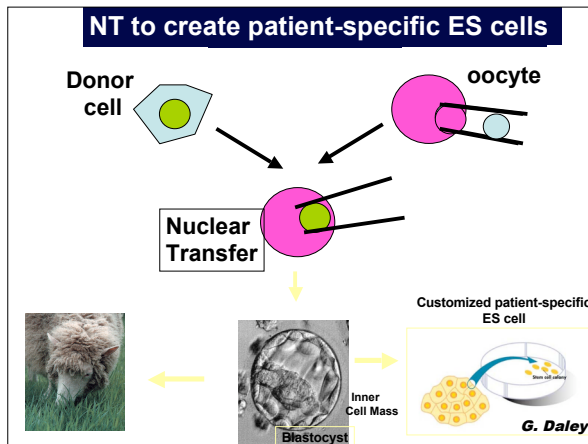


Stem Cells and Cancer

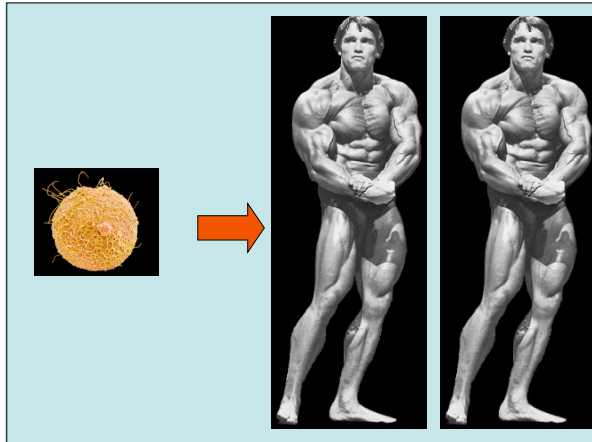
THERAPEUTIC CLONING

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

Stem cell

Differentiated cell
Liver, blood, nerve

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

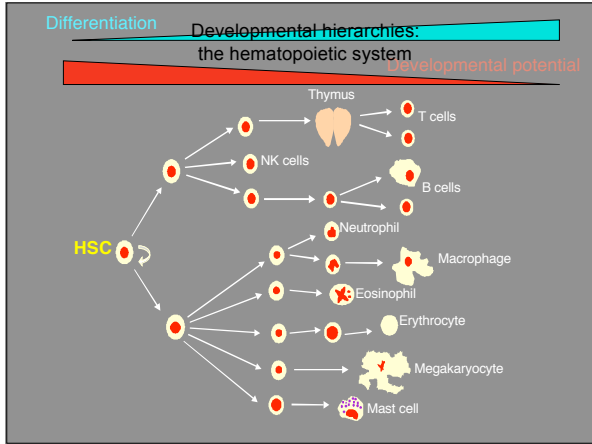
Embryonic stem cells

Endoderm: Liver, Gut, Pancreas

Mesoderm: Blood, Muscle, Bone

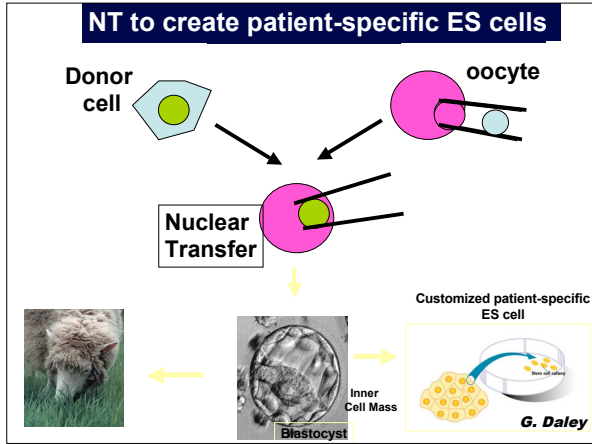
Ectoderm: Nervous system, Skin

Developmental potential



Embryonic versus adult

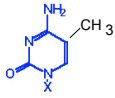
- Isolated from early embryos
- Can expand indefinitely in culture
- Can give rise to all cell types
- Isolated from adult human tissue
- Can not be expanded in culture
- Can only give rise to same tissue



WHY ORGANISM CLONING MIGHT NOT WORK

- TECHNICAL REASONS---
- 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

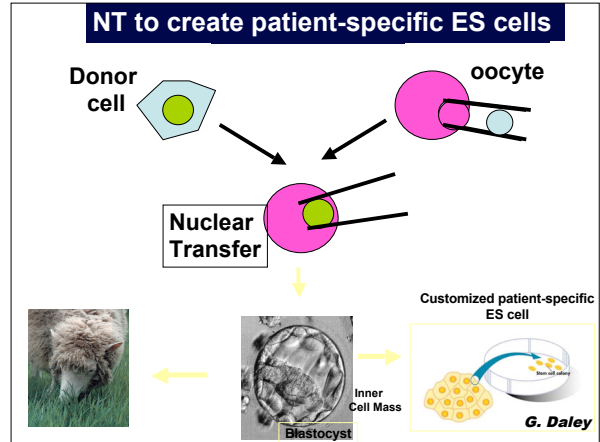
Xist RNA "paints" the inactive X-chromosome in mammals

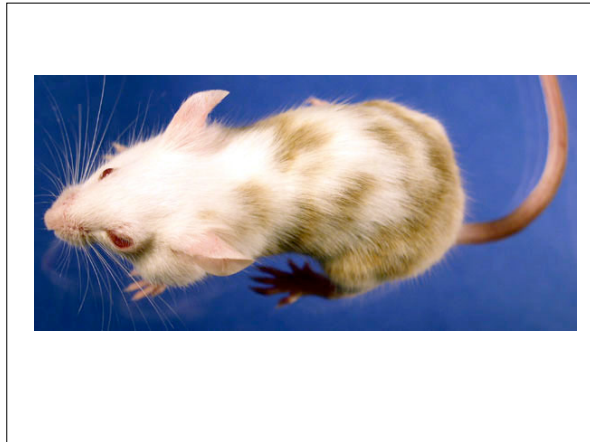
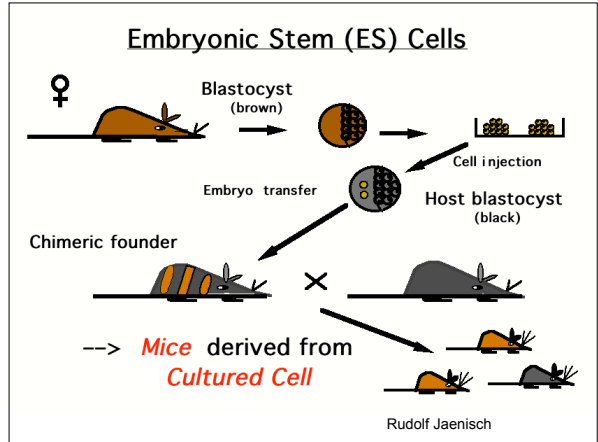
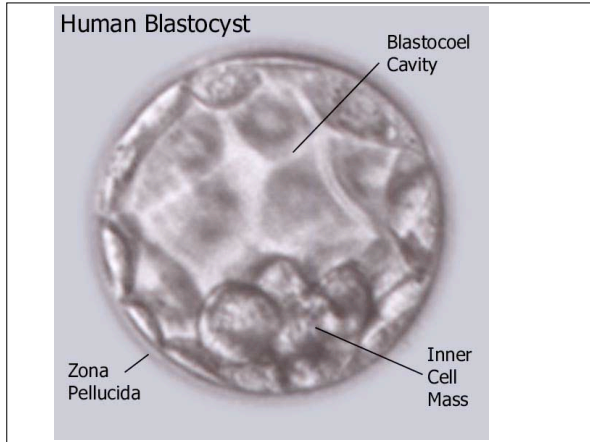
The *Xist* gene on one of the two X-chromosomes only is active- the Xist RNA (green) moves in cis and helps establish inactivity of other genes on that X-chromosome

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

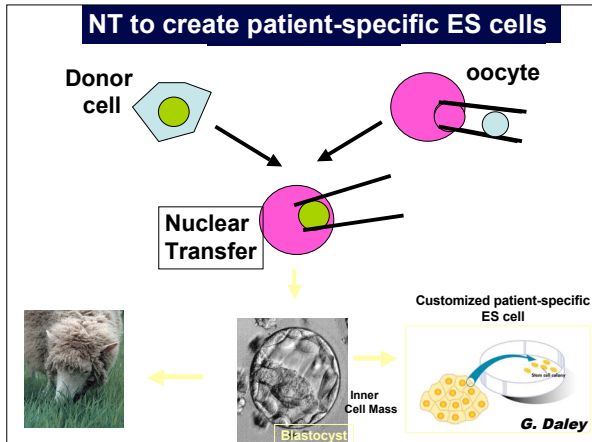
Inactive X-chromosome in mitotic cell of female mouse

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 calico 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 calico cats are virtually nonexistent.



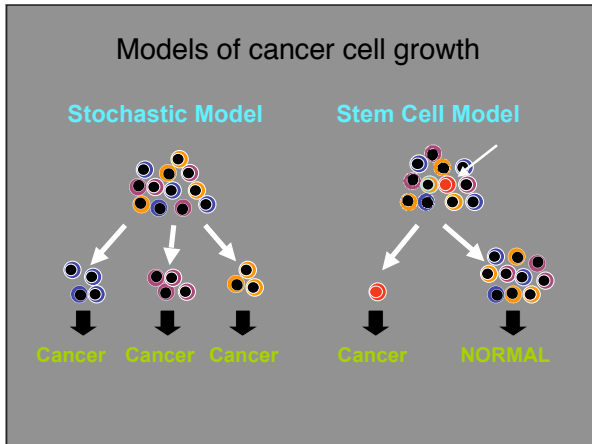


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Cancer as a stem cell disease?

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



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)

