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THE PROMISE OF HUMAN EMBRYONIC STEM CELL RESEARCH

HEARING

BEFORE A

SUBCOMMITTEE OF THE

COMMITTEE ON APPROPRIATIONS

UNITED STATES SENATE

ONE HUNDRED ELEVENTH CONGRESS

SECOND SESSION

SPECIAL HEARING

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THE PROMISE OF HUMAN EMBRYONIC STEM CELL RESEARCH

THURSDAY, SEPTEMBER 16, 2010

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

The subcommittee met at 10:05 a.m., in room SD–124, Dirksen Senate Office Building, Hon. Tom Harkin (chairman) presiding.

Present: Senators Harkin, Murray, Specter, and Cochran.

Also present: Senator Wicker.

OPENING STATEMENT OF SENATOR TOM HARKIN

Senator HARKIN. Good morning. The Senate Appropriations Subcommittee on Labor, Health and Human Services, and Education will now come to order.

Well, this is the 21st hearing that this subcommittee has held on human embryonic stem cells starting back in December 1998, 1 month after Dr. Jamie Thompson of the University of Wisconsin announced that he had isolated them for the first time. And I want to note for the record that it was Senator Specter who led this subcommittee at that time, who led the hearings beginning then and on through the remainder of the 1990s and into the 2000s, and then when the gavel changed hands, I picked up from him and we have kept this effort going on. At that time, it was a very bipartisan basis. And so I just want to acknowledge the great leadership role that Senator Specter has played in this whole effort on embryonic stem cell research.

It is a shame that we have to revisit this issue under the circumstances in which we find ourselves today. When President Obama lifted the Bush administration's restrictions on stem cell research a year and a half ago, most of us thought the fight was finally over. At last, we thought, there was a new approach to scientific research in this country, one that was dictated not by politics or ideology, but by ethical science. At last, we thought, our brightest young minds could enter this field without worrying that they would go to the lab one day and find the doors ordered shut by someone in Washington, DC. At last, we thought, we could begin to realize the promise of embryonic stem cell research. And we were on track to do that. The National Institutes of Health (NIH) instituted new guidelines to ensure that this research would be conducted ethically and responsibly. The number of stem cell lines eligible for federally funded research rose from 21 to its current

total of 75. And the scientific community has responded, applying for and receiving NIH grants that are moving this research forward in robust and exciting ways.

At the same time, of course, NIH continued to fund research on adult stem cells and on induced pluripotent cells (iPS) and numerous other approaches to regenerative medicine that could lead to treatments and cures.

Embryonic stem cells have very special properties that no other cells can match, and that is why they offer so much hope to people who are suffering. That is why so many scientists are excited to have access to these stem cell lines and to see what they can learn from them.

Then out of the blue came the preliminary injunction from District Judge Royce Lamberth. That action, once again, has placed a cloud of uncertainty over this entire scientific field. Thanks to a temporary stay by the D.C. Circuit Court, human embryonic stem cell research is, for the time being anyway, progressing just as it was before Judge Lamberth's ruling. But how long that will last is anybody's guess.

Well, I can say this. We have come too far to give up now. If we do not win this battle in the courts, we will have to take it up in Congress. This research must continue. The politicians and activist judges who oppose it need to respect the views of the overwhelming majority of the American people who want this research to go forward. People across America—and I am one of them—have too many loved ones and friends who have died from ALS, from Parkinson's, from spinal cord injuries, and other diseases that might one day respond to treatments made possible by embryonic stem cell research.

I remember Christopher Reeve testifying before this subcommittee several years ago. I wish we still had him around today. I remember Rob Borsellino, a newspaper man from Iowa who had ALS, testified before our subcommittee. I wish we had him around still too.

As long as there is a reasonable chance that this research could help ease human suffering and save lives, I believe we have a moral responsibility to pursue it.

The purpose of today's hearing is to examine the promise of human embryonic stem cell research. We will look at the science. We will not relitigate the ongoing court case. None of the witnesses is prepared to discuss the legal arguments for or against the injunction. So I ask members of this subcommittee to refrain from asking them questions that are not in their area of expertise. And I say to our witnesses if you receive such questions regarding legality or court decisions, you should not feel required to answer them in any way. We want to stick to the science, where we are in the science, what is happening with all forms of stem cell research, what role embryonic stem cell research is playing in that whole area today.

So before we begin, I would like to turn to Senator Cochran for any opening remarks he would like to offer.

Senator COCHRAN. Mr. Chairman, thank you very much. We appreciate your calling this hearing, to give us an opportunity to further explore options for the Congress in dealing with the difficult

choices we have to make in supporting research that is so important in finding cures for illnesses.

I know when we first started looking into this area of stem cell research, my brother-in-law was dying of leukemia. Buzzy Clayton was one of the finest young men our State had produced, at that time, and he just had an outstanding future and was a wonderful person in every way. I am sure that is something that I will always keep in mind and remember his great loss. And there are many others like Buzzy Clayton who might benefit—we hope would benefit—from findings that are made through additional and more aggressive research on how to combat these terrible illnesses.

I thank my colleague, Roger Wicker, who is here today to be our lead-off witness in this hearing. He has been a leader in this area for some time, and we commend him for his successes in his efforts.

Senator HARKIN. Thank you, Senator Cochran.

I say to other people on the panel if you want to incorporate your statements into your opening questions, that would be fine too.

But before we go to our panels, Senator Roger Wicker of Mississippi has asked to make a brief opening statement and we certainly welcome our colleague to this panel. Senator Wicker, if you have a statement, it will be made a part of the record in its entirety, and please proceed as you so desire. But welcome.

Senator WICKER. Thank you very much, Mr. Chairman, and I appreciate the opportunity to be back with you. As you know, I served on the subcommittee in the House that is the counterpart of this subcommittee, and so it is wonderful to be here today. If I am doing something wrong on the microphone, maybe I will be the guinea pig and it will be ready for the rest of the panel.

I appreciate the opportunity to appear on the subject of embryonic stem cell research. As you know, in 1995 I co-authored an amendment to the Labor, Health and Human Services, and Education, and Related Agencies Appropriations Act prohibiting the use of taxpayer funds to create human embryos for research or support any research in which human embryos are harmed, destroyed, or subjected to risks not permitted for unborn children. This so-called Dickey-Wicker language has remained the law of the land for a decade and a half.

In my opinion, the body of scientific evidence developed since 1995 has served only to strengthen the argument in favor of Dickey-Wicker, but the basic premise for the provision has not changed. It is this.

Number one, the destruction or cloning of human embryos for research purposes raises profound moral and ethical challenges.

Number two, the Federal Government should not be involved in subsidizing this controversial life-altering research with taxpayer dollars.

Number three, there are limited Federal funds available for health-related research.

Number four, if human embryonic stem cellresearch is to be done at all, it should be paid for with nontaxpayer funds.

The chair mentioned Dr. James Thompson. He was the first to isolate human embryonic stem cells and one of the scientists who discovered the groundbreaking embryo-free way to produce genetically matched stem cells, known as iPS cells. iPS cells are adult

cells that have been genetically reprogrammed to an embryonic stem cell-like state. This discovery has changed the debate on embryonic stem cells.

When discussing the ethics surrounding embryonic stem cell research, Dr. Thompson himself said "If human embryonic stem cell research does not make you at least a bit uncomfortable, you have not thought about it enough." Recent polling proves that embryonic stem cell research makes many Americans uncomfortable. According to a 2010 Rasmussen poll, 57 percent of Americans oppose taxpayer funding of embryonic stem cell research. In other words, the majority of Americans support the current ban on using taxpayer dollars to fund research in which embryos are destroyed.

The question is, if we can use adult stem cells, reprogram them to act like embryonic stem cells, and avoid the ethical challenges, then why would we not take that approach?

Some people would have us think that prohibiting Federal funding of embryonic stem cell research is stopping science entirely. I disagree. As we all know, private funds can be used for this research and are being used for this purpose. The distinction is whether or not the Federal Government should be subsidizing controversial, life-altering research with taxpayer dollars, especially when the majority of Americans oppose such a move.

Federal funding is scarce. Indeed, because of funding limits, we simply are unable to afford all the research we would like to do. I submit that we should use limited taxpayer dollars on already proven research demonstrated in areas like adult stem cells. Adult stem cells are the ones that are treating people right now. In fact, treatments have been so effective that many doctors have turned to adult stem cell transplants as a standard life-saving therapy for hundreds of thousands of people, people suffering from dozens of diseases and conditions, including cancer, juvenile diabetes, Parkinson's, multiple sclerosis (MS), leukemia, lymphoma, spinal cord injuries, and corneal regeneration, among others are turning to adult stem cell treatments for help.

An estimated 50,000 adult stem cell transplants are occurring annually worldwide using stem cells from bone marrow, umbilical cord blood, and other tissues. Research with adult stem cells has produced therapies for more than 70 afflictions and demonstrated promising results.

Advancements in this field are happening every day. Just 3 months ago, researchers reported they had restored vision to people whose eyes were damaged from chemicals. Doctors took stem cells from the patient's healthy eye and multiplied them in a lab to transplant to the damaged eye where they grew into healthy corneal tissue.

Preclinical trials to treat spinal cord injury patients have also proven to be promising in recent years. At age 16, Laura Dominguez was paralyzed from the neck down in a car accident. Doctors treated Laura for spinal cord injury using her own nasal adult stem cells. As a result of the surgery and extensive physical therapy, Laura has regained feeling and movement in her lower body and she continues to make progress.

iPS research is another promising field. iPS cells are producing unprecedented opportunities in medicine, toxicology, and drug dis-

coveries. All over the world, hospitals and laboratories are developing IPSCs from individuals with various diseases. For example, a clinic in Ontario, Canada, has already created more than 130 IPSC lines for 11 diseases. This clinic is also working on making lines to address diseases such as autism and schizophrenia. If there are additional funds, Mr. Chairman, Congress should invest in this type of groundbreaking research.

Supporters of embryonic stem cell research would like to ignore such accomplishments. They would suggest that providing Federal tax dollars on embryonic stem cell research is the only means of getting results. However, the accomplishments among adult and pluripotent stem cells versus embryonic stem cells prove otherwise.

I am proud to say that for a decade and a half, the Dickey-Wicker amendment has protected life. This debate involves profound ethical and moral questions. This is a matter of conscience for me, but more importantly, it is a matter of conscience for millions of Americans who are deeply troubled by the idea that their taxpayer dollars may be used to destroy another human life when there are other proven techniques available.

Mr. Chairman and members of this subcommittee, I want to thank you very much for your time, and I appreciate the opportunity to testify on this important issue.

Senator HARKIN. Senator Wicker, thank you very much for your statement, and I know of your long-term interest in this area. And we thank you for your appearance before the subcommittee.

I know you have a lot of important things and you are a busy person like everyone else, and so we thank you for being here. Thank you for your testimony. And you are excused, if you would like, unless you have something else you would like to add as an emphasis point or something like that.

Senator WICKER. Thank you very much.

Senator HARKIN. All right. Thank you very much, Senator Wicker.

Now we will call our first panel and that will be Dr. Francis Collins. Dr. Collins is no stranger to all of us here and certainly not to this subcommittee. Dr. Collins was sworn in last year as the 16th Director of the NIH, a physician geneticist noted for his discoveries of disease genes and of course for his outstanding leadership of the Human Genome Project. And prior to becoming the NIH Director, he served as the Director of the National Human Genome Research Institute at NIH.

Dr. Collins received his B.S. from the University of Virginia, an M.D. from the University of North Carolina at Chapel Hill, and a Ph.D. from Yale.

As I said, last August he was confirmed unanimously by the United States Senate to be our 16th Director of the NIH.

So, Dr. Collins, welcome back. Your statement will be made a part of the record in its entirety. I have got the clock set at 10 minutes. Please take at least that amount of time. If you need a few more, we will give you that too to give us your thoughts and your views on where we are with embryonic stem cell research and the whole area of stem cell research and what the status is right now. Dr. Collins, welcome back.

STATEMENT OF FRANCIS S. COLLINS, M.D., Ph.D., DIRECTOR, NATIONAL INSTITUTES OF HEALTH, DEPARTMENT OF HEALTH AND HUMAN SERVICES

Dr. COLLINS. Thank you. Good morning, Chairman Harkin, distinguished members of this subcommittee. I will make an abbreviated version of what is in the written statement, but thank you for the opportunity to describe some of the exciting science that surrounds human embryonic stem cell research. And I have some visual aids that perhaps will assist in terms of conveying some of these points, and you should have hard copies of those visuals in front of you.

It is truly an honor to appear before you today to discuss this topic, and I would like to thank this subcommittee for its steadfast support of the NIH's mission, discovering fundamental knowledge about living systems and then applying that knowledge to fight illness, reduce disability, and extend healthy life.

I also want to thank you for your leadership in advancing human embryonic stem cell research. From your very first hearing in December 1998, as the chairman has already referred to, this subcommittee has provided a forum for discussing the great promise of this research and has enabled NIH to invest more than $500 million in this promising research.

But today there is a cloud hanging over this field. The preliminary injunction issued on August 23, now stayed pending further order from the court of appeals, has created deep uncertainty in the field of human embryonic stem cell research. Some of our Nation's most promising researchers such as these stem cell scientists you see here working in the laboratories of Drs. Morrison, Daley, and Melton are now asking should I even bother to submit my new ideas to NIH. And young scientists who were excited about careers in stem cell research are now worried about going into this field given the legal uncertainty.

But let us keep the focus of this discussion where it belongs. The real reason for distress about the current legal uncertainty is that patients may have to put hope on hold. While we continue through this legal process, we must keep patients and their families foremost in our thoughts. Patients, after all, are at the heart of the NIH mission and are the ones who stand to benefit the most or to lose the most by the stem cell policies we are discussing today.

I am not a lawyer. I speak to you today as a doctor and a scientist, and I appreciated the Chairman's exhortations that for the witnesses at this table, myself and Dr. Daley and Dr. Morrison, Dr. Peduzzi Nelson, and our wonderful advocate who is herself affected by a spinal cord illness, that we should stick to the science, and that is my goal.

But I want to take a few minutes to outline for you the promise of human embryonic stem cell research, research that could be, frankly, hobbled permanently unless stable Federal funding can be assured over the long term. So let us go through this.

There are three different types of human stem cells. All of them are interesting. All of them are important, and it is important to describe the properties of each.

HUMAN EMBRYONIC STEM CELLS

Let us begin with human embryonic stem cells since that is the main topic of this morning's hearing. I will begin with a brief overview of the remarkable properties of these cells and then describe how they can be used to understand the molecular basis of development and disease to regenerate and repair tissue and to screen for new therapeutics.

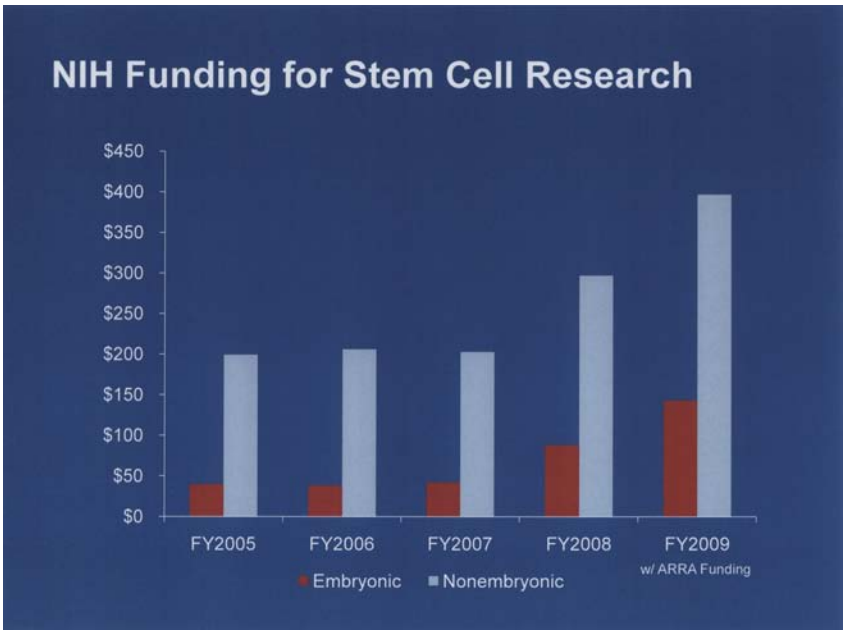
Human embryonic stem cells possess several unique characteristics. First, these cells are called pluripotent, a word which means they have the potential to become nearly every one of the different types of cells in the human body, as you see here.

Second and importantly, these cells are self-renewing. That means they are able to multiply in essentially limitless numbers in the lab over many years and to be shared with researchers around the world.

Now, before I go on to describe the potential applications of human embryonic stem cell research, let me emphasize, though, that as scientists, we are also intensely interested in other types of stem cells. Each has different properties, different potential applications. So let me speak for a moment about adult stem cells.

ADULT STEM CELLS

These are found in various organs and tissues throughout the body. These cells have been studied for more than 50 years and have saved many lives through procedures such as bone marrow transplantation. But because they do not divide indefinitely and produce only a limited repertory of cell types, they are called multipotent rather than pluripotent. And that limitation makes them less than ideal for some types of research.



But let me be clear and demonstrate it by the graph you see here. NIH is strongly committed to research using adult stem cells (in blue) because there may be other clinical applications for which they prove useful that we do not know about yet. So as you can see from this graph, we have been spending considerably more on adult stem cell research (in blue) than on human embryonic stem cell research (in red) for the last several years.

INDUCED PLURIPOTENT STEM CELLS

Now a new and third category of stem cells are these so-called iPS cells, which is what I will call them now. These were created as a direct result of the knowledge gained from studying human embryonic stem cells and understanding their biology. This type of stem cell was only first produced in 2007 when scientists used a virus to insert molecular instructions into the DNA of skin cells, instructions that, amazingly enough, turned back the cells' developmental clock. These new iPS cells possess many properties of human embryonic stem cells. They continue to divide indefinitely and they have the potential to give rise to nearly all the cells of the human body. iPS cells have the added potential clinical benefit of avoiding transplant rejection since they can be derived directly from the patient. But let us be clear. They are not well understood yet. There is growing evidence, including from one of the members of the next panel, for subtle differences between iPS cells and human embryonic stem cells. Whether this will matter for clinical applications is not yet clear, but virtually all investigators working in the field agree that ongoing comparisons between iPS cells and human embryonic stem cells are critically important because human embryonic stem cells remain the gold standard for pluripotency. So to prohibit work on human embryonic stem cells will, thus, do severe collateral damage to the new and exciting research on iPS cells.

THREE KEY USES OF HUMAN ES CELLS

Now I want to turn to the first of three key uses of human embryonic stem cells, going back to talk specifically about them for the rest of my comments.

