A microscopic image of a neural network. The image shows a dense collection of neurons. The cell bodies (soma) are stained blue, while the axons and dendrites are stained in various colors including red, green, and yellow. The overall appearance is a complex, interconnected web of fibers.

Stem Cells: Introduction and Prospects in Medicine

Ode to a Stem Cell, Part II

by VCW

There once was stem cell stuck in the 'hood'
Dividing endlessly, but only wishing he could
Become something else, a skin cell, a hair cell, or some other type
But for weeks he sulked and uttered this gripe
“Why am I not needed?” to his friends he would say
Isn't there a call for a specialist somewhere today?
Well, if you really want to leave to get a new start,
You must change your tune, for surely there is an art
To consider what signals you hear and choices you make.
Divide once more for the special journey you take.
Dare to be different, as you differentiate!

Overview

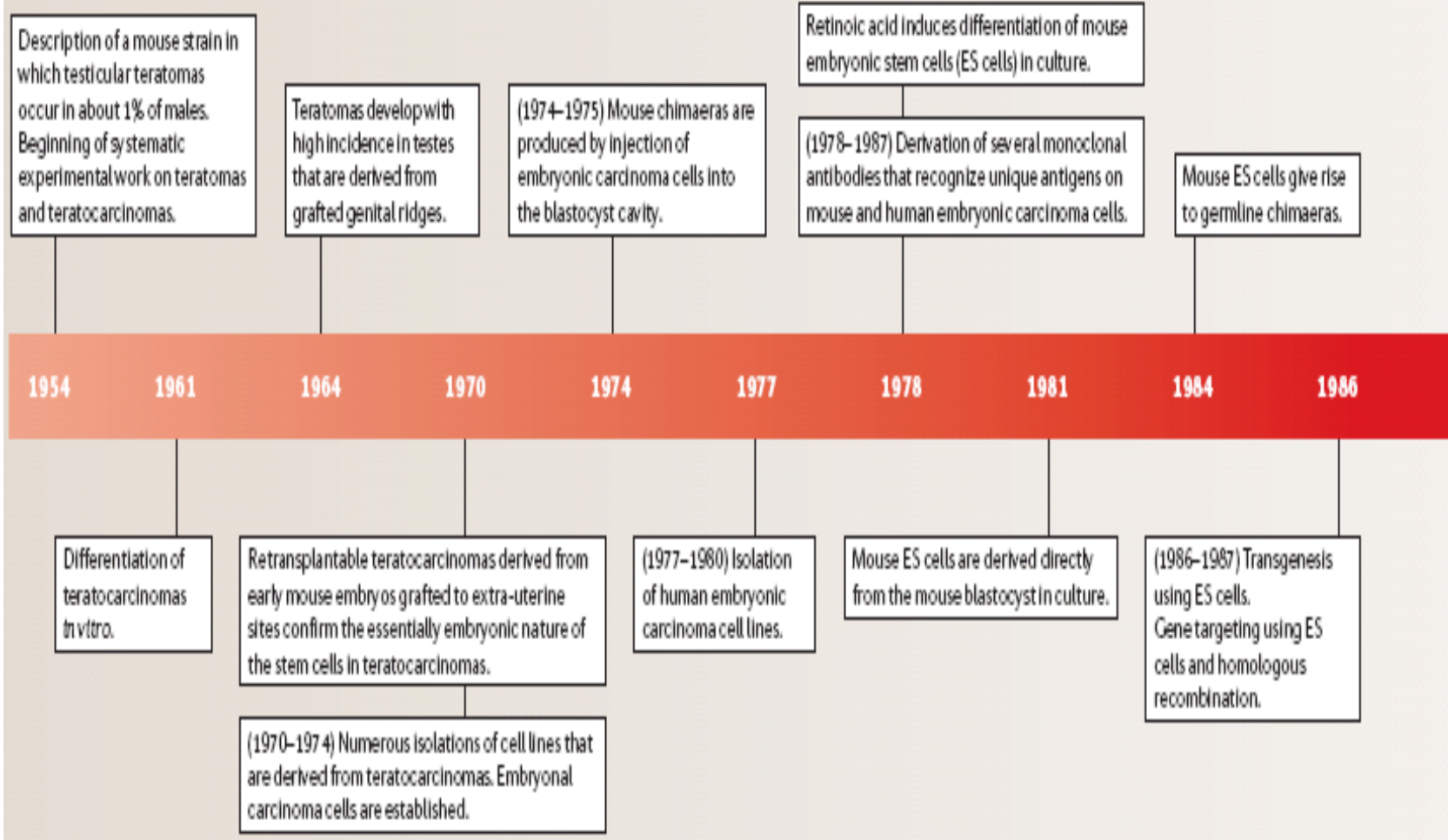
- **Setting the stage for the discussion:** historical perspective and prospects in regenerative medicine
- **Stem Cell Basics:**
 - What are stem cells?
 - Where do stem cells come from?
- **Stem Cell Advances in the News!**
- **Stem Cell Research Challenges**

