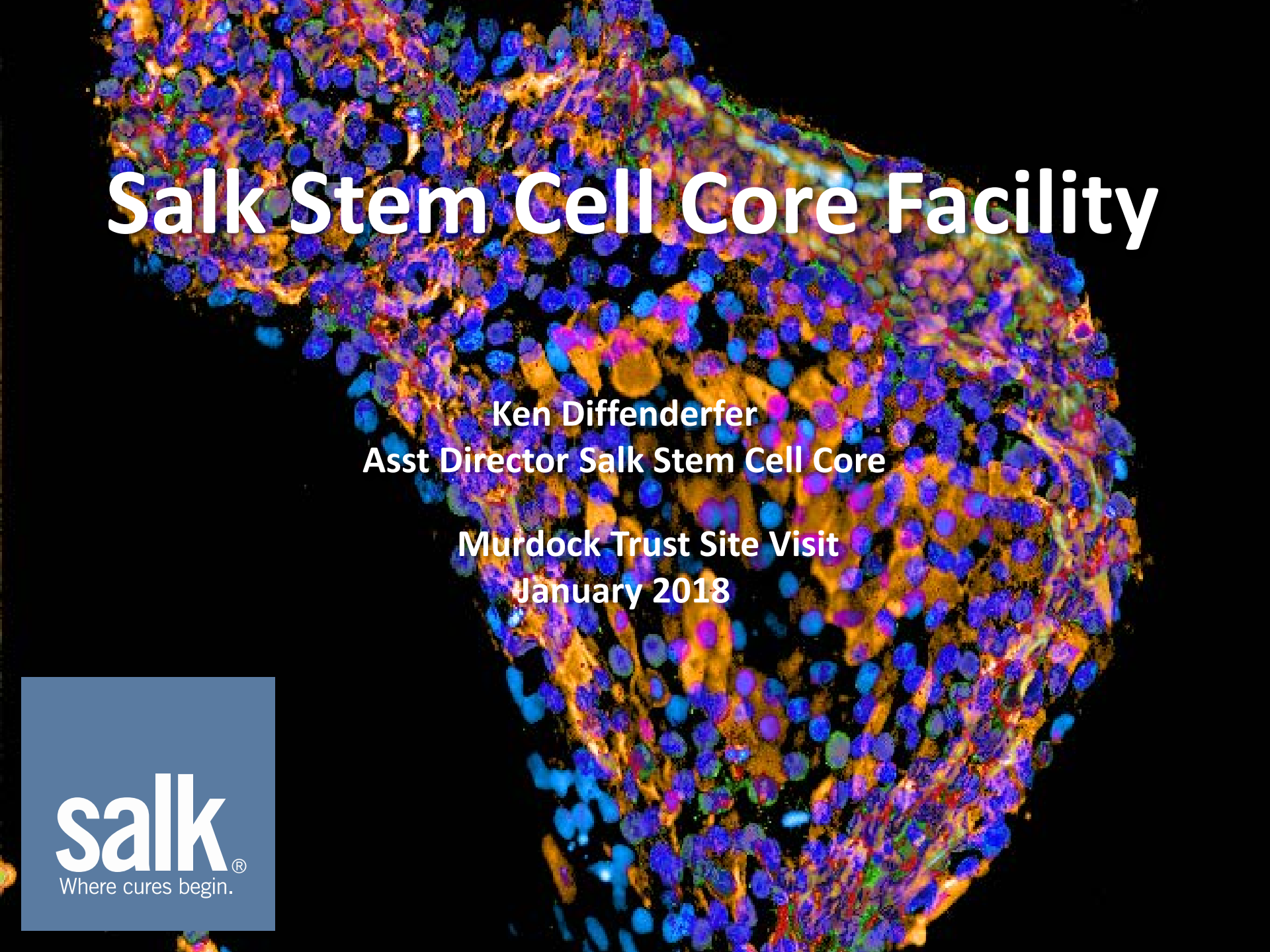


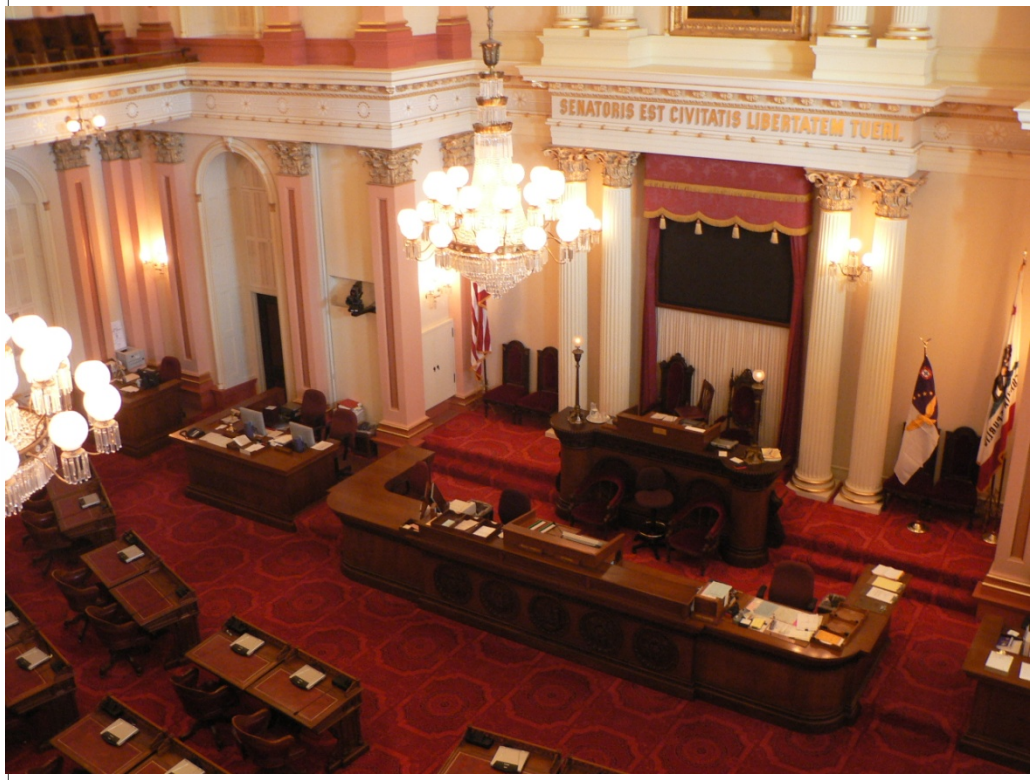
Salk Stem Cell Core Facility

Ken Diffenderfer
Asst Director Salk Stem Cell Core

Murdock Trust Site Visit
January 2018

salk®
Where cures begin.

Why should you care?


SENATORIS EST CIVITATIS LIBERTATEM TUERI.


VOTE
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VOTE

YOU

What are stem cells? What are the different types of stem cells?

Why should we study stem cells?

What Are Stem Cells?

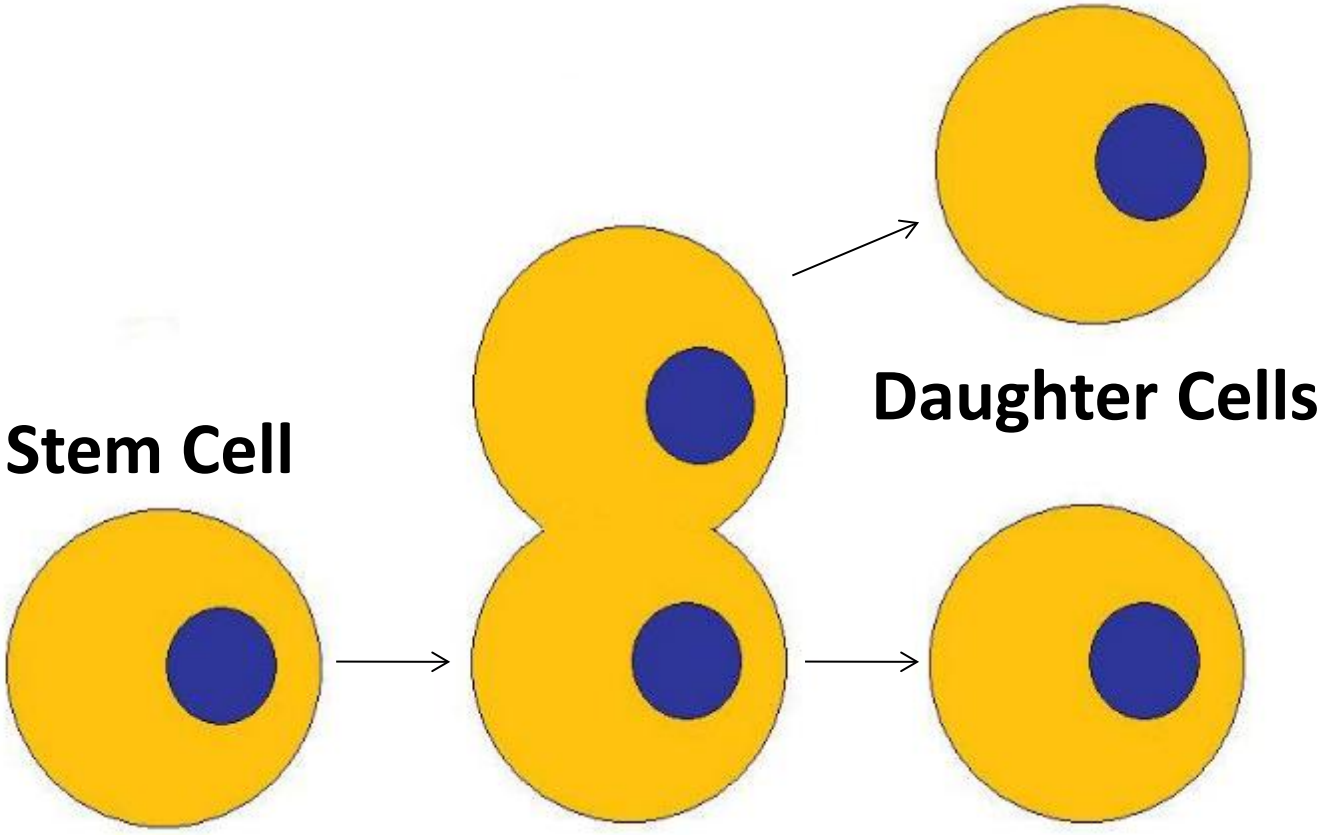
1. Self-Renew

2. Differentiate

What Are Stem Cells?