Their value in understanding the molecular pathways and development in disease is the first of these three. So, for example, you might ask, what genes are expressed in human embryonic stem cells and how is that programming altered as these cells move down pathways to become blood cells, muscle cells, or brain cells, and how does that go awry in the presence of a disease mutation and cause an illness or a birth defect? One of the very best windows we have now into human development is through these human embryonic stem cells. For example, scientists are using these cells to study diseases such as Fragile X syndrome, which is a developmental disability, a rather common one affecting primarily boys; Rett syndrome, a debilitating brain disorder affecting primarily girls; and Huntington's disease, a late-onset neurodegenerative disease.

A second area, an exciting one and the one that has probably generated the greatest public excitement, is regenerative medicine, the idea that human embryonic stem cells could actually be used

as a cell therapy to replace damaged tissues for somebody with Parkinson's disease or diabetes. We might someday be able to regenerate damaged heart muscle tissue in heart attack patients.

One of the most exciting and most advanced possible therapeutic applications of human embryonic stem cells is for patients who have been paralyzed by catastrophic spinal cord injury. And here in this x-ray is an example of what that has done in this patient to disrupt the spinal cord. Researchers at the University of California-Irvine and the biotech company, Geron, as well as at several other universities and companies around the country, are pursuing the possibility that human embryonic stem cells can be directed to generate spinal cord cells for transplantation. And this summer, this being rather a landmark year, Geron began phase I clinical trials of its techniques for converting human embryonic stem cells into a type of neuronal cell called an oligodendrocyte, which is a bit of a mouthful, that is intended for injection into the patient's spinal cord at the site where injury has occurred.

And I am going to show you a computer animation that will show you what this looks like. So we are now going to zero in on some neurons and their axons, which are transmitting electrical signals, which in the spinal cord have to cross great distances. And there, that is an oligodendrocyte that provides the insulation that allows those signals to pass. If the spinal cord is injured, the signals cannot go through. So adding these human embryonic stem cells that have been turned into oligodendrocytes should—and this has been documented in animals—allow a repair of what is otherwise a blocked signal, so that it can reach the limbs of the affected individual.

The potential of this approach in restoring limb function has been repeatedly demonstrated in animal tests, some of which are pretty dramatic. But no one is sure whether this will work in humans with severe spinal cord injury, and even if it does, it will take years of additional rigorous research and testing before a standardized therapy can be developed. Yet, I think anyone looking at this opportunity would say the potential here is truly amazing.

HIGH-THROUGHPUT DRUG SCREENING

A third area of opportunity for human embryonic stem cells and one that has not received as much attention—but I thought you should know about it, because it is actually quite exciting for scientists involved in this, is the potential to catalyze dramatic advances in therapeutics by using these cells as a tool to search for new drugs. Let us consider a specific example.

We desperately need new drugs for a disease called amyotrophic lateral sclerosis (ALS). You mentioned you have had a witness on this very topic speaking about that, who is no longer with us, and this is a disease which, unfortunately once it appears, progresses rapidly. This is Lou Gehrig's disease. It is characterized by the progressive loss of motor neurons in the spinal cord which normally provide the connection between the brain and the muscles of the body.

Now, ideally we would like to find a drug that stabilizes those human motor neurons against this kind of cell death, but how? Well, suppose you could test a library of hundreds of thousands of

candidate drug compounds, knowing that somewhere in there, there might be one that would be valuable encouraging motor neurons to survive. That would be a very attractive approach to ALS. Well, can we actually do that?

I am showing you now a video of three hard-working and uncomplaining yellow robots who are doing high-throughput drug screening, and this is in a facility right up in Gaithersburg, Maryland. This is done in a miniaturized format, supported by NIH, that allows researchers to test the effect of more than 100,000 drug compounds in 48 hours and can, therefore, save months or years of time.

This is not a pipe dream. It is a reality. Lee Rubin's lab at Harvard is carrying out exactly this kind of experiment for ALS right now. The possibility that human embryonic stem cell research might one day enable us to identify a therapy for the disease that claimed the lives of so many, including Senator Jacob Javits, gives you some hope that this new application may provide answers that we desperately need.

CONCLUSION

So in conclusion, Mr. Chairman, I would like to emphasize that human embryonic stem cell research provides enormous but mostly untapped promise for medicine, but this field has been thrust into a precarious state. If this research is slowed or halted, the greatest loss will be suffered by the millions of Americans with conditions that might be helped by human embryonic stem cells. Such people include those suffering from heart disease, from diabetes, from liver disease, from vision problems, along with those afflicted by spinal cord injuries and neurodegenerative conditions like ALS and Parkinson's disease.

The many messages I have received from patients since the issuance of the preliminary injunction on August 23 reflect these deep concerns. Let me just read you part of one such message written to me by the mother of two boys who have juvenile diabetes, and she suffers from early-onset Parkinson's disease. Here is what she says:

"I have held my breath with hope that my sons would benefit from the early stem cell research. I watched as American scientists and science fell further behind on the global scene during the past decade. In 2009, I had such hope that once again our medical schools and universities would begin to attract the best and brightest young minds to work in this exciting and promising area of research."

She finishes with this:

"This week's news was devastating to me. I had no idea how strongly I would be affected by it. Your message of support for the research once again gives me hope, hope that there will be change, hope that we will see effective treatments in our lifetimes for these devastating diseases."

PREPARED STATEMENT

Hope, Senator. When someone is seriously ill or has a loved one who is facing a life-threatening disease, it is often hope that sustains them, provides the strength and determination to prevail. Moving forward responsibly with all types of stem cell research gives us and them good reason for hope, hope that is informed by science, rigorous science. Patients and their families are counting

on the research community to find those cures and treatments. Please help us do our part to turn that hope into reality.

Thank you, Mr. Chairman, for your strong support of stem cell research, and I would be happy to answer any questions.

[The statement follows:]

PREPARED STATEMENT OF FRANCIS S. COLLINS

Good morning, Chairman Harkin and distinguished members of the subcommittee. It is an honor to appear before you today to discuss human embryonic stem cell research. First, I'd like to thank this subcommittee for its steadfast support of the National Institutes of Health's (NIH) mission: discovering fundamental knowledge about living systems and then applying that knowledge to fight illness, reduce disability, and extend healthy life. NIH is grateful for the confidence that Congress—and this subcommittee in particular—has shown in our ability to achieve this mission, as evidenced by our current $31 billion budget, and the $10.4 billion provided to NIH through the American Recovery and Reinvestment Act. Your support makes our mission possible, and we are very grateful.

Nowhere has this support been more evident than in this subcommittee's leadership in advancing human embryonic stem cell research. From your first hearing in December 1998, this subcommittee has provided a forum for discussing the great promise this research holds. With your steadfast support, NIH has invested more than $500 million in human embryonic stem cell research; one of the most promising research avenues of recent times.

The preliminary injunction issued on August 23 by U.S. District Court Judge Royce Lamberth in the *Sherley* v. *Sebelius* case, now stayed pending further order from the Court of Appeals, has created uncertainty in the field of human embryonic stem cell research. Many researchers across the country have considered modifying their research plans to turn away from an area of research that, while promising, is now fraught with uncertainty. Some of our Nation's best researchers, who have written grant applications proposing innovative new ideas, are now asking, "Should I even bother to submit my proposal to NIH?" Likewise, young scientists excited about careers in stem cell research are concerned about going into this field, given the legal uncertainty.

But the real reason for distress about the current legal uncertainty is that patients may have to put hope on hold. While we continue through the legal process, I hope that we can keep the patients and their families in our thoughts. They are at the heart of the NIH mission, and they are the ones who stand to benefit the most, or lose the most, by the stem cell policies we are discussing today.

I am not a lawyer, and I speak to you today as a doctor and a scientist. In that capacity, I want to outline for you the promise of human embryonic stem cell research—research that could be hobbled permanently unless stable Federal funding can be assured over the long term.

I want to begin with a brief overview of the remarkable properties of human embryonic stem cells and then describe how research using these cells will:

—provide key insights into the molecular pathways in development and disease;
—allow for the development of tissue replacement or regenerative medicine; and
—enable more targeted and efficient screening of new drug candidates.

Human Embryonic Stem Cells

Human embryonic stem cells possess several unique characteristics. First, these cells are pluripotent, which means that they have the potential to become nearly every one of the different types of cells in the human body. Second, these cells are self-renewing, which means that they are able to multiply in essentially limitless numbers in the lab over many years and to be shared with many researchers around the world.

To be sure, scientists are also interested in other types of stem cells. Adult stem cells are found in various organs and tissues throughout the body. These cells, also sometimes referred to as multipotent or somatic stem cells, can develop into a limited number of specific cell types, depending upon the organ or tissue from which they are derived. However, adult stem cells are less than ideal for many types of research and therapy because they do not divide indefinitely in culture, and they produce only a limited number of cells and cell types.

In considering the relative benefits of adult and embryonic stem cell research, keep in mind that research on the most abundantly available source of adult stem cells, hematopoetic stem cells in bone marrow, began more than a half-century ago. In fact, Drs. E. Donnall Thomas and Joseph Murray were awarded the Nobel Prize

in Medicine in 1990, "for their discoveries concerning organ and cell transplantation in the treatment of human disease." Indeed, this research has produced clinically validated and widely used treatments that reconstitute the immune system after leukemia, lymphoma, and various blood or autoimmune disorders have been treated with chemotherapy.

NIH is strongly committed to research using adult stem cells because there may be other clinical applications for which they prove useful. NIH has invested many hundreds of millions of dollars over the years in adult stem cell research. Indeed, annually we are spending almost three times as much on adult stem cell research as on human embryonic stem cell research.

A new and third category of stem cells are induced pluripotent stem (iPS) cells, which were created as a direct result of the knowledge gained from studying human embryonic stem cells. This type of stem cell was first produced in 2007, when scientists discovered that it is possible to instruct adult skin cells to return to a very early developmental stage. They accomplished this by using viruses to insert molecular instructions into the DNA of skin cells—instructions that acted to turn back the cells' developmental clock. These new cells possess many properties of human embryonic stem cells: they continue to divide indefinitely and are pluripotent, with the potential to give rise to all the cells of the human body.

While induced pluripotent stem cells are of great interest to scientists, and have the added potential clinical benefit of avoiding transplant rejection since they can be derived directly from the patient, they are not well understood yet. A growing body of research, including a publication just 2 months ago from Dr. George Daley, who is here today, and his collaborators suggests that there are subtle, but potentially important differences between iPS cells and human embryonic stem cells. On close examination with powerful molecular fingerprinting, it seems that iPS cells retain some memory of the tissue from which they were derived. Whether this will matter for clinical applications is not clear, but virtually all investigators working in the field agree that additional comparisons between iPS cells and human embryonic stem cells are critically important. Human embryonic stem cells remain the gold standard for pluripotency: to prohibit work on human embryonic stem cells will thus do severe collateral damage to the new and exciting research on iPS cells.

Molecular Pathways in Biological Development and Human Disease

While many researchers are focused on coaxing human embryonic stem cells to develop into a particular cell type, such as insulin-secreting cells or liver cells, understanding the basic biology of stem cells themselves will be extremely valuable to understanding human development. We have learned much about the genes required for pluripotency, but there is much more to understand. For example, what genes are expressed in human embryonic stem cells? How is that program altered as these cells move down pathways to become blood cells, muscle cells, or brain cells? How are these steps regulated? What happens if one of the genes doesn't function properly? Our best window into human development is using human embryonic stem cells.

In addition to understanding normal human development more completely, human embryonic stem cells are providing key tools to help us study the origins of many devastating diseases that afflict babies and young children. Such research may even help to uncover targets for drug development. We now have a number of human embryonic stem cell lines that are known to carry mutations that cause specific diseases. For example, scientists are studying cell lines with a mutation in the FMR1 gene that causes Fragile X, a developmental disability. The FMR1 gene normally makes a protein that the brain needs to develop properly. However, the Fragile X mutation in the FMR1 gene causes the body to make only a little or none of the protein. Research using human embryonic stem cells with this mutation showed that although the FMR1 gene is expressed normally in Fragile X, it is turned off after the cells begin to differentiate. How this happens is something we can study using human embryonic stem cell lines. Dr. Daley also studies a number of human embryonic stem cell lines with various genetic mutations, and I am sure he can tell you more about his research.

One ongoing NIH grant focuses on Rett syndrome, a debilitating, developmental brain disorder generally afflicting young females and caused by mutations in a gene called MECP2. This research uses human embryonic stem cells to generate human brain cells with a deficiency in the MECP2 gene, and then studies the effects of this deficiency on the development and functions of these brain cells. Such research could improve our understanding of Rett syndrome, and facilitate the development of therapies for it.

Another research team has recently generated human embryonic stem cell lines containing mutations in the HTT gene that causes Huntington's disease, a late-

onset neurodegenerative disease. Huntington's disease has been studied for a long time, but the normal function and pathogenesis of the protein coded for by the HTT gene is not fully understood.

Tissue Replacement or Regenerative Medicine

One of the more exciting and high-profile potential applications of human embryonic stem cell research is the possibility that such cells can be programmed to replace or regenerate tissues damaged by disease or injury. For example, we might one day be able to regenerate damaged heart muscle tissue in heart attack patients, develop insulin-producing pancreatic beta cells to replace those lost or damaged in people with Type 1 diabetes, or restore spinal cord neural connections in patients paralyzed by catastrophic spinal cord injury.

Part of the devastation that heart attack victims suffer is that, because of restricted blood flow and oxygen deprivation, their heart muscle cells die, leaving the heart much weaker and less able to pump blood throughout the body. Today we are studying the tantalizing possibility that human embryonic stem cells, or perhaps adult stem cells or iPS cells, might be programmed to replace damaged or destroyed heart muscle cells, known as myocardial cells. The prevalence of heart disease, along with the scarcity of hearts and heart tissues available for transplantation and the associated clinical and autoimmune problems of transplantation, make this line of research imperative.

Type 1 diabetes is a disease in which a specific type of cell, insulin-producing pancreatic beta cells, is damaged or destroyed by the patient's own immune system. A major challenge is to understand the autoimmune response that kills these cells in children who then develop Type 1 diabetes, but human embryonic stem cells offer the hope that we might one day produce replacement cells that avoid the autoimmune challenges associated with today's rudimentary transplantation therapies. To do that, we need to know more about how stem cells are genetically programmed, how they differentiate, and how they renew themselves; but as our understanding and ability to work with these cells expands, we are laying the foundation for an entirely new—and much more effective—way to address the devastation of Type 1 diabetes.

One of the most exciting—and most advanced—possible therapeutic applications of human embryonic stem cells is for patients who have been paralyzed by catastrophic spinal cord damage. Researchers at the University of California—Irvine and at the biotech company Geron Corp., as well as at other universities and companies around the country, are pursuing the possibility that human embryonic stem cells can be directed to generate spinal cord cells for transplantation.

This summer, Geron began phase I safety trials of its technique for converting stem cells into a type of neuronal cell, known as oligodendrocytes, intended for injection into the patient's spinal cord at the site where it has been severed by injury. The hope, which has been repeatedly demonstrated in animal tests, is that the newly injected oligodendrocytes might repair the damaged insulation around the severed nerve cells of the spinal cord, and thereby enable those cells to once again send signals to the patient's limbs and organs. We are not sure that this approach will work, and even if it does, it will take years of additional research and testing before we can develop a standardized therapy using these techniques. Still, the potential that this research holds is truly amazing.

For all of these efforts, there are many scientific challenges that must be addressed. We need to figure out how to get human embryonic stem cells to differentiate down specific pathways in a well-controlled process. We also need to make sure that the resulting cells behave in predictable ways. Because human embryonic stem cells are immortal and can proliferate endlessly—much like cancer cells—we need to be sure that they or their differentiated "daughter" cells do not produce tumors or otherwise harm patients. The field of regenerative medicine is young. It is unreasonable for us to think we will have cures within a set time period. It is also wrong to overpromise on the speed and scope of such research to patients and their families. But we must persevere and move this research forward in a strong and consistent manner. That is why the delay and uncertainty associated with the current legal situation is so disheartening for both researchers and patients. As I said at the time the injunction was issued, this unexpected development is like pouring sand into the engine of discovery.

Targeted, Efficient Screening of New Drug Candidates

Recently, human embryonic stem cells have received increasing attention as a tool for drug screening. High throughput drug screening is done in a miniaturized format that allows researchers to test the effect of more than 100,000 chemicals on a gene, protein, cell, or organism of interest. It is a highly automated process that can

test in one day what would otherwise take a researcher months or years. Because human embryonic stem cells can differentiate into specific human cell types in large quantities, they provide the foundation for high throughput screening of candidate drug compounds for a given disease. This means that we now have the capacity to identify efficiently drugs that work in a targeted cell type.

This is not a promise, it is reality. Human embryonic stem cells are currently being used to identify drug candidates that can slow or stop the progression of amyotrophic lateral sclerosis (ALS). Also called Lou Gehrig's disease, ALS is an ultimately fatal disease characterized by the progressive loss of motor neurons, which provide the connection between the brain and the muscles of our body. The possibility that human embryonic stem cell research might one day enable us to identify a therapy for the disease that afflicts astrophysicist Stephen Hawking and claimed the life of Senator Jacob Javits, gives you some sense of the hope this new application might provide.

There are very few drugs available for ALS, and none that prolong the patient's life for more than a few months. Dr. Lee Rubin, a researcher at Harvard's Stem Cell Institute, and his colleagues have developed an elegant set of studies to screen for drugs that prevent motor neuron death. The scientists differentiated mouse embryonic stem cells into large numbers of motor neurons and exposed them to thousands of compounds to find the ones that improve the survival of these vital cells. Dr. Rubin and his team identified a handful of promising compounds that they then tested in motor neurons derived from human embryonic stem cells. The most promising of these can now be moved further along the pipeline from drug discovery to clinical trials.

Drugs fail for many reasons: lack of efficacy in humans is responsible for 30 percent of drug failures, and unpredicted toxicity is responsible for more than 20 percent of failures. The traditional methods of using animal or abnormal human cell lines for safety and efficacy testing provide a poor model of how a human will respond to a particular drug. Human embryonic stem cells can generate the appropriate cell type and even disease cell lines for efficacy testing early on, as in the case of the ALS study. They are also being used to understand the toxicity of promising compounds in the early stages of drug development. For example, liver toxicity is a common cause of drug failure. Human embryonic stem cells can be differentiated into human liver cells, or hepatocytes, which are then exposed to novel drugs to identify any obvious liver toxicity and provide early insight on how a drug will be metabolized by the liver. In this manner, human embryonic stem cells provide drug developers and researchers a model of how actual human livers will respond to a drug. Our hope is this will reduce the number of drugs that fail in human clinical trials because of low efficacy or unacceptable toxicity.

