

# CAN CONGRESS HELP FULFILL THE PROMISE OF STEM CELL RESEARCH?

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## JOINT HEARING

BEFORE THE

COMMITTEE ON HEALTH, EDUCATION,  
LABOR, AND PENSIONS

AND THE

SUBCOMMITTEE ON LABOR, HEALTH AND HUMAN  
SERVICES, EDUCATION AND RELATED AGENCIES

OF THE

COMMITTEE ON APPROPRIATIONS

UNITED STATES SENATE

ONE HUNDRED TENTH CONGRESS

FIRST SESSION

ON

EXAMINING STEM CELL RESEARCH, FOCUSING ON ONGOING FEDERAL  
SUPPORT OF BOTH EMBRYONIC AND NON-EMBRYONIC STEM CELL  
RESEARCH AND SCIENTIFIC PROGRESS, INCLUDING RECENT FIND-  
INGS ON AMNIOTIC FLUID STEM CELLS

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JANUARY 19, 2007

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Printed for the use of the Committee on Health, Education, Labor, and Pensions



Available via the World Wide Web: <http://www.gpoaccess.gov>

U.S. GOVERNMENT PRINTING OFFICE

32-808 PDF

WASHINGTON : 2007

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# C O N T E N T S

## STATEMENTS

FRIDAY, JANUARY 19, 2007

	Page
Kennedy, Hon. Edward M., Chairman, Committee on Health, Education, Labor, and Pensions, opening statement .....	1
Enzi, Hon. Michael B., a U.S. Senator from the State of Wyoming, opening statement .....	3
Harkin, Hon. Tom, a U.S. Senator from the State of Iowa .....	4
Specter, Hon. Arlen, a U.S. Senator from the State of Pennsylvania .....	6
Landis, Story C., Ph.D., Director, National Institute of Neurological Disorders and Stroke (NINDS), Department of Health and Human Services, Wash- ington, DC .....	7
Prepared statement .....	9
Daley, George Q., M.D., Ph.D., Associate Professor of Pediatrics, Children's Hospital, Boston, MA .....	13
Prepared statement .....	15
Stanford, Lauren, Juvenile Diabetes Patient, Plymouth, MA .....	16
Wagner, John E., Jr., M.D., Professor of Pediatrics, University of Minnesota Medical School, Minneapolis, MN .....	19
Prepared statement .....	21

## ADDITIONAL MATERIAL

Statements, articles, publications, letters, etc.:	
RAND Research Brief .....	35
Letter from David A. Prentice and Gene Tarne with supporting mate- rials .....	51
Response to Questions of Senator Enzi by George Q. Daley, M.D., Ph.D. ..	76
Response to Question of Senator Cochran by George Q. Daley, M.D., Ph.D. ....	77
Response to Questions of Senator Enzi by Lauren Stanford .....	77
Response to Questions of Senator Enzi by John E. Wagner, Jr., M.D. ....	78
Response to Questions of Senator Cochran by John E. Wagner, Jr., M.D. .	79

## **CAN CONGRESS HELP FULFILL THE PROMISE OF STEM CELL RESEARCH?**

**FRIDAY, JANUARY 19, 2007**

U.S. SENATE,  
COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS,  
COMMITTEE ON APPROPRIATIONS,  
SUBCOMMITTEE ON LABOR, HEALTH AND HUMAN SERVICES,  
*Washington, DC.*

The committees met, pursuant to notice, at 9:33 a.m. in Room SD-192, Dirksen Senate Office Building, Hon. Edward Kennedy, presiding.

Present: Senators Kennedy, Harkin, Brown, Lautenberg, Reed, Sanders, Enzi, Specter, Stevens, Isakson, Murkowski, Coburn, Hatch, and Allard.

### **OPENING STATEMENT OF SENATOR KENNEDY**

The CHAIRMAN. Good morning. We'll come to order.

This is a very special day for not only the very important subject that we're considering, stem cell research, but for those of us on these two committees: our Health, Education, Labor, and Pensions Committee, and the Appropriations Committee, which Senator Harkin and Senator Specter are leaders in the Senate and have done an extraordinary job over the period of these years, in terms of giving focus and life to this subject matter. We're all partners, working closely together. We have a great admiration for the leadership that Senator Harkin and Senator Specter have provided in moving us all toward this place where we are today, really on the eve, almost, of Senate consideration of this legislation. And we're enormously grateful to my colleague and friend Senator Enzi, who has been the chairman of our committee, and who is my partner in so many of these health issues and has been a valid and important ally in this undertaking.

So, I'll make a brief comment and ask my colleagues if they would be good enough to say a brief word, and we'll move forward with a very, I think, distinguished panel that can be very helpful in bringing us up to date with the great sense of opportunity about stem cell research.

Today's hearing is really about hope. And hope is what stem cell research brings to millions of Americans who seek cures for cancer, diabetes, spinal cord injury, many other serious conditions—hope for those with Parkinson's disease—the tremors of that disease can be cured; hope that spinal injury—spinal cord injuries can be healed; hope for children with diabetes. The constant worry and

vigilance required to cope with their disease will be a thing of the past.

A week ago, a solid bipartisan majority, in the House of Representatives, voted for hope and new progress in these battles against illness, by approving legislation to unlock the potential of stem cell research. Now the challenge is before the Senate, and we, too, must respond. Many of the Senate's staunchest of supporters of stem cell research are here today. We represent diverse backgrounds and many faiths. We have come to our support of stem cell research by different paths, but we have all concluded that this research is one of the great potential breakthroughs of modern medicine, that it brings the potential of fuller, longer life for countless people who suffer from debilitating diseases.

Many of those who oppose this research are here today, too, and we welcome their perspective. Those who oppose the research do so out of deeply held moral convictions, and we respect their views, even as we differ with them. Today, we'll also hear from the leading scientists about recent advances in stem cell research, their potential to help Americans whose lives have been devastated by disease and injury. Some have suggested these new developments avoid the need for the use of stem cells derived from embryos, and we will hear the scientific community's evaluation of that possibility.

We welcome Dr. Story Landis, who will be the director of the—she is the director of the National Institute of Neurological Diseases and Stroke, as well as Dr. George Daley, of the Children's Hospital in Boston, Dr. George Wagner, the University of Minnesota. All of them are leaders in the field of stem cell research.

But today's hearing is not just a celebration of research, it's a call for change in the search for new cures that have been severely limited by the restrictions that President Bush imposed on stem cell research 6 years ago when he limited the use of funds to the inadequate number of cell lines existing at the time. Last year, President Bush vetoed the bipartisan legislation to end those restrictions and offer the hope of fuller and longer lives to millions of our citizens.

Today, we'll hear of that hope from Lauren Stanford, of Plymouth, Massachusetts. We'll hear of her courage and dignity in the face of diabetes. I was profoundly moved by the letter that she sent me during the stem cell debate, last year, describing her hope that stem cell research might allow her to live a future free of her illness. I'm sure our colleagues on our two committees will welcome the opportunity to hear her words, too.

Lauren is not alone. She joins Nancy Reagan, dozens of Nobel laureates, thousands of scientists, millions of patients across the Nation, in calling for an end to the restrictions that have hobbled the search for new cures. The debates that we have held in recent years have already led many of our colleagues who opposed the research in the past to support it now. It may be too much to hope that President Bush will join those ranks, but if he could be here today to hear the hopes and dreams of patients like Lauren, surely he would have to re-examine his conscience and reconsider the restrictions imposed on the research. Let us all hope that, in a private moment, the President will undertake that re-examination

and signal the acceptance of our new bipartisan stem cell legislation and the hopes of millions of Americans it represents.

Time has come for Congress and the President to join together to unchain the creative energies of America's scientists and allow them to pursue the promise of stem cell research. There could be fewer greater triumphs of bipartisan progress than to have the Stem Cell Research Enhancement Act signed into law.

Senator Harkin.

Senator Enzi.

#### OPENING STATEMENT OF SENATOR ENZI

Senator ENZI. Thank you, Mr. Chairman, for holding this hearing. I want to thank the witnesses for coming.

Throughout the history of our Nation, generations of American scientists have looked for ways to improve human condition and address the problem of disease and afflictions of old age. As they conducted their research, each scientist's work built on the discoveries that preceded it, and the results they achieved over the years have enabled us to live longer, healthier, more productive lives. From time to time, there's a breakthrough, or possible breakthrough, in medical science that has the potential to revolutionize not only our ability to diagnose or treat an affliction, but our basic understanding of how the human body operates. When that occurs, a debate ensues as society attempts to evaluate the new procedure's potential to address the diseases that threaten our health, as well as the ethics of putting the new procedures into practice. Such a possible breakthrough is stem cell research.

At present, its promise and potential for changing the way we view health and disease seems limitless. In theory, stem cells may be capable of doing everything we can possibly imagine, and more. Unfortunately, there's often a wide gap between what's possible in theory and what's practical and possible in the real world. What the future of stem cells will be, no one knows for certain. Still, the possibilities are more than intriguing, and certainly worth an in-depth look.

The research that's been conducted into stem cells so far has been so exciting because of the very nature of these cells. Stem cells have the capacity to renew themselves and then become specialized cells. Most of the cells that are in the body are created and committed to performing a specific function. The stem cell remains on the fence, uncommitted, until given a signal by the body to develop into a specialized cell. We've all heard the saying, "You don't have to be a weatherman to know which way the wind's blowing." As for the research, however, you really do need a strong background in science to understand fully the specifics of stem cell research and its implications for the future.

Fortunately, we're not here to predict the impact stem cells will have on the healthcare system in the years to come, we're here to discuss if it is appropriate to use Federal taxpayer dollars to finance additional work in this area, and there is a big difference. In discussing stem cell today, we're not making a judgment about the science itself; rather, we're considering what science should be supported by Federal taxpayer dollars. We're considering the appropriate political oversight and public fiscal support of the work

of those scientists in manipulating and possibly even destroying the basic building blocks of human life. We're considering if we should pass legislation that will be vetoed by the President or legislation that will move this research field forward. We're reaffirming how we, as a society, view the human embryo and its function. Without question, science must be guided by morality. There have been too many instances, over the course of human history, in which terrible things have been done in the name of science.

In determining how to proceed, we, of course, must consider the promise of stem cell research generally and embryonic stem cell really specifically. But, in considering that promise, we must make it clear that, while stem cells may someday lead to therapeutic advancements for devastating diseases, like Alzheimer's, diabetes, Parkinson's, leukemia, and spinal cord injuries, that that day has not come. We must be careful not to oversell the promise of this research to the American people. While several nonembryonic stem cell therapies are now in practice, every reputable scientist will admit that possible cures or advanced treatment, using embryonic stem cells are many years away. So, while the research provides great hope for millions of Americans, at this point the full benefits have not been realized. They fire our imagination as we consider the possibilities that may or may not come to pass. If we truly trust science, then we should give science a chance to solve the dilemma before we reach the issue of public funding of embryonic stem cell research.

As outlined by the report from the President's Council on Bioethics, and is highlighted again with the recent announcement by Dr. Atala and others, related to amniotic stem cells—researchers are exploring a multitude of different ways by which we can create embryonic-like stem cell lines without harming or destroying embryos. Further, States and private research organizations are already plowing billions of dollars into human embryonic stem cell research that goes beyond the parameters of President Bush's policy. Let those efforts continue while we continue working in Congress to support stem cell research that doesn't involve harming or destroying an embryo, which is something that the vast majority of Americans could support.

Thank you all for coming today. I look forward to the ongoing discussion.

The CHAIRMAN. Thank you very much, Senator Enzi.

And, as I mentioned earlier, Senator Harkin and Senator Specter played a special role in keeping this issue in the forefront here in the Senate, and we work very closely together. We're delighted that we've been able to work so that the members of both committees could hear our excellent witnesses.

Senator Harkin.

#### OPENING STATEMENT OF SENATOR HARKIN

Senator HARKIN. Well, thank you very much, Mr. Chairman. You've been a leader on so many health issues for so many years, and I want to thank you for suggesting that we team up our two committees together on this joint hearing.

This marks the 20th hearing that Senator Specter and I have held on human embryonic stem cells, dating back to December



1998, 1 month after Dr. Jamie Thompson, from the University of Wisconsin, announced that he had isolated them, for the first time ever. Since that time, I've talked to hundreds of patients and their family members about their hopes for this research. I've visited laboratories and talked to scientists. I've heard from ethicists and religious leaders. And every day, I become more and more convinced that we, in Congress, need to do all we can to promote this possible life-saving, life-enhancing research.

Meanwhile, the opponents have become more and more desperate. We saw that earlier this month during the hysteria over Dr. Anthony Atala's new research on amniotic stem cells. Opponents breathlessly claimed that, on the basis of this one paper, embryonic stem cell research should be abandoned, even though Dr. Atala himself completely disagrees with that conclusion. Dr. Atala wrote, "It is essential that National Institutes of Health-funded researchers are able to fully pursue embryonic stem cell research as a complement to research into other forms of stem cells."

That's a direct quote from Dr. Atala.

A few days later, the White House released a 60-page polemic against embryonic stem cell research, in which it touted research by Dr. Kevin Eggan, of Harvard, who testified before our subcommittee last year. Here's what Dr. Eggan wrote in response to that White House report. And Dr. Eggan was just in my office last week to substantiate it further. But here's what Dr. Eggan wrote,

"We are disappointed that the White House Office of Domestic Policy gave us no opportunity to correct the report's clear misrepresentation of our work. On the contrary, we assert that human embryonic stem cells hold great promise to find new treatments and cures for diseases, and we support the Stem Cell Research Enhancement Act."

The House overwhelmingly passed that bill earlier this month, and the Senate will pass it soon. There's no question about that. The only question is what the President will do when the bill reaches his desk. Most people assume that he'll veto it. I'm not so sure.

Earlier this month, White House spokeswoman Jeannie Mamo was quoted in a Gannett news story as saying this about stem cell research,

"The President has said that, after careful and thoughtful deliberation with government and outside experts, there was only one moral line he said he would not cross, and that is that Federal taxpayer dollars should not be used in the destruction of embryos."

Well, this is a very interesting statement, because, if it's true, the President should have no problem signing our bill. S.5 would not allow Federal funding to be used for the destruction of embryos. That's prohibited by what's called the Dickey Amendment, which is included every year in our appropriations bill. Our stem cell bill doesn't have anything to say about the Dickey Amendment. We're only talking about using embryos that are going to be destroyed anyway. Every day, IVF clinics discard embryos that are no longer needed for fertility treatments. All we're asking is to use stem cells from some of those excess embryos for research that would save people's lives. No Federal tax dollars would be used to derive the stem cells. That work would be done using non-Federal funding.

So, either this spokeswoman misrepresented the President's position, in which case, I assume she's been taken out to the woodshed, or the White House just opened the door to signing our bill. And I hope it's the latter. I hope that President Bush will listen to the scientists at NIH and elsewhere, so many Nobel laureates all around this country and around the world, who want this research to proceed. Most important, I hope he'll listen to millions of Americans who suffer from juvenile diabetes and spinal cord injuries and ALS and Parkinson's and cancer, who view this stem cell research as their best hope for a treatment or a cure.

I want to thank all the witnesses who have taken the time to give testimony before us today. We have an outstanding group of scientists, all of whom I've met before at some point over the years. I hadn't met Lauren Stanford until this morning, but I feel like I know her, because Senator Kennedy and I talked about her a lot on the Senate floor last year, and I believe her story helped us pass H.R. 810, and will do so again.

So, again, Mr. Chairman, thank you very much. I look forward to the testimony of our witnesses.

The CHAIRMAN. Senator Specter.

#### OPENING STATEMENT OF SENATOR SPECTER

Senator SPECTER. Thank you, Mr. Chairman.

I believe that we are setting a record here this morning, on a Friday, in the U.S. Senate, to have 13 Senators present for a hearing. I believe that is solid testimony to the importance of this subject, and I believe it signifies a tremendous interest in utilizing Federal funds for embryonic stem cell research.

We found out about stem cells when the scientists told us about them in November 1998, and, within a few days, the appropriations subcommittee held the first hearing, in this room, and this is our 20th hearing. And I believe that sets something of a record, too.

I agree with Senator Kennedy on his call for hope. I would supplement that with a call for political pressure. We are within close range of overriding a presidential veto. Sixty-three Senators voted in favor of use of Federal funds for embryonic stem cell research last year, and we're within shouting distance, in the House, of having enough votes to override a presidential veto.

Sometimes we forget that we live in a representative democracy, and that means that the people decide what the government is going to do. We had a clarion call on that, on the last election, where the American people spoke out on Iraq. I'm not sure that it's been heard in all quarters, but the American people did speak out. And they also spoke out, in a number of States, on the issue of stem cell research. And I believe, if some of the Republican candidates, to put it candidly and bluntly, had been for stem cell research, I'd still be chairman of the Judiciary Committee.

[Laughter.]

Now, it's a very basic matter of fact that there are 400,000 embryos that are frozen, and almost all of them will be thrown away if they're not used. The subcommittee put up \$2 million for an embryo adoption program, and, since that time, only about 100 have been adopted. So, it's a simple matter of either to use them or lose them. If these embryos were going to create life, no one would be

in favor of using them for research. And as Senator Harkin points out, this bill clearly does not allow Federal funding for the destruction of embryos.

We have increased NIH funding on initiatives originating in this room with our subcommittee, raising the funding from \$12 to \$29 billion, and it is scandalous that those funds are not available for embryonic stem cell research. In 1970, President Nixon declared war on cancer, and, had we pursued that war with the same intensity we pursue other wars, cancer would have been cured by now. And, frankly, I'm madder than hell about our failure to prosecute that war. I'm one of the victims of the failure to prosecute that war. I have urged the advocacy groups to organize a million-person march on the Mall loudly enough to be heard in the second floor of the living quarters of the White House. It's close to the Mall. And it is really reprehensible that the National Cancer Institute was cut last year by \$50 million, which goes to the NIH funding issue and the stem cell issue. But I think that, properly organized and with the pressure being put on the Members of Congress who have voted no, and ultimately on the White House, it's a matter of when, not if, we'll be using Federal funds for embryonic stem cell research.

Thank you, Mr. Chairman.

The CHAIRMAN. Thank you very much.

Our first witness, Story Landis, who's the director of the National Institute of Neurological Disorders and Stroke. Dr. Landis has been the director since September 1, 2003, and, as director of NINDS, Dr. Landis oversees an annual budget of a billion and a half dollars and a staff of more than 900 scientists—physicians, scientists, and administrators. The Institute supports research by investigators, public and private institutions across the country, as well as by scientists working in intramural laboratories and branches in Bethesda, Maryland. The Institutes' mission is to reduce the burden—neurological disease, a burden borne by every age group, by every segment of society, by people all over the world.

Ms. Landis, thank you very much for being here.

Ms. LANDIS. Thank you very much—

The CHAIRMAN. We look forward—

Ms. LANDIS [continuing]. For inviting me.

The CHAIRMAN [continuing]. And for your service.

**STATEMENT OF STORY C. LANDIS, PH.D., DIRECTOR, NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE (NINDS), DEPARTMENT OF HEALTH AND HUMAN SERVICES, WASHINGTON, DC**

Ms. LANDIS. Mr. Chairman, Senator Specter, Senator Enzi, and members of the subcommittee, I'm pleased to appear before you today to testify about the science of stem cell research. I look forward to discussing the compelling need to pursue both embryonic and nonembryonic stem cell research and the scientific challenges and progress, including a recently published scientific finding on amniotic-fluid stem cells.

So, both embryonic and nonembryonic stem cells show promise for developing treatments for human diseases and injuries, and at

the present time, we can't predict which type of stem cell will be best for treating a given disease, nor, to be perfectly honest, is it likely that any one type of stem cell will be best for all uses of stem cells. Therefore, NIH should support research on stem cells from both embryonic and other sources.

Now, the most obvious use of stem cells, which has captured the public's attention, is to replace specific types of cells which are damaged by disease or injury, and my written testimony describes recent progress in preclinical animal studies using embryonic stem cells to replace dopamine-producing nerve cells that are lost in Parkinson's, motor neurons, and supporting cells that are damaged in spinal cord injury, and liver cells that are affected by chronic liver diseases.

However, beyond replacing cells or tissue, stem cell biology has many other potential applications. We could, for example, speed drug development by testing potential drugs in cell culture on specific kinds of human cells that are affected by disease, and stem cells represent a source of the necessary cells.

Studies of human embryonic stem cells also yield information about the complex events that occur during human development, including the molecular mechanisms through which these pluripotent cells generate the hundreds and thousands of different kinds of cells that make up the human body. This knowledge will not only help us control stem cells from both embryonic and non-embryonic sources, but also will help us better understand the cause of many diseases, and that, in turn, will lead to more effective treatments.

Finally, another potential application of stem cell biology is to learn how to encourage the stem cells that are present in even the adult human brain to repair damage. And this approach has recently shown promise in animal experiments in Parkinson's disease and also stroke.

But to realize the potential promise, the promise of stem cell biology for treating disease, scientists must learn how to reliably manipulate stem cells to have the characteristics necessary for each of these applications. We have to learn how to control stem cell proliferation to generate sufficient quantities of cells, we have to learn how to control their differentiation, create recipes for specific classes of cells. We also have to enable stem cells to survive after we transplant them, to integrate into the surrounding tissue, and to function for extended periods of time. Finally, we must control stem cell behavior to avoid harming the recipient, whether by generating tumors—and I'm sure this is an issue that will come up—by forming faulty nerve cell connections, or in any other way.

I'd like to speak briefly about amniotic-fluid-derived stem cells. This is a topic that's received a great deal of attention recently.

In a recently published article in *Nature Biotechnology*, Dr. Atala and his colleagues at Wake Forest University described how they isolated and characterized stem cells from the amniotic fluid that cushions the developing fetus in the uterus. This fluid is collected from pregnant women during amniocentesis, when they ask to be tested for a variety of congenital and developmental diseases and disorders.

