

# STEM CELLS

Definition?

Where from?

What's for?

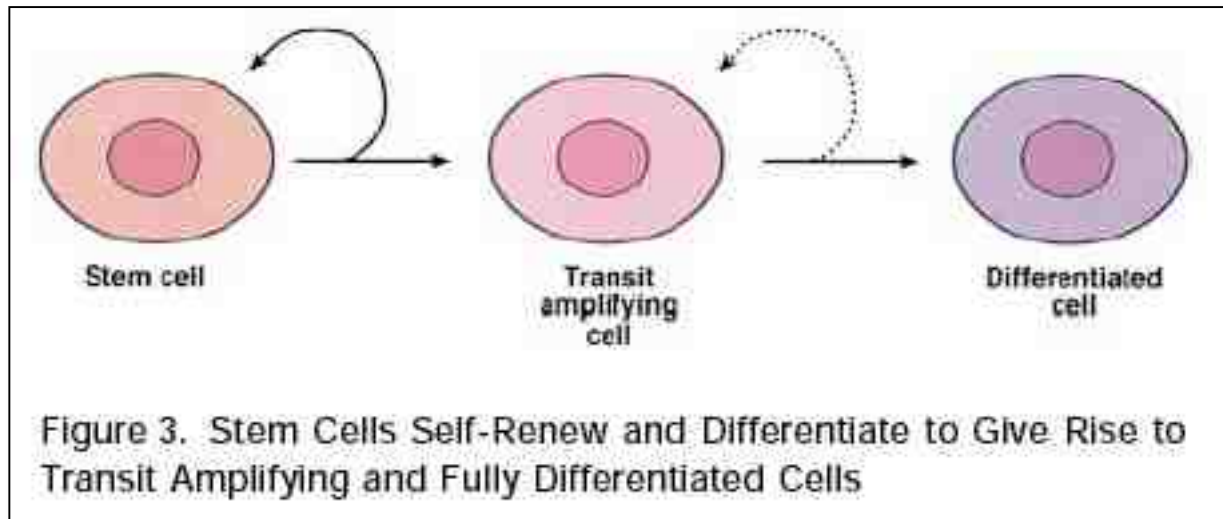
Where are we?

# Definition?

It is now well accepted that a stem cell must fulfill three criteria:

1. First, it must be capable of self-renewal, i.e., undergoing symmetric or asymmetric divisions through which the stem cell population is maintained.
2. A single cell must be capable of multilineage differentiation.
3. In vivo functional reconstitution of a given tissue.

The definition of ‘stem cell’ is essentially **functional**: “rather than referring to a discrete cellular entity, a stem cell most accurately refers to a biological function that can be induced in many distinct types of cells, even differentiated cells”



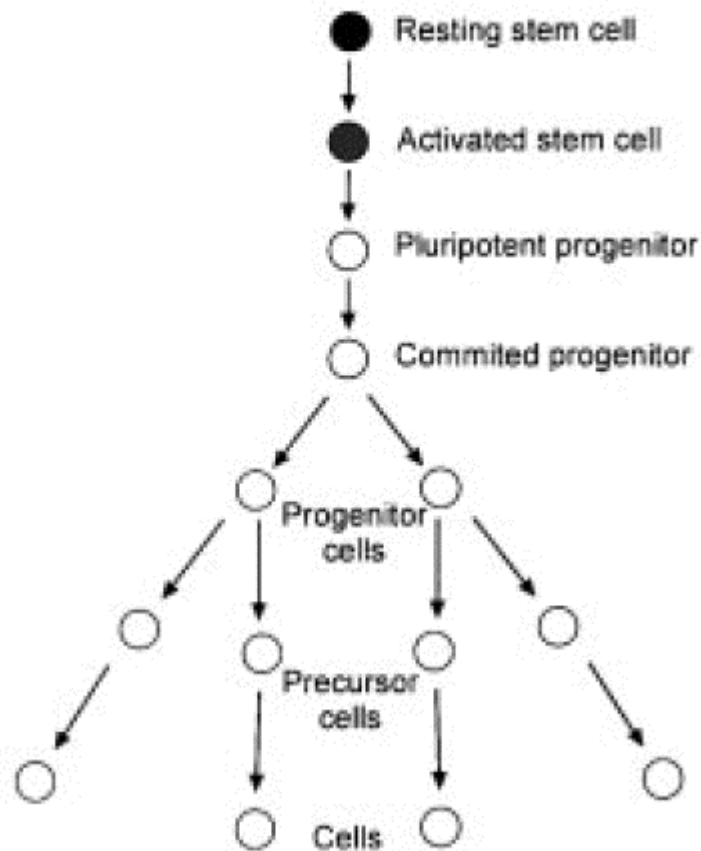
✓ stem cells are **relatively uncommon**, with frequencies varying from roughly 0.0001% to roughly 5% of the total cells in a tissue—accordingly, tissue-specific stem cells may be difficult to isolate;

✓ stem **cells cycle relatively slowly**, and often we see transit amplifying (TA) cells dividing more often than stem cells;

✓ stem cell activity is governed by the cells' microenvironment or '**niche**', comprising cell-adhesion molecules, cell–cell signals and growth factors; and