The NIH Stem Cell Guidelines

President George W. Bush first funded research on human embryonic stem cells—but that decision only allowed the use of cell lines that had been derived before August 9, 2001. Ultimately, that only amounted to 21 cell lines, and as science moved forward it was clear that this somewhat arbitrary time stamp was significantly inhibiting the field. On March 9, 2009, President Barack Obama issued Executive Order 13505, Removing Barriers to Responsible Scientific Research Involving Human Stem Cells. The Executive Order states that the Secretary of Health and Human Services, through the Director of NIH, may support and conduct responsible, scientifically worthy human stem cell research, including human embryonic stem cell research. This Executive Order prompted a rapid expansion of scientific effort and progress.

The President asked NIH to review existing human stem cell research guidelines and issue new guidelines, consistent with the President's Executive order, within 120 days. NIH immediately began a comprehensive review that resulted in draft guidelines that were published in the Federal Register for public comment on April 23, 2009. After careful analysis of more than 49,000 comments from scientific, patient advocacy, medical, and religious organizations, as well as private citizens and members of Congress, NIH published final guidelines, effective July 7, 2009. The guidelines provide a framework for funding scientifically worthy research using responsibly derived human embryonic stem cells. The guidelines restrict Federal funding to cell lines derived from embryos that: were created for reproductive purposes and were no longer needed for that purpose; were donated for research by individuals who sought reproductive treatment; and for which the donors gave voluntary written consent. Since the President issued his Executive order and NIH implemented its guidelines, 75 human embryonic stem cell lines have been approved for use in NIH-funded research. All were reviewed rigorously and found to meet the high ethical standards laid out in the NIH guidelines. The review process is so rig-

orous that 48 stem cell lines have not been approved for use in federally funded research. Prior to the court's order, in fiscal year 2010, NIH funded 199 grants for research on human embryonic stem cells totaling $137 million. These grants support a broad range of research including studies to improve stem cell technologies, studies to compare different types of stem cells, and studies to develop cell types for use in treating debilitating diseases and disorders such as diabetes, liver failure, and neurodegenerative diseases.

If the Government is not successful in defending the guidelines in this litigation, and NIH will have to withdraw future NIH support for all grants involving human embryonic stem cell research, drastic scientific consequences will occur. Since funding for these projects would be discontinued mid-stream, all the funds that have been put in accounts or already drawn down—$270 million over the 2- to 5-year life of these grants, including what has been provided fiscal year 2010—would have been wasted. The research momentum that this subcommittee worked so hard to achieve would be lost.

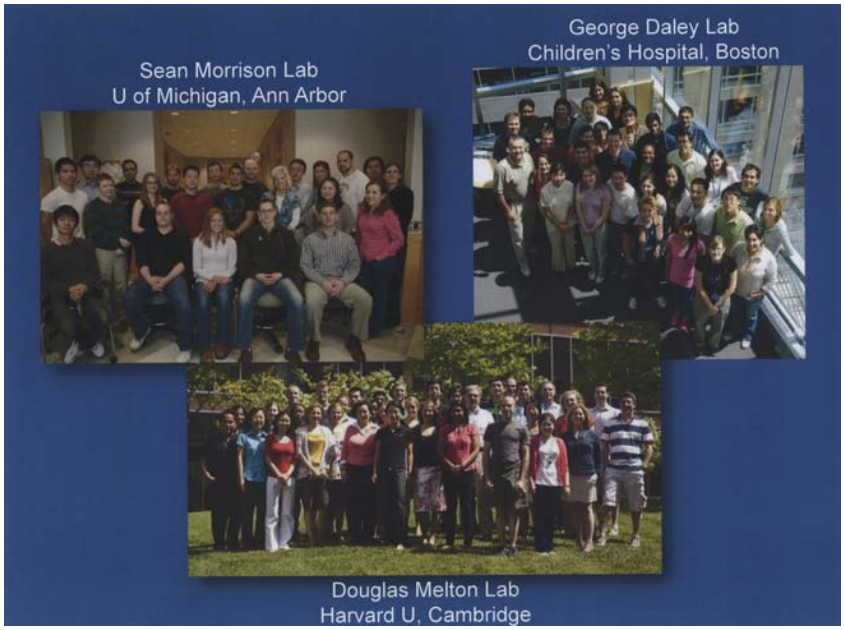
Young scientists may opt out of this field due to the chaos of stopping, then starting and now stopping again. More senior investigators may look to other countries, such as Singapore, China, and the United Kingdom to pursue their work. The greatest loss, however, will be for the millions of Americans with conditions currently under study with human embryonic stem cells. Such people include those suffering from heart disease, diabetes, liver disease, and vision problems, along with those afflicted by spinal cord injuries and neurodegenerative conditions like ALS and Alzheimer's disease. The many messages I have received from patients since the issuance of the preliminary injunction reflect these deep concerns. Here is part of just one such message:

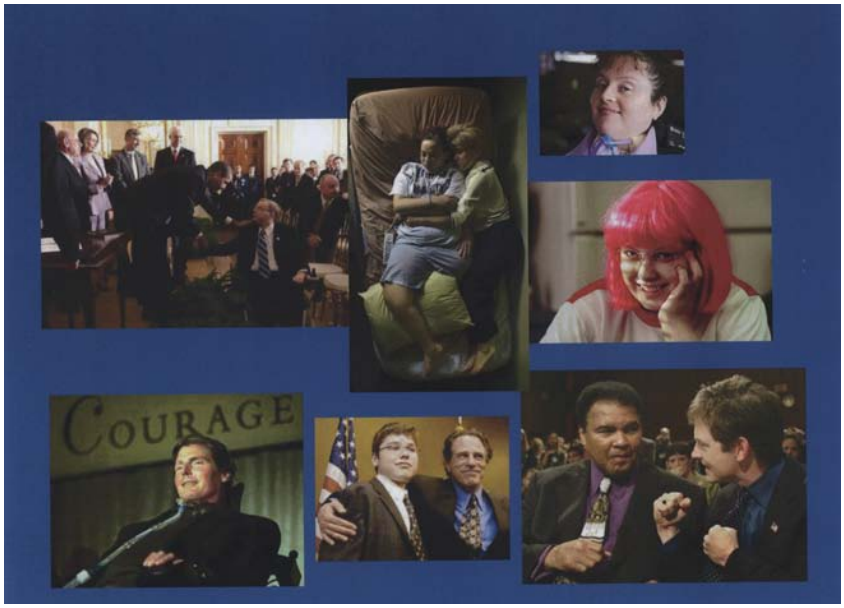
"I am a mother of two adult sons with Type I diabetes (since age 7), and a person with young onset Parkinson's disease. I have watched as my oldest son moved from taking the old beef/pork insulin to taking genetically engineered insulin, and have held my breath with hope that my sons would benefit from the early stem cell research.

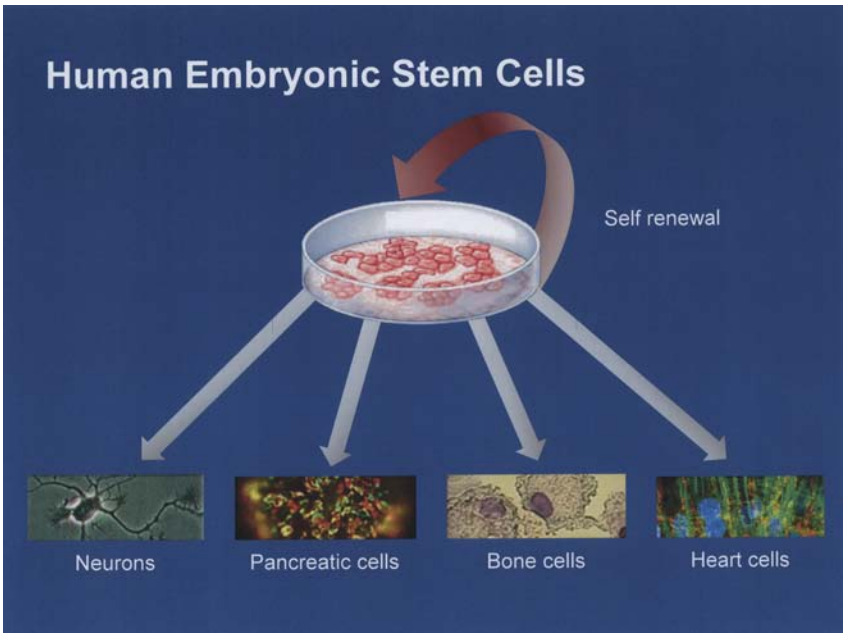
"I watched as American scientists and science fell farther behind on the global scene during the past decade. In 2009, I had such hope that once again our medical schools and universities would begin to attract the best and brightest young minds to work in this exciting and promising area of research.

"This week's news was devastating to me. I had no idea how strongly I would be affected by it. Your message of support for the research once again gives me hope. Hope that there will be change. Hope that we will see effective treatments in our lifetimes for these devastating diseases."

Thank you, Mr. Chairman, for your strong support of stem cell research. I would be happy to answer any questions.

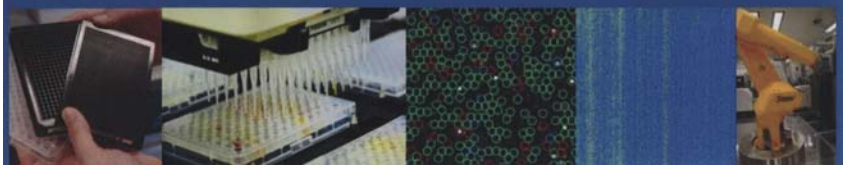

George Daley Lab
Children's Hospital, Boston
Sean Morrison Lab
U of Michigan, Ann Arbor
Douglas Melton Lab
Harvard U, Cambridge

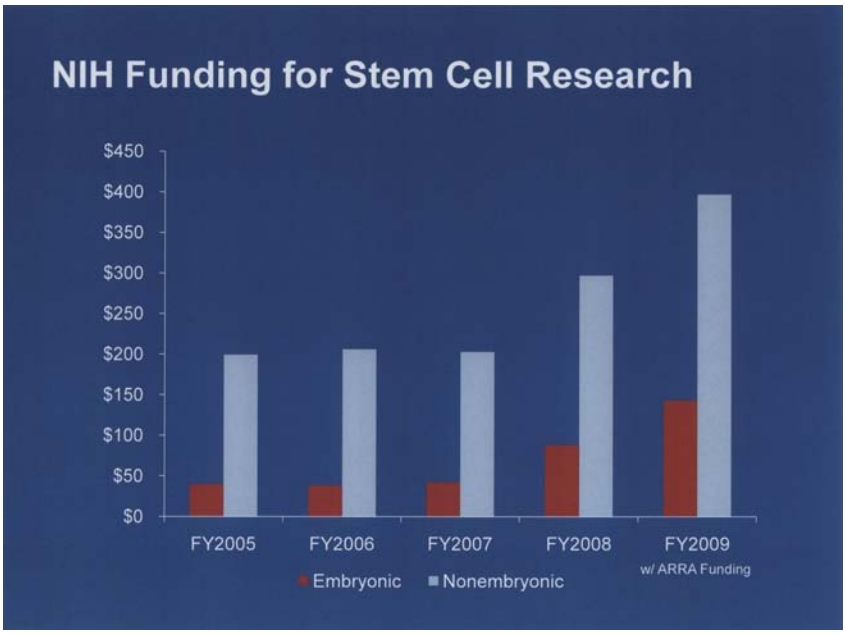

COURAGE

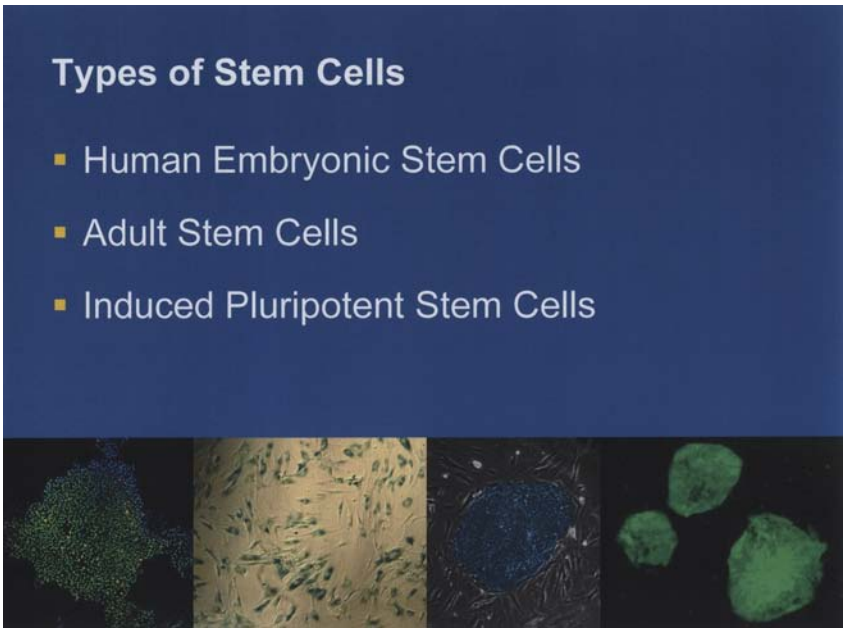


Uses of Human Embryonic Stem Cells

- Understand molecular basis of development and disease
- Regenerate and repair tissue
- Screen for new therapeutics




NIH Funding for Stem Cell Research
$450
$400
$350
$300
$250
$200
$150
$100
$50
$0
FY2005
FY2006
FY2007
FY2008
FY2009
w/ ARRA Funding
Embryonic
Nonembryonic


Types of Stem Cells
Human Embryonic Stem Cells
Adult Stem Cells
Induced Pluripotent Stem Cells

Uses of Human Embryonic Stem Cells

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- Regenerate and repair tissue
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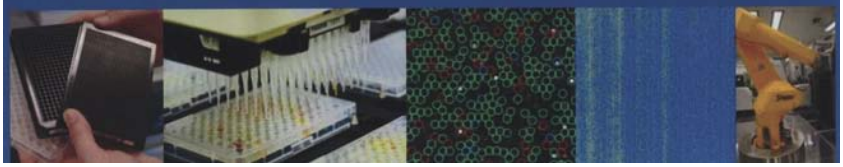
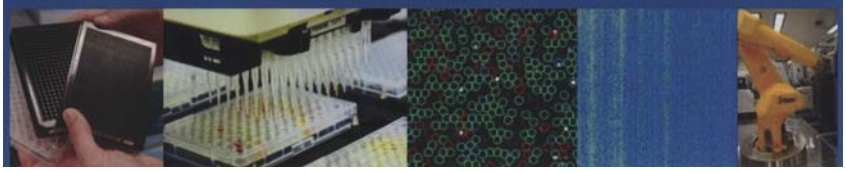


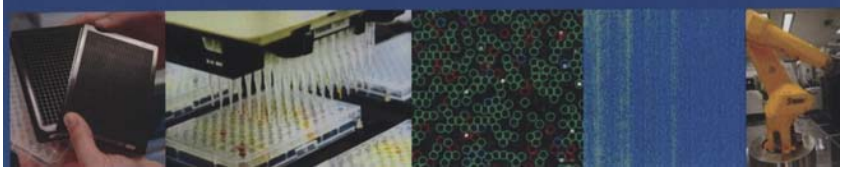
Uses of Human Embryonic Stem Cells

- Understand molecular basis of development and disease
  - Fragile X
  - Rett Syndrome
  - Huntington's Disease

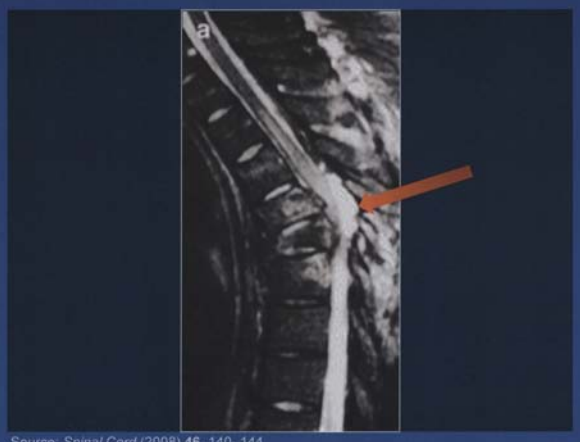


Uses of Human Embryonic Stem Cells

- Understand molecular basis of development and disease
- Regenerate and repair tissue
- Screen for new therapeutics



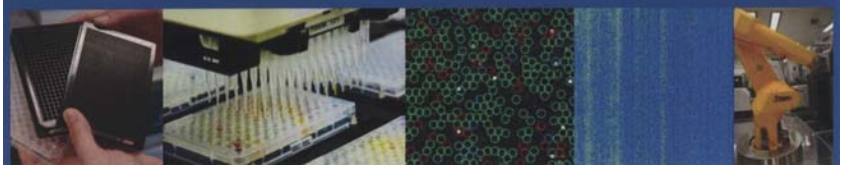
Regenerating Tissue



Source: *Spinal Cord* (2008) **46,** 140–144

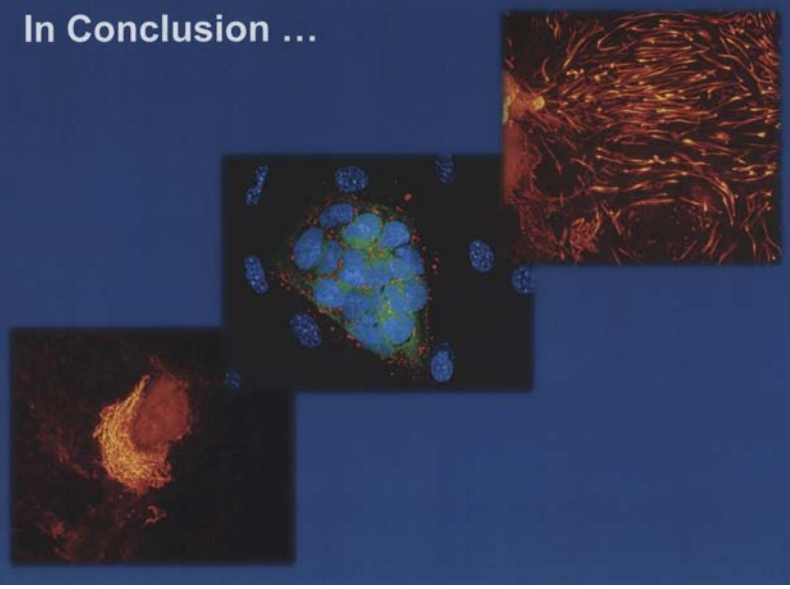
Uses of Human Embryonic Stem Cells

- Understand molecular basis of development and disease
- Regenerate and repair tissue
- Screen for new therapeutics



Screening for Therapeutics

In Conclusion …

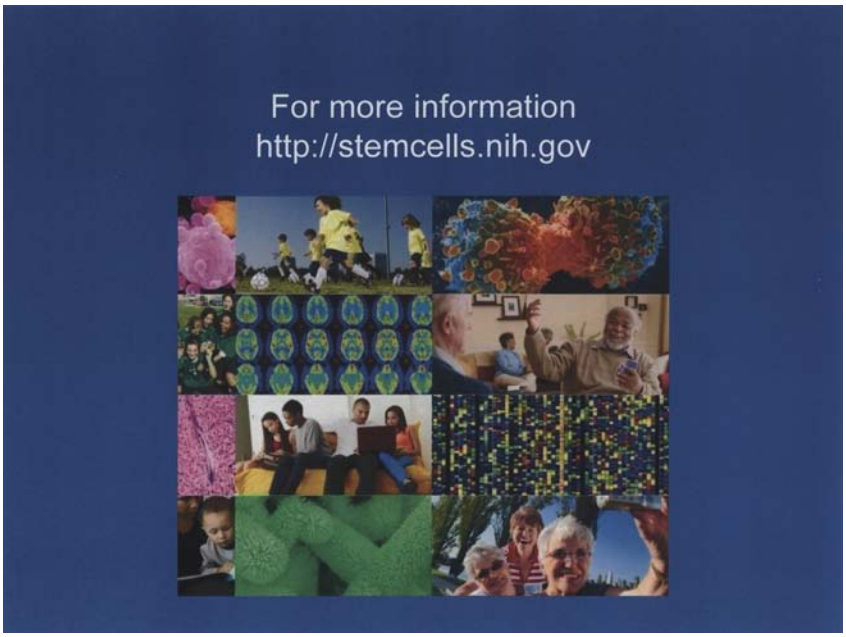


Message of Hope

This week's news was devastating to me. I had no idea how strongly I would be affected by it. Your message of support for the research once again gives me hope.

