IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

DR. JAMES L. SHERLEY, et al.,	Plaintiffs,	
v.		Civil Action No. 09-CV-01575-RCL
KATHLEEN SEBELIUS, et al.,	Defendants.	

DECLARATION OF DR. JAMES SHERLEY
IN SUPPORT OF PLAINTIFFS' COMBINED REPLY IN SUPPORT OF SUMMARY JUDGMENT, OPPOSITION TO DEFENDANTS' MOTION FOR SUMMARY JUDGMENT, AND RESPONSE TO AMICI CURAIE

I, Dr. James L. Sherley, declare as follows:

1. I am a plaintiff in this action, and I am over the age of eighteen and competent to testify. I am knowledgeable about the facts set forth herein, and make this declaration in support of Plaintiffs' Reply in Support of Motion for Summary Judgment, Opposition to Defendants' Motion for Summary Judgment, and Response to Amici Curaie.

2. I have experienced increased competition as a result of the NIH Guidelines because the adult stem cell research that I conduct is in direct competition with human

embryonic stem cell research ("hESCr"). As an example, two of my recently submitted applications overlap substantially, in terms of goals and hoped-for achievements, with hESCr, making hESCr a uniquely substantial competitor for the NIH funds I seek. The research reflected in my grant application 1DP1OD008154-01, Pioneering Bioengineered Streaming Cell Tissue Bioreactors, submitted September 8, 2010, is in competition with hESCr scientists who think they can make mature human liver cells for use in drug evaluations and transplantation therapies. Given the present state of scientific knowledge, stem cells are the most likely source for producing such liver cells, so it is inevitable that my grant application will be in competition with hESCr grant applications. Similarly, my grant application GRANT10709545, Engineered Stem Cell Transplantation for Diabetes, submitted October 5, 2010, will inevitably be in competition with grant applications from hESCr scientists who think they can make pancreatic beta cells from hESCs. These two applications are merely examples of the cross-over between adult stem cell and hESC research, and illustrate the increased competition that now exists as a result of the NIH Guidelines.

3. I have experienced concrete harm as a direct result of the implementation of the NIH Guidelines. For example, I have had four adult stem cell research grant applications go unscored since the Guidelines were implemented. During this period, my success rate was significantly lower than my earlier above-average success rate. The first unscored application was an investigator-initiated R01 (1R01CA144018-01A1; 6/10/09, not scored). I appealed the decision without success during the period after the Guidelines were instituted. NCI Council did not provide me the courtesy of a decision on the appeal. In fact, they gave me no answer at all, leaving me in limbo. Subsequently, I have submitted a revised application and am awaiting review. The second was an investigator-initiated R01 (1R01DK087986-01; 10/5/09, not scored).

The third was an investigator-initiated R01 for the ARRA funding (1RC1CA146089-01; 7/20/09, not scored). Fourth, the program project grant for which I was the Principal Investigator was not scored. In addition, the application I co-submitted on April 5, 2010 received an unfundable score. The shared instrumentation grant for which I did receive funding included ten other Boston Biomedical Research Institute investigators, with only one other adult stem cell research project included.

4. As a result of the increased competition and direct harm I have experienced due to the NIH Guidelines, I have had to alter my practices regarding applications for NIH funding. For instance, I have submitted more grant applications than ever before in my career: Currently, I have four NIH grant applications pending, two foundation grant applications pending, and I am submitting a fifth NIH grant application to meet an October 27th deadline. In all of my applications to NIH, moreover, I must make a concerted effort to minimize the harmful impact of NIH's misperception that embryonic stem cell research is preferable to adult stem cell research (a perception that is shown by, among other things, the Guidelines themselves and the efforts of NIH Director Collins and NINDS Director Landis in their declarations to exaggerate the accomplishments and promise of embryonic stem cell research while downplaying the accomplishments and promise of adult stem cell research).

5. Defendants continue to mischaracterize the scientific literature and facts regarding embryonic and adult stem cell research. For example, Defendants cite a single small study regarding generation of "Natural Killer, or 'NK' cells, a kind of white blood cell that destroys cancer, [which] found that the hESC-derived cells were better at destroying leukemia than cells derived from another type of stem cells." (Mem. in Support of Defs.' Mot. for Summ. J. & in Opp'n to Pls.' Mot. for Summ. J. ("Defs.' Mem. & Opp.") at 4–5.) What Defendants fail to

mention is that the other type of stem cells used for comparison—umbilical cord blood stem cells—were not purified before use, in contrast to the purified hESC-derived cells. Defendants further fail to mention that the study was halted after only a few weeks, making it impossible to assess the tumor-forming ability of the hESC-derived cells. In addition, Defendants neglect to mention that the test was done on only a few immune-deficient mice in order to overcome the natural immune reaction to hESC cells, a problem that the published paper and its authors admit.[1]

6. The Landis Declaration cites the NK study as evidence that hESC are supposedly superior to non-embryonic stem cells, including induced pluripotent stem cells ("iPSC"), for research purposes. (Declaration of Story Landis ("Landis Decl.") ¶ 21). Unfortunately, the Landis Declaration fails to mention the limitation of hESCr posed by the likelihood of immune rejection, a limitation pointed out by the study's authors. The authors also note the potential of iPSC to circumvent this limitation.[2]

7. Defendants assert that "[r]esearchers have made significant progress in differentiating hESC lines into 'beta cells,' that is, the type of cell in the pancreas that produces insulin," but cite no scientific evidence for that proposition. (Defs.' Mem. & Opp. at 5). Indeed, Defendants' only reference for that assertion is a statement in a public educational pamphlet that

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[1] *See* Deane Morrison, "Researchers derive cancer-killers from human embryonic stem cells," http://www1.umn.edu/news/features/2009/UR_CONTENT_107683.html (last visited Oct. 10, 2010) ("Nevertheless, hESCs present problems as a source of NK cells for clinical use, the researchers say. For one thing, any cells derived from an unrelated donor's hESCs could be eliminated by the patient's immune system."); Woll, et al., "Human embryonic stem cells differentiate into a homogeneous population of natural killer cells with potent in vivo antitumor activity," *Blood* 113, 6094, 6100 (2009) ("hESC's have been proposed as an alternative source of cells for clinical therapy. However, these cells are like other cells used for clinical transplantation, limited by their potential to evoke an allogeneic immune response.").

[2] *See* Woll et al., *Blood* 113 at 6100–01.

contains no scientific citations. (*See id.* (citing *Understanding Stem Cells* at 17)).

8. In fact, contrary to Defendants' assertions, the published scientific literature shows that the best embryonic stem cell experiment for diabetes in mice[3] produced only transient correction of blood glucose levels in the mice, and concludes that embryonic stem cells "possess limited functionality" in this context.[4] The study also notes that "[r]ecipients were sacrificed at 3–4 weeks post-transplantation, because most recipients developed teratomas."[5] Tumor growth in animals receiving even differentiated hESC is a persistent problem, and this problem was observed in experiments in which mice were injected with insulin-secreting cells derived from hESC.[6]

9. In contrast, insulin-secreting cells have been derived from both mouse adult stem cells, which restored normal blood glucose in mice,[7] and human adult stem cells.[8] Furthermore, patients with type I (juvenile) diabetes have achieved insulin-independence using their own adult stem cells. (*See* Comments of Do No Harm, et al. at G-6). Unlike embryonic stem cells, these adult stem cells pose no risk of immune rejection or tumor formation.

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[3] A.S. Boyd, et al., A Comparison of Protocols Used to Generate Insulin-Producing Cell Clusters from Mouse Embryonic Stem Cells, *Stem Cells* 26, 1128–1137 (2008).

[4] *Id.* at 1128.

[5] *Id.* at 1134.

[6] E. Kroon, et al., "Pancreatic endoderm derived from human embryonic stem cells generates glucose-responsive insulin-secreting cells in vivo," *Nat. Biotech*. 26, 443–52, (2008).

[7] T. Tayaramma, et al., "Chromatin-Remodeling Factors Allow Differentiation of Bone Marrow Cells into Insulin-Producing Cells," Stem Cells 24, 2858–67 (2006).

[8] L. Denner, et al., "Directed engineering of umbilical cord blood stem cells to produce C-peptide and insulin," Cell Prolif. 40, 367–80 (2007); Y. Li, et al., "Generation of Insulin-Producing Cells From PDX-1 Gene-Modified Human Mesenchymal Stem Cells," Journal of Cellular Physiology 211, 36–44 (2007).