Now, scientists had previously shown that some of these cells could turn into fat cells, muscle cells, bone cells, and cells of the nervous system, but what Dr. Atala has done is to devise a method to select, from those multiple kinds of cells in the fluid, those cells which have the most stem-cell-like property, and then, also, he has extended our understanding of the kinds of properties of these cells, and what they can turn into.

So, he and his colleagues have demonstrated that amniotic-fluid-derived stem cells could produce several different adult cell types—nerve cells, liver, cells, bone-forming cells—and, in the case of nerve cells, that they make proteins characteristic of nerve cells and that they can be integrated into the nervous system, that they're self-renewing and maintain the normal number of chromosomes. But these cells are not equivalent to pluripotent embryonic stem cells. They have some of the properties, but not all. And, as we've already heard, he has concluded that these cells complement, but do not replace, human embryonic stem cell research.

So, in conclusion, NIH places a very high priority on both embryonic and nonembryonic stem cell research that will be useful for basic, translational, and clinical studies. Science works best when scientists can pursue all avenues of research. And if I could be so presumptuous as to borrow a metaphor that Senator Harkin used in hearings in 1997 on the importance of funding basic science research, if the cure for Parkinson's disease or juvenile diabetes lay behind one of four doors, wouldn't you want the option to open all four doors at once instead of one door? And stem cell research is the same.

Thank you very much.

[The prepared statement of Ms. Landis follows:]

PREPARED STATEMENT OF STORY C. LANDIS, PH.D.

#### OPENING REMARKS

I am pleased to appear before you today to testify about the science of stem cell research. I look forward to discussing ongoing Federal support of both embryonic and nonembryonic stem cell research and scientific progress, including the recently published findings on amniotic-fluid stem cells and other studies raising the possibility that nonembryonic stem cells have similar properties allowing them to differentiate into many different cell types.

#### THE NEED FOR RESEARCH TO EXPLORE THE POTENTIAL OF HUMAN STEM CELLS

Stem cells are cells that can multiply without changing, that is, self-renew, or can differentiate to produce specialized cell types. Stem cells have been derived from both embryonic and nonembryonic tissues, and these cells have different characteristics. Both embryonic and nonembryonic stem cells show potential for developing treatments for human diseases and injuries. Because of this, this Administration in 2001 became the first to fund research on human embryonic as well as adult stem cells. There are many ways in which human stem cells might be used in basic and clinical research. However, only further research will overcome the technical hurdles between the potential of stem cells and the realization of these uses.

The most obvious potential application of human stem cells would be the generation of cells and tissues for cell-based therapies. Stem cells, directed to differentiate into specific cell types, offer the possibility of a renewable source of replacement cells and tissues to treat a number of common diseases and disorders, including Parkinson's disease, spinal cord injury, stroke, burns, heart disease, diabetes, osteoarthritis, and rheumatoid arthritis.

To realize the potential of stem cell-based therapies for pervasive and debilitating diseases, scientists must learn to reliably manipulate stem cells so that they possess the necessary characteristics for successful differentiation, transplantation, and engraftment. Although scientists are making progress, we cannot yet control the dif-

ferentiation of stem cells adequately. To be useful for transplant purposes, stem cells must:

- Proliferate extensively and generate sufficient quantities of specialized cells.
- Differentiate into the desired cell type(s).
- Survive in the recipient after transplant.
- Integrate into the surrounding tissue after transplant.
- Function appropriately for extended periods of time.
- Avoid harming the recipient in any way.

Stem cells have many other potential uses. Studies of human embryonic stem cells, for example, yield information about the complex events that occur during the initial stages of human development. A primary goal of this research is to identify the molecular mechanisms that allow undifferentiated stem cells to differentiate into one of the several hundred different cell types that make up the human body. Scientists know that turning genes on and off is central to this process. A significant challenge for stem cell research is that scientists do not yet fully understand the signals that turn specific genes on and off to influence the differentiation of the stem cell into a specialized cell with a specific function, like a nerve cell. This knowledge not only offers the opportunity to learn how to control stem cells from both embryonic and nonembryonic sources, but also to better understand the cause of a number of serious diseases, including those that affect infants and children, which in turn could lead to new and more effective intervention strategies and treatments.

Among other applications, human stem cells could also be used to speed the development of new drugs. Initially testing thousands of potential drugs on cells in cell culture is potentially far more efficient than testing drugs in live animals. *In vitro* systems are useful in predicting *in vivo* responses and provide the benefits of requiring fewer animals, requiring less test material, and enabling higher throughput. New medications could be tested for safety on the specific types of human cells that are affected in disease by deriving these cells from human stem cell lines. Other kinds of cell lines are already used in this way. Cancer cell lines, for example, are used to screen potential antitumor drugs. The availability of useful stem cell lines could allow drug testing in a wider range of cell types. However, scientists must learn to control the differentiation of stem cells into the specific cell type on which drugs will be tested.

#### FEDERAL FUNDING OF STEM CELL RESEARCH

NIH has acted quickly and aggressively to provide support for this research in accordance with the President's 2001 stem cell policy. Since 2001, NIH has invested nearly \$3 billion on all forms of stem cell research. Within this total, NIH has contributed more than \$130 million in research studying human embryonic stem cells, more than \$1.1 billion on research using human nonembryonic stem cells, nearly \$509 million on nonhuman embryonic, and more than \$1.2 billion on nonhuman nonembryonic stem cells.

Additionally, in fiscal year 2007, it is projected that NIH will spend more than \$30 million on human embryonic stem cell research and about \$200 million on human nonembryonic stem cell research, while also investing nearly \$100 million on nonhuman embryonic stem cell research and more than \$270 million on nonhuman nonembryonic stem cell research.

In addition to this ample support, NIH has encouraged stem cell research through the establishment of an NIH Stem Cell Task Force, a Stem Cell Information Web Site, an Embryonic Stem Cell Characterization Unit, training courses in the culturing of human embryonic stem cells, support for multidisciplinary teams of stem cell investigators, and a National Stem Cell Bank and Centers of Excellence in Translational Human Stem Cell Research, as well as through extensive investigator initiated research. NIH determined that access to hESC lines listed on the NIH Stem Cell Registry and the lack of trained scientists with the ability to culture hESCs were obstacles to moving this field of research forward. To remove these potential barriers, the National Stem Cell Bank and the providers on the NIH Stem Cell Registry together have currently made over 700 shipments of the hESC cell lines that are eligible for Federal funding, as posted on the NIH Stem Cell Registry Web site. In addition, the NIH-supported hESC training courses have taught over 200 scientists the techniques necessary to culture these cells. We plan to continue to aggressively fund this exciting area of science.

NIH-supported scientists have developed efficient techniques to derive dopamine-producing nerve cells from human embryonic stem cells. The loss of dopamine-producing nerve cells is responsible for the movement problems of Parkinson's disease. When grafted into the brain of a rat model for Parkinson's disease, the stem

cell-derived dopamine cells significantly improved the animals' movement. However, after 3 months of transplantation, the scientists found that treated rats' brains contained groups of undifferentiated cells that had become tumors. (*Nature Medicine* 12:1259–1268, laboratory of S. Goldman). This had not been observed in other studies that transplanted neural stem cells and emphasizes the need for scientists to learn to better regulate cell division in transplanted pluripotent stem cells, whatever the source, before they may serve as a renewable source of replacement dopamine-producing nerve cells to treat Parkinson's disease in humans. These results demonstrate both the potential and the challenge of stem cell research.

In recent years, NIH-supported scientists have demonstrated that even the adult human brain can generate new nerve cells. Studies focused on encouraging the innate potential of stem cells that are normally present in the adult brain are another avenue of research that has also shown potential for treating Parkinson's disease. In recent experiments, researchers used drugs to activate adult stem cells in the brains of adult rats with experimental Parkinson's disease, which increased the proliferation of replacement cells and improved movement (*The Journal of Neuroscience* 26:7272–7280, laboratory of C. Eckman).

Currently, scientists are also using stem cells from a variety of sources to help animals with spinal cord injuries regain movement. Human embryonic stem cells have been coaxed into becoming a type of cell that repaired damaged nerve fiber insulation called myelin (*The Journal of Neuroscience* 25:4694–4705, laboratory of H.S. Keirstead). Human nonembryonic-neural stem cells helped replace damaged rat spinal cord nerve cells and myelin (*Proceedings of the National Academy of Sciences of the USA* 102:14069–14074, laboratory of A.J. Anderson). NIH-supported scientists now report that they can use mouse embryonic stem cells to make functional motor neurons, which are the spinal cord cells that send long nerve fibers called axons (the threadlike extensions on a neuron, or nerve cell, which conducts nerve impulses) to connect with leg muscles and other muscles used to move the body. The scientists combined several methods to coax the mouse embryonic stem cells to become motor neurons, to overcome molecules that restrain axon growth in adults, and to attract the motor neuron axons to the correct muscles. Previously paralyzed rats treated with the motor neurons were able to move their legs again, although they could not walk or grip with their feet as well as uninjured rats. This research gives scientists insight on how they might one day replace human motor neurons damaged by spinal cord injuries and motor neuron diseases such as Lou Gehrig's disease (amyotrophic lateral sclerosis, or ALS) and spinal muscular atrophies. (*Annals of Neurology* 60(1):32–44, laboratory of D. Kerr)

Japanese and NIH-funded scientists used mouse embryonic stem cells to make liver-like cells to create an implantable bioartificial liver. Chronic liver diseases such as cirrhosis and hepatitis affect 25 million Americans and scientists hope to overcome the shortage of organs available for transplants by using liver cells derived from stem cells to replace lost liver function. This implanted device uses liver cells to replace some liver function. Ninety percent of mice with liver failure that were implanted with the bioartificial liver survived at least three times longer than the untreated mice. If scientists can repeat these results with liver cells made from human stem cells, the technique offers potential both to individuals born with liver problems and to those who develop liver disease later in life. (*Nature Biotechnology* 24:1412–1419, laboratory of I. Fox).

#### AMNIOTIC-FLUID-DERIVED STEM CELLS

As you all know, there has been much interest in the recently published article in *Nature Biotechnology* by Dr. Anthony Atala and colleagues at Wake Forest University regarding stem cells isolated from the amniotic fluid that cushions the developing fetus in the uterus. Amniotic fluid is collected from pregnant women during amniocentesis to test for a variety of congenital and developmental diseases and disorders. Scientists have previously reported that some of these cells can differentiate into fat, muscle, bone, and nerve cells. Dr. Atala's work extends our knowledge of the properties of these amniotic-fluid-derived stem cells (AFS).

Dr. Atala and colleagues showed that AFS could produce cells that originate from each of the three embryonic germ layers that give rise to all of the cells in the body. More specifically, the scientists were able to develop in vitro conditions that produced nerve cells, liver cells, and bone-forming cells from AFS. The AFS-derived human nerve cells were able to make proteins typical of specialized nerve cells and were able to integrate into a mouse brain and survive for at least 2 months, although it is not yet clear whether these cells have all the properties of normal neurons. They also showed that AFS cells were also self renewing and maintained the normal number of chromosomes after a long time in culture over many cell divi-

sions. However, undifferentiated AFS did not make all of the proteins expected in embryonic stem cells, and they were not shown to form a teratoma (a germ cell tumor), one of the essential characteristics of embryonic stem cells. Thus, given the characteristics of AFS, scientists conclude that these cells may be multipotent rather than pluripotent. Although scientists do not yet know how many different cell types AFS are capable of generating, banked AFS may one day enable the generation of tissue-matched cells for transplantation into humans.

#### CONCLUSION

Since 2001, NIH has aggressively pursued research using embryonic and non-embryonic stem cells that will be useful for basic, translational, and clinical studies. We are continuing to move this research forward through training programs, the establishment of the NIH stem cell characterization unit, and the many grants that have been made to scientists to explore stem cell research. With NIH support, scientists have already made remarkable progress in understanding human embryonic stem cells, and we will provide continued support for these research efforts, consistent with Administration policy.

I will be more than happy to answer any questions.

The CHAIRMAN. Thank you very much.

I'm going to ask if you'd be joined by George Daley, who's the associate professor at Harvard Medical School, President-elect of the International Society of Stem Cell Research; Lauren Stanford, to join you—Lauren Stanford, who has courageously fought juvenile diabetes and her letter has moved the entire Senate; and Dr. John Wagner, who's a professor of pediatrics, University of Minnesota, an internationally respected researcher—stem cells. And we'll hear from them, and then have the questions from the committees—for any of our panelists.

We'll start with Dr. Daley, if you'd be good enough—please——

Dr. DALEY. Thank you.

The CHAIRMAN [continuing]. Welcome, from Boston.

Dr. DALEY. Thank you, Senator Kennedy. I appreciate the opportunity to speak here. I was given the instructions that I could not read my testimony, so I will not.

The CHAIRMAN. That's right.

Dr. DALEY. I just have some notes.

The CHAIRMAN. Well, we're trying something—there are a lot of people around that come up here and don't know a great deal about it, and they spend a lot of time reading long dissertations on it that are rather dull and——

Dr. DALEY. Yeah.

The CHAIRMAN [continuing]. Not terribly informational.

[Laughter.]

Dr. DALEY. I——

The CHAIRMAN. And our staffs could work out of that, so——

Dr. DALEY [continuing]. I'm worried——

The CHAIRMAN [continuing]. We have a rule on our committee——

Dr. DALEY. I'm certainly worried about being dull.

The CHAIRMAN [continuing]. That unless you can speak on your subject for 5 minutes, we're not going to spend the time. If you want to file other statements—but that is not——

Dr. DALEY. Thank you.

The CHAIRMAN [continuing]. Guidance for any—we have a brilliant panel here.

[Laughter.]

And some of us have read extensively about your works, and——



Dr. DALEY. Well——

The CHAIRMAN [continuing]. Are enormously grateful. I just——

Dr. DALEY [continuing]. At the risk of being dull——

The CHAIRMAN. Well, I'd divert you for 1 minute. I do have to mention about getting testimony in on time. We are really going to try and do this. It makes a great deal of difference to our ability to prepare. And, in this instance, some of the material didn't get in until 8:30 last evening, and we were in, ourselves, late. We're really going to insist on that for our hearings in the future, and we are going to let people know, in the future, that we are going to insist on it.

But I thank all of you. It was basically the NIH, and—I've been around here long enough—it isn't NIH, it's OMB clearing NIH, so I—we know who the culprits are. So——

[Laughter.]

Culprits be warned.

Dr. Daley——

Dr. DALEY. OK.

The CHAIRMAN [continuing]. Carry on, please.

Dr. DALEY. Thank you very much.

**STATEMENT OF GEORGE Q. DALEY, M.D., PH.D., ASSOCIATE  
PROFESSOR OF PEDIATRICS, CHILDREN'S HOSPITAL,  
BOSTON, MA**

Dr. DALEY. As you said, I'm here as a physician scientist from Children's Hospital, Harvard Stem Cell Institute. I am the President-elect of the International Society for Stem Cell Research, and I'm here representing the American Society of Cell Biology, whose 10,000 members include some of the world's leading stem cell scientists.

And I was asked to make some comments that would be pertinent to the current aspects of the stem cell debate, and to reinforce the need for expanded funding for embryonic stem cell research.

The media has covered a remarkable array of supposed breakthroughs over the last many years that purport to announce cells that could replace the need for embryonic stem cells in research. A number of years ago, it was the multipotential adult progenitor cell from Catherine Verfaillie's lab in Minnesota; we'll hear more about that in the coming days. Then it was the fat stem cell, and clearly there's a lot of fat stem cells around. And then it was umbilical-cord-blood stem cells, and then testis stem cells, and, only more recently, the amniotic-fluid stem cells. These are all fascinating and important tools for research, but none of them are embryonic stem cells.

Stem cells, in fact, I want to point out, is really a category of cells, and the term "stem cells" is inexact. And it's really more akin to the term "seeds." We appreciate that not all seeds are alike. An apple seed makes apple trees, an orange seed makes orange seeds. And when we talk about apples and oranges, we don't get them confused. Well, the distinctions between seeds are essential to the biologist, just as the distinctions among different stem cell types are essential. And yet, in the public debate, I think, we lose the

sense of refinement about what different types of stem cells actually are.

So, after many years of competing claims, embryonic stem cells remain the most versatile stem cell, they remain the gold standard of this fascinating biological concept of pluripotency. And, after 20 years of research in the mouse, we know that embryonic stem cells can make any cell type in the body. Routinely, in my laboratory, we move from an embryonic stem cell in a petri dish to an entire mouse within a month. Those cells, we know, can make every cell type.

So, embryonic stem cells have unique properties, and they will fulfill a unique purpose in research, a purpose that, I would argue, will not be replaced by all of these other types of stem cells. As was pointed out by Dr. Landis, human embryonic stem cells are important tools for basic research. We spend an enormous amount of time talking about their therapeutic value. All of the different stem cell types will have, we hope, 1 day, therapeutic value. But unique aspects of embryonic stem cells pertain to their ability to model the earliest steps of human development. If you really want to understand the genetic regulation and the diseases that set in during those first few days of human development, then studying amniotic-fluid stem cells and fat stem cells will not get you to those answers. Embryonic stem cells, therefore, are unique.

Now, it's often said, by opponents of embryonic stem cell research, that embryonic stem cells have never yielded a treatment, have never cured a patient. And that's true, but I think it's a patently unfair criticism, because human embryonic stem cells have only been around for 9 years. Actually, in the last year, if you just look at the medical literature, human embryonic stem cells have been used to generate a whole variety of human cell types—blood cells, heart muscle cells, nerve cells, and many, many more. So, they're beginning to yield their fruits in basic research, and I think it's only a matter of time before we see an impact on therapy. But to criticize embryonic stem cell value for medical research is to trivialize the enormous contribution of mouse ES cells for the past 20 years.

Scientists have generated literally thousands of strains of knockout mice, which all derive from mouse embryonic stem cells. And these have been used to model human cancer, neurodegenerative disease. And, just a few years ago, there was a publication that reported that knockout mouse strains validate the targets of the hundred best selling drugs. So, where it's true that human embryonic stem cells have not yet yielded cures in the form of cell therapy, I think it's clear that embryonic stem cells have already had a revolutionary effect on biology, and they have saved lives—not directly, through cell replacement, but indirectly, through insights into disease and the development of drugs.

So, I want to close by saying that I believe there are no credible scientific arguments which say that we should be studying adult stem cells at the exclusion of embryonic stem cells. And I'm looking forward to answering questions pertaining to those issues. We must promote embryonic stem cell research and adult stem cell research with equal vigor. And Senate passage of S.5 would be a very healthy start.

Thank you very much.  
 [The prepared statement of Dr. Daley follows:]

PREPARED STATEMENT OF GEORGE Q. DALEY, M.D., PH.D.

My name is Dr. George Q. Daley and I'd like to begin by thanking the members of the committee for inviting me here today. I believe passionately in the scientific value of stem cell research, and I am eager to present my views to the committee.

I am an Associate Professor at the Harvard Medical School based at the Boston Children's Hospital. I am Associate Director of the Children's Hospital Stem Cell Program and a founding member of the Harvard Stem Cell Institute. I serve on the Public Policy committee of the American Society for Cell Biology, which represents over 10,000 scientists, and I am President-Elect of the International Society for Stem Cell Research, the world's leading organization of stem cell scientists, which has grown to over 2,500 members in just over 4 years.

As a practicing physician-scientist, I run a busy research laboratory at the Children's Hospital, where we study adult stem cells of the blood—both their normal regulation and their pathology, as in leukemia—and we study the formation of blood during embryonic development. For this, we use embryonic stem cells. I also care for adults and kids with malignant and genetic bone marrow conditions—diseases like leukemia and lymphoma, immune deficiency, and sickle cell anemia. Many of these diseases can be cured by bone marrow transplantation—a form of stem cell therapy that harnesses the power of adult blood stem cells, or as you will hear (or have heard) from Dr. Wagner, from stem cells in Umbilical Cord Blood. While transplants are effective for some, the reality is that marrow replacement represents a heroic attempt at a life saving therapy for fatal diseases. The transplantation regimen itself is highly toxic. I would not wish this therapy on anyone who was not otherwise facing a potentially terminal illness. As a direct response to these shortcomings of adult stem cell therapies, my lab investigates the formation of blood stem cells from embryonic stem cells, and is pursuing strategies for making rejection proof, autologous tissues for transplantation. Our current treatments for many blood diseases are stone age, and only through research can we hope to make progress. I believe that embryonic stem cell research holds the key to treating many blood diseases.

Stem cells come in many varieties. Even the term “stem cell” is a very general term. It defines a generic category of cells that has many members with different properties. It's about as specific as the category “seed.” Seeds of all types share many properties, but an apple seed makes apple trees and an orange seed makes oranges. When we compare apples and oranges no one confuses the two. To a biologist, the distinctions between seeds are crucial, as are the distinctions between different types of stem cells. No credible biologist would argue that one type of seed can teach you all you need to know about all seeds and all fruit. Yet somehow, when we speak about stem cells in the current debate, people tend not to appreciate the differences, and consider them all interchangeable.

The media has covered a long list of “breakthroughs” that purportedly represent new sources of stem cells that substitute for embryonic stem cells. Initially, it was the Multipotential Adult Progenitor Cell from Catherine Verfaillie's lab in Minnesota, later it was the fat stem cell, then umbilical cord blood stem cells, and stem cells from testes. Just last week we heard reports about stem cells from amniotic fluid. All of these new types of stem cells are important tools for research and may even one day yield new therapies. However, none of them is the equivalent of embryonic stem cells. Perhaps they can do some of the things that embryonic cells can do, but they cannot do all of them. The differences between these other stem cells and embryonic stem cells are very, very important.

We have also heard that there are alternative means of generating embryonic stem cells without sacrificing embryos. There have been exciting recent developments that claim “reprogramming” of adult cells back to their primitive embryonic state, either by cell fusion with existing embryonic stem cells, or by introducing a small number of genes. Again, these achievements are noteworthy and fascinating, but they have not yet produced cells that faithfully mimic or replace the functions of true ES cells.