Hope that there will be change. Hope that we will see effective treatments in our lifetimes for these devastating diseases.

~ Woman with early onset Parkinson's disease
and mother of two sons with Type 1 diabetes



THE NEED FOR ADDITIONAL STEM CELL LINES

Senator HARKIN. So, Dr. Collins, thank you. As usual, a very lucid and understandable presentation of a very complex issue and complex science.

We will begin a round of 5-minute questioning. We have two votes, I think, starting at 10:45 a.m., if I am not mistaken. So we will do as much as we can, and then we will return.

Because of the Executive order signed, the number of stem cell lines eligible for Federal funding rose from 21 to 75. Dr. Collins, why is this important to scientists? What can researchers do with these additional lines they could not do before? Would it help to have even more lines?

Dr. COLLINS. I think President Bush deserves credit for being the first to provide Federal funds for human embryonic stem cell research, and that did lead to these 21 lines that have been utilized over the course of several years. But they were derived a long time ago and many of them under circumstances that today we would say are less than ideal. There are many advances in the science over that time table, and many other stem cell lines being derived during that time table since 2001 were not available to scientists who had great interest in studying them.

In particular, to be able to have available human embryonic stem cell lines that have specific genetic mutations in them would be a great advance in terms of the ability to study certain diseases such as Fragile X, for instance, or Huntington's disease, and such were not in the collection of 21 lines.

Furthermore, those 21 lines were very nondiverse in terms of their origins, nearly all of them coming from individuals of North-

ern European background, and if you were seriously thinking about the possibility of utilizing these therapeutically, as Geron is now doing for spinal cord injury, that could greatly limit the ability to use them for people of different backgrounds. So there is enormous enthusiasm and intense interest on the part of the scientific community to have this panel broadened, and the Obama Executive Order of March 2009 made that possible under carefully described conditions to maintain the most ethical standards in terms of how such lines would have to have been derived in order to qualify for Federal funding. And NIH now has on its registry 75 lines that have met those standards and more to come.

LIMITATIONS OF ADULT STEM CELLS

Senator HARKIN. Very good.

In Senator Wicker's opening statement, he said the following:

"People suffering from dozens of diseases and conditions, including cancer, juvenile diabetes, Parkinson's, MS, leukemia, lymphoma, spinal cord injuries, and corneal regeneration, among many others, are turning to adult and induced pluripotent stem cell treatments for help."

My understanding has been that while adult stem cells are used routinely to treat blood diseases, this is not the case for any other type of disease. Could you please enlighten us on that aspect?

Dr. COLLINS. Sure. Adult stem cell research has been studied now for more than 50 years——

Senator HARKIN. You said that.

Dr. COLLINS [continuing]. And certainly has been primarily utilized clinically for bone marrow transplantation where it has been of great value. We are, as you saw from the graph, spending almost $400 million a year on non-embryonic stem cell research, looking for additional applications where adult stem cells could also be of benefit. And the Senator's opening statement mentioned some areas of potential interest, but they are far from being what you would call standardized care yet. They are experimental.

I think one of the unfortunate aspects of the discussion about human embryonic stem cells is that it has somehow implied that scientists are opposed to research on adult stem cells. Not at all. Speaking for myself and the others who will be here today, we celebrate all of the ways that every kind of stem cell can be utilized for effective research, but should we not be pursuing the most exciting options in parallel and not assuming that we know one of them is going to be better than the other? Because right now, we have absolutely no reasons to say that. And I think most would assume that, depending on the application, adult stem cells may be better in one instance; embryonic stem cells may be better in another. We will never know if we are not allowed to do the research.

Senator HARKIN. So it is not just two different camps. It is a blending of all of this.

Dr. COLLINS. Absolutely. Dr. Daley would probably tell you he has made major advances in both those fields, and he would be right.

IMPORTANCE OF FEDERAL FUNDING

Senator HARKIN. Lastly, we sometimes hear opponents of this research say Federal funding is not needed. There are other potential

sources of money in the private sector. How would you respond to that?

Dr. COLLINS. Well, of course, that was an argument that basically prevailed before there was any allowance for Federal funding for human embryonic stem cells and led to some States taking action. But most of the really critical observations that need to be made in terms of understanding the potential of human embryonic stem cells are unlikely to happen without the kind of Federal support in our best universities and medical centers around the country. That is where the talent often lies for doing those really fundamental explorations of the nature of these cells. To assume that private sector investment, although it is critical in terms of those ultimate translational steps, is going to be sufficient is to not understand the many steps that we need to pursue now in order to fully flesh out the potential of this approach to treating a long list of conditions.

Senator HARKIN. Thank you very much, Dr. Collins. My time is out. I do have a couple of follow-up questions, but I will wait my turn. I will turn to Senator Cochran for his.

Senator COCHRAN. Dr. Collins, we were talking specifically today about the options for Federal support for research and specifically using embryonic stem cell therapy. What in your judgment would happen if we did not approve Federal funding or, if for some reason, the funding sources in the Federal Government to support this kind of research dried up for whatever reason—action of Congress or, heaven forbid, running out of money?

Dr. COLLINS. If Federal funds were terminated for the support of human embryonic stem cell research, that would be an absolutely devastating outcome. You would see large numbers of scientists who have already developed a lot of momentum in this field becoming extremely disillusioned. You would see many of them potentially moving into other research areas or moving overseas. Most importantly, you would see that hope for the treatment of many diseases that we currently lack effective ways to intervene being dashed.

I do not want to overstate here the potential for human embryonic stem cell research to solve all those problems because we just do not know, and we have to be careful that our hope does not turn into hype, and I think people here will be careful about that. But you know, if you were living in 1950 and somebody said, you know, those iron lungs are working pretty well, maybe we do not need to do anything more about polio, what a terrible mistake that would have been. So we have some science now that is working in some areas, but we have this new potential to do something really that is game-changing. To have that cut off at the knees would be a devastating blow.

And let me say one other thing that I tried to put into my statement which I think has not been appreciated. It is not sufficient to say, well, we now have iPS cells, so we do not need human embryonic stem cells anymore. We have to compare those side by side, every step of the way right now, because we do not understand the subtle differences between them and what that might mean, and if we give up doing that comparison to the gold standard for

pluripotency, we may damage the potential of iPS cells just as they are beginning to gather momentum.

Senator COCHRAN. Well, I appreciate very much your being here today. I think your testimony has helped us understand in a real way, a practical way, what the consequences are for a breakdown in Federal support for this research. Thank you very much.

Dr. COLLINS. Thank you, Senator.

Senator HARKIN. Senator Specter.

Senator SPECTER. Thank you, Mr. Chairman. I thank you for your generous comments and for scheduling this early hearing to take up the important subject of embryonic stem cell research. I look forward to debating with Senator Wicker the issues which he has raised more appropriately on the Senate floor than in this hearing, I think, and would ask unanimous consent that a commentary by Bob Schieffer on 60 Minutes be included in the record where there is a comparison between those who oppose stem cell research with those who challenged the use of Galileo's telescope because they believed their doctrines and tradition had already told them what was necessary to be seen.

[The information follows:]

[From www.cbsnews.com, August 29, 2010]

STEM CELL INJUNCTION DICTATED BY DOCTRINE

(By Bob Schieffer)

Last week two people I know were diagnosed with colon cancer, one of the deadliest of all cancers.

Because my wife and I are cancer survivors, and because my mother died of cancer because she was afraid to go to the doctor, I've come to know a little about the disease.

My friends have a serious illness, but there is a path to recovery that was not there not so long ago. And as I talked to them last week, I was again struck by the remarkable progress science is making to give them that path.

Being told we have cancer no longer means we've been given the death penalty.

Like all scientific breakthroughs, advances in cancer research began and depend on basic research—science's ability to go not where doctrine or tradition dictates, but where research takes it.

Ironically, my friends were diagnosed about the time a Federal judge issued the injunction placing limits on stem cell research, an area that holds the greatest possibilities for medical breakthroughs since penicillin.

I have the greatest respect for those who disagree, but to me putting restraints on stem cell research is not far from those who refused to look through Galileo's telescope because they believed their doctrines and tradition had already told them what they would see.

Their beliefs, too, were deeply held—but where would the store of knowledge be had their view prevailed?

As we again try to untangle the arguments over stem cells, let us also consider this: No civilization, no society, has survived if its people came to believe they knew enough and needed to know nothing more.

IMPACT OF JUDICIAL DECISIONS

Senator SPECTER. The decision by the district court in the District of Columbia has had a very serious impact on the research. May the record show a nod by Dr. Collins. And I will ask him specifically about that. But in our informal discussion, he said that while they have been able to proceed with the expenditure of Federal funds with the circuit stay, that the researchers are very, very concerned about their ability to move forward. And we have a stay

which has been issued until next Monday, September 20, and we do not know what will happen after that.

That is why I moved very promptly, as soon as we were in session—on Monday of this week we went into session at 2:30 p.m., and before 3 o'clock I had to go to the floor to introduce legislation to overturn the court decision because Congress has the authority to make this determination. It is not constitutional issue. It is a matter of statutory interpretation. And the evidence is overwhelming about the importance of embryonic stem cell research to deal with the maladies of the world. And if there are 400,000 frozen, which will be lost and that we are not dealing with human life—if they would be turned into human life, no one would suggest using them for medical research.

The vicissitudes of the legal battle are very, very uncertain as to what will happen in the circuit court, whether the stay will be maintained or whether the Supreme Court might issue a stay. There have been surprising stays issued by the Supreme Court in the past several months. There was an Arizona campaign finance law which provided for public funding where the Court of Appeals for the Ninth Circuit upheld the law, overruling the district court, and the Supreme Court of the United States, without even a petition for certiorari filed, intervened in the case to grant a stay—really unheard of—on ideological grounds.

We had a trial in process before Chief Judge Walker in San Francisco on the issue of gay marriage, and the Supreme Court intervened to stop televising on closed circuit television.

So the legislature, the Congress, had better get busy and it better act on this subject so we do not await court action. We do not put the scientists under the pressure of knowing what may or may not happen.

I have a couple of questions for you, Dr. Collins. The first question relates to the impact of the judicial decision, and I have gotten the information that more than $500 million has been expended on embryonic stem cell research. Well, actually three questions.

Question number one is what has the impact been on the scientists now using NIH funding for embryonic stem cell research in terms of the uncertainty of the future.

Number two, what results have been taken in a positive sense, which I know are very good for the more than $500 million already expended?

And what has been the consequence of the $10 billion in the stimulus package where you informally told me that it has created a tremendous excitement and a new wave of enthusiasm by researchers who had been discouraged by the failure of Congress to keep the pace, which we had moved from $12 billion to $30 billion, but failure to keep the pace in funding since 2003?

THE EFFECT OF THE PRELIMINARY INJUNCTION ON NIH EMBRYONIC STEM CELL RESEARCH

Dr. COLLINS. Well, Senator, thank you for the question, and let me first say how appreciative I am personally and everyone at NIH is for the strong leadership you have shown over these years and your advocacy for the value of medical response and especially, because we are talking about it today, for stem cell research. That

has been much appreciated and your articulation of the importance has always been right on target, as it just was here in your opening statement. And we are all grateful, indeed, for the way that you have shown that leadership. And you, together with our chairman, have played such a significant role in NIH being at this exciting place that we are right now in terms of medical research opportunities that, frankly, I did not dream we would be at 10 years ago.

But we also are here with this cloud over the enterprise in this very specific area of human embryonic stem cell research.

When the judge issued that preliminary injunction, we were stunned, and basically after interpretations by the Department of Justice, took steps that we felt we had to with intramural researchers who were working with Federal funds at that very time doing embryonic stem cell research. We had to ask them to stop. With extramural grantees, if they had already received a grant and were spending down the dollars that they had already been allocated, they could continue, but they would need to come back for a renewal on an annual basis, and we basically said within a year, there will be no more funds because those annual renewals cannot be adhered to. And frankly, we had a bunch of new grants and renewals right in front of us, about 244 grants, adding up to about $200 million, that were immediately put on hold, not to mention a whole other set of grants that were ready for peer review that we had to stick on the shelf because we felt the judge's order prevented us from acting on them.

Fortunately and to our great relief, although temporary relief it apparently is, the stay on that particular injunction last week allowed us to catch up and to go back to doing what we had been doing, and we are working vigorously to be sure that we are doing the right thing here in terms of supporting the research that we had always intended to.

But there is this cloud of uncertainty that hangs over the situation because there is not a clear path forward. And I think as you will hear from others at this hearing, that is creating great anxiety particularly amongst young scientists who are wondering, "Do I have a career path here or is this something I better just not get involved in because it is too uncertain?"

So the impact so far has been quite significant and is uncertain going forward. We are, as I tried to show in the graph in the opening statement, spending in the neighborhood of $188 million—sorry—$138 million on nonembryonic—I am sorry—on embryonic and other types of nonadult—let me try that again. We are spending $138 million on human embryonic stem cell research and all of that was put into jeopardy. And that is an estimate for fiscal year 2010.

AMERICAN RECOVERY AND REINVESTMENT ACT (ARRA) AT NIH

In terms of your question about the ARRA dollars that have flowed to NIH, that has been an enormous infusion of energy and capability and excitement in a community that had, frankly, been struggling after 5 years of flat budgets and many innovative ideas lacking support. The infusion of that money has made it possible to put into place a whole host of innovative projects.

One of the things I have done in my first year as NIH Director is to read a lot of those grants that came in because of ARRA to see what was there. And it is some of the most exciting science that you can imagine, and we have used it specifically to encourage people to put forward out-of-the-box ideas that might otherwise have not seemed worth trying in a very tough budget climate. This has supported breakthroughs in cancer, in heart disease, in diabetes, in autism, things that really have changed the whole landscape because of this opportunity to empower the community in ways that they had not been previously been able to do. And I want to thank you for your remarkable leadership in making that possible.

Of course, we have another anxiety there, that the 2 years of ARRA are coming to a close, and the momentum that was started is now somewhat in question.

Senator SPECTER. You testified about the advances generally, but specifically on stem cells with the $500 million expended, tell about the big results there.

Senator MURRAY. Mr. Chairman, before Dr. Collins answers that, a vote has been called and I want to go to the floor. So I just want to say really quickly——

Senator HARKIN. Yes.

Senator MURRAY [continuing]. That, Dr. Collins, your testimony is extremely compelling and understandable, and I really appreciate it. I think it clarified a lot for me.

I want to thank Senator Harkin for his leadership on this, but I especially want to thank Senator Specter too whose voice we will miss on this panel. And we will continue to carry your spirit forward on this critical issue. I just wanted to say thank you very much.

We do have a vote and I want to make sure we get to the rest of the panel.

ADVANCES IN EMBRYONIC STEM CELL RESEARCH

Senator SPECTER. Thank you, Senator Murray.

Well, just focus for a moment, if you would, on the $500 million already expended on embryonic stem cell research and what tremendous advances have been made there.

Dr. COLLINS. So that is a long list. It has given us the opportunity at the basic level to begin to understand what it is that takes this cell with all of this potential and triggers it to become a neuron or a muscle cell or a pancreatic beta cell that makes insulin. Those signals, those elaborate pathways of development, are now being sorted out by researchers working on that with very powerful technologies, some of them coming from the genome project.

And in terms of specific applications, you have heard of the application to spinal cord injury which is now in its Phase I clinical trial. That is the first one which has actually made it through that. That was a lot of Food and Drug Administration (FDA) review, believe me. But there are also applications which are looking very promising for eye diseases and for Type 1 diabetes where human embryonic stem cells have been differentiated into the cells needed in that circumstance and have then been used in an animal model

to show clear benefit and rigorous science, setting the stage then for human clinical trials in the not-too-distant future.

On top of all that, human embryonic stem cells are being used, as I mentioned, to do drug screening because if you are looking for a drug that might help somebody with a muscle disease, you would really like to test and see does that work in human muscle cells? Well, we now have the ability to make human muscle cells because you can take human embryonic stem cells and tweak them to do that and then test hundreds of thousands of compounds to see what is there that would stabilize a muscle cell, make it healthy or make it better able to survive. A huge opportunity in drug screening which is happening both in the private sector and in academia. All of those things add up to that roughly $500 million and some, but we think we are just scratching the surface of the potential here.

Senator SPECTER. Thank you, Dr. Collins. That is powerful.

Senator HARKIN. Thank you, Senator Specter.

Dr. Collins and others, we have a vote. There are two votes. So we have about 6 or 7 minutes left in this vote. So I will recess the panel. We will go vote on one, and then we will vote on the next one. So it will be probably 15 minutes before we get back here. So I would like to say if anybody needs to use the facilities or something, we will be back in 15 minutes.

What I would like to ask, Dr. Collins—I hate to impose on you, but there are a lot of things we need to cover. I would like to ask if you could stay during our second panel. I would appreciate that very much if you could. I am not going to put the guards at the door, but I would really like to have you stay.

While we are gone, I am going to ask the staff to go ahead and put the other nameplates of the second panel up there.

But I do have some follow-up questions for you, Dr. Collins, when we come back.

Dr. COLLINS. No guards needed. I am happy to stay.

