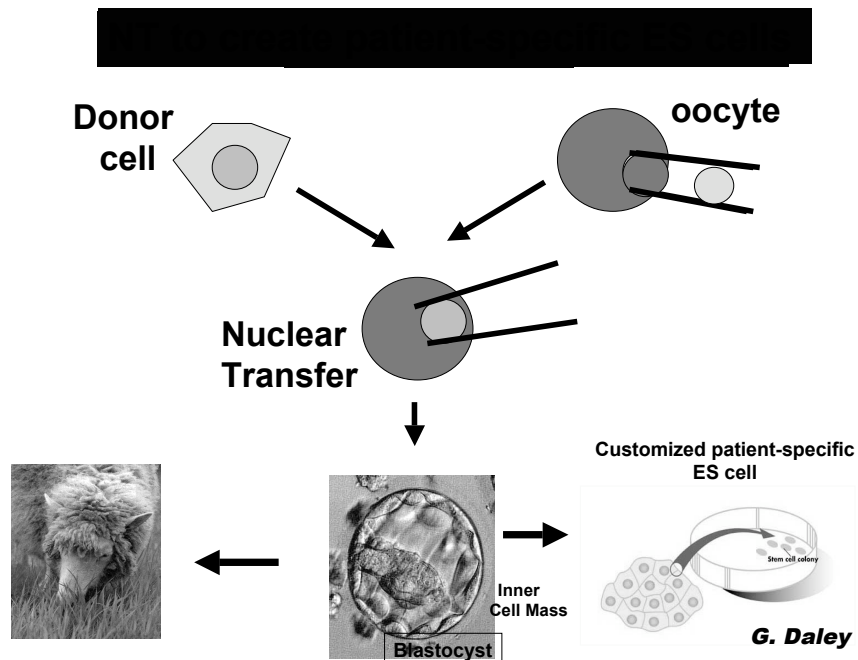


Stem Cells and Cancer

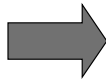
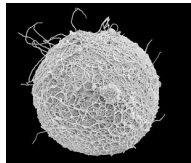
THERAPEUTIC CLONING

ORGANISM CLONING



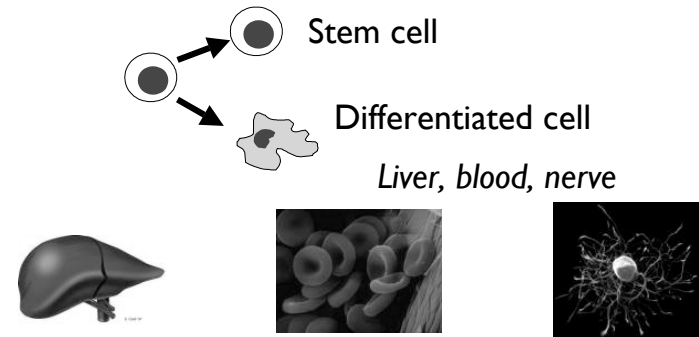
Potential therapeutic uses of stem cells

- Transplantation of bone marrow for muscular dystrophies
- Direct injection of bone marrow stem cells for cardiac regeneration
- Bone marrow injections for neurodegenerative diseases



What are stem cells?

Units of development and regeneration

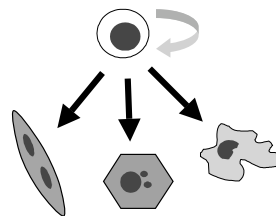


What are stem cells?