After many years of competing claims, ES cells remain the most versatile of all stem cells. ES cells are the gold standard for the biological concept of pluripotency, and it has been known from over 20 years of research in the mouse that ES cells can make all the cells of the body. ES cells have unique properties and they fulfill a unique purpose in biological research. Human ES cells are irreplaceable tools for understanding the earliest stages of human development. They are unique precisely because they come from the earliest human embryos—before implantation into the

womb, before even the most rudimentary human form has begun to take shape. Understanding how these primitive cells orchestrate the process of human development represents one of the greatest goals of modern biology. Figuring out how amniotic stem cells work or fat stem cells work will not teach us about the earliest days of human development. Many different types of stem cells—adult and embryonic—may prove useful for therapies. But embryonic stem cells are the only stem cells that have been proven to form all cells in the body, and this feature alone makes them worthy of study.

With regards to medicine, it is sometimes said by opponents of ES cell research that ES cells have never cured anyone. This is a patently unfair assertion because human ES cells have only been around for 9 years, and even now cannot be considered routinely available to scientists in the United States. However, the detractors of ES cells are naive in trivializing the contributions that ES cells have made to biomedical research. Mouse ES cells have been used extensively to model human disease and to study how gene variations influence cancer, heart disease, neurodegeneration, metabolic disease, and many, many others. Indeed, a paper published in 2003 reported that gene knock-out strains of mice, which derive from ES cells, provided key target validation for the effects of the 100 best selling drugs (Zambrowicz and Sands, *Nature Reviews*, 2003). It is therefore fair to say that ES cells have already saved lives—not directly through cell replacement therapies—but indirectly through key insights into human disease and the development of new drugs.

In closing, I want to stress that there is no credible scientific argument that would justify studying only adult stem cells to the exclusion of embryonic stem cells. Medical science does not advance fastest by cutting off fruitful avenues of research that the overwhelming majority of scientists and leading scientific societies like the ASCB and the ISSCR believe are vital. We must promote embryonic and adult stem cell research with equal vigor. We need a more conducive Federal policy for human embryonic stem cell studies, and Senate passage of Stem Cell Bill would be a healthy start. This vital research should not be left up to the States to fund. We need to stop making pseudo-scientific arguments against embryonic stem cell research, and get on with the scientific challenges ahead.

Thank you.

The CHAIRMAN. Thank you very much, Dr. Daley. Very, very helpful.

We have Lauren Stanford, here, a freshman at North Plymouth High School. And we welcome her mother and father. I hear your grandfather was William Ohrenberger, who was the superintendent of schools in Boston, and a very enlightened and courageous one, for many, many years, one of the great educators in Boston, who also played professional football in the 1920s. He was quite a guy. And Lauren follows in a very wonderful tradition of public interest. She was good enough to write a very moving letter, a year or so ago, when we were—had these issues on the floor, and we've invited her back. We want to welcome her parents.

This is the first day of school that she's been absent in I don't know how many years. But, Lauren, we—you're among friends here, and so, we hope you'll relax and, sort of, enjoy it, too. It might not seem that way, but we want—

[Laughter.]

We want you to know that you're among friends, and you're very welcome here. You've got a very, very, very important message, and you've taken the time to give this a good deal of thought, and we're very thankful for your being here.

#### **STATEMENT OF LAUREN STANFORD, JUVENILE DIABETES PATIENT, PLYMOUTH, MA**

Ms. STANFORD. Thank you.

I'd like to thank Senators Kennedy, Harkin, Specter, and Enzi for inviting me to appear before your committees today. It's won-

derful to live in a Nation where the cares of a 15-year-old girl from a small town are heard in the U.S. Senate, and that is because of leaders like you. I admire and respect all of you so much.

To see me sitting here, you'd think I'm just a normal American teenager. And, in most ways, I am. I play tennis and field hockey, I swim, and I ski. I'm pretty much addicted to Instant Messaging. [Laughter.]

I cannot survive without my cell phone nearby. Yes, on the surface I'm just another American girl.

But inside me, a battle has been raging for 10 years now, because, just after my 6th birthday, I was diagnosed with Type 1 diabetes. Type 1 isn't something you do wrong to get, it isn't something you can change your habits to avoid. In the past 10 years, diabetes has sent me to the hospital 14 times, twice to intensive care; it has pricked my fingertips over 30,000 times; it has injected needles in me tens of thousands of times; and it has forced me to learn to change my own pump catheter every 2 days, from the time I was just 7 years old. It has forced my mother to be a part of my life in a constant way, every hour of every day. Now, imagine accepting that, as a 15-year-old girl.

Diabetes has, indeed, ruled every minute of my life. Every 2 months, doctors peer deep into my eyes waiting for the time when they can tell me it's begun to break down my eyesight. They poke at my feet and my hands to see if it's robbed me of my circulation yet. They test my kidneys to see how far its assault on them has gone. And through all of this, I walk and talk and try to live in the world as just another American girl.

But time is not on my side, and I know that my only hope for a cure lies in medical research. My parents—my family has helped me learn about research over the years. And my friends and I have raised a lot of money to help fund it. My group, called "Got Islets: Lauren's League for a Cure," has raised hundreds of thousands of dollars for the Juvenile Diabetes Research Foundation since I was diagnosed, and we are just a bunch of kids. But we kids can't do it alone. We need the Government to help by allowing scientists to fully unleash the potential of embryonic stem cell research. This research could hold the key to a change in, not just my life, but in the life of so many Americans.

Imagine if it can help get to the source of what causes diabetes and stop it before it starts. Imagine if it can find a way to create new islet cells so my destroyed ones can be replaced with working ones. I cannot imagine what it's like to have 1 day—just 1 day when I was not sick. That's because I've had diabetes for longer than I can remember. Now is the time to expand the current stem cell research policy, not just because I want to know firsthand what a healthy day feels like, but because scientists believe they can make real advances in the search for cures for diabetes and for other diseases, as well.

While I wait for scientific advances, I really am doing all I can to help keep myself alive. Recently, I took a brave new step in fighting diabetes, and it has not been easy. I am now wearing what is called the Continuous Glucose Monitoring System, and I'm one of the first kids in the Nation to do it. This means I have a radio transmitter strapped to my side 24/7, in addition to my insulin

pump. Attached to it is a wire probe that I insert under my skin every few days—again, on my own, doing something most would need medical staff for. It helps me see, more often, what my blood sugar is, and it helps me keep my blood sugar in better control. But it's not a cure. It's a step forward in helping me take better care of myself until scientists find a cure, because, even though I have more information from it, it's not stopping diabetes from attacking my body.

I still get high and low. I still need insulin. I still fear the future, because, you see, I have hopes and dreams for a future, like most other kids. I want to go to a great college, but I have to worry about how to balance my constant care with life in the dorms. I want to get married and have children, but I have to worry about: How will I make that happen? Women with diabetes can have children now, but only with a constant and very invasive care. I want to be a Senator, like you, but I have to worry if my body will hold up long enough to help me get the experience I need to even try for that.

I have to admit, I am lucky in some ways. Living in Massachusetts and near Boston means I am very close to some of the best care in the world. At my diabetes camp and through my advocacy, I've met kids who are not that lucky. They don't have a good team to help them take care of themselves and try new treatments, they don't meet with great researchers like we have at Harvard. I worry for them, too. How will they achieve their dreams if I'm worried about mine?

I'm also very lucky that my parents are willing and able to work very hard to pay for all the things that diabetes demands, because, even with good insurance, it's expensive. Pump supplies, needles, insulin, test strips, and more, it all adds up to tens of thousands of dollars my parents spend. What about the kids who are not lucky enough to afford that?

Embryonic stem cell research could be a key answer to all of this. As I try my hardest to take the best care of myself I can, and those thousands of kids out there who are not as lucky as me do best in their situations, I hope that the Government will do its part by giving our best scientists the best tools to get a cure as soon as possible.

One of the best tools out there is definitely embryonic stem cell research. With it, with our great Nation and brilliant scientists, I can go on and live the life that I dream of. Will I go to a good college? Maybe. Will I get married and have kids? Hopefully. Will I be a Senator? We shall see. But one thing is for sure—once stem cell research helps us cure diabetes, I'll be that one thing I truly dream of being: just another American girl.

The CHAIRMAN. Very good, Lauren.

[Applause.]

Very well done.

John Wagner, professor of pediatrics, University of Minnesota, we welcome your testimony.

**STATEMENT OF JOHN E. WAGNER, JR., M.D., PROFESSOR OF  
PEDIATRICS, UNIVERSITY OF MINNESOTA MEDICAL  
SCHOOL, MINNEAPOLIS, MN**

Dr. WAGNER. Thank you, Senator Kennedy, Senator Enzi, Senator Specter—

The CHAIRMAN. Push the button. Push the button.

Dr. WAGNER [continuing]. Thank you for allowing me to speak today. As was said, my name is John Wagner. I'm a professor of pediatrics. I'm a co-director of the Stem Cell Institute at our institution, as well as the head of the Bone Marrow Transplant Program.

Over the past decade, there have been several major events. One is breaking down the genetic code, and the second is stem cell therapy. I take care of patients with incurable diseases, and I'm here to represent many of those patients, who are looking for cures, whether it be spinal cord injury, diabetes, Parkinson's, whatever the disease.

We're looking for new strategies that give them hope, and, as others have already said, I think we're on the cusp of seeing this become a reality. But I'm also here as a staunch advocate of adult stem cells. Clearly, there is a role for adult stem cells. We've seen a great deal of promise in all the publications that have been coming out over the past couple of years. These clearly need to be explored. But it needs to also be unequivocally clear that there is only one proven cure, that's been documented, with stem cell therapies from adult or neonatal tissues, and that's in the setting of bone marrow transplantation for the treatment of leukemia, lymphoma, sickle cell disease, immune deficiency. Clearly, what we're doing there is, we're replacing diseased bone marrow with bone-marrow stem cells or cord-blood-derived stem cells. Now, that's the only proven cure. And as Dr. Daley said, you know, "Well, what have you shown us, in terms of cures, with embryonic stem cells?" Well, clearly lots of work needs to be done, both with embryonic stem cells, but with adult stem cells, as well.

Many different trials are being conducted right now looking at the use of adult stem cells in the treatment of heart disease, in the treatment of spinal cord injury, bone disorders, genetic diseases. Clearly, they need to be explored. But have we proven any success yet? No, we haven't. But I think that we need to also step back for a second, because I'm a clinical trialist, I'm the one who actually designs new therapies and tries them out for the first time. Some of the families of my patients are actually right here, because they've actually tried brand new things, because there is no cure for their underlying disease. So, we try new things, and it doesn't always work.

I think that there are a few obstacles and a few things about moving this field forward. One, is that—What are realistic expectations? When we do stem cell therapies, whether it be adult stem cells, as we're doing very much today, or embryonic stem cells, perhaps in the future, you don't expect home runs to occur the first time you test them out.

Let me give you one example. What I did, and what I am a pioneer in, is the use of umbilical-cord blood as a source of stem cells for treating patients with leukemia. If you go back and look where

we were in 1990, when I performed the first cord-blood transplant for a child with leukemia in the world, the patient didn't survive. Did we give up? No, we continued. And, just a year ago, there—with the Stem Cell Act, we were able to actually markedly expand the collection and storage of umbilical-cord blood. And why did we do that? It's because we've actually been able to show, now, through our work at the University of Minnesota, that others are now replicating—we've tripled the survival in adult patients with leukemia and lymphoma. We've now been able to improve upon the overall survival rates with children. And we now are able to address the concerns of access to stem cell therapies to patients of ethnic and minority descent. We can find donors for almost everyone, which we could not previously do. So, we've made substantial progress, despite the fact that the first trials were failures.

There are other obstacles, however, that you have to keep in mind. One of the things that's touted as a benefit of adult stem cells, which is probably still a benefit of adult stem cells, is the fact that there could be tissue matching. I could collect stem cells from every one of you in this room and actually be able to create a multipotent adult stem cell that we could actually then re-infuse into your diseased heart or whatever the organ that needs to be fixed. Now, one thing we've also learned is that the immune system, unfortunately, attacks those cells, as well, even if it's from your own body. There's something peculiar about the stem cell that we have to address. The fact that it's matched, the fact that it's from your own body, doesn't mean that it won't be immune-rejected.

Well, what we've also learned is strategies to make this work. And, in fact, over the next year, I hope I can say to you that we will have done the first trials with the multipotent adult stem cell that was discovered in our institution by Cath Verfaillie. It will then be tested in patients who are undergoing chemotherapy and radiation, as a way of tissue repair. The advantage of that setting is because of the fact that these patients will also be immune-suppressed and hopefully given the chance, the best chance, for these stem cells to engraft, to divide, to replicate, and to repair tissue.

But what happens if it doesn't work? Do we give up? No, we continue. And, in fact, probably the first trials won't work. The first trials are actually a safety study. But this will be one of many generations of trials. Just like with cord blood, 16 years ago, when we did that first transplant, this will be an evolutionary process.

The last thing, because one of the tasks today was—I was asked, Can Congress help fulfill the promise of stem cell research? And this goes back to Dr. Landis, is the fact that—you know, where are we, in terms of NIH dollars? We are still inhibited by—we have our hands tied by the amount of funding that's available for this research. And, in fact, although I am an example of a successful candidate for getting research for clinical trials, unfortunately not a single trial has been designed by me, at least in the past, that has been substantial enough to be able to pay for the clinical trial itself. It requires multiple sources of funding for every clinical trial that we do, or I have to design the trial such that it's a small trial that can be within the confines of what the NIH will allow me in their cap.



But if we want to move these cell therapies forward, we have to invest in them, we have to recognize the obstacles, you have to understand the translational pipeline and its current problems. And how do we make this work? We have the tools to do that, and we're here to help you, if you want us to.

But every single one of us, in conclusion, will be faced with a disease that will be amenable to stem cell therapy. It might be our child, it might be our spouse, it could be us. Adult stem cells and cord-blood stem cells have benefits in the treatment of blood cancers. We know that. What we have to do is to be able to explore other diseases outside the context of bone marrow transplantation. It's essential that Federal funds be devoted to this. I think that you support it. We have to make it move forward, but also have real expectations. We do this for ourselves, for the science, but, most importantly, for the children and our families.

Thank you.

[The prepared statement of Dr. Wagner follows:]

PREPARED STATEMENT OF PROFESSOR JOHN E. WAGNER, JR., M.D.

#### EXECUTIVE SUMMARY

Over the past decade, two major events promise to revolutionize the practice of medicine—unraveling the genetic code and the isolation of the stem cell. Today, there is only one proven use of adult stem cells and that is in the context of blood and marrow transplantation to treat diseases such as leukemia, lymphoma, sickle cell disease and various other blood and immune disorders.

Accomplishments using stem cells from adult and neonatal tissues include: (1) our demonstration of their capacity to differentiate into cells of multiple tissues, (2) their safety and efficacy in laboratory models of disease, and (3) procedures for manufacturing stem cells for human testing.

There are many new adult stem cell projects moving to clinical trials. It is unrealistic to expect that there will be home runs; and, it may take several generations of studies to make a new therapy work. The Stem Cell Therapeutic and Research Act of 2005 authorized substantial funds to be used to increase the Nation's inventory of cord blood by 150,000 units. The NCI and NHLBI are supporting multi-institutional trials in children and adults to validate these results pioneered at the University of Minnesota. This is an example of what your support has accomplished and what it takes to move stem cell therapeutics from concept to clinical testing to standard of care.

We are now ready to test the multipotent adult stem cell, the cells discovered by Dr. Verfaillie and colleagues. But, importantly we have also identified obstacles, reasons why these may fail to repair injured tissues. While it is touted as one more advantage of adult stem cells over ES cells, it is now clear that the most primitive adult stem cells, even those directly from the patient, are susceptible to immune attack. This serves as a clear example of why it is not enough to show that a cell can differentiate into a tissue, the right models need to be used to predict clinical outcome.

Gap funding for Phase I clinical trials is an obstacle to our success. Currently, the Federal grants are too small to complete the trials and we must compile several funding sources to move forward.

There are things we can do now that will speed the process of moving new laboratory discoveries to clinical trials. First, you need to understand the translational pipeline, its components, how it is funded, and the potential obstacles. Second, it is necessary to understand why there are disincentives for clinicians and basic scientists to engage in this translational research—as this will help identify solutions. Third, and perhaps most important, you must be able to differentiate speculation from fact, as it pertains to stem cells, as there is a considerable misinformation and misunderstanding out there on what adult stem cells can and cannot do.

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Senator Kennedy, Senator Harkin, Senator Enzi, and Senator Spector, thank you for the opportunity to speak today. My name is John Wagner. I am the Director of Hematology/Oncology and Blood and Marrow Transplantation Program and Sci-

entific Director of Clinical Research for the Stem Cell Institute at the University of Minnesota.

Over the past decade, two major events promise to revolutionize the practice of medicine—unraveling the genetic code and the isolation of the stem cell. The rate that new genes are discovered and their function understood have been extraordinary. Take for example, BRCA2—the breast cancer gene. In my own clinic in the treatment of children with rare life threatening disorders, we have learned that this genetic defect is not only associated with breast and ovarian cancer in adults but also leukemia, brain tumors and kidney tumors in very young children. In fact, detection of this genetic defect in young children has allowed me to predict with high certainty what cancers will develop and when. This is powerful information because it has allowed me the opportunity to pre-emptively intervene and alter the future predicted by these genes. One intervention has been the use of stem cells.

Today, there is only one proven use of adult stem cells and that is in the context of blood and marrow transplantation to treat diseases such as leukemia, lymphoma, sickle cell disease and various other blood and immune disorders. This has been known for 40 years. For these diseases, we infuse stem cells to repair marrow that has either been destroyed by the disease itself or by treatments, such as high doses of chemotherapy and radiation. These blood producing stem cells come from adult marrow or cord blood (the blood left in the placenta after a baby is born).

A year and a half ago I presented before Senators Harkin and Spector to defend the vital importance of embryonic stem cell research. While I unequivocally support embryonic stem cell research, it must also be clear that adult stem cells have an important place in medicine as well. While adult stem cells do not replace the need for ES cells, they will likely complement it.

The principal accomplishments over the past 5 years using stem cells from adult and neonatal tissues (such as cord blood, amniotic fluid and the cord itself) include: (1) our demonstration of their capacity to differentiate into cells of multiple tissues (e.g., mesenchymal cells into neurons; cord blood stem cells into cells of the lung); (2) their safety and efficacy in laboratory models of disease, and (3) procedures for manufacturing stem cells for human testing. In fact, the first clinical trials have already been initiated in acute heart disease (heart attacks) and chronic heart failure, acute brain injury and lung injury. In addition, clinical trials with organ-specific stem cells are already being studied in diabetes in addition to those in bone marrow transplantation.

With National Institute of Health (NIH) research dollars and other governmental and nongovernmental support as well as philanthropic support, there are many new projects moving to clinical trials. At our own laboratory, we are collaborating with investigators at Johns Hopkins, helping to develop clinical manufacturing methods for testing cardiac stem cells; we are collaborating with investigators at Tulane, developing stem cell populations for treatment of genetic disease and bone repair; and, we are working with industry, such as Athersys, manufacturing multipotent adult stem cells for treatment of radiation and chemotherapy injury. Significant progress has been made.

It is unrealistic to expect that there will be home runs; and, it may take several generations of studies to make a new therapy work. As an example, cord blood used to treat leukemia and lymphoma took years before it reached its current success. In 1990, I performed the first cord blood transplant in the world for a child with leukemia. While this child unfortunately died of his underlying disease, scientifically it was a success—thereby giving us a reason to push forward. Eight clinical trials later, we made modifications that have led to extraordinary survival rates in adults with leukemia. Now, patients from all over the world are now receiving this therapy. In addition, the “double cord blood” platform, has solved the problem of access—permitting us to find donors for more than 80 percent of patients, particularly important for patients of ethnic and racial minority descent.

The Stem Cell Therapeutic and Research Act of 2005 authorized substantial funds to be used to increase the Nation’s inventory of cord blood by 150,000 units. The NCI and NHLBI are supporting multi-institutional trials in children and adults to validate these results pioneered at the University of Minnesota. This serves as just one example of what your support has accomplished and what it takes to move stem cell therapeutics from concept to clinical testing to standard of care.

After 5 years of intense study, we are now ready to test the multipotent adult stem cell, the cells discovered by Dr. Verfaillie and colleagues. We are about to submit our first application to the U.S. Food and Drug Administration. Over the past 2 years, we have compiled safety and efficacy data in laboratory models and developed the procedures for reliably producing these cells for individual patients. The first trials will take place in the setting of radiation and chemotherapy injury and the goal is to demonstrate safety and hopefully signs of tissue repair. Will it cure

patients—may be not. Do we give up—no. As in the early trials with cord blood, we have to carefully design the right studies that will insure that we learn why the cells work or why they don't work should that occur. We already know in laboratory models that multipotent adult stem cells will home preferentially to areas of tissue injury.

But, importantly we have also identified obstacles, reasons why these may fail to repair injured tissues. While it is touted as one more advantage of adult stem cells over ES cells, it is now clear that the most primitive adult stem cells, even those directly from the patient, are susceptible to immune attack. This serves as a clear example of why it is not enough to show that a cell can differentiate into a tissue, the right models need to be used to predict clinical outcome. For this reason, our first trial with the multipotent adult stem cell will be in immune suppressed patients with tissue injury, giving every chance for these stem cells to engraft into damaged tissues and effect tissue repair.

It is not enough to give hope based on the results from a Petri dish. We must have better models to move the science forward. It is exactly this stage of research that is sorely lacking in funding—this in between stage. Gap funding for Phase I clinical trials is an obstacle to our success. Currently, the Federal grants are too small to complete the trials and we must compile several funding sources to move forward.