Senator HARKIN. All right, thanks, Dr. Collins.

We will be right back.

EMBRYONIC STEM CELLS AS A RESEARCH TOOL

Senator HARKIN. The subcommittee will resume its sitting. I thank everyone for their indulgence.

Dr. Collins, just two other things I wanted to cover with you. One, in your testimony—and you mentioned it also in the slides—was the power of embryonic stem cells as a research tool. It sounds like even if these cells never actually end up being used as therapies in which they are transplanted into human beings, they could still teach us valuable information that could lead to treatments and cures. I just want to ask is that correct and just a slight elaboration on that.

Dr. COLLINS. That is correct, and in two ways.

One is that human embryonic stem cells, because they represent that most pluripotent, most undifferentiated cell type, but can be encouraged to go down various pathways to become muscle cells or brain cells or blood cells, they give us a window into how that development happens in humans in a way that we did not have before. And again, if you are able to understand what those signals

are, you can also infer what goes wrong if one of those signals misfires, and many birth defects and many genetic diseases are in that category.

The second way, which I also mentioned, is the ability to use these cells particularly if you turn them into neurons or muscle cells, or whatever it is that you need to study most to screen for new drug therapies. The way we got drugs in the past involved a variety of approaches, trying to identify a small molecule, an organic compound that would have the right properties to do something you want it to, but you have often had to try that in an animal model. These are human cells and they are human cells that you can convince to behave pretty much the way they would in a person except they are there in your dish, so you can do this without the risks of toxicity. A very powerful new way to find the next generation of drugs.

THE ETHICS OF HUMAN EMBRYONIC STEM CELL RESEARCH

Senator HARKIN. Very good.

Dr. Collins, on a kind of a more personal note, opponents of human embryonic stem cell research sometimes argue that it is immoral. They have raised it into a moral issue. Quite frankly, I have a number of friends, but I have one very close family friend who had a lot of trouble conceiving a child. She and her husband tried many different things. They finally went to a fertility clinic, and through in vitro fertilization, she was able to conceive and have a wonderful child. Actually twins who are very healthy. And so that is a real blessing that science was able to help them.

Now, I do not know this for a fact, but in many of these cases, a lot of the embryos are left over from a process of in vitro fertilization. And at some point, the donors are asked what they want to do with them. And obviously, they are not going to keep them in liquid nitrogen forever, and so they are discarded. Some time ago, my friend said to me, well, but I understand they could be used for embryonic stem cell research that might help someone who is suffering. And I said, well, yes, that is true. She said, well, I would much rather do that.

So it seems to me there is some morality there that we have not thought about, and as you know, under the guidelines that were issued only stem cells derived from leftover in vitro fertilization could be used with full consent of the donors and with no monetary consideration and could not be transplanted into a uterus. It had to only be used for stem cell derivation. So those are the ethical guidelines. Well, I just thought I would lay that out. A lot of people do not understand that.

But you are well known not only as one of the world's foremost scientists, but as a man of faith. I actually did read your book. I thought it was very good, The Language of God. I think it is just one of the wonderful crossover books between science and faith. It is just a wonderful book.

Can you talk about why you personally as a pre-eminent scientist are comfortable with this research? How do you reconcile your advocacy for embryonic stem cell research with your own faith and your own moral judgment?

Dr. COLLINS. Thank you, Senator. I think you have already articulated the issues extremely well.

I do believe that the human embryo deserves moral respect. It is a potential human being. This coming together of sperm and egg is the way we all got started, and that is not something to be taken lightly. But when you look at the circumstances that you have just outlined in terms of the consequences of in vitro fertilization efforts, benevolent as they are, giving couples a chance to have children who otherwise could not, one of those consequences is the existence of hundreds of thousands of frozen embryos that are being discarded potentially all the time.

And then faced with the ethical choice in that situation, I have come to the conclusion as a person of faith that the alternative of discarding this embryo that is clearly not going to get used versus, for a small number of these, trying to turn them into a stem cell line that might ultimately teach us something about human development in medicine and ultimately help us come up with a treatment for Parkinson's disease or diabetes or spinal cord injury or some eye disease or liver disease, which of those is the more ethical choice?

I think it is too easy to simply say, well, the embryo is an entity that is a potential human and therefore any consideration of using the word "research" in the same sentence is something we should be opposed to. We are not really being given that as an alternative. These embryos exist. They are going to continue to exist as long as in vitro fertilization goes forward, and it is. And certainly it has given many couples a chance for a new life in their families.

So putting the reality test here, I believe that most people who look carefully at the issues, whether from a faith perspective or a purely humanistic perspective, come up with a conclusion that what is potential here justifies what we are talking about in terms of Federal funding of human embryonic stem cell research.

Senator HARKIN. Well, thank you very much for that profound statement. Thank you very much, Dr. Collins. We have statements submitted from Senators Murray and Feinstein to be included in the record.

[The statements follow:]

PREPARED STATEMENT OF SENATOR PATTY MURRAY

Thank you, Senator Harkin, for holding this hearing. Stem cell research is not just about science—it's about hope. The hope of millions Americans who are suffering from diseases like Alzheimer's, Parkinson's, and diabetes. The hope of their friends, families, and loved ones who can't bear to see them in pain another day. And the hope of a scientific and medical community that is fighting against the clock to save lives and reduce suffering.

Stem cell research offers this hope because it is one of the most promising fields in medical research today. And we simply cannot afford to allow potential cures to be slowed down or halted by the political process.

That's why I was so glad when President Obama issued an Executive order in March of last year to lift the restrictions on funding for human embryonic stem cell research. This action took the handcuffs off of our scientists and made sure we were exploring every option for finding cures to debilitating diseases. Because as so many of us know, limiting Federal support of this research will continue to push embryonic stem cell research overseas. And our country will continue to fall behind in a critical, growing, and cutting-edge field.

Because of the arbitrary limits on stem cell research that were imposed in the past, we are already getting off to a slow start—and we can't afford to fall any far-

ther behind. Because in addition to helping patients—cutting-edge research also creates jobs and boosts the economy.

My home State of Washington is home to world-class research institutions like the University of Washington and the Fred Hutchinson Cancer Research Center, just to name a few. They want to help patients. They want to do this research to help cure debilitating diseases, but we need to make sure they have the resources they need to succeed. And that great institutions in Washington State and across the country continue leading the way in science, research, and medical cures.

Nothing sums this issue up better than a letter I received from a mom named Suzanne, from Seattle, whose 16-year-old son has diabetes.

She wrote to me and said:

"For our family, embryonic stem cell research offers the hope that by the time our son finishes graduate school, scientists will be developing new therapies or even a cure for his diabetes. Every year that researchers are denied full access to the best cellular material, and the funds with which to study it, is a year wasted, and a year denied to my son to live outside the burden of his disease . . . Please keep hope alive for Charlie, and millions of kids like him."

Once again, this is about hope.

I am going to keep fighting to make sure this hope stay alive for Suzanne and millions of others.

And I am going to keep working to make sure nothing stands in the way of our medical researchers and doctors developing cures and reducing suffering.

Thank you, again, Senator Harkin, for holding this hearing, and I look forward to continuing to work with you on this issue.

PREPARED STATEMENT OF SENATOR DIANNE FEINSTEIN

I want to thank Chairman Harkin for calling this hearing today.

Last month, the U.S. District Court for the District of Columbia issued an alarming decision that temporarily halted Federal funding of human embryonic stem cell research. That opinion has now been stayed pending appeal, but it should serve as a wake-up call to us all.

We must do everything we can to protect this funding, which is essential to life-saving research innovations.

Human embryonic stem cells have the potential to become any type of cell in the human body, meaning that the potential for treatment of disease is unlimited. This kind of research is vital to finding cures for Alzheimer's, Parkinson's disease, diabetes, spinal cord injuries, and numerous other illnesses.

National Institutes of Health (NIH) funding of these research projects holds out the possibility of a cure for millions of Americans. In the last year alone:

—1.5 million Americans were diagnosed with cancer;

—60,000 Americans were diagnosed with Parkinson's;

—12,000 Americans suffered spinal cord injuries; and

—1.6 million adults were diagnosed with diabetes.

Those are just the new diagnoses—think of all the other Americans who continue to suffer from cancer, heart disease, Alzheimer's, Parkinson's, spinal cord injuries, and other catastrophic diseases who could potentially be helped by embryonic stem cell research.

There is no question but that this research must be conducted within strict ethical guidelines, and these guidelines must, in my view, take into account the millions of people whose lives human embryonic stem cell research may dramatically improve or even save.

President Obama's 2009 Executive order on research involving human stem cells paved the way for responsible scientific research and removed critical barriers to potential breakthroughs from this research.

Under the Executive order, the strictest guidelines were put in place. Any embryo used must be left over following fertility treatment; it must be clear that the embryos would otherwise be discarded; individuals providing the embryos must provide written consent; and the donors may not be compensated for their donation.

The District Court's decision, and its unprecedented and highly restrictive interpretation of the Dickey-Wicker amendment, cast all of this aside and placed in peril hundreds of millions of dollars in research grants.

If the decision is not overturned:

—50 requests for new NIH research funding will not be considered;

—Roughly 12 requests that were likely to be approved will be frozen;

—22 grants totaling about $54 million that are due for renewal in September will be cut off; and

—Another 199 grants already awarded for about $131 million will be at risk next year.

The Justice Department continues to fight the decision, and I, along with Senators Harkin, Specter, Boxer, and others, are committed to working to pass legislation in the Senate that ensures that Federal funding can continue.

The United States has long been a leader in biomedical research and innovation. We have many of the best and brightest medical researchers in the world who are working to end suffering from all kinds of diseases. We should give them every tool we can to advance their work for the millions of American patients who are hoping and praying that they will find a cure.

I want to thank Chairman Harkin again for holding this hearing, and I look forward to working together to protect and promote this vital research.

Senator HARKIN. Now I will introduce our panel here, and then we will have our testimonies. Dr. George Daley, professor of Hematology and Oncology at Children's Hospital in Boston and the Dana Farber Cancer Institute, also professor of Biological Chemistry and Molecular Pharmacology at Harvard Medical School. Dr. Daley is past president of the International Society for Stem Cell Research and chaired the International Task Force that wrote ethical guidelines for human embryonic stem cell research. He received his Ph.D. in biology from MIT and his M.D. degree from Harvard Medical School.

Dr. Sean Morrison, Director of the University of Michigan Center for Stem Cell Biology, where he is also a professor of Medicine and a professor in the Life Sciences Institute. Dr. Morrison is also a director of the International Society for Stem Cell Research. He received his Ph.D. in immunology from Stanford University.

Jean Peduzzi Nelson is an associate professor at the Department of Anatomy and Cell Biology at Wayne State University School of Medicine. Dr. Peduzzi Nelson received her B.S. from the University of Michigan and her Ph.D. from Wayne State University.

Ms. Cody Unser is the founder of the Cody Unser First Step Foundation, an organization dedicated to raising research funds and public awareness for people afflicted with spinal cord-related paralysis. Ms. Unser graduated in May from the University of the Redlands with a degree in biopolitics. She is now a graduate student at the George Washington University School of Public Health studying health policy.

I thank you all for being here today, and I thank you for your indulgence because of our votes. I will make sure that all of your statements are made a part of he record in their entirety. And starting with you, Dr. Daley, working down, if you could sum up in 5 minutes or so—I will not hold you to an exact time, but we will start with 5 minutes and try to get it there so we can open it up for some discussion and questions. But again, Dr. Daley, no stranger to this subcommittee, welcome back.

STATEMENT OF GEORGE Q. DALEY, M.D., Ph.D., DIRECTOR, STEM CELL TRANSPLANTATION; ASSOCIATE DIRECTOR, STEM CELL PROGRAM, CHILDREN'S HOSPITAL BOSTON, BOSTON, MASSACHUSETTS

Dr. DALEY. Thank you very much. Chairman Harkin, thank you for the invitation to testify.

I am here to assert that human embryonic stem cells offer unique advantages for understanding human diseases and are essential to a vigorous national portfolio of stem cell research.

However, recent upheavals in the Federal funding are disrupting our research. They are dissuading scientists from entering the field and they are threatening American pre-eminence in the research.

As director of the Stem Cell Transplant Program at Children's, I wish to first speak to the success we have in using adult stem cells. And we are using adult stem cells to cure kids with a variety of life-threatening diseases. We perform some 80 stem cell transplants per year for childhood leukemia, genetic diseases, and indeed, we have cured many kids. I was on rounds last week. I met an adorable little girl. She was about to receive her transplant for a very rare genetic immune disorder, and I found out she was the second in her family that we could very confidently say we would cure. So it is very, very heartening to save the life of a child.

But I am also here to advocate as a scientist, and as a scientist I am sobered by the statistic that fewer than half of all patients treated with stem cells are cured, and despite 50 years of research in adult hematopoietic stem cell transplants and practice—this is our most successful form of transplant—blood cancers still relapse and patients still die. So as a scientist, I am working to improve these treatments through research on adult stem cells, embryonic stem cells, and iPS cells.

I think it is a flawed argument to say that scientists should restrict their focus to adult stem cells, and I think it is a mistake to cast the different types of stem cells as competing priorities. Adult stem cells are not better than or more promising than embryonic stem cells. Embryonic stem cells are different, and to many scientists, they offer more hope in certain diseases like diabetes. Would it make sense as a Federal policy to fund cancer and cardiovascular research but not diabetes research? All of these are essential research avenues, and the most successful strategy to advancing cures is to let scientists decide which cells to study.

Now, I have been a student of the hematopoietic stem cell, the adult stem cell, for 25 years, but starting about 15 years ago, I began envisioning a new approach to the research to generating blood stem cells from embryonic stem cells. And the idea was that we could generate customized blood stem cells in a way that would solve the immune rejection problems, solve the donor shortages, and allow us to perform gene repair, together with bone marrow transplantation.

Now, we have succeeded in mice, and we have a lot of promise in humans. In 2007, I was one of three laboratories to produce iPS cells, and in 2008, my lab produced the first large repository of human disease-specific iPS cells.

So why, given that I have pioneered the development of both adult stem cells and iPS cells, do I continue to advocate for human embryonic stem cells?

Well, there are several reasons, and the first is that iPS cells and many other future areas of research are founded on the knowledge we have gained from human embryonic stem cells.

Second, my own research and that of others is pointing to important differences between iPS and embryonic stem cells.

And third, some diseases are simply more effectively modeled with human embryonic stem cells than iPS cells. We recently showed that you could model human Fanconi anemia, a disease that predisposes kids to leukemia, as well as Fragile X syndrome, which is the most common genetic cause of autism and mental retardation, and these were better modeled with human embryonic stem cells.

So when we have so much to learn from embryonic stem cells, how can we conclude that we do not need to fund the research? We are told that restrictions on Federal funding will not inhibit stem cell research and that private philanthropy will fill the gap, but realistically research careers are founded on the architecture of Federal support. Investment by the NIH has made U.S. research preeminent. It has given us domination in the Nobel Prizes, and it has been an engine for our very vigorous biotechnology industry.

Now, opponents of embryonic stem cell research will argue that adult stem cells are more promising, that embryonic stem cells have yet to cure anyone. Well, this is like arguing why try to develop new classes of antibiotics when we have got penicillins and cephalosporins. Let us continue to work to improve those.

It is very curious. The only time I confront the argument that adult stem cells are superior and that embryonic stem cells should be replaced is at hearings like this. At scientific meetings, we discuss and debate adult and embryonic and iPS cells as all complementary aspects of cell and developmental biology.

In my opinion, the arguments that adult stem cells obviate the need for embryonic stem cells are not scientifically driven. They are ideologically driven arguments to suppress embryonic stem cell research. And no matter how much progress is made with other forms of stem cells, embryonic stem cells will remain a vital research tool. embryonic stem cells are not contestants on Survivor that should be voted off the island. Expelling embryonic stem cells from the researchers' toolkit will gravely weaken the search for cures.

Now, President Obama's policy has expanded access to more embryonic stem cell lines, and the court challenge has really come on us as a major blow. We have had immediate disruptions, but the long-term uncertainty is even more insidious. And I have several trainees who have toiled to make their projects on human embryonic stem cells work, and the uncertainty has really compelled some of them to abandon those plans. So these decisions which are driven by politics and not science are deeply disturbing.

PREPARED STATEMENT

So let me finish by saying that although the injunction has been stayed, with the latest upheavals, we are again reminded that human embryonic stem cell research is on fragile and fickle footing and that new legislation is needed to sustain the momentum of embryonic stem cell research and to allow scientists and not politicians and not judges to determine which research priorities to pursue.

Thank you.

Senator HARKIN. Dr. Daley, once again thank you for a very profound statement and for all the work that you have been doing in this area.

[The statement follows:]

PREPARED STATEMENT OF GEORGE Q. DALEY

Chairman Harkin and distinguished members of the subcommittee, thank you for the invitation to testify today on the subject of human embryonic stem (embryonic stem) cells. I am here to assert that human embryonic stem cells offer unique advantages for understanding a number of human diseases and are essential to a vigorous portfolio of stem cell research here in the United States. I also wish to recount how recent upheavals in Federal funding have disrupted our research and how ambiguous Federal policy saps the motivation of junior scientists and threatens American pre-eminence in this vital field of biomedical research.

My name is George Daley and I am the Samuel E. Lux IV Professor of Hematology/Oncology and Director of the Stem Cell Transplantation Program at the Children's Hospital Boston and the Dana Farber Cancer Institute. I am also Professor of Biological Chemistry and Molecular Pharmacology at Harvard Medical School, Principal Faculty and founding member of the Executive Committee of the Harvard Stem Cell Institute, and an investigator of the Howard Hughes Medical Institute. I am past president of the International Society for Stem Cell Research (ISSCR; 2007–2008), the major international organization of stem cell scientists with more than 3,000 members worldwide. I chaired the international task force that wrote ethical guidelines for human embryonic stem cell research (ISSCR Guidelines for Human Embryonic Stem Cell Research 2006)[1] and as ISSCR President empanelled and participated in the international task force that wrote guidelines for the responsible clinical translation of stem cell therapies (ISSCR Guidelines for the Clinical Translation of Stem Cells 2008.).[2] I am here representing the American Society for Cell Biology, whose members number some 10,000 scientists.

As Director of the Stem Cell Transplantation Program at Children's Hospital I speak as a doctor who uses adult stem cells to treat patients with life-threatening blood diseases—including leukemia, sickle cell anemia, immune-deficiency, bone marrow failure, and others—but I also speak as a scientist working to improve those treatments through research on adult stem cells, embryonic stem (embryonic stem) cells, and induced pluripotent stem (iPS) cells. Stem cell research is important to real live patients, and I believe to my core that stem cell research offers tremendous promise for curing a range of diseases. It is a mistake to cast the different types of stem cells as competing priorities. Adult stem cells are not better than or more promising than embryonic stem cells. And iPS cells do not obviate the need for embryonic stem cells. Would it make sense to fund cancer and cardiovascular research but not diabetes research? All are essential research avenues. The most successful strategy to advance stem cell research is to let scientists decide which cells to study.

