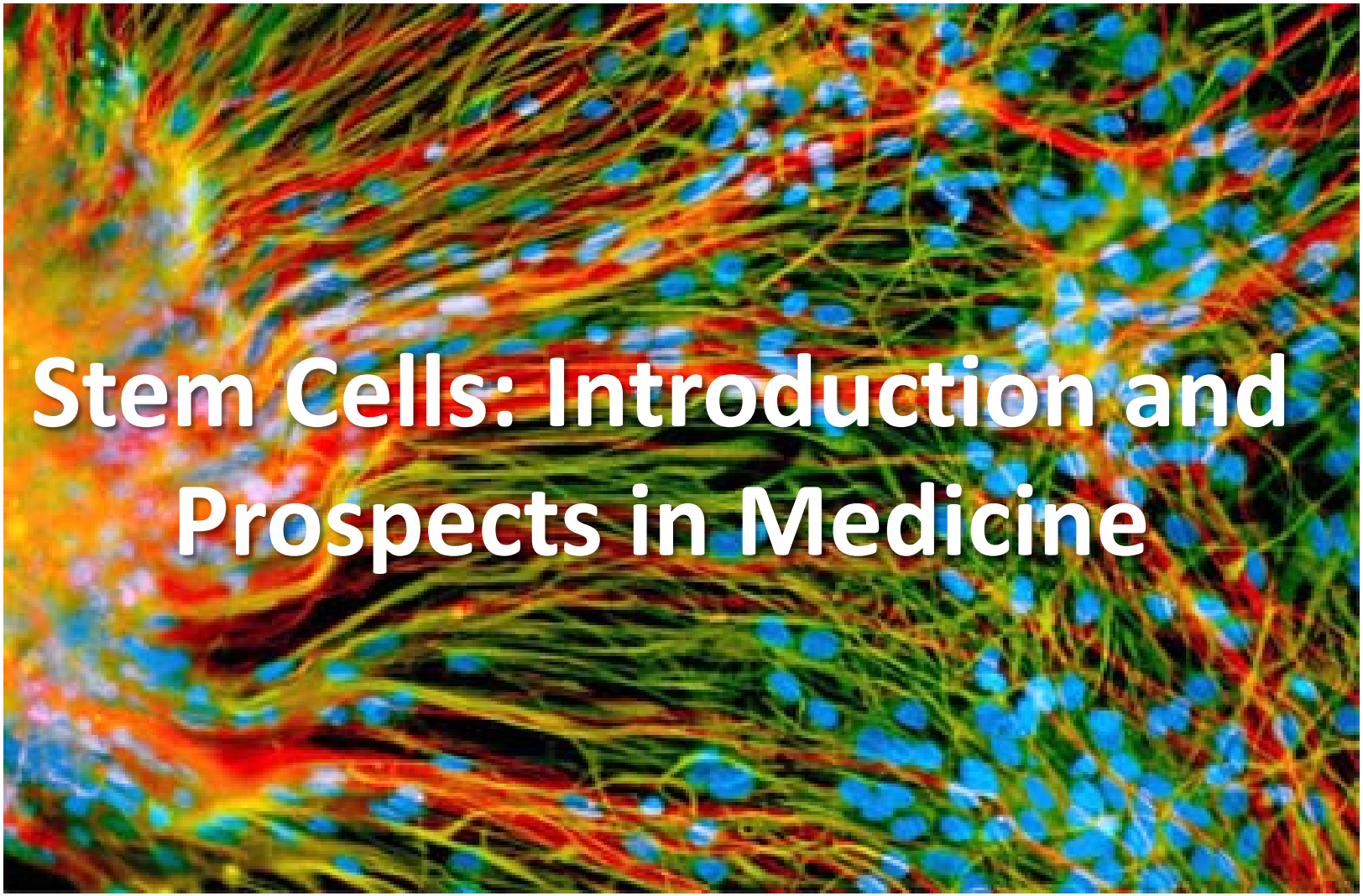


Stem Cells: Introduction and Prospects in Medicine

Professor Vassie Ware, 2012
Department of Biological Sciences

www.gothamgazette.com/.../stemcell/stem_cell.jpg

Overview

- **What's the Big Deal? A Historical Perspective and Future Prospects in Regenerative Medicine**
- **Stem Cell Basics**:

  What are stem cells?

  Where do stem cells come from?