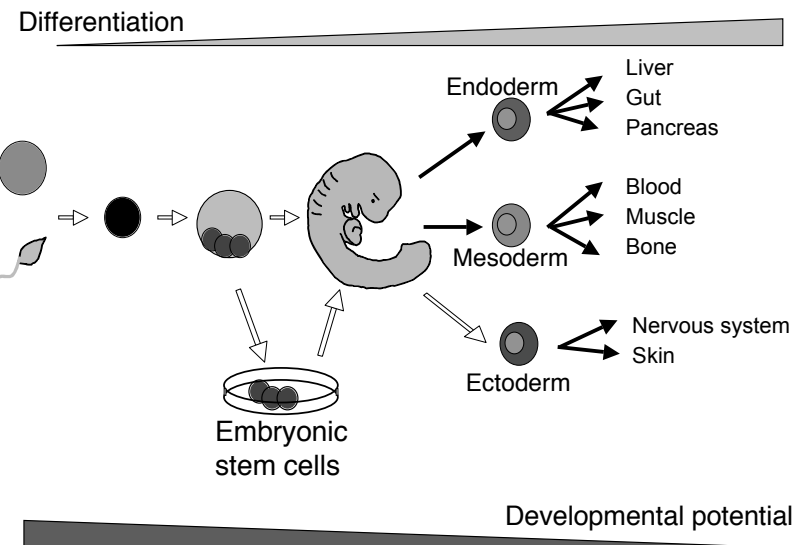
Units of development and regeneration

Why are stem cells unique?

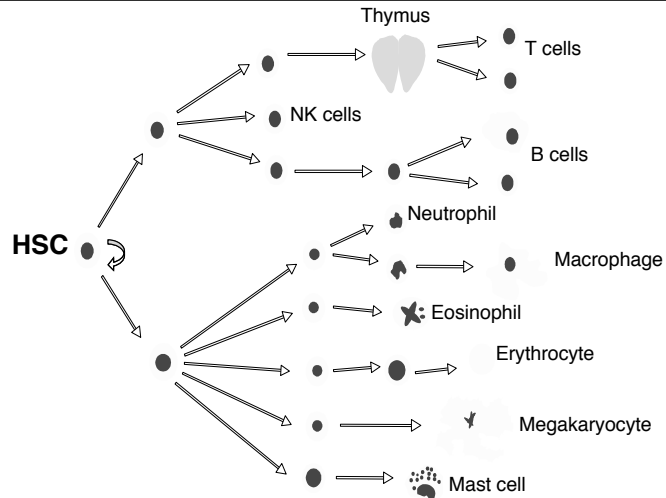
1. They are unspecialized
2. They can produce more stem cells
3. They can produce specialized cells



Human development: a stem cell hierarchy

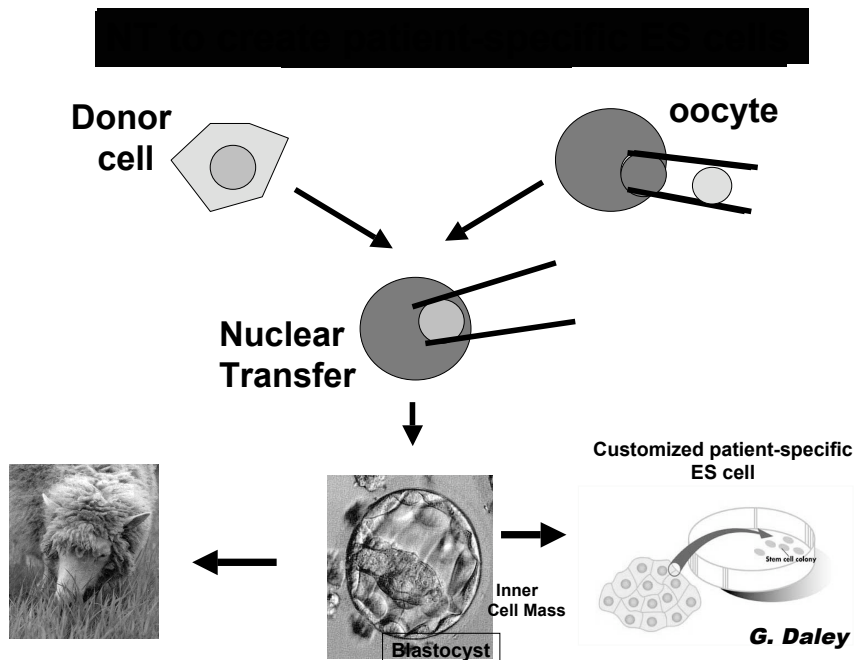


Differentiation **Developmental hierarchies:**
 the hematopoietic system **Developmental potential**