Let me first speak to the success and the limitations of adult stem cell therapies. Hematopoietic stem cells harvested from bone marrow, mobilized peripheral blood, and umbilical cord blood are the most successful adult stem cell treatments, and potentially curative for cancers of the blood and some genetic diseases. At Children's we perform some 80 stem cell transplants per year for childhood leukemia and conditions like immune deficiency. Casting our success in a positive light, we have cured many kids over the years. On transplant rounds last week, I was heartened to meet a little girl about to receive her transplant for a rare inherited immune condition, the second in her family that we will likely cure. Saving the life of a child is deeply gratifying. However, confronting our shortcomings, we must acknowledge that fewer than half of all patients treated with hematopoietic stem cell transplants are cured. Despite 50 years of research and practice in hematopoietic stem cell transplantation, blood cancers still relapse, and patients still die or become severely disabled because the transplant regimens are so toxic. Many patients who might benefit never make it to the transplant stage because they are too sick or lack a suitable donor.

Such limitations of even our most successful adult stem cell therapies for blood diseases drive me, as a medical research scientist, to seek improvements through stem cell research. I have been a student of the hematopoietic stem cell for 25 years,

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[1] Daley, G.Q., et al., Ethics. *The ISSCR guidelines for human embryonic stem cell research*. Science, 2007. 315(5812): p. 603–4.

[2] Hyun, I., et al., *New ISSCR guidelines underscore major principles for responsible translational stem cell research*. Cell Stem Cell, 2008. 3(6): p. 607–9.

and I remain an ardent advocate for research on adult stem cells. But starting more than fifteen years ago, I began to explore a new approach to bone marrow transplant based on making blood stem cells from embryonic stem cells. I envisioned one day generating customized stem cells perfectly matched to my patients, thus bypassing the challenge of immune matching, eliminating the problems of donor shortages, and making transplants safer because they would be performed with a patient's own cells. Moreover, for patients with genetic diseases, this new approach offered potentially safer ways to repair gene defects and to return healthy cells to the patient. Indeed, we have succeeded in treating mice with genetic immune deficiency with this strategy, and we are making headway towards the goal of developing similar treatments with human cells.

Opponents of embryonic stem cell research will argue that adult stem cells are more promising, that embryonic stem cells have yet to cure anyone, and that with iPS cells in hand, embryonic stem cells are no longer needed. By similar reasoning, why try to develop new classes of antibiotics? Let's just keep trying to improve penicillin. The only time I confront the argument that adult stem cells are superior to embryonic stem cells and should replace embryonic stem cells is at hearings like this. At scientific meetings, discoveries with adult and embryonic stem cells are discussed and debated as integrated and complementary aspects of cell and developmental biology, not as contestants on American Idol. In my opinion, such arguments are not sound scientific advice, but rather ideologically driven attempts to prohibit scientists from using embryonic stem cells to search for new cures. No matter how much progress is made with other forms of stem cells, embryonic stem cells will remain a vital research tool, and any expulsion of embryonic stem cells from the researcher's toolkit would gravely weaken stem cell research overall.

Embryonic stem cells are valuable because they are pluripotent, that is, able to make any tissue in the human body, and can grow indefinitely in a petri dish. In contrast, adult stem cells show a restricted potential for generating cells of a given tissue, and are difficult to propagate in a petri dish and thus available in limited quantities. Not all tissues regenerate from adult stem cells, which is a major reason why we need embryonic stem cells. Indeed, in juvenile diabetes, there is little or no regeneration of the insulin-producing beta cells that have been destroyed by immune attack. We are technically capable of transplanting a whole pancreas or isolated pancreatic islets to replace beta cells, but there is a shortage of these organs for transplanting even the most severe diabetics. Consequently, embryonic stem cells are being developed by the biotechnology company Novocell as an alternate and more readily available source of beta cells for treatment of diabetes.

Only 3 years ago, a new form of pluripotent stem cell was introduced into stem cell research, the induced pluripotent stem cell, popularly called the iPS cell. At the end of 2007, my lab was one of three worldwide to report the successful derivation of human iPS cells,[3] and in 2008, my lab was the first to produce a repository of customized iPS cells from patients with a range of diseases like Parkinsons, diabetes, and immune deficiency.[4] iPS cells share the defining features of embryonic stem cells-pluripotency and limitless growth, and one goal of stem cell research is to refine techniques for making iPS cells that are indistinguishable from embryonic stem cells. Thus, given that iPS cells exist, why is there a need for human embryonic stem cells, and what is the value of continued development of new human embryonic stem cell lines?

First, it is important to note that the iPS breakthrough was founded upon the study of embryonic stem cells, and isolation of human iPS cells depended upon specific culture conditions for human, not mouse, embryonic stem cells. Today, human embryonic stem cells remain the gold standard against which our cultures of human iPS cells are compared. Human embryonic stem cells hold many more secrets, and no one can be sure where the next breakthrough will emerge.

Second, it is not clear that even ideal iPS cell lines are identical in all respects to embryonic stem cells. My lab and that of Konrad Hochedlinger recently demonstrated that iPS cells tend to retain chemical modifications of their DNA reminiscent of their tissue of origin, so that when the iPS cells are differentiated in the petri dish, they reflect a preference to form the tissues from which they were derived.[5–6] This so-called "epigenetic memory" dictates that iPS cells made from blood

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[3] Park, I.H., et al., *Reprogramming of human somatic cells to pluripotency with defined factors*. Nature, 2008. 451(7175): p. 141–6; online Dec. 23, 2007.

[4] Park, I.H., et al., *Disease-specific induced pluripotent stem cells*. Cell, 2008. 134(5): p. 877–86.

[5] Kim, K., et al., *Epigenetic memory in induced pluripotent stem cells*. Nature, 2010 online July 19.

cells make better blood than iPS cells made from skin cells. We are working towards ways to erase these memories, but these data teach us that in practice, iPS cells harbor important differences from embryonic stem cells that influence their behavior and potential utility in research and therapy.

Third, although iPS cells provide a flexible alternative to embryonic stem cells in modeling human diseases, not all diseases are readily modeled with iPS cells. One of the first diseases we attempted to model with human iPS cells was a fascinating but rare condition called Fanconi anemia that leaves kids with bone marrow failure and a predisposition to leukemia and various cancers. Despite repeated attempts, we have been unable to generate iPS cells from patients with Fanconi anemia, and last year the laboratory of Juan-Carlos Izpisua-Belmonte published that Fanconi anemia cells were resistant to iPS generation.[7] Mice that lack the same genes as human Fanconi patients do not develop the same marrow failure and leukemia of human patients. Thus, we turned instead to modeling Fanconi anemia by depleting the relevant genes from human embryonic stem cells, and then examining the effects on human blood formation in the petri dish. Using genetically modified human embryonic stem cells, we discovered that Fanconi anemia alters the earliest stages of human embryonic blood development, teaching us that the condition develops in utero, such that children are born with stem cell deficiency, a new insight for a condition thought to develop only later in childhood.[8]

Another example where human embryonic stem cells offer an advantage over iPS cells is in the study of Fragile X syndrome, the most common genetic cause of mental retardation. Fragile X is caused by a defect in the FMR1 gene, which is expressed early in human development, but in affected individuals becomes aberrantly silent in adult tissues, including nerve cells. My Israeli colleague, Nissim Benvenisty, had generated human embryonic stem cells from discarded embryos that carried the gene defect. When these embryonic stem cells were differentiated in the petri dish, the gene shut off, just as it does during human development. In collaboration with the Benvenisty lab, we asked what would happen to the FMR1 gene in iPS cells made from skin cells of Fragile X individuals. To our surprise, the gene remained silent in iPS cells, showing that Fragile X-iPS cells differed from Fragile X embryonic stem cells, with only the embryonic stem cells reflecting the dynamic FMR1 gene silencing observed in human development.[9] For studying gene silencing in Fragile X, human embryonic stem cells provide a unique advantage.

Finally, human embryonic stem cells remain valuable tools for research. There is still much to be learned about human embryonic stem cells, and about how stem cells derive from human embryos. Only recently have we learned that human embryonic stem cells are markedly different from mouse embryonic stem cells, and represent a distinct type of pluripotent stem cell. Only recently have we learned that deriving human embryonic stem cells in reduced oxygen conditions preserves two active X chromosomes, which is the natural embryonic state, leaving us to question whether any of the existing human embryonic stem cells have been derived in an optimal way.[10] When we still have so much to learn, how can we conclude that embryonic stem cells are no longer needed?

We are told that restrictions on Federal funding do not inhibit stem cell research because private philanthropy fills the gap. Realistically, however, research careers are built upon the architecture of Federal grant support. Investment by the NIH has made the United States the pre-eminent incubator for biomedical research, has produced American dominance in Nobel prizes in medicine, and has contributed directly to our robust biotechnology industry. Medical research is one of the chief sectors projecting job growth over the next decade, and one of the few areas of technological innovation where U.S. leadership remains largely uncontested. A loss of Federal funding threatens American competitiveness in stem cell research.

Unfortunately, during the last decade prohibitions and restrictions on Federal funding for human embryonic stem cell research has greatly restricted progress and dissuaded numerous scientists from entering the field. President Bush allowed funding for a very restricted set of cells—in practice only a small handful—but prohibited funding for the more than 1,000 human embryonic stem cell lines generated

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[6] Polo, J.M., et al., *Cell type of origin influences the molecular and functional properties of mouse induced pluripotent stem cells*. Nat Biotechnol, 2010. 28(8): p. 848–55.

[7] Raya, A., et al., *Disease-corrected haematopoietic progenitors from Fanconi anaemia induced pluripotent stem cells*. Nature, 2009. 460(7251): p. 53–9.

[8] Tulpule, A., et al., *Knockdown of Fanconi anemia genes in human embryonic stem cells reveals early developmental defects in the hematopoietic lineage*. Blood, 2010. 115(17): p. 3453–62.

[9] Urbach, A., et al., *Differential modeling of fragile X syndrome by human embryonic stem cells and induced pluripotent stem cells*. Cell Stem Cell, 2010. 6(5): p. 407–11.

[10] Lengner, C.J., et al., *Derivation of pre-X inactivation human embryonic stem cells under physiological oxygen concentrations*. Cell, 2010. 141(5): p. 872–83.

since his policy was enacted on August 9, 2001. Many of these embryonic stem cell lines have important advantages for medical research, like carrying the precise gene defects responsible for human disease. President Obama's policy has expanded access to many more lines and has succeeded in bringing many dozens of additional laboratories into the field, as evidenced by the new grants submitted or approved for research in the last year.

Against this backdrop of rising enthusiasm after nearly a decade of frustration for patients, their families, their physicians, and the research community, the announcement of the injunction against Federal funding came as a major blow. I was justifiably confused by what the injunction meant for our research program, which depends heavily on Federal grant dollars, and personally, I was deeply discouraged and worried for the future of human embryonic stem cell research.

Several cases illustrate the immediate harm to our research program and the potential harm to the careers of young scientists by the current confusion. A doctoral student in my lab has just completed nearly a year of work mastering a protocol for generating red blood cells from human embryonic stem and iPS cells, a critical step in her research on sickle cell anemia. Because of variability among the iPS lines, human embryonic stem cells are essential for her studies, and she has just started to have success with the H1 line of human embryonic stem cells. However, because she is being paid by Federal dollars and the future prospects are so uncertain, she has abandoned the use of human embryonic stem cells, and is instead restricting her efforts to iPS cells that may give sub-optimal red blood cell production. Such a compromise—driven by politics and not science—is deeply troubling. Several other scientists in my lab have altered their projects out of concern for a loss in Federal funding. Two scientists being funded on Federal training grants abandoned plans to test human embryonic stem cells for their response to a unique cocktail of growth factors that had stimulated blood stem cell formation from mouse embryonic stem cells. Moreover, I face losing my largest NIH grant, which is aimed at defining the precise similarities and differences between embryonic stem and iPS cells. I have been scrambling to come up with private funding so that I don't have to lay anyone off. I wrote to my seven co-investigators on this project and warned them not to expect funding for the second year, which would stop cold major new research collaborations that have already proven remarkably productive. Scientific research is challenging enough without adding the uncertainty and fickle nature of Federal support for one's research to the task.

With the recent upheavals, scientists have again been reminded that human embryonic stem cell research is on fragile and fickle footing. The cloud that hangs over the field saps enthusiasm for planning a long-term program of NIH grant-funded human embryonic stem cell research, which is the bedrock of most research careers. Younger researchers are discouraged from entering the field, while established researchers like myself are spending a disproportionate amount of time on regulatory compliance, legal interpretation, program management, and external fundraising. With the economy in turmoil, private funding for stem cell research has become scarce. Ambiguity about Federal policy itself has a negative impact that extends beyond the practical restrictions of legislation. Having devoted the last 25 years of my career to aspects of adult and embryonic stem cell biology, I am convinced that human embryonic stem cells are critical to a multi-faceted portfolio of NIH stem cell research, and in the long run will save lives. New legislation is needed to sustain the momentum of human embryonic stem cell research in the United States, and to allow scientists—not politicians and judges—to determine which research priorities to pursue.

Senator HARKIN. Now we turn to Dr. Morrison. Dr. Morrison, welcome. Proceed.

STATEMENT OF SEAN J. MORRISON, Ph.D., DIRECTOR, CENTER FOR STEM CELL BIOLOGY, UNIVERSITY OF MICHIGAN, LIFE SCIENCE INSTITUTE, ANN ARBOR, MICHIGAN

Dr. MORRISON. Thank you, Senator Harkin, for the opportunity to testify today.

I have spent my entire career doing stem cell research, almost exclusively adult stem cell research. The research in my lab has won a number of awards, including a Presidential Early Career Award from President Bush in 2003.

Nonetheless, like nearly all leading stem cell researchers, I believe the Federal Government must support all forms of stem cell research, including human embryonic stem cells. We simply do not yet know what kinds of stem cells will yield the breakthroughs of the future and must pursue all forms of stem cell research to develop new therapies sooner rather than later.

Stem cell scientists do not cluster into adult versus embryonic camps. This framing of the debate comes from political lobbyists. I interact regularly with hundreds of the leading stem cell scientists throughout the world, and virtually all of them believe that research must continue with all types of stem cells for the reasons George just articulated.

Stem cell research is a remarkably fast-moving field that has taken a series of unexpected twists and turns over the past several years. There is no point in the last 10 years where we could have predicted even 2 years down the road where the field would be. Yet, at every point there have been people who believe they could predict the future and who could tell us which avenues of research should be abandoned. But until the research is done, we do not know what the answers will be.

Think about the arguments that opponents have made as alternatives to embryonic stem cell research.

First, they suggested that umbilical cord blood cells could replace embryonic stem cells. Yet, my lab has studied cord blood, and I can tell you that there was never any scientifically plausible basis for the argument that cord blood cells could do what embryonic stem cells can do. And you no longer hear much about cord blood as an alternative.

Instead, they subsequently suggested that amniotic cells could replace embryonic stem cells, but those cells are biologically different from embryonic stem cells and, again, were never a plausible alternative. And again, you never hear about those cells anymore.

Then opponents circulated lists of more than 70 diseases they claim could be cured with adult stem cells. What they do not tell you is that only diseases of the blood-forming system are routinely treated with adult stem cells and that many of the other "treatments," in quotation marks, they cite are highly speculative, are often not based on sound science, and are prohibited from being sold to patients in this country by our FDA.

The reality is that many types of stem cells are likely to yield scientific advances and potentially new therapies. And it would be foolish to place all of our bets on certain stem cells at such an early stage in the development of this field.

For this reason, the International Society for Stem Cell Research has repeatedly recommended that all forms of stem cell research must be pursued and that patients should be cautious about claims regarding unproven adult stem cell therapies that are offered overseas. Where would we be right now if you had taken the advice of opponents of embryonic stem cell research and directed the NIH to focus their funding on umbilical cord blood cells or on amniotic cells? Promising research would have been abandoned in favor of the alternative du jour, sacrificing scientific progress and the opportunity to develop new therapies.

The award my lab received from President Bush was for our work studying stem cells that give rise to the peripheral nervous system. One of the things we discovered is that a birth defect called Hirschsprung disease is caused by defects in the function of these neural stem cells during fetal development. In kids with Hirschsprung disease, the neural stem cells fail to migrate into part of the intestine, rendering that segment of the intestine nonfunctional. Our work suggested that we might be able to bypass that defect by transplanting neural stem cells into the nonfunctional portion of the gut. The problem is that neural stem cells with the right properties only exist during fetal development. So we decided to generate those cells by deriving them from human embryonic stem cells.

Now, I want to emphasize this point because for the therapy we want to use a tissue-specific stem cell, a cell that in the newspaper is generally referred to as an adult stem cell. And yet, we have to obtain it from embryonic stem cells. So this illustrates why it is scientifically meaningless to frame this debate as a choice between adult and embryonic stem cells because we sometimes need embryonic stem cells to derive the adult cells that we want to use in the therapy.

So this research in my lab is funded by the NIH, but it has suffered from repeated delays. First, the grant was delayed while NIH put in place its new embryonic stem cell policy. Then we received the grant but we were unable to spend the money until NIH had the opportunity to review and approve new stem cell lines for funding. And finally, we were able to start the research, but just 8 months later, the Federal injunction was issued.

In the first few days after the injunction, I told my lab that if our funding were cut off, we would abandon our work on Hirschsprung disease. I have with me today Jack Mosher from my laboratory. Jack, you might want to stand up for a second. Jack is the guy in my lab who does this work. The project I have been telling you about is Jack's work, and his salary comes exclusively from this grant. Jack has dedicated the last 9 years of his life to studying peripheral nervous system development, culminating in this project, attempting to translate the basic science that we have done to the benefit of patients. Yet, in those early days after the injunction, Jack did not know whether his work would survive the injunction, whether he would still have a salary, or what would happen to his career.

PREPARED STATEMENT

So I would just sum up by saying that American science is the envy of the world because it is a meritocracy in which there is fierce competition to fund the best ideas. If we accept the principle that those who are not judged to have the best ideas can obtain judicial relief that blocks funding of the best ideas to allow the lesser ideas to compete, this will erode the very heart of American competitiveness. We owe more to the patients suffering from incurable diseases. We owe it to them to support all forms of stem cell research so that no matter where the science leads and where the cures come from, we can follow the most promising avenues of discovery.

So I would urge you to clarify the Dickey-Wicker amendment so there can be no question regarding Congress' intent to fund the most meritorious science.

Senator HARKIN. Thank you very much, Dr. Morrison.

