

## Activity 3: Communications in the Stem Cell Research Community

### Assignment 1: Journal Club Presentations

Scientific communications are tailored to specific audiences, such as students, laypersons, or other scientists. Information can be conveyed via textbooks, scientific research literature, review articles, or oral presentations. Venues that allow for scientific discussion include scientific journal club meetings in which scientists read and present recent work to one another, and meetings sponsored by professional societies in which researchers present and challenge preliminary work presented in abstracts, poster sessions, and oral presentations.

This assignment mimics a journal club meeting, in which members of a laboratory or research group meet to discuss the state of a particular field, each one being assigned a different research article to present to the group. Various textbook chapters may help you decipher the research articles which were written over a course of a few years by many groups of researchers. The main focus of these studies is to determine the degree to which stem cells are capable of adopting different cell fates and the molecular mechanisms that can be manipulated to instruct these cells to adopt a specific fate *in vitro* and *in vivo*. This field has not yet resolved the identity of the signaling molecules capable of producing only one cell fate. Understanding the process of stem cell differentiation will lead the way for development of treatments and preventions of disease as well as cell lines that can measure the efficacy of novel drugs and the harmful effects of environmental toxins. Given the controversies surrounding federal funding of embryonic stem cell research this field has gained the interest of the general public and patient advocacy groups as well as basic science researchers, and it is important for you to become part of this discussion.

In completing the reading for this assignment, you might take for granted that a paragraph in a textbook is clearly presented, free of ambiguities or conflicting data. You might be surprised to learn that several years of research and many papers by professional scientists, post-doctoral fellows, and students contributed to that one paragraph. Still more surprising is that just one paragraph represents the final consensus regarding data that came from collaborating or competing research groups who didn't always agree about the interpretation of their results. What is not always obvious is that the paragraph distills the findings presented in numerous research articles written by developmental biologists, cell biologists, and geneticists.

Each of these articles contains a good deal of highly specific scientific language because it is tailored for those currently conducting stem cell research. These articles aim to report a unique contribution to the field and focus on the technical details of a particular experiment and the wider implications of those results. Manuscripts were submitted for publication and underwent peer review indicating that the research was conducted in a rigorous manner upheld by those in the field. After publication, the article may have received commentary by other researchers in the field and these can be found alongside responses in subsequent issues of the journal. Collectively, these research articles document the incremental process of scientific discovery and present alternative points of view and are referred to as the "primary literature" of the stem cell field.

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In addition to the research articles a few review articles are also assigned and, by contrast, these articles are written to attract the interest of scientists and students who are not experts within a particular field. These articles usually provide a synopsis of the state of affairs within that field, and give the non-expert an overview of recent advances, setbacks, and controversies. These review articles are referred to as the “secondary literature.”

When conducting research in an unfamiliar field of biology, then, it is useful to start with review articles and then move on to research articles. In reading the literature assigned here, compare the genres and notice particularly the differences in titles, formats, and language that reflect the purposes of the different genres.

### Instructions

1. Your instructor will assign each student or groups of students assigned text sections, some review articles, and one primary research article listed below (suggestions for textbook readings and article selection may be found in the Teaching Notes to Activity 3).
2. A study guide, **Resource Seven: Worksheet for Reading Primary Literature**, is provided to help you decipher the meaning of the primary research article and understand the relationships between the figures, tables, and text.
3. Each student or group will complete the reading and develop an oral 10-minute PowerPoint presentation and/or written report that summarizes the assigned article and addresses these questions:
  - What questions or problems are the researchers interested in addressing? (place this in the context of the larger field of stem cell research)
  - What methods or approaches did they use? (consider experimental system, sample size, and controls)
  - What was the most significant finding of the paper in your opinion and why? (How convincing were the data? What else would you have liked to see done?)
  - What questions remain unanswered or are in need of further studies?
4. Students, or small groups, report their findings to the rest of the class. Each will give a 10-minute oral and visual presentation via PowerPoint and spend five minutes answering questions from the audience. This will be done in succession and will take the form of a discussion: questions and ambiguities of one group may be addressed by another group.
5. Each group or individual may be asked to write a summary report based on their research and PowerPoint presentation and will include a bibliography.

