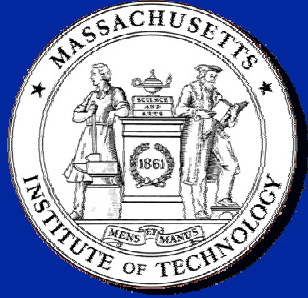
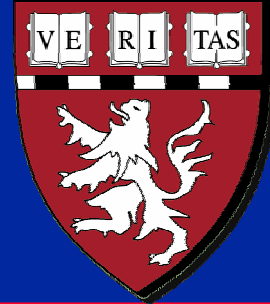


Harvard-MIT Division of Health Sciences and Technology  
HST.535: Principles and Practice of Tissue Engineering  
Instructors: E. Marsilio and Myron Spector



**Massachusetts Institute of Technology**  
**Harvard Medical School**  
**Brigham and Women's Hospital**  
**VA Boston Healthcare System**



**2.782J/3.961J/BEH.451J/HST524J**

**TISSUE ENGINEERING**  
**IV. Stem Cells**

**E. Marsilio, Ph.D. and M. Spector, Ph.D.**

# ELEMENTS OF TISSUE ENGINEERING/ REGENERATIVE MEDICINE

- **MATRIX (SCAFFOLD)**
  - Porous, absorbable synthetic (*e.g.*, polyglycolic acid) and natural (*e.g.*, collagen) biomaterials
- **CELLS (Autologous or Allogeneic)**
  - Differentiated cells of same type as tissue
  - Stem cells (*e.g.*, bone marrow-derived)
  - Other cell types (*e.g.*, dermal cells)
- **SOLUBLE REGULATORS**
  - Growth factors or their genes
- **ENVIRONMENTAL FACTORS**
  - Mechanical loading
  - Static versus dynamic (“bioreactor”)

# **CELLS FOR TISSUE ENGINEERING/REGENERATIVE MEDICINE**

- **Autologous (from the same individual)**
- **Allogeneic (from a different individual)**
- **Xenogeneic (from a different species)**
  - **Differentiated specialized cells of same or other tissue type, such as heart, muscle etc.**
  - **Undifferentiated unspecialized or uncommitted cells such stem cells.**

# **NEED FOR STEM CELLS IN TISSUE ENGINEERING/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.**

## **WHY STEM CELLS?**

**Stem cells have the capacity to regenerate or repair tissues that have been destroyed or damaged by injury or disease such as cartilage, spinal cord etc.**

**Stem cells are specially important in tissues that do not have the ability to regenerate.**

# WHAT ARE STEMS CELLS?

**“Stem cells are self-renewing unspecialized cells that can give rise to multiple types of specialized cells in the body”**

## WHAT IS THE DIFFERENCE?

- **Specialized cells are cells “committed” to perform a specific function e.g. heart muscle cell, skin cell, neuron etc.**
- **Stem cells are “uncommitted” cells. They remain “uncommitted” until they receive signals from their environment to develop into specialized cells.**

<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.