[The statement follows:]

PREPARED STATEMENT OF SEAN J. MORRISON

My name is Sean Morrison and I'd like to begin by thanking Senator Harkin and the members of the subcommittee for inviting me to testify. By way of introduction, I am the Director of the University of Michigan Center for Stem Cell Biology, where I am also the Henry Sewall Professor of Medicine, a Professor in the Life Sciences Institute, and a Professor of Cell and Developmental Biology. I am also an Investigator of the Howard Hughes Medical Institute, a Director of the International Society for Stem Cell Research, and a member of the American Society for Cell Biology Public Policy Committee.

I have spent my entire career doing stem cell research, almost exclusively adult stem cell research. The adult stem cell research in my laboratory has won many awards, including a Presidential Early Career Award from President Bush in 2003. Nonetheless, I'm here today to tell you that like nearly all leading stem cell researchers, I believe that the Federal Government must support all forms of stem cell research, including human embryonic stem cell research. We simply do not yet know what kinds of stem cells will yield the scientific breakthroughs of the future or what kinds of stem cells will yield new treatments for disease. Therefore, we must pursue all forms of stem cell research in order to have the greatest chance of developing new therapies sooner rather than later.

Stem cell scientists do not cluster into "adult" versus "embryonic" camps—this framing of the debate comes from political lobbyists. I interact regularly with hundreds of leading stem cell scientists from all over the world and virtually all of them believe that research should continue with all types of stem cells.

Stem cell research is a remarkably fast-moving field that has taken a series of unexpected twists and turns over the past several years. There is no point over the past 10 years during which we could have predicted where the field would be, even two years down the road. Yet, at every point there have been people who believed that they could predict the future and could tell us which avenues of research should be abandoned. But until the research is done, we don't know what the answers will be.

Think about the alternatives that have been offered by opponents of embryonic stem cell research.

—First, they suggested that umbilical cord blood could replace embryonic stem cells. Yet as somebody whose laboratory has studied umbilical cord blood I can tell you that there was never any scientifically plausible basis for suggesting that cord blood cells could replace embryonic stem cells. The opponents of embryonic stem cell research never talk about cord blood anymore.

—Instead, they subsequently suggested that amniotic cells identified by Dr. Anthony Atala could replace embryonic stem cells. But those cells are biologically different from embryonic stem cells and were never a plausible alternative. Even Dr. Atala has gone on record stating they are not an alternative to embryonic stem cells. Again, you never hear about those cells anymore.

—Then, opponents of embryonic stem cell research circulated lists of more than 70 diseases they claimed could be cured with adult stem cells. What they don't tell you is that only diseases of the blood-forming system are routinely treated with adult stem cells, and that many of the other "treatments" they cite are highly speculative and often not based upon sound science.

—Most recently, opponents of embryonic stem cell research have suggested that reprogrammed adult cells, so-called iPS cells, should be studied instead of embryonic stem cells. While these reprogrammed cells are very promising, George Daley and others have recently shown that their properties are somewhat different from embryonic stem cells.

The reality is that all of these types of stem cells are likely to yield scientific advances, and potentially new therapies, but it would be foolish to place all of our bets on a single type of stem cell at such an early stage in the development of this field. For this reason the International Society for Stem Cell Research, a society representing thousands of stem cell scientists all over the world, has repeatedly recommended that all forms of stem cell research must be pursued, including adult and embryonic stem cells, and that patients should be cautious about claims regarding unproven adult stem cell therapies.

Where would we be right now if you had taken the advice of opponents of embryonic stem cell research and directed the National Institutes of Health (NIH) to focus their funding on umbilical cord blood cells or amniotic cells? Promising research would have been abandoned in favor of the alternative du jour, sacrificing scientific progress and the opportunity to develop new therapies. We remain unable to predict the future. So blocking Federal funding for embryonic stem cell research at this juncture will certainly block scientific progress and will likely delay the search for new therapies.

The Presidential Early Career Award that my lab received was for our work studying the stem cells that give rise to the peripheral nervous system. One of the things we discovered is that a birth defect called Hirschsprung disease is caused by defects in the function of these peripheral nervous system stem cells during fetal development. Hirschsprung disease affects 1 in 5,000 newborns and is caused by a defect in the development of the portion of the peripheral nervous system that regulates intestinal function. In kids that have Hirschsprung disease, the neural stem cells fail to migrate into the large intestine, rendering that segment of intestine nonfunctional because of the lack of nervous system in that segment. Surgery to remove the nonfunctional segment of intestine can save these kids' lives, but for many of these kids, their guts never quite work right, leading to life-long problems.

We figured that if Hirschsprung disease is caused by a failure of stem cells to migrate into the large intestine, that we might be able to by-pass this migratory defect by transplanting stem cells into the nonfunctional portion of gut, and that this cell therapy might improve the treatment of kids with Hirschsprung disease. The problem is that neural stem cells with the right properties to correctly innervate the intestines only exist during fetal development. So where would we get the neural stem cells for therapy? We don't want to use aborted human fetal tissue. George Daley's recent results have raised the concern that if reprogrammed adult cells are not generated from peripheral nervous system stem cells that they might have difficulty making the correct types of neural cells to regulate intestinal function. Thus, the most prudent way of generating peripheral nervous system stem cells is by deriving them from human embryonic stem cells.

I want to emphasize this point—we wish to use tissue-specific stem cells (often described as "adult" stem cells in the newspaper) for the therapy, but we will obtain them from embryonic stem cells. This illustrates why it is scientifically meaningless to frame this debate as a choice between adult and embryonic stem cells. We sometimes need embryonic stem cells to generate adult cell types for therapy.

We are funded by the National Institutes of Health (NIH) to try to develop a cell therapy for Hirschsprung disease, using human embryonic stem cells to derive neural stem cells for transplantation. But our research has suffered from repeated delays. First, the awarding of this grant was delayed while NIH put in place its new embryonic stem cell research policy, after the repeal of the Bush administration policy. After the new NIH policy was established, we received the grant, but were unable to spend any of the money until NIH had the opportunity to review and approve embryonic stem cell lines for funding. Finally, lines were approved and we were able to start the research, then just 8 months later the injunction was issued.

In the first few days after the injunction was issued none of us knew exactly what research would be blocked, or how the ruling would be interpreted by NIH. During this period, I told my lab that if our funding were cut off as a result of the injunction, and if the injunction could not soon be lifted, that we would abandon our work on Hirschsprung disease. I have with me today Jack Mosher from my laboratory. The project I have been telling you about is Jack's work, and his salary comes almost exclusively from this grant.

Jack completed his undergraduate work at Allegheny College in Pennsylvania, then a Ph.D at the University of North Carolina. He came to my lab in 2001 as a postdoctoral fellow and was ultimately promoted into a faculty position at the University of Michigan. He has dedicated the last 9 years of his life to studying peripheral nervous system development, culminating in this project, trying to translate our results to help patients. Yet in those early days after the injunction he did not know whether his work would survive the injunction, whether he would still have a salary, or what would happen to his career. Since the injunction, many students, postdoctoral fellows, and junior faculty have had similar conversations in scores of laboratories across the country.

It turns out that because of the timing of our annual review, we received our second year of funding just before the injunction. As a result, our funding was not interrupted. But this is not the way in which funding decisions for medical research should be determined. American science is the envy of the world because it is a meritocracy in which there is fierce competition to fund the best ideas. As a con-

sequence, American scientists lead the world in virtually every measure of scientific impact and America is the world's engine of scientific discovery.

If we accept the idea that those who do not have the best ideas can obtain judicial relief that blocks NIH funding for the best ideas, to help the lesser ideas compete, this will erode the very heart of American competitiveness.

We don't know yet whether the cell therapy we are attempting to develop will work, or whether it will ultimately be performed with embryonic stem cells, reprogrammed adult cells, or other cells. That's why they call it research. The point is that we're never going to find out until we do the research. Yet instead of devoting ourselves to trying to make a difference for kids with Hirschsprung disease, Jack and I now find ourselves talking about the uncertain future of embryonic stem cell research, whether legislative and judicial delays will continue on-and-off indefinitely, and whether his career would be better served by working in a different area.

I'd like to leave you with one last story. Opponents of embryonic stem cell research frequently repeat the argument that this research is less promising than adult stem cell research because adult stem cells are already used to treat patients whereas embryonic stem cells are not. The problem is that adult stem cells have been studied for decades while we have only had human embryonic stem cells since 1998, 12 years. So let's examine this argument for a moment.

The adult stem cell therapy that is routinely used clinically is blood-forming stem cell transplantation (formerly known as bone marrow transplantation) to restore the blood forming systems of patients after cancer therapy or to treat various diseases of the blood-forming system. This is indeed a great success: while it's not perfect it does save thousands of lives each year. What did it take to get to this point?

After many years of research, the first bone marrow transplant among unrelated patients was attempted in 1955 by Donnall Thomas. All of the patients died. Dr. Thomas went back to the laboratory to figure out why he couldn't just randomly transplant bone marrow cells from one patient into another. He discovered that donor and recipient had to be matched, so that their immune systems didn't attack each other. The first successful bone marrow transplant between an unrelated donor and recipient was performed in 1969—14 years later. Thus if we were to take the advice of opponents of embryonic stem cell research, and abandon lines of research that do not lead to cures within 12 years, none of the adult stem cell therapies that they exalt would exist today and Donnall Thomas would never have won the Nobel prize.

Science takes time, and the path to cures is uncertain and fraught with setbacks. American science is the envy of the world because it has fostered creativity and innovation, amidst constant competition and peer review to invest the public's limited resources in the most promising ideas. We owe nothing less to the patients suffering from incurable diseases. For this reason, we must support all forms of stem cell research so that no matter where the cures come from, we can get there sooner rather than later. I urge you to clarify the Dickey-Wicker amendment so that there can be no question regarding Congress' intent to fund the most meritorious science.

Senator HARKIN. Dr. Mosher, welcome, and thank you. I may even have a question for you when we get to the questions here.

Now we turn to Dr. Peduzzi Nelson and welcome and please proceed.

STATEMENT OF JEAN PEDUZZI NELSON, Ph.D., ASSOCIATE PROFESSOR, DEPARTMENT OF ANATOMY AND CELL BIOLOGY, WAYNE STATE UNIVERSITY SCHOOL OF MEDICINE, DETROIT, MICHIGAN

Dr. PEDUZZI NELSON. Thank you very much, Chairman Harkin, for the opportunity to present this information today.

I am a translational neuroscientist from Wayne State University, and today I am—there are two types of stem cells, embryonic stem cells from embryos and adult stem cells. Today I am going to talk about adult stem cells, and we use the term "adult stem cells" to mean not just stem cells from adults, but also from children, umbilical cord, from blood.

What you have to understand is that the first human adult stem cell was isolated in 1992. Now, we do have a long history of doing bone marrow transplants, which contain stem cells, but adult stem

cells are actually, in terms of looking at other diseases and injuries, a new field. And it was only in the late 1990s did we realize the potential for other diseases other than cancer and various blood disorders.

Yes, most of the Federal funding does go to adult stem cells, but the majority of that goes to old but very important studies in terms of treating cancer and blood diseases. The big disadvantage for adult stem cells is often there is not intellectual property. So the biotech industry that has a much larger budget for research than Federal funding is not interested in most cases in adult stem cells. And we only have a limited amount of Federal funding available.

And where we are in adult stem cells—I am sure the members have seen previously that there are some examples of people being treated with adult stem cells where there is considerable improvement. But the research is going from isolated incidents, and I am going to present clinical trial data in respectable journals where we need to move through clinical trials to standard of care. And to move from a basic science study is relatively inexpensive, several hundred thousand dollars, but for each clinical trial, you need billions of dollars. So we need a lot more Federal support to move forward with adult stem cells.

This is an example of one of the patients. Well, this would have been an example of one of the patients that was treated, a quadriplegic that was treated, using a procedure that was developed in Portugal by Dr. Carlos Lima and his team. And this is a picture. I think we do have a poster of this gentleman that I met several years ago. And he was treated with his own adult stem cells 2 years after his injury. And 2 years after his injury, this gentleman is now shown standing up without anyone supporting him. He is not waving, but he was in the video. And with only braces on his—a foot ankle brace. So he is standing up maintaining balance, and he can now walk with a walker. Amazing, a quadriplegic walking with a walker without assistance, and this is the progress.

But this is not an isolated incident. If you look at the two publications that have been published in peer-reviewed journals——

Senator HARKIN. Dr. Peduzzi, could I just interrupt for a quick question?

Dr. PEDUZZI NELSON. Yes.

Senator HARKIN. Was he treated with what I would refer to as autologous stem cells?

Dr. PEDUZZI NELSON. Yes, he was. And these autologous stem cells were obtained from inside of his nose and used to treat his spinal cord injury.

But this, as I said, is not an isolated incident. There are peer-reviewed publications and a larger number of patients, and I would love the opportunity to bring this forward in the United States after completing a safety study so patients do not have to go to other countries to have this done.

Another example. This is Doug Rice, and he had several heart attacks and had chronic heart failure. And he was told in 2002 that he had 2 years to live. He went to another country and had a treatment done, and he is alive and doing well. At the time he had the procedure done, he could barely walk. But this is also not an isolated example.

This is a published, peer-reviewed article of a study where they used 191 patients who had adult stem cells and compared to 200 patients with similar heart conditions. And the treated patients lived longer and also could exercise more.

Now, I have to move to a somewhat gross picture, and I apologize for that. But this is corneal blindness, and this is the second leading cause of blindness in the country. And on the left side, it shows eyes of patients who had several surgeries that were unsuccessful and were blind in that eye. But using adult stem cells from their other eye, this shows the results several years later. This particular one was 112 patients, and more than 75 percent of the time it was successful. And many of the patients regained normal vision in their eye.

And let me just go to another example. This is the study, the published study, that was published of these 112 patients in the New England Journal of Medicine.

I will go to one more patient. I am showing these sort of poster patients or poster examples, but now they are supported by results from clinical trials. In the middle between his parents is Joe Davis, and he had very severe sickle cell anemia and his parents were told that Joe might not live to his teens. So he had the procedure using his brother's umbilical cord blood cells, and Joe is absolutely doing fine right now and has no sickle cell symptoms.

There have been two published studies for sickle cell, which is a very painful condition. This first study, 6 out of 7 patients no longer have sickle cell symptoms.

And another study—this particular study was by NIH scientists and published in the New England Journal of Medicine in 10 adults with sickle cell anemia. Most of these patients—9 out of 10 of these patients—no longer had sickle cell symptoms.

The last patient that I would like to show is Barry Goudy and he had MS. He went to Northwestern Memorial Hospital. His symptoms of MS have disappeared. And he was part of a larger study that was published in a peer-reviewed journal, in Lancet, and these patients showed significant functional improvement and no one got worse in this degenerative disease.

Senator HARKIN. Dr. Peduzzi Nelson, I have to ask you to wrap up. I would like to get to the last—we just have some more votes that just——

PREPARED STATEMENT

Dr. PEDUZZI NELSON. Okay. This is just another study supporting that. I will not talk about the amazing results in newly diagnosed juvenile diabetes in JAMA.

But I would just like to conclude that we need more Federal funding. We need more NIH funding so patients do not have to go to other countries and so these amazing results that I presented can go to clinical trials and become standard of care for U.S. patients that need their support.

Senator HARKIN. Thank you very much, Dr. Peduzzi Nelson.

[The statement follows:]

PREPARED STATEMENT OF JEAN PEDUZZI NELSON

Thank you Chairman Harkin, Senator Cochran, and distinguished subcommittee members for the opportunity to present this information to you today. My name is Jean Peduzzi Nelson from Wayne State University. Please note that the testimony I am giving today is my own opinion and not necessarily that of the university. I am a translational neuroscientist who is working to bring using one's own olfactory mucosal adult stem cells for spinal cord injury, head injury, and radiotherapy damage.

There are two major categories of stem cells: embryonic and adult. Human embryonic stem cells are derived from human embryos and remain controversial. I want to focus my comments on the science of adult stem cells that are treating patients for many diseases. This second category of stem cells can be obtained from adult tissues, as well as tissues from children. For my purposes, I will use "adult stem cells" to refer to these as well as stem cells from umbilical cord blood.

I wanted to share with you pictures of some brave pioneers who first explored the potential of adult stem cell treatment. The progress of adult stem cells has gone so far beyond these particular patients to long-term follow-up results of numerous patients in peer-reviewed published clinical trials.

Stem cells are cells that can generate lots of cells and, under the right conditions, become one of the many cell types in the body. Adult stem cells are stem cells obtained from adults, children, even infants and umbilical cord after birth. These include cells from the bone marrow, nose, fat tissue, umbilical cord, and other places. The great thing about these cells is that a person's own cells can be used which eliminates the problem of immune rejection and tumor formation sometimes observed with other types of stem cells. Adult stem cells are the best stem cells to replace lost or damaged cells in our bodies.

The financial challenge with adult stem cells is that usually when you use your own cells, there is no intellectual property or patents. So, the biotech industry that invests billions in research often does not fund this research.[1] Millions of dollars are needed to complete each clinical trial so all patients can benefit from a treatment, not the lucky few, and so that billions can be saved in healthcare costs. The National Institute of Health (NIH) has developed new programs to encourage translational research and clinical trials, but has a much smaller budget than private industry.[2] Much of the funding for adult stem cells by NIH is directed at older, but important uses of bone marrow stem cells that were developed in the 1950s and 1960s for leukemia and other cancers. While bone marrow transplants have been used in patients for years, the successful isolation and characterization of adult stem cells is a very recent science. The first mouse adult stem cell was successfully isolated and purified in the laboratory in 1983.[3] The first human adult stem cell was first successfully isolated and characterized in the laboratory in 1924.[4] New uses of adult stem cells for other diseases and injuries only started in the 1990s, but have already reached patients with various diseases and injuries as I will demonstrate.

I would like to tell you about five patients who have been helped by adult stem cells. These patients were either part of a clinical trial, and their results are now published in a peer-reviewed journal, or sometimes a similar procedure was done in a clinical trial that is now published.

The first patient is Silvio who I met several years ago. I have been working with a group in Portugal led by Dr. Carlos Lima.[5–6] Dr. Lima, Dr. Pratas-Vital, Dr.

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[1] "In 2004, the top twenty companies spent a combined total of over $56 billion on research and development." York University (2008, January 7). Big Pharma Spends More On Advertising Than Research And Development, Study Finds. ScienceDaily. Retrieved September 10, 2010, from http://www.sciencedaily.com-/releases/2008/01/080105140107.htm.

[2] ". . . growth in the National Institutes of Health (NIH) budget would slow sharply to just 2.7 percent in fiscal year 2004 from just-approved fiscal year 2003 level, to $27.9 billion." NIH Budget Growth Slows to 2 Percent in fiscal year 2004, AAAS R&D Funding Update on R&D in the fiscal year 2004 NIH Budget—REVISED AAAS Report XXVIII: Research and Development fiscal year 2004, http://www.aaas.org/spp/rd/nih04p.pdf.

