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President

Nancy Berliner, MD
Chief, Hematology Division
Brigham & Women's Hospital
75 Francis Street
Boston, MA 02115-6110
phone 617-732-5840
fax 617-264-5215
nberliner@partners.org

President-Elect

Hal E. Broxmeyer, PhD
Walther Oncology Center
Indiana University School of Medicine
950 W. Walnut Street, Room 302
Indianapolis, IN 46202
phone 317-274-7510
fax 317-274-7592
hbroxmey@iupui.edu

Vice President

J. Evan Sadler, MD, PhD
Washington University Medical School
660 South Euclid Avenue, Box 8125
Saint Louis, MO 63110-1093
phone 314-362-9029
fax 314-454-3012
esadler@im.wustl.edu

Secretary

Charles S. Abrams, MD
University of Pennsylvania
School of Medicine
421 Curie Boulevard, #912
Philadelphia, PA 19104-6140
phone 215-898-1058
fax 215-573-7400
abrams@mail.med.upenn.edu

Treasurer

Linda J. Burns, MD
Division of Hematology,
Oncology, and Transplantation
University of Minnesota
420 Delaware Street, SE
Mayo MC 286/Room 14-154A Moos Tower
Minneapolis, MN 55455-0341
phone 612-624-8144
fax 612-626-9988
burns019@umn.edu

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Executive Director

Martha L. Liggett, Esq.
American Society of Hematology
1900 M Street, NW, Suite 200
Washington, DC 20036
phone 202-776-0544
fax 202-776-0545
mliggett@hematology.org

NIH Stem Cell Guidelines Working Group
MSC 7997, 9000 Rockville Pike,
Bethesda, Maryland 20892-7997

May 21, 2009

The American Society of Hematology (ASH) appreciates the opportunity to review and provide comments on the National Institutes of Health (NIH) Guidelines for Human Stem Cell Research (Guidelines). ASH represents over 16,000 clinicians and scientists committed to the study and treatment of blood and blood-related diseases such as leukemia, lymphoma, sickle cell disease, anemia and hemophilia. The Society's members have been pioneers in the fields of bone marrow transplantation, gene therapy, and stem cell research.

As an organization of physicians who care for desperately ill patients and scientists devoted to understanding the basic mechanisms of disease and discovering new therapies, ASH is excited about the scientific potential of all avenues of stem cell research, particularly human embryonic and adult stem cells. ASH believes that stem cell research offers a significant degree of promise and hope to the approximately 100 million Americans suffering from deadly and debilitating diseases, including cancer, stroke, heart attack, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, diabetes, and traumatic brain and spinal cord injury. The Society supports federal funding of all avenues of stem cell research performed under NIH federal research guidelines and with appropriate public oversight. At this time, there is sufficient evidence to conclude that research into both embryonic and reprogrammed adult stem cells (induced pluripotent stem cells or iPS cells) is warranted to reach the goal of developing new therapies for patients with devastating diseases.

To this end, ASH applauds the NIH for their efforts to develop guidelines that have the potential to greatly expand the list of human embryonic stem (hES) cell lines that are eligible for federal research funding and provide new opportunities for scientific advancement. However, the Society would like to express some concerns about the current draft of the Guidelines and offer recommendations below.

Recommendation 1: The final Guidelines should clarify the NIH's expectation that other federal agencies that fund human embryonic stem cell research will adopt the same principles.

ASH recommends the NIH to clarify the Summary section of the Guidelines that state that the Guidelines will pertain only to the extramural NIH-funded research to include NIH's expectation that other federal agencies that fund human embryonic stem cell research will adopt the same principles.

Recommendation 2: Federal funds should be allowed for research using all existing human stem cell lines created by following ethical practices at the time they were derived. The derivation and documentation requirements outlined in the final NIH Guidelines should be applied only to hES cell lines generated henceforth.

ASH is concerned that the language of the proposed Guidelines suggests that federal funding will be allowed for research on hES cell lines already in existence only if such cell lines were derived (and the derivation process documented) according to these draft Guidelines (Section II.B). As many of the current hES lines were derived at a time when no such guidelines were available, it is important the NIH recognize that there are many stem cell lines currently in use in research, which were responsibly derived but may not meet all of the specific informed consent criteria in the draft Guidelines, or that the stem cell line owners may not have documentation of all criteria. The Society is concerned that a strict interpretation of the draft Guidelines could result in a situation where potentially no stem cell lines that are currently in use by federal grantees would be eligible for continued federal funding and many ongoing research studies that have been underway for several years will be disrupted. ASH urges the NIH to allow federal funds for research using all existing hES cell lines, provided they were obtained following ethical practices standards of the grantee institution, as defined by the standards defined in 2001.

