DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892
www.nih.gov

May 14, 2004

The Honorable Diana DeGette
and
The Honorable Michael Castle
House of Representatives
Washington, D.C. 20515

Dear Ms. DeGette and Mr. Castle:

The President asked me to respond to your April 28 letter regarding human embryonic stem cell (hESC) research.

The President and the National Institutes of Health (NIH) share your enthusiasm about the promise that stem cells may offer in treating diseases and disorders. In putting into place his policy in August 2001, the President made clear his intention to "explore the promise and potential of stem cell research without crossing a fundamental moral line." He determined that the policy was predicated on the notion that taxpayer funds should not "sanction or encourage further destruction of human embryos that have at least the potential for life."

Through the President's leadership and the extraordinary efforts of the NIH, we are making good progress in meeting the potential of this exciting new field of science—a field that had not been federally funded prior to the President's historic address to the Nation on August 9, 2001.

As you know, 78 hESC derivations met the criteria established by the President on that date. Although some have been withdrawn or have failed to expand, many lines are currently being used for research into diseases such as diabetes and Parkinson's. Eligible lines are also being used in private sector research and in research using funding from other Federal sources.

Expanding and characterizing cells derived from human embryos is a process that consumes both time and resources. In April 2002, only one line was available. To help make more hESC lines available, the NIH supports "Human Embryonic Stem Cell Research Resource Infrastructure Enhancement Awards" that assist sources of human embryonic stem cells to scale-up and distribute cell lines. To date, NIH has awarded nine infrastructure grants. As a result, hESC providers have made 19 hESC lines widely available for commercial distribution to researchers in this country and abroad. As of February 2004, hESC providers had shipped more than 400 lines to researchers. I

anticipate that more lines may become available in the future, as some are in the early phases of development and have not yet been expanded or characterized to the point where they could be readily distributed to the research community.

In fiscal year 2003, NIH supported 118 research projects that were using hESCs. NIH continues to receive investigator-initiated research grant applications and supports numerous studies using human embryonic stem cells. We have also issued administrative supplements to existing grant awards. These supplements enable experienced researchers in different academic institutions to rapidly extend their ongoing federally supported research to include human embryonic stem cells. This enables scientists to develop their skills working with these difficult-to-use cells and develop some preliminary data—both key steps to future research success.

The NIH Human Embryonic Stem Cell Characterization Unit within NIH's own intramural laboratories is conducting side-by-side analyses to comprehensively determine the properties of cell lines available for shipment to researchers. This will provide researchers with the information they need to select the cell line, or lines, most useful for their specific experiments. In addition to the efforts of the Characterization Unit, the number of intramural NIH laboratories conducting research using human embryonic stem cells has grown from one to nine.

NIH also established and funds three Exploratory Centers for Human Embryonic Stem Cell Research. These Centers will promote multi-disciplinary research on hESCs, improve understanding of the basic biology of stem cells, promote the use of these cells as a model system for studying health and disease, and train scientists to work with stem cells and develop tools for studying them.

In 2002, I established a Stem Cell Task Force within the NIH to continually monitor the state of this rapidly evolving area of science. The purpose of the Task Force is to enable and accelerate the pace of stem cell research by identifying rate-limiting resources and developing initiatives to overcome these barriers to progress. The Task Force seeks the advice of scientific leaders in stem cell research about moving the stem cell research agenda forward and exploring strategies we may pursue to address the needs of the scientific community.

In fiscal year 2003, NIH supported $24.8 million in hESC research. This represents an increase of $14.1 million for hESC, or 132 percent, over fiscal year 2002 spending. We also supported $190.7 million in human non-embryonic stem cell (adult stem cells, including cord blood, placental, bone marrow, etc.) research in fiscal year 2003.