Embryonic versus adult

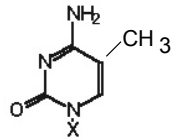
- | | |
|--|---|
| <ul style="list-style-type: none"> • Isolated from early embryos • Can expand indefinitely in culture • Can give rise to all cell types | <ul style="list-style-type: none"> • Isolated from adult human tissue • Can not be expanded in culture • Can only give rise to same tissue |
|--|---|



WHY ORGANISM CLONING MIGHT NOT WORK

1. TECHNICAL REASONS---
2. GENES OR CHROMOSOMES ARE LOST OR CHANGED IN DEVELOPMENT

DNA IS MODIFIED DURING DEVELOPMENT



5- methylcytosine

IN HUMAN FEMALES ONE X INACTIVATED IN DEVELOPMENT

Xist transcripts

Xist RNA “paints” the inactive X-chromosome in mammals

The *Xist* gene on one of the two X-chromosomes only is active- the Xist RNA (green) moves in cis and helps establish inactivity of other genes on that X-chromosome

Xist RNA (green) associates with the Barr body (red) in human female cells

Inactive X-chromosome in mitotic cell of female mouse

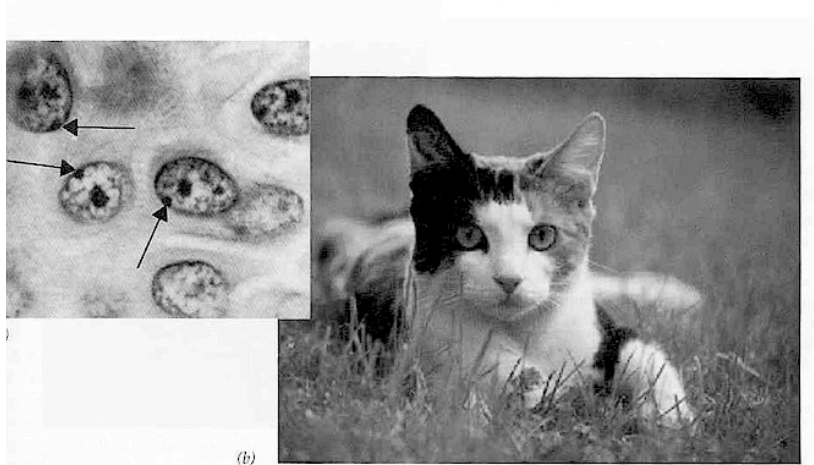
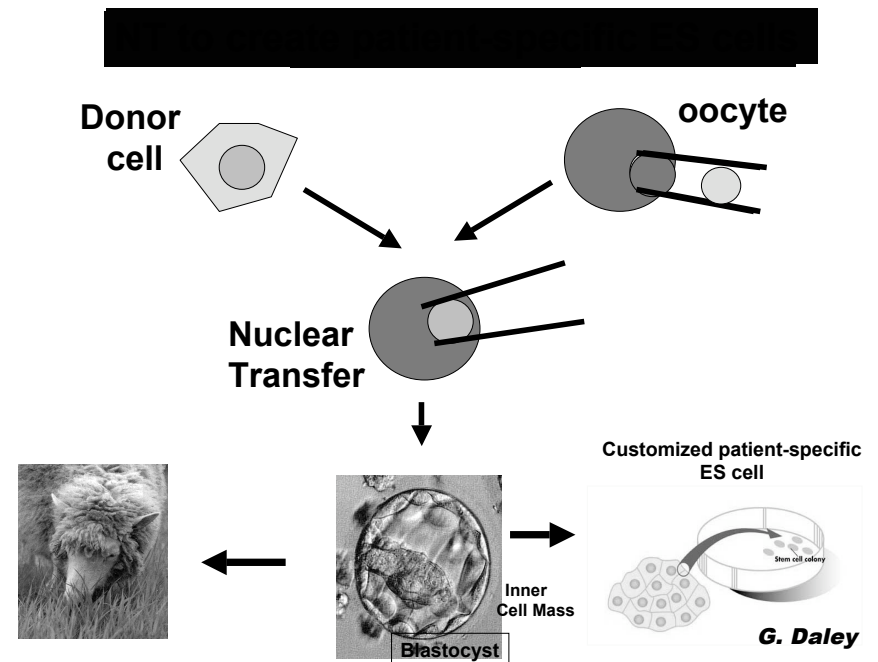
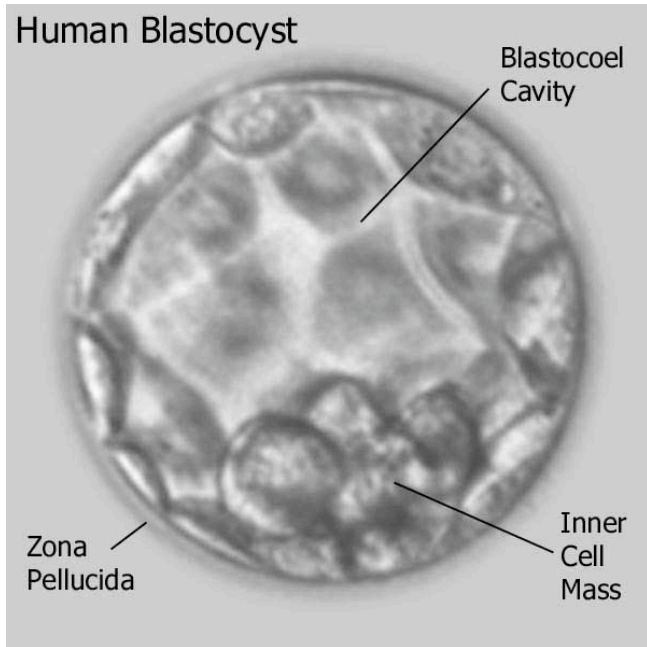