Historical Perspective and Prospects for Regenerative Medicine

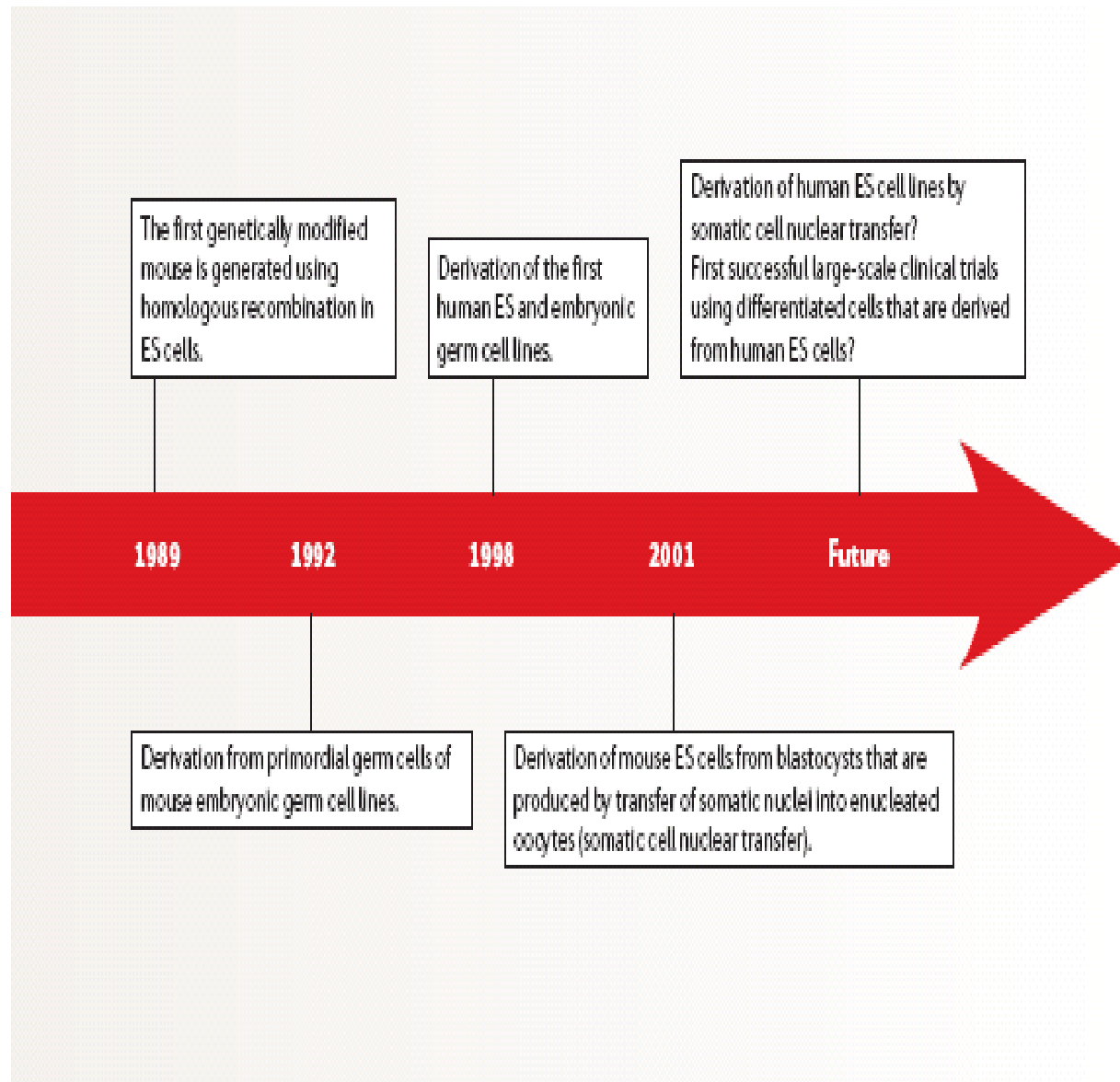
Historical Perspectives

- Major changes in regenerative medicine (replacement of damaged or diseased cells and tissues with new cells and tissues) due to advances in stem cell technologies
- Some stem cell therapies in existence for over 50 years. First successful bone marrow transplant done in 1956 on leukemia patient. Bone marrow contains **adult-derived** hematopoietic stem cells (able to regenerate tissues similar to the specialized tissues in which they are found).
- **Embryonic stem cells** believed to have greater potential. This line of stem cell research has been the most controversial.

Timeline | The history of embryonic stem cell research



From Solter, D. 2006 *Nature Reviews Genetics* 7, 319-327.



