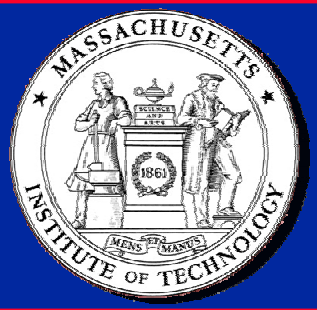
Harvard-MIT Division of Health Sciences and Technology
HST.535: Principles and Practice of Tissue Engineering
Instructor: Myron Spector



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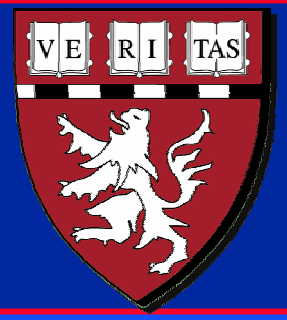

HST 535

TISSUE ENGINEERING: Cells

M. Spector, Ph.D.

CELLS FOR TISSUE ENGINEERING/REGENERATIVE MEDICINE

- Autologous (from same individual)
  - Differentiated cells of same or other tissue type
  - Stem cells (*e.g.*, from bone marrow, fat or other tissue, or saved from umbilical cord)
- Allogeneic (from another individual)
  - Differentiated cells of same or other tissue type
  - Fetal stem cells
  - Embryonic stem cells
- Xenogeneic (from another species)
  - Same as allogeneic

CELLS FOR TISSUE ENGINEERING/REGENERATIVE MEDICINE

Autologous vs. Allogeneic vs. Xenogeneic Cells

	Advantages	Disadvantages
Auto	No disease transmission	Donor site morbidity
Allo	Large available pool Less expensive	Disease transmission Immune reaction Heterogeneous pop. (genetic anomalies)
Xeno	Largest pool Least expensive	Disease transmission Immune reaction

CELLS FOR TISSUE ENGINEERING/REGENERATIVE MEDICINE

Stem Cells Versus Differentiated Cell Types

	Advantages	Disadvantages
Diff.	Already display the desired phenotype More expensive procedure	Donor site morbidity Difficulties in growth *in vitro*
Stem	Several sources Easier to obtain Less expensive Can be used for many applications; undiff. and diff.	May not differentiate as desired Uncontrolled growth *in vivo*

NEED FOR STEM CELLS IN TISSUE ENGINERING/REGENERATIVE MEDICINE

Problems in Using Differentiated Cells

- Limited availability of differentiated autologous cells.
- Morbidity of a harvest procedure and donor site.
- Limited proliferative capacity and biosynthetic activity.

http://stemcells.nih.gov/

NATIONAL INSTITUTES OF HEALTH
May 2000

Stem Cells: A Primer

Definitions

Stem cells - cells that have the ability to divide for indefinite periods in culture and to give rise to specialized cells.

- **Multipotent** -giving rise to many cell types.
- **Pluripotent** -capable of giving rise to most tissues of an organism.
- **Totipotent** - having unlimited capability. Totipotent cells have the capacity to specialize into extraembryonic membranes and tissues, the embryo, and all postembryonic tissues and organs.

In the political debate over the use of embryonic stem cells, some opponents claim that malleable adult cells can take the place of their embryonic cousins. Many scientists aren't so sure

Can Adult Stem Cells Suffice?

Science 292: 1820 (2001)

- Stem cells can be found in many tissues of the body and developing embryos and fetuses
  - ES cells are **pluripotent**; with the correct cues they can give rise to any kind of cell in the body
  - Adult stem cells are **multipotent**; they can produce many, but not all, cell types
- Adult bone marrow cells have been in use for more than a decade, whereas embryonic stem (ES) cells were isolated for the first time 3 years ago
- Surprising flexibility of adult stem cells found in many tissues
- ES cells multiply more readily and seem far more proficient in producing certain specialized cell types

CELLS BEING REFERRED TO AS "STEM CELLS"

- Can divide in culture for only a limited number of passages and still be induced to differentiate into selected cell types (*i.e.*, cannot divide indefinitely).
- Can only be induced to differentiate into only a few specialized cell types.
- Most tissues appear to contain such cells.