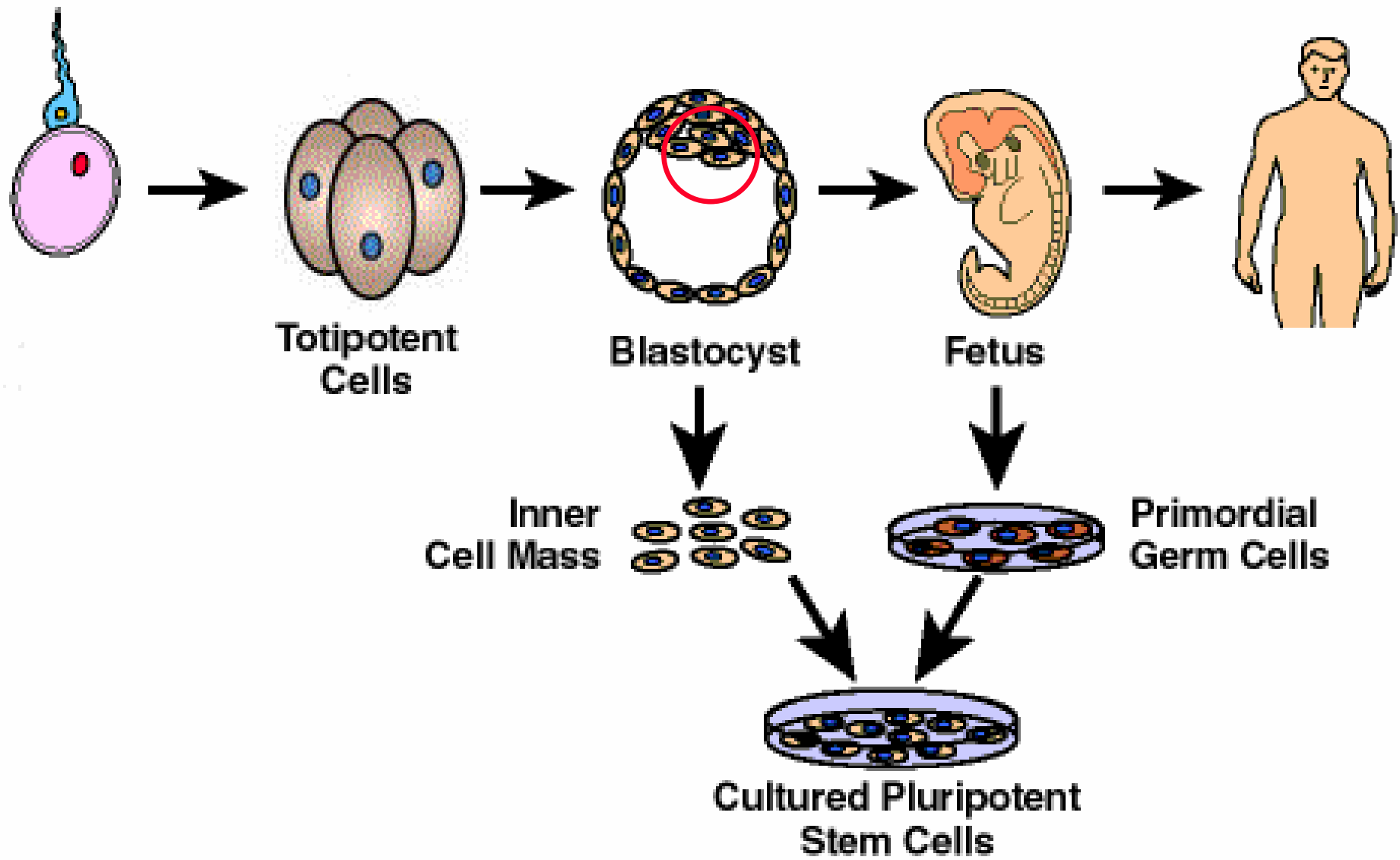
# STEM CELL SOURCES

**Stem cells are derived from:**

- Embryo (pluripotent)**
- Fetal tissue (pluripotent, multipotent)**
- Adult tissue (multipotent)**

# How are pluripotent stem cells derived?

- Pluripotent stem cells can be isolated directly from the inner cell mass of human embryos at the blastocyst stage and cultured to produce a pluripotent stem cell line.
- Pluripotent stem cells can be isolated from fetal tissue obtained from terminated pregnancies. Cells can be taken from the region of the fetus that is destined to develop into the testes or the ovaries.



# Potential Applications of Pluripotent Stem Cells

- **Help to understand the events that occur during development.**
  - identification of the factors involved in the cell specialization; "decision-making" genes .
- **Change the way drugs are developed and tested for safety.**
  - new medications could be initially tested using human cell lines.
- **Generation of cells and tissue that could be used for so-called "cell therapies."**
  - donated organs and tissues are often used to replace ailing or destroyed tissue.
  - the number of people suffering from these disorders far outstrips the number of organs available for transplantation.