  Types of stem cells:

  embryonic stem cells (ESCs)

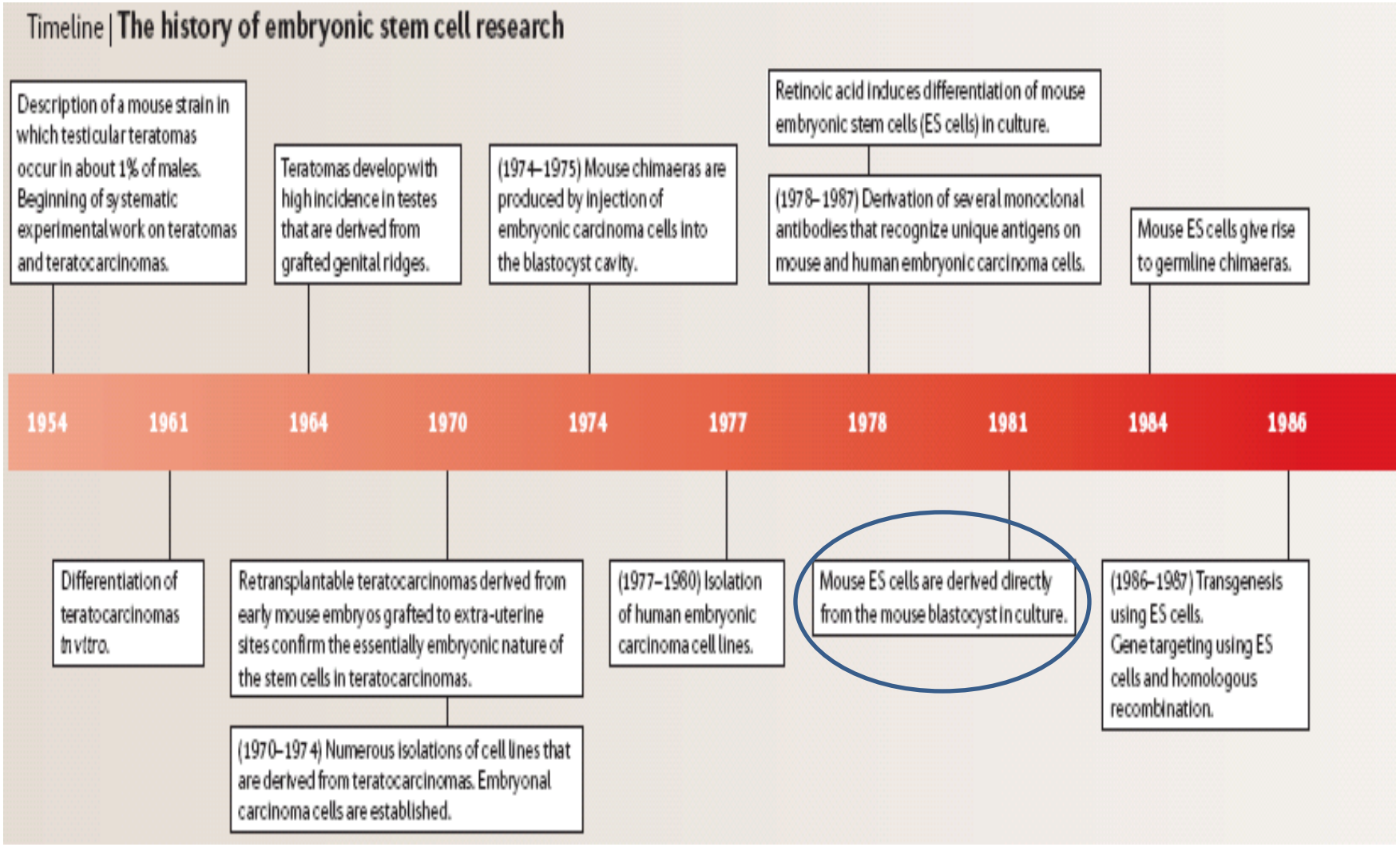
  adult-derived stem cells (ASCs)

  induced pluripotent stem cells (iPSCs)
- **Adult Stem Cell Advances in the News!**
- **Stem Cell Research Challenges**
- **Summary**