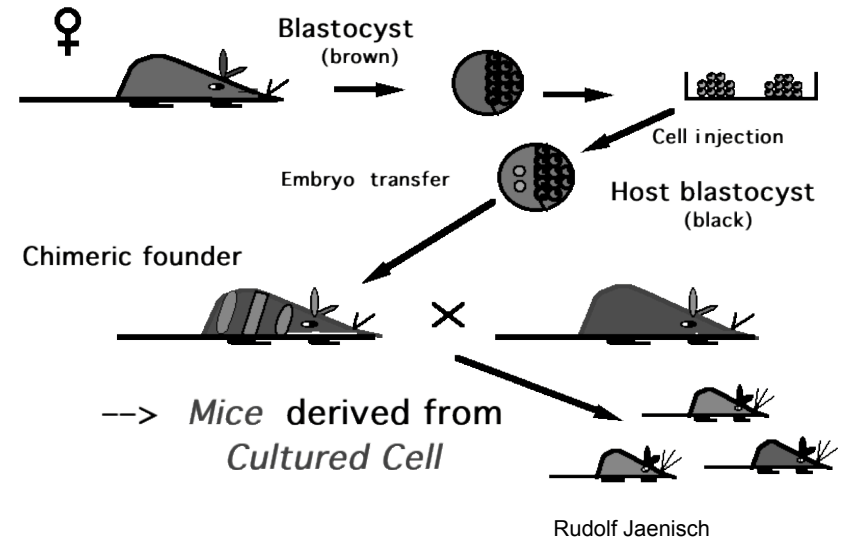
Figure 12.14 The inactive X chromosome: an example of facultative heterochromatin. (a) The inactivated X chromosome in the nucleus of a woman’s cells appears as a darkly staining heterochromatic structure, called a Barr body (arrows). (b) A calico cat. Random inactivation of either X chromosome in different cells during early embryonic development creates a mosaic of tissue patches. Each patch comprises the descendants of one cell that was present in the embryo at the time of inactivation. These patches are visually evident in tortoiseshell cats, which have an allele for black coat color residing on one X chromosome and an allele for yellow coat color on the other X. This explains why male tortoiseshell cats are virtually nonexistent.