# Adult Stem Cells

- Multipotent stem cells can be found in some types of adult tissue. In fact, stem cells are needed to replenish the supply cells in our body that normally wear out (*e.g.*, the blood stem cell).
- Multipotent stem cells have not been found for all types of adult tissue, but discoveries in this area of research are increasing.
  - neuronal stem cells have been isolated from the rat and mouse nervous systems. The experience in humans is more limited.
  - a kind of cell that may be a neuronal stem cell has been isolated from adult brain tissue.

# The Mesengenic Process

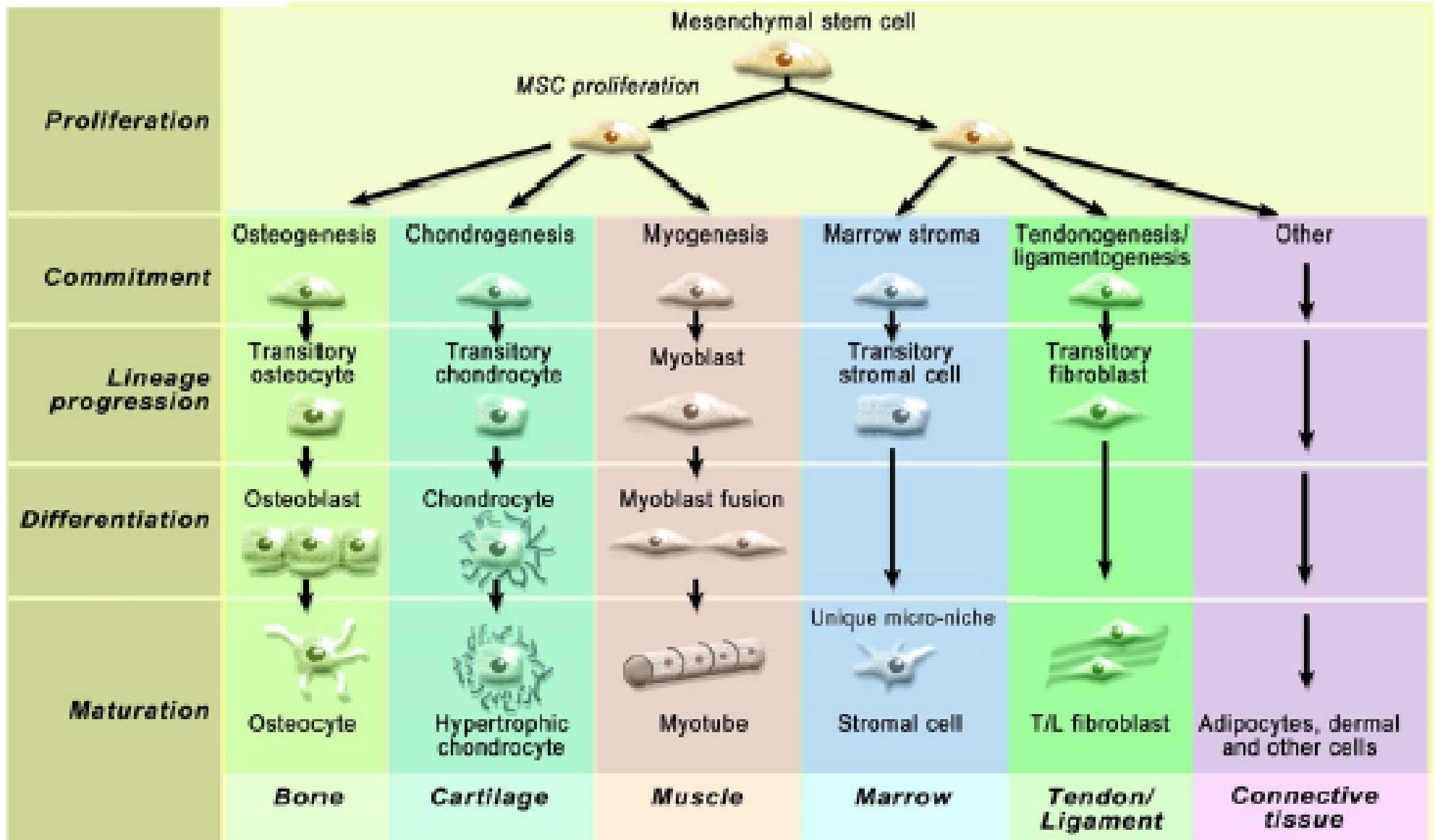


Figure by MIT OCW.

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

# **Do adult stem cells have the same potential as pluripotent stem cells?**

- **Until recently, little evidence that multipotent cells such as blood stem cells could change course and produce cells other than a blood stem cell or a specific type of blood cell.**
  - **In animals, it has been shown that some adult stem cells are able to develop into other types of specialized cells.**
  - **In mice neural stem cells placed into the bone marrow appeared to produce a variety of blood cell types.**
  - **In rats, stem cells found in the bone marrow were able to produce liver cells.**
- **Even after a stem cell has begun to specialize, the adult stem cell may, under certain conditions, be more flexible than first thought.**