✓ more controversially, stem cell populations are **selfmaintaining**, in that each stem cell division, on average, generates one stem cell and one TA cell, or each two stem cell divisions, on average, generate two stem cells and two TA cells

## Traditional View



## Evolving View

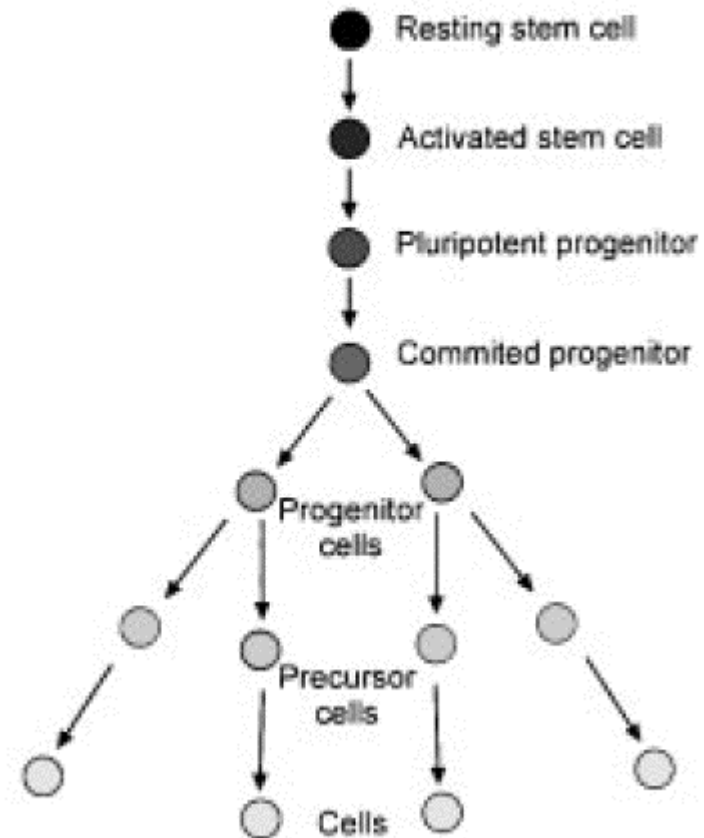
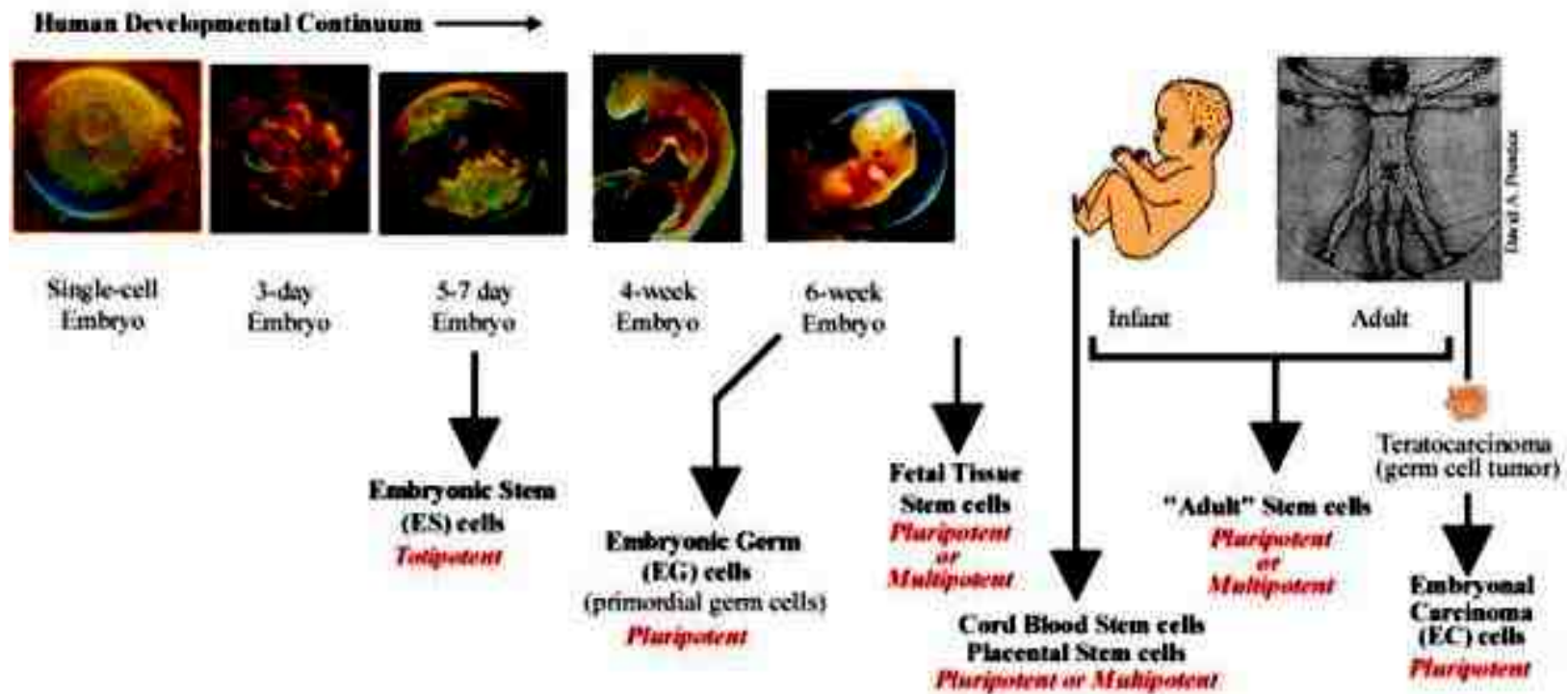