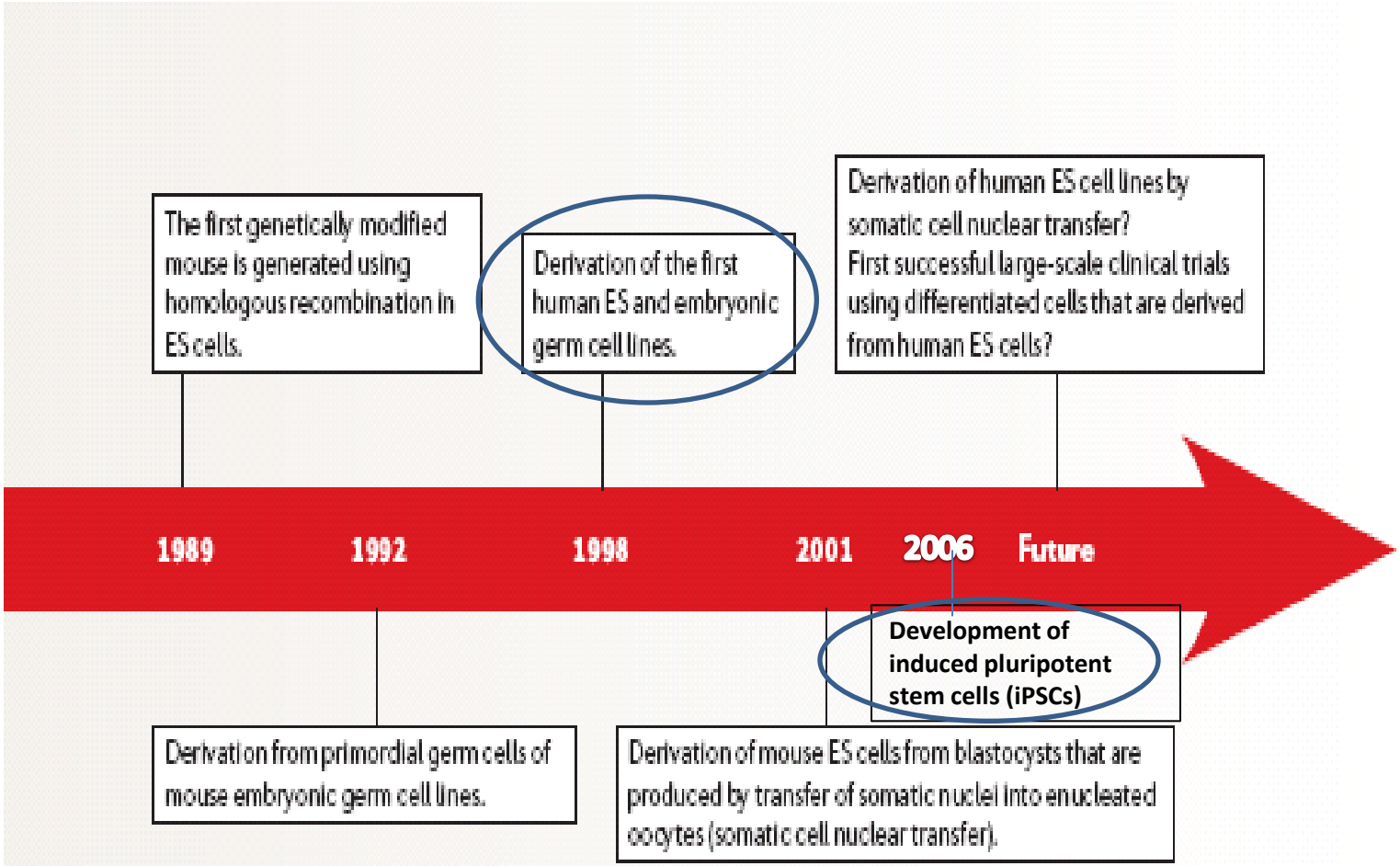
Historical Perspective and Prospects for Regenerative Medicine

Historical Perspectives

- Major changes in cell-based therapies 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, adult stem cells,** and **induced pluripotent stem cells** are believed to have great potential for regenerative medicine.



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



2007 Nobel Prize in Medicine

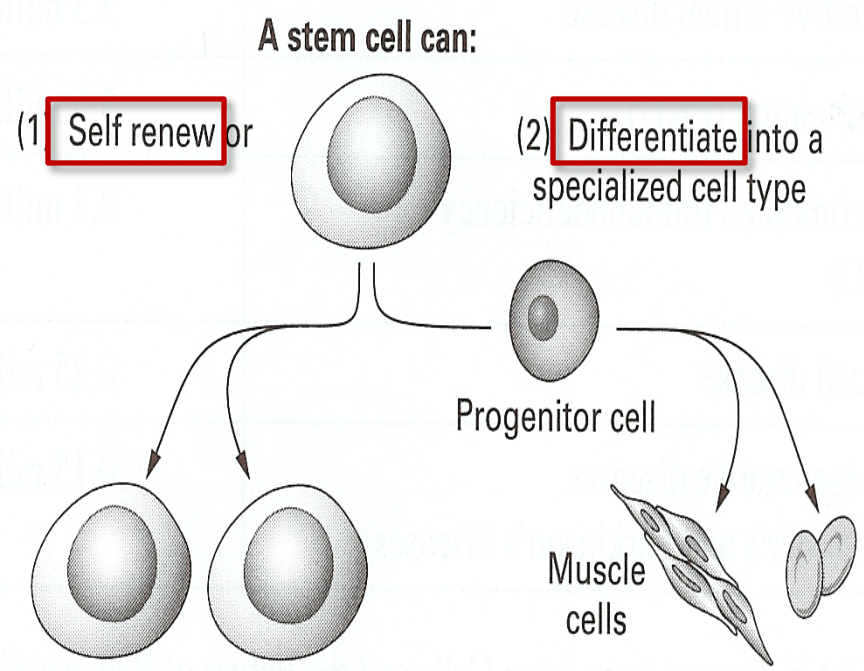
Mario R. Capecchi, **Martin J. Evans** and **Oliver Smithies** for their discoveries of the principles for introducing specific gene modifications in mice by the use of embryonic stem cells.