1. Self-Renew

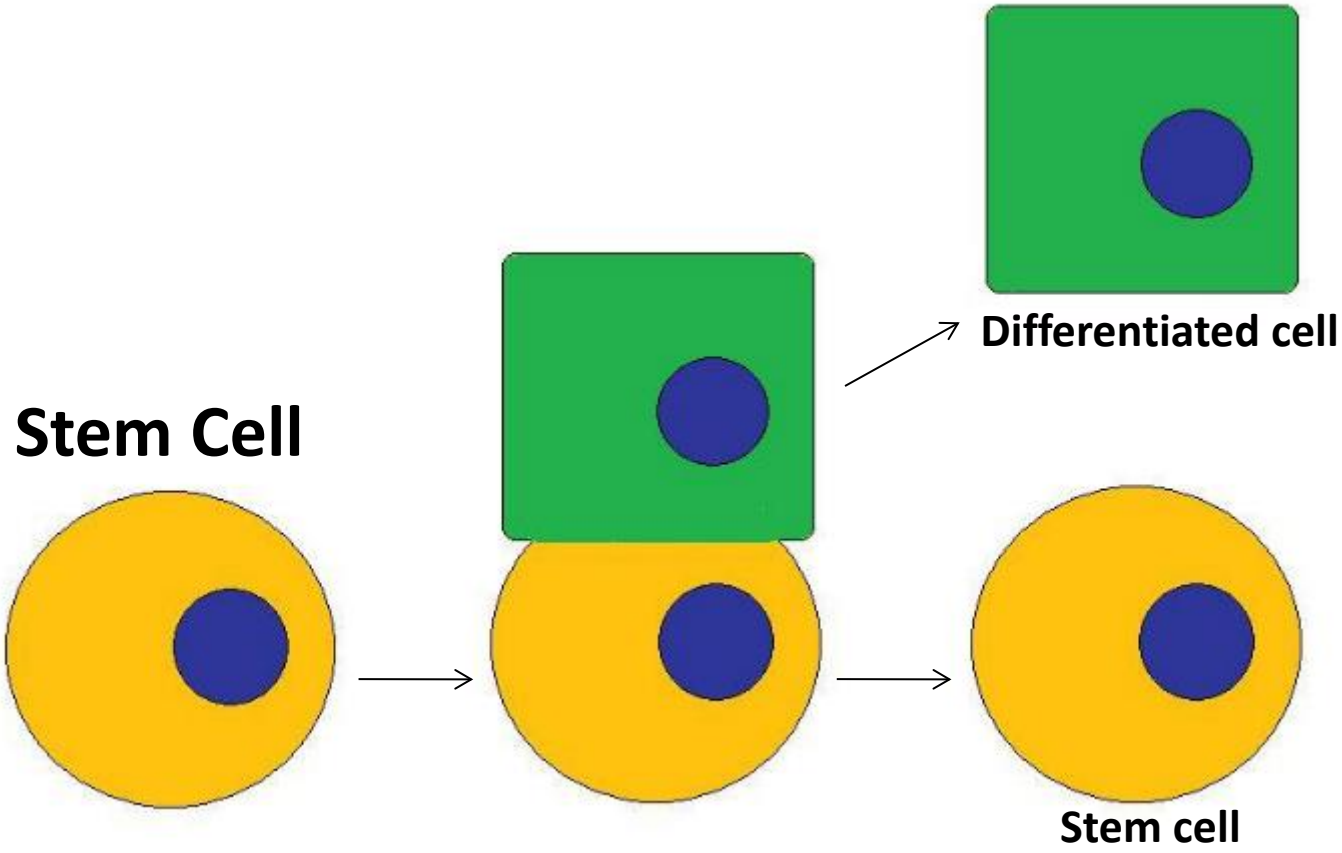
Symmetric Division



What Are Stem Cells?

2. Differentiation

Asymmetric Division



Stem Cell Types

- Tissue-Specific (Adult) – multipotent: can only turn into a limited number of cell types (blood, brain, liver, etc.)
- Embryonic – pluripotent: can turn into any cell type in the human body
- Induced Pluripotent – engineered by scientists to act like embryonic stem cells

Stem Cell Types

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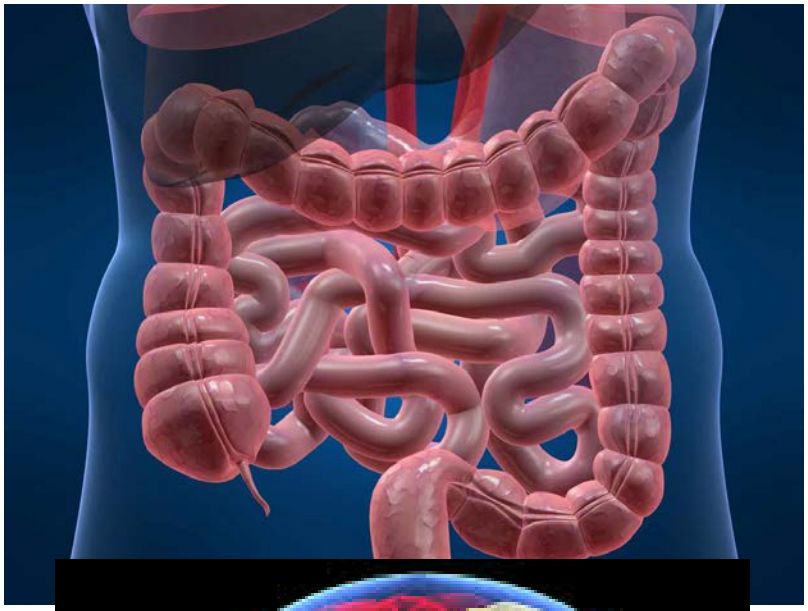
Adult Stem Cells



Where do they come from?

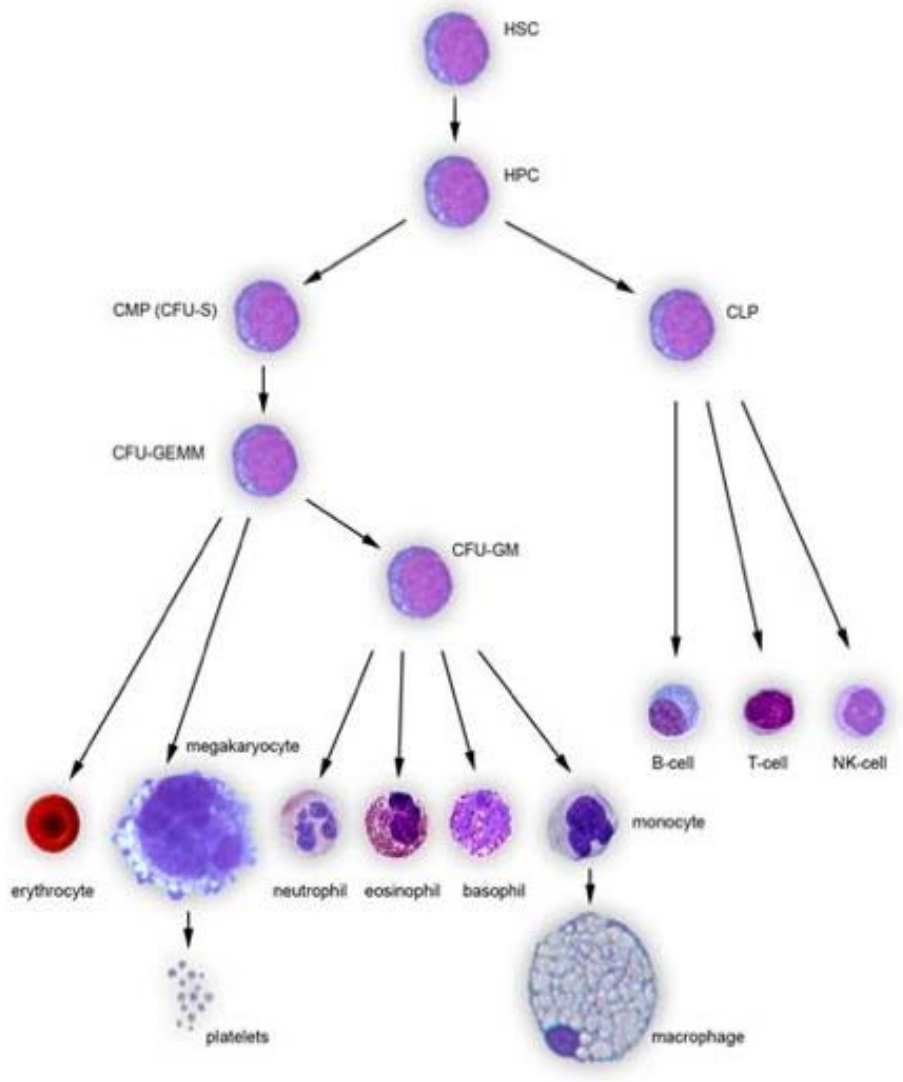
- Specific areas of the human body (bone marrow, gut, brain)

What do they do?