Figure 1. Two concepts of stem cells. On the left is the traditional view of stem cells, showing an irreversible loss of potency in maturing stem cells. On the right is an evolving view postulated by Blau et al. whereby stemness is a biological function that progressively degenerates over time but remains potentially recruitable within even differentiated cells in particular contexts. Redrawn with substantial modification from Fig. 7 in Blau HM, Brazelton TR, Weimann JM. 2001. The evolving concept of a stem cell: Entity or function? *Cell* 105:829–841, with permission of Elsevier.

# STEM CELLS

## Where from?



A human embryo, at the “blastocyst” stage, used to create new stem cell lines.



[www.sciencemag.org](http://www.sciencemag.org) SCIENCE VOL 282 6 NOVEMBER 1998

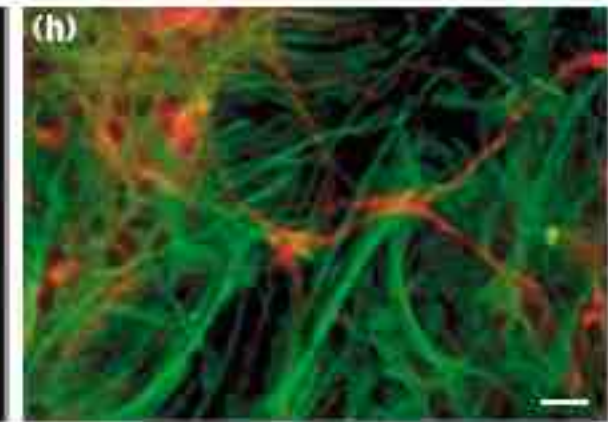
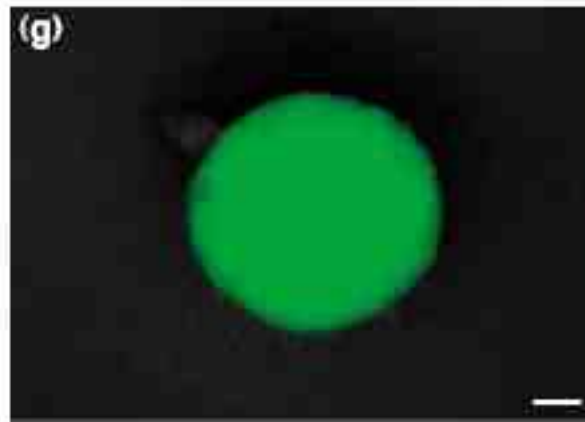
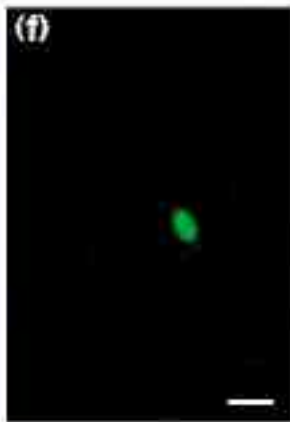
## **Embryonic Stem Cell Lines Derived from Human Blastocysts**

