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May 26, 2009

Dr. Raynard S. Kington
NIH Stem Cell Guidelines, MSC 7997
9000 Rockville Pike
Bethesda, Maryland, 20892-7997

Dear Dr. Kington:

On behalf of the Massachusetts Life Sciences Center, and in consultation with the Massachusetts Department of Public Health, I write to comment on the National Institutes of Health Guidelines for Human Stem Cell Research (Guidelines), issued in response to President Obama's Executive Order 13505, *Removing Barriers to Responsible Scientific Research Involving Human Stem Cells*.

We commend NIH for taking this important step towards remediating years of undue restrictions on human embryonic stem cell research. We believe strongly that scientific research and discovery have been seriously slowed since the Bush Administration promulgated its policies in 2001. We are encouraged greatly by President Obama's decision to overturn those policies. However, we believe that the proposed guidelines run the risk of realizing some significant unintended consequences, potentially placing human embryonic stem cell researchers in an even more restrictive environment than they found themselves in prior to March 9th, 2009, when President Obama issued his Executive Order.

Background: The Massachusetts Life Sciences Center ("the Center") is a quasi-public agency of the Commonwealth of Massachusetts, created by the Massachusetts Legislature in June 2006 to promote the life sciences within the state. The Center is the hub of the state's \$1 billion Life Sciences Initiative and is tasked with investing in life sciences research and economic development. This work includes making financial investments in public and private institutions growing life sciences research, development and commercialization as well as building ties among sectors of the Massachusetts life sciences community – including those in the stem cell community.

Our investments include the funding of the Massachusetts Human Stem Cell Bank at the University of Massachusetts Medical School ("the Bank"). The Bank provides the biomedical research community with expertly maintained human ES (hES) and reprogrammed (iPS) cell lines to facilitate studies into the properties and potential

therapeutic applications of pluripotent stem cells. The Bank cultures, characterizes and distributes quality controlled hES and iPS cell lines derived in Massachusetts and beyond. It is a 15,000 square foot facility that contains research and training space for visiting investigators. In addition to federal hES policy, the Bank must comply with state law governing hES research.

On May 31, 2005, Massachusetts amended and clarified its own laws on stem cell research when our Legislature enacted Chapter 27 of the Acts of 2005, An Act Enhancing Regenerative Medicine in the Commonwealth (the “Act”). Specifically, section 1 of the Act added a new chapter to the General Laws, Chapter 111L, which states in its opening section: “It shall be the policy of the commonwealth to actively foster research and therapies in the life sciences and regenerative medicine by permitting research and clinical applications involving the derivation and use of human embryonic stem cells, including research and clinical applications involving somatic cell nuclear transfer, placental and umbilical cord cells and human adult stem cells and other mechanisms to create embryonic stem cells which are consistent with this chapter. It shall further be the policy of the commonwealth to prohibit human reproductive cloning.”

Chapter 111L addresses several other matters related to stem cell research in Massachusetts, including registration of institutions conducting human embryonic stem cell research; human embryonic stem cell research methods that are permitted and those that are prohibited; informed consent protections for individuals undergoing infertility treatment and for individuals donating genetic material and pre-implantation embryos for research; the protection of employees of research institutions performing human embryonic stem cell research; the establishment of a public Institutional Review Board (IRB) at the University of Massachusetts Medical School at Worcester; the establishment of a public bank for the purpose of collecting and storing umbilical cord blood and placental tissue; and the establishment of a Biomedical Research Advisory Council to advise the General Court and the Governor on matters related to stem cell research.