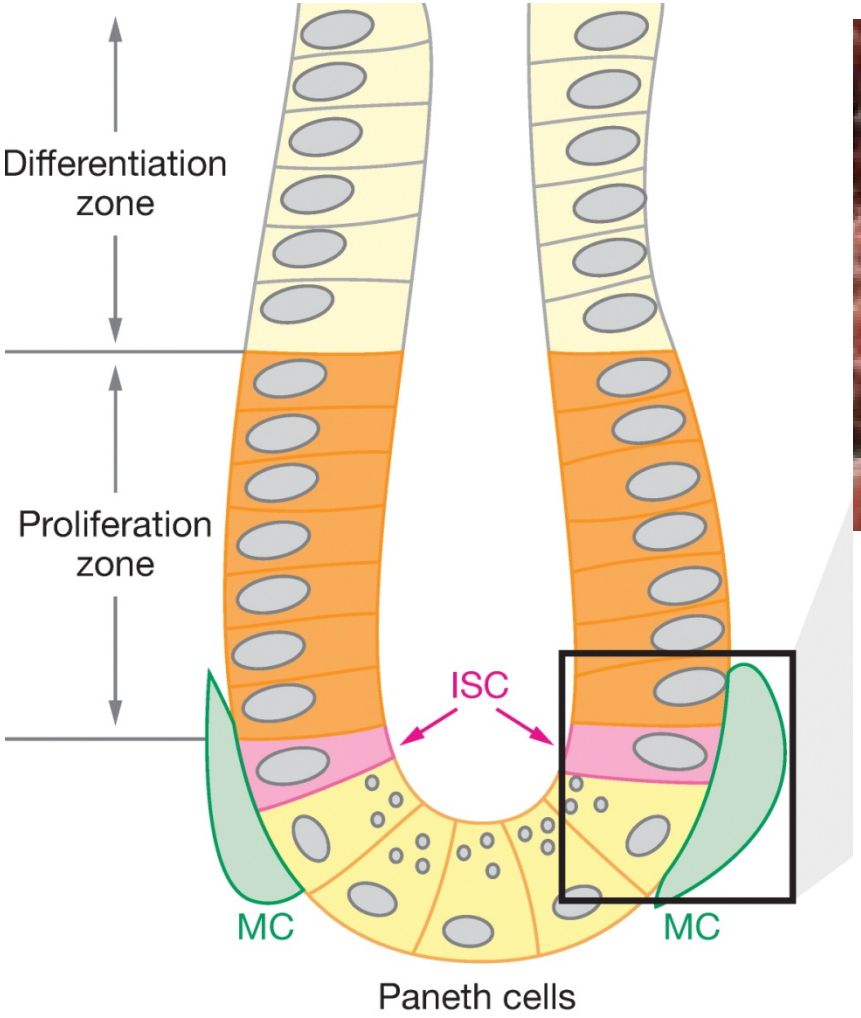
- Self-renew
- **MULTI**potent – differentiate into a few related cell types

Blood Stem Cells (aka Hematopoietic Stem Cells)

- Blood stem cells live in the bone marrow
  - 1 in 10,000 to 15,000 bone marrow cells
- Source of all blood and immune cells
- Theraopeutic source – Bone Marrow Transplant



Gut Stem Cells (Intestinal Stem Cells)

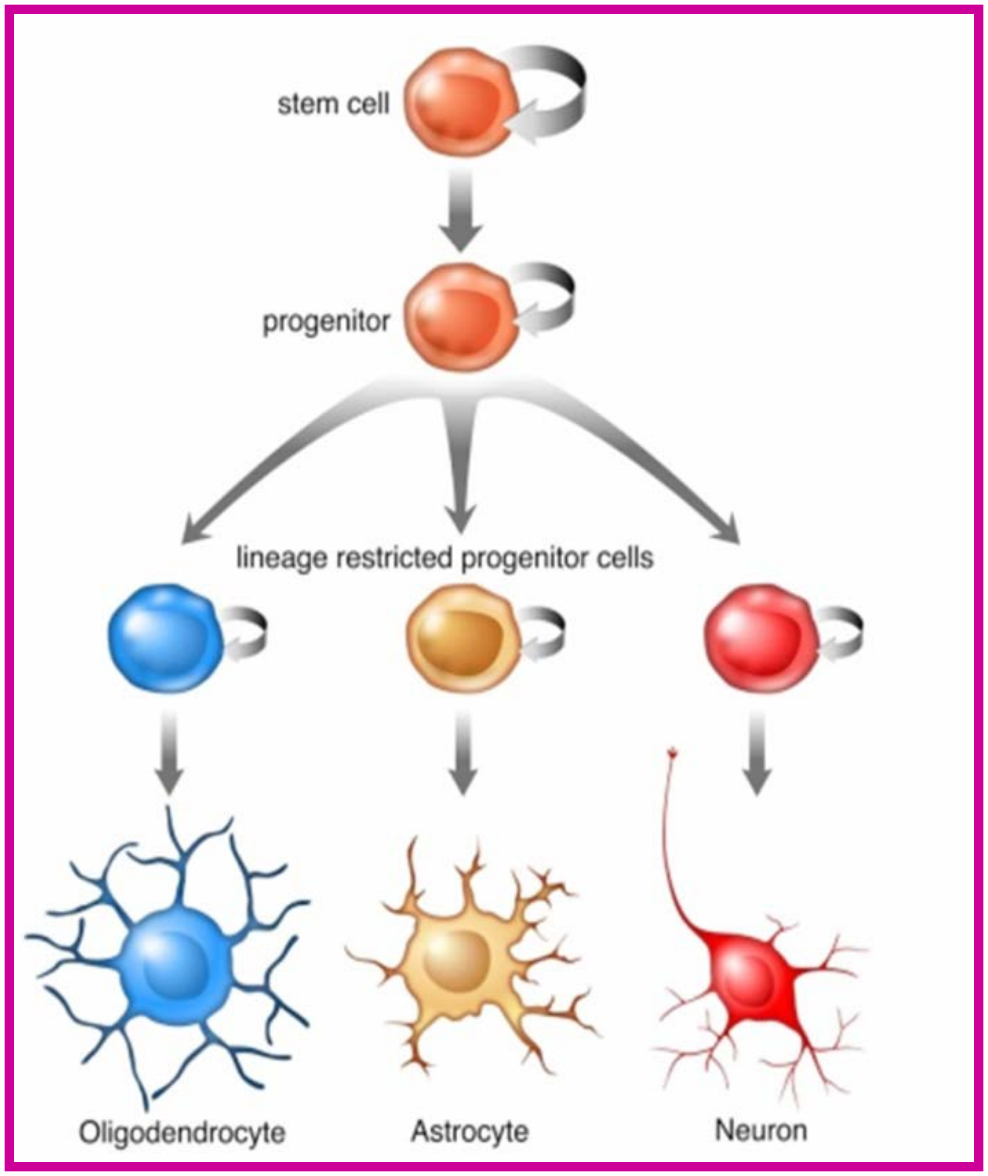


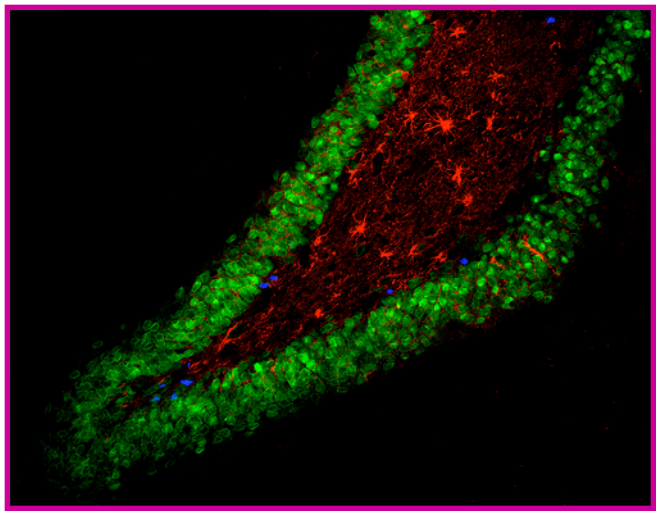
Intestines lined with 1000s of vili.

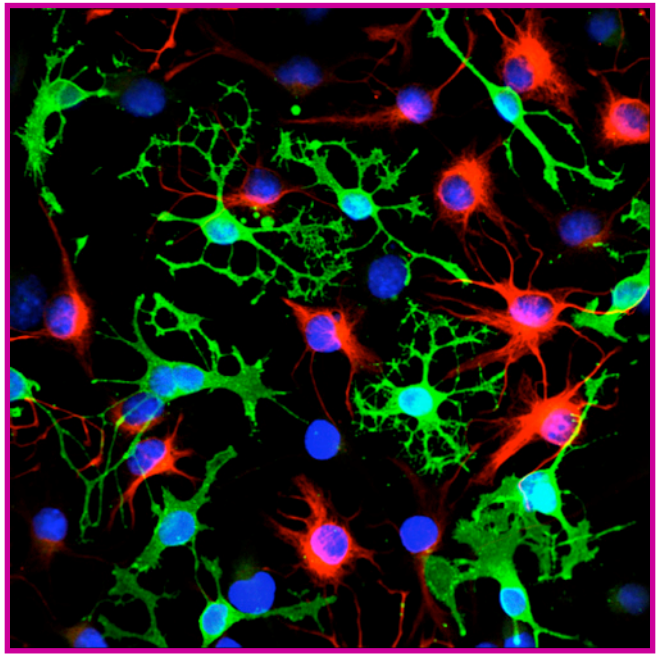
Intestinal lining is replace ever 3-5 days.

Li L, Xie T. 2005.
Annu. Rev. Cell Dev. Biol. 21:605–31

Stem cells in the adult brain







Stem Cell Types

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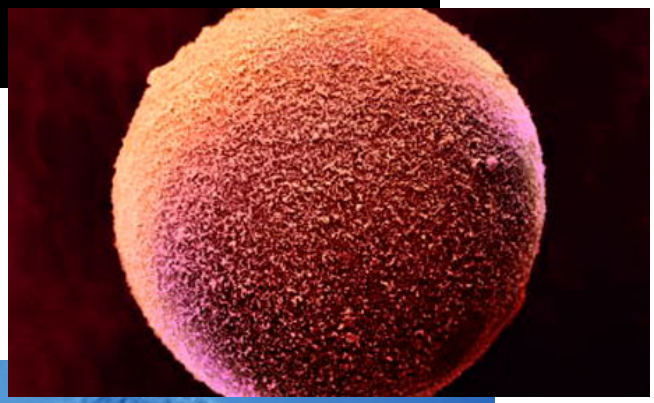
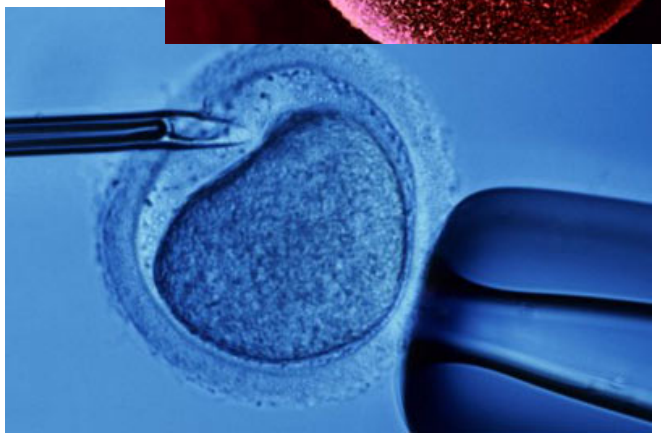
Embryonic Stem Cells

Where do they come from?