# Why not just pursue research with adult stem cells?

- They are multipotent cells and can give rise to many different cell types.
- The use of autologous cells will avoid rejection by the immune system.
- Adult bone marrow derived cells have been used for over a decade compared to embryonic cells.
- “Reduce or even avoid the practice of using stem cells derived from human embryos or human fetal tissue, sources that trouble many people on ethical grounds.”

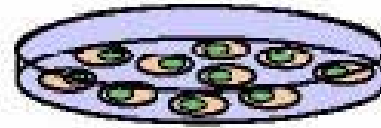


# **TECHNICAL CHALLENGES**

- **Adult stem cells are found in tissues at a low number.**
- **The isolation and identification process is not well defined.**
- **Adult stem cells ability to proliferate in culture is less than in the living organism.**

# The Promise of Stem Cell Research

Drug Development  
and Toxicity Tests

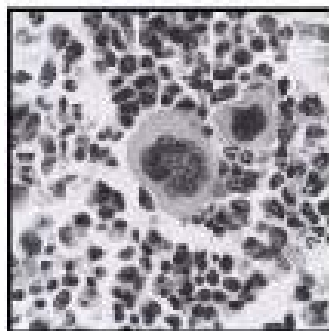


Experiments to  
Study Development  
and Gene Control

Cultured Pluripotent  
Stem Cells



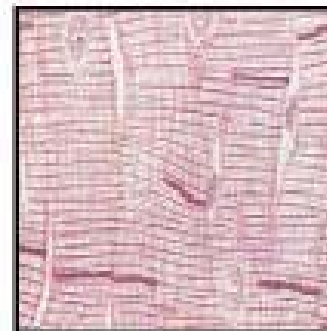
Tissues/Cells for Therapy



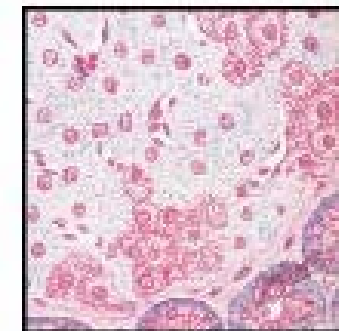
Bone Marrow



Nerve Cells



Heart Muscle  
Cells



Pancreatic  
Islet Cells

# CONCLUSION

Stem cell research is still relatively at a young stage. Progress is being made at a rapid pace.

The potential for new therapies that can be derived from using either pluripotent or adult stem cells is great.

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