# Stem cell research

Isolation

Proliferation

Differentiation



EGFP+ single cell

EGFP+ single cell

EGFP+ neurosphere

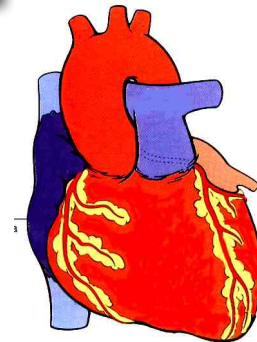
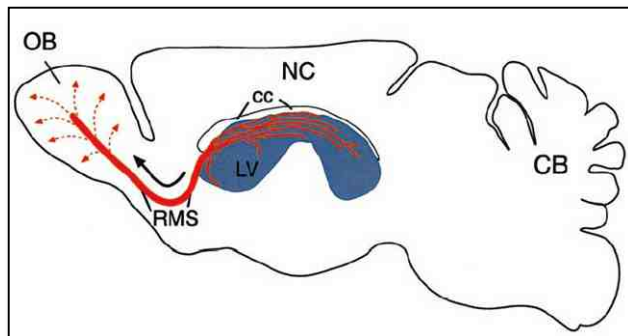
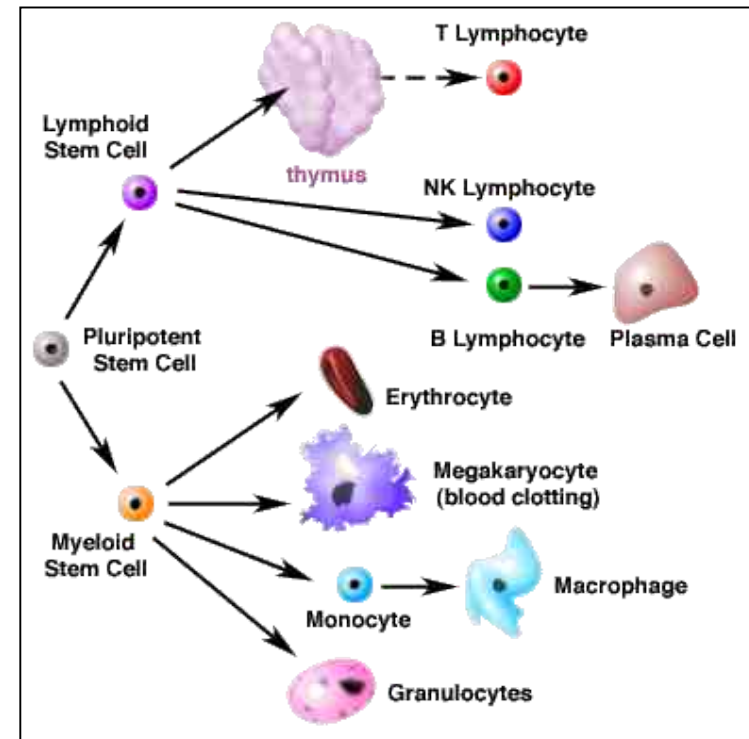
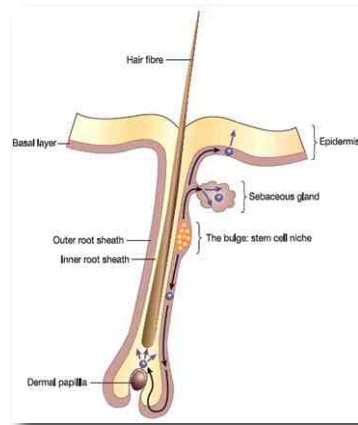
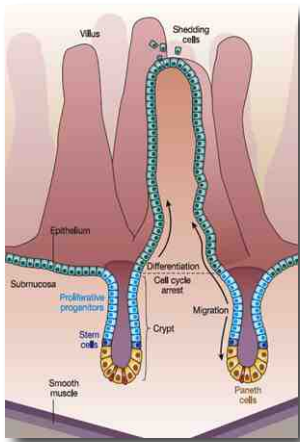
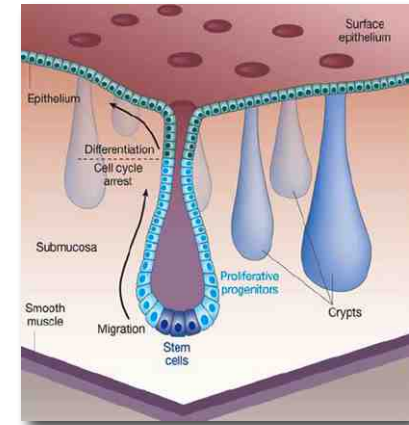
GFAP-TuJ