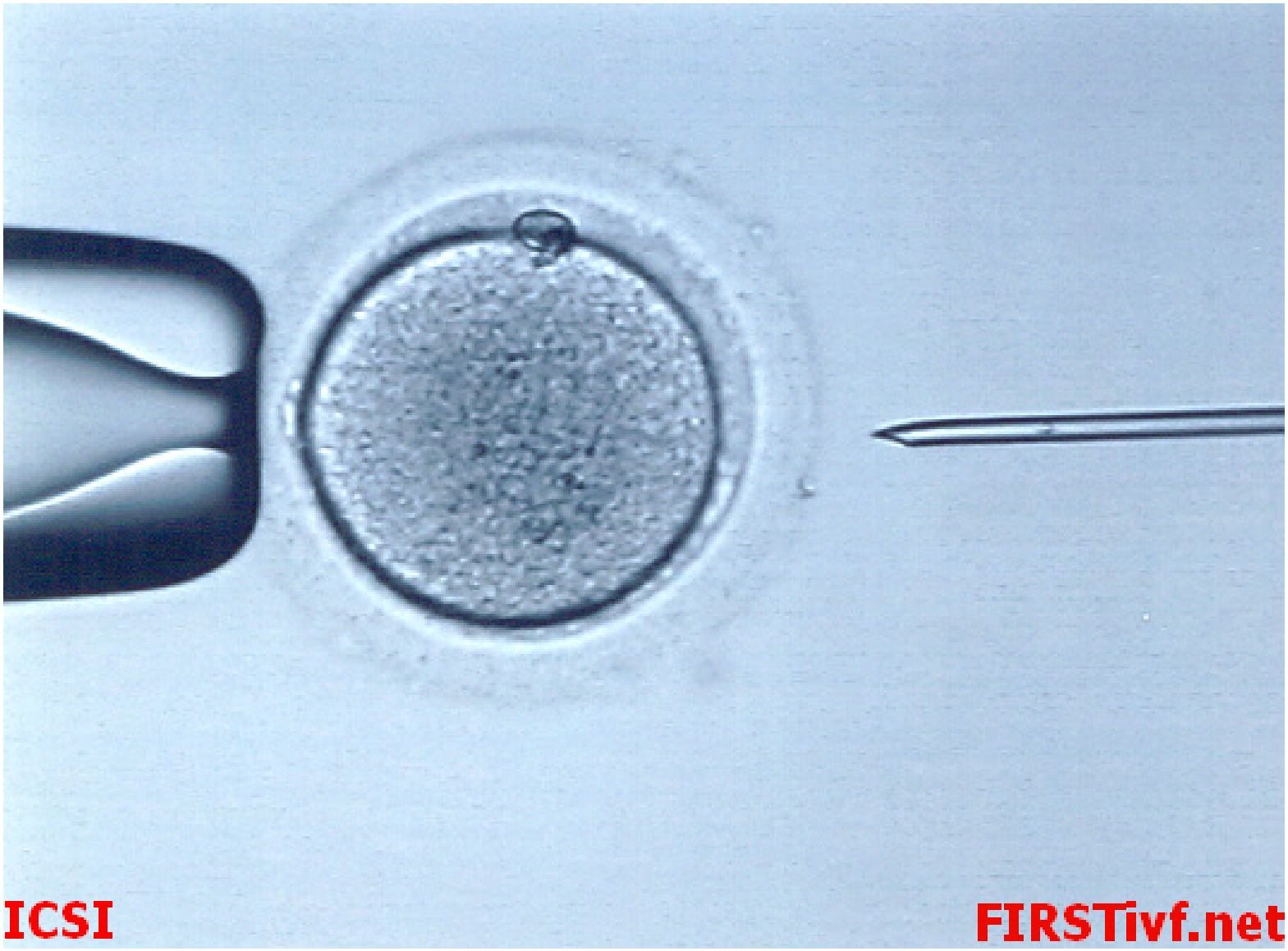
•Unused material from the in-vitro fertilization process (IVF)

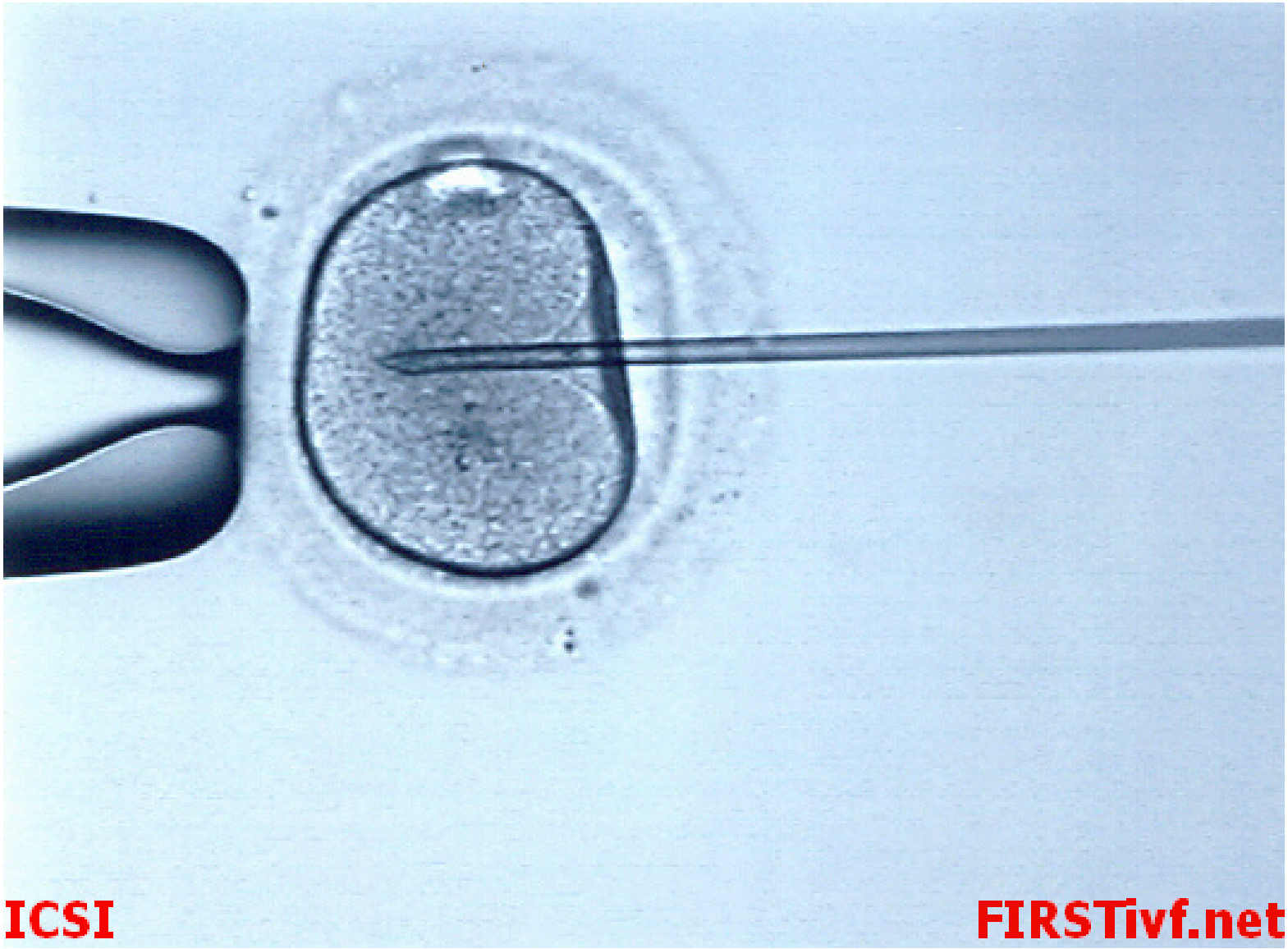




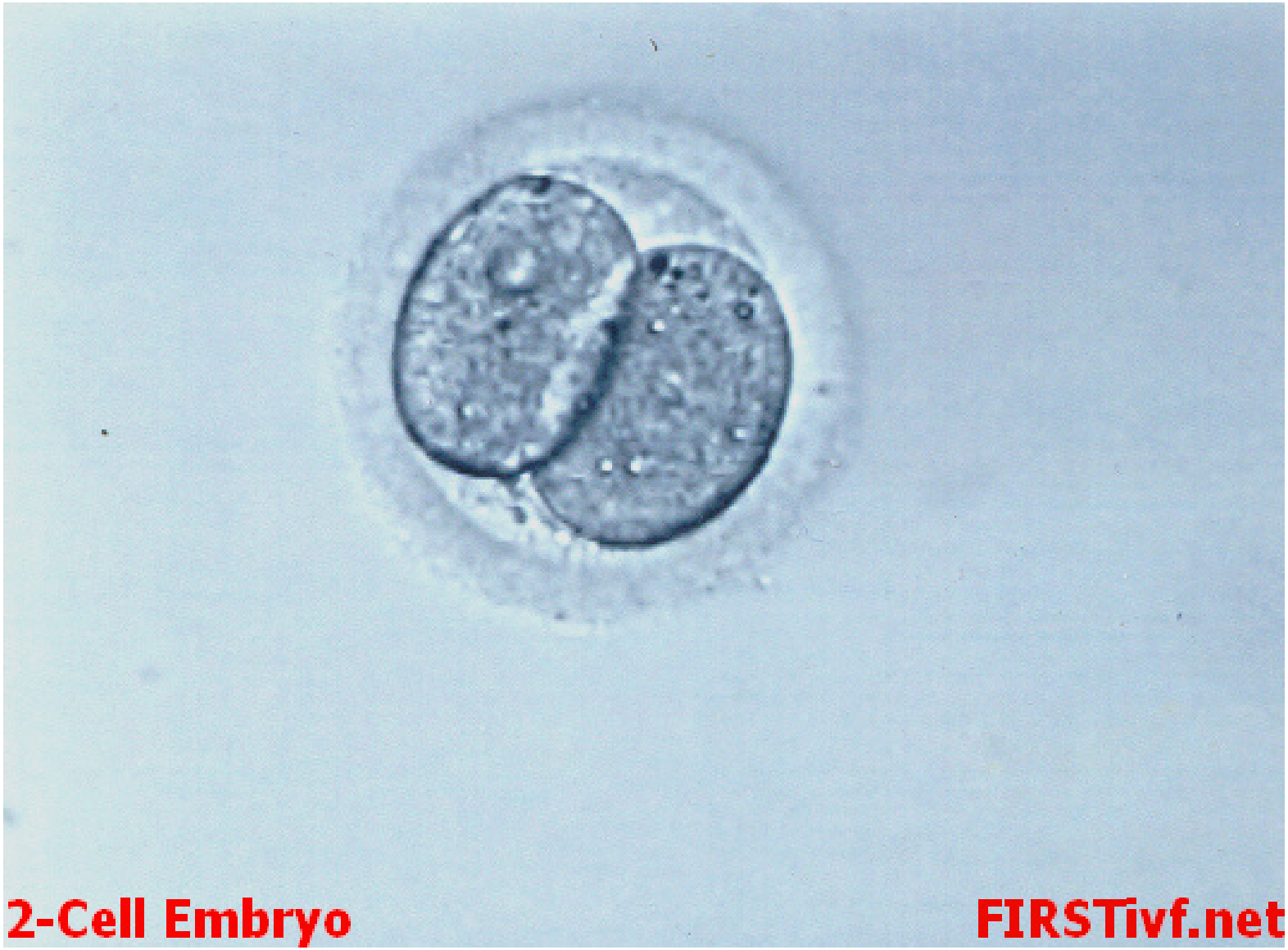
What do they do?