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2007 Nobel Prize in Medicine

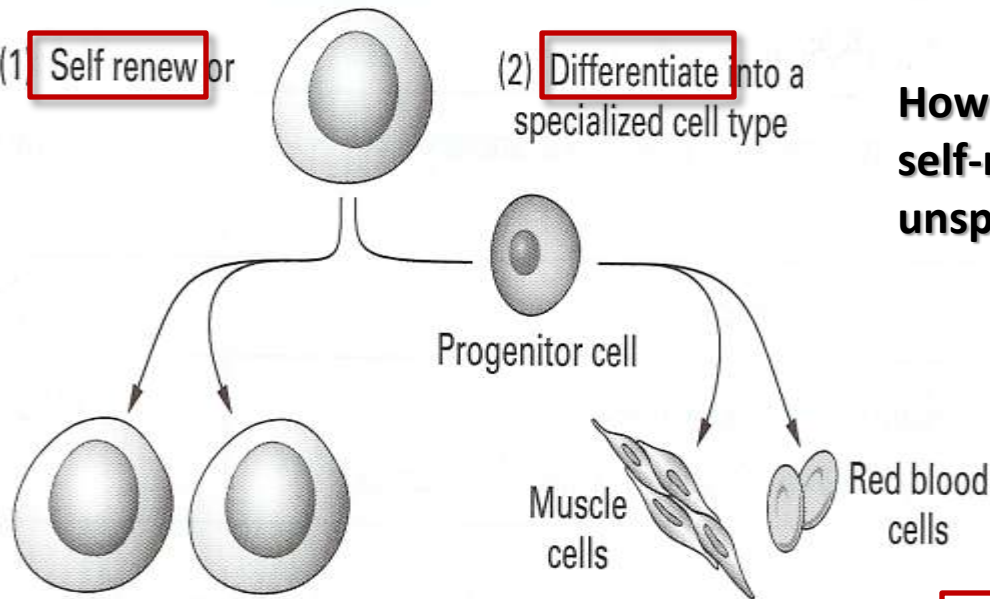
Mario R. Capecchi, Martin J. Evans and Oliver Smithies for their discoveries of the principles for introducing specific gene modifications in mice by the use of embryonic stem cells.

STEM CELL BASICS

I. What are stem cells?

Basic Characteristics of Stem Cells

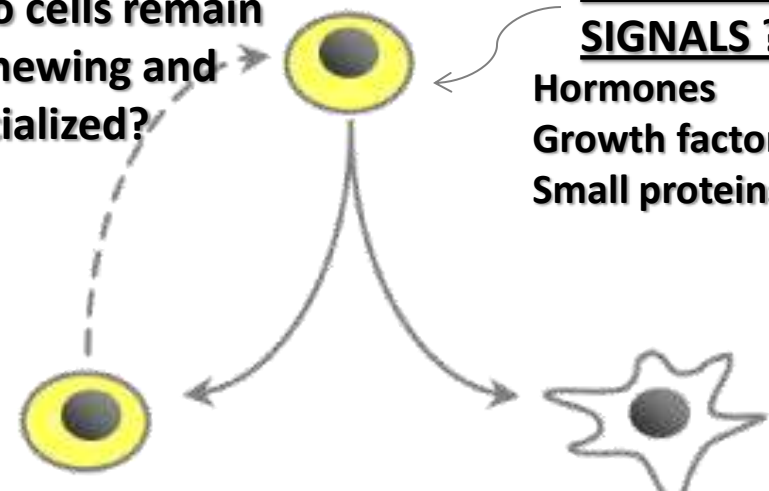
A stem cell can:



How do cells remain self-renewing and unspecialized?

STEM CELL

What are the SIGNALS ???
Hormones
Growth factors
Small proteins



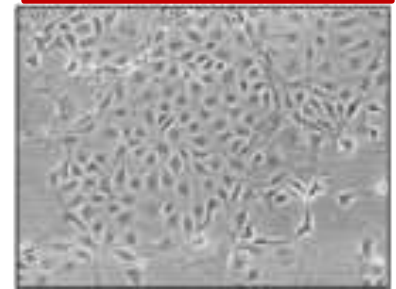
Stem cells properties:

1. Capable of dividing and renewing for long periods
2. They are unspecialized.
3. They give rise to specialized cells.

SELF-RENEWAL

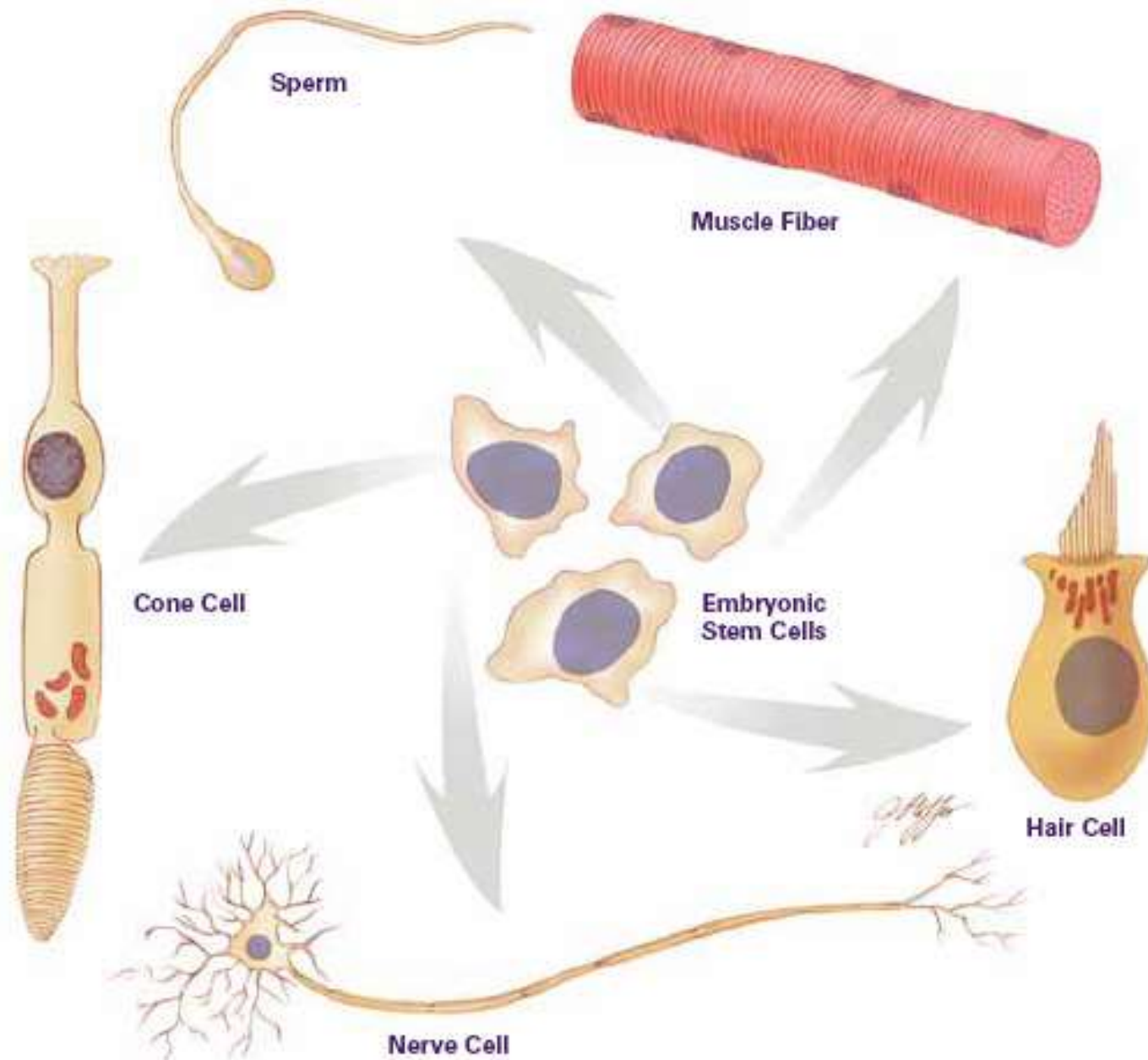


DIFFERENTIATION





<http://gajitz.com/?s=rube+goldberg>



Remember:

Unlike gametes (egg and sperm cells), all other cells (somatic cells) have the same DNA content and the same genes.

Since **DNA** → **RNA** → **protein**, then how can we account for different protein patterns in different types of cells?

The expression pattern of genes within different types of cells is NOT identical.