Neuronal stem cell

Neurosphere

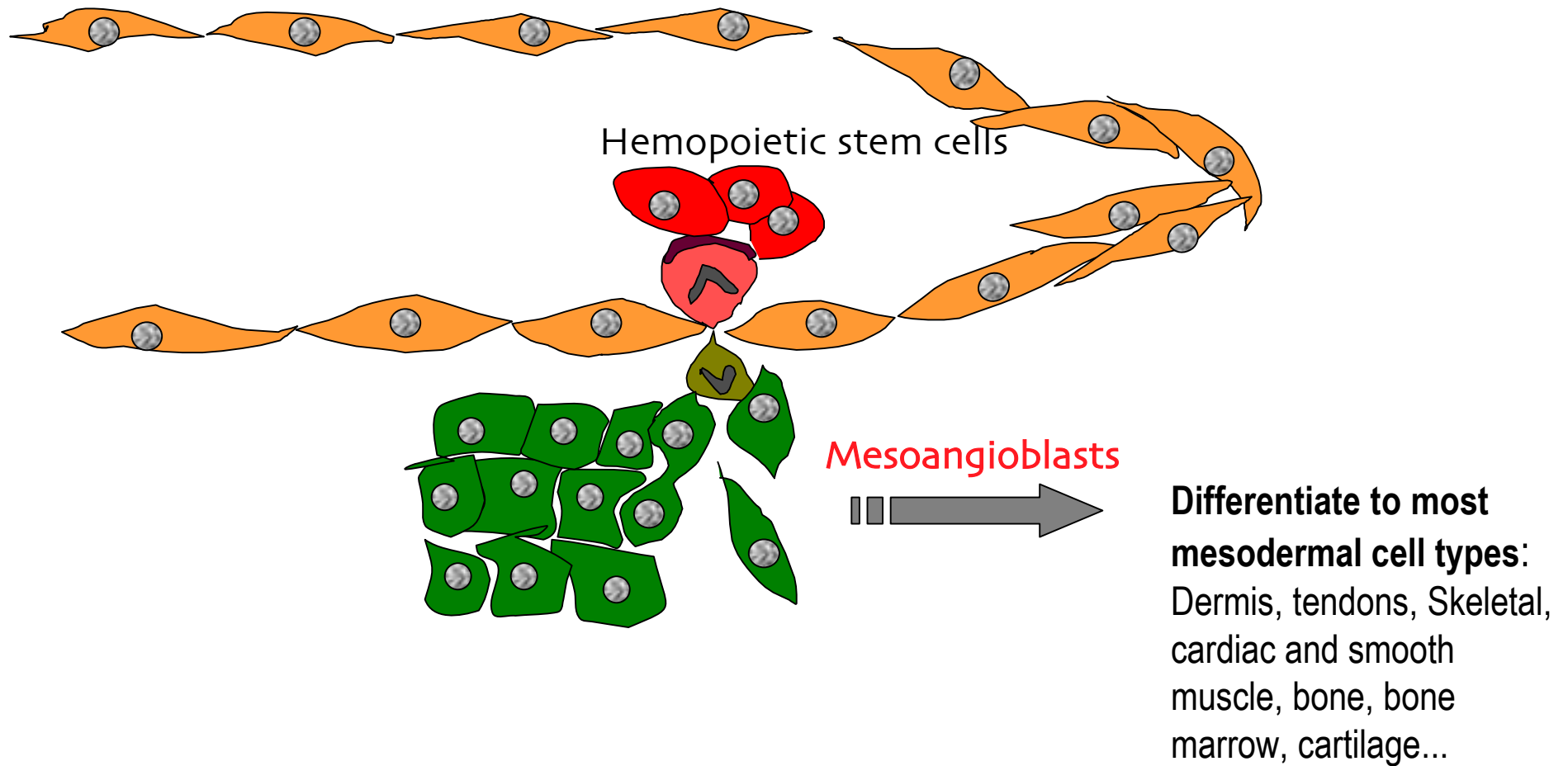
Neurons and  
glial cells

The most extensively studied adult stem cell is the **hematopoietic stem cell** (HSC). **Neural stem cells** (NSC) give rise to neurons, astrocytes, and oligodendrocytes. **Mesenchymal stem cells** (MSC) differentiate into fibroblasts, osteoblasts, chondroblasts, adipocytes, and skeletal muscle. Other stem cells have been identified, including **gastrointestinal stem cells**, **epidermal stem cells**, and **hepatic stem cells** (also called oval cells).



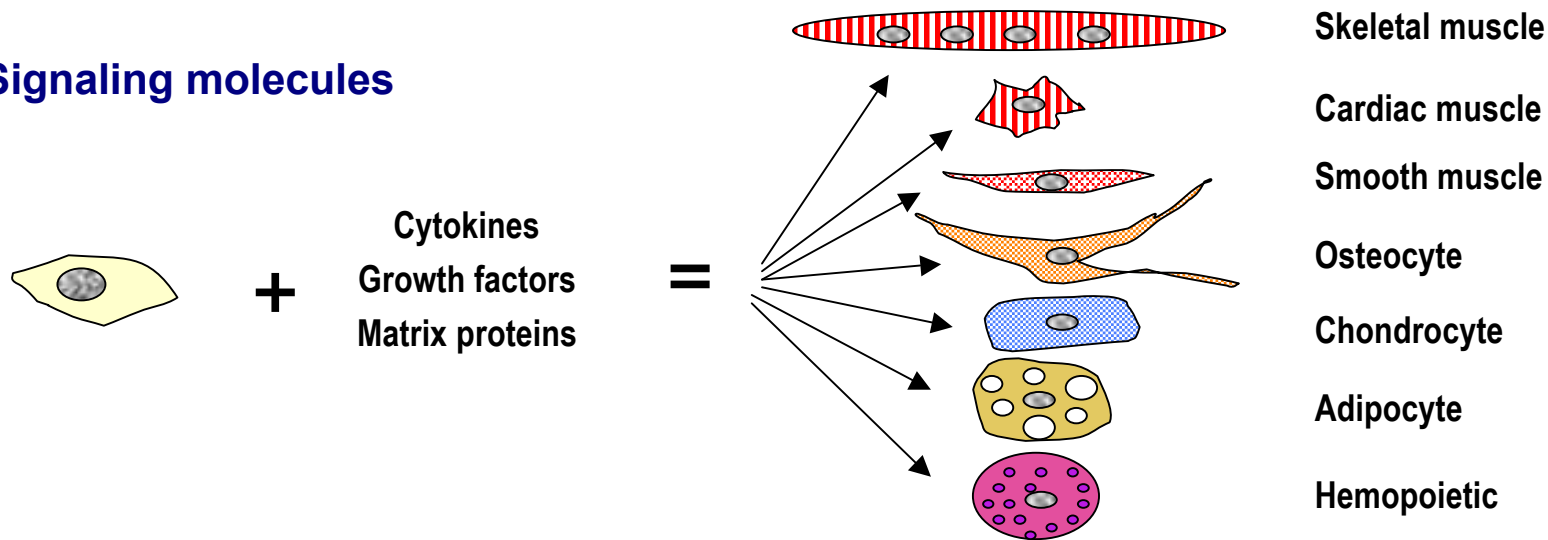


Vessel associated progenitor cells may enter surrounding tissues and adopt the local fate