### Readings

#### Review Articles

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1. Kenny, P.A., et al. (2006). "The ecology of tumors." *The Scientist* 20(4):31-35. This article reviews the history of stem cell biology and its intimate relationship with oncogenesis.
2. Mikkers, H. et al. (2005). "Deconstructing stemness." *The EMBO Journal* 24 (15): 2715-2719. OR Zipori, D. (2005). "The stem state: Plasticity is essential, whereas self-renewal and hierarchy are optional." *Stem Cells* 23: 719-726. These articles discuss the murky definition of a stem cell.
3. Lanza R. and Rosenthal, N. (2004) "The Stem Cell Challenge." *Scientific American* 290(6): 92-100 This review is appropriate for non-biology majors. [http://www.sciam.com/print\\_version.cfm?articleID=000DFA43-04B1-10AA-84B183414B7F0000](http://www.sciam.com/print_version.cfm?articleID=000DFA43-04B1-10AA-84B183414B7F0000).
4. Stojkovic, M. et al. (2004). "Derivation, growth and applications of human embryonic stem cells." *Reproduction* 128(3): 259-267. This review is appropriate for biology majors. <http://www.reproduction-online.org/cgi/reprint/128/3/259>
5. Rohm, W. (2004). Seven Days of Creation. *Wired*. 12.01 January. This feature article is part of a cover story on cloning and reviews the work of Chung at Advanced Cell Technology. <http://www.wired.com/wired/archive/12.01/clones.pr.html>.
6. Vogelstein, B., Alberts, B., and Shine, K. (2002). "Please don't call it cloning!" *Science* 295 (5558): 1237. This article suggests new nomenclature for stem cell research that does not invoke the concept of reproductive clones.
7. O'Mathuna, D. (2002). "What to call human cloning." *EMBO Reports* 3 (6): 502-505. This article is in response to the Vogelstein et al. article and states that ethical issues can not be skirted by changing the vocabulary. <http://www.nature.com/cgi-taf/DynaPage.taffile=/embor/journal/v3/n6/full/embor136.html>.
8. Blau, et al. (2001). "The evolving concept of a stem cell: Entity or function?" *Cell* 105(7): 829-41. This review has a nice figure illustrating a reversible path for differentiation.

### Primary Research Articles

#### Seminal and Historical

1. Martin G. (1981). "Isolation of a pluripotent cell line from early mouse embryos cultured in medium conditioned by teratocarcinoma stem cells." *PNAS* 78(12): 7634-7638.
2. Shambloott et al. (1998). "Derivation of pluripotent stem cells from cultured human primordial germ cells." *PNAS* 95: 13726-13731. <http://www.pnas.org/cgi/content/full/95/23/13726>
3. Thomson J. et al. (1998) "Embryonic stem cell lines derived from human blastocysts." *Science* 282: 1145-1147.
4. Munsie et al. (2000). "Isolation of pluripotent embryonic stem cells from reprogrammed adult mouse somatic cell nuclei." *Current Biology* 10(16): 989-992. AND Cibelli et al. (2001). "Somatic cell nuclear transfer in humans: Pronuclear and early embryonic development." *The Journal of Regenerative Medicine* 2: 25-31.

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<http://pippo.catchword.com/v1=2912331/cl=23/nw=1/rpsv/catchword/mal/15248909/v2n5/s5/p25>

- Hwang, W. S. et al. (2004). "Evidence of a pluripotent human embryonic stem cell line derived from a cloned blastocyst." *Science* 303 (5664): 1669-1674. Originally published on February 12, 2004 in *Science Express* and retracted in January 2006.
- Hwang, W.S. et al. (2005). "Patient-specific embryonic stem cells derived from human SCNT blastocysts." *Science* 308(5729): 1777-1783. Originally published on May 19, 2005 in *Science Express* and retracted in January 2006.
- Stojkovic, M. et al. (2005). "Derivation of a human blastocyst after heterologous nuclear transfer to donated oocytes." *Reproductive BioMedicine Online* 11(2): 226-231.

### Stem Cells and Muscle Cell Differentiation

- Gussoni et al. (1999). "Dystrophin expression in the mdx mouse restored by stem cell transplantation." *Nature* 401(6751): 390-394.
- Seale et al. (2000). "Pax7 is required for the specification of myogenic satellite cells." *Cell* 102 (6): 777-786.
- Torrente et al. (2001). "Intraarterial injection of muscle-derived CD34+ Sca-1 stem cells restores dystrophin in mdx mice." *Journal of Cell Biology* 152(2): 335-348.

### ESCs and Neuronal Differentiation

- Bjorklund et al. (2002). "Embryonic stem cells develop into functional dopaminergic neurons after transplantation in a Parkinsonian rat model." *PNAS* 99(4): 2344-2350. [www.pnas.org/cgi/doi/10.1073/pnas.022438099](http://www.pnas.org/cgi/doi/10.1073/pnas.022438099) (review article, Vogel, G. (2002) "Rat Brains Respond to Embryonic Stem Cells." *Science* 295(5553): 254-55.).

### Signaling Factors and Differentiation

- Schudliner et al. (2000). "Effects of eight growth factors on the differentiation of cells derived from human embryonic stem cells." *PNAS* 97(21): 11307-11312. <http://www.pnas.org/cgi/content/abstract/97/21/11307> (review of the work <http://www.hhmi.org/news/melton.html>)

### Adult Cell Plasticity and Differentiation

- Bjornson et al. (1999). "Turning brain into blood: A hematopoietic fate adopted by adult neural stem cells *in vivo*." *Science* 283 (5401): 534-6.
- Terada, N., et al., (2002) "Bone marrow cells adopt the phenotype of other cells by spontaneous cell fusion." *Nature* 416(6880): 542-45.
- Ying, Q. et al. (2002) "Bone marrow cells adopt the phenotype of other cells by spontaneous fusion." *Nature* 416(6880): 545-548.
- Mezey et al. (2003). "Transplanted bone marrow generates new neurons in human brains." *PNAS* 100:1364-1369. <http://www.pnas.org/cgi/content/abstract/100/3/1364>

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17. Weimann, J.M. et al. (2003). "Contribution of transplanted bone marrow cells to Purkinje neurons in human adult brains." *PNAS* 100(4): 2088-2093.  
<http://www.pnas.org/cgi/content/abstract/100/4/2088>.
18. Constans A. (2005). "Another chapter in going from blood to brain." *The Scientist* 19 (21): 20.

