Learning Activity 2: Hope v. Hype & Care v. Cure

Disease, Disability, & Immortality: Hope & Hype Module

by Katayoun Chamany & Adrienne Asch Updated July 2017

As advances in stem cell research (SCR) move from the lab to the clinic, a number of professional organizations, governments, and patient advocacy organizations continue to invest in efforts to bring forth the promise of cure for those living with disease and disability. In California, Proposition 71 created a funding stream to support translational research at a time when the state was cutting social services due to the economic recession. Voter support was partly the result of a campaign that highlighted studies in which embryonic derived stem cells could repair spinal cord injury in rodents. These results combined with the rousing testimonies of high profile actors in Hollywood living with disease and disability, such as Christopher Reeve and Michael J. Fox, led voters to believe that cures were just around the corner and that the California Institute of Regenerative Medicine (CIRM) could also heal an ailing state economy. The hype surrounding stem cell research expanded globally as can be seen by the "Connect, Collaborate, and Cure" tag line of the World Stem Cell Summit, designed to bring industry, academia, regulatory officials, and patient advocates together to promote stem cell research. As research accelerated, some clinics began offering stem cell therapies without adequate testing or attention to good manufacturing practices. In response, the International Society for Stem Cell Research launched a watchdog site intended to list those clinics that were not able to provide the ISSCR with literature and results supporting their claims. The site was taken down after the society became concerned about litigation costs associated with "black listing" clinics.

In an age of remarkable scientific innovation, how can society provide hope for those seeking treatments and refrain from hype using the biomedical approach to health? Furthermore, how can SCR move forward without neglecting efforts to provide care using a social model of health for those currently living with disease and disability? More generally, how do we avoid these dangerous dichotomies that position options as "either/or?"

PART I: Diversity in Disability & Stem Cell Research
PART II: Stem Cell Therapy: Fact or Fiction?

At the completion of this activity you will be able to:

- Recognize the difference between the biomedical and social models of health.
- Map the dichotomies of medical v. social, cure v. care, and hope v. hype to the arguments made by members of the disability rights and the stem cell research communities.
- Provide evidence for a diversity of viewpoints *within* communities that share common identities (those living with disability, disability rights scholars, stem cell researchers, bioethicists).
- Generate questions about the types of disease and disability that could be best addressed by either the biomedical or social model of health.
- Describe how advances in stem cell research can both challenge and confirm stereotypical views of those that live with disease and/or disability.
- Recognize the influence that advances in basic science, law, business, human rights, and medicine can have on one another and how this informs an address of disease and disability.

- Understand how basic science reveals the underlying cell signaling pathways necessary to stimulate regeneration in the body and how this work informs the development of transplant and drug therapies.
- Describe how the value of various bodily tissues has shifted from waste or unwanted entities to useful resources for stem cell research.
- Compare the ethical issues associated with procurement processes for each type of stem cell used in therapy.
- Compare the therapeutic potential and range of side effects of different stem cell transplant therapies.

PART I: Diversity in Disability & Stem Cell Research

View the documentary film *Terra Incognita: The Promise and Perils of Stem Cell Research,* which depicts individuals whose lives were touched by disability and stem cell research. Two individuals shifted their career paths to SCR after experiencing frustration in their relationships with those living with spinal cord injury. One is a developmental biologist, Jack Kessler, who became a stem cell researcher when his daughter became disabled, and another is Vicki Tysseling-Mattiace, who left her career as a physical therapist to obtain a PhD in neuroscience in the Kessler lab. The other two individuals are young women who experienced spinal cord injury acquired through recreational activities, one of which is the daughter of Jack Kessler, Alison Kessler. Also view the trailer to the documentary film *Hope Deferred,* which takes its title from the Proverb 13:12 "Hope deferred makes the heart sick, but a longing fulfilled is a tree of life." In the trailer, Doug Melton, another developmental biologist who switched research focus when his children developed diabetes, argues that stem cell research should be pursued. The Brooke Ellison Project produced the film. Brooke, who acquired spinal cord injury as a child, served on the New York Empire State Stem Cell Ethics Committee and is a strong advocate for embryonic stem cell research.

The readings provide a fuller view of the multiple narratives presented in these films, highlighting the diversity of opinion *within* communities that have a shared identity. The Hahn and Belt study uses qualitative research methods to assess the attitudes of those living with disability and the role that disability plays in shaping their identities. In the book review by Edwards, Tom Shakespeare's critical analysis of the social model of disability is reviewed within the context of interdisciplinary scholarship across disability studies, genetics, and bioethics, and the more recent review of Shakespeare's work by Goodley provides a response from a disability studies scholar. Scherman analyzes the way that language separated Christopher Reeve from disability rights activists and squarely addresses the care v. cure dichotomy in this context. The articles under *Hope v. Hype* display a diversity of opinion among stem cell advocates. The Jakimo and Fernandez piece counters disability rights advocacy with stem cell advocacy propelled through a stem cell accelerator platform, while other scientists and researchers call for a more balanced address of the potential of stem cell research. Some highlight the challenges of access, while others caution that clinicians may need to narrow the scope of applications. The remaining articles extend the stem cell research presented in the *Terra Incognita* film in a series of science news articles (Pail, Anonymous), a scientific research article co-authored by Tysseling-Mattiace, and a contemporary review of the combinatorial nanotech and cell-based therapeutic approaches to spinal cord injury.

After reading these resources, your instructor may ask you to discuss them using the **Thought Questions** that follow and/or write a response essay.

Readings:

Care v. Cure

1. **Film.** Siegel, J. 2008. Hope Deferred. Trailer Link (2:23 min)

2. **Research Article:** Hahn, H. & Belt, T. 2004. Disability identity and attitudes toward cure in a sample of disabled activists. *Journal of Health and Social Behavior.*45:453-464. Link
3. **Book Review:** Edwards, S. 2008. Disability rights and wrongs. *Journal of Medical Ethics*. 34(3): 222. Link
4. **Book Review:** Goodley, D. 2014. Disability rights and wrongs revisited. *Disability & Society*. 29(4): 659-661. Link
5. **Article:** Scherman, E. 2009. The speech that didn't fly: Polysemic readings of Christopher Reeve's speech to the 1996 Democratic National Convention. *Disability Studies Quarterly.* 29 (2): (~10 pages) Link

Hope v. Hype

1. **Article:** Jakimo, A. and Fernandez A. 2011. Innovation in stem cell advocacy: You only get what you can measure. *Regenerative Medicine 6 (6 Supplement)*: 127-132. Link
2. **Review:** King, M. & Perrin, J. July 7, 2014. Ethical issues in stem cell research and therapy. *Stem Cell Research & Therapy*. 5 (4): 85(1-6). Link
3. **Professional Society Blog**: Barfoot, J. July 30, 2015. Stem Cell Research: Promise, Progress, and Hype. *Stem Cells in Focus Blog*. International Stem Cell Research Society. Link
4. **CIRM Blog:** McCormack, K. Dec 11, 2015. The "Right to Try" Laws Are More Feel Good Than Do Good. *The Stem Cellar*. Link
5. **Research Article:** Kamenova, K. and Caulfied, T. 2015. Stem cell hype: Media portrayal of therapy translation. *Science Translational Medicine.* 7 (278): 278: 278ps4. Link

Kessler Lab Terra Incognita + Follow Up

1. **Film:** *Terra Incognita: The Promise and Perils of Stem Cell Research.* Cancer Finitzo, M. (Director) 2007. Independent Lens/ Kartemquin Films; PBS. Trailer Link
2. **News:** Paul, M. April 2, 2008. Promising New Stem Cell Nanotechnology For Spinal Cord Injury. *Northwestern University News*. Link
3. **News:** Anonymous. 2008. Top down bottom up bridging two cultures. *Nature Nanotechnology.* 3(6): 317. Link
4. **Research:**Tysseling-Mattiace, V. et al. April 2, 2008. Self-assembling nanofibers inhibit glial scar formation and promote axon elongation after spinal cord injury. *Journal of Neuroscience*. 28(14): 3814-3823. Link
5. **Review:** Assuncao-Silva, R. et al. June 1, 2015. Hydrogels and cell based therapies in spinal cord injury regeneration. *Stem Cells International*: 1-24. Link

Thought Questions

1. What is health and why is it valued? Reflect on the *Lancet* Editorial "What is Health: The Ability to Adapt"?
2. What is the connection in people's minds between some level of health and some level of social functioning – in school, family, work, politics, and civic life? An array of characters appears in the film, but they do not share the same views. How does life experience influence their views?
3. How does the film help you understand the lives of people living with disability? How, for example, does it affect the goal of obtaining higher education?
4. How does disability intersect with other identities such as age, gender, and socioeconomic class?
5. How should people who are not "healthy" or "normal" by some definitions think about themselves, and how should society think about their situation? Do the answers vary depending upon the characteristics of the health condition in question: physical, mental, emotional, sensory?; congenital or acquired?; early-onset or late-onset?; static or progressive?; visible or invisible?; ultimately fatal or not?

6. Is what we call a disability inevitably a disadvantage, a “handicap”, or a problem, or does its impact upon a person’s life depend upon non-medical facets of the society in which they are living? Again, the characters in this film do not necessarily agree; where do you see conflict or difference?

7. Some of your readings and some of the characters in this movie consider the stage in life at which someone acquires an impairment (early in childhood or adolescence versus later) as contributing to the difference in how people make sense of disability. How does the film portray this? What does the film leave out? What questions does it make you want to ask about other disabilities?

8. If the United States is interested in promoting health, what actions could it or should it take to change conditions that cause harm to people’s health? Why does society appear to be more interested in some therapies, such as stem cell research or genetic alteration, than in making safer products?

9. Are there some conditions that could be prevented or supported by environmental, product, lifestyle changes?

10. Does it make any sense to think of characteristics like spinal cord injury, diabetes, schizophrenia, Parkinson’s disease, or cystic fibrosis with the same attitude we take toward variations in ethnicity, religion, height, gender, sexual orientation, or age? How do we as a society link disability with other forms of diversity/social justice, and is this appropriate?

11. There is some genetic research that purports that there might be risk-taking genes? What do you think people will do with that knowledge? How might it be applied? What would the characters in this film support in terms of risk taking genes?

PART II: Stem Cell Therapy: Fact or Fiction?

While advances in spinal cord injury repair are slow going given the complexity of biological processes associated with scar tissue formation and cell differentiation, more encouraging results have emerged in applications using stem cells from unlikely sources such as adipose and fetal tissue. With respect to adipose tissue, a Fat Industry has emerged replete with devices and reagents designed to isolate, amplify, and enhance these stem cells to function in breast reconstruction, muscle and cartilage regeneration, neural regeneration, and cardiac repair. As of 2015, over 152 clinical trials were underway worldwide investigating the application of adipose derived stem cells in transplant therapy. With respect to fetal tissue, cells acquired from five to ten fetal brains can be directly injected into the brains of those living with Parkinson’s to reduce the severity of muscle spasm. Though it is not known whether these cells survive and reestablish brain function or secrete factors that stimulate the host cells to regenerate, the results suggest that further studies should be conducted. The recent, but false, accusation that Planned Parenthood was involved in the sale of fetal tissue has made access to this tissue more challenging, despite the fact that donation of fetal tissue for research and treatment is legal in the United States. Given that there is minimal manipulation of cells used in these transplant therapies, a number of clinics have emerged offering these services. However, the US Food and Drug Administration has found that not all clinics are using good manufacturing practices, nor are their results subjected to FDA review. Those clinics that have refused to provide the FDA with appropriate documentation have incurred injunctions, and as a result have either shut down or relocated to countries with more lenient regulation.

A collection of resources will showcase the degree to which unproven therapies have been marketed and used thus far and efforts to curtail these practices. *Please note that the 60 minutes videos require paid registration.*

1. **60 Minutes Script and Main Site:** Sept. 12, 2010. 21st Century Snake Oil.60 Minutes. *CBSnews.com* Link
    a. **Video** Sept. 12, 2010. 21st Century Snake Oil. Part 1 Reveal. 60 Minutes. CBSnews.com. *YouTube* (13:23 min) Link
    b. **Video** Sept. 12, 2010. 21st Century Snake Oil. Part 2 Reveal. 60 Minutes. CBSnews.com. *YouTube* (12 min) Link
2. **60 Minutes Script:** Jan 9, 2012. Stem Cell Fraud. 60 Minutes. *CBSnews.com* Link
    a. **Video** Jan 8, 2012. Stem Cell Fraud. 60 Minutes. *CBSnews.com* (15 min) Link
1. **News:**Cyranoski, D. 2010. FDA challenges stem-cell clinic. *Nature*. 466 (7309):909.
2. **News:**Ledford, H. June 30 2011. Stem-cell scientists grapple with clinics. *Nature*. 474:550. Link
3. **Article:** Nov 6, 2011. European medicines agency, CAT secretariat & US food and drug administration. 2011. *Regenerative Medicine.*6(6 Suppl):90-96. Link
4. **News:** Cyranoski, D. July 6, 2012. Patients Seek Stem-Cell Compensation. *Nature News Blog.* Link
5. **News:** Cyranoski, D. Aug 2, 2012. FDA's claim over stem cell upheld. *Nature.* 488:14. Link
6. **Article:**Turner, L. 2015. US stem cell clinics, patient safety, and the FDA. *Trends in Molecular Medicine.* 21(5):271-273. Link
7. **Article:** Kuriyan, A, et al. 2017. Vision loss after intravitreal injection of autologous "stem sells" for AMD. New England Journal of Medicine. 376 (11):1047-1053. Link
8. **News:** Service, K. June 15, 2017. Texas has sanctioned unapproved stem cell therapies. Will it change anything? Science News. Link

After reviewing the resources below, you will apply this knowledge to create **a presentation** that integrates the biological, ethical, legal, and social dimensions associated with a specific stem cell therapy. Depending on your course, you may be asked to design a presentation or summary for a single type of stem cell based therapy or you may be asked to collaborate with your peers on a single source, or generate a narrative for each source over the course of the semester. Additional resources to those listed below each stem cell source are the Timelines and PPT Slide Sets at *Stem Cells Across the Curriculum.* Your presentation should address:

1. **The Source:** The starting material for the source of stem cells, the manipulations, and the technologies involved in bringing it to the lab or clinic.

2. **The Process:** The steps involved in procurement of the tissue/cells and any related activities.

    a. Was any money exchanged? Are there any excess, extra, or by-products, and how are they managed?
    b. What policies are associated to derive or deliver stem cells from this source?
    c. The key points at which decisions are made.

3. **Biology Characteristics:** What is useful about this specific source for basic biological research.

    a. What is the cell fate potential?
    b. What does the genetic content for cells from this source relate to the recipient?
    c. Are there animal components present?

4. **Scientific Potential**: Characteristics that make this source useful for basic scientific research.

a. How can the source expand our knowledge base of human development, disease, etc.?
b. How can working with these cells expand our tool kit in scientific experiments?

5. **Therapeutic Potential**: Characteristics that make this source useful for biomedicine or future therapies.

    a. If used for transplant therapy or enhancement would they be universally immunocompatible?
    b. Are the cells easily retrieved? Are the stem cells plentiful? Do they need to be amplified?
    c. Is there potential for the development of unwanted outcomes such as tumor formation?

6. **Banking and Access:** Where are the potential products stored and how they are used/ administered for scientific research and therapeutic purposes.

7. **Public or Private:** Are the cells obtained within the public and private sector, and why relegated to one or the other?

8. **Social Views**: The ways that this source may challenge and/or confirm stereotypical views on the role of females in society and tissues and cells associated with female bodies, waste, or reproduction.

Resources:

Embryonic Stem Cells Derived Treatment for Spinal Cord Injury (Human/Geron/Asterias Bioetherapeutics)

1. **Video:** UC Irvine Hans Keirstead. Stem Cells Restore Mobility in Neck Injured Rats. UCI News. Link
2. **Infographic**: Chamany, K. et al. 2013. Embryo.IVF.Extranumerary Embryo AND PGD. ZoomGraphics. Stem Cells Across the Curriculum. Link
3. **News:** Woodbury, M.A. 2009. Hans Keirstead Can Make Mice Walk Again. Esquire.com. (1p) Link
4. **News:** Pollack, A. 2009 Milestone in Research With Stem Cells. *New York Times*: B1 Link
5. **News:** Pollack, A. 2010. Stem Cell Trial Wins Approval of F.D.A. *New York Times*. Link
6. **Feature:** Regalado, A. June 21, 2011. Stem-Cell Gamble. *MIT Technology Review*. Link
7. **Tutorial with Animation and Film:** Eurostemcell. April 2, 2015. Spinal Cord Injuries: How could stem cells help? Link
8. **Perspective:** Scott, C., & Magnus, D. 2014. Wrongful termination: Lessons from the Geron clinical trial. *Stem Cells Translational Medicine.* 3(12):1398-1401. Link
9. **News:** Dubnicoff, T. Oct 22, 2015. New Video: Spinal Cord Injury and CIRM-funded Stem Cell Based Trial. *Stem Cell Cellar. CIRM.* Link

Adipose (Fat) for Spinal Cord Injury & Other Disabilities (Animal & Human)

1. **Infographics**: Chamany, K. et al. 2013. Adult Stem Cell Source. Fat Stem Cells ZoomGraphic. Stem Cells Across the Curriculum. Link
2. **Review:** Gimble, J et al. 2007. Adipose-derived stem cells for regenerative medicine. *Circulation Research*.100 (9):1249-1260. Link
3. **Review:** Gimble, J. et. al. 2011.Taking stem cells beyond discovery: A milestone in the reporting of regulatory requirements for cell therapy. *Stem Cells and Development.* 20 (8): 1295-1296. Link
4. **Article:** Ra, J. et al. 2011. Safety of intravenous infusion of human adipose tissue-derived mesenchymal stem cells in animals and humans. *Stem Cells and Development*. 20(8): 1297-1308. Link
5. **Review:** Mizuno, H. et al. 2012. Concise review: Adipose-derived stem cells as a novel tool for future regenerative medicine. *Stem Cells*. 30 (5): 804-10. Link

6. **Review:** Nordberg R. & Loboa E. 2015.Our fat future: Translating adipose stem cell therapy. *Stem Cells Translational Medicine* 4: 974-979. Link
7. **Perspective:** Taylor-Weiner, H & Zivin J. 2015. Medicine's wild west—unlicensed stem-cell clinics in the United States. *NEJM*. 373(11):985-87. Link
9. **Review:** Bora, P., & Majumdar, A. S. 2017. Adipose tissue-derived stromal vascular fraction in regenerative medicine: A brief review on biology and translation. *Stem Cell Research & Therapy*. 8:145. Link

Fetal Stem Cell Transplants for Degenerative Diseases

1. **Infographics**: Chamany, K. et al. 2013. Fetal Stem Cell Source. Fetus.ZoomGraphic. Stem Cells Across the Curriculum. Link
2. **News:** Lindvall, O. et al. 1990. Grafts of fetal dopamine neurons survive and improve motor function in Parkinson's Disease. *Science*. 247 (4942): 574-77. Link
3. **Research Article:** Shamblott, M. et al.1998. Derivation of pluripotent stem cells from cultured human primordial germ cells. *Developmental Biology.* 95: 13726-3731. Link
4. **News:** Anonymous. Oct 27, 2011. A priceless resource. *Nature* 478:427. Link
5. **News:** Anonymous. Oct 26, 2011. Tissue-bank shortage: Brain child. *Nature* 478 :4242-443. Link
6. **Research Article:** Lu J. et al. May 25, 2011. Generation of neural stem cells from discarded human fetal cortical tissue. *Journal of Visual Experiments.* 51 (e2681). Link
7. **Review:** Wadman, M. June 26, 2013. Medical research: Cell division. *Nature*. 498:422-426. Link
8. **Research Article**: Barker, R. et al. 2013. Fetal dopaminergic transplantation trials and the future of neural grafting in Parkinson's Disease. *The Lancet Neurology.* 12: 84-91. Link
9. **Research Article:** Hsieh, J. & Schneider, J. 2013. Neural stem cells, excited. *Science* 339:1534-535. Link

