

Activity 3: Communications in the Stem Cell Research Community

Assignment 2: Writing a Review Article

Scientific communications are tailored to specific audiences, such as students, laypersons, or other scientists. Information can be conveyed via textbooks, scientific research literature, or oral presentations. One of the most challenging types of communication is the review article. A review article must attract and maintain 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, giving the non-expert an overview of recent advances, setbacks, and controversies.

These review articles, referred to as the “secondary literature,” compile information from a series of research articles. Collectively, the research articles document the incremental process of scientific discovery and present alternative points of view and are referred to as the “primary literature.” Each of the articles in this assignment contains a good deal of highly specific scientific language, because they are tailored for stem cell researchers. 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.

Though the review article is an important part of communication within the scientific community, it serves those outside of the community as well. When targeting the general public, the review article might take the shape of a feature story, incorporating social, ethical, and political perspectives. The feature story might also move away from more technical language and provide more background than a science review article.

This assignment asks students to read a number of primary research articles, address a set of questions, and write a review article. Since the stem cell research field is large, the research articles have been categorized and may focus on just one aspect of the field, such as seminal work, stem cell characterization, clinical applications, cell plasticity, and/or cell differentiation. 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*. To help you get started, a few review articles have been assigned. But as the field is always moving forward, they provide only a glimpse of the field at a particular point and time. Your task here is to write an up-to-date review. Please note that various textbook chapters may help you decipher the research articles, and additional web sites are also listed as resources. When beginning research in an unfamiliar field of biology, it is useful to start with review articles and textbooks to gain a sense of the larger issues and historical background.

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

Activity 3: Communications in the Stem Cell Research Community

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. It is important for you to become part of this discussion.

Instructions

1. Read the assigned text section, review articles, and primary research articles listed below. Your instructor may choose to assign a few or only one category (suggestions for textbook readings 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 these papers and understand the relationships between the figures, tables, and text.
3. The following questions should be used to guide your writing of the review article:
 - The articles below demonstrate that embryonic stem cells are capable of adopting cell fates that represent those arising from the three primordial germ layers. What concerns do researchers in the field have about the accuracy of these studies? In terms of clinical applications, why must we proceed with caution?
 - There appear to be two schools of thought about adult stem cell plasticity: those who believe that adult stem cells can be reprogrammed to adopt very different cell fates and those that believe that the encouraging results are due to fusion events occurring between adult stem cells and feeder cells. Provide evidence that supports each view.
 - Which experimental methods were used to better understand stem cell biology? Were these experiments conducted *in vivo* or *in vitro*. Which of these do you feel need to be explored further?
 - How do these findings affect future methodologies in this field and potential clinical applications?
 - How do genetics and cell biology work together to establish “stemness?”
4. Using **Resource Six: Self-assessment of Writing**, write a review article using a “News and Views” *Nature* format or a “Perspectives” *Science* format. Be sure that your review does the following:
 - Reviews the current state of research in this area.
 - Provides biological and historical significance for the data presented in the primary literature.
 - Makes the distinction between experiments that are purely biochemical and those that are more functionally relevant such as transplantation assays.
 - Clearly distinguishes which results are convincing and which are not, providing reasoning.
 - Use persuasive language and data to indicate which studies you find more convincing or conclusive.

Activity 3: Communications in the Stem Cell Research Community

- Points to future directions of basic science research and application to society
 - Contains citations and a bibliography.
5. You may be asked to exchange this review article with a peer and critique one another's work. Even if you are not asked by your instructor to do this, it is a common practice in writing and in science to obtain feedback from others in the field before completing a final draft. If you are required or interested in peer-review, use **Resource Five: Peer-assessment of Writing**.
 6. Submit your review for a grade.

Readings

Review Articles

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. 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>
4. 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>.
5. 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.
6. 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>.
7. 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.

Activity 3: Communications in the Stem Cell Research Community

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.
<http://pippo.catchword.com/vl=2912331/cl=23/nw=1/rpsv/catchword/mal/15248909/v2n5/s5/p25>
5. 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.
6. 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*.
7. 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

8. Gussoni et al. (1999). "Dystrophin expression in the mdx mouse restored by stem cell transplantation." *Nature* 401(6751): 390-394.
9. Seale et al. (2000). "Pax7 is required for the specification of myogenic satellite cells." *Cell* 102 (6): 777-786.
10. 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

11. 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 (review article, Vogel, G. (2002) "Rat Brains Respond to Embryonic Stem Cells." *Science* 295(5553): 254-55.).

Signaling Factors and Differentiation

12. 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

13. Bjornson et al. (1999). "Turning brain into blood: A hematopoietic fate adopted by adult neural stem cells *in vivo*." *Science* 283 (5401): 534-6.

Activity 3: Communications in the Stem Cell Research Community

14. Terada, N., et al., (2002) "Bone marrow cells adopt the phenotype of other cells by spontaneous cell fusion." *Nature* 416(6880): 542-45.
15. Ying, Q. et al. (2002) "Bone marrow cells adopt the phenotype of other cells by spontaneous fusion." *Nature* 416(6880): 545-548.
16. 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>
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 Applications 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.

Activity 3: Communications in the Stem Cell Research Community

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

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 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.

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>