[3] Spangrude GJ, et al., Purification and characterization of mouse hematopoietic stem cells, Science 241, 58 (1988).

[4] Baum CM, et al., Isolation of a candidate human hematopoietic stem-cell population, Proc. Natl. Acad. Sci. USA 89, 2804 (1992).

[5] Lima, C., P. Escada, J. Pratas-Vital, C. Branco, C.A. Arcangeli, G. Lazzeri, C.A.S. Maia, C. Capucho, A. Hasse-Ferreira, and J.D. Peduzzi (2010) Olfactory Mucosal Autografts and Rehabilitation for Chronic Traumatic Spinal Cord Injury. Neurorehab & Neural Repair 24:10–22.

[6] Lima, C., J. Pratas-Vital, P. Escada, A. Hasse-Ferreira, C. Capucho and J.D. Peduzzi. Olfactory mucosa autografts in human spinal cord injury: a pilot clinical study, J Spinal Cord Medicine, 29(3):191–203, 2006.

Escada, Dr. Capucho, and Dr. Hasse-Ferreira have been using a person's own tissue from inside of the nose as a way of delivering adult stem cells. Silvio had a spinal cord injury at the base of his neck [cervical level 6/7, American Spinal Injury Association Impairment Scale (AIS) A, complete injury. Grade A is considered the worst, which indicates a "complete" spinal cord injury where no motor or sensory function is preserved in the sacral segments S4–S5.]. Silvio was left with no movement of his legs and minimal movement of his fingers. At 2 years after injury, he received his own adult stem cells and partial scar removal after intensive rehab failed to lead to an improvement.

Today he can maintain standing position and wave without help. With a walker and short braces, he can walk more than 30 feet without anyone helping him. He can now move his fingers, which he could not do before. Because he was in a wheelchair for 2 years before treatment and could only move the chair using his wrists,

a special rehab program called BIONT (brain initiated non-robotic/non-weight supported training) was used at Centro Giusto in Italy so he could learn to walk again. Dr. Arcangeli and Dr. Lazzeri have developed an effective rehab program that, when combined with adult stem cells, helps patients recover. BIONT therapy is being used on some U.S. patients who had this procedure in Portugal at Walk the Line in Detroit. With NIH and/or the Department of Defense (DOD) I would like to bring olfactory mucosal stem cell treatment to the people in the United States.

This is much more remarkable than a treatment of an acute spinal cord injury within the first few weeks after injury. More than 15 percent of the patients who are American Spinal Injury Association Impairment Scale (AIS) grade A improve in their classification in the first year after injury.[7] If a treatment is given acutely or subacutely, it is difficult to separate normal recovery and effects of a treatment unless a large number of patients are enrolled in the clinical trial and randomly assigned to treatment or control. If a treatment is given at 1 year or greater after spinal cord injury, only 5.6 percent of AIS A (32/571 patients) improve in grade from year 1 to year 5 after spinal cord injury.[8]

Silvio is not an isolated case. Here are the two peer-reviewed publications from the Journal of Spinal Cord Medicine and Neurorehabilitation and Neural Repair which reveal that more than half of AIS A patients improved in grade compared to the normal 5 percent without treatment. When the adult stem cells are combined with an effective rehab program, 12/13 AIS A improved in AIS grade and all of the patients regained some muscle movement in their legs. These findings were documented with EMG and SSEP recordings.

The next picture is Doug Rice who was told in 1998 that he had 2 years to live due to chronic heart failure after multiple heart attacks. At that time he could hardly walk. He did not qualify for any U.S. clinical trials, so he went to Thailand to have a treatment with adult stem cells. The cells were sent to a company in Israel where the cells were purified and allowed to multiply, then sent back to Thailand for injection. Since that time, he has more energy and is enjoying life. However, this is also not an isolated incident. This year an article was published in the European Journal of Heart Failure reporting the followup of 191 patients who received adult stem cells from their own bone marrow compared to 200 patients with comparable symptoms.[9] These adult stem cell treated patients lived longer and had a greater capacity to do exercises. Their heart functioned much better based on a large number of tests (left ventricular ejection fraction, cardiac index, oxygen uptake, and left ventricle contractility). This report of the STAR-heart study provides the controlled clinical trial data, and new trials are now proceeding in the United States.

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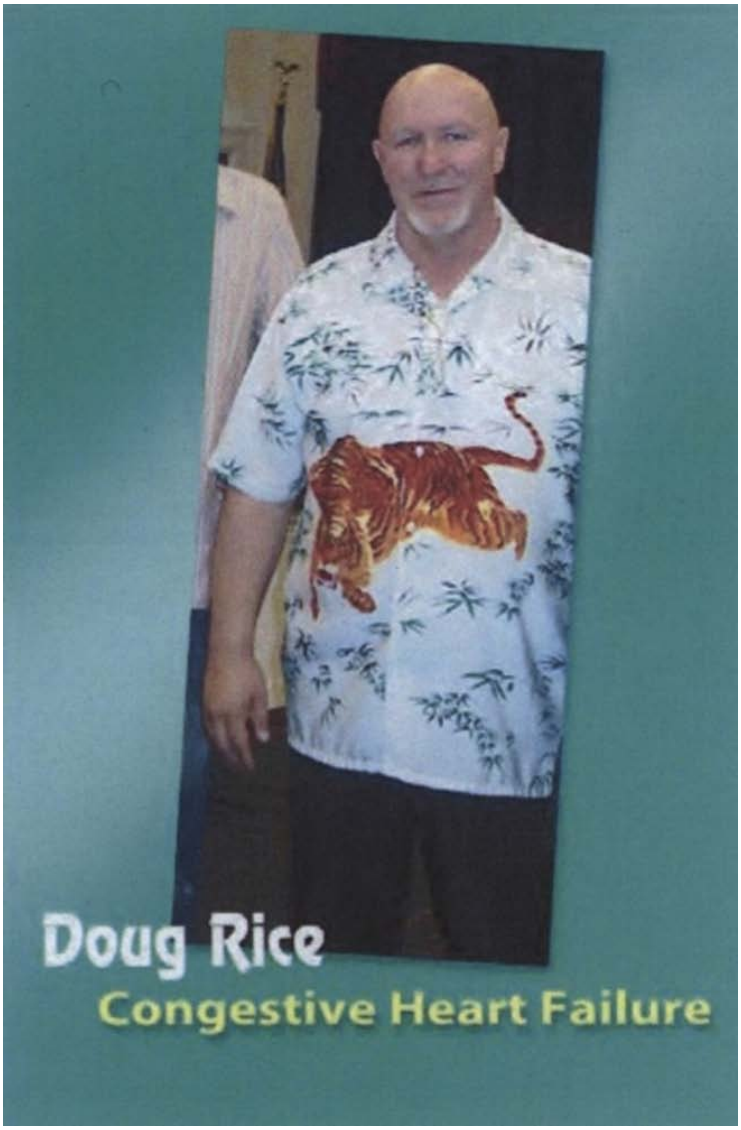
[7] Marino RJ, Ditunno JF Jr, Donovan WH, Maynard F Jr. Neurologic recovery after traumatic spinal cord injury: data from the Model Spinal Cord Injury Systems. Arch Phys Med Rehabil. 1999;80(11):1391–6.

[8] Kirshblum S, Millis S, McKinley W, Tulsky D. Late neurologic recovery after traumatic spinal cord injury. Arch Phys Med Rehabil 2004;85:1811–7.

[9] Strauer BE, Yousef M, Schannwell CM. The acute and long-term effects of intracoronary stem cell transplantation in 191 patients with chronic heARt failure: the STAR-heart study. Europ. J Heart Failure (2010)12:721–29.



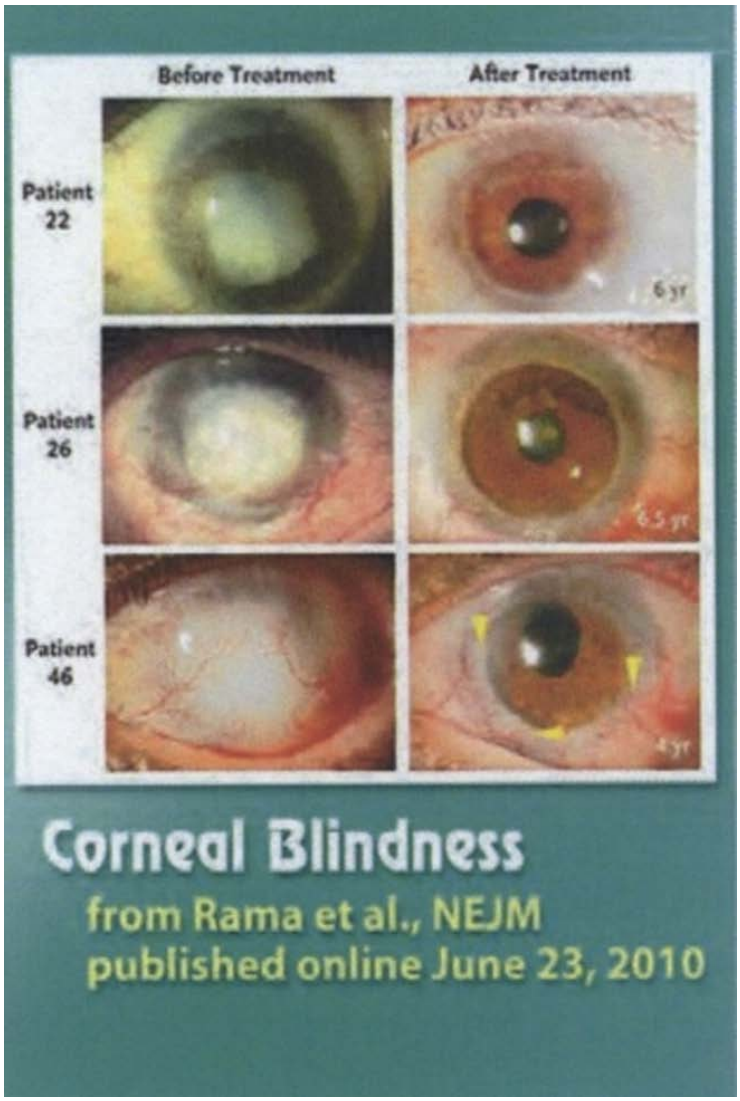
I have to apologize for the next picture. It isn't a photo of a single patient, but somewhat gross pictures of the eyes of three patients with corneal blindness from an article just published in the New England Journal of Medicine.[10] Corneal disease is the second leading cause of blindness after cataracts in the world.[11] Corneal transplants are commonly used, but the transplants are rejected in about 20 percent of the cases.[12] On the left are pictures of the eyes of patients who had severe burns

[10] Rama, P, S. Matuska, G. Paganoni, A. Spinelli, M. De Luca and G. Pellegrini. Limbal Stem-Cell Therapy and Long-Term Corneal Regeneration N Engl J Med 2010; 363:147–55.

[11] Whitcher, JP, M. Srinivasan, & MP Upadhyay. Corneal blindness: a global perspective. Bulletin of the World Health Organization, 2001, 79 (3):214–221.

[12] Facts About The Cornea and Corneal Disease, NIH, National Eye Institute http://www.nei.nih.gov/health/cornealdisease/#4.

or damage to their eye and suffered from corneal blindness. These patients had surgery on their eyes, but these surgeries did not help. Several years later, adult stem cells were removed from the opposite eye and implanted in the damaged eye. The results of the adult stem cell transplant are shown on the right several years after the procedure. The patients went from barely being able to see hand movements to normal sight in these eyes. This procedure was successful in more than 75 percent of the 112 patients. Some of these patients were followed for 10 years. We need more clinical studies in the United States to treat U.S. patients with corneal blindness.



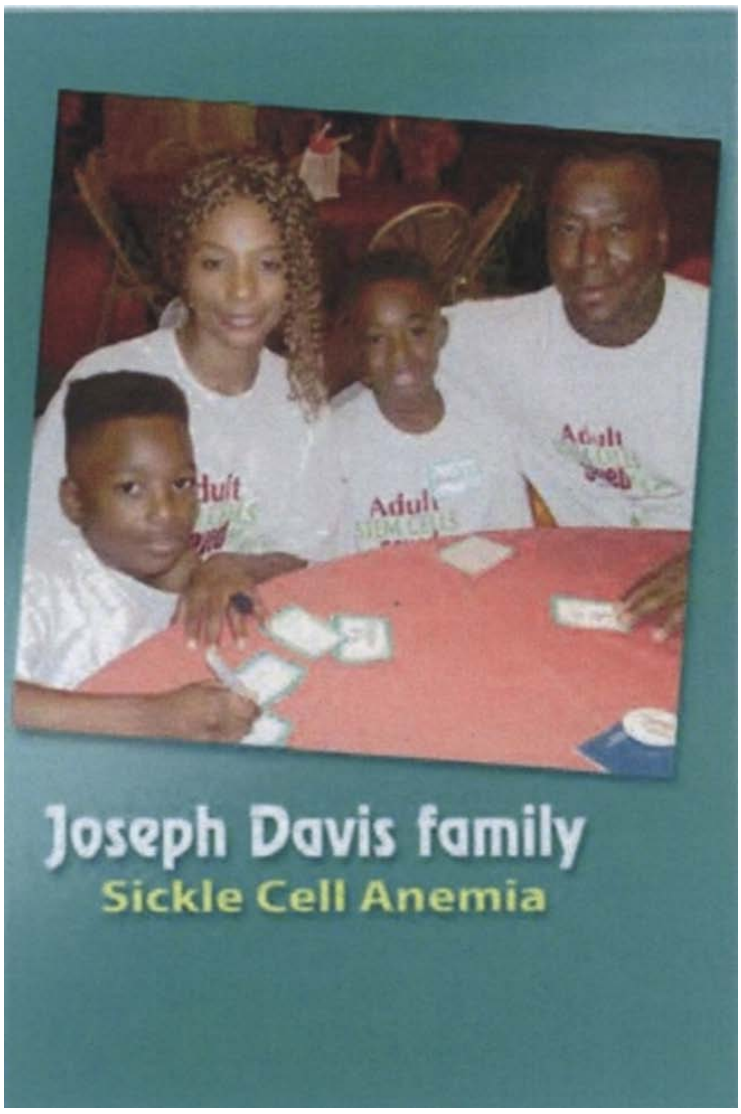
The next patient is Joe Davis, Jr. Joe is the boy between his mom and dad; he was born with severe sickle cell anemia. Sickle cell anemia is a blood disease that affects 1/500 African Americans. The doctors thought that Joe might not live to see his teens. When Joe was 2 years old in 2002, he received a transplant of stem cells from his younger brother's umbilical cord. Joe no longer has sickle cell anemia. So, where are we now? About 72,000 people in the United States have sickle cell anemia

that causes pain, chronic tiredness from anemia and severe infections, usually beginning when they are babies.[13] In a published study last year in the New England Journal of Medicine that was supported by NIH, 10 adults were treated with adult stem cells from their brother or sister. Of these patients, nine no longer had symptoms of sickle cell anemia and were doing well at 4 years after their treatment.[14] A similar study was published in 2008 showing that 6/7 of the children with severe sickle cell anemia treated in a similar manner were without sickle cell symptoms when they were examined at 2–8 years after treatment.[15] It would be great if we could have everyone with sickle cell anemia treated.

[13] Anemia, sickle cell, http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gnd&part=anemiasicklecell.

[14] Hsieh, MM, EM Kang, CD Fitzhugh, Allogeneic hematopoietic stem-cell transplantation for sickle cell disease. N Engl J Med 2009;361:2309–2317.

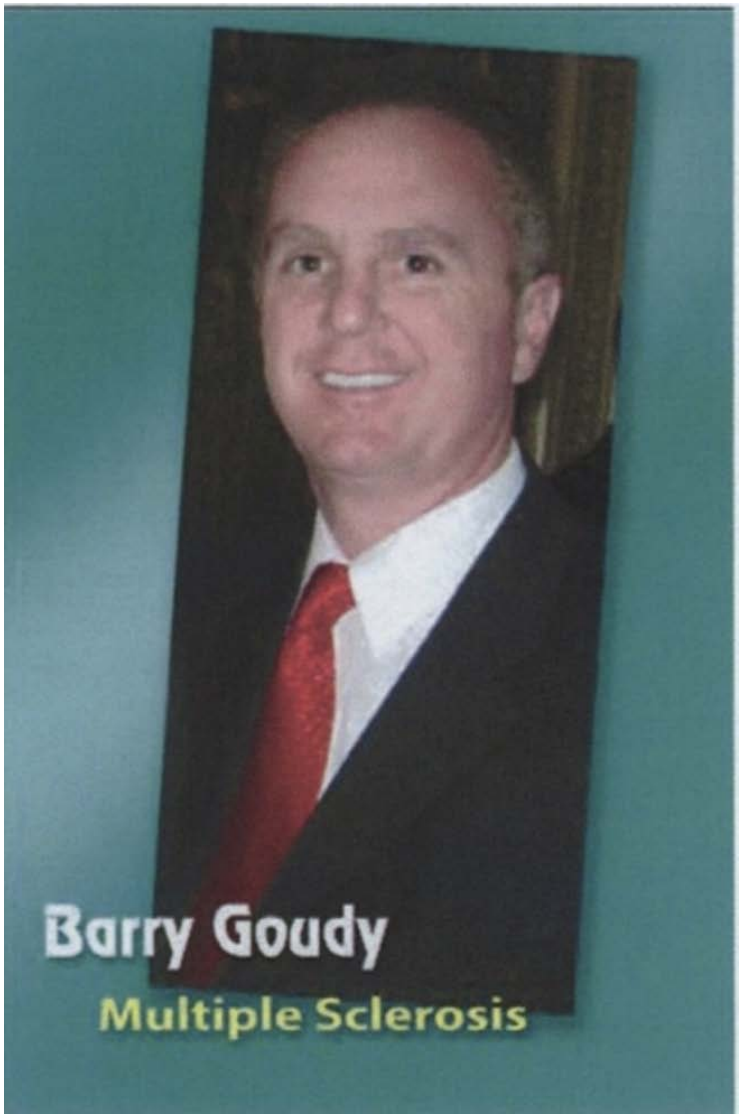
[15] Krishnamurti L, Kharbanda S, Biernacki MA, Zhang W, Baker KS, Wagner JE, Wu CJ. Stable long-term donor engraftment following reduced-intensity hematopoietic cell transplantation for sickle cell disease. Biol Blood Marrow Transplant. 2008 Nov;14(11):1270–8.



The last picture is Barry Goudy who was suffering from multiple sclerosis (MS). He had numerous relapses and the medication was not helping his condition. He was part of a study conducted at Northwestern Memorial Hospