Re: Review of NIH’s “Guidelines for Research Using Human Pluripotent Stem Cells.”

Dear Dr. Kirschstein,

The use of federal funds to support human embryonic stem cell research is illegal, unethical, and unnecessary. On behalf of Do No Harm: The Coalition of Americans for Research Ethics, the purpose of this letter is to advise the agencies reviewing NIH’s “Guidelines for Research Using Human Pluripotent Stem Cells,” 65 Fed. Reg. 51976 (“Guidelines”), of recent scientific developments that further demonstrate the immense potential of stem cell research that does not entail the destruction of human embryos, and of the concomitant absence of any medical need or justification for the federal funding of destructive human embryonic stem cell research.

Since February 22, 2000, the end of the comment period on the draft Guidelines, research using human stem cells not derived from human embryos has confirmed what prior evidence had long suggested: that adult stem cells (and other “post-natal” stem cells) have vast biomedical potential to cure diseases such as diabetes, Parkinson’s, heart disease, and other degenerative diseases. This biomedical potential is as great as or greater than the potential offered by human embryonic stem cell research. Simply stated, adult stem cell research is a preferable alternative for progress in regenerative medicine and cell-based therapies for disease because it does not pose the medical, legal, and ethical problems associated with destructive human embryonic stem cell research.

Among the justifications stated in the Guidelines for pursuing human embryonic stem cell research was the allegedly limited potential of adult stem cells as compared to the purportedly enormous, yet speculative, potential of embryonic stem cells. In particular, NIH’s response to comments urging the benefits of adult stem cell research highlighted four alleged shortcomings...
related to the biomedical potential of adult stem cells. 65 Fed. Reg. 51976. The agency stated that adult stem cells (1) had not been found in all cell types, (2) appear in limited numbers and can be difficult to harvest and grow in time for treatment, (3) are likely to pass on genetic defects, and (4) may not have the capacity to multiply as do “younger cells.” Id. Recent scientific developments now support the contention, however, that these claims about the shortcomings of adult stem cells are not true, are not relevant to their therapeutic potential, and/or overstate the differences between adult stem cells and embryonic stem cells. Significantly, human adult stem cells can be pluripotent and have the ability to transform from one cell type into another, a fact largely unrecognized by the Guidelines. The scientific record now indicates that the supposed shortcomings NIH perceived in adult stem cell research either are illusory or can be overcome.

Moreover, an impressive volume of scientific literature attests to the fact that human adult stem cells -- unlike human embryonic stem cells -- are currently being used successfully in clinical trials to combat many of the very diseases that embryonic stem cells only prospectively promise to treat. Animal research strongly suggests that more therapeutic applications of adult stem cell research will follow.

Finally, the potential biomedical application of human embryonic stem cell research faces risks that are unique to embryonic stem cells, such as the tendency toward tumor formation. In addition, embryonic stem cells face the very real possibility of immune rejection, while use of a patient’s own adult stem cells is free from this problem. Consequently, adult stem cells have several advantages as compared with embryonic stem cells in their practical therapeutic application for tissue regeneration.

Thus, contrary to the suggestions by supporters of destructive human embryonic stem cell research, federal funding of such research is not a necessary, or even a wise, use of limited federal research dollars. Other forms of stem cell research are more promising, are demonstrably more successful at producing beneficial treatments that are actually in use today, and do not present the significant problems and uncertainties (to say nothing of the ethical and legal problems) posed by destructive human embryonic stem cell research.

1. Adult stem cells have been located in numerous cell and tissue types and can be transformed into virtually all cell and tissue types

Although it is true that human adult stem cells have not been found in every cell type, they have been found in many cell and tissue types including, but not limited to: brain (and other nervous system), muscle, retina, pancreas, bone marrow and peripheral blood, cornea, etc.

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can effect transplant-mediated remyelination of demyelinated CNS axons,” 123 Brain 1581 (Aug. 2000) (identifying human “olfactory ensheathing cell,” the cell type which has been used successfully in animals to repair spinal cord damage); C.B. Johansson et al., “Neural stem cells in the adult human brain”; 253 Exp. Cell Res. 733 (Dec. 1999) (discussing different regions in the adult brain in which stem cells have been isolated); see also, C.J. Hodge, Jr. and M. Boakye, “Biological Plasticity: The future of science in neurosurgery,” 48 Neurosurgery 2 (Jan. 2001) (reviewing science regarding the plasticity of neural cells in humans and animals); see generally, App. A, Refs. 106-135 (collecting published papers using non-embryonic neural stem cells from human adults and animals).


5 See e.g., A. A. Kocher et al., “Neovascularization of ischemic myocardium by human bone-marrow-derived angioblasts prevents cardiomyocyte apoptosis, reduces remodeling and improves cardiac function,” 7 Nature Medicine 430 (April 2001) (experiment using bone marrow cells); see generally, App. A, refs. 160-207 (collecting papers using non-embryonic human and animal adult bone marrow and peripheral blood stem cells).

blood vessels (endothelial cells), fat, dental pulp, spermatogonia, and placenta. In essence, where scientists have devoted time and resources to the identification of human adult (and other non-embryonic) stem cell types, they have generally found them.

Moreover, experiments using animals have recently isolated many additional adult stem cell and tissue types, including, but not limited to: skin, liver, and mammary gland. Given the impressive pace of adult stem cell identification in the past few years -- which invariably followed the pattern of (1) identification and isolation of the stem cell in animals, followed by (2) identification and isolation of the stem cell in humans -- the imminent identification and isolation of the human adult stem cells of these cell and tissue types is highly likely.

Even more important than the identification of human adult stem cells in most cell types is the fact that adult stem cells can regenerate healthy tissue and many can transform from one cell type into another. Thus, many types of human adult stem cells -- including stem cells from fat -- exhibit the ability to transform from one tissue type into many others. For example,

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11 Based on press releases from AnthroGen indicating that scientists have isolated stem cells in placenta that have been induced to form bone, nerve, cartilage, bone marrow, muscle, tendon, and blood vessel. This press release is available at <http://www.mcpf.org/AnthroGen%20Discovery.htm>. AnthroGen has also posted articles based on that press release at <http://www.anthrogenesis.com/page411559.htm>.

12 See, e.g., H. Oshima et al., “Morphogenesis and renewal of hair follicles from adult multipotent stem cells,” 104Cell 233 (Jan. 2001) (studies showing that the skin/hair follicle cell is multipotent and can form epidermis, hair follicles, sebaceous glands, and all structures of the hairy skin).

13 See, e.g., N. N. Malouf et al., “Adult-derived stem cells from the liver become myocytes in the heart in vivo,” 158 American Journal of Pathology, 1929 (June 2001); see generally, App. A, refs. 208-213 (collecting papers discussing liver stem cells).

plentiful adult stem cells from fat have been transformed into cartilage, muscle, and bone. Readily accessible human adult bone marrow stem cells have been transformed into smooth muscle, cardiac tissues, neural cells, liver, bone, cartilage, and fat. Human adult neural stem cells have been reprogrammed to form skeletal muscle and have the ability to form all neural types. Human adult stem cells from skeletal muscles can be coaxed into forming skeletal myotubes, smooth muscle, bone, cartilage, and fat. Human adult stem cells from human dental pulp can be induced to differentiate into tooth structures. And stem cells from placenta are reported to have been induced to form bone, nerve, cartilage, bone marrow, muscle, tendon, and blood vessels.

In fact, animal research indicates that adult neural and bone marrow stem cells may be able to generate virtually all adult tissues, including heart, lung, intestine, kidney, liver, nervous system, muscle, and the gastrointestinal tract (including esophagus, stomach, intestine, and

15 See P.A. Zuk et al., supra at n. 8.
21 Id.
22 Id.
24 Pagano, supra at n. 1.
25 Williams, supra at n. 2.
26 S. Gronthos et al., supra at n. 9.
27 See AnthroGen press release, supra at n. 11.
Clarke suggests that “stem cells in different adult tissues may . . . have a developmental repertoire close to that of [embryonic stem] cells.” The recent rapid pace of discovery of adult stem cells for a variety of tissue types, combined with their ability to form many, if not all, adult tissues, suggests that adult stem cells will ultimately be found in or be capable of transforming into every significant tissue type.

In particular, the Guidelines evince concern that no pancreatic or cardiac adult stem cells had been identified. In fact, however, human pancreatic and cardiac stem cells have been identified. Indeed, scientists have actually reversed diabetes in mice using the animal’s own adult pancreatic stem cells. This animal research has led to evidence of adult human pancreatic stem cells, which have been grown in culture and induced to differentiate into insulin-producing cells. In fact, in 1999, well before the NIH published the Guidelines, the NIH was funding research involving insulin-producing adult human pancreatic stem cells. These cells are available for use in potential technologies to reverse diabetes in humans.

Recent evidence also indicates the ability of stem cells to transform into heart cells. Added to the numerous studies done in animals since 1995, these reports indicate that adult stem cells from skeletal muscle, bone marrow, liver, and the heart itself have the capacity to regenerate cardiac tissue and repair heart damage. More recently, new evidence has emerged


29 Clarke et al., supra at n. 28.


31 See references cited in n. 4, supra.

32 See Grant Number 5R21DK57173-02 to Lawrence K. Olson, Michigan State University, “Pluripotent Human Pancreatic Ductal Cells,” Project Start Date, September 30, 1999 (available at NIH website).

suggesting the existence of a human heart stem cell. This research promises potential biomedical application to treat heart disease. In fact, myoblast transplantation has already been used in the first successful clinical application of human adult stem cells for treatment of cardiac damage.

Contrary to the impression created by advocates of destructive human embryonic stem cell research, these results for adult stem cell research are far more promising than any results obtained thus far through embryonic stem cell research. Indeed, researchers have yet to publish any evidence that human pancreatic cells can be generated from human embryonic stem cells, and have yet to show any evidence that human cardiac cells generated from embryonic stem cells in culture can form functional tissue in the body. The case for diverting scarce research dollars away from promising avenues of research and instead into human embryonic stem cell research in order to “cure” diabetes or heart disease is weak indeed.

2. Adult stem cells can be reproduced to create a “virtually limitless” supply

Contrary to the assumptions expressed in the Guidelines, recent scientific evidence indicates the ability of adult stem cells to rapidly expand and implies that adult stem cells can be produced in ample quantities for biomedical applications. To be sure, adult stem cells are present in finite amounts throughout the human body, but the supply of human adult stem cells immediately available is much greater than previously thought. Moreover, the number of available adult stem cells can be expanded greatly in culture. In March of 2000, researchers identified the conditions necessary to allow for a large-scale expansion (a billion-fold in a few weeks) of adult stem cells in culture. Other researchers have confirmed the ability to rapidly

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34 See A. P. Beltrami et al., “Evidence That Human Myocytes Divide After Myocardial Infarction,” 344 New England Journal of Medicine 1750 (June 7, 2001) (research indicating that the adult human heart may have its own stem cell).


and significantly expand the numbers of adult stem cells in culture, so that sufficient numbers of a variety of adult stem cells can be produced for clinical applications.38

Thus, scientific reports make clear that adult stem cells are readily accessible, can create a “virtually limitless” supply, and can even be transformed into other tissue types with use of a simple protocol.39 Indeed, animal studies indicate that a single stem cell is sufficient to repopulate adult bone marrow,40 generate nerves,41 and participate in tissue repair in a variety of tissues throughout the body.

In a nutshell, the arguments for federal funding of destructive human embryonic stem cell research rely on an outdated understanding that markedly underestimates the number of adult stem cells present in an adult human and the efficiency with which those cells can be reproduced. Studies published since the close of the Guidelines’ comment period indicate that there will be no shortage of adult stem cells for clinical use.

3. **The pluripotent nature of adult stem cells alleviates concerns about the difficulty of harvesting neural stem cells from humans**

As discussed above, adult stem cells show great potential to transform from one tissue type into multiple other tissue types. Thus, at least some adult stem cells can be pluripotent in the sense that they can develop into cells and tissues of the three primary germ layers -- the ectoderm, the mesoderm, and the endoderm. For example, as noted above, human adult bone

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39 D. Woodbury, *supra* at n. 18.


marrow stem cells have the capacity to transform into the following tissue types: muscle, cardiac blood vessels, neural cells, liver, bone, cartilage, and fat. See supra, § 1. Animal research suggests that the bone marrow stem cell could transform into virtually all tissue types.42 Such research also indicates that adult neural stem cells have the ability to transform into virtually all tissue types.43

The Guidelines evinced a concern that adult neural stem cells were impracticable in clinical application because neural cells would be difficult to harvest. A finding of pluripotency for adult stem cells would make this and similar concerns irrelevant. If neural stem cells can easily be created from readily accessible adult bone marrow stem cells in human beings,44 it will not matter whether the harvesting of neural cells directly from adult humans would require difficult procedures such as surgery.

Aside from creating neural cells through a transformation of cell type, adult brain cells have also been isolated at locations that are more accessible and safer to harvest.45 Indeed, researchers have determined that human adult neural stem cells can be isolated from cadavers.46 Thus, as with other concerns discussed above, the suggestion that adult stem cell research and clinical applications suffer from a lack of adequate supply is not supported by the available evidence.

4. Treatments using adult stem cells will not be prohibited by risks of “duplicating genetic error”

The Guidelines asserted that adult stem cells are likely to be ineffective at combating genetic diseases because the patient’s own stem cells would likely contain the same genetic error, making cells from the patient inappropriate for transplantation. But evidence from clinical studies to date belies this assertion. The first successful human gene therapy used “remedied” adult stem cells -- not embryonic stem cells -- to cure severe combined immunodeficiency syndrome.47 Not only can genetic error be remedied while adult stem cells are in culture, but in many cases the correction of the genetic defect may not be necessary to effect a cure with adult stem cells. For example, patients with systemic lupus have been treated with their own adult


43 See, e.g., Clarke, supra at 28.

44 See, e.g., D. Woodbury, supra at n. 18.

45 Pagano, supra at n. 1.

46 Palmer, supra at n. 1.

bone marrow stem cells which repaired organ damage that was previously considered permanent. This repair occurred without correcting the genetic defect present in the bone marrow cells.\textsuperscript{48}

In sum, a patient’s genetic deficiency does not preclude the use of his or her own stem cells for therapeutic purposes. In fact, as discussed below, the use of one’s own stem cells is medically and scientifically preferable to the use of embryonic stem cells derived from another human being, because the transplantation of embryonic stem cells may carry with it a severe risk of immune rejection and tumor formation.

5. \textbf{Adult stem cells have been used in many clinical trials with great success}

Contrary to the impression created by advocates of destructive human embryonic stem cell research, the biomedical potential of embryonic stem cells remains entirely speculative, because such cells have never been successfully used in clinical applications with human patients. \textit{See infra}, § 7. By contrast, adult stem cells already have been used in a variety of human clinical trials and applications with considerable success. Indeed, because researchers have found that stem cells in the bone marrow were the chief therapeutic agent in whole marrow transplants, many treatments which previously relied on transplant of unfractionated bone marrow now use transplants of bone marrow stem cells instead. Such treatments include applications for various types of cancer, including but not limited to: brain tumors,\textsuperscript{49} retinoblastoma,\textsuperscript{50} ovarian cancer,\textsuperscript{51} various solid tumors,\textsuperscript{52} testicular cancer,\textsuperscript{53} multiple myeloma and leukemias,\textsuperscript{54} breast cancer,\textsuperscript{55} neuroblastoma,\textsuperscript{56} non-Hodgkin’s lymphoma,\textsuperscript{57} and renal cell carcinoma.\textsuperscript{58} Adult stem cells have also been used in treatment of autoimmune diseases such as multiple sclerosis, systemic lupus, rheumatoid arthritis, and juvenile rheumatoid

\textsuperscript{49} App. A, refs. 1-3.
\textsuperscript{50} \textit{Id.} at refs. 4-5.
\textsuperscript{51} \textit{Id.} at refs. 6-7.
\textsuperscript{52} \textit{Id.} at refs. 8-12.
\textsuperscript{53} \textit{Id.} at refs. 13-14.
\textsuperscript{54} \textit{Id.} at refs. 15-24.
\textsuperscript{55} \textit{Id.} at refs. 25-28.
\textsuperscript{56} \textit{Id.} at ref. 29.
\textsuperscript{57} \textit{Id.} at refs. 30-32.
\textsuperscript{58} \textit{Id.} at refs 33-34.
arthritis, immunodeficiencies and anemias, stroke, and cartilage and bone diseases. Adult stem cells have been used to regenerate corneas, restoring sight to previously blind patients, and also to combat blood and liver diseases. Recently the positive results from the first successful human trials of adult stem cells to treat cardiac damage were published.

Simply stated, adult stem cells are already being used in a wide array of human clinical trials, with many therapeutic applications having moved well beyond the experimental stage. Thus, adult stem cells are presently providing the results only promised by advocates of destructive embryonic stem cell research. There can be little doubt that as we learn more about adult stem cells, they will be even more successfully employed to fight the diseases noted above and to combat other diseases and conditions, such as diabetes and paralysis.

6. Adult stem cells have been used successfully in treatment of numerous animal models of disease

The scientific record provides strong evidence for the conclusion that adult stem cells will be applied to biomedical technologies to treat a host of other human diseases and conditions. Adult and other non-embryonic stem cells have already been used successfully in treatment of various animal models of disease, including nerve and spinal cord damage, retinal damage, Parkinson’s disease, heart damage, muscular dystrophy, diabetes, stroke, and liver

59 Id. at refs. 35-47.
60 Id. at refs. 49-58.
61 Id. at ref. 48.
62 Id. at refs. 60-61.
63 Id. at refs. 62-68.
64 Id. at refs. 69-70.
65 See P. Menasché, supra at n. 35; see generally, App. A, Refs. 72-76 (collecting reports regarding clinical treatment of heart damage using non-embryonic human stem cells).
67 Id. at ref. 130.
68 Id. at ref. 108.
69 Id. at refs. 139-141, 143-144, 150-152, 161-163, 169.
70 Id. at refs. 142, 146, 147.
71 Id. at ref. 159.
72 Id. at refs. 164, 165, 228.
disease. Adult stem cells also appear to possess an ability to “home” to sites of damaged tissue in the body, repairing damaged tissue and even attacking tumors.

There is every reason to believe that these studies will yield positive results in human application as well. As these studies move from animal models to clinical application, adult stem cells will be our best hope for fighting those diseases in the near term.

7. **By contrast, human embryonic stem cells have never successfully been used in clinical trials, have had lackluster success in combating animal models of disease, and carry significant risks, including immune rejection and tumor formation**

Human embryonic stem cells have never been used successfully in clinical trials. Thus, unlike adult stem cells, their biomedical potential is purely speculative. And any speculative clinical use remains a distant hope. Indeed, in contrast to human adult stem cells, human embryonic stem cells have not been successfully coaxed to transform into pure populations of most cell and tissue types, even in treatment of animal models of disease.

Although human embryonic stem cells exhibit impressive plasticity due to their potency, this plasticity has proven to be a double-edged sword, as embryonic stem cells have been difficult to control in laboratories. The inability to successfully control embryonic stem cells in the controlled atmosphere of a laboratory does not suggest that they have a high probability of

73 *Id.* at ref. 211.

74 *Id.* at refs. 111, 142, 160, 164, 171, 172, 228.

75 In fact, these experiments have yielded disastrous results, as implanted embryonic stem cells have literally killed the cells of their host after transplantation. *See, e.g.*, G. Vogel, “Stem Cells: New excitement, persistent questions,” 290 Science 1672 (Dec 1, 2000) (describing an experiment performed at Geron Corp. implanting human embryonic stem cells into rats, where the implanted embryonic stem cells “did not readily differentiate,” and instead caused the neural cells “near them . . . to die”). In stark contrast, experiments in which human adult bone marrow stem cells were injected into rat brains to repair damaged brain tissue -- experiments performed over 3 years ago -- yielded remarkably successful results. *See, e.g.*, S.A. Azizi *et al.*, “Engraftment and migration of human bone marrow stromal cells implanted in the brains of albino rats-similarities to astrocyte grafts,” 95 Proc. Natl. Acad. Sci. USA 3908 (March 1998) (reporting that human bone marrow stromal cells had the ability to repair damaged rat brain tissue without inflammatory response or rejection).

76 *See, e.g.*, M. Schuldiner *et al.*, “Effects of eight growth factors on the differentiation of cells derived from human embryonic stem cells,” 97 Proc. Natl. Acad. Sci. USA 11307 (Oct. 10, 2000) (study using human embryonic stem cells indicated that “none of the eight growth factors tested directs a completely uniform and singular differentiation of cells”); G. Vogel, *supra* at n. 42 (“And so far, reports of pure cell populations derived from either human or mouse ES cells are few and far between -- fewer than those from adult cells.”).
successful use in therapeutic treatments. In contrast, adult stem cells have proven to be relatively easy to control.

Fetal tissue transplants provide a cautionary example of the potential for problems using developmentally-young cells such as embryonic stem cells, which are difficult to direct along specific and controlled developmental pathways. In one instance, fetal tissue derived from early fetuses was transplanted into an individual’s brain, resulting in no viable neurons but instead producing non-specific differentiation into numerous non-brain tissues within the patient’s brain.\textsuperscript{77}

Moreover, in the most extensive controlled study of fetal brain tissue transplantation for Parkinson’s disease, the transplants showed little or no benefit to most patients. Fetal brain tissue was transplanted into the brains of patients to regenerate or replace the cells missing or damaged due to Parkinson’s disease, the theory being that these young cells would take over production of the missing brain chemical dopamine. However, there were horrific results for some patients, with transplanted fetal cells going out of control and producing irreversible and devastating changes in the patients’ brains.\textsuperscript{78}

Significantly, embryonic stem cells also face a substantial risk of immune rejection, similar to the risks present in organ transplantation.\textsuperscript{79} These risks include the rejection of the transplanted tissue, as well as the possibility of the transplant attacking the host, or even forming tumors.\textsuperscript{80} In stark contrast, the re-transplantation of a patient’s own adult stem cells carries with it no risk of immune rejection since the cells are the patient’s own.


\textsuperscript{80} See, e.g., Johns Hopkins Medical Institutions Office of Communications and Public Affairs, “New Lab-Made Stem Cells May Be Key To Transplants,” (Dec. 25, 2000) (quoting embryonic stem-cell researcher Dr. Michael Shamblott as stating, when “coaxing [embryonic [Footnote continued on next page]
Scientists have not developed an effective strategy to combat the problems of tumor formation and immune rejection. Until they do, human embryonic stem cells have no realistic potential to be used for therapeutic purposes.

Indeed, advocates of destructive embryonic stem cell research have recently stated that embryonic stem cell regenerative technologies will, by themselves, be unable to provide effective therapeutic treatments. Instead, they claim, embryonic stem cell technology must be applied to human embryos produced by cloning if it is to achieve biomedical application. The reason is simple: although human embryonic stem cells exhibit tremendous plasticity, they lead to immune rejection. A cloned embryo, however, has the same genetic code as the donor, and thus transplantation of a pluripotent cell from this embryo into its “original” may “avoid complications due to immune response rejection.” Thus, embryonic stem cell research may be merely a tool to understanding how pluripotent cells function, a stepping stone to open the door for what some call “therapeutic cloning.”

But this door is closed, providing further confirmation that the NIH should not waste precious research dollars funding speculative embryonic stem cell research that will never result in effective medical treatments. The Bush Administration has announced its opposition to human cloning for any purpose, including research purposes. If the ultimate goals and

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stem cells] to differentiate -- to form nerve cells and the like -- you risk contaminating the newly differentiated cells with the stem cells. . . . Injected into the body, stem cells can produce tumors”); G. Vogel, “Can Adult Stem Cells Suffice?,” supra at n. 42 (“E[mbryonic ]S[tem] cells have a disturbing ability to form tumors, and researchers aren’t yet sure how to counteract that”).

81 See Okarma, supra at n. 79 (“Somatic cell nuclear transfer [i.e., cloning] is essential if we are to achieve our goals in regenerative medicine.”) (emphasis added).