It is not a question of whether this new knowledge will “translate” into a useful clinical treatment but rather—when? I receive hundreds of emails and letters monthly asking for direction, help and above all—hope. As a physician who sees patients for whom there is no known treatment, I explore the unknown. I have to keep trying. For the most part, I have made some good decisions and patients have benefits. While it will never be fast enough, there are things we can do now that will speed the process of moving new laboratory discoveries to clinical trials. First, you need to understand the translational pipeline, its components, how it is funded, and the potential obstacles. Second, it is necessary to understand why there are disincentives for clinicians and basic scientists to engage in this translational research—as this will help identify solutions. Third, and perhaps most important, you must be able to differentiate speculation from fact, as it pertains to stem cells, as there is a considerable misinformation and misunderstanding out there on what adult stem cells can and cannot do.

It must be clear that no study with adult or cord blood stem cells outside the context of bone marrow transplantation has proven efficacy. While there are claims to suggest otherwise, the results are either contradictory or too preliminary. While I wish that I could tell you otherwise, speculation seems to get confused with fact. While promising, adult stem cells do not exhibit all the capacities of ES cells. For example, we have yet to see stem cells from cord blood or adult tissues (outside the heart) differentiate into heart muscle cells that spontaneous beat, as has been shown repeatedly with ES cells.

*Can Congress Help Fulfill the Promise of Stem Cell Research?—Absolutely.* We are here today to help you understand what we know, what we think we know and how you might help translate this hope of stem cells into reality. In addition, it is important to know exactly how much is currently being spent on stem cell research. This involves separating how much is spent on adult/cord blood versus ES stem cells and separating adult/cord blood stem cells into hematopoietic (bone marrow transplant) and nonhematopoietic. In my opinion, this is not clear to the public.

Every single one of us will be faced with a disease amenable to stem cell therapy. It may be our child, our spouse, our friend or even ourselves. Adult and cord blood stem cells have proven benefits in the treatment of blood cancers and other disorders and perhaps even in tissue repair that has yet to be clearly proven. It is essential that Federal funding be devoted to stem cell biology and therapeutics. All the required components to make this work already exist—we just need to bring them together. There are patients in this room today and parents of children who have passed away looking for a chance to see this hope move into a reality. The results are extraordinary; we have to make it happen now on their behalf. For them, the stakes are unimaginable.

The CHAIRMAN. Well, thank you. Thank you very much. Very good panel.

We've got 12 members here. I thought we'd just do 4 minutes, so everybody gets—tries, basically, a question and a followup. That's still 48 minutes, but at least we'll give everybody, hopefully, an opportunity. And then, for those that want to—are able to re-

main, and our panel remain, then we'll stay here afterwards, but permit everyone.

I'd like to ask, Dr. Landis, Do you believe that restricting the NIH funding to the small number of cell lines included in the current policy allows the federally funded scientists to explore the full healing potential of a remarkable new field? Are we missing out on possible breakthroughs under the current policy?

Ms. LANDIS. Yes, we are missing out on possible breakthroughs. From a purely scientific perspective, Federal funding of additional cell lines is necessary to advance the field. The cell lines that are eligible for NIH funding now have been shown to have genetic instabilities; in particular, with respect to epigenetic changes in methylation. NIH—scientists who are funded by NIH would also like to have access to cell lines that have been derived without the use of feeder cell lines or animal products. And, finally, there are a number of cell lines—many cell lines that have been generated since the President's policy was put in place that have in them mutations specific to human diseases, like Huntington's and ALS and Parkinson's. That would be extraordinarily useful for learning about the progression of disease and testing drugs, and those are not available either. So, yes, more cell lines would be incredibly important.

The CHAIRMAN. Dr. Daley, what happens to the best of the American researchers—give us—with the current policy? Where—has this research been going abroad? Tell us what's happening to the young, ablest, most gifted researchers. Will they get into this field, or are—

Dr. DALEY. Yeah.

The CHAIRMAN [continuing]. Or are they going into other areas?

Dr. DALEY. Yeah, you know, we, in the United States, enjoy a remarkable luxury of support from the Federal Government for our research. And because we have, I think, some of the best research infrastructure, the best universities, we tend to attract the top young scientists from all over the world. Increasingly, though, when I interview researchers from Europe or from Asia, they ask whether or not there is a supportive enough environment in the United States that they should commit their careers to coming to the United States to do embryonic stem cell research. I can't say—or give you a number of the ones who decide against coming. The ones who do come to my lab are those intrepid few who are so caught up in the excitement of the science—and I say there are a remarkable number of scientists internationally who are voting with their feet to study these cells, they are fascinating cells. But I have every sense, every belief, that there are people who are being dissuaded from this very interesting new area of science because of the political climate here in the United States.

The CHAIRMAN. Lauren, a young lady of courage and fearlessness, if you had the President here today, what do you think you'd tell him to encourage him to support this program?

Ms. STANFORD. I think I'd probably just tell him about the struggles that I've gone through and about how passing this bill would be very important to me and all the other people with diabetes around the world, and it would be a big help if he just didn't veto the bill.

The CHAIRMAN. Very good to hear.

My time is up.

Senator Enzi.

Senator ENZI. Thank you, Mr. Chairman.

I recognize the message that everyone's given, that more money needs to be spent on all kinds of stem cell research. And I don't think there's, probably, anybody that disagrees that if there was more spent, there would be more discoveries, and we'd know more. One of the difficulties is allocating more money to some things, when we're requested to do it for everything. We have to recognize that there is a significant group of people out there that feel that embryonic stem cell research would be very similar to the other end of the spectrum, where people might go through nursing homes and find people who no longer can talk, probably close to death, they're just going to be thrown away, and perhaps they could be used for research, but not with their permission. That group of people will object to spending taxpayers' dollars on similar procedures for embryonic research.

The more people that agree that there are moral ways to do this, the more support there'll be for it. I want to congratulate Senator Isakson for the work that he's done to try and come up with some compromises and expand the capability of research. A bill that, I think, has the capability of bringing more money into the system.

Professor Wagner, I want to thank you for coming, and I want to thank the patients that joined with you today, as well. It does sound like you're making great progress with the adult stem cell research. I know that you recognize embryonic stem cell research is important, as well. But do you think an expansion of adult stem cell research will lead to more therapies in the next 10 years, perhaps more quickly than embryonic stem cell research? Realistically, are there any particular treatments, other than the ones you're working on, that you're intrigued by and excited about seeing put into the clinical setting?

Dr. WAGNER. Well, Senator Enzi, I mean, first off, you know, as you stated, I mean, I think that we should be exploring both embryonic stem cell research, as well as adult stem cell research. Clearly, more money in adult stem cell research will obviously help us advance that, perhaps more quickly, because of the very fact that there's less money for embryonic. On the other hand, with that said, it clearly is a supporter for both, but yet, adult stem cell work is now being explored not only for, you know, correcting bone disease, liver disease, lung disease, it's also now being explored for a way of treating patients with diabetes, as well.

But we're at the very earliest phases. The fact is, that it's still quite speculative. You know, I'm not saying that it will ever achieve the same status as an embryonic stem-cell-derived therapy, but clearly we need to explore all the options, and everything is wide open. Many people are working on all these areas simultaneously.

Senator ENZI. Very quickly, Dr. Landis, we're operating under CR now, which limits the amount of money. There's no expansion of money. Were we to end the embryonic stem cell Federal funding prohibition, what research would you cut in order to get the research done on that?

Ms. LANDIS. That's a very challenging question that we're facing every day at my Institute. If we do this, what won't we do? What NIH does, in general, is to not set aside specific pots of money for particular projects, but to fund the very best science. And, as we've heard, some of the very best scientists are incredibly excited about human embryonic stem cells, and expansion of the lines would enable them to write wonderful applications, which we would review and hopefully have the money to fund.

Senator ENZI. Thank you.

And my time is expired.

The CHAIRMAN. Senator Harkin.

Senator HARKIN. Thank you, Mr. Chairman.

I just want to respond a little bit to what was just said. You know, this image is always brought up of old people, as if we're going to use them for experimentation and stuff. Let's just keep in mind what we're talking about here. We're talking about a blastocyst with about 150 cells, has absolutely no human form whatsoever. Does it contain all the genetic material and stuff? Yes, it does, just like a sperm and an egg does. That's what we're talking about here.

So, I listened to the debate that was on the House floor last year on this, and one speaker got up and talked about destroying fetuses. This is the kind of misinformation that gets out all over America, that we're going to destroy a fetus. And they said it clearly on the House floor, that that's what this was about. So, you know we've got to continually combat this kind of misrepresentation of what we're talking about here.

One other thing we have to clear up is the fact that the Federal Government is already spending U.S. Federal tax dollars on embryonic stem cell research. We already are, on 21 outdated contaminated lines that were derived prior to 9 p.m., August 9, 2001. So, don't tell me that we can't spend U.S. Federal taxpayers' dollars on stem cell research. We're already doing it. The fact is, we're only doing it on those that were derived prior to 9 p.m., August 9, 2001. Somehow, that's moral. But to do it on those derived after August 9, 2001, 9 p.m., is immoral. I don't know why that is a dividing line of morality. I've often asked, "Why wasn't it 9:05 p.m., 9:30 p.m.?" "Midnight, 8 p.m." Why was it 9 p.m., August 9, 2001, that somehow is the dividing line?

Well, when that happened, I said, we thought 70-some lines were available—I thought that might be enough. But now we know it's only 21, and every one's been contaminated and will probably never lead to any kind of human therapies. So, we have to keep in mind that we already are spending taxpayer dollars on embryonic stem cell research. All we're asking is, let's expand that, and let's get new lines, that are not contaminated, some that are healthy and vibrant, that have been derived already by private sources. That's what we're talking about. So, I continue to try to clear this up, to point out that NIH funds are already available for this.

Now, I was just figuring out the budget here, Dr. Landis. Last year, about 2 percent—my figure—of the entire NIH budget went for all forms of stem cell research—adult, animal embryonic, animal nonembryonic, all of it. It was about 2 percent.

I just think that that is woefully inadequate. And I just won't buy this argument that somehow we're so limited by the budget that we can't do this, when we're spending \$8 billion a month on the war in Iraq. Eight billion a month? And we're spending \$637 million, last year, total, on all stem cell research? Don't tell me the budget's limiting us. It's the priorities we have as a Nation, and it's the priorities we set as a Senate and a House, that determines how much we spend. There's no magic thing out there that says you can't spend more than this on research.

Well, I've used up my time, and I didn't even get to ask a question, but there is one I just want to ask.

[Laughter.]

Dr. Daley, I wanted to ask you this. Some people say we don't need more Federal support of embryonic stem cell research because States and private resources are funding it. California's jumped in. Wisconsin's jumped in. New York's jumped in. I don't know if Massachusetts has.

Dr. DALEY. Not yet, but I hope so.

Senator HARKIN. Well, okay. So, maybe we don't need more Federal funding. Let the States do it.

Dr. DALEY. No, actually, this is not an issue for the States. I mean, who's to say that the breakthroughs are going to come in California or New Jersey? And I have outstanding colleagues who are in other States—Michigan, Arkansas, Iowa. Those researchers in those States should be allowed to obtain Federal funding. This is a Federal issue. The Federal Government is the lifeblood of scientific research. Virtually all of my funding comes through the Federal Government. It's a reliable source, it's subject to peer review, it's subject to ethical oversight. It's very hard to raise private money, and it's taken outside of those oversight processes when it's—when the research is done privately.

Senator HARKIN. Thank you, Doctor.

Thank you, Mr. Chairman.

The CHAIRMAN. Thank you. Thank you very much.

Senator SPECTER.

Senator SPECTER. Thank you, Mr. Chairman.

Thank you very much for coming in, Ms. Stanford. I'm very interested to hear your desire to become a U.S. Senator.

[Laughter.]

You're 15, you'll be eligible to run in 15 years. I just want to offer a word of caution, that Senator Kennedy will still have a decade left—

[Laughter.]

Under Senator Thurmond's tenure.

[Laughter.]

So, be patient.

[Laughter.]

Lauren, when we have these hearings we wonder what their impact is. Speaking, perhaps, for many people in your situation, does this hearing give you more hope? Does it encourage you that something really may be done to deal with your diabetes problem?

Ms. STANFORD. Well, just coming here and talking, I know that my voice is being heard, and that gives me a lot of hope that something may happen in the future and I may have impacted some-

one's opinion on something else or a choice to make, and it makes me feel good about myself and good about the future.

Senator SPECTER. Dr. Wagner, you testified that you infuse stem cells into the heart or other organs which need to be repaired. Could you be specific as to what prospects there are—I know it's subject to experimentation, but what prospects there are to deal with Lauren Stanford's diabetes, or what the prospects are to deal with Arlen Specter's Hodgkins disease?

Dr. WAGNER. Well, you've asked quite a few questions right there. I mean, but in terms of the prospects for——

Senator SPECTER. I've only got 4 minutes.

[Laughter.]

Dr. WAGNER. Well, clearly, the one we know is actually Arlen Specter's cancer, because if it's a lymphoma, then clearly we have tried-and-true therapies, though I don't know the details. But, on the other hand, we have—we do have therapeutic—proven results in patients with lymphoma leukemia.

The question then is, is that—Where do we go outside the context of the classic bone marrow transplantation, such as in diabetes or in heart disease? What I can specifically address right now is that there are a number of studies, both at our institution and others, where we're specifically taking stem cell populations, whether it be cardiac stem-cell-derived, or whether it be mesenchymal stem-cell-derived, and actually inputting them into patients with heart failure. Have we proven benefit? The results are mixed. But this—again, this is a step one. But we are moving these cell therapies into clinical testing. It will be only time before we know the true benefit in that speculation, at this point.

Senator SPECTER. Dr. Daley, this is your fourth appearance before this subcommittee—in 2002, in 2005, in 2006. Are you getting a little tired of coming here without better results? Can you be a little more persuasive on this thing?

Dr. DALEY. Yes, I——

[Laughter.]

Well, I have to say that I think it's been a bit frustrating that the political—or the—let me say it directly—I think the politicians have been lagging somewhat behind the American public. We've been out there, as a scientific community, trying to speak out on these issues, trying to educate, trying to justify the importance of stem cell research.

Senator SPECTER. Dr. Daley, let me interrupt you——

Dr. DALEY. And——

Senator Specter [continuing]. Because I've only got a few seconds left, and I want to ask Dr. Landis a question.

You are the vice chair of the NIH Stem Cell Task Force?

Ms. LANDIS. Yes.

Senator SPECTER. The subcommittee has polled all of the institutes, and it's gotten responses almost everywhere, "Please give us embryonic stem cells." The question is raised, Where are you going to get the money? As a matter of priorities, isn't it true that many of the institutes would put embryonic stem cell research at a higher priority and make some funding available?

Ms. LANDIS. Yes, we absolutely would. In fact, in NINDS we have several program announcements with setasides specifically for



enhancing the likelihood of investigators working in this area that they would get funded.

Senator SPECTER. Thank you, Mr. Chairman.

The CHAIRMAN. Thank you.

Senator Brown.

Senator BROWN. Thank you, Mr. Chairman. And thank you for calling this hearing, the joint hearing.

I am—

The CHAIRMAN. I have Senator Brown, Coburn, Lautenberg, and Isakson. If there's a difference in that, or someone has a particular schedule, if they want to just have their staff let us know, and we'll try.

Thank you.

Senator BROWN. Thank you.

I sat on the House Subcommittee on Health for many years and it's heard several hearings on this whole issue of embryonic stem cell research. Of all the issues we discuss in healthcare and in other issues in the Senate and in the House when I was there, few issues seem so clear cut to me as this one. From all the substantive questions, we talk about how the position of our Federal Government on embryonic stem cell is almost for sure causing some very young—for some young, very bright scientists to look elsewhere. We lose that potential. Some evidence of some scientists going overseas to Singapore, others—perhaps overstated, but some evidence of that. I hear Senator Harkin and then Dr. Landis repeating the four-door metaphor, if you will. All this is—as I said, of all the issues that come in front of this committee and other committees, this one seems so clear cut to me, and it's so discouraging, having just gone through a campaign talking about this issue and seeing overwhelming public support for it, that we can't get further along than we have.

Dr. Daley, would you give us some very specific, understandable-to-the-public, recent breakthroughs or about-to-happen breakthroughs that can help us along with this, to go home and talk about in continuing to educate the public, who will then continue to educate the President and other policymakers about the importance of stem cell, if you would.

Dr. DALEY. Yeah, I would point to the papers, just in the last year, that have highlighted the formation of specific cells from human embryonic stem cells. It's the beginning. You know, are they breakthroughs? This is the hard work of basic science. But the fact that you can make human skin cells, tendon cells, bone cells, liver cells, muscle cells, dopaminergic neurons, motor neurons—I have a list here. This is a graph that shows the publications, by year, for different stem cells. Look at the inflection point here. It's just growing exponentially, the number of publications around embryonic stem cells. And there are breakthroughs among them. I would point to any number of diseases where understanding the cellular basis is really advanced by these types of publications.

Senator BROWN. Thank you.

Thank you, Mr. Chairman.

The CHAIRMAN. Senator Coburn.

Senator COBURN. Thank you. Senator Kennedy, if I might, I might yield to Senator Isakson. I believe he has a plane to catch.

The CHAIRMAN. Fine.

Senator ISAKSON. Good, absolutely. Thanks, Senator Coburn.

First of all, I thank all the—I thank the Chairman for calling the hearing today, and all the other chairmen and ranking members—

[Laughter.]

Their testimony. I don't want to make any of them mad. And thank all the panelists. Lauren, you were terrific. I'm glad you are in Massachusetts and Senator Kennedy has to worry about you.

[Laughter.]

If you move to Georgia, I'm in big trouble, and I know that.

[Laughter.]

And I have to say, personally, to Dr. Wagner, on a personal note, my sister's life was saved because of bone marrow transplant therapy that was developed in the 1990s and tried at the University of Nebraska Medical Center in Omaha, where I spent 3 weeks staying with her when that happened. So, I'm very grateful for the work that you do, and the advancement of the work that you do.

Dr. Landis, it's my understanding that one of the benefits of any NIH investment is, it takes the information that is gained from the research and puts it in the public domain; whereas, if it's done strictly privately or overseas, that information remains proprietary. Is that correct?

Ms. LANDIS. So—there are differences in publication strategies used by people funded by NIH, versus people who work at companies, so that's true. And NIH investigators, more and more, are being asked to put information in the public domain. So, in—as a generalization, that is true.

Senator ISAKSON. Dr. Daley, not—I appreciate your comments on the recent articles on “amniotonic”—if that's the right—

Dr. DALEY. Amniotic.

Senator ISAKSON [continuing]. Pronunciation. This question does not relate to that. But on deriving embryonic stem cells for research purposes, which is something everybody, I think, is for, there are—the differences come down on the destruction-of-embryos question that Senator Harkin, Senator Kennedy, and Senator Enzi have all made very quality statements, on both sides of that particular issue.

At the University of Georgia, three lines, which do receive NIH funding, were developed—or embryonic stem cell lines done specifically in diabetes research with eminent scholars—were derived from the extraction of embryonic stem cells from level-three Gardner-principle grading in the in vitro fertilization process. Do you have—that's one known alternative that does not involve the destruction of an embryo that can be implanted or frozen. Do you know of others?

Dr. DALEY. Yeah. I mean, I know of Dr. Stice's work, in Georgia. In our own lab, we have actually derived five new lines from embryos that were considered such poor quality that they would even be discarded before freezing, they're just not even part of the IVF process. We have derived lines.

There are a number of issues. The efficiency with which you can derive those lines is significantly lower than using the embryos that are frozen, the embryos that have been judged to be of suffi-

cient quality for clinical use, but which would otherwise be discarded. I think our preference would be to take advantage of the hundreds of thousands of embryos that are destined for medical waste. We can use those and make good lines.

We need new lines. I just had our—our lab had a meeting yesterday, where we talked about the crazy H9 cells. My lab now has been growing this one NIH line, H9, for 6 years. It's now so distorted that we call it "crazy H9." I mean, we really—we really—you know, we're handcuffed if we can't continue to innovate in the area of stem cells. There are many, many new lines—and the lines that model genetic disease, as Dr. Landis spoke of, these are enormously valuable, and, Why can't we use our Federal dollars to study them?

The CHAIRMAN. Could I ask—if the Senator would yield—could you expand? You said that the efficiency is not as good. As I got the thrust of the question, does not destroy the embryo, but that was the—as I understood what—the Senator has spoken to me about this. I'm interested in your responses. I wrote down "the efficiency is not as good, and we ought to"——

Dr. DALEY. Yeah.

The CHAIRMAN [continuing]. "Be able to deal with the others." Can you still do it?

Dr. DALEY. Well, they——

The CHAIRMAN. I mean, is it a way of proceeding [inaudible]?

Dr. DALEY. So, one——

The CHAIRMAN. And what would be the disadvantage?

Dr. DALEY. Right. One——

The CHAIRMAN. Excuse me.

Dr. DALEY [continuing]. Strategy that's been put forth as a—and considered as possibly ethically more acceptable than using viable embryos is to use the embryos that are deemed of poor clinical quality. So, at day three in an in vitro fertilization lab, the embryologists will look at the embryos and they'll judge whether the cells are intact or whether they're fragmented or not. And if they're given a choice, they'll pick ones that look viable, and the ones that have fragmented will be discarded. We get those embryos, and we use them.

Now, we believe that they will allow us to make normal stem cell lines, but I'm not necessarily certain that there aren't hidden genetic defects in those cells. For some reason, those embryos didn't form.

The CHAIRMAN. Yeah.

Dr. DALEY. And so, not only is it much less efficient—it's about 1 percent of those poor-quality embryos that we can make yes-cells from. I'm not only concerned about the efficiency, I'm really concerned about the integrity of those lines.

The CHAIRMAN. Senator Lautenberg.

Senator LAUTENBERG. Thanks, Mr. Chairman.

I listened with interest to the testimony of each one of you, and I congratulate you for doing it.

