Regenerative medicine in neuroscience

The Ohio State Stem Cell Education Program (OSCEP) team

For inquiries contact:
Dr. Elizabeth Kirby, PhD
Department of Psychology
The Ohio State University
Kirby.224@osu.edu

All content is published under CC BY-NC-SA 4.0 license terms, unless cited as from another source. https://creativecommons.org/licenses/by-nc-sa/4.0/
Questions for today

• What is a stem cell?
• What kinds of stem cells are there?
• How can stem cells help us? How can’t they help us?
• What are the barriers to getting more stem cell-based treatments?
“I didn’t have any kind of plan for the future,” he said of his mindset before the gene therapy. “I didn’t think I was going to need one. I was more focused on the ‘right then’ — getting healthy right then. ... I’d never thought that long-term before because I’d been sick for so long.”

Dorothy O’Connell

- Arthritic back and neck pain
- Given injections of umbilical cord blood as a source of stem cells
- Within in days, hospitalized for vomiting and intense body-wide pain
- Now has permanent damaged vision, hearing loss and impaired balance

Source: https://www.washingtonpost.com/national/health-science/miraculous-stem-cell-therapy-has-sickened-people-in-five-states/2019/02/26/c04b23a4-3539-11e9-854a-7a14d7fec96a_story.html
What is a stem cell?
What is a stem cell?

A cell with the ability to self-renew and differentiate into many different cell types.
Stem cells can be a source of new cells

1 stem cell

Self renewal - maintains the stem cell pool

4 specialized cells
Differentiation - replaces dead or damaged cells throughout your life
Potential uses of Stem cells

- Stroke
- Traumatic brain injury
- Learning defects
- Alzheimer's disease
- Parkinson's disease
- Missing teeth
- Wound healing
- Bone marrow transplantation (currently established)
- Spinal cord injury
- Osteoarthritis
- Rheumatoid arthritis
- Crohn's disease
- Amyotrophic lateral sclerosis
- Myocardial infarction
- Muscular dystrophy
- Diabetes
- Multiple sites: Cancers
- Baldness
- Blindness
- Deafness

Image from: https://www.unmc.edu/stemcells/educational-resources/importance.html
True or false: Stem cells are in some food products.
False!

Some companies used human kidney cells that have been “immortalized” in a dish to test artificial flavors and sugars on live human cells. These cells originally came from aborted fetuses in the 1970s.

Types of Stem Cells

1. Embryonic stem cells
2. Adult tissue stem cells
3. Induced pluripotent stem cells
Types of Stem Cells

1. Embryonic stem cells
2. Adult tissue stem cells
3. Induced pluripotent stem cells
Embryonic Stem Cells

Stage: 1 Zygote Mouse: E0.5
Stage: 2 2-cell E1.5
Stage: 3 4-cell E2.0
Stage: 4 Morula E2.5
Stage: 5 Compacted morula E3.0 E4
Stage: 6 Early blastocyst E3.5 E4-5
Stage: 7 Late blastocyst E4.5 E5

Embryonic stem cells
Embryonic Stem Cells
Embryonic Stem Cells

Day 5 blastocyst

Inner cell mass

Trophoblast

Embryonic stem cells

Cell culture dish
Embryonic Stem Cells

ES cells can differentiate into all possible types of specialized cells. They are pluripotent.
Where do scientists get human embryonic stem cells?
Let’s watch!
Dr. Renee Reijo Pera, PhD
Vice President of Research and Economic Development,
California Polytechnic State University
If ESCs could treat so many diseases and they can be obtained from left over IVF blastocysts, what’s the catch?
Major challenges to using ESCs for therapy

Ethical questions

Regulatory changes
Funding fluctuations

Medical/scientific challenges
Immune rejection of transplants
Controlling ESC differentiation
Tumor formation
Types of Stem Cells

1. Embryonic stem cells
2. Adult tissue stem cells
3. Induced pluripotent stem cells
Types of Stem Cells

1. Embryonic stem cells
2. Adult tissue stem cells
3. Induced pluripotent stem cells
Adult tissue stem cells

• Adult (tissue) stem cell is an undifferentiated, self-renewing cell found in tissues and organs.