Protein Profiles Differ in Different Cell Types

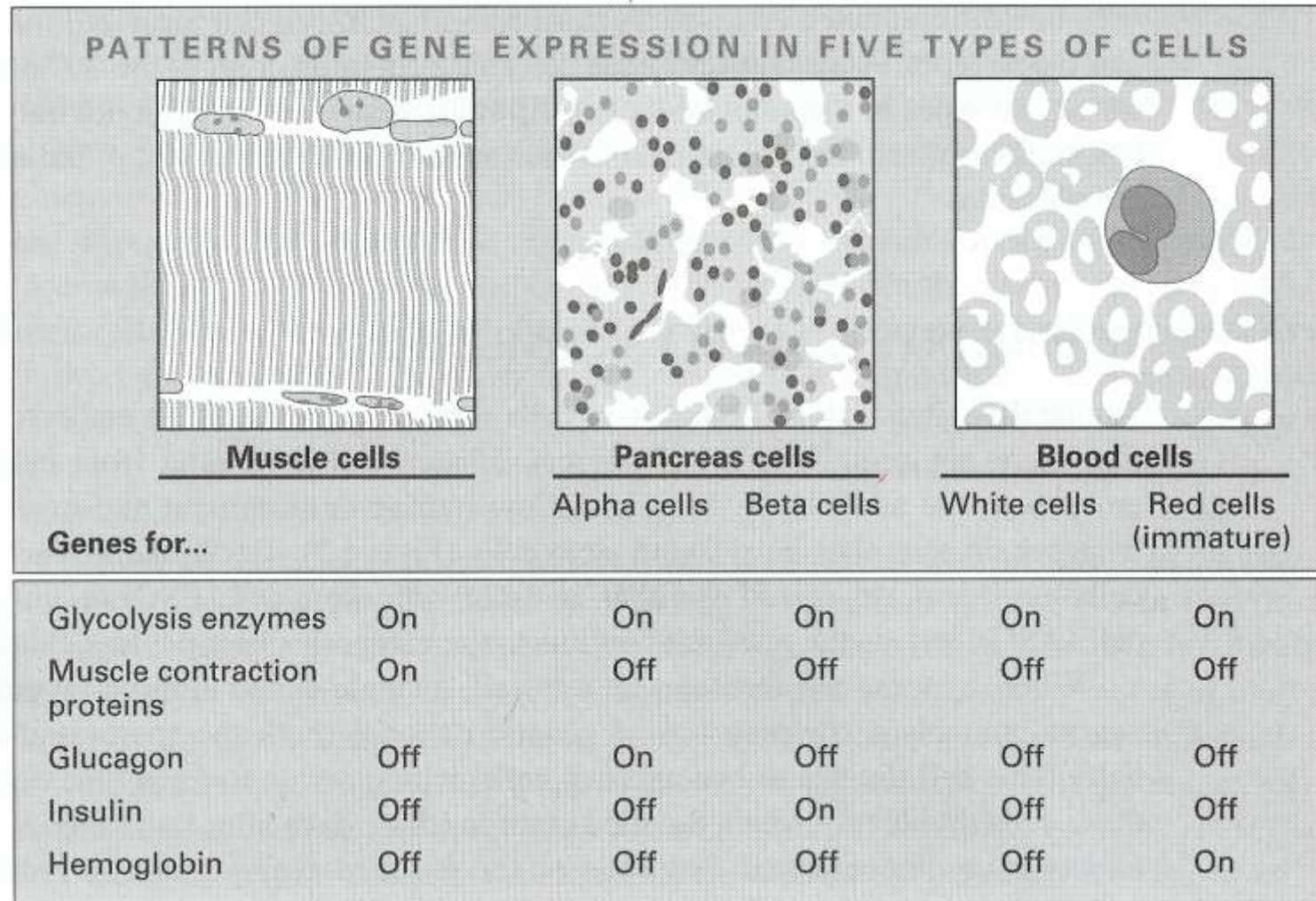


Figure from *Stem Cells and Cloning* by K.A. Hogan

All stem cells are not alike!

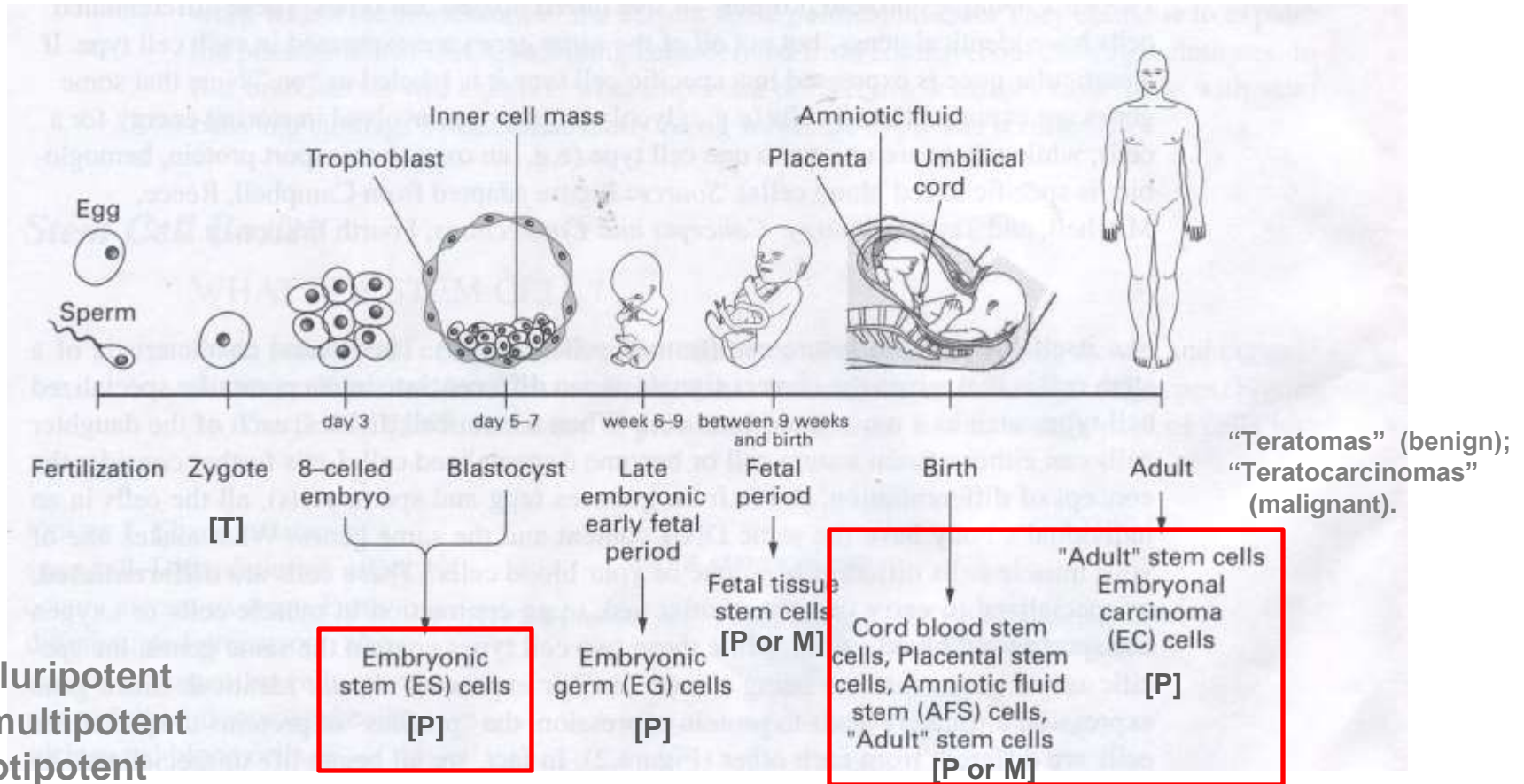
- Some stem cells have more potential than others. **POTENCY** describes this flexibility.
- **Unipotent** stem cells form only one type of specialized cell type.
- **Multipotent** stem cells can form multiple types of cells and tissue types.
- **Pluripotent** stem cells can form most or all cell types in the adult.
- **Totipotent** stem cells can form all adult cell types as well as the specialized tissues to support development of the embryo (e.g., the placenta)