82 Id.

83 Mr. Okarma explains the process as follows: “Once we fully understand re-programming[, the process of making a differentiated cell a pluripotent cell[,] we will be able to develop specific cells[, using the knowledge that will be acquired from studying embryonic stem cells[,] for transplantation without immune rejection.” Id. Thus, advocates of destructive human embryonic stem cell and cloning research seek to learn technologies from cells created through the destruction of human embryos that then can be applied to technologies using clones -- individuals who will necessarily be destroyed as they are used for research purposes -- all in an attempt to avoid immune rejection and tumor formation, side effects to regenerative therapies that are already avoidable by employing effective autologous transplants using adult stem cells. See, e.g., Azizi, supra at n. 75.

84 Claude Allen, Prepared Witness Testimony before the Subcommittee on Health (hearings regarding H.R. 1644, Human Cloning Prohibition Act of 2001) (June 20, 2001) (speaking on behalf of the administration, stating that “we oppose the use of human somatic cell nuclear
hypothetical applications of human embryonic stem cell research depend on cloning, which is
directly contrary to the position of this Administration, it would be wholly inappropriate -- and
directly contrary to the Administration’s policy on cloning -- to fund embryonic stem cell
research.

Finally, the Guidelines assert that adult stem cells may be more difficult to grow and may
contain more DNA abnormalities than younger, embryonic stem cells. Although these assertions
are of questionable merit, it is important to note that embryonic stem cells in fact suffer from
these defects that the Guidelines attribute to adult stem cells alone.

As demonstrated above, adult stem cells have proven to be relatively easy to grow. See
supra, § 2. In contrast, even proponents of embryonic stem cell research have noted that
embryonic stem cells are “tedious to grow,” and that “simply keeping human embryonic stem
cells alive can be a challenge.”85 Not only is there difficulty in consistently coaxing human
embryonic stem cells to differentiate into the desired cell and tissue type, but there is the more
fundamental problem of keeping embryonic stem cell lines alive.

In addition, embryonic stem cells face the risk of mutation with every successive
generation. Thus, “[c]ells derived from stem cells that have replicated through many generations
will have accumulated mutations and be susceptible to cancer or have decreased viability.”86
The phenomenon of mutation is controlled by the number of divisions a cell line has undergone,
and not its chronological age.87 Thus, an embryonic stem cell line, kept alive in a lab for
successive generations, has an equal or greater chance of exhibiting undesirable characteristics
compared to the adult stem cells harvested from a patient for purposes of autologous
transplantation.

Conclusion: Compared with embryonic stem cells, adult stem cells have at least as
great, if not greater, potential for biomedical application, but without the medical
risks or the ethical controversy

The biomedical potential of adult stem cells is enormous. Adult stem cells have been
used in treatments for diseases such as lupus, renal cell carcinoma, and breast cancer, with
encouraging results. Moreover, animal models using adult stem cell treatments indicate that

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transfer cloning techniques either to assist human reproduction or to develop cell- or tissue-
based therapies,” because cloning “would pose deeply troubling moral and ethical issues for
humankind”).

85 G. Vogel, “Stem cells: New excitement, persistent questions,” supra at n. 75 (quoting Peter
Andrews of University of Sheffield, England).

86 L. Roccanova, P. Ramphal, P. Rappa III, “Mutation in Embryonic Stem Cells,” 292 Science
438 (Apr. 20, 2001).

87 Id. (citing J. Smith, O. M. Pereira-Smith, 273 Science 63).
therapeutic treatments for pernicious diseases such as diabetes, heart disease, and stroke are well within the vast therapeutic capabilities of adult stem cells.

Moreover, science is continuing to discover human adult stem cells for an increasing number of cell and tissue types. Furthermore, studies of the pluripotent nature of human adult stem cells as readily accessible as stem cells from fat or bone marrow are yielding impressive results, and strongly suggest that some adult stem cells have the capacity to transform into all significant cell and tissue types. This transformative power of adult stem cells, unrecognized by the Guidelines, has caused one reviewer to remark that “[r]ecent studies have revealed that much of this remarkable developmental potential of embryonic stem cells is retained by small populations of cells within most tissues in the adult.”

Whereas human adult stem cells continue to surpass the Guidelines’ expectations and amaze observers, embryonic stem cells have yet to live up to their billing as the new fountain of youth. Embryonic stem cells have proven to be difficult to work with, and carry with them significant risks that cast doubt upon their therapeutic viability. Indeed, some now say that human cloning might be necessary if embryonic stem cells could ever have clinical application to human beings -- a result that is directly contrary to the stated policy positions of this Administration. The shortcomings of embryonic stem cells, contrasted with the capability of adult stem cells, have led scientists to conclude that “adult stem cells have several advantages as compared with embryonic stem cells in their practical therapeutic application for tissue regeneration.”

Finally, it is worth noting that the National Bioethics Advisory Commission (“NBAC”), which recommended federally funding research using embryonic stem cells under the assumption that embryonic stem cells “offer greater promise of therapeutic breakthroughs,” noted that “the derivation of stem cells from embryos . . . is justifiable only if no less morally problematic alternatives are available for advancing the research.” There can be little doubt at this time that adult stem cells provide equal, if not greater, potential for biomedical application as compared with embryonic stem cells. Thus, applying NBAC’s own standard, the scientific record indicates that federal funding of destructive human embryonic stem cell research is not

89 See generally, G. Vogel, “Stem cells: New excitement, persistent questions,” supra at n. 75.
justifiable. Indeed, less morally problematic alternatives for advancing the research are available, due to the stunning promise of research using adult stem cells.

Because federal funding of research using human embryonic stem cells is illegal, unethical, and unnecessary, we respectfully urge the NIH and the Department of Health and Human Services to withdraw the Guidelines authorizing such funding.

Sincerely,

Eugene Tarne
Communications Director
Do No Harm: The Coalition of Americans for Research Ethics

Attachment

Cc: President George W. Bush
   Vic President Richard Cheney
   The Hon. Tommy Thompson
   The Hon. John Ashcroft
   The Hon. Sam Brownback
   The Hon. Thad Cochran
   The Hon. Mike DeWine
   The Hon. Bill Frist
   The Hon. Charles Grassley
   The Hon. Orrin Hatch
   The Hon. Trent Lott
   The Hon. John McCain
   The Hon. Don Nickles
   The Hon. Dick Armey
   The Hon. Jim Barcia
   The Hon. Tom DeLay
   The Hon. J. Dennis Hastert
   The Hon. Joseph Pitts
   The Hon. Christopher Smith
   The Hon. Bart Stupak
   The Hon. J.C. Watts
   The Hon. Dave Weldon
ATTACHMENT A

Selected References Documenting the Scientific Developments Related to Research Using Cells Derived From Sources Other Than Embryos

This attachment contains a selected list of references that catalogs many of the scientific developments related to research using stem cells that are derived from sources other than embryos. Most of the sources cited in this reference list are articles published in peer-reviewed scientific and medical J.s. Some are reviews of scientific research. This document is organized by subject area, so some references may appear more than once.
I. **CURRENT CLINICAL APPLICATIONS SUCCESSFULLY USING HUMAN ADULT STEM CELLS TO COMBAT DISEASES AND CONDITIONS**

A. CANCER TREATMENTS

(1). Brain Tumors

**References:**


(2). Retinoblastoma

**References:**
4. Hertzberg, H et al.; “Recurrent disseminated retinoblastoma in a 7-year-old girl treated successfully by high-dose chemotherapy and CD34-selected autologous peripheral blood stem cell transplantation”; Bone Marrow Transplant 27(6), 653-655; March 2001.


(3). Ovarian Cancer

**References:**

(4). Solid Tumors

References:


(5). Testicular Cancer

References:


(6). Multiple Myeloma; Leukemias

References:


18. Bensinger, WJ et al.; “Transplantation of bone marrow as compared with peripheral-bone marrow as compared with peripheral-blood cells from HLA-identical relatives in patients with hematologic cancers”; New England J. of Medicine 344, 175-181; Jan. 18, 2001 (review of new procedures involving stem cell transplantation).


(7). Breast Cancer

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