• **Multipotent** - Able to produce several types of mature cells rather than all or many types.
Where can they be found?

Multipotent stem cells are found in stem cell niches throughout the body.
Types of Adult SC’s (two examples)

• Hematopoietic

• Neural
Stem cell differentiation from bone marrow

- Hematopoietic stem cell
  - Myeloid progenitor cell
    - Megakaryocyte
    - Eosinophil
    - Basophil
    - Erythrocytes
    - Monocyte
    - Neutrophil
    - Platelets
    - Dendritic cell
    - Macrophage
  - Lymphoid progenitor cell
    - T cell
    - B cell
    - NK cell
    - Plasma cell
Hematopoietic stem cell transplants

1. Collect the blood stem cells from the bloodstream or bone marrow
2. Freeze the blood stem cells until they are required
3. Administer chemotherapy to remove or partially remove the immune system
4. Return thawed blood stem cells by infusion into the vein
HSC transplant plus gene therapy

1. Blood stem cell collection
2. Pre-infusion conditioning
3. Transduced stem cells infusion
4. Immune system reconstitution

Patient treatment

Treatment manufacturing

Viral particle with therapeutic gene

Transduction

Stem cells

Transduced stem cells
Types of Adult SC’s (two examples)

- Hematopoietic
- Neural
Neural stem cell differentiation

Neural stem cell

- Neuronal progenitor cell
- Astroglial progenitor cell
- Oligodendrocyte progenitor cell

- Neuron
- Astrocytes
- Oligodendrocytes
If adult tissue SCs can be obtained without destroying an embryo, why are there so few therapies using them?
Major challenges to using adult SCs for therapy

- Limited access to some stem cell types
- Problems shared with ESCs
  - Immune rejection of transplants
  - Controlling SC differentiation
  - Tumor formation
- Multipotency
  - Limited potential cell types
- Limited access to some stem cell types
Types of Stem Cells

1. Embryonic stem cells
2. Adult tissue stem cells
3. Induced pluripotent stem cells
Types of Stem Cells

1. Embryonic stem cells
2. Adult tissue stem cells
3. Induced pluripotent stem cells
Induced pluripotent stem cell (iPSC)

- Divide and self-renew
- Differentiate into any tissue in the adult body
iPSCs turned science upside down!
The potential of iPSCs
If iPSCs can be obtained without destroying an embryo and can differentiate into anything, why are there no therapies using them?
Major challenges to using iPSCs for therapy

Problems shared with ESCs and adult SCs
- Immune rejection of transplants
- Controlling SC differentiation
- Tumor formation

Low efficiency of making iPSCs

Cost of treatments
Getting stem cells to patients in need
How are medical treatments approved?
Are stem cells drugs?

Yes!

The FDA regulates the manufacturing and marketing of medical treatments, including HCT/P.
Are stem cells drugs?

Yes!

The FDA regulates the manufacturing and marketing of medical treatments, including HCT/P

Unless it is **minimally manipulated** and **homologous use**
Organ transplant

A classic example of **minimal manipulation** and **homologous use**
Can stem cell treatments be homologous and minimally manipulated?

Yes!

Bone marrow transplants

1. Collect the blood stem cells from the bloodstream or bone marrow
2. Freeze the blood stem cells until they are required
3. Administer chemotherapy to remove or partially remove the immune system
4. Return thawed blood stem cells by infusion into the vein
Brenden Whittaker

- X-linked chronic granulomatous disease (X-CGD)
- Treated with his own blood (hematopoietic) stem cells that were genetically modified

Homologous use?
Minimally manipulated?