STEM CELL BASICS

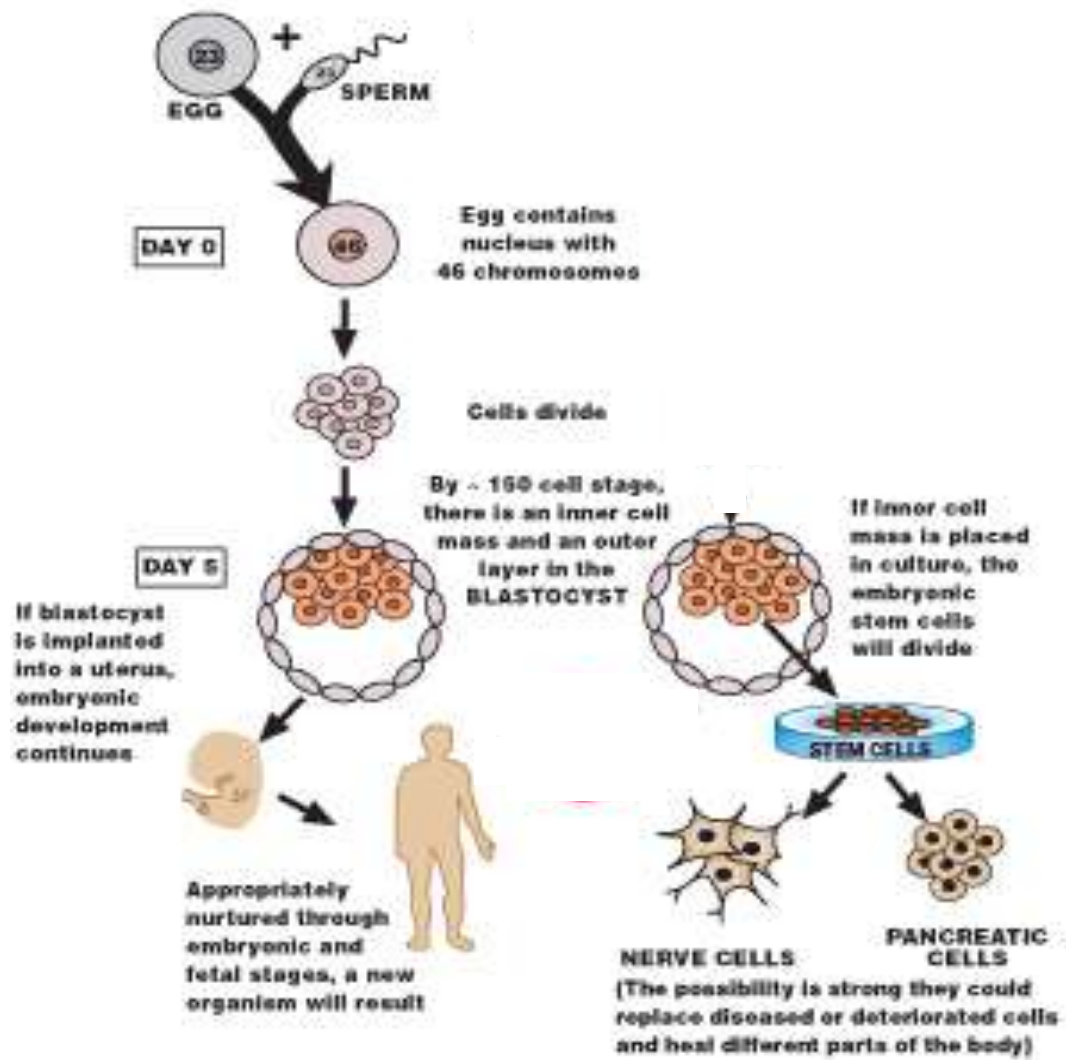
II. Where do stem cells come from?