But, in particular, Lauren, your story will be listened to by lots of people. They'll hear your voice, and we're very proud of you. And I reach out to you, because I'm a grandfather of 10 grandchildren,

and I realize how lucky we are that they're without any difficulty like the one you have.

And, to Mr. and Mrs. Stanford, I want you to know this. We've heard the discussion about money, about resources, and how, "We just don't have the money." What we're saying to you, in body, is that your priority for Lauren doesn't compare to the priority of making a war that over two-thirds of the American people reject. That would represent 200 million people in our society who don't want us to carry on the war as it is. But we can't afford to spend more than \$130 million on embryonic stem cell research? I find it difficult to understand, and I find it shocking. And I defy any member of the U.S. Senate to tell you that that priority, with that beautiful young woman, that intelligent young woman, who can make such a contribution to our society, doesn't rank with a war that's really distasteful to most of the people in the country.

Mr. Daley, the lack of the proper investment in stem cell research has slowed progress. Is there any judgment, any guess, about how much we've lost by not paying attention to this, by not making the proper investments to find out what's there?

Dr. DALEY. It's always difficult to answer a question about what might have been, what could have been, if we had had more resources. I can speak very personally, that this has led to countless hours of delay working through various institutional review boards to get approval to do nonpresidential—what we call nonpresidential work. Raising private money takes enormous, enormous amounts of time.

We have to set aside, in our laboratory, behind a black curtain, a room exclusively for privately funded embryonic stem cell research, where every single pipette, every single bottle, every single piece of equipment is labeled with a big sign that says, "NP," which classifies as the nonpresidential resources. It's an enormous obstruction to progress in this very vital area of research.

Senator LAUTENBERG. Mr. Chairman, as we sit here, we hear about the possibilities that might be there, about relieving young people, like Lauren, from having to stick their fingers and so forth. We also know, or we believe, that we're going to be facing a request for \$100 billion for a supplemental for the war in Iraq, primarily. Yet still, out of \$3 billion invested in stem cell research, only 4 percent was allowed to be invested in embryonic stem cell research. Thank you.

And thank you, Mr. Chairman, for holding this hearing.

The CHAIRMAN. Thank you. Thank you very much, Frank. Thank you.

Senator Coburn.

Senator COBURN. Thank you.

First of all, let me say how much I appreciate each of you, in terms of your dedication to what you're doing. The area of expertise that you're in today is going to be critical for our future.

And, Lauren, I want to tell you, I've delivered 4,000 babies—I diagnosed a 6-month-old with type-1 diabetes before, and cared for her until she graduated from college. You have a great future in front of you, and you can have all the children you want, with today's management techniques. So, don't worry about that. And I'd

love to see you up there, instead of Senator Kennedy, I promise you.

[Laughter.]

Besides being a lot better to look at—

[Laughter.]

A couple of points I want to make, and then I want to ask a couple of questions.

First of all, let's make sure we understand the dividing line on this debate. Some of us very earnestly believe life begins at conception. At the moment that sperm and egg divide—combine, we believe there's life there. And so, that's where the ethical problem is. And we want to work as hard as we can to get around that and not rationalize away the fact that we believe that's life. And that has to be respected. That position is not taken lightly. Everything about our life revolves around some of those critically held beliefs. And so, I won't demean anybody who disagrees with that, but you—we can't be demeaned because we believe that. And I hope we'll respect that opinion. That says nothing about us not wanting to get everywhere you all want to get, in terms of cures.

I'm a two-time cancer survivor. I may be a two-time cancer survivor, we don't know yet. But the point is—and I have family—sister-in-law and sister with breast cancer—I mean, you know, I don't have a very good set of genes, quite frankly. But the point is, we have hope, too, even those that oppose this on this very ideal and heartfelt thinking of the value of the initiation of life.

And I think Senator Isakson is really on to something. And I think we have a way that we can move a President to sign money for research, even though it might be harder, but the idea of non-viable, nonlife-giving embryos to be used to develop stem lines. And, as you said, Dr. Daley, you don't know yet whether or not they're a compromised cell line. Well, let's find out.

I can tell you that there's—you're going to get a veto. That's No. 1. So, let's send him something that he won't veto that helps move us down the track. What I would hope is that you all would agree to work with us to try to come to that point. Senator Isakson and Senator Coleman have worked hard on what looks like a great compromise, which we'll be discussing with people. I can certainly live with it, given my beliefs, and I'd hope you all would.

The other thing that I want to talk about, and I guess I'd better ask my question—let me ask my question, and then, if I get a chance to talk about it again, I will.

Autologous transfer. Dr. Wagner's talked about rejection with what they've seen so far. But there is no question, there is more rejection, within the body, of foreign protein than there is autologous protein. Is that not true?

Dr. WAGNER. That's generally correct. However, it may be different for stem cells.

Senator COBURN. Right. But the fact is, everything we know about immunology today is, if you put foreign protein into the body, you're going to have a greater reaction than if you put your own protein into your body. And so, we have to believe, until your research proves otherwise, that there's less likelihood to be a rejection if you were using autologous cells, if, in fact, we can use autologous cells. And I mean cells that come from your own body.

And the reason I'm a big believer in the research that's going—I don't discount, for a minute, the great work that's going to come from biochemical studies, drug studies, disease-treatment studies, and disease treatment from embryonic stem cell research. And I wouldn't discount that for a minute. But the real cures, in my belief, based on rejection and the potential for rejection being less with autologous cells, I believe, is going to come from some type of nonembryonic stem cells, but maybe more potent or pluripotent, not totipotent cells.

And I'd just like your comments on what you know in the literature, in terms of rejection, in terms of mitochondrial DNA that's going to be a factor in anything that we do, in terms of embryonic stem cells, in terms of transplantation. And just a comment on that, for a minute, if you would.

Dr. WAGNER. To whom?

Senator COBURN. Either one.

Dr. WAGNER. Well, can I start first?

Well, first off, you know, although I didn't get into the details, the one thing that we also know, based on our work, is that, because stem cells lack class-one antigens—and I know that's—doesn't really matter to the majority of you—

[Laughter.]

However, it will be eradicated by natural killer cells. So, even if it's autologous, it will have an immune reaction.

The second thing is, it's a misconception that if you believe that—the future is going to be, you know, individual autologous products, we—it's too expensive and too difficult to do for each individual patient. Yes, proof of principles can be established using that, but, in the great future, we're going to have to do an off-the-shelf product that will not be completely matched, even with autologous stem cells.

Dr. DALEY. Yeah, I would just second that. I would agree with that.

Senator COBURN. Thank you.

The CHAIRMAN. Senator Sanders.

Senator COBURN. Senator Kennedy, I would also like to submit for the record the RAND study on the availability of embryos—

The CHAIRMAN. Be so included.

Senator COBURN [continuing]. That are out there.

The CHAIRMAN. Be so included.

[The information previously referred to follows:]

# LAW & HEALTH *Research Brief*

The Law & Health Initiative is a collaboration of the RAND Institute for Civil Justice and RAND Health

## How Many Frozen Human Embryos Are Available for Research?

Frozen human embryos have recently become the focus of considerable media attention. Frozen embryos are a potential source of embryonic stem cells, which can replicate themselves and develop into specialized cells (e.g., blood cells or nerve cells). Researchers believe that such cells might be capable of growing replacement tissues that could be used to treat people suffering from a number of diseases, including cancer, Alzheimer's disease, and diabetes. Among the most contentious issues in the stem cell debate are whether frozen embryos should be used to produce stem cells for research purposes and whether it is appropriate to use federal funds for research involving human embryos.

Many of the proposed resolutions to the embryonic stem cell debate are based on assumptions about the total number of frozen human embryos in the United States and the percentage of that total that is available for research. Accurate data on these issues, however, have not been available. Guesses on the total number of embryos have ranged wildly from tens of thousands to several hundred thousand.

RAND researchers Gail L. Zellman and C. Christine Fair, together with the Society of Assisted Reproductive Technology (SART) Working Group led by David Hoffman, MD, have completed a project designed to inform the policy debate by providing accurate data on the number of frozen embryos in the United States and how many of those embryos are available for research purposes. Their findings include the following:

- Nearly 400,000 embryos (fertilized eggs that have developed for six or fewer days) have been frozen and stored since the late 1970s.

- Patients have designated only 2.8 percent (about 11,000 embryos) for research. The vast majority of frozen embryos are designated for future attempts at pregnancy.
- From those embryos designated for research, perhaps as many as 275 stem cell lines (cell cultures suitable for further development) could be created. The actual number is likely to be much lower.

### Vast Majority of Frozen Embryos Are Held for Family Building

The practice of freezing embryos dates back to the first infertility treatments in the mid-1980s. The process of *in vitro* fertilization often produces more embryos than can be used at one time. In the United States, the decision about what to do with the extra embryos rests with the patients who produced them.

The RAND-SART team designed and implemented a survey to determine the number and current disposition of embryos frozen and stored since the mid-1980s at fertility clinics in the United States and the number of those embryos designated for research. The survey was sent to all 430 assisted reproductive technology facilities in the United States, 340 of which responded. Estimates for nonresponding clinics were developed using a statistical formula based on a clinic's size and other characteristics. The results show that as of April 11, 2002, a total of 396,526 embryos have been placed in storage in the United States. This number is higher than expected; previous estimates have ranged from 30,000 to 200,000.

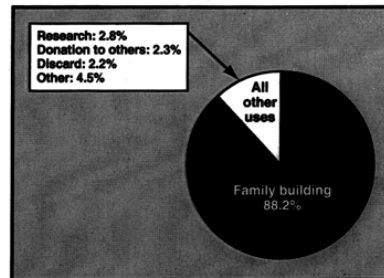
RAND research briefs summarize research that has been more fully documented elsewhere. This brief summarizes RAND-SART research reported in the following article: Hoffman DI, Zellman GL, Fair CG, Mayer JF, Zeitz JG, Gibbons WE, and Turner TG. May 2003. Cryopreserved Embryos in the United States and Their Availability for Research. *Fertility and Sterility* 79 (5): 1063-1069.

Although the total number of frozen embryos is large, the RAND-SART survey found that only a small percentage of these embryos have been designated for research use. As the figure illustrates, the vast majority of stored embryos (88.2 percent) are being held for family building, with just 2.8 percent of the total (11,000) designated for research. Of the remaining embryos, 2.3 percent are awaiting donation to another patient, 2.2 percent are designated to be discarded, and 4.5 percent are held in storage for other reasons, including lost contact with a patient, patient death, abandonment, and divorce.

#### Embryos Available for Research Do Not Have High Development Potential

Although the 11,000 embryos designated for research might seem like a large number, the actual number of embryos that might be converted into stem cell lines is likely to be substantially lower. Because assisted reproductive technology clinics generally transfer the best-quality embryos to the patient during treatment cycles, the remaining embryos available to be frozen are not always of the highest quality. (High-quality embryos are those that grow at normal rates.) In addition, some of the frozen embryos have been in storage for many years, and at the time that some of those embryos were created, laboratory cultures were not as conducive to preserving embryos as they are today. Some embryos would also be lost in the freeze-and-thaw process itself.

To illustrate how such laboratory conditions might limit the number of embryos available for research, the RAND-SART team performed a series of calculations. Drawing upon the few published studies in this area, they estimated that only about 65 percent of the approximately 11,000 embryos would survive the freeze-and-thaw process, resulting in 7,334 embryos. Of those, about 25 percent (1,834 embryos) would likely be able to survive the initial stages of development to the blastocyst stage (a blastocyst is an embryo that has developed for at least five days). Even fewer could be successfully converted into embryonic stem cell lines. For example, researchers at the University of Wisconsin needed 18 blastocysts to create five embryonic stem cell lines, while researchers at The Jones Institute used 40 blastocysts to create three lines.



Designated Use of Frozen Embryos in the United States as of April 2002

Using a conservative estimate between the two conversion rates from blastocyst to stem cells noted above (27 percent and 7.5 percent), the research team calculated that about 275 embryonic stem cell lines could be created from the total number of embryos available for research.<sup>1</sup> Even this number is probably an overestimate because it assumes that all the embryos designated for research in the United States would be used to create stem cell lines, which is highly unlikely.

#### Conclusion

The RAND-SART survey found that almost twice as many frozen embryos exist in the United States as the highest previous estimate. Only a small percentage of these embryos are available for research because the vast majority are reserved for family building. Among those that are in principle available for research, some have been in storage for more than a decade and were frozen using techniques that are less effective than those that are currently available.

<sup>1</sup>It should be noted that these conversion-rate estimates are based upon the conditions under which cryopreserved embryos were frozen as well as current techniques to create stem cell lines from such embryos. It is possible that as freezing procedures and laboratory techniques to create stem cell lines improve, the conversion rate could increase over time.

RAND's Law & Health Initiative brings together policy researchers with expertise in civil justice and health care issues to analyze the resolution of health care disputes and the effects of law and litigation on health care quality, cost, and access. Law & Health materials are available online at <http://www.rand.org/lh/> and <http://www.rand.org/health/>. RAND is a nonprofit institution that helps improve policy and decisionmaking through research and analysis. RAND® is a registered trademark.

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RB-9038 (2003)

Senator SANDERS. Thank you, Mr. Chairman, for holding this important hearing. Let me concur with colleagues in congratulating this extraordinarily wonderful panel for your testimony.

The House of Representatives recently voted, 253 to 174, to lift the current limits on Federal funding for embryonic stem cell research. And I have every reason to believe that the U.S. Senate is also going to vote in that direction. I certainly will vote for that.

Unfortunately, we have a situation—and Senator Coburn just told you what I suspect is the truth—that we have a President of the United States who will likely veto this legislation. I think that that is a tragedy, but that is the apparent reality.

The President regards this issue as murder. I, myself, have a little bit of difficulty understanding that. And the question that I



wanted to ask Dr. Daley is, Isn't it simply true that embryonic stem cells which are not implanted are simply discarded and thrown into the trash? Is that the case, or is that not the case?

Dr. DALEY. Well, I mean, there—one has to figure out what to do with the many, many tens of thousands—some would say hundreds of thousands—of embryos that are frozen. They're—a very, very tiny percentage would be adopted by others, a small number will be used by the couples themselves in future pregnancies, but the vast majority will be essentially destined for medical waste, discarded.

Senator SANDERS. And these are cells which you are telling us, today, could possibly lead to huge breakthroughs in a whole host of diseases which plague millions of Americans and people throughout the world, is that the case?

Dr. DALEY. Well, I mean, I think the extension is that there are enormous opportunities for using those embryos in medical research, whether it's for deriving stem cells, which is only one aspect of embryo research, these are enormously valuable tools and objects for study.

Senator SANDERS. So, on one hand, we are looking at these cells being discarded, destroyed; on the other hand, we are looking at these cells being used for research which can make major breakthroughs in some of the most terrible diseases facing humanity. Is that really the equation that we're looking at?

Dr. DALEY. I believe that is the direct——

Senator SANDERS. Well, you know——

Dr. DALEY [continuing]. Equation.

Senator SANDERS [continuing]. On many issues, the United States is being seen in a lower and lower light all over the world. And I have to say that when people around the world—when serious people are trying to deal with some of the worst illnesses and diseases facing humanity, they are wondering what is going on in our great Nation. And I would hope very much that all over our country people begin to stand up and express the long-held faith that we, as Americans, have had in basic science; that we try to continue the traditions that we have had as being a nation leading the world in breakthrough scientific research; and that we give the President of the United States all of the reasons in the world, scientific and political, that he should not veto this legislation.

Thank you very much, Mr. Chairman

The CHAIRMAN. Thank you very much.

Senator Hatch.

Senator HATCH. Well, thank you, Mr. Chairman.

A lot of my questions have been asked, but I'd like to just take this time to make some points.

I want to thank all of our distinguished scientists for taking the time to join us. And I especially want to thank you, Lauren, for being here—your testimony is very important to me, and, I think, to all of us here—for gracing us with your presence.

Mr. Chairman, this hearing is important, because opponents of embryonic stem cell research point to the fact that there are no treatments with embryonic stem cells—they say that it's a failed science. I say it's a handcuff science. And I've brought——

[Laughter.]

These handcuffs, from one of my Secret Service buddies, to make that point.

[Laughter.]

Now, think of these handcuffs while you listen to the expert scientists assembled here. They will tell us that they and their colleagues are holding the line against spinal cord injuries, Parkinson's disease, diabetes, and other illnesses. They are exploring the potential of stem cells from umbilical-cord blood, of stem cells from amniotic fluid, and, of course, of stem cells taken from adults, all of which we think is crucial and important, but they are not advancing as rapidly against these afflictions as they could by ethically using frozen cells from—stem cells from frozen and unused embryos, because their hands are bound.

While all forms of stem cell research should be aggressively pursued, scientists see great potential in the use of embryonic stem cells because they have the unique ability to become any kind of cell in the body, yet we are placing unnecessary and potentially disastrous obstacles in the way of scientists who wish to pursue this research to develop breakthrough treatments.

Let me give you just a few examples.

Dr. Marie Csete is an anesthesiologist and cell biologist from Emory University who works with embryonic stem cells. She tells us that the restrictions that current Federal policy places upon her and her colleagues are, in her words, "so odious that many scientists just do not try." I'll bet you agree with that.

Dr. DALEY. Yeah.

Senator HATCH. OK. We are wasting researchers' time, we are wasting their resources, and, in the final analysis, we are wasting the lives of many people who could be saved.

Now, I commend President Bush for authorizing Federal funds to study approved human embryonic stem cell lines isolated before August 2001. He's the only President who has allowed this. But this was hardly the key to unlock the treatments of the future. In 2001, there were 71 approved stem cell lines, that has since dwindled to 21 usable lines. And an NIH-funded stem cell researcher at the University of Texas, Dr. Ping Wu, told me that, in reality, there are only 12 usable lines, the others will not grow. Dr. Wu says the few usable cell lines are not enough to represent the general population in any way. Furthermore, these lines are contaminated with animal cells, mouse feeder cells, if you will, and, therefore, can never be placed in humans.

Dr. Linda Kelley, who happens to be here today, is an associate professor of medicine at the University of Utah, somebody I greatly admire. She told me that the approved cell lines are so unstable that—I know I'm taking a little more time. Is that all right, Mr. Chairman?

The CHAIRMAN. That's—you're always——

[Laughter.]

You always have something useful to say.

[Laughter.]

And so, we're glad to——

Senator HATCH. He doesn't dare prohibit me, I'll tell you. I know how to get to him.

The CHAIRMAN. Yeah.

[Laughter.]

Senator HATCH. But Dr. Kelley is an associate professor of medicine at the University of Utah. She told me that the approved cell lines are so unstable that, in her words, "You are lucky if you can recover 10 percent of the cells they send to you." Now, she said the cells have been reused for so long that they have degraded and no longer represent the human population at all. And I'll bet you agree with that.

Another unintended consequence of the President's policy is the creation of monopolies. Many owners of these few approved stem cell lines have used their monopoly to make the cells very expensive and difficult to obtain.

Dr. Rick Wetsel, at the University of Texas Health Center, told me about paying \$5,000 for one approved cell line, only to find that the cells were worthless, forcing him to pay another \$5,000 and wait 6 months for a new batch. Another scientist, Dr. Csete, who I mentioned before, was charged \$20,000 for what should have been a \$500 cell line. The cells they've purchased have been reproduced so many times that they do not live very long and cannot be used with normal laboratory techniques. So, they are spending more money for less valuable material.

These restrictions also waste time and effort. NIH funds are the bedrock of every university's research program. Hardly a piece of equipment or a technician in a medical school, is not in some way, supported by NIH. You agree with that, don't you? You bet your life.

Ms. LANDIS. Yes.

[Laughter.]

Senator HATCH. Medical school deans and scientists are afraid of violating Federal law by allowing equipment and personnel funded by the NIH to touch a nonapproved cell line. You all agree with that.

Dr. Wetsel, in Houston, spent several years obtaining enough funds from a private donor to work with a fresh cell line derived from a discarded frozen embryo. He was forced to use most of the precious funds to buy duplicate equipment and then place it in a small laboratory that was isolated from the rest of his NIH-funded facility.

Dr. Csete told me that she is unable to send her doctors-in-training to study stem cell techniques in expert laboratories that work with nonapproved lines, because their salaries were funded by NIH.

Scientists in the United States are either walking away from embryonic stem cell research or they're walking away from the United States.

Now, Mr. Chairman, let me just cite one more proof of how our current policy is handcuffing this promising research.

In the first 6 years after human embryonic stem cells were discovered, at the University of Wisconsin in 1998, half of the 20 most quoted publications on this research came from the United States. But a closer look at these publications is troubling. Seven of those ten U.S. publications came from the University of Wisconsin and Geron Corporation, both heavily endowed with private funding. Only 3 of the 125 U.S. academic medical centers contributed a top

human embryonic stem cell publication in the 6 years after their discovery. If the United States is to remain among the world's leaders in this research, that simply must change. We must give scientists who want to work with embryonic stem cells a chance, just like we do for stem cells from cord blood, amniotic fluid, and from adults, all of which I support strongly.

As Professor Kelley told me, "There is so much to be learned, and it is terribly frustrating." It shouldn't be that way. It doesn't have to be that way. And I think we've got to unlock these handcuffs and let our scientists find these treatments and cures that'll help Lauren and others similarly situated. And that's all you want, is a chance to really make these things go.

And last, but not least, I said, after we had won this debate on the floor of the Senate—in the press conference afterwards, I said, "Look, there are at least 300 embryonic stem cell lines that are fertile and working in our society today. Why can't we, since the Government had not participated in the destruction of the embryo, allow NIH to partner with those 300—with those companies and those 300 lines that would partner with them"—and I think they all would—"so that we can push this research forward?" That's what was the theory behind the original 71 stem cell lines that the President said we could have. Why not do that? And I don't think it's a good answer to say, "Well, that would encourage them to continue to destroy embryos."

I just want to tell you how much your testimonies, all of you, have meant. And the leadership of these fellows sitting up in front here—and we're happy to have Bernie Sanders with us. I've got to admit, I was worried about that, but I—

[Laughter.]