Treated as part of a CGD clinical trial at Dana-Farber/Boston Children’s Cancer and Blood Disorders Center
Dorothy O’Connell

- Arthritic back and neck pain
- Given injections of umbilical cord blood as a source of stem cells

Homologous use?  
Minimally manipulated?

Purchased an **unapproved** umbilical cord derived product, ‘Liveyon ReGen’, sold by Liveyon LLC and administered by her doctor.

*It was infected with bacteria during manufacturing.*

Source: https://www.washingtonpost.com/national/health-science/miraculous-stem-cell-therapy-has-sickened-people-in-five-states/2019/02/26/c04b23a4-3539-11e9-854a-7a14d7fec96a_story.html
Stem Cell Clinics: Tourism and domestic

- **Tourism** – Patients travel to other countries with fewer restrictions to receive stem cell therapies
- **Domestic** – Clinics that offer unproven stem cell treatments in the US
Stem Cell Clinics: hallmarks of a sketchy clinic

- Too good to be true treatments
- Advertise treatment of diseases that stem cells have not yet been approved to treat
- Exaggerate the benefits and dismiss the risks
- Offer no long-term patient information
- Clinicians often do not have relevant expertise
Let’s explore:
https://www.phenicell.com/
How do stem cell clinics get away with this?
They are constantly expanding in number
They are constantly expanding in number

And changing their names!
Let’s explore:
https://www.phenicell.com/

From phenicell.com on 06/02/2021
WELCOME TO CSCI
The #1 Stem Cell Institute in the World!
No one has stepped up to stop them

Not equipped to police an expanding and shifting number of clinics

- Oversees all doctors, M.D and D.O, working in the U.S
- Have not historically pursued licence suspension for bad stem cell practitioners
What are proven uses for stem cells for right now?

• Bone marrow transplants
• Some bone, skin and corneal transplants

All other “stem cell” treatments are unproven and should be viewed as highly experimental
Stem Cells: What do you know?
A stem cell is...

A. A cell that is only present in the embryonic stage
B. A cell that is capable of making many different cell types
C. A cell that is found in the xylem of plants
A. A cell that is only present in the embryonic stage

B. A cell that is capable of making many different cell types

C. A cell that is found in the xylem of plants
Once a stem cell is differentiated, it cannot become undifferentiated

- False! Scientists have recently discovered a way to take differentiated cells, like skin, and make them pluripotent.
There is only one type of stem cell

- False! There are embryonic stem cells, adult stem cells, and induced pluripotent stem cells.
Embryonic stem cells cannot make which of the following tissues

A. Bone  
B. Skin  
C. Red blood cells  
D. Brain  
E. None of the above, embryonic stem cells can make all tissue types
Embryonic stem cells cannot make which of the following tissues

A. Bone
B. Skin
C. Red blood cells
D. Brain
E. None of the above, embryonic stem cells can make all tissue types
True or false: There are many FDA approved stem cell therapies available

• False. Only bone marrow transplants are currently FDA approved
True or false: Stem cells treatments are risk-free if they come from your own body

• False!

• Even when the stem cells come from your own body, there is a lot of research to be done regarding the risks associated with the transplant process.
The Ohio State Stem Cell Education Program (OSCEP) team

**PhD students and postdoctoral fellows**
- Tyler Dause
  - PhD student
  - Department of Psychology
- Dr. Jiyeon Denninger, MD PhD
  - Postdoctoral Fellow
  - Department of Psychology
- Josh Rieskamp
  - PhD student
  - Department of Psychology

**Undergraduates**
- 2019
  - Valerie Burch
  - Grace Campbell
  - Daniel Dodd
  - Kelly Dubay
  - Samantha Loeffler
  - Zach Smotzer
  - Angel White
- 2020
  - Grant Goodman
  - Andrew Hakopian
  - Sarah Imwalle
  - Samantha Loeffler
  - Hrushil Patel
  - Angel White

**Funding from the National Science Foundation**