Different sources of stem cells during development

Adapted from *Stem Cells and Cloning* by K.A. Hogan



Origin of Human Embryonic Stem Cells



Isolation of Human Embryonic Stem Cells

First done by Dr. James Thomson and colleagues at the University of Wisconsin (1998).

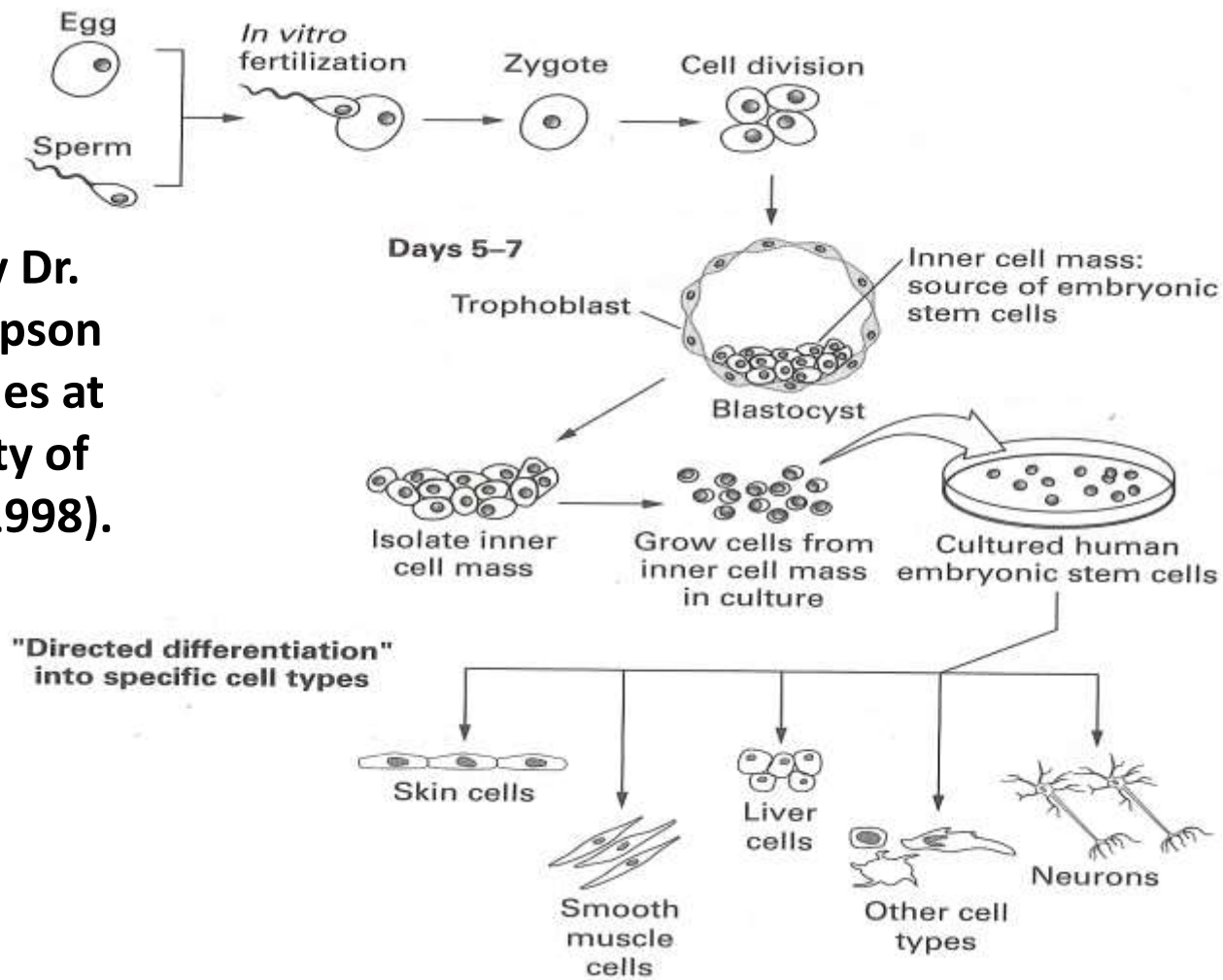


Figure from *Stem Cells and Cloning* by K.A. Hogan

Properties of Human Embryonic Stem Cells in Culture

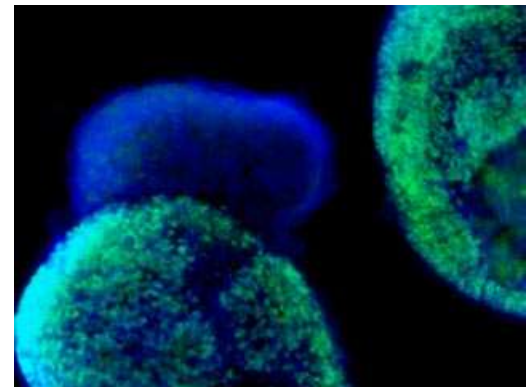
- **Pluripotent** – able to form any of ~200 different types of cells of the body
- **Self-renewing *in vitro*** – can propagate or proliferate indefinitely in the undifferentiated state
- **Express** the enzyme **telomerase** (required to maintain the ends of chromosomes) and ***Oct4*** (a master regulator of ESC pluripotency)
- **Maintain normal chromosome structure and complement** even after long periods in culture (unlike many other tissue culture cell lines)

Stem Cell Research in the News!