I appreciated his comments this morning.

But I want to thank each of you. I think you've made excellent statements. They're straightforward, they're honest, and, frankly, accurate and true.

Sorry, Mr. Chairman, I took too long, I know that.

The CHAIRMAN. Well, thank you. We'll forgive that extra time, as long as you get the SCHIP out of the Finance Committee to look at our health insurance for the—

[Laughter.]

Senator HATCH. Well, we got it out before.

The CHAIRMAN. That's right.

Senator Allard, thank you for your patience and for joining our committee. I look forward to hearing from you.

Senator ALLARD. Well, thank you, Mr. Chairman. And I appreciate the fact that you're holding this hearing. It's the first opportunity I've had to listen to testimony from the NIH.

And I'm going to, kind of, steer away from the political arguments and focus a little bit on the science and kind of look at it from a practical aspect.

It's obvious that we've got a problem with the number of dollars that you can use for research; you have to set priorities. The other challenge that I see are that we have an ethical concern raised by some members of this committee. I know, in the scientific community, we also have those ethical concerns.

So, the question that I see before us is, How do we take a patient like Lauren—by the way, I'm a veterinarian, so I've had some medical training—but how do you take a patient like Lauren, and how do you most quickly get a remedy for her juvenile diabetes?

And I'd also bring out another axiom, in veterinary medicine, when we use a more specific treatment, the fewer side effects we're going to deal with. That's true in immunology, too. We're developing vaccines whose antigens are more specific, so you have fewer reactions to it.

As I picked up from your testimony, we have a huge immunological problem here. It seems to me that we would do best to focus on stem cells for islet cells than we would to focus our efforts on a pluripotent type of cell, that, in the long run, the chances of coming up with a treatment that would have fewer immunological problems would be to take a specific approach like that.

My question to both of the physicians that are here is, In your research, in trying to set priorities, have you thought about taking this type of approach, as opposed to an omnipotent approach and if you have, how far along are you in this? I mean, have we identified—the questions have come up—have we identified stem cells for islet cells, or have we identified stem cells for pancreatic cells, in general? Just how far along are we in that? And I think that would help us in our debate.

Dr. DALEY. Yeah. So, if we speak about type-1 diabetes, which is the loss of insulin-producing beta cells, and the best hope for cure for Lauren is to replace those beta cells. It is currently highly controversial as to whether or not her body, or any of our bodies, actually possess stem cells that regenerate insulin-producing beta cells. Highly controversial. It is, however—

Senator ALLARD. So, some are saying that they believe there is that—

Dr. DALEY. Some are saying it's—

Senator Allard [continuing]. Possibility, some say that it—

Dr. DALEY. And it's—

Senator Allard [continuing]. Doesn't.

Dr. DALEY. And so—

Senator ALLARD. Yeah.

Mr. DALEY [continuing]. The way to balance the priorities of research are to let expert scientists make those decisions. I don't think those priorities are well decided here in the Halls of Congress. And that's done through a very extensive and rigorous peer-review system that the NIH has pioneered. I think that's where the decisions should be made.

Dr. WAGNER. But just to further that, when stuff—basically, you know, all those avenues are being pursued, perhaps at one institution, or many institutions. But I can tell you, even at our own institution, we're exploring not only islets, as a form of therapy gotten from the patient—him or herself—we're also exploring the use of sibling donors, also exploring unrelated donors for islets, as well as porcine donors, the pig donors, for islets, as a strategy for treating human patients with diabetes, in addition to multipotent adult stem cells, in addition to embryonic stem cells. But going back to the analogy that Mr. Harkin had, you know, stated years ago, Why would we ever want to close any of those doors, when we don't

know which one will be the true therapy that will have the most benefit for the patients with diabetes? We don't want to close any door. And that's what the scientists are asking for, that ability.

Senator ALLARD. Well, the problem I have with that is you know, maybe not close the door, but what you need to do is, you need to look at where you're going to most likely get the best results from the taxpayer dollars that you're spending. I mean, that's—

Dr. WAGNER. But we don't—

Senator Allard [continuing]. That's the challenge we have. And I think it's—

Dr. DALEY. Right.

Senator Allard [continuing]. Your challenge, as researchers—

Dr. DALEY. And that's the challenge—

Senator Allard [continuing]. To convince us—

Mr. DALEY [continuing]. Of the peer-review process—

Senator ALLARD. Yeah—is to convince us—

Mr. DALEY [continuing]. To determine the right—

Senator ALLARD [continuing]. As scientists—

Dr. DALEY [continuing]. Priority.

Senator ALLARD [continuing]. That you have that plan and you've given that some thought. And that's the reason I bring up the arguments in the way I did, because the challenge I think you have, as scientists, to present to us, as policymakers, Where you are going to get the best results that'll get the quickest cure for Lauren while realizing we have a limited resource in taxpayer dollars. We just can't—we can't open every door—

Dr. WAGNER. Sure.

Senator ALLARD [continuing]. So we have to take a look at those doors that most likely will open up to a quicker solution.

Dr. WAGNER. Well, in response to that, I think that, you know, we're already doing it. All the doors are open. It's just some of the doors are being markedly slowed down.

But the fact is, is that you're asking for the answer before the researchers know what the answer is. We don't know what the best therapy will be. Of course, in the meantime, we explore what we can do, and that is, we can look at islets as a form of cellular therapy. But I would believe, based on the results that we have so far, that islet transplants themselves are a short-term fix, they don't reproduce themselves for the life of the patient. Maybe we'll figure out a way of doing that in the future, but right now we don't know. And how can I speculate what I don't know? So, we have to explore all the options. And I think that we're doing that.

Ms. LANDIS. So, if I could just add, for nervous-system diseases, the evidence is pretty clear that adult stem cells, and even, most recently, the amniotic-fluid-derived stem cells, really aren't going to provide us with the tools that we need. We now have recipes to create dopamine neurons for Parkinson's, motor neurons for spinal cord injury, oligodendrocytes, or ensheathing cells, for spinal cord injury, retinal progenitor cells. And that's been done within the 5 years since the President's policy was put—

Senator ALLARD. Yeah.

Ms. LANDIS [continuing]. In place.

Senator ALLARD. Yeah.

Ms. LANDIS. And if, with Senator Hatch's handcuffs, we've been able to do that, imagine what the opportunities are without the handcuffs.

Senator ALLARD. Thank you.

The CHAIRMAN. Thank you.

Senator Hatch.

Senator HATCH. Mr. Chairman, could I just ask the whole panel—the three doctors one question?

The CHAIRMAN. Certainly.

Senator HATCH. Sorry to go out of turn, but—

Dr. Landis, we'll start with you. In your opinion—and I think this is an important question—if NIH funds were made available for research, you know, on all ethically obtained embryos from in vitro fertilization, would the probability of finding treatments and/or cures, we'll put it that way—for human diseases, increase or decrease?

Ms. LANDIS. Absolutely it would increase. There's no question about that.

Senator HATCH. Just barely, or would you have a real opportunity to—

Ms. LANDIS. We would have a real opportunity. I can give you one specific example. Huntington's disease is an inherited disease, triplet repeat disease, causes a particular kind of death of neuron in the brain. We have no good animal models. We don't know why those cells die. We don't know how to stop that process. If we had embryonic stem cells derived from discarded embryos that were not implanted, we would be able to make extraordinary inroads into therapeutics for that disease.

Senator HATCH. Dr. Daley.

Dr. DALEY. I would say, in general, any investment in basic biomedical research is an incredibly important investment for this country. It pays off handsomely, in terms of human health. It's now an issue of national security, given the issues around bioterrorism. And we, in general, will derive enormous economic benefit, long-term economic benefit, from raising the overall NIH budget, not just stem cells.

Senator HATCH. For embryonic stem cells.

Mr. Wagner.

Dr. WAGNER. The first thing that I'd do, like Dr. Kelley, would be to actually derive cell lines that would be perfect for use in clinical settings and for patients, which—none of them currently exist today. Second thing I'd do is, I would actually then make you also think about that this is more than just a cell therapy. As Dr. Daley previously mentioned, these cells also give us an unprecedented ability to look at new drugs. We can look at molecular events and better understand why diseases occur. So, it's much more than just a cell therapy.

So, it would have a profound effect. But, also, from a practical point of view, right now the restrictions that we have are, as you've heard, just getting the ability to be able to take the cell that's newly derived and be able to give it to our neighbor in Iowa or to be able to then give it to the lab next door, outside the confounds of what the Government will allow us, because these are NIH-fund-

ed labs, would make it just extraordinarily easy for us to make advances rapidly.

Senator HATCH. Lauren, we want to help all people like you. And these great scientists can do it, if their hands are not handcuffed. And we've just got to make sure they're not handcuffed. We're going to win on this, but it's a shame that it's been 3, 4 years since we really started putting a drive on it. And, for the life of me, I can't understand how some of my friends believe that discarding, as hospital waste, 7,000 to 20,000 embryos a year is the right thing to do. We ought to be utilizing them for Lauren and people who similarly suffer. We've just got to wake up on this; untie your hands and allow you to really do the research that has to be done.

This group—many in this hearing today are really dedicated to trying to do that. And others are very sincerely on the other side, but it's just a matter of time. We've just got to move this forward.

And I particularly appreciated your testimony in front of NIH today. I know it took a lot of courage for you to do that.

The CHAIRMAN. Thank you.

Senator HATCH. Thank you.

The CHAIRMAN. Senator Hatch, like our colleagues Senators Harkin, Specter, and others, has been a real leader in this whole—

Senator HATCH. Thanks.

The CHAIRMAN [continuing]. And I want to pay tribute to his leadership. It's been very, very important.

And I had just one final question, if I could. All of you have been extremely patient. And that is, Dr. Landis, could we talk about those ethical restrictions that we have in the research now that guide Federal research, not necessarily applicable to other research? One of the powerful arguments that can be made is, with the Federal research, on that, there are going to be the appropriate kind of ethical guidelines which are so—

Ms. LANDIS. Right.

The CHAIRMAN [continuing]. Important, in a major—

Ms. LANDIS. Right.

The CHAIRMAN [continuing]. New area—

Ms. LANDIS. Right.

The CHAIRMAN [continuing]. Of research.

Ms. LANDIS. So, I—

The CHAIRMAN. Just—

Ms. LANDIS [continuing]. I think it's very—

The CHAIRMAN [continuing]. Just briefly—

Ms. LANDIS [continuing]. Clear that federally funded research has monitoring, oversight, and transparency that privately funded research will not necessarily have, and that, to the extent that embryonic stem cell research is funded by Federal dollars, then that research will benefit from those oversight procedures.

The CHAIRMAN. I think it's very important that it's been included in the legislation from the beginning.

Tom.

Senator HARKIN. Mr. Chairman, again, I want to thank everyone for being here and for hanging in there on this and continuing to inform us and enlighten us on the various aspects of all the different forms of stem cell research. And I just want to make it clear for the record, from my standpoint, this Senator's standpoint, I'm



a strong supporter of all stem cell research. I made that clear from the very beginning, whether it's adult stem cell, amniotic, cord blood—I think these are all worthy of the most profound research that we can do in our society. And they can all lead to different things. Some may be good here. You used the analogy of the seeds. Some may be good here, Dr. Wagner, for what you're doing out there; some may be good some other place.

But I think what Senator Hatch said was really very important and we've got to keep it in mind. I had asked Dr. Daley this question before, about why don't we just leave it to the States and private entities? Senator Hatch, I think you've really hit upon a key part of that, and that is—and I've heard this from scientists around the country that, because NIH funding is so pervasive through universities and academic research centers and everything else, that if they want to do this kind of research, the hoops they've got to go through. If California moves ahead on what they're doing, they will be building separate buildings, separate research centers just to do this. What a waste of money and resources. Scientists right now have to set up different rooms and different labs, and they can't use their computers at night, because those computers are used also for NIH-funded research, so they can't get online and do that.

Last, one of the analogies I would make on why this is so important for Federal research, is that this committee funded the first money into the human genome research in 1989. Dr. Watson came to see us. We started putting money in it. And out of that came the human genome center at NIH and the mapping and sequencing of the human gene. What's so wonderful about that is not only the knowledge that we've gained from that, but the fact that it's free for everybody. It's out there. Anyone, anywhere in the world, can go in there and find all that information. Now, if we had left that just to the private sector—and, believe me, I love Craig Venter, he's been a friend of mine, he's done great research, but the fact is that we would have had snippets, perhaps, of different parts of the genome that would have been available, at a great, high price that Senator Hatch was talking about, and others, but we might not have had the whole genome mapped and sequenced. But the fact is, you can go online right now, and you can find any one of those 3 billion pairs anywhere, and it's available for research. It seems to me, stem cell research lends itself to this kind of thing. And I don't mean just embryonic stem cells, I mean all stem cell research, that if it's done by NIH, and funded by NIH, you get it done ethically, you have monitoring, you don't have duplication, it's much more efficient and effective, you have scientists talking to one another in free form, and all the results of that information is available to the public. It's available to anyone.

And, who knows, there might be a young Lauren someplace who's just a budding young scientist, not bound by old concepts and old ways of doing things, that sees some research being done there and say, "I think I can do something different with that." It's one of those young scientists that's going to find how to take some of these cells and move them in different directions. That, to me, is the promise of all this.

I love the handcuffs. I mean, I think that was really illustrative of what we're talking about here, Senator Hatch, and getting the handcuffs off of the Federal Reserve.

Dr. DALEY. Senator Harkin.

Senator HARKIN. Who said something?

Dr. DALEY. I'm sorry, if I could just return to your issue of the ethical oversight of stem cell research, I want to make the point that scientists are very motivated to do the research in a climate of rigorous and ethical oversight, and the International Society for Stem Cell Research is about to announce a set of guidelines to govern the conduct, to establish rules of play for scientists. These are guidelines that have been vetted through an international committee. And what we're hoping is that scientists all over the world, well beyond the reach of U.S. oversight, will agree to the same common set of ethical principles so that the public, worldwide, can really embrace this science.

Senator HARKIN. Well, I pointed out before that the bill that we're talking about here, that we passed last year, the same one we're talking about now, has stronger ethical guidelines and strictures on it than what's in existing law right now. Very strong ethical guidelines. As you know, the research can only be done on those embryos left over in in vitro fertilization clinics and has to have the fully informed written consent of the donors. No money can change hands, so there can't be any farming and that kind of stuff; it has to be done voluntarily with fully informed written consent and only with those embryos that would be discarded anyway. And last, they can only be used for stem cell research—can't be used for implantation and other things, only be used for stem cell research. To me, these are pretty tough ethical guidelines, right there. Tougher than what we have in existing law right now. I always say to my friends that if they want more ethical standards, well, we have them in our bill, and they're there.

Well, Mr. Chairman, again, thank you very much for this joint hearing. We will continue to pursue this on both levels, on yours and on the Appropriations Committee. And, of course, we are hoping, Dr. Landis, with your great leadership, and the whole NIH, that we can have a better budget for NIH, this next year. It's unconscionable to me, and I know it is to my good friend Arlen Specter, that we are fighting, right now, just to get funding for NIH at the 2005 level. It's not that we're asking for a big increase, we're just trying to get back to the 2005 level in the budget. Hopefully this year we can move it ahead, and more aggressively. And again, if we do that and open up these doors, perhaps we can make some really, really significant progress so that Lauren can become that Senator in Massachusetts.

[Laughter.]

The CHAIRMAN. That's good.

Senator HARKIN. So, thank you very much.

The CHAIRMAN. Tom, thanks so much. You can feel Senator Harkin's passion about this issue, and can see why he's such a leader in this undertaking.

Senator Hatch just has a final few questions and—like to address the panel.

Senator HATCH. I'm sorry to keep you a little bit longer, but this is an important question. We'll start with you, Dr. Wagner, and then have the three doctors give a crack at this.

I don't know if you're all aware of it, but the Web site for the organization called Do No Harm lists 71 diseases that are treatable by adult stem cells. Among the diseases listed spinal cord injury, stroke, and Parkinson's disease. Now, three clinical scientists from three separate academic medical centers reviewed this Web site and concluded that adult stem cells were clinically proven, and FDA approved to treat only 9 diseases, not 71.

So, my question on that is this. Which is the correct number? How many diseases are you aware of that are treatable by adult stem cells currently? I'm for pushing adult stem cell research as fast as we can, as far as we can, but I don't want to have misrepresentations if these doctors are right, that there are only 9 diseases and not 71.

Dr. WAGNER. Well, I think that within the context, as I presented, the context of using adult stem cells, the only proven use of adult stem cells is in the setting of bone marrow transplant to treat leukemia——

Senator HATCH. Right.

Dr. WAGNER [continuing]. Bone-marrow failure. As far as I know, there is no proven use of adult stem cells. However, are there FDA-sponsored or, you know, monitored trials that are ongoing to ask the question, you know, Would this be useful therapy? Yes, there's quite a few different therapies currently being explored, but are not yet definitive.

Senator HATCH. But to say that there are 71 currently in use would not be a good representation by a scientist.

Dr. WAGNER. No, it's misleading. Seventy-one may be under study, but certainly have not been proven.

Senator HATCH. Dr. Daley.

Dr. DALEY. Yeah, I mean, with all due respect to Dr. Wagner's fabulous contributions to bone marrow transplantation, this is not a panacea, this is a heroic, highly toxic form of therapy which is really used in an attempt to save people with fatal diseases. To say that we don't need embryonic stem cells, because look at all this success with adult stem cells, is really to deny the fact that the current therapies are inadequate. They are just grossly inadequate. The future is in pushing research so that we can truly have curative therapies for those 71 diseases.

Senator HATCH. Do you agree with that?

Ms. LANDIS. So, I actually have the letter to Science—it was in the July 13 issue—in front of me, from Smith, Neaves, and Teitelbaum, which lists the evidence indicated that there are 9 and not 71, and you might want to have it introduced into the record.

Senator HATCH. I'll ask the Chairman to introduce it in the record.

**[Editor's Note: The information previously referred to can be found at [www.sciencemag.org](http://www.sciencemag.org).]**

**[Response by Prentice and Tarne to the above letter can be found in Additional Material.]**

Ms. LANDIS. And it's very clear that there are nine approved—FDA-approved, clinically tested treatments, but that is all that

presently exist. NIH believes it's critical to continue to fund all kinds of stem cell research so that, again, we can move that 9 closer to the 71.

Senator HATCH. Dr. Landis, are you aware of any young scientists who have redirected their research interest because of the lack of Federal funding for embryonic stem cell research?

Ms. LANDIS. I know of many young scientists who are finishing their training who are very reluctant to move into, or retain activities in, human embryonic stem cell research, because of all of the complexities that you've heard to date.

Senator HATCH. Well, now, Dr. Daley, let me just finish with these questions. Really, this panel has been one of the best panels I've ever heard on healthcare. And I've heard a lot of them over the last 30 years with my friends on my left here. And we've sat through a lot of hearings, and this has been a great panel. But, Dr. Daley, opponents of embryonic stem cell research have made much of the fact that these cells are reported to produce tumors in experimental animals. What are scientists' views on this problem? And how do you think the potential for amniotic stem cells may prove to stack up against embryonic stem cells as potential therapies, or is it too early to tell?

Dr. DALEY. We know about this issue, that embryonic stem cells form a type of benign encapsulated mass, which is called a tumor. We have strategies for dealing with that. No one is thinking about any kind of cell therapy that would involve transplanting the undifferentiated stem cells. You predifferentiate, you make the tissue of interest, the highly specialized insulin-producing cell or blood cell—those are not tumorigenic cells. It's an issue of safety, it's an issue of clinical testing. We're at the earliest stages, we know about it, and we're going to anticipate it, and we're going to look very, very hard for ways to get around it.

Senator HATCH. Then you believe you can solve that problem.

Dr. DALEY. We do believe we can solve that problem, yes.

Senator HATCH. OK. Now, what about the potential for amniotic stem cells that—how may they prove to stack up against embryonic stem cells as potential therapies or—again, is it too—

Dr. DALEY. Yeah.

Senator HATCH [continuing]. Early to tell?

Dr. DALEY. Well, amniotic stem cells are fascinating. They are not embryonic stem cells. They will not do everything that embryonic stem cells do. But we have work, at the Children's Hospital, with kids who are diagnosed with diaphragmatic hernias, in ultrasound, in utero. You can take the amniotic cells, you can grow a patch to be used in that child. This is a very exciting application of this work. In no way should one choose embryonic over amniotic. They both need to be studied, and we need more funding to do it.

Senator HATCH. So, they're complementary.

Dr. DALEY. They're complementary, not competitive.

Senator HATCH. Do either of the other two doctors care to comment about that?

Dr. Wagner?

Ms. LANDIS. So, if I could just say, there's a paper recently that's received a lot of attention. Cells differentiated into dopamine neurons transplanted in human embryonic stem cells, differentiated

into dopamine neurons transplanted into a rat model of Parkinson's, and they did, in fact, see tumors. I would say that this is one of a number of studies, and, in the other studies, there was no evidence of a teratoma or a tumor. And the point that Dr. Daley has made is that almost certainly undifferentiated cells were transplanted, and, by selecting the differentiated from the undifferentiated, you can prevent tumor formation. So, this is——

Senator HATCH. OK.

Ms. LANDIS [continuing]. An unusual——

Senator HATCH. But you can use embryonic stem cells to reach the differentiated status, is——

Ms. LANDIS. Right.

Senator HATCH [continuing]. What I——

Ms. LANDIS. Right.

Senator HATCH [continuing]. Understand——

Ms. LANDIS. Right. Right.

Senator HATCH [continuing]. Dr. Daley said.

Dr. Wagner, we'll finish with you.

Dr. WAGNER. My only comment was really to emphasize that, you know, all the data suggests, exactly as Dr. Daley had indicated, that there are strategies that we can employ to overcome this issue of teratomas from the embryonic stem cells. Furthermore, you know, the idea of using amniotic stem cells as a future therapy currently is—certainly needs to be explored, but it's currently all speculative, at this point, where it will go. Again, we need to explore all the options.