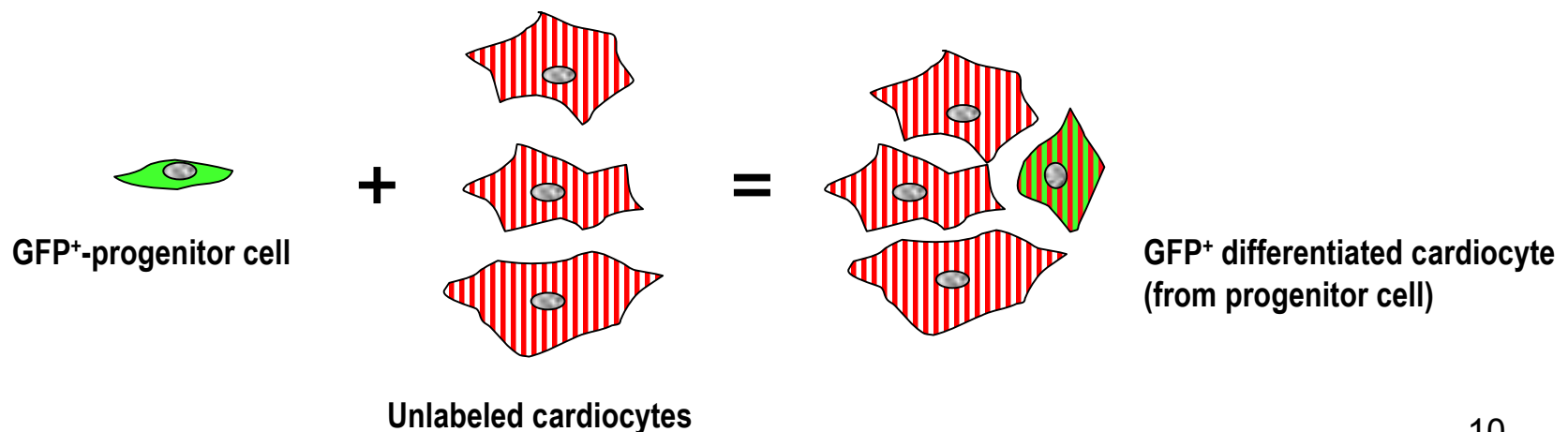


# Different signaling processes may activate different fates in pluripotent progenitors

## Signaling molecules



**Co-culture test for pluripotency:** Progenitor cells are recruited to a given differentiation pathway, e.g. cardiogenesis, by neighboring differentiating cells (e.g. cardiocytes)



# Leukaemia stem cells and the evolution of cancer-stem-cell research

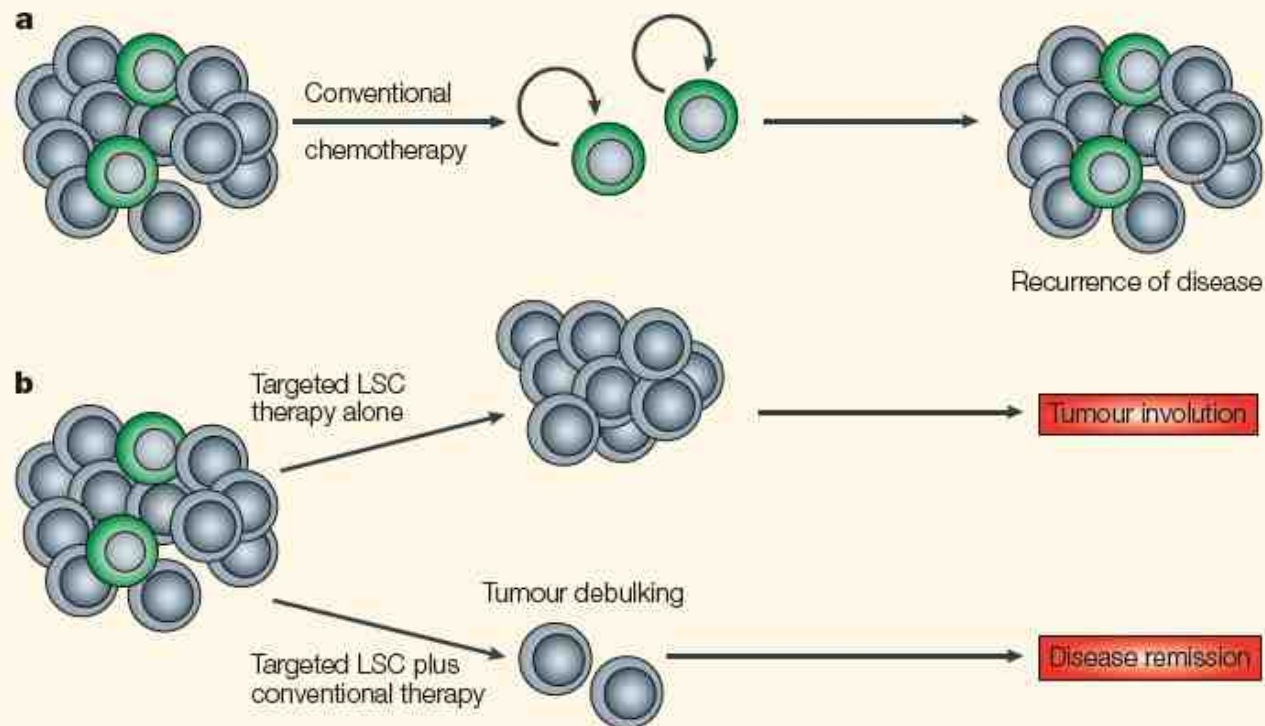
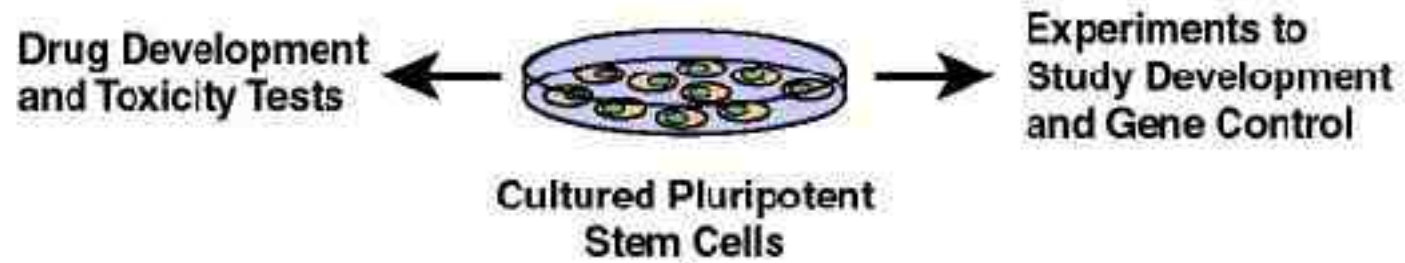