Human Blastocyst

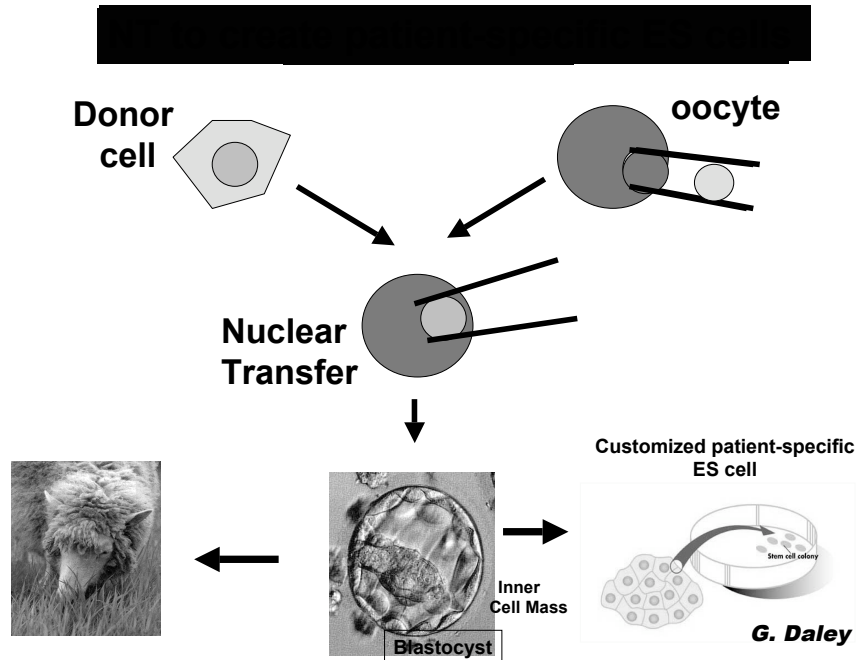


Embryonic Stem (ES) Cells



Potential therapeutic uses of stem cells

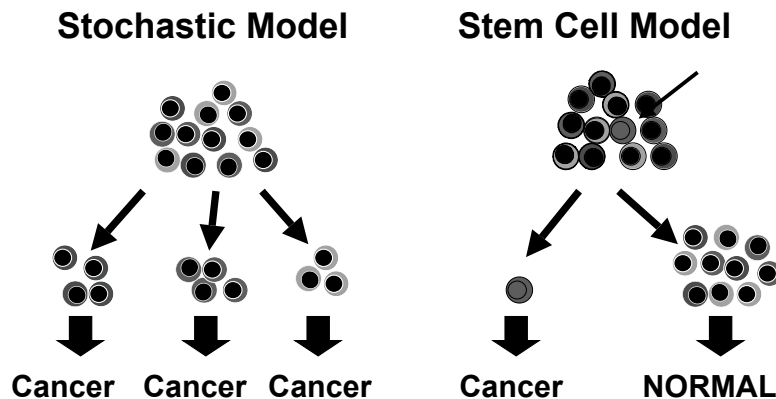
- Transplantation of bone marrow for muscular dystrophies
- Direct injection of bone marrow stem cells for cardiac regeneration
- Bone marrow injections for neurodegenerative diseases



Cancer as a stem cell disease?

- Low clonogenic ability of tumors in vitro
- Most tumors are morphologically heterogeneous

Models of cancer cell growth



Experimental evidence of cancer stem cells

- Acute myeloid leukemia: $CD34^+ CD38^{neg}$ cells are tumor initiating (only 0.1% of total tumor cells)
- Breast cancer: $CD44^+ CD24^{neg}$ (2% of all tumor cells)
- Brain cancer: $CD133^+$ (~20% of all tumor cells)