A. Support of Scientifically Worthy Research

As the agency charged with implementing and enforcing Chapter 111L, our Massachusetts Department of Public Health seeks to promote all ethically responsible scientifically worthy research in the Commonwealth. To this end, it has promulgated regulations permitting the creation of embryos for research by stem cell researchers and issued an advisory ruling clarifying that oocyte donors may be reimbursed their direct medical and out-of-pocket costs related to a donation to research. Under Massachusetts law, research and clinical applications involving somatic cell nuclear transfer, and parthenogenesis are considered scientifically worthy research that may be conducted ethically if conducted pursuant to the informed consent requirements of Chapter 111L, which largely track the informed consent principles of the federal

Common Rule. Somatic cell nuclear transfer involves placing patient-specific genetic material from adult cells into eggs that have been cleared of their own genetic material and stimulating the egg to produce embryonic stem cells. As yet, this has not been achieved with human cells and eggs, but such research holds the promise of greater understanding of complex diseases such as Lou Gehrig's, Parkinson's disease and Type 1 diabetes and of issues related to reprogramming and differentiation. Parthenogenic stem cell lines hold similar promise and actually currently exist. Reliable patient-specific stem cell lines derived from these clinical research applications could also lead to the development of cell transplantation therapies without fear of immune rejection.

It is our belief that **NIH should recognize that the derivation of SCNT and parthenogenic lines represent scientifically worthy research. Further, NIH should allow funding for the use of parthenogenic lines and signal that it would support the creation of SCNT lines provided that the materials were procured in accordance with federal and state law at the time of donation, including IRB approval of the donation protocol, and/or conform with the final NIH informed consent standards.**

B. Ethical Standards for Research and Informed Consent

We have heard concern from the research community that existing stem cell lines derived under close scrutiny of oversight bodies and pursuant to national and international guidelines for stem cell research developed after extensive deliberation and consultation will no longer be eligible for federal funding under the detailed informed consent guidelines in the draft Guidelines. For example, the following lines may meet particularly thoughtful self-regulated standards, but may not meet all of the requirements delineated in the proposed Guidelines:

- Eligible lines approved for research use between 2001-2008;
- Eligible lines derived in the United States;
- Eligible lines derived outside the United States;
- Eligible donated blastocysts currently stored in tissue banks.

Federal law (the Common Rule) provides a regulatory framework for protecting research participants. The Common Rule requires institutional review boards ("IRBs") to review and approve the process for obtaining voluntary informed consent from individuals participating in research, including the donation of cells and tissues. Massachusetts researchers, pursuant to Chapter 111L, conduct research under the oversight of expert review bodies, following the principles of informed consent enunciated in the Common Rule. The Common Rule supports ethically responsible and scientifically worthy research by:

- Requiring independent oversight such as through IRBs which have extensive experience reviewing informed consent in the context of human tissue research;
- Ensuring a process for voluntary informed consent including the review of consent procedures performed outside the United States;
- Requiring no undue inducements to donors.

Simply reiterating the informed consent requirements of the Common Rule and acknowledging that existing independent oversight mechanisms such as IRBs are sufficient in the NIH Guidelines, rather than setting new and unique requirements, would support ethically responsible oversight. As you know, informed consent as mandated by the Common Rule includes:

- A statement that the study involves research
- An explanation of the purposes of the research
- The expected duration of the subject's participation
- A description of the procedures to be followed
- Identification of any procedures which are experimental
- A description of any reasonably foreseeable risks or discomforts to the subject
- A description of any benefits to the subject or to others which may reasonably be expected from the research
- A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject
- A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained
- For research involving more than minimal risk, an explanation as to whether any compensation is offered, and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained
- An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject.
- A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits, to which the subject is otherwise entitled.

It is our position that lines derived pursuant to the principles of the Common Rule, under vigorous scrutiny by IRBs and other comprehensive oversight bodies, and adhering to model guidelines of self-regulation designed pursuant to extensive deliberation and public consultation, should be afforded the opportunity to compete for federal funds as ethically derived lines. In absence of such a standard, some of the most heavily used and studied hESC lines, some of

which have been studied for many years both in the US and abroad, will be rendered ineligible for NIH funding.

We truly appreciate the opportunity to comment on these guidelines which are so critical to the furtherance of scientific discovery in the United States. Thank you, in advance, for your consideration of these comments.

Very truly yours,

Susan Windham-Bannister
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