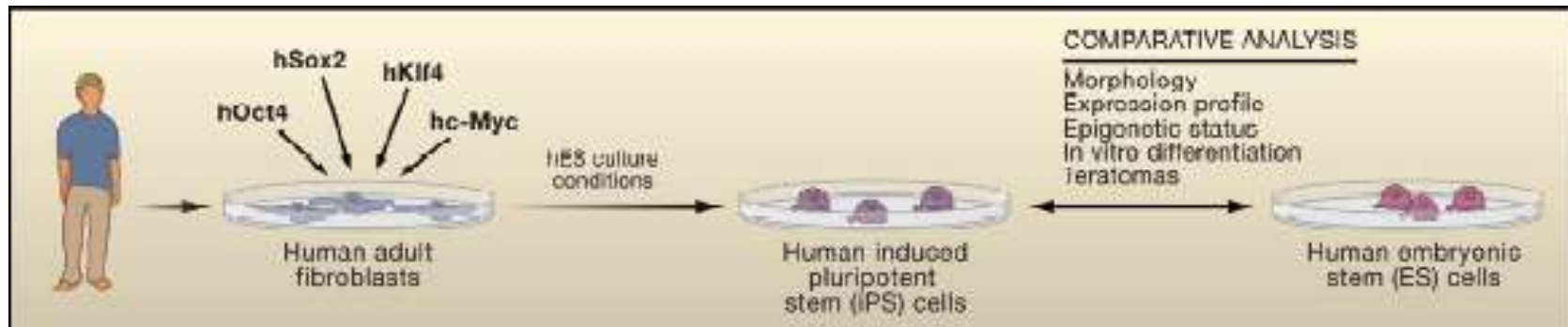
Selected News about Stem Cells

†

- “Scientists Find Way to Track Stem Cells in Brain”
(*Science*, November 2007)
- “Stem Cells Restore Memory in Mice”
(*Journal of Neuroscience*, October 2007)
- “Researchers Isolate Adult Stem Cells for First Time in Tendon”
(*Nature Medicine*, September 2007)
- “Stem Cells From Testes Produce Wide Range of Tissue Types”
(*Nature*, September 2007)
- “Scientists Turn Human Skin Cells into Stem Cells”
(*Science; Cell*, November 2007)
- “First Neurons Created from ALS Patient’s Skin Cells”
(*Science*, July 2008 [online])



“Scientists Turn Human Skin Cells into Stem Cells”



Induction of Pluripotency: From Mouse to Human

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IMPACT :

- Understanding birth defects
- Possibility of generating patient-specific stem cell lines to study the mechanism of different diseases in the laboratory
- Creation of models for drug discovery and testing the toxic effects of drugs
- Tissue engineering (e.g., use of progenitor cells to make artificial bladders)
- Does this alter the debate about the use of human ES cells or not?

Parkinson's Disease (PD): Stem Cell Insights

Source cells	Differentiated Cell type	Host animal receiving brain transplant	Results
Monkey ESCs	Dopamine-producing neurons	Monkey model of PD	Diminished PD symptoms; low survival rate of transplanted cells
Human ESCs	Dopamine-producing neurons	Rat model of PD	Significantly improved muscle coordination; tumor formation in brains
Human neural progenitor cells from fetal tissue engineered to express a "survival factor"	N/A	Rat and monkey models of PD	Improved symptoms of PD; new dopamine-producing neurons generated; effects not long lasting
Adult human brain biopsy cells	Neural progenitor cells	Mouse	New neurons generated
Mouse or human neural ASCs	N/A	Mouse model of related disease, Sandhoff's disease	Increased life span; delayed loss of motor function; no tumors
Human ESCs	Neural progenitor cells	Mouse model of Sandhoff's disease	Increased life span; delayed loss of motor function; no tumors

adapted from K.A. Hogan, *Stem Cells and Cloning*.

Stem Cell Therapy Challenges

- Ethical considerations for ESC research
- Safety challenges – Use of ESCs or differentiated cells derived from ESCs for therapy? Considerations to avoid tumor formation. Immune system challenges to avoid rejection of foreign cells.
- Understanding the basic mechanisms that underlie stem cell biology

Summary:

- **Stem cell therapies offer regenerative prospects for numerous human diseases**
- **Stem cells are capable of renewal and differentiation.**
- **Stem cells are derived from numerous sources and have different potency capacities.**
- **Adult stem cells (ASCs) have been detected in numerous tissues.**
- **Considerable debate surrounds the use of embryonic stem cells. Adult stem cells may offer similar prospects for therapy as do as ESCs, yet a complete understanding of stem cell applications will require a basic understanding of differentiation and renewal mechanisms in ASCs and ESCs as well.**

Additional resources: <http://stemcells.nih.gov/info/basics/>

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