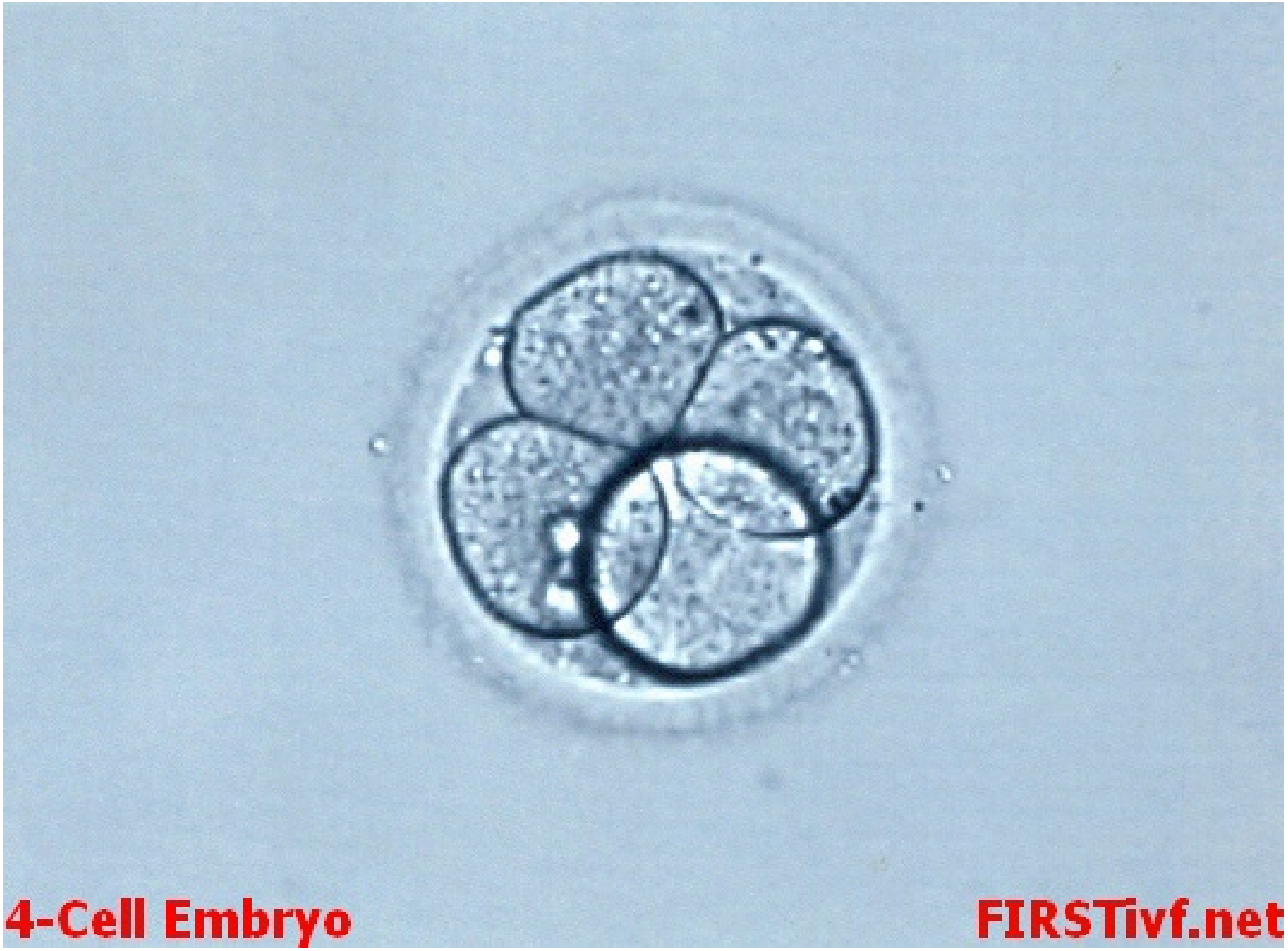
- Self-renew
- Divide indefinitely
- Turn into any cell in the body
- **PLURI**potent