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

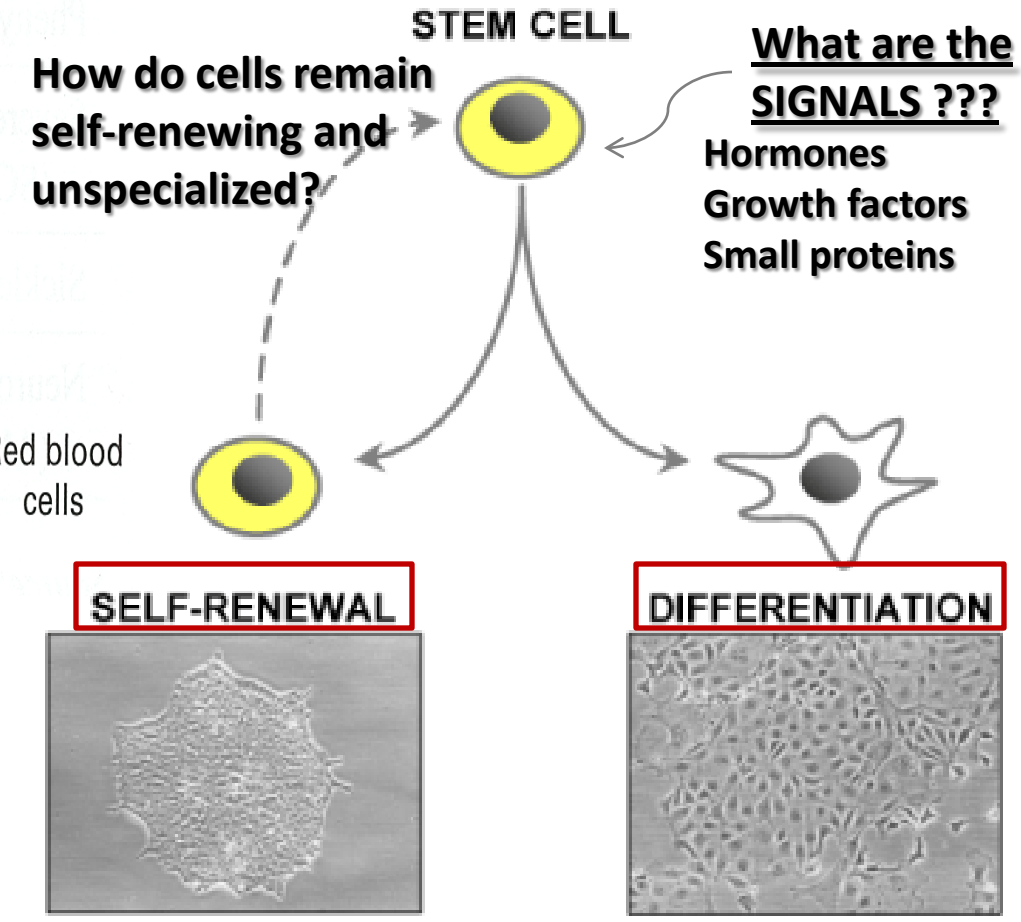
STEM CELL BASICS

I. What are stem cells?

Basic Characteristics of Stem Cells



Stem cell "niche" (neighborhood)

