Stem Cell Instructor Reference Sheet and Slide Guide

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Cell Review [Slides 6-8]

In order to thoroughly discuss stem cells and their functions/uses, it is important to recall the mammalian cell structure and function. The cell is the smallest basic unit of life. The organelles inside the cell serve a similar purpose to the organs inside the body. The cell's organelles perform specific functions inside the cell, like storing DNA, producing energy, and deconstructing proteins. The first reference provides more information on all organelles, their functions, and provides clear visuals to help students see the bigger picture.

A review of mitosis may also set a good precedent before discussing stem cells, with a reference for that information below.

Content Citations:

1. Rachael. "Cell organelles and their functions." Rs' Science, 15 Sept. 2021. https://rsscience.com/cell-organelles-and-their-functions/.
2. "Phases of mitosis." Khan Academy. https://www.khanacademy.org/science/ap-biology/cell-communication-and-cell-cycle/cell-cycle/a/phases-of-mitosis.

Image Citations:

1. Images created with BioRender.com.

Stem Cells [Slides 9-11]

The healing process is a good example to demonstrate stem cells in active use. When the body endures a cut for example, healing will follow a generalized pathway in order to return to homeostasis. After the cut, you need to regrow the skin cells lost in that cut. In order to do that, new skin cells need to be generated. This is where stem cells come in! Stem cells become active participants in the proliferation and remodeling stages, as the body has natural stem cell niches (to be discussed later) that house stem cells in case of instances like a wound. Other examples where stem cells are used regularly include bone remodeling, skin replacement, hair growth, among others.

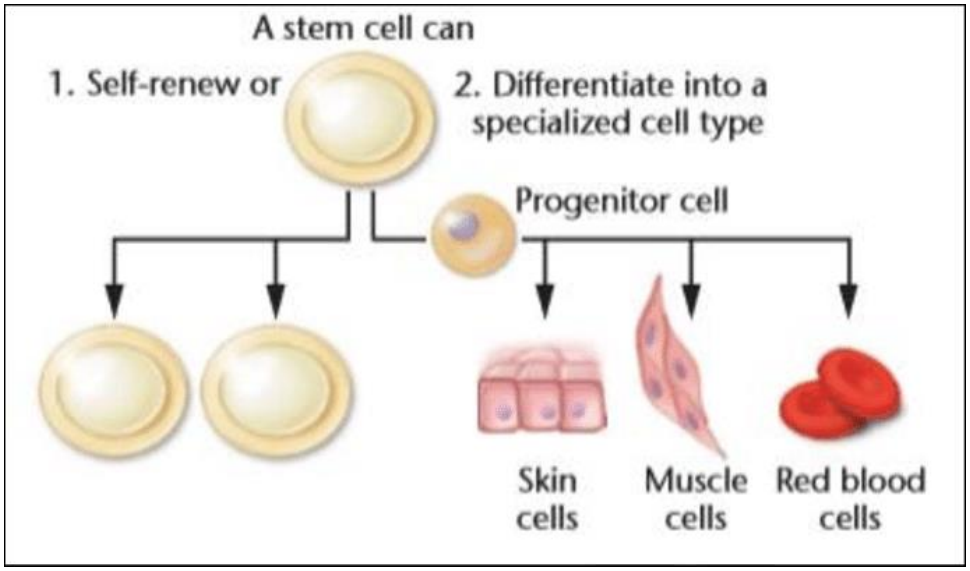
Image Citations:

1. Images created with BioRender.com.

Citations links active as of May 2022.

What do stem cells do? [Slides 12-17]

Stem cells are defined by their ability to differentiate (begin down the path to a specific cell type such as a skin cell, heart cell, etc.) and self-renew (produce more stem cells with the same abilities). The image below helps to visualize this process where self-renewal displays symmetric division, where the stem cell produces a daughter stem cell through mitotic division. Stem cells can also divide asymmetrically where they can produce daughter cells that are distinct from the original stem cell. This begins with production of a progenitor cell, which is a descendent of the stem cell that has begun down the path to the target differentiated cell. Progenitor cells are slightly more specific than stem cells, but not fully differentiated into the final cell type. A good analogy for stem cell differentiation is described in slides 10-11, where a student becomes more specialized, the more school and jobs she experiences. Once the student goes into a full-time job, they have a specific role and function in society. This is just like the stem cell, which differentiates into a specific cell type and functionality in the body!



Content Citations:

1. *NCI Dictionary of Cancer terms*. National Cancer Institute. (n.d.). Retrieved May 3, 2022, from https://www.cancer.gov/publications/dictionaries/cancer-terms/def/hematopoietic-stem-cell
2. Prasanta, M., "Stem Cells and Its Applications." Agriculture & Food: e-newsletter. Sept. 2019. https://www.researchgate.net/figure/Fig-1-Characteristics-of-a-Stem-Cell-Self-renewal-and-differentiation-into-different_fig1_343975500.

Image Citations:

1. Images created with BioRender.com.
2. Prasanta, M., "Stem Cells and Its Applications." Agriculture & Food: e-newsletter. Sept. 2019. https://www.researchgate.net/figure/Fig-1-Characteristics-of-a-Stem-Cell-Self-renewal-and-differentiation-into-different_fig1_343975500.

Other stem cell functions in the body [Slide 18]

These are just some of the few examples of everyday use of stem cells found in the body. In each example, stem cells would reproduce asymmetrically (to address the injury, organ, etc) and symmetrically (to replenish the stem cell supply).

Content Citations:

1. The Public Engagement team at the Wellcome Genome Campus. (2021, July 21). *What is a stem cell?* Facts. Retrieved May 4, 2022, from https://www.yourgenome.org/facts/what-is-a-stem-cell.

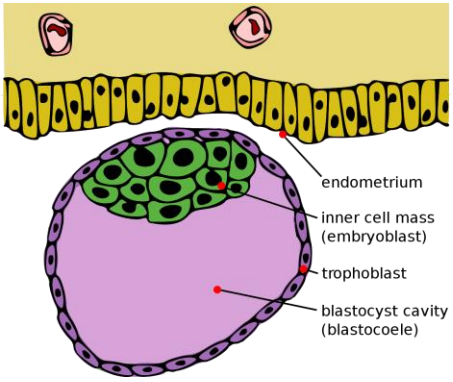
Image Citations:

1. Images created with BioRender.com.

Stem Cell Types [Slides 19-23]

Embryonic [Slide 20]

Embryonic stem cells (ESCs) are extracted from the inner cell mass of the blastocyst of a human embryo (seen in the image below).The blastocyst is a structure of cells that forms around 4-7 days after fertilization. It is the inner cell mass that gives rise to the developing fetus, making embryonic stem cells pluripotent, meaning they can differentiate into any body cell. During early embryogenesis, three germ layers form which eventually give rise to the fetus. For more information on this topic, please refer to the first reference.



Some pros of embryonic stem cell usage is that these fertilized blastocysts provide for easy access to the stem cells and they are from left over in vitro fertilization (IVF). Additionally, the stem cells are multipotent, so they can differentiate into any type of cell. These stem cells are said to be immortal because they can proliferate indefinitely. One of the largest cons however, is that use of these stem cells tends to produce a higher instance of teratoma formation, or tumor growth. This is because the cells are completely undifferentiated and can develop into any cell type. There is one point of contention with using ESCs, regarding ethical concerns with the question of when life begins. While religion and science can sway these opinions, the blastocysts used in research are from discarded IVF, not intended to be implanted.

Content Citations:

1. Winograd, C. “Anatomy & Physiology.” *Britannica*. https://www.britannica.com/science/germ-layer.
2. Pennings, S. “The Stem Cell Niche: Interactions between Stem Cells and Their Environment.” *Stem Cells International*, Aug. 2018. https://www.hindawi.com/journals/sci/2018/4879379/.

Image Citations:

1. Images created with BioRender.com.
2. “Inner cell mass.” *WikiDoc*. Inner cell mass - wikidoc.

Adult Stem Cells [Slide 21]

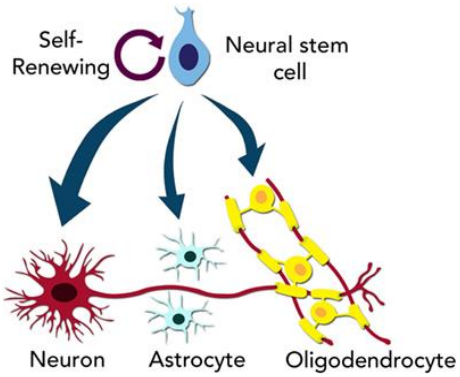
Adult stem cells are present in various forms throughout the body. Depending on the type and region of location, they are mostly multipotent, meaning they can differentiate into many cell types, but not all. These regions where stem cells are found are known as a specific stem cell niche, which provides the right microenvironment for the stem cells to grow and reproduce.

For instance, you could isolate epithelial stem cells from the bulge of the hair follicle. In the lab, this stem cell could go on to become a hair cell, skin cell, or even line the intestines. Each type of stem cell is found in a niche, which are all over the body. As far as pros and cons, adult stem cells are less ethically controversial, as they are coming from a living adult, with no harm to the patient in the obtaining of the stem cells. This is also a con in itself, in the sense that a sick adult may not be able to utilize their own stem cells. In addition, some of these stem cells can be hard to find in the body and more difficult to isolate, as some niches are deep in the body.

Adult Stem Cell Types [Slide 22]

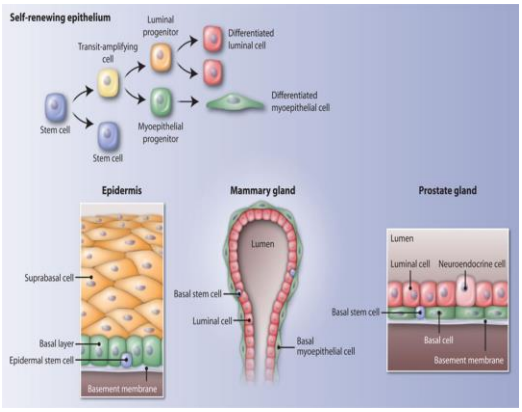
Neural

These stem cells will eventually give rise to neurons and the support cells of the nervous system (astrocytes, oligodendrocytes, glia, etc.). Neural stem cell niches are found in the subventricular and subgranular zones of the brain. This makes isolation of stem cells on a living patient extremely difficult.



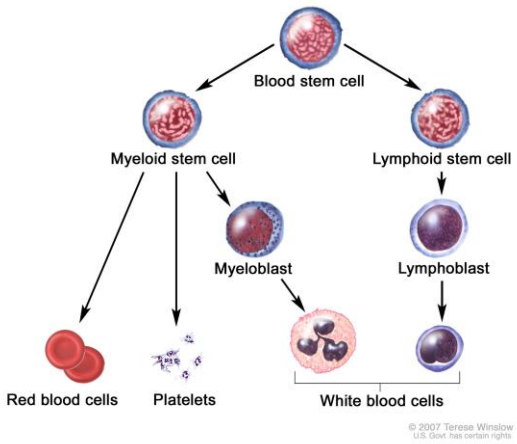
Epithelial

Become cells of the skin, intestinal, gland, & vessel lining, as well as the hair. They can therefore be found in various niches that house these adult cells. Epithelial stem cells are relatively easy to find and isolate.



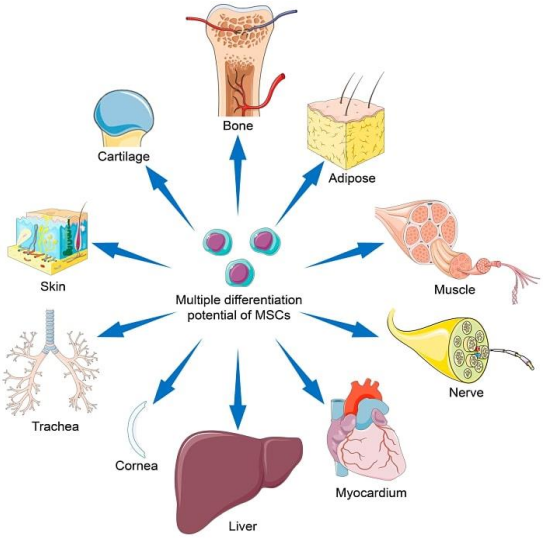
Hematopoietic

This group of stem cells gives rise to the cells that make up the blood (myoblast, red blood cells, etc.) They are found mostly in the bone marrow of a living adult and umbilical cord blood.



Mesenchymal

These diverse stem cells can differentiate into cells of the muscle cartilage, fat, heart tissue, among others. They are also found in the bone marrow, along with adipose tissue, and umbilical cord blood.



Content Citations:

1. Mayo Foundation for Medical Education and Research. (2022, March 19). *Answers to your questions about Stem Cell Research*. Mayo Clinic. Retrieved May 3, 2022, from https://www.mayoclinic.org/tests-procedures/bone-marrow-transplant/in-depth/stem-cells/art-20048117

Image Citations:

1. Images created with BioRender.com.
2. Authors Janet Y. Le, Authors Udochukwu Amanamba, Authors Hiba Hasan, & Authors Bianca Westhoff. (n.d.). *What are neural stem cells, and why are they important?* Frontiers for Young Minds. Retrieved May 3, 2022, from https://kids.frontiersin.org/articles/10.3389/frym.2016.00020
3. *Maintaining epithelial stemness with p63 - science.org*. (n.d.). Retrieved May 4, 2022, from https://www.science.org/doi/10.1126/scisignal.aaa1033
4. *Maintaining epithelial stemness with p63 - science.org*. (n.d.). Retrieved May 4, 2022, from https://www.science.org/doi/10.1126/scisignal.aaa1033
5. *What are mesenchymal stem cells (mscs)?* What are Mesenchymal Stem Cells (MSCs)? (n.d.). Retrieved May 2, 2022, from https://www.dvcstem.com/post/what-are-mesenchymal-stem-cells