Muscle, Military Defense, & Sports

1. **Research Article**: Quintero, A. et al. 2009. Stem cells for the treatment of skeletal muscle injury. *Clinical Sports Medicine.* 28 (1): 1-11. Link
2. **Article:** Dean, W. 2011. The armed forces institute of regenerative medicine: A collaborative approach to department of defense-relevant research. *Regenerative Medicine.* 6(6 Suppl):71-74. Link
3. **News:** Drummond, K. Sept 24, 2012. World's Most Wired War Healer. *Wired.com.* Link
4. **News:** Fountain, H. Sept 17, 2012. Human Muscle, Regrown on Animal Scaffolding. *New York Times*: A1. Link
5. **Video:** Singh, V. Sept 24, 2012. Extracellular Matrix. *New York Times Video Science*. Link
6. **Video:** Ley, B. Jan 22, 2012. Outside The Lines. The Stem Cell Salvation as seen on YouTube.ESPN2 (20 min) Link
7. **Review.** Best T. et al. 2013. Stem cells, angiogenesis, and muscle healing: A potential role in massage therapies. *British Journal of Sports Medicine.* 47(10): 656. Link
8. **Animations and Post**: Lewis, R. & Barefoot, J. July 23, 2014. Stem Cells and Sports Medicine: An Overview. EuroStemCell. Link
9. **Research Article:** Zhao, T. et al. Sept 3, 2015. Humanized mice reveal differential immunogenicity of cells derived from autologous induced pluripotency. *Cell Stem Cell*. 17(2):353-9. Link

Stem Cells for Genetic Diseases (Animal & Human)

1. **Video News:** Baker, M. Dec 23, 2009. Method of the Year 2009: IPS Cells. Link
2. **Video:** April 2, 2010.Thirteen/Education Broadcasting Corporation (Producer). *Religion and Ethics Weekly: Embryonic Stem Cell Controversy.* Link

3. **Conference Video:** Sugarman, J., Zoloth, L. & Hempel, C. October 4 2010. The Immortal Life of Henrietta Lacks - lessons for stem cell researchers and patients. World Stem Cell Summit, Pasadena, CA. *Stem Cells Across the Curriculum.* Link (Chris Hempel last 20 minutes)
4. **Infographic**: Andrews, P. & Gokhale, P. 2011.From teratomas to embryonic stem cells: Discovering pluripotency. Macmillan Publishers and *Nature Reviews Molecular Biology*. Link
5. **Review:** Pagliuca, F. & Melton D. 2013. How to make a functional β-cell. *Development.* 140(12) 2472-83. Link
6. **Review:** Sterneckert J. et al. 2014. Investigating human disease using stem cell models. *Nature Reviews Genetics*. 15:625-639. Link
7. **Review:** Munoz, J. et al. 2014. Concise review: Umbilical cord blood transplantation: Past, present, and future. *Stem Cells Translational Medicine*. 3(12):1435-1443 Link
8. **Blog Post:** June 22, 2015.Updates on Harvard's Diabetes Stem Cell Research from ADA 2015. *diaTribe* Link
9. **Article:** Agulnick, A. et al. Oct 4, 2015. Insulin-producing endocrine cells differentiated in vitro from human embryonic stem cells function in macroencapsulation devices in vivo. *Stem Cells Translational Medicine*. 4 (10):1214-22. Link
10. **Review:** Ballen, K. May 2017. Umbilical cord blood transplantation: Challenges and future directions. *Stem Cells Translational Medicine*. 6(5):1312-1315. Link