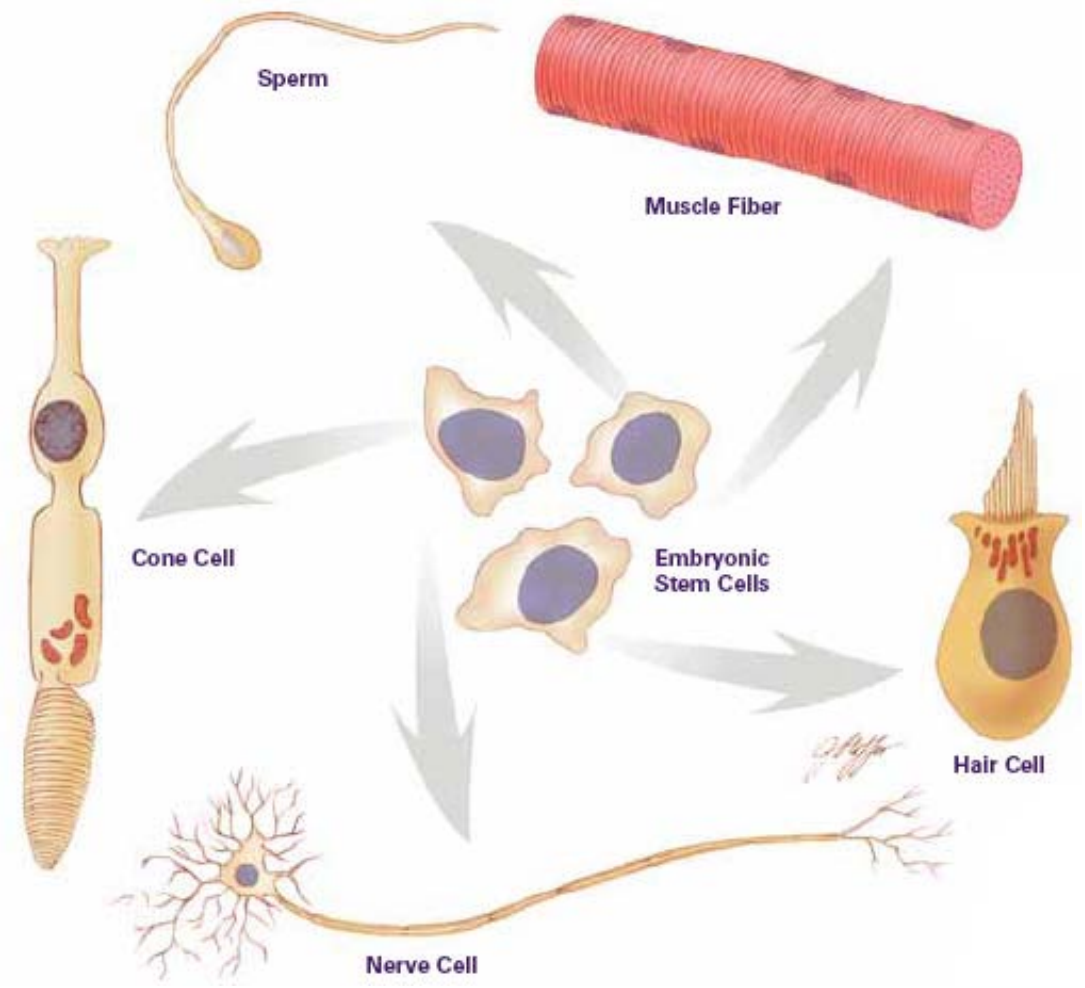


Stem cells properties:

1. Capable of dividing and renewing for long periods
2. Are unspecialized.
3. Give rise to specialized cells.

Adapted from *Stem Cells and Cloning* by Kelly A. Hogan;
http://stemcells.nih.gov/info/basics/basics2.asp

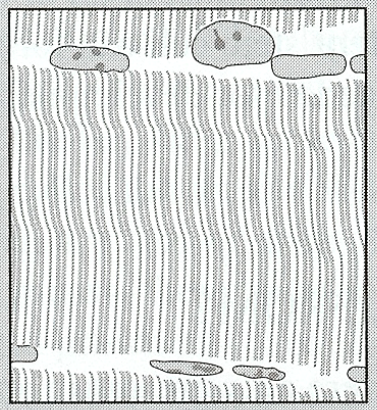
What distinguishes cell types from one another?

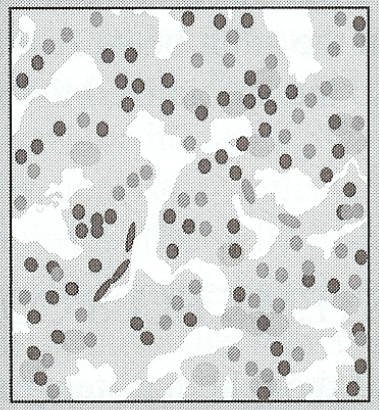


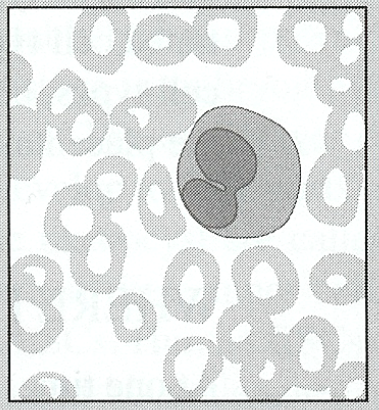
http://creationwiki.org/index.php/Stem_cell

