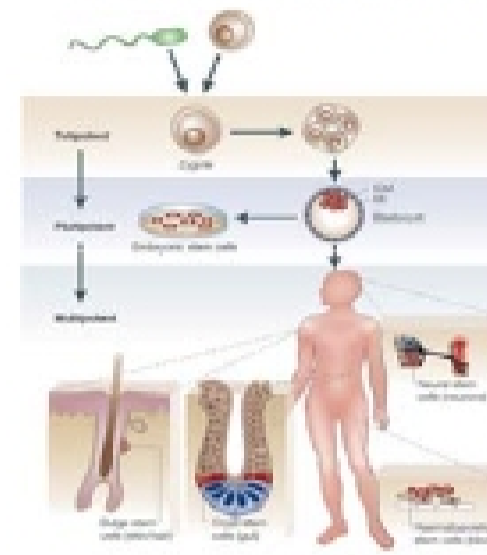


How do we define a Stem Cell?

- A cell that is capable prolonged self-renewal
- A cell that is able to differentiate into one or more lineages



Differentiation Potential of Stem Cells

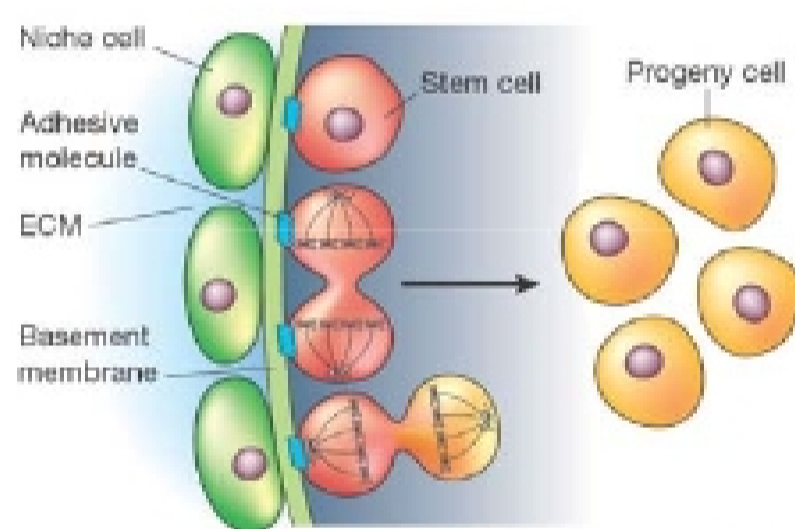


- **Totipotent**- ability to give rise to all embryonic and extra-embryonic tissues
- **Pluripotent**- ability to give rise to embryonic tissues (3 germ layers-ectoderm, endoderm, mesoderm)
- **Multipotent**- can produce cells of closely related family of cells
- **Unipotent**- can produce only one cell type, have property of self-renewal

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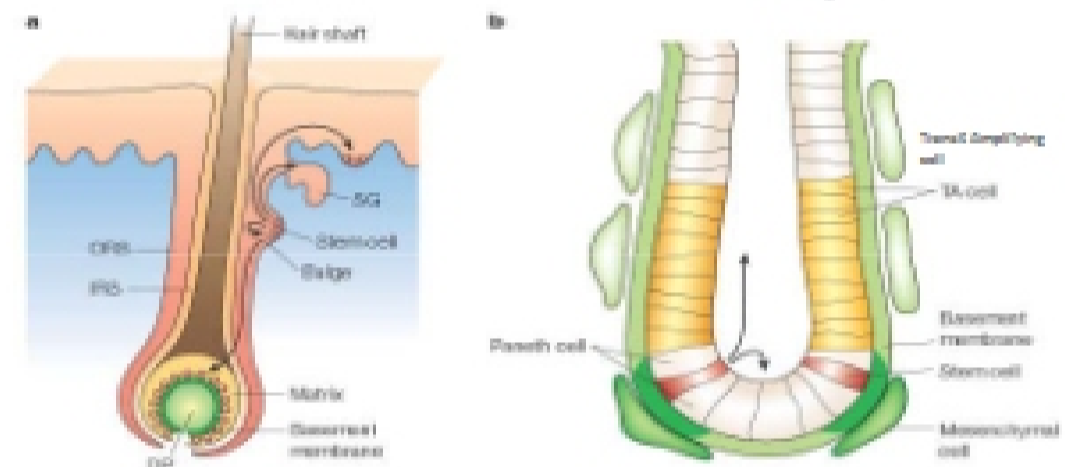
Beckfeldt (2008) Nature Reviews: MCB 8:728