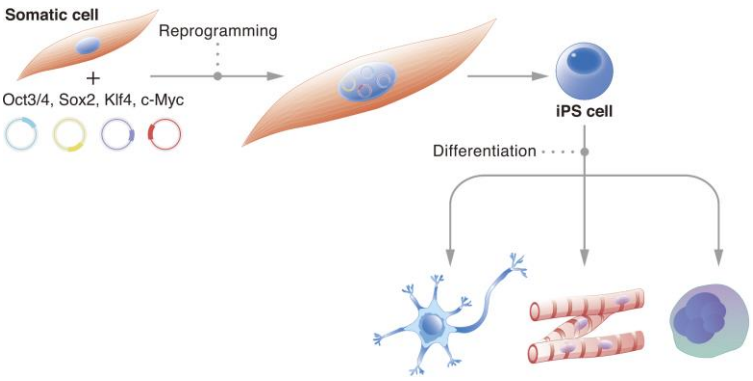
Induced Pluripotent Stem Cells [Slide 23]

Commonly noted as iPS cells, these specialized stem cells utilize innovative technology to reprogram already differentiated somatic cells into pluripotent stem cells. The resulting iPS cell, which is pluripotent, has similar potential to embryonic stem cells. This process of converting an adult stem cell into a stem cell with greater potency is known as transdifferentiation and is

centralized in the nucleus of these cells. More information about this process is detailed in the first reference below.

These somatic cells are typically isolated from a niche that is relatively easy to access such as the skin or blood. They are reprogrammed using the transcription factors Oct ¾, Sox2, c-Myc, and Klf4. These transcription factors are introduced to the somatic cells and bind to the DNA in the nucleus. This specific combination changes gene expression, and in turn increases the potency of these cells.

These reprogrammed cells are now pluripotent, meaning they can differentiate into any type of cell. There are similar pros and cons for iPS cells to embryonic stem cells. They are considered to be pluripotent and immortal, as they can continue to self renew. In addition, they are easily located and isolated as somatic cells. Yet, one major fallback is the potential for teratoma growth, due to the presence of undifferentiated iPSCs that are able to self-replicate indefinitely.



Content Citations:

1. Ye, L. "Induced Pluripotent Stem Cells and Their Potential for Basic and Clinical Sciences." *Current Cardiology Reviews*, Feb. 2013. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3584308/#:~:text=INTRODUCTION-,Induced%20pluripotent%20stem%20(iPS)%20cells%2C%20are%20a%20type%20of,defining%20properties%20of%20ES%20cells.

Image Citations:

1. Images created with BioRender.com.
2. *JMA Journal. (n.d.). Google search. Retrieved May 2, 2022, from https://www.google.com/search?q=induced%2Bpluripotent%2Bstem%*

Why we care in medicine [Slides 24-27]

This section is meant to demonstrate various real life examples of stem cells and stem cell therapies present in medicine. The following references provide more information about the different types of stem cell therapy applications. Below there are references for Alzheimer's [1], blindness [2], cancer [3,4], diabetes [5], heart attacks [6], and vascular grafts [7].

Content Citations:

1. Cona, L. "Stem Cell Therapy for Alzheimer's." *DVC Stem*, March 2021. https://www.dvcstem.com/post/stem-cell-therapy-for-alzheimers.
2. "The eye and stem cells: the path to treating blindness." *EuroStemCell*. https://www.eurostemcell.org/eye-and-stem-cells-path-treating-blindness#:~:text=Holoclar%C2%AE%20is%20currently%20the,the%20eye%20lacking%20these%20cells.
3. "Stem Cell Transplants in Cancer Treatment." *National Cancer Institute*, April 2015. https://www.cancer.gov/about-cancer/treatment/types/stem-cell-transplant.
4. Walcher, L. "Cancer Stem Cells – Origins and Biomarkers: Perspectives for Targeted Personalized Therapies." *Frontiers in Immunology*, Aug. 2020. https://www.frontiersin.org/articles/10.3389/fimmu.2020.01280/full.
5. "Diabetes." *A Closer Look at Stem Cells*. https://www.closerlookatstemcells.org/stem-cells-medicine/diabetes/.
6. Buckles, S. "Mayo Clinic research discovers how stem cells repair damage from heart attacks." *Mayo Clinic*, March 2020. https://newsnetwork.mayoclinic.org/discussion/mayo-clinic-research-discovers-how-stem-cells-repair-damage-from-heart-attacks/#:~:text=Stem%20cells%20restored%20cardiac%20muscle,caused%20by%20a%20heart%20attack.
7. Wang, L. "Fabrication of tissue-engineered vascular grafts with stem cells and stem cell-derived vascular cells." *Expert Opinion on Biological Therapy*, Aug. 2015. https://pubmed.ncbi.nlm.nih.gov/26560995/.

Image Citations:

1. Images created with BioRender.com.

Additional Notes

For a more interactive presentation and to encourage more participation, teachers can use Nearpod.com.