Figure 4 | **Targeting leukaemia stem cells.** **a** | At present, treatment for leukaemia uses chemotherapeutic agents that target all leukaemia cells (grey), based on properties such as their increased proliferation and entry into the cell cycle. However, it is likely that this approach spares the population of leukaemia stem cell (LSCs; green), which are responsible for the continued growth and propagation of the tumour. In many instances, this leads to recurrence of the disease. **b** | A greater understanding of LSC biology will allow us to design therapeutic agents that specifically target the LSC populations. Such therapies used alone, or in combination with conventional chemotherapeutic agents that reduce tumour burden, should lead to tumour involution or disease remission, respectively. Both of these approaches could improve both initial response rates and overall survival, through a decrease in the relapse of disease.

# What's for?

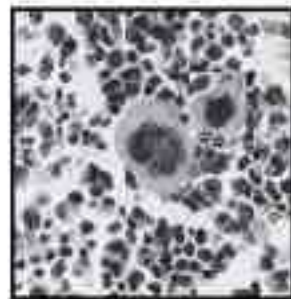
## The promise of Stem Cell Research

Embryonic stem cells



Adult stem cells

Tissues/Cells for Therapy



Bone Marrow



Nerve Cells

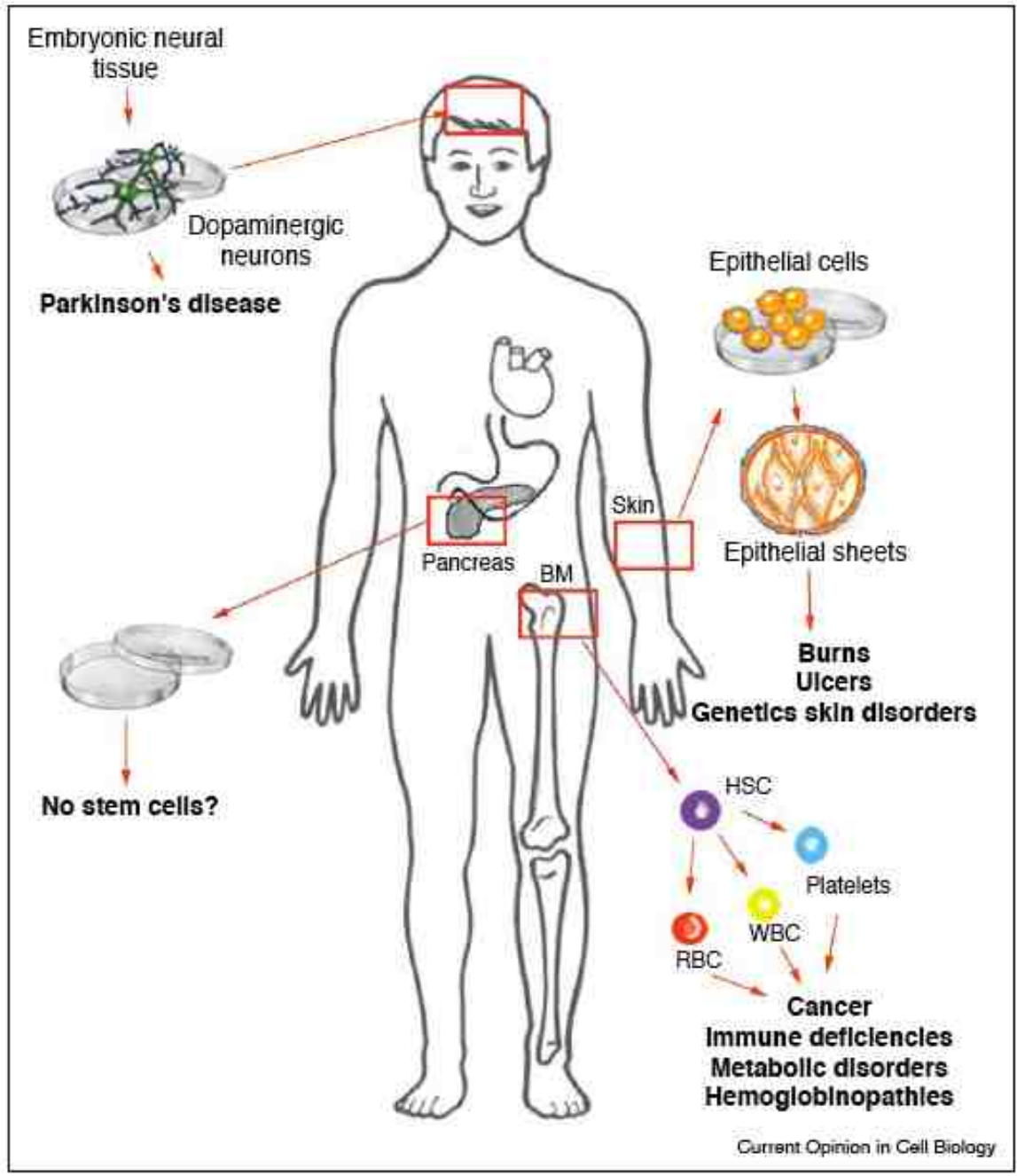


Heart Muscle Cells

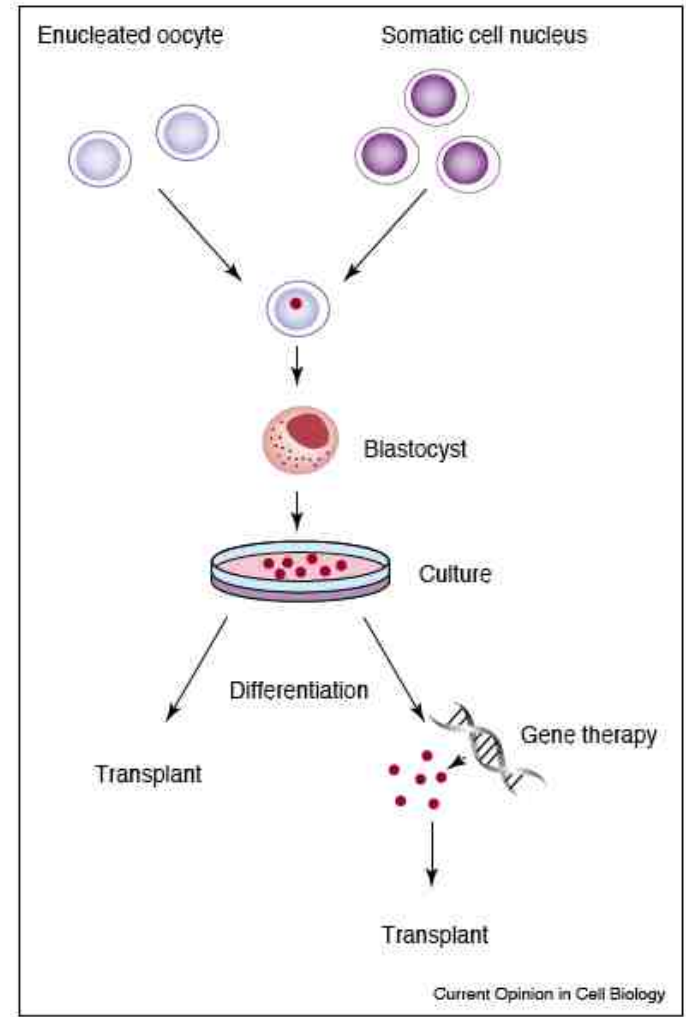


Pancreatic Islet Cells

# Reconstructive therapy



# Gene therapy



Nature January 2006

## Generation of a functional mammary gland from a single stem cell

Mark Shackleton<sup>1,2</sup>, François Vaillant<sup>1,2</sup>, Kaylene J. Simpson<sup>3†</sup>, John Stingl<sup>4,5</sup>, Gordon K. Smyth<sup>1</sup>, Marie-Liesse Asselin-Labat<sup>1,2</sup>, Li Wu<sup>1</sup>, Geoffrey J. Lindeman<sup>1,2</sup> & Jane E. Visvader<sup>1,2</sup>

A LacZ- outgrowth arising from transplantation of 13 visualized, double-sorted Lin-CD29<sup>hi</sup>CD24<sup>+</sup> cells.