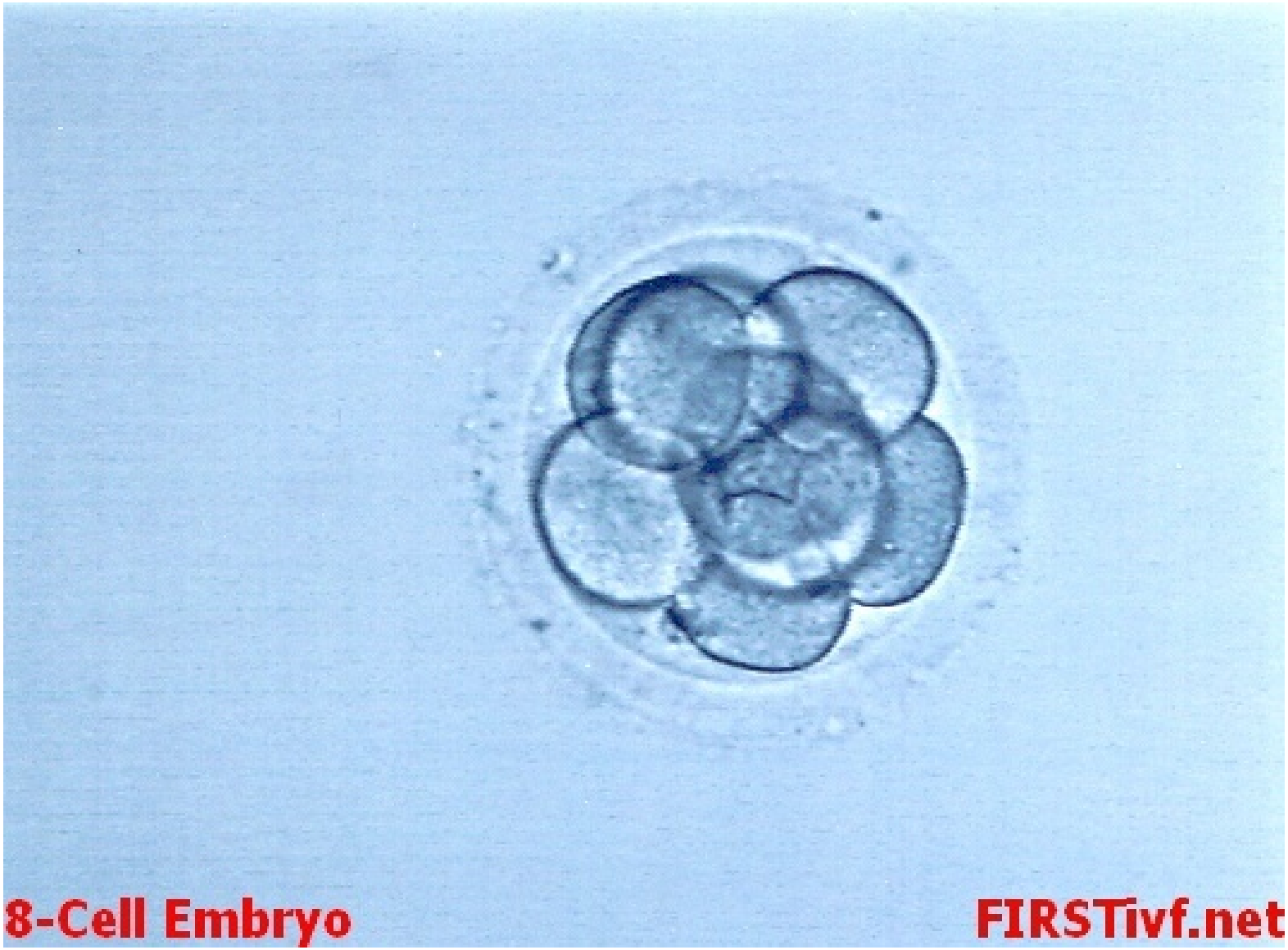

ICSI
FIRSTivf.net

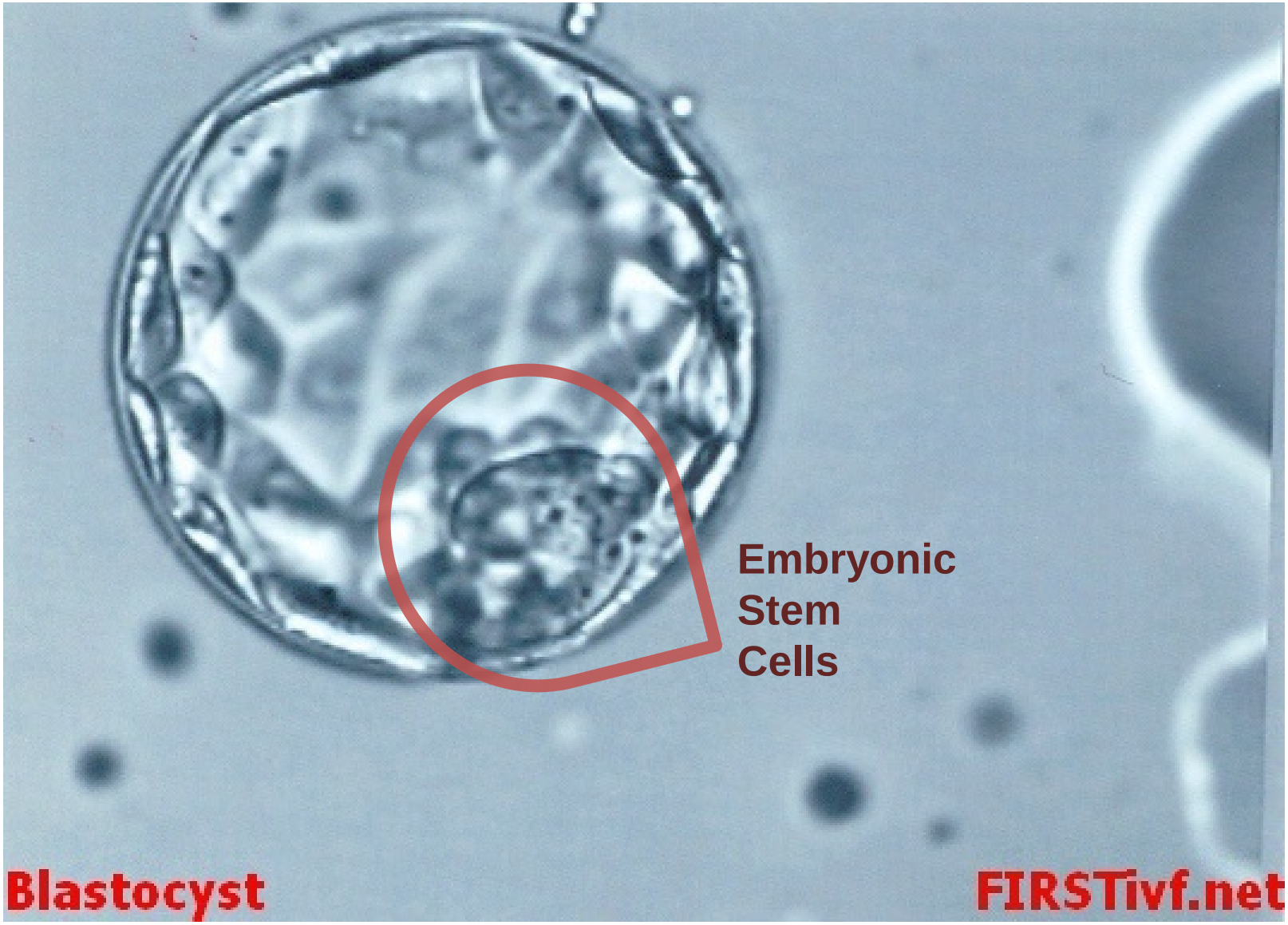

ICSI
FIRSTivf.net

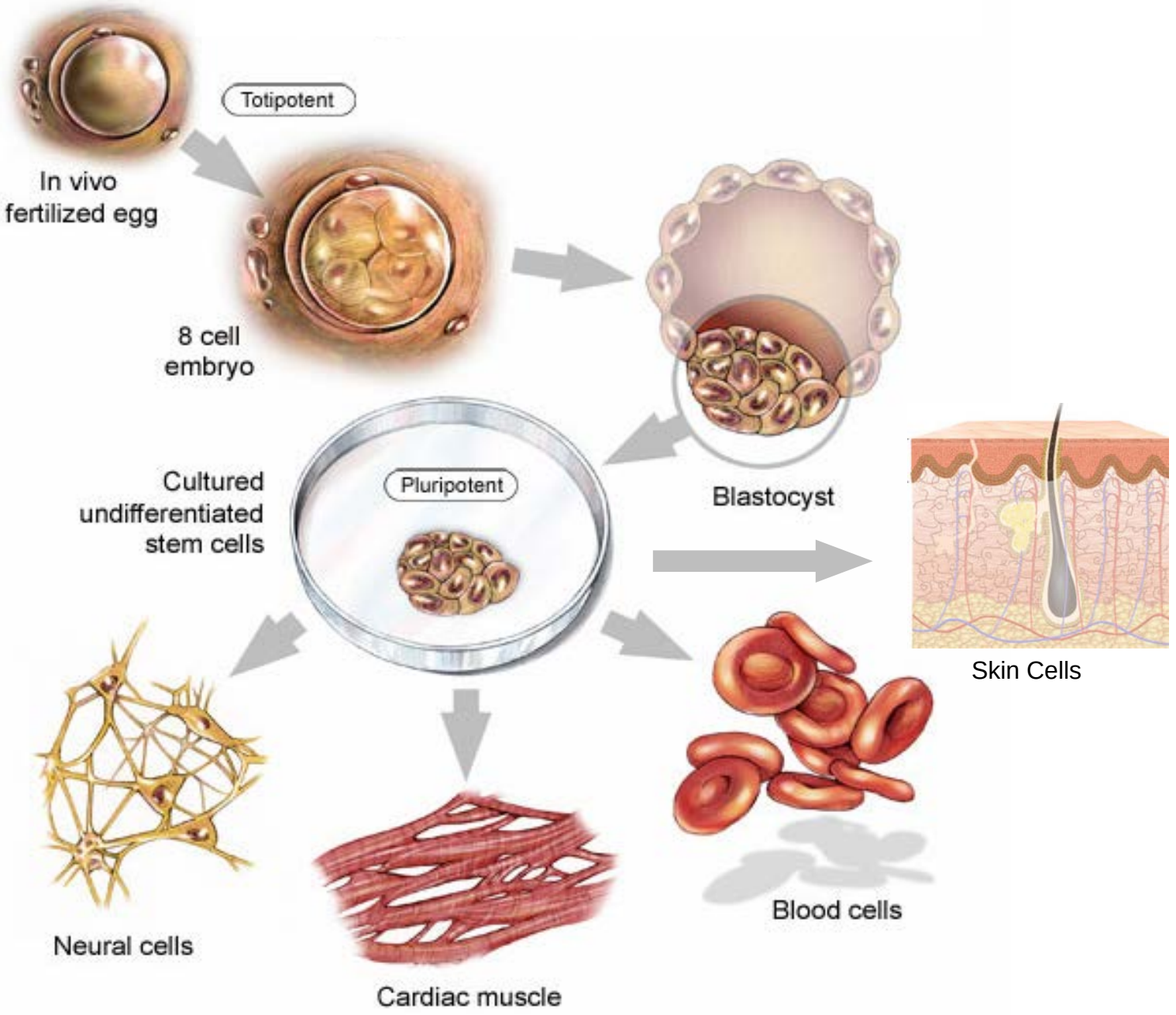

Fertilized Egg
FIRSTivf.net

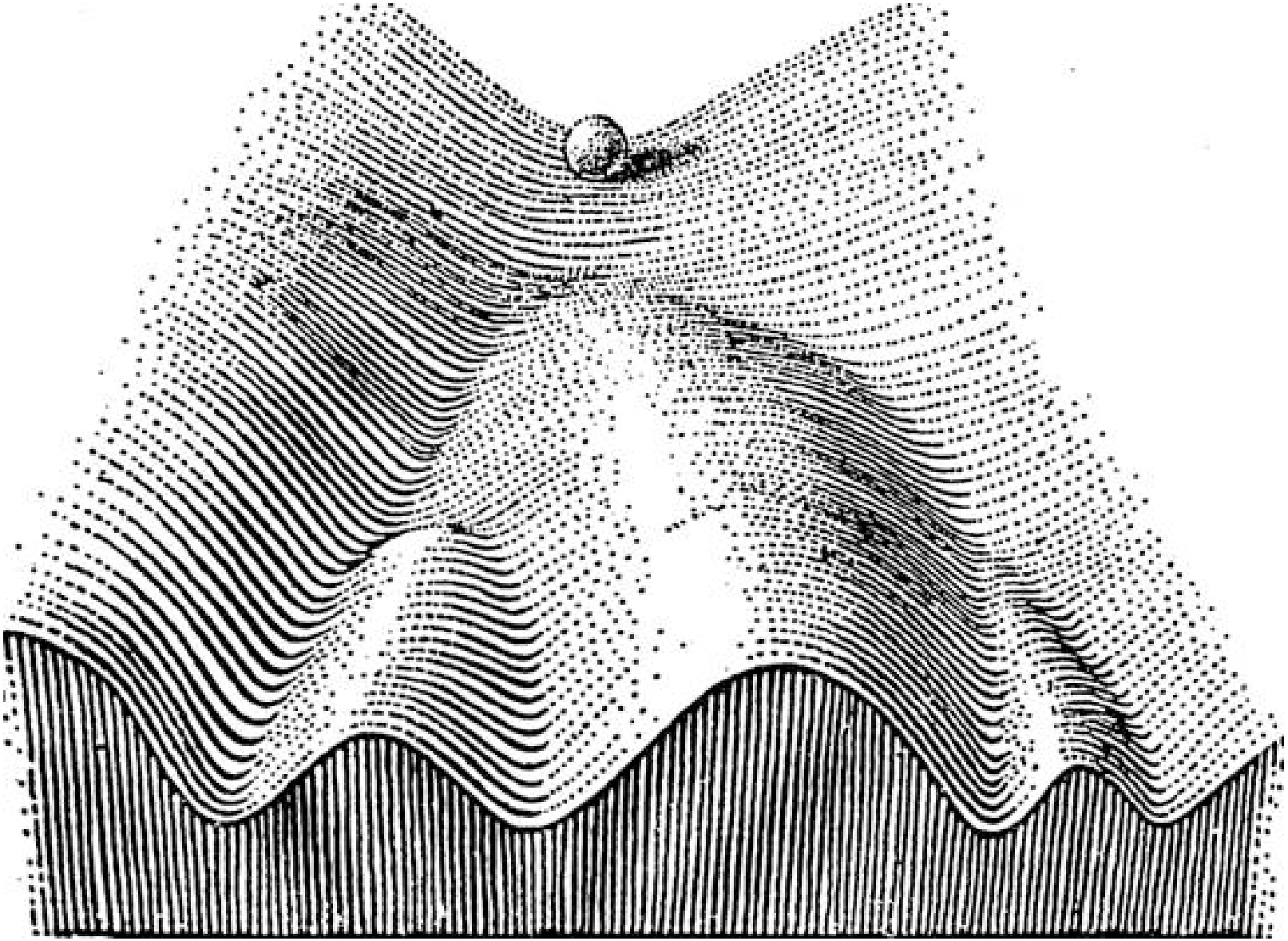

2-Cell Embryo
FIRSTivf.net


4-Cell Embryo
FIRSTivf.net


8-Cell Embryo
FIRSTivf.net


Embryonic
Stem
Cells
Blastocyst
FIRSTivf.net


Totipotent
In vivo fertilized egg
8 cell embryo
Blastocyst
Cultured undifferentiated stem cells
Pluripotent
Skin Cells
Neural cells
Cardiac muscle
Blood cells