Senator HATCH. But without exploring it, we will never——

Dr. WAGNER. We'll never know.

Senator HATCH [continuing]. Be able to know whether we can arrive at these treatments or cures that could save us trillions of dollars in healthcare costs and maybe make a lot of the current surgical procedures and other procedures not necessary. I see this as the only way we're going to stop our healthcare budget from just consuming the whole Federal budget. But it's going to take years. That's what science is all about. It's not something you snap your fingers about, it's something that takes years and years, by brilliant people, who basically never give up, and who can get around these so-called "problems" by continued research.

And I just want to compliment all of you here today. And, Lauren, thank you for taking time to be here. You're the most sophisticated—and you're in ninth grade, you say?

Ms. STANFORD. Uh-huh.

Senator HATCH. You're the most sophisticated ninth grader I've ever met in the Senate, so I just want you to know that.

[Laughter.]

The CHAIRMAN. So, thank you.

Just concluding, I'm a great believer that we are in the life-science century, and we have—the opportunities for breakthroughs are unlimited, and the impact that it can have on the quality of life in our families and for our country, and, as was pointed out, for our economy, in—an innovative new economy with all the implications that that has in—for people that are working in this and for leading the world, and demonstrate our interest in helping to solve the human condition in other parts of the world. We have——

all of this is a breathtaking possibility. And this is an aspect of it, in terms of the stem cell research that is just an indispensable aspect of it. So, we are very strong supporters.

What I want to just say is, we have every intention, for those that are here today, of having this on the Senate floor. This is a—priorities in the House, and we have talked to the leadership, our Democratic leader, hopefully with our Republican leader, as—that I mentioned, Senator Hatch has been a strong leader on this issue. We've had a very strong bipartisan commitment. But this is going to be on the—this is a high priority, and we expect this to be considered—the earlier the better, but certainly in February. And so, this is moving ahead, and this hearing will be really instrumental.

And we want to just conclude by congratulating Lauren's parents, too, for doing a great job.

The committee stands in recess.

[Additional material follows:]

## COMMENTARY

Learning languages

332

Animal health  
and poverty

333



LETTERS | BOOKS | POLICY FORUM | EDUCATION FORUM | PERSPECTIVES

## LETTERS

edited by Etta Kavanagh

## Treating Diseases with Adult Stem Cells

IN THEIR LETTER "ADULT STEM CELL TREATMENTS FOR DISEASES?" (28 JULY 2006, P. 439), S. Smith *et al.* claim that we misrepresent a list of adult stem cell treatments benefiting patients (1). But it is the Letter's authors who misrepresent our statements and the published literature, dismissing as irrelevant the many scientists and patients who have shown the benefits of adult stem cells.

We have stated that adult stem cell applications have "helped," "benefited," and "improved" patient conditions. Smith *et al.*'s Supporting Online Material (2) repeatedly notes patient improvement from these cells (3). We have never stated that these treatments are "generally available," "cures," or "fully tested in all required phases of clinical trials and approved by the U.S. Food and Drug Administration (FDA)." Some studies do not require prior FDA approval (4), and even the nine supposedly "fully approved" treatments acknowledged by Smith *et al.* would not be considered "cures" or "generally available" to the public at this stage of research.

The insistence that no benefit is real until after FDA approval is misplaced. Such approval is not a medical standard to evaluate patient benefit, but an agency determination that benefits outweigh risks in a broad class of patients. Physicians and patients use an evidentiary standard. Our list of 72 applications, compiled from peer-reviewed articles, documents observable and measurable benefit to patients, a necessary step toward formal FDA approval and what is expected of new, cutting-edge medical applications.

Smith *et al.* also mislead regarding citations for testicular cancer and non-Hodgkin's lymphoma, referring to "[t]he reference Prentice cites..." as though only one reference existed in each case, and not mentioning four other references that, according to their own SOM, show "improved long-term survival" of patients receiving adult stem cells. There are currently 1238 FDA-approved clinical trials related to adult stem cells, including at least 5 trials regarding testicular cancer and over 24 trials with non-Hodgkin's lymphoma (5). They also disregard studies showing successful stimulation of endogenous cells for Parkinson's.

"The ethical and political controversy surrounding embryonic stem cell research makes scientific claims especially prone to exaggeration or distortion. All such claims should receive careful scrutiny..."

—Prentice and Tarne

The ethical and political controversy surrounding embryonic stem cell research makes scientific claims especially prone to exaggeration or distortion. All such claims should receive careful scrutiny, as recently acknowledged by the editors of this journal after two articles claiming human "therapeutic cloning" success were revealed to be fraudulent. This scrutiny should be directed equally to all sides. We note that two of our critics, Neaves and Teitelbaum, are founding members of a political group whose Web site lists over 70 conditions that "could someday be treated or cured" using embryonic stem cells (6). High on this list is Alzheimer's disease, acknowledged by experts as a "very unlikely" candidate for stem cell treatments, with one NIH expert describing such a scenario as a "fairy tale" (7). The entire list, in fact, is based on no evidence of benefit in any human patient from embryonic stem cells and little evidence for its claims in animal models. No one should promote the falsehood that embryonic stem cell cures are imminent, for this cruelly deceives patients and the public (8).

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## References and Notes

1. Posted at the web site of Do No Harm: The Coalition of Americans for Research Ethics: [www.stemcellresearch.org](http://www.stemcellresearch.org).
2. Available at [www.sciencemag.org/cgi/content/full/1129987/DC1](http://www.sciencemag.org/cgi/content/full/1129987/DC1).
3. See Table S1 in the Supporting Online Material on Science Online at [www.sciencemag.org/cgi/content/full/315/5810/328b/DC1](http://www.sciencemag.org/cgi/content/full/315/5810/328b/DC1); seven applications were not analyzed in the editorial update of 12 July 2006.
4. E.g., for studies done outside the United States. FDA approval is irrelevant; also see, e.g., 21 CFR 1271.10, 21 CFR 1271.15, 21 CFR 1271.3.
5. See [www.clinicaltrials.gov/ct/search?term=stem+cell](http://www.clinicaltrials.gov/ct/search?term=stem+cell) (accessed 13 October 2006); initial search shows clinical trials recruiting patients; click box in upper left to show all trials, including those no longer recruiting patients.
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## Moving Toward Decarbonization

CONCENTRATED SOLAR THERMAL (CST) ENERGY, such as that used at the SEGS solar energy plants, is not new. What appears to be new is R. Shinnar and F. Citro's suggestion that oil at a temperature of >800°F can be stored for hours or days before being used to generate steam ("A road map to U.S. decarbonization," *Policy Forum*, 1 Sept. 2006, p. 1243).

Tucson, Arizona, at 32°N latitude has average daily solar insolation of 2,000 Btu/ft<sup>2</sup>. This is the highest level in the United States and occurs only in the southern half of Arizona and a small part of New Mexico. During the peak summer periods, the rate of solar energy falling on a given land area is more than five times the rate in winter. Further, about 60% of the solar energy comes between 10 a.m. and 2 p.m.

Consequently much of the oil would be heated to >800°F during midday in summer and stored for use in the winter. The amount of hot oil storage required to provide 50% of U.S. energy consumption is enormous and impractical.

## SUPPORTING MATERIAL FOR TREATING DISEASES WITH ADULT STEM CELLS

DAVID A. PRENTICE AND GENE TARNE

TABLE S1. DISEASE AND CONDITION CHART

List of conditions in which adult stem cell use produced therapeutic benefit for human patients (1)

Disease or Condition	Quotes from Smith, Neaves, Teitelbaum (emphasis added) (2)	Additional Comments
Brain Tumors ..... (Medulloblastoma and Glioma) (3–5) ...	Two clinical studies and one literature review indicated that some patients who have their brain cancers treated with high-dose chemotherapy show <b>improved long-term survival rates</b> when transplants of adult stem cells from bone marrow or blood are used to alleviate side effects of the chemotherapy.	Clinical improvement shown by peer-reviewed reference.
Retinoblastoma (6–7) .....	Two clinical reports indicated that a small group of patients with malignant retinoblastoma show <b>improved survival rates</b> when transplants of adult stem cells from bone marrow or blood are used to alleviate side effects of chemotherapy.	Clinical improvement shown by peer-reviewed reference.
Ovarian Cancer (8–9) .....	One clinical study and one literature review indicated that a subset of ovarian cancer patients <b>responds better to high-dose chemotherapy when treatment is followed by adult stem cell transplants</b> .	Clinical improvement shown by peer-reviewed reference.
Merkel Cell Carcinoma (10) .....	A case study reporting that a single Merkel cell carcinoma patient showed a <b>longer-than expected survival time</b> when given an adult stem cell transplant after chemotherapy.	Clinical improvement shown by peer-reviewed reference.
Testicular Cancer (11) .....	Bhatia <i>et al.</i> described a clinical evaluation showing <b>improved long-term survival</b> of relapsed testicular cancer patients following a radical therapy that included a transplant of adult stem cells from bone marrow or blood.	One technical reference removed. Remaining reference not mentioned by Smith <i>et al.</i> in letter.
Lymphoma (12–14) .....	Three clinical reports of various lymphoma types and patient numbers indicated that some patients show <b>improved long-term survival</b> when adult stem cell transplants follow high-dose chemotherapy.	Clinical improvement shown by peer-reviewed reference.
Non-Hodgkin's Lymphoma (15–18) .....	Three clinical studies reported that some non-Hodgkin's lymphoma patients show <b>improved long-term survival</b> when adult stem cell transplants follow high-dose chemotherapy.	One technical reference removed. Three references not mentioned by Smith <i>et al.</i> in letter.
Hodgkin's Lymphoma (19–20) .....	Two clinical studies indicated that some patients with Hodgkin's lymphoma show <b>overall improved survival rates</b> when transplanted with adult stem cells from blood.	Clinical improvement shown by peer-reviewed reference.
Acute Lymphoblastic Leukemia (21–23)	Two clinical studies, each incorporating multiple leukemia types, indicated that adult stem cell transplants from bone marrow or umbilical cord blood <b>improve the survival</b> of children with leukemia when the transplants are performed during the early phase of disease. Adult stem cell transplants from bone marrow or blood <b>can induce lasting remission</b> when leukemias are diagnosed early.	Clinical improvement shown by peer-reviewed reference. FDA-approved through phase IV clinical trials according to Smith <i>et al.</i>



TABLE S1. DISEASE AND CONDITION CHART—Continued

List of conditions in which adult stem cell use produced therapeutic benefit for human patients (1)

Disease or Condition	Quotes from Smith, Neaves, Teitelbaum (emphasis added) (2)	Additional Comments
Acute Myelogenous Leukemia (24–27) ..	Three clinical studies indicated that AML patients who receive adult stem cell transplants after initial disease remission demonstrate <b>improved overall survival</b> . Adult stem cell transplants from bone marrow or blood can accomplish <b>significant improvements in the survival</b> of early-stage AML.	Clinical improvement shown by peer-reviewed reference. FDA-approved through phase IV clinical trials according to Smith <i>et al.</i>
Chronic Myelogenous Leukemia (28–29)	Two clinical studies, each incorporating multiple leukemia types, indicated that adult stem cell transplants from bone marrow or umbilical cord blood <b>improve the survival</b> of children with leukemia when the transplants are performed during the early phase of disease. Adult stem cell transplants from bone marrow or blood <b>can induce lasting remission</b> when leukemias are diagnosed early.	Clinical improvement shown by peer-reviewed reference. FDA-approved through phase IV clinical trials according to Smith <i>et al.</i>
Juvenile Myelomonocytic Leukemia (30)	Two clinical studies, each incorporating multiple leukemia types, indicated that adult stem cell transplants from bone marrow or umbilical cord blood <b>improve the survival</b> of children with leukemia when the transplants are performed during the early phase of disease. Adult stem cell transplants from bone marrow or blood <b>can induce lasting remission</b> when leukemias are diagnosed early.	Clinical improvement shown by peer-reviewed reference. FDA-approved through phase IV clinical trials according to Smith <i>et al.</i>
Angioimmunoblastic Lymphadenopathy (31).	A case study reported that a single AILD patient experienced an <b>extended disease-free period</b> after receiving high-dose chemotherapy and a transplant of stem cells derived from blood.	Clinical improvement shown by peer-reviewed reference.
Multiple Myeloma (32–33) .....	Vesole <i>et al.</i> showed that a high-dose chemotherapy regimen followed by transplanting adult stem cells from blood resulted in <b>modest survival improvements</b> in half of study participants.	Clinical improvement shown by peer-reviewed reference; updated. FDA-approved through phase IV clinical trials according to Smith <i>et al.</i>
Myelodysplasia (34–35) .....	Two clinical studies, each incorporating a small number of patients with myelodysplasia, suggested that high-dose chemotherapy in combination with adult stem cell transplants from bone marrow or umbilical cord blood <b>improve the survival of myelodysplasia patients</b> , particularly when this treatment is performed during the early phase of disease. Adult stem cell transplants from bone marrow or blood enable myelodysplasia patients to withstand a higher dose of chemotherapy, thereby <b>increasing the chances of the treatment inducing lasting remission</b> .	Clinical improvement shown by peer-reviewed reference. FDA-approved through phase IV clinical trials according to Smith <i>et al.</i>
Breast Cancer (36–39) .....	Four clinical studies reported that patients with high-risk or advanced breast cancer had <b>improved survival rates</b> when intensive radiation and/or chemotherapy was followed by a transplant of adult stem cells derived from bone marrow or blood.	Clinical improvement shown by peer-reviewed reference.

TABLE S1. DISEASE AND CONDITION CHART—Continued

List of conditions in which adult stem cell use produced therapeutic benefit for human patients (1)

Disease or Condition	Quotes from Smith, Neaves, Teitelbaum (emphasis added) (2)	Additional Comments
Neuroblastoma (40) .....	A clinical study indicated that transplantation of adult stem cells derived from blood is associated with <b>improved survival rates</b> for a specific kind of high-risk neuroblastoma.	Clinical improvement shown by peer-reviewed reference.
Renal Cell Carcinoma (41–44) .....	One clinical study and one case report indicated that, in patients with metastatic renal cell carcinoma, transplants of donated adult stem cells from blood delayed cancer spread and resulted in <b>overall increase in long-term survival</b> of some patients.	Clinical improvement shown by peer-reviewed reference; updated.
Soft Tissue Sarcoma (45) .....	One clinical study indicated that some STC patients exhibited <b>higher survival rates</b> when treated with adult stem cells from blood after high-dose chemotherapy.	Clinical improvement shown by peer-reviewed reference.
Various Solid Tumors (46–50) .....	Four clinical studies evaluating the safety and/or efficacy of adult stem cell transplants as a treatment for various solid tumors (inc. breast, ovarian, pediatric brain cancers) showed that adult stem cell transplants may <b>reduce chemotherapy-related side effects</b> for some cancer patients.	Clinical improvement shown by peer-reviewed reference.
Waldenstrom's Macroglobulinemia (51)	One clinical study indicated that some WM patients receiving both high-dose chemotherapy and a transplant of bloodforming stem cells showed <b>improved survival rates</b> .	Clinical improvement shown by peer-reviewed reference.
Hemophagocytic Lymphohistiocytosis (52).	A case study reported that a child with HLH received a transplant of stem cells donated by the patient's mother 2 months after a transplant of liver tissue from the same parent. The patient was <b>disease-free for 4 months post-stem cell transplant</b> .	Clinical improvement shown by peer-reviewed reference.
POEMS Syndrome (Osteosclerotic Myeloma) (53).	An initial clinical study indicated that transplants of adult stem cells from blood <b>alleviated some of the symptoms of POEMS</b> .	Clinical improvement shown by peer-reviewed reference.
Systemic Lupus (54–62) .....	Early reports suggest that <b>immune reconstitution by adult stem cell transplants may induce an extended disease-free period in some lupus patients</b> who have failed conventional therapies.	Clinical improvement shown by peer-reviewed reference.
Sjogren's Syndrome (63) .....	"Resetting" the immune system with chemotherapy and an adult stem cell transplant <b>may induce an extended disease-free state in some patients</b> with Sjorgen's syndrome.	Clinical improvement shown by peer-reviewed reference.
Myasthenia (64) .....	.....	Clinical improvement shown by peer-reviewed reference.
Autoimmune Cytopenia (65–66) .....	"Resetting" the immune system with chemotherapy and an adult stem cell transplant <b>may induce an extended disease-free state in some patients with this disease, and a more recent clinical study suggests that such treatment can confer benefit to some patients in spite of a risk of severe side effects</b> .	One technical reference removed. Clinical improvement shown by peer-reviewed reference; updated.

TABLE S1. DISEASE AND CONDITION CHART—Continued

List of conditions in which adult stem cell use produced therapeutic benefit for human patients (1)

Disease or Condition	Quotes from Smith, Neaves, Teitelbaum (emphasis added) (2)	Additional Comments
Scleromyxedema (67) .....	More recent evidence indicates that high-dose chemotherapy followed by transplants of blood-forming stem cells <b>reverse many disease symptoms for an extended period, but this treatment is not curative.</b>	Clinical improvement shown by peer-reviewed reference.
Scleroderma (68–69) .....	Two literature reviews written by the same first author described early clinical studies of adult stem cell transplants as a treatment for various autoimmune diseases. The authors propose that these transplants can <b>cause disease remission in some patients.</b>	Clinical improvement shown by peer-reviewed reference.
Crohn's Disease (70–73) .....	Initial, small-scale clinical evaluations suggest that this combination approach <b>can suppress disease in some patients who fail standard treatments</b> , but the adult stem cell transplants are intended to help patients survive the immune suppressive regimen, not directly treat the disease.	Clinical improvement shown by peer-reviewed reference.
Behcet's Disease (74) .....	"Resetting" the immune system with chemotherapy and an adult stem cell transplant <b>has been observed to induce an extended disease-free state in some patients with Behcet's disease.</b>	Clinical improvement shown by peer-reviewed reference.
Rheumatoid Arthritis (75–81) .....	Five early clinical studies and two literature reviews indicated that transplants of adult stem cells, either donated or from the patient him/herself, in combination with radical use of conventional therapies (e.g., immune suppression, chemotherapy and/or radiation) <b>delay the course of rheumatoid arthritis in some patients with advanced disease.</b> More recent evidence suggests that some patients with severe rheumatoid arthritis who have failed conventional therapies <b>can experience an extended disease-free period</b> when adult stem cell transplants are used as part of a radical treatment protocol.	Clinical improvement shown by peer-reviewed reference.
Juvenile Arthritis (82–84) .....	More recently, adult stem cell transplants have been used in combination with immune suppression or radiation treatment. Results indicate that <b>about half the patients show disease remission following this treatment.</b>	Clinical improvement shown by peer-reviewed reference; updated.
Multiple Sclerosis (85–90) .....	The combination of adult stem cell transplantation and radical therapy <b>decreased the number of observable MS lesions</b> , but following the extent of disease-free remission would have required further study. More recent research indicates that radical treatments that include adult stem cell transplants <b>can improve the overall quality of life of patients with severe multiple sclerosis (for whom there are no effective alternative treatments).</b>  However, the transplant's ability to reverse the onset of MS remains unproven, and in most cases the transplant is intended to help alleviate the side effects of harsh chemotherapy and/or immune suppression.	Clinical improvement shown by peer-reviewed reference.

TABLE S1. DISEASE AND CONDITION CHART—Continued

List of conditions in which adult stem cell use produced therapeutic benefit for human patients (1)

Disease or Condition	Quotes from Smith, Neaves, Teitelbaum (emphasis added) (2)	Additional Comments
Polychondritis (91) .....	The single patient included in the cited study was reported to have achieved an <b>extended disease-free period</b> .	Clinical improvement shown by peer-reviewed reference.
Systemic Vasculitis (92) .....	“Resetting” the immune system with chemotherapy and an adult stem cell transplant <b>has been observed to induce an extended disease-free state in some patients with systemic vasculitis</b> .	Clinical improvement shown by peer-reviewed reference.
Alopecia Universalis (93) .....	This reference was a case study reporting that a lymphoma patient who received a bone marrow transplant also <b>experienced hair regrowth</b> .	Clinical improvement shown by peer-reviewed reference.
Severe Combined Immunodeficiency Syndrome-X1 (94–95).	<b>In some patients, this therapy is curative</b> , though immune rejection concerns persist throughout the life of the patient.	Clinical improvement shown by peer-reviewed reference. FDA-approved through phase IV clinical trials according to Smith <i>et al</i> .
X-Linked Lymphoproliferative Syndrome And X-Linked Hyperimmunoglobulin M Syndrome (96–97).	<b>In some patients, this therapy is curative, though it remains experimental.</b> Immune rejection concerns persist throughout the life of the patient, and it is not a suitable treatment option for all patients.	Clinical improvement shown by peer-reviewed reference.
Sickle Cell Anemia (98–103) .....	One case report and one observational clinical study (totaling experience with 5 patients) indicated that adult stem cell transplants from bone marrow or umbilical cord blood <b>can provide some benefit to sickle cell patients</b> . A third literature review proposed that adult stem cell transplants hold the potential to treat sickle cell anemia because sickle cell results from a defect in blood-forming stem cells in bone marrow, <b>restoring healthy stem cells to a patient's bone marrow can reverse the disease</b> .	Clinical improvement shown by peer-reviewed reference; updated.
Sideroblastic Anemia (104–105) .....	These references were two small clinical studies suggesting that transplants of adult stem cells from bone marrow or blood <b>can reverse sideroblastic anemia for an extended period</b> .	Clinical improvement shown by peer-reviewed reference.
Aplastic Anemia (106–107) .....	Combinations of immune suppression and adult stem cell transplantation <b>can improve the long-term survival of aplastic anemia patients</b> .	Clinical improvement shown by peer-reviewed reference. FDA-approved through phase IV clinical trials according to Smith <i>et al</i> .
Red Cell Aplasia (108) .....	Transplants of donated blood-forming stem cells in combination of chemotherapy <b>may improve the long-term survival of some patients</b> .	Clinical improvement shown by peer-reviewed reference; updated.
Amegakaryocytic Thrombocytopenia (109).	Combinations of chemotherapy, immune suppression and adult stem cell transplants have been <b>proposed as a potentially curative treatment</b> . However, due to the small number of patients affected by this disease, this treatment protocol remains experimental.	Clinical improvement shown by peer-reviewed reference.