### Clinical Perspectives of Stem Cell Research

19. Rideout et al. (2002) "Correction of a genetic defect by nuclear transplantation and combined cell and gene therapy," *Cell* 109(1): 17-28.

### Characterization of Stem Cells

20. Ivanova, N.B. et al. (2002). "A stem cell molecular signature." *Science* 298(5593): 601-604.
21. Ramalho-Santos, M. et al. (2002). "Stemness: Transcriptional profiling of embryonic and adult stem cells." *Science* 298(5593): 597-600.
22. Fortunel, N. et al. (2003). "Comment on "'Stemness': Transcriptional profiling of embryonic and adult stem cells and "A stem cell molecular signature."(I)." *Science* 302(5644): 393b.
23. Evsikov, A. et al. (2003). "Comment on "'Stemness': Transcriptional profiling of embryonic and adult stem cells and "A stem cell molecular signature."(II)." *Science* 302(5644): 393c.
24. Ivanova, N.B., et al. (2003). "Response to Comments on "'Stemness': Transcriptional Profiling of Embryonic and Adult Stem Cells" and "A Stem Cell Molecular Signature"." *Science* 302(5644):393d.
25. Sato, N. et al. (2003). "Molecular signature of human embryonic stem cells and its comparison with the mouse." *Developmental Biology* 260(2): 404-413.
26. Love, L. (2003). "Rockefeller News Release: Genetic Clues to Stem Cells' Unlimited Potential." Online. Rockefeller. July 3, 2003.  
<http://www.rockefeller.edu/pubinfo/070303.php> .

### Embryonic Stem Cell Lines Without Embryo Destruction

27. Solter, D. (Dec 1, 2005). Politically correct human embryonic stem cells. *New England Journal of Medicine* 353(22): 2321-23.
28. Weissman, I. (2006). "Politic stem cells." *Nature* 439 (7073): 145-148.
29. Meissner, A. et al. (2006). "Generation of nuclear transfer-derived pluripotent from cloned Cdx2 deficient mouse blastocysts." *Nature* 439 (7073): 212-215.
30. Klimanskaya, I., et al. (2006). "Human embryonic stem cell lines derived from single blastomeres." *Nature* 05142. Chung, Y. et al. (2006). "Embryonic and extraembryonic stem cell lines derived from single mouse blastomeres." *Nature* 439 (7073): 216-219.

### Web Sites

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University of Michigan. (2006). "Stem Cells Explained and Explored." Online. University of Michigan. March 21. This site has an extensive interactive tutorial for stem cell production and use. [http://www.umich.edu/news/stemcells/022706\\_TabA.html](http://www.umich.edu/news/stemcells/022706_TabA.html) or <http://www.lifesciences.umich.edu/research/featured/tutorial.html>.

Public Broadcasting Service. (2001). "Life's Greatest Miracle." Online. VHS. Erikson & Nilsson Production et al. Part 4 "The First Two Weeks" and Part 5 "The Embryo Takes Shape." VHS. Contains 4:58 and 7:47 minute video clips respectively. 20 November. <http://www.pbs.org/wgbh/nova/miracle/program.html>

Sumanas Inc. "Human Embryonic Stem Cells." Online. NIH. This site has a narrated animation of the methods used to isolate and culture embryonic stem cells. [http://www.sumanasinc.com/scienceinfocus/sif\\_stemcells.html](http://www.sumanasinc.com/scienceinfocus/sif_stemcells.html) .

Dolan DNA Learning Center. "How Embryonic Stem Cells Are Made." Cold Spring Harbor Laboratory. This site contains six slides. <http://www.dnalc.org/stemcells.html>

Dolan DNA Learning Center. "Cloning 101." Cold Spring Harbor Laboratory. This site demonstrates the Roslin and the Honolulu cloning techniques with animations. <http://www.dnalc.org/stemcells.html>

"What Is A Stem Cell?" Online. Genetics Science Learning Center at the Eccles Institute of Human Genetics University of Utah. This animation is somewhat juvenile but really gets some important points across about differentiation. It is extremely interactive and accompanied by extensive text. Clicking on the word "animation" which lets the viewer see more details and process. <http://gslc.genetics.utah.edu/units/stemcells/whatissc/>

(2001). "Appendix A, Early Development" as seen in *Stem Cells: Scientific Progress and Future Research Directions*. National Institutes of Health. Washington DC. This site contains a number of figures and diagrams that depict fertilization, implantation, embryogenesis, and genomic imprinting. <http://stemcells.nih.gov/info/scireport/appendixa.pdf>