Waddington, *The Strategy of the Genes*, 1957

Stem Cell Types

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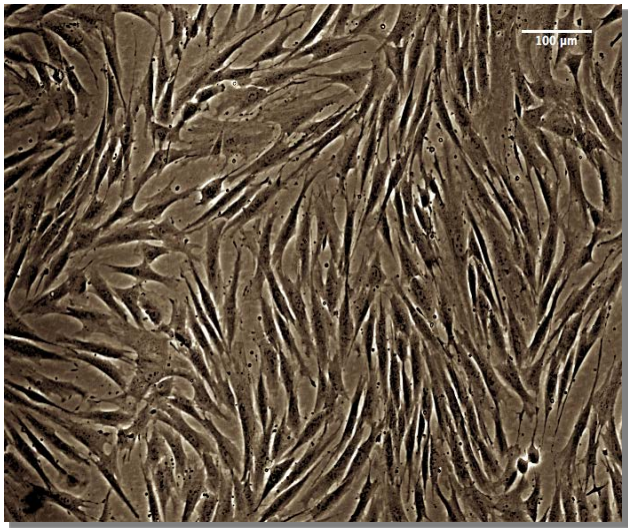
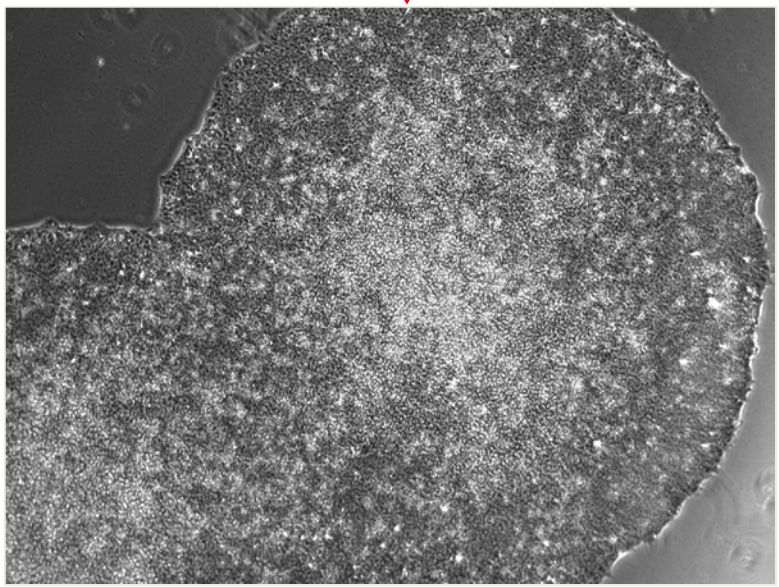
Induced Pluripotent Stem Cells



Where do they come from?

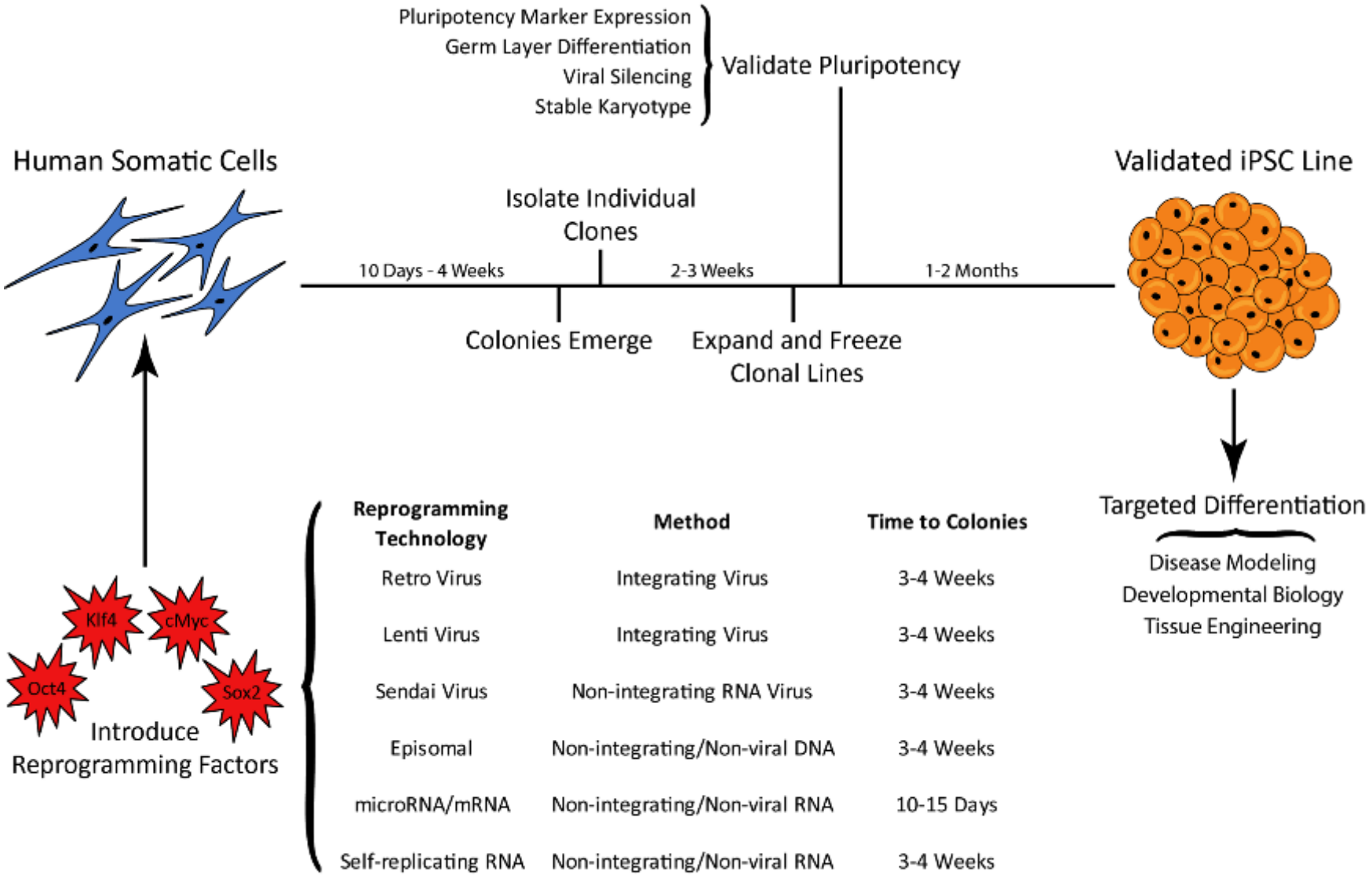
- Generated from patient skin cells (or blood cells… even FAT!)
- Any somatic tissue



What do they do?

- Self-renew
- Divide indefinitely
- Turn into any cell in the body
- **PLURI**potent