Where Do Stem Cells Reside?



Sprengel et al., Nature 414, 95 (2001)

Stem Cell Niche

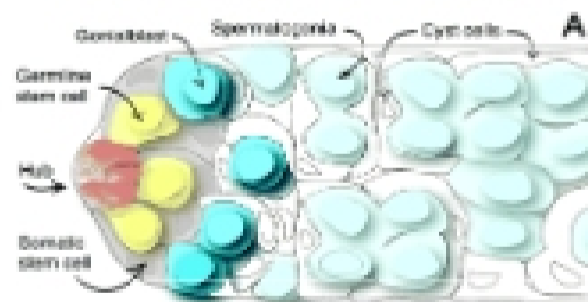


Mammalian Epidermal Stem Cells (Hair Follicle)

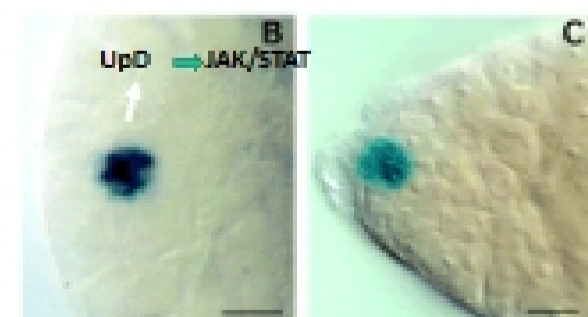
Mammalian Gut Crypt

Sprengel et al., Nature 414, 95 (2001)

Stem Cell Self-Renewal in Niche

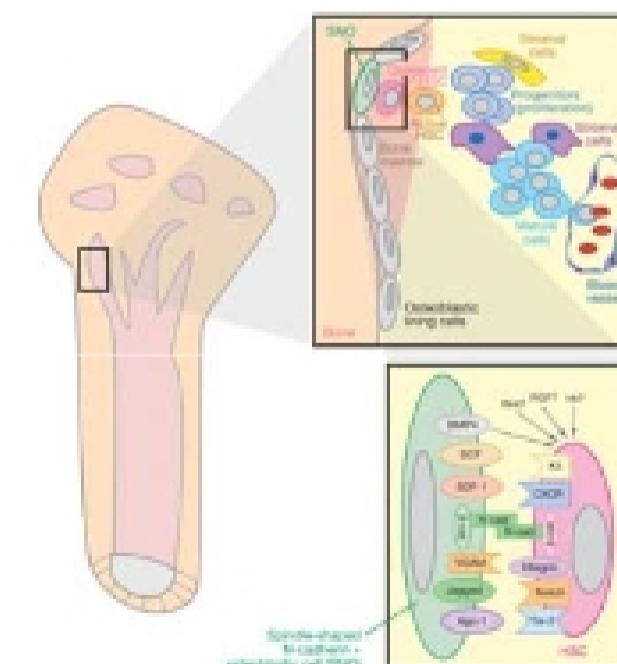


Control of Stem Cell Self-Renewal in *Drosophila* Spermatogenesis by JAK-STAT Signaling



Kiger et al:
Science 294, 2542 (2001)
Tulina & Matunis:
Science 294, 2548 (2001)

Niche for HSC



Osteoblast cells are the top candidate for the "Niche cells" in the bone marrow.

These cells likely provide some of the signals responsible for HSC self-renewal and proliferation