10. Defendants assert that significant progress has been made in turning hESC into dopamine neurons and treating Parkinson's disease in experimental animals. (*See* Defs.' Mem. & Opp. at 5; Landis Decl. ¶ 18). Yet Defendants cite only a single limited study regarding the animal experiment, and fail to mention that the study was only a few weeks in duration and thus incapable of truly assessing the tumor risk posed to the animals. Defendants also fail to cite a similar study in rats that found dopamine neurons derived from hESC resulted in growing clusters of cells in 100% of the rats.[9] The study noted that "the grafts exhibited expanding cores of undifferentiated mitotic neuroepithelial cells, which can be tumorigenic."[10] In layman's terms, the rats were at substantial risk of developing tumors.

11. The Landis Declaration further asserts that dopamine-secreting cells to treat Parkinson's cannot be generated from adult stem cells, stating that "dopamine neurons . . . cannot at this time be obtained from bone marrow." (Landis Decl. ¶ 18). This assertion ignores the substantial scientific literature showing that adult stem cells can indeed form neurons, and specifically dopamine-secreting neurons, including adult stem cells from bone marrow, solid umbilical cord, and nasal olfactory mucosa; in each case the induced neurons produced behavioral recovery in Parkinson's animals.[11] The first published report of a Parkinson's patient treated with his own neural adult stem cells appeared in 2009, noting improvement in symptoms

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[9] N.S. Roy, et al., "Functional engraft of human ES cell-derived dopaminergic neurons enriched by coculture with telomerase immortalized midbrain astrocytes," Nature Medicine 12, 1259–68 (2006).

[10] *Id.*

[11] *See* M. Dezawa, et al., "Specific induction of neuronal cells from bone marrow stromal cells and application for autologous transplantation," Journal of Clinical Investigation 113, 1701–10 (2004); M.L. Weiss, et al., "Human Umbilical Cord Matrix Stem Cells: Preliminary Characterization and Effect of Transplantation in a Rodent Model of Parkinson's Disease," Stem Cells 24, 781–92 (March 2006); W. Murrell, et al., "Olfactory Mucosa Is a Potential Source for Autologous Stem Cell Therapy for Parkinson's Disease," Stem Cells 26, 2183–92 (June 2008). *See also* Comments of Do No Harm, et al. at G-2–G-3.

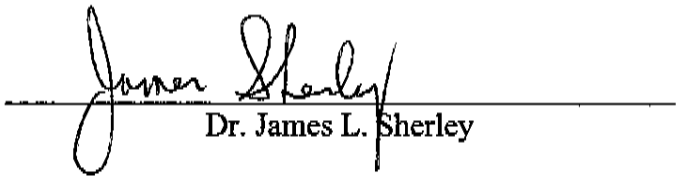
for almost five years.[12] Thus, unlike embryonic stem cells, adult stem cells are actually being used with success in the treatment of individuals suffering from Parkinson's Disease.

12. Defendants also assert that hESC have been used to develop neurons that "may lead to a safe and effective form of treatment for stroke victims," citing a single limited study of short duration in mice. (*See* Memo. & Opp. at 5). But adult stem cells have *already* been shown to be effective in treating strokes by numerous animal studies (*see* Comments of Do No Harm, et al. at G-2) as well as in an early clinical trial (*see id.* at G-7).[13]

13. Attached as Exhibit A is a true and correct copy of a letter from Dr. Kate A. Berg, Deputy Scientific Director of the NCHGR, to Dr. Wendy Fibison of Georgetown University Medical Center, dated October 10, 1996.

14. Attached as Exhibit B is a true and correct copy of *Utah Ethicist Heads Stem Cell Panel*, a Press Release from the University of Utah, dated September 23, 2009.

I declare under penalty of perjury under the laws of the United States that the foregoing is true and correct. Executed on October 13, 2010.



Dr. James L. Sherley

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12 M.F. Lévesque, et al., "Therapeutic Microinjection of Autologous Adult Human Neural Stem Cells and Differentiated Neurons for Parkinson's Disease: Five-Year Post-Operative Outcome," The Open Stem Cell Journal 1, 20–29 (February 2009). *See also* Comments of Do No Harm, et al. at G-8.

13 *See also* Christi Myers, "Houston doctors use stem cells in new way," Apr. 17, 2009, at http://abclocal.go.com/ktrk/story?section=news/health&id=6754833 (last visited Oct. 13, 2010); "Stroke Patient's Own Stem Cells Used In Trial For First Time," ScienceDaily, Apr. 16, 2009, at http://www.sciencedaily.com/releases/2009/04/090415162654.htm (last visited Oct. 13, 2010).