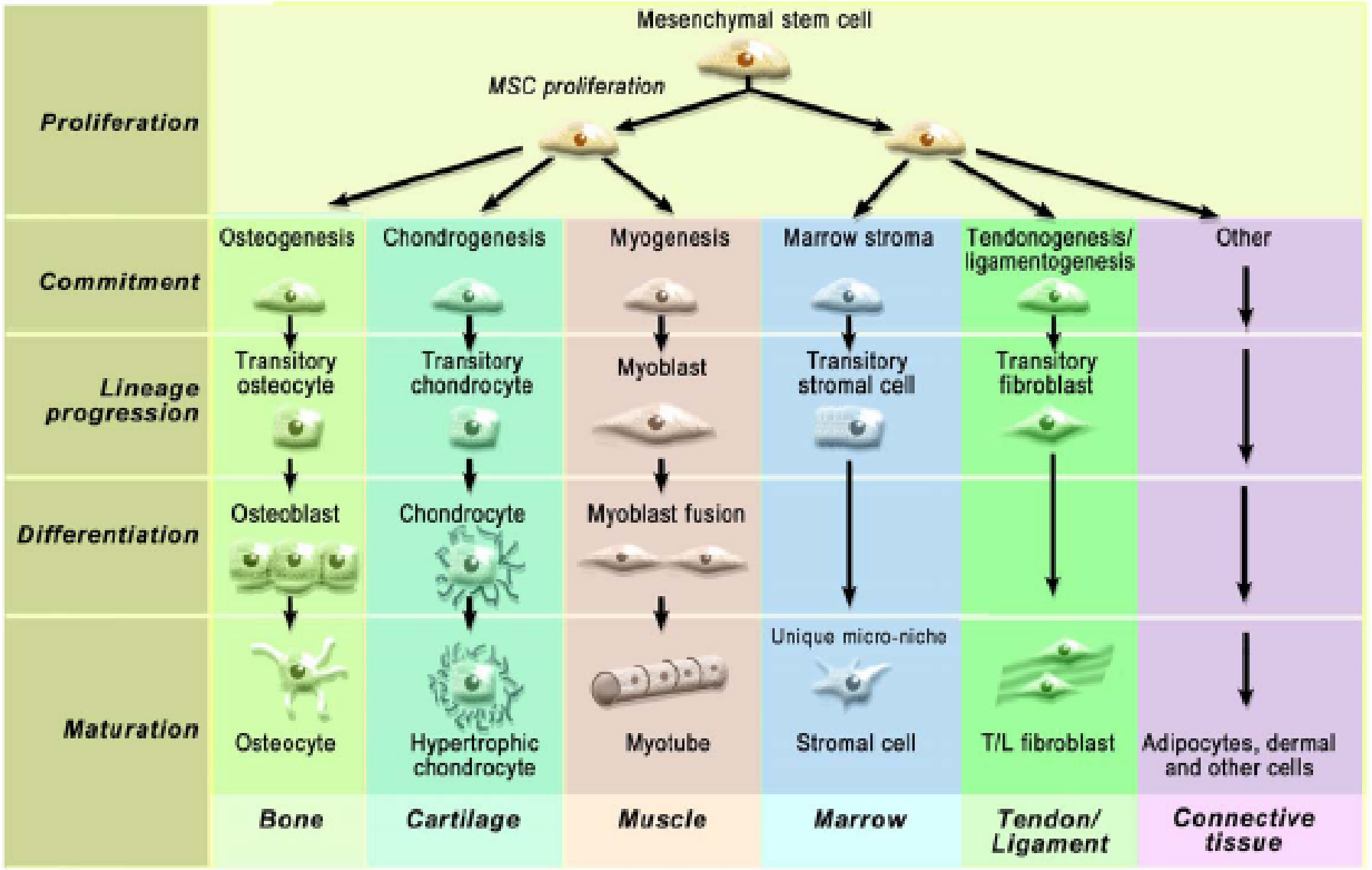

Figure by MIT OCW.

AI Caplan and SP Bruder, Trends Mol. Med., 7:259;2001

STEM CELLS FROM MARROW
Rationale for Clinical Value

Historical Perspective

1869 Autologous marrow induces bone at heterotopic sites (E. Goujon)

1919 Marrow has osteogenic activity (A Keith)

1961 Osteogenic properties of marrow (RG Burwell)

1986 Intra-op centrifugation of marrow and percutaneous injection for treating non-unions (J Connolly, et al., Neb. Med. J. 71:105)

1995 Marrow infiltrating into defects in articular cartilage provide stem cells for chondrogenesis

MSC Differentiation Assays *In Vitro*

Hyaline Cartilage

Photo removed for copyright reasons.

B. Kinner, ECR 2002;278:72

Fat

Photo removed for copyright reasons.

Bone

Photo removed for copyright reasons.

Von Kossa

Chondro-induced adult canine MSCs in a Type II Collagen-GAG matrix after 2 weeks (+100ng/ml of IGF-1) Safranin O staining