Those standards are:

- The stem cells must have been derived from an embryo that was created for reproductive purposes;
- The embryo was no longer needed for these purposes;
- Informed consent must have been obtained for the donation of the embryo;
- No financial inducements were provided for donation of the embryo.

The mechanism for providing assurance of adherence to these standards could include the review by the institution's Institutional Review Board (IRB). ASH believes that the IRB assurance of ethical development of stem cell lines is appropriate and sufficient. ASH strongly recommends that all existing ethically-derived hES lines should be "grandfathered" to be eligible for federally-funded research, and the derivation and documentation requirements listed in the final Guidelines should be applied only to hES cell lines generated henceforth.

Recommendation 3: Federal funds should be allowed for research using human stem cell lines derived from sources other than excess IVF embryos, such as somatic cell nuclear transfer (SCNT), parthenogenesis, and embryos created for research purposes.

The Society also believes that the final Guidelines should permit federal funding for human stem cell lines derived from sources other than excess IVF embryos, such as

somatic cell nuclear transfer (SCNT), or parthenogenesis, or embryos created for research purposes. ASH strongly believes that these promising techniques for deriving stem cells have scientific potential, especially for creating patient-specific and disease-specific lines by SCNT and parthenogenesis. Section II.B and IV of the draft Guidelines do not permit federal funding for such lines and ASH strongly urges the NIH to allow federally-funded research on human stem cell lines created in other ways. The lack of stem cell lines created by a variety of methods eligible for federal funding has created roadblocks and slowed medical and scientific progress in an era where patient-specific therapies can be pursued through research on iPS cell lines and lines derived by SCNT and parthenogenesis. ASH firmly believes that with more hES cell lines available for federal funding, new opportunities will become available for scientific advancement. Likewise, with the ability to develop additional embryonic stem cell lines, more investigators will be attracted to careers in stem cell research in the United States. The Society believes that more US researchers using new hES cell lines should ultimately equate to further scientific and medical progress that is beneficial to patients.

Recommendation 4: The NIH should clarify definitions of “donor(s) and individual(s) seeking reproductive services” and their informed consent requirements and protections in Section II.B.

ASH recommends that NIH clarify the definition of *donor(s) and individual(s) seeking reproductive services* whose informed consent is required under section II.B. It is currently unclear whether donors of both gametes from which the embryo was created from are required to provide consent, and, if so, anonymous gamete donors should be exempt from this provision. The donor(s) should also be protected from any outcomes (beneficial or harmful) of potential treatments using hES cells derived from their donated embryo (Section II.B.7.f).

ASH also asks the NIH to clarify informed consent requirement outlined in section II.B.4:

...There was a clear separation between the prospective donor(s)'s decision to create human embryos for reproductive purposes and the prospective donor(s)'s decision to donate human embryos for research purposes.

ASH is concerned that this separation clause will be difficult to document. Furthermore, some donor(s) may seek reproductive services with a dual purpose: to create embryos for intra-uterine transfer and to donate extra embryos for research. ASH suggests deleting this condition.

Recommendation 5: The final Guidelines should include a continuation of NIH-funded registry that will list the human stem cell lines eligible for research using NIH funds.

ASH is concerned that the draft Guidelines do not appear to contain the continuation of a stem cell registry of approved lines. Without such a registry, each institution will be required to review each stem cell line's derivation process and informed consent compliance, regardless of how widely that line is used elsewhere for NIH-funded research. This will create a significant burden on institutions and researchers and slow the pace of potentially life-saving research. ASH urges the NIH to continue to maintain a list of approved hES lines; or, alternatively, the final Guidelines should include some other "safe harbor" provision that does not require each research institution to start from scratch in reviewing a cell line, especially when they have been reviewed by another institution for NIH-funded research. Additionally, the extramural grantees should not be required to re-review the derivation consent process for cell lines being used in the NIH intramural program.

Recommendation 6: The NIH should monitor developments in the area of stem cell research, review and update its Guidelines periodically as the research in this area progresses.

ASH enthusiastically supports the continued development of the field of stem cell research and applauds the NIH in taking an important first step towards achieving this goal. To this end, ASH strongly urges the NIH to monitor scientific developments in the area of stem cell research and update its Guidelines periodically, as stated in the President Obama's March 9, 2009 Executive Order, as this the research progresses.

Thank you for the opportunity to submit these comments. Please contact ASH Scientific Affairs Manager, Ulyana Vjugina, PhD, at (202) 776-0544 or uvjugina@hematology.org for any additional information.

Sincerely,



Nancy Berliner, MD
President