Protein Profiles Differ in Different Cell Types

PATTERNS OF GENE EXPRESSION IN FIVE TYPES OF CELLS







Genes for...	Muscle cells	Pancreas cells: Alpha cells	Pancreas cells: Beta cells	Blood cells: White cells	Blood cells: Red cells (immature)
Glycolysis enzymes	On	On	On	On	On
Muscle contraction proteins	On	Off	Off	Off	Off
Glucagon	Off	On	Off	Off	Off
Insulin	Off	Off	On	Off	Off
Hemoglobin	Off	Off	Off	Off	On

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

Remember:

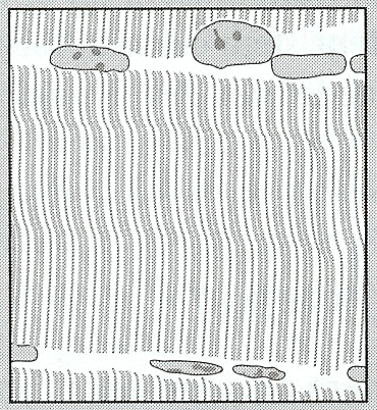
Unlike gametes (egg and sperm cells), all other cells (somatic cells) have the same DNA content and the same genes.

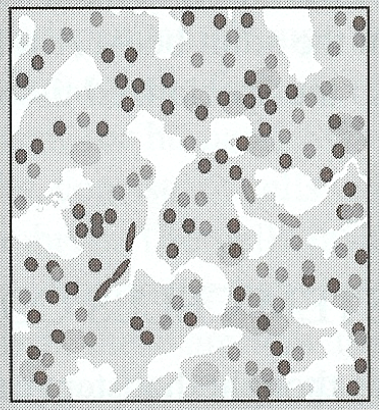
We can account for different protein patterns in different types of cells:

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

Protein Profiles Differ in Different Cell Types due to differential gene expression

PATTERNS OF GENE EXPRESSION IN FIVE TYPES OF CELLS





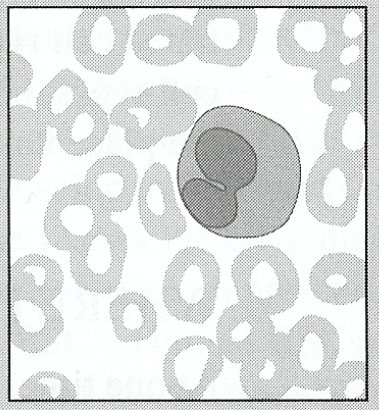


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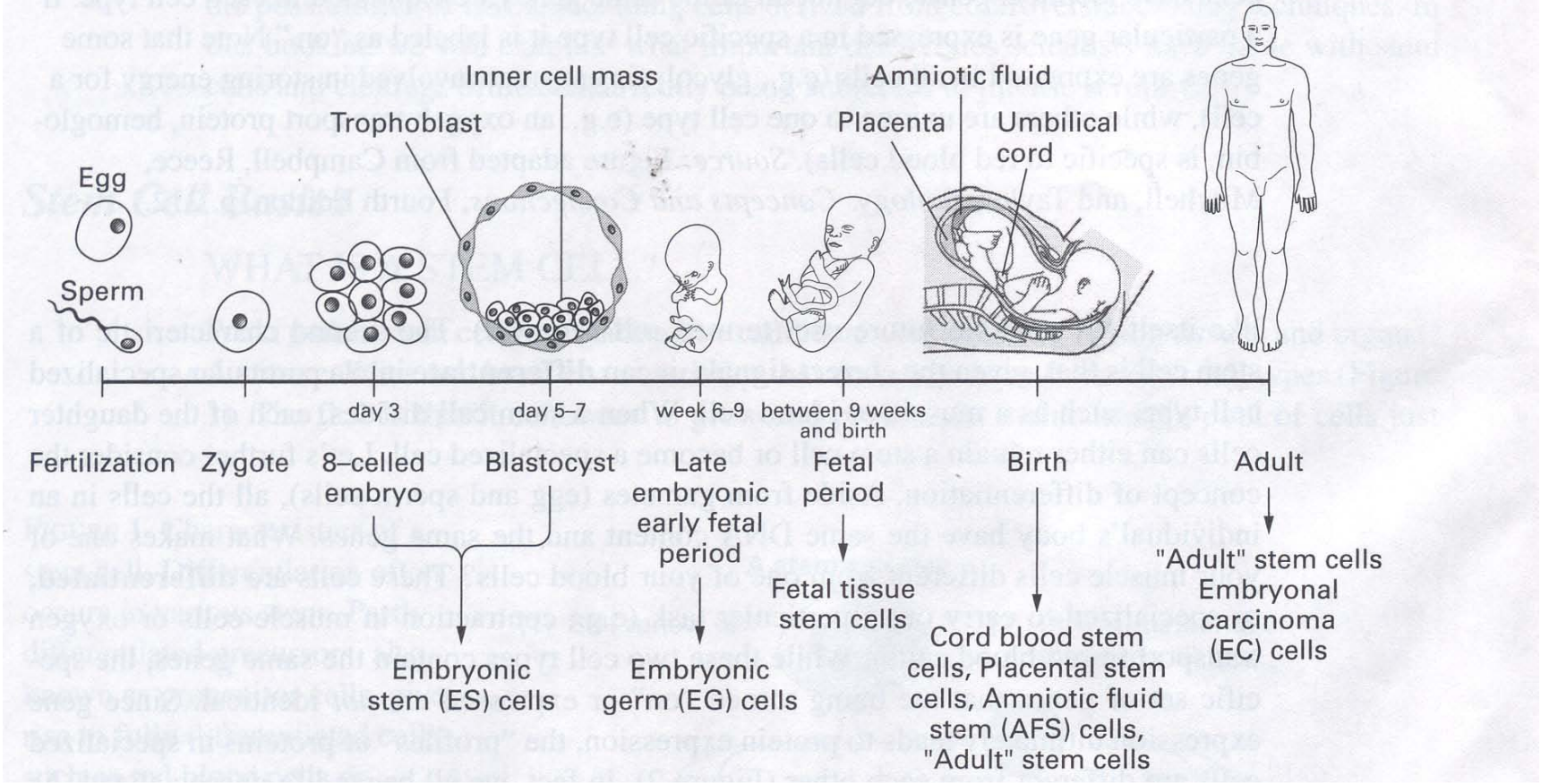
Figure from *Stem Cells and Cloning* by K.A. Hogan