In your letter, you suggest that there are several challenges with regard to the current policy. In particular, you mention the fact that currently only 19 of the 78 eligible lines are available to researchers. To this point, it is important to reiterate that by putting this policy into place, the President opened up an unlimited source of Federal funds for

meritorious research using eligible hESCs. Today, much of the basic research that needs to be done can be and is being supported with Federal funds under the President's policy. In the three years since the President announced his policy, this science has advanced. Yet we still do not know with certainty what we will or will not be able to accomplish with 19 lines or 23 lines or more. And although it is also fair to say that from a purely scientific perspective more cell lines may well speed some areas of hESC research, the President's position is still predicated on his belief that taxpayer funds should not "sanction or encourage further destruction of human embryos that have at least the potential for life."

With regard to your concern about exposure of cells to mouse feeder cells, last year the NIH Stem Cell Task Force and the NIH hESC infrastructure awardees met to discuss whether hESCs grown on human feeder layers could be used more readily and with greater safety than hESCs grown on mouse feeder layers. At that meeting, FDA representatives asserted that cell lines grown on human feeder layers are not necessarily safer for clinical trials than stem cells grown on mouse feeder layers. Either mouse or human feeder layers might harbor pathogens that could be transmitted to the hESCs grown on them. In either case, the FDA would evaluate a proposed clinical investigation prior to such a study proceeding. The FDA's evaluation would include information related to safety issues, such as the characteristics of the stem cells, how the stem cells were derived, the properties of any feeder layer used to propagate the cells, potential contaminants introduced through the media or sera used in culture, and the presence of infectious agents transmitted from feeder layer cells to cultured hESCs. It is important to note that there are living cellular products currently in clinical trials that have been developed using culture techniques that involve living animal cells. Thus, the FDA's regulatory approach does not preclude the development and clinical testing of cellular products from hESC lines grown on either mouse or human feeder layers as long as appropriate safety issues are addressed. Contact with feeder cells is one of many safety considerations that need to be assessed before clinical application of this technology.

With regard to your point about attracting new scientists into this area of research, NIH is taking the lead in the Government's effort to enable scientists to study the biology of hESCs. As is true for any new area of research, progress depends on attracting outstanding scientists to design and perform basic research studies, which may eventually translate into treatment methods. Because the hESC field is at an early stage, there is a shortage of researchers with expertise in this area. This shortage is currently a rate-limiting factor in advancing embryonic stem cell research. Simply growing embryonic stem cells to the state where they can be used for experimentation requires substantial knowledge, training, and experience. To help increase the number of scientists who know how to grow hESCs, NIH is funding five courses to provide research scientists with hands-on experience with hESC culture procedures.

We are is striving to make stem cell research attractive to the most talented research scientists, whose creativity in developing investigator-initiated research will move the

research agenda forward. To this end, NIH is providing opportunities for the scientific community to develop training courses for researchers to acquire the skills needed to culture embryonic stem cells, as well as opportunities to support stem cell research career pathways. Given the complexity of stem cell biology, we are supporting grants that use a multi-disciplinary, multi-investigator team approach to conduct hESC research by way of the exploratory centers I described earlier. In addition to these initiatives, we are stimulating the research field by issuing numerous other announcements for research on all types of stem cells, including embryonic and adult cells, both from animals and humans.

Finally, you suggest that this promising field is moving overseas. I agree that it is essential for the U.S. to maintain its scientific and technological leadership. With regard to stem cell biology, we have been making every effort to monitor international research and can assure you that the U.S. remains a major force in this research area. Many of the major advances in hESC research are emerging from research laboratories in this Country.

The NIH stem cell Web site at http://stemcells.nih.gov is an excellent source of information on stem cell research. It contains links to the NIH hESC Registry, to the NIH Stem Cell Task Force, and to information on stem cell research supported by the NIH. As we learn more, we will ensure that that new information is posted on the Web site in a timely fashion.

Thank you for your continued support for biomedical research. Please let me know if you have further questions.

Sincerely,

Elias A. Zerhouni, M.D.
Director

cc:
All Co-Signatories