Induced Pluripotent Stem (iPS) Cells

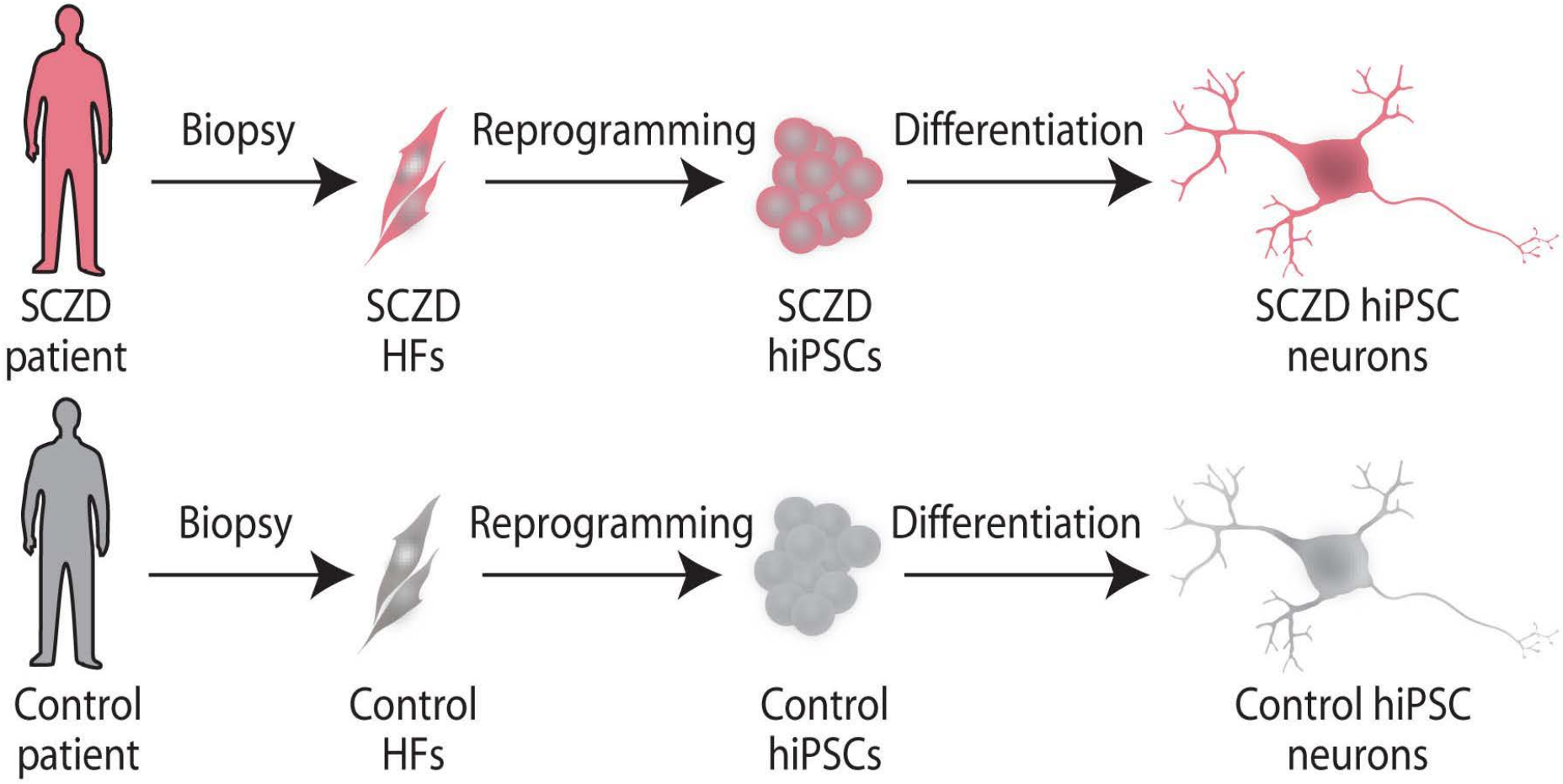


Reprogramming Technology	Method	Time to Colonies
Retro Virus	Integrating Virus	3-4 Weeks
Lenti Virus	Integrating Virus	3-4 Weeks
Sendai Virus	Non-integrating RNA Virus	3-4 Weeks
Episomal	Non-integrating/Non-viral DNA	3-4 Weeks
microRNA/mRNA	Non-integrating/Non-viral RNA	10-15 Days
Self-replicating RNA	Non-integrating/Non-viral RNA	3-4 Weeks

Application of Human Stem Cells

- Basic Biology: Further our understanding of human development
- Biomedical Research:
  - Disease modeling
    - Further understanding of disease development
    - Platform for drug discovery
  - Tissue replacement therapy
    - Adult Stem Cells
    - Pluripotent Stem Cells (hESC and hiPSC)

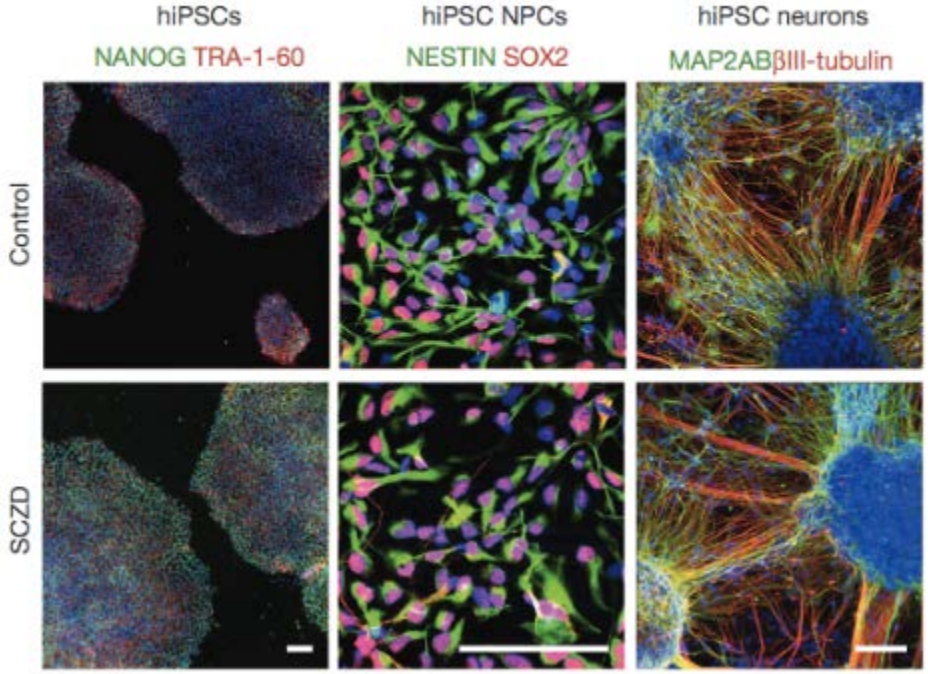
Modeling Human Disease in a Dish



Modelling schizophrenia using human induced pluripotent stem cells

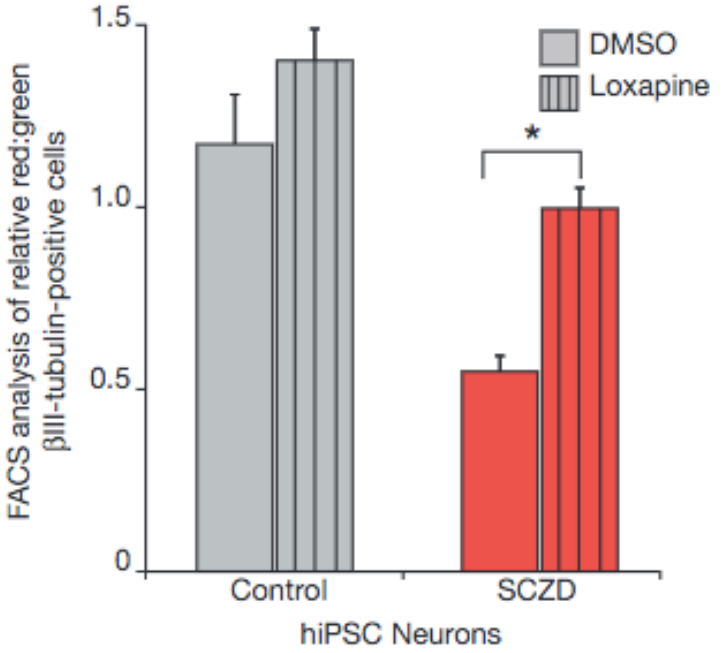
Kristen J. Brennand[1], Anthony Simone[1]*, Jessica Jou[1]*, Chelsea Gelboin-Burkhart[1]*, Ngoc Tran[1]*, Sarah Sangar[1], Yan Li[1], Yangling Mu[1], Gong Chen[2], Diana Yu[1], Shane McCarthy[3], Jonathan Sebat[4] & Fred H. Gage[1]

Patient Specific hiPSCs, NPCs, and neurons



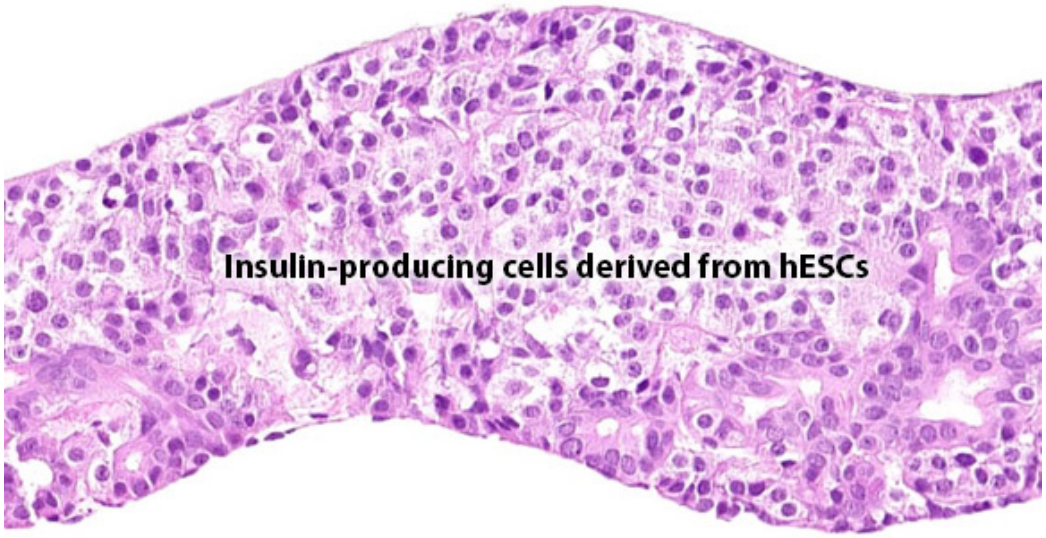
Brennand et al., Nature, May 2011

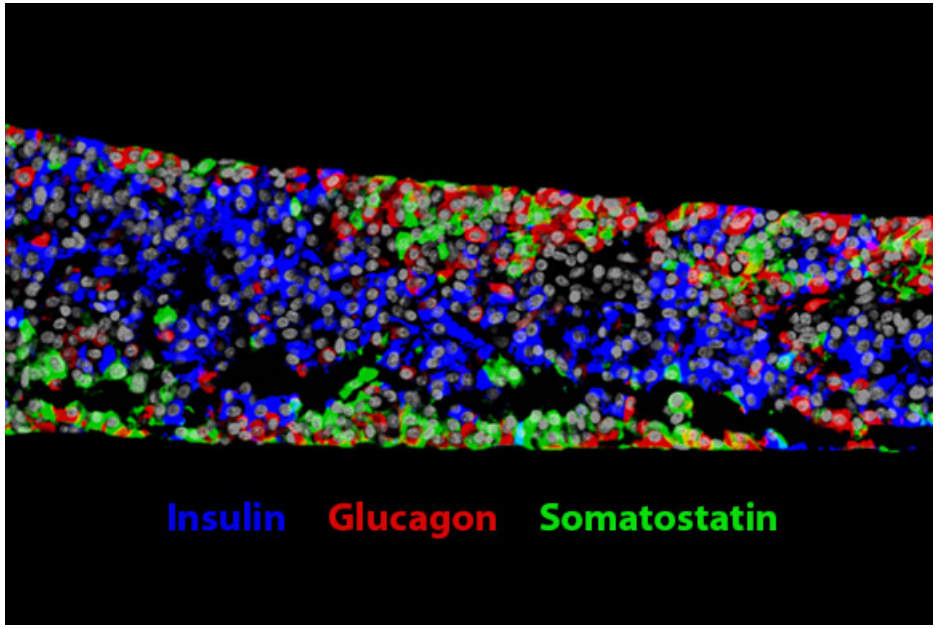
Connectivity Deficit with SCZD Neurons



Using Embryonic Stem Cells to Treat Diabetes

Viacyte





Delivering Therapeutic Cells to Patients