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

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)

Isolation of Human Embryonic Stem Cells

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

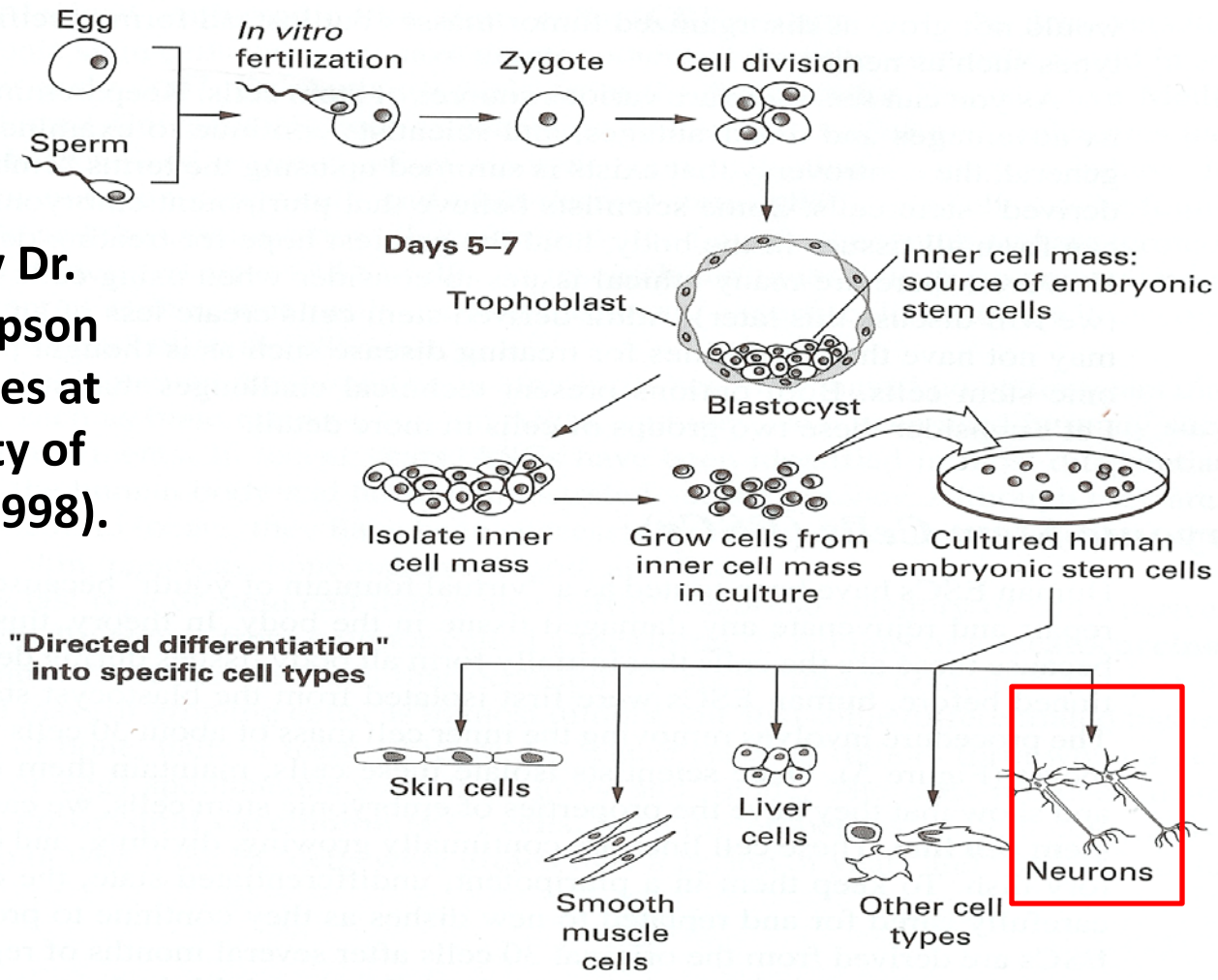
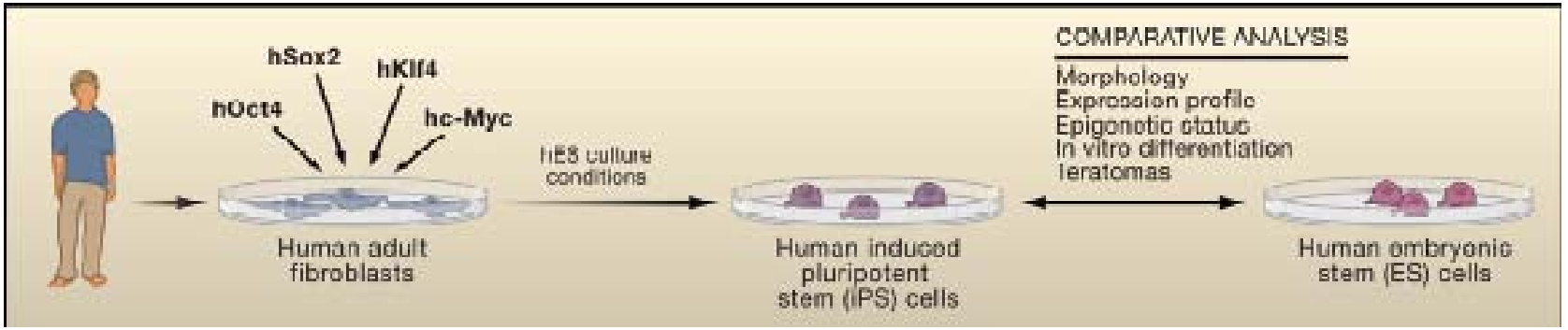


Figure from *Stem Cells and Cloning* by K.A. Hogan

“Scientists Turn Human Skin Cells into Stem Cells”



Induced pluripotent stem cells (IPSCs or IP cells)

Induction of Pluripotency: From Mouse to Human

Holm Zaehres[1] and Hans R. Schöler[1,*]
[1]Max Planck Institute for Molecular Biomedicine, Department of Cell and Developmental Biology, Münster, NRW 48149, Germany
*Correspondence: schoeler@mpi-muenster.mpg.de
DOI 10.1016/j.cell.2007.11.020

Adult Stem Cell Research in the News!

Selected News about Adult 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)

"First Neurons Created from ALS Patient's Skin Cells"
(*Science*, July 2008 [online])

"Wisconsin team grows retina cells from skin-derived stem cells"
(*PNAS*, August 2009 [online])

"Mouse Study: Uterine Stem Cells Used To Treat Diabetes"
(*Molecular Therapy*, August 30, 2011)

"Scientists Discover New Class Of Stem Cell-Like Cells In Spinal Cord"
(PLoS ONE September 12, 2011)

"Long-Distance Growth and Connectivity of Neural Stem Cells after Severe Spinal Cord Injury"
(*Cell* September 12, 2012)

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*.

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, retinas)
- To what degree do advances in adult stem cell research alter the debate about the use of human ES cells or not?

Stem Cell Therapy Challenges

- **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**
- **Social, ethical, political considerations for ESC research**

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 ethical debate surrounds the use of embryonic stem cells. Adult stem cells may offer similar prospects for therapy as do 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/
www.stemcellresearchnews.com

TAKE-HOME LESSON:

Ode to a Stem Cell, Part II©
by VCWare

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!

Rap performed by Isadore Carrie
Lehigh University, Class of 2013