TABLE S1. DISEASE AND CONDITION CHART—Continued

List of conditions in which adult stem cell use produced therapeutic benefit for human patients (1)

Disease or Condition	Quotes from Smith, Neaves, Teitelbaum (emphasis added) (2)	Additional Comments
Thalassemia major (110) .....	This reference is a case report indicating that a transplant of donated blood-forming stem cells <b>suppressed disease in two thalassemia patients</b> . Severe thalassemia is often treated by bone marrow transplantation, although this procedure carries considerable risk and is not suitable for all patients.	Clinical improvement shown by peer-reviewed reference. FDA-approved through phase IV clinical trials according to Smith <i>et al.</i>
Primary Amyloidosis (111) .....	This reference is a literature review proposing that transplants of adult stem cells from blood and high-dose chemotherapy provide an improved treatment for primary amyloidosis. On a small scale, adult stem cell transplants have been <b>shown to benefit patients with advanced disease</b> , though significant treatment-related side effects were reported.	Clinical improvement shown by peer-reviewed reference.
Diamond Blackfan Anemia (112) .....	Adult stem cell transplants <b>can reverse bone marrow failure in some patients</b> , but they do not alter the genetic defect underlying the disease and so are not curative.	Clinical improvement shown by peer-reviewed reference.
Fanconi's Anemia (113–115) .....	Adult stem cell transplants <b>can reverse bone marrow failure in some patients</b> , but they do not alter the genetic defect underlying the disease and so are not curative.	Clinical improvement shown by peer-reviewed reference; updated.
Chronic Epstein-Barr Infection (116–117).	High-dose chemotherapy and bone marrow replenishment has been reported to <b>reduce the amount of active virus in the body and can improve survival of some patients</b> .	Clinical improvement shown by peer-reviewed reference.
Hurler's Syndrome (118–120) .....	One retrospective analysis and one small clinical study indicated that adult stem cell transplants protected some of the tissues attacked by Hurler's syndrome but provided little relief to other tissues. <b>Long-term survival was improved</b> , with the greatest benefit seen in children transplanted early in life.	Clinical improvement shown by peer-reviewed reference; updated.
Osteogenesis Imperfecta (121–123) .....	Three clinical studies, all from the same first author, suggested that transplants of bone-forming stem cells from bone marrow are feasible and <b>can improve the bone growth of children suffering from osteogenesis imperfecta</b> .	Clinical improvement shown by peer-reviewed reference.
Krabbe Leukodystrophy (124–125) .....	Two early clinical studies reported that <b>cognitive impairments from Krabbe's disease are reduced</b> when children are treated with transplants of donated umbilical cord blood stem cells.	Clinical improvement shown by peer-reviewed reference.
Osteopetrosis (126–128) .....	These references were one retrospective analysis and one small clinical study indicating that transplants of adult stem cells from bone marrow (either donated or from the patient him/herself) <b>improve the long-term survival of some children with a certain kind of osteopetrosis</b> .	Clinical improvement shown by peer-reviewed reference; updated.

TABLE S1. DISEASE AND CONDITION CHART—Continued

List of conditions in which adult stem cell use produced therapeutic benefit for human patients (1)

Disease or Condition	Quotes from Smith, Neaves, Teitelbaum (emphasis added) (2)	Additional Comments
Cerebral X-Linked Adrenoleukodystrophy (129).	This reference was one retrospective analysis indicating that transplants of adult stem cells from blood <b>improve the long-term survival</b> of some patients with early-stage cerebral Xlinked adrenoleukodystrophy. Roughly half of study subjects ultimately succumbed to the disease, and the transplant therapy was shown to be significantly less effective for children with advanced disease.	Clinical improvement shown by peer-reviewed reference.
Sandhoff Disease .....	.....	Removed from list awaiting peer-reviewed report.
Corneal Regeneration (130–138) .....	<b>All papers reported regeneration of the cornea and improved vision</b> in a subset of patients.	Clinical improvement shown by peer-reviewed reference. Smith <i>et al.</i> misstate repetition of reports.
Limb Gangrene (139) .....	One pilot study reported that implantation of bone marrow stem cells into non-healing skin ulcers <b>restored some blood flow to the affected area and accomplished moderate repair.</b>	Clinical improvement shown by peer-reviewed reference.
Surface Wound Healing (140) .....	.....	Switched animal & clinical paper. Clinical improvement shown by peer-reviewed reference; updated.
Jaw Bone Replacement (141) .....	A case report detailed a tissue engineering approach to making a new jaw for a patient who had lost his to cancer. By this technique, a jaw-shaped metal frame is seeded with bone marrow stem cells and growth-promoting drugs before implantation in the patient's shoulder. <b>After 7 weeks bone grew over the frame and was then removed from the shoulder and installed as the patient's new jaw.</b>	Clinical improvement shown by peer-reviewed reference.
Skull Bone Repair (142) .....	A case report described a tissue engineering approach to closing a large skull fracture. The open portion of the patient's skull was covered with a protein-based glue that had fat stem cells seeded within it. <b>New bone growth was observed 3 months after this procedure.</b>	Clinical improvement shown by peer-reviewed reference.
Acute Heart Damage (143–159) .....	Seven experimental or early phase clinical studies, including one placebo-controlled clinical trial, indicated that transfusion of a patient's own bone marrow-derived stem cells into the heart shortly after heart attack is relatively safe and is associated with regeneration of heart tissue and improved heart function.  The cited studies suggest that transplantation of adult stem cells from bone marrow is associated with <b>improved recovery after heart attack.</b>	Clinical improvement shown by peer-reviewed reference.
Stroke (160–163) .....	Three experimental studies reported that <b>implantation of brain stem cells into the brains of long-term stroke patients was feasible and relatively safe.</b>	Clinical improvement shown by peer-reviewed reference; updated.

TABLE S1. DISEASE AND CONDITION CHART—Continued

List of conditions in which adult stem cell use produced therapeutic benefit for human patients (1)

Disease or Condition	Quotes from Smith, Neaves, Teitelbaum (emphasis added) (2)	Additional Comments
Parkinson's Disease (164–166) .....	.....	Removed abstract & 2 Congressional testimonies. Valid stimulation of endogenous stem cells not mentioned by letter authors. Clinical improvement shown by peer-reviewed reference; updated.
Spinal Cord Injury (167) .....	.....	Removed 3 Congressional testimonies. Clinical improvement shown by peer-reviewed reference.

NOTES: Column 1 shows the disease or condition listed as treated, with peer-reviewed sample references. Column 2 lists comments validating patient improvement from the supplement of Smith, Neaves and Teitelbaum. Column 3 provides additional information regarding listed references.

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## RESPONSE TO QUESTIONS OF SENATOR ENZI BY GEORGE Q. DALEY, M.D., PH.D.

*Question 1.* Professor Daley, sometimes I wonder if we are being realistic about the short foreseeable advances from stem cell research, in terms of it always seems medical research is a slow endeavor. For instance, some adult stem cell therapies have been in commercial investigation for the past 10 years and not yet reached the market. My staff reports that there are 1,229 publicly available adult stem cell trials of which 614 are currently enrolling patients. Are there any embryonic stem cell therapies that are in early clinical trials now? Do you have a realistic best case thought when an embryonic stem cell therapy might be widely used?

Answer 1. Medical research is a slow, methodical, step wise endeavor to ferret out the biological basis of disease, and to translate those basic insights into new forms of diagnosis or treatment. All new medical technologies take years, sometimes decades to realize their full clinical potential.

Embryonic stem cell research will pay off both in the near term and the long-term. Near-term, scientists are already using embryonic stem cells to unravel the secrets of early human development and cell differentiation—to learn how the cells of the human embryo first become specialized into nerves, muscle, blood, and more. Such basic research is certain to yield insights into miscarriage and infertility, chromosomal abnormalities, intra-uterine growth defects, tissue generation and regeneration, and cancer. Drugs that are currently being used clinically are being tested in various in vitro assays that employ embryonic stem cells, and we might learn that existing drugs can stimulate stem cell function and encourage tissue repair. In the long-term, we hope that scientists will learn how to coax embryonic stem cells to become specific tissues for therapy—skin cells, blood cells, nerve cells and many others.

It is impossible to predict with any certainty when embryonic stem cells will themselves serve as a source of specialized cells for cell replacement therapy. Geron, a leading biotechnology company that has pioneered embryonic stem cell research, has stated publicly that they wish to begin human trials of specialized tissues from human embryonic stem cells for the treatment of spinal cord injury within the next 2 years. My best estimate is that products derived from embryonic stem cells will be tested in patients within the next 5 to 7 years, but that effective cell-based therapies cannot be expected for at least a decade or more.

The history of biomedicine teaches us that most new forms of therapy take many years to evolve and bear fruit. This was true for the translation of recombinant DNA into new protein-based drugs (insulin, interferon, erythropoietin), for monoclonal antibodies, and I believe will be true for embryonic stem cell-based therapies.

*Question 2.* Professor Daley, the Administration's current stem cell policy does not prevent any embryonic stem cell research. Accordingly, States and private foundations are supporting some research. State funding alone is expected to add up to several billions of dollars of funding in the next few years. Accordingly, I noticed some of your work is supported by private foundations. It seems to me that many of these foundations that help fund disease research are wonderful drivers of innovation. Is there anything we can do in Congress to encourage foundations like those to be created?

Answer 2. Unfortunately, the Administration's current stem cell policy does indeed effectively prevent an enormous amount of embryonic stem cell research. Federal funds are essential to virtually every major biomedical research laboratory, and are used to purchase equipment and supplies and to pay scientists' salaries. Because no Federal money can be used for any embryonic stem cell research that does not narrowly conform to the administration's policy (that is, purely in vitro research on a small number of lines created prior to August 9, 2001), any so-called nonconforming "nonPresidential" research must be performed with entirely separate equipment and supplies by personnel whose salary comes from private sources. Because only a few laboratories and institutions have the resources to duplicate equipment,



space, supplies, and personnel, the vast majority of American scientists cannot and do not act on the creative experimental ideas they might have for working in non-conforming areas of research. The power of the purse is extremely strong, and serves to limit innovation and intellectual creativity.

State funds and private foundations are not a solution for funding areas of research that are in the vital national scientific interest. For scientists outside of a few exclusive States like New Jersey, Connecticut, and California, no significant alternative funds exist. Thus the scientists of States like Wyoming and many others are largely excluded from new and exciting areas of embryonic stem cell science that fall outside the narrow funding guidelines of the administration policy. All but a few foundations have endowments large enough to have a substantive impact on biomedical research, and altogether will not be able to make up for the absence of funding through the National Institutes of Health.

*Question 3.* Professor Daley, as a physician-scientist, do you think we are doing enough to develop adequate numbers of physician scientists to fulfill the promise of stem cell research? Can you suggest any changes we might make to encourage more doctors to pursue innovative research like you are doing?

*Answer 3.* The dark storm-clouds over the current NIH funding climate serve as the greatest hindrance to developing more physician-scientists. Physician-scientists must train for many years before achieving independence, and they depend upon Federal grant dollars to initiate their new research programs. The doubling of the NIH budget created an enormous new flow of research and allowed for the development of many new scientists. But given that the NIH budget is no longer even matching the rising costs due to inflation, everyone's budgets are being cut across the board, and junior investigators are being hit the hardest. Moreover, the political controversy over stem cell research dissuades all but the most idealistic and motivated scientists from pursuing stem cell research.

*Question 4.* Dr. Daley, in your research efforts at the Boston Children's Hospital, you are using embryonic stem cells to replace problematic genes in certain diseases, such as sickle cell disease and leukemia. In your estimation, how close are you to a breakthrough that will improve the health of patients with these diseases?

*Answer 4.* Our research aims to combine gene therapy and cell therapy, so that patients with genetic diseases can be treated with their own genetically-repaired cells in a way that is safe and effective. We are working on technology platforms that could be applied to any one of dozens of bone marrow diseases, with sickle cell anemia, immune deficiency, and leukemia are but a few. We are working diligently in hopes of achieving breakthroughs that will help improve the health of my patients. No one knows for certain when breakthroughs will happen, but in my estimation, I expect to see such advances within my career, and hopefully within the next decade or two. Basic research is a long-term investment, but such investments have paid off handsomely for the United States.

RESPONSE TO QUESTION OF SENATOR COCHRAN BY GEORGE Q. DALEY, M.D., PH.D.

*Question.* I would address this question to any of our panel members today, has new scientific research emerged to support or negate the need for additional embryonic stem cell lines to further your research efforts?

*Answer.* I would argue that no research has emerged that would negate the need for additional embryonic stem cell lines, as the many so-called "alternatives" to embryonic stem cells are not perfect substitutes. Ample evidence exists and has been published that many of the current NIH-approved "Presidential" embryonic stem cell lines develop genetic defects when cultured for prolonged periods. This fact alone argues that a new supply of lines is needed. Moreover, there have been many new lines established since the administration's policy of August 9, 2001 was put in place, and many of these new lines have advantageous properties for stem cell research: for instance, they carry specific gene defects for human disease, making them extremely valuable for medical research, or they have been derived under improved, animal-free conditions that make them particularly favorable for clinical use.

RESPONSE TO QUESTION OF SENATOR ENZI BY LAUREN STANFORD

*Question.* I want to join the other Senators and thank you for coming here to testify. You are saluted for active participation in the political process and for raising money for diabetes research. I also wish you the best of luck in becoming a Senator. What advice would you have for other teenagers who have been diagnosed with Diabetes?

Answer. I think I would tell other teens with diabetes two things. First, don't lie to your parents about things like your blood sugars. If you feel like it's all too much you are better off just telling them the truth so they can help you. I made that mistake 2 years ago of not telling them that I was sick of it and not giving myself the insulin I needed and I almost died. It's better to just be honest and get some help. Second, I would tell them that their voices are important too. When we are little kids we all do the diabetes walks and speak up and all that, but it seems like as soon as a lot of us get to be teens we stop speaking out. It's hard to be different when you are a teen, but I think people really listen to us. So keep speaking up about needing a cure and then you won't have to be sick of diabetes anymore, once it is cured.

RESPONSE TO QUESTIONS OF SENATOR ENZI BY JOHN E. WAGNER, JR., M.D.

*Question 1.* Professor Wagner, thank you for coming and I wanted to thank your patients that joined you today. It sounds like you are making great progress with adult stem cell research. I know you recognize embryonic stem cell research is important, but do you think an expansion of adult stem cell research will lead to more therapies in the next 10 years? Realistically, is there any particular treatments, other than the ones you are working on, that you are intrigued by and excited about seeing tried in a clinical setting?

Answer 1. Without question, there are a number of adult stem cell therapies outside the ones I am working on that are either in the planning stage or in progress that bear close monitoring. For example, adult stem cell therapies are being planned for spinal cord injury, neurodegenerative disease, type I diabetes and vascular injury. Trials are underway evaluating adult stem cell therapies for acute and chronic heart failure, bone and joint cartilage repair, and acute brain injury. However, it must be unequivocally clear that these therapies are as yet unproven in terms of efficacy. Certainly, the field of adult stem cell research is extraordinarily exciting and deserves heightened funding in order to capitalize on its full potential. But, this in no way deters from the pressing need for greater embryonic stem cell research. ES cells offer opportunities that are either not possible with adult stem cells, such as the development of disease specific ES cell lines with which to identify pathological mechanisms sensitive to novel pharmacologic agents, or may later prove to be better than adult stem cells for specific diseases. It is possible, for instance, that ES cells have a greater capacity to make heart muscle than adult stem cells. Or, have a greater capacity to make islets for treatment of diabetes. Also, there may be circumstances that adult stem cells may be less prone to immune attack, making that a better source for other diseases. Based on work done at the University of Minnesota and elsewhere, I believe that we will see major breakthroughs in adult and embryonic stem cell research over the few years that will lead to an increasing number of clinical trials.

*Question 2.* Professor Wagner, we all saw Professor Atala announce his breakthrough regarding amniotic stem cells and that advance got an awful lot of press. In addition to your own work, should we expect other announcements that also have potential to generate new methods of generating stem cells in the not to distant future?

Answer 2. Professor Atala's report several weeks ago did get a great deal of press. I know of other research here at the University of Minnesota and elsewhere specifically evaluating other potential stem cell sources as well as improved methodologies for isolating and expanding stem cell populations from umbilical cord blood, the umbilical cord itself and various adult tissues. However, it is important to recognize that we do not yet know how the various stem cell populations compare with each other or whether one source or isolation/expansion methodology offers a true advantage in terms of treating patients with disease. All these announcements are exciting but be very careful about what is in the press as it may not accurately reflect what is known versus what is pure speculation. As a scientist, I am asked to speculate as to the meaning of a particular discovery, but it's just that—speculation. Sometimes, the press may interpret speculation as fact inappropriately. In my own experience, some have taken our own discoveries on adult stem cells and used them to nullify the critical importance of ES cells.

There is purposeful misinformation that scientists, focused on "finding truth," often find themselves too ill-equipped to respond to. So, while these new discoveries with adult stem cells are promising, such as that reported by Professor Atala, it is way too premature to suggest that they replace ES cells in our collective efforts to reduce suffering and disease.

*Question 3.* Professor Wagner, I'd like to ask you the same question I asked Professor Daley, it seems like in order to deliver on the promise of stem cell research, we need more physician investigators like yourself. Can you suggest anything Congress should consider to encourage physicians to pursue the development of innovative therapies like you have?

*Answer 3.* It should be clear that we are all devoted to reducing suffering and minimizing the impact of debilitating diseases, such as cancer, diabetes, and heart failure. The list of diseases is long and the number of affected people asking for a chance to live healthy, productive lives, is enormous. I know that you and others genuinely want to help us to do just that—the goals are clear and the rewards will be immeasurable.

First, allow us to pursue all promising avenues. We did this with cancer and we did this with AIDS. Today, survival rates are the highest ever. Is there more work to do—obviously, yes. But, the achievements to date can be attributed to the breadth of the attack. Rather than limit science, the science was embraced. Rather than limit funding, the funding was dramatically augmented.

In my opinion, the stem cell and its impact upon science and medicine will be revolutionary. It promises to fundamentally change the way we understand disease and the practice of medicine. Just as the Nation dreamed about the limits of space five decades ago, we dream about the limits of stem cells today. Could President Kennedy have imagined the gains we have made in telecommunications when he proposed the development of NASA? Could he know that there would be a phone at every ear and GPS device in every car? No. But he did know that space was worth the investment because the returns 1 day could be spectacular.

*Question 4.* What can Congress do to encourage physicians to develop innovative stem cell therapies?

*Answer 4.* As a physician, I would start by eliminating the barriers and provide incentives for collaborations between basic scientists and clinical investigators and invest in such translational research. Piecemeal approaches will beget mediocre progress. Substantial and strategically focused efforts, free of politics, and supportive of both adult and ES cell basic, translational and clinical research are required. Right now, the effort is diluted between industry and the various institutes of the NIH. Just as Congress needs to be united, so does the NIH. The potential impact of this research is unprecedented and for that reason, a focused effort is required. Whether this should manifest itself as a new Institute for Stem Cell Research or as an additional line item allocation, Congress needs to address the gaps in the stem cell translational pipeline.

RESPONSE TO QUESTION OF SENATOR COCHRAN BY JOHN E. WAGNER, JR., M.D.

*Question.* I would address this question to any of our panel members today, has new scientific research emerged to support or negate the need for additional embryonic stem cell lines to further your research efforts?

*Answer.* Without a doubt, all stem cell science benefits from the work we do in any one area. We will never know the full potential of adult stem cells unless we have the chance to compare them side by side with embryonic stem cells. Just as we have tested the limits and possibilities of bone marrow versus cord blood for transplantation, we must allow the full vetting of the scientific potential of this science. Indeed, while embryonic stem cells are clearly the “gold standard” against which all other stem cell sources are compared, today's researchers' hands are tied as the population of embryonic stem cells available for Federal funding are less than optimal either for basic research or clinical testing. We need to manufacture new cell lines that will (1) broaden genetic, racial and ethnic diversity, (2) be free of animal tissues, and (3) have a defined history both in terms of proven gamete donor consents as well as reagent exposures and number of passages. Embryonic stem cell lines and its derivatives are more than simple sources of tissues for repair; they provide us with an unprecedented resource for understanding mechanisms of disease and development of targeted treatment strategies to modify or prevent disease. We have the knowledge and know-how now. While there may be political reasons, there is absolutely no objective, scientific research that negates the need for more embryonic stem cell research and the development of new cell lines. Without question, the “Presidential” stem cell lines are suboptimal. Acquisition of genetic defects after years of passaging in culture and their derivation on murine feeder layers are two reasons that make them suboptimal. Yet, these are the only cell lines for which Federal dollars can be used. Without question, no adult stem cell population, outside the context of bone marrow transplantation, has any proven efficacy. Certainly, work is on-going to determine the place of adult stem cells. It is important to under-

stand that every discovery with embryonic stem cells has only enhanced our own work with adult stem cells. These facts are uncontestable!

As proposed by some, why not first determine the true capacity of adult stem cells and potentially eliminate the ethical issues associated with embryonic stem cells? The argument has three major drawbacks: (1) without ES research, how will we ever determine how far adult stem cells can go in the treatment of disease?; (2) deleterious impact upon our efficiency in moving stem cell therapies forward; and (3) without the unbiased pursuit of knowledge, how can science move forward?

[Whereupon, at 11:41 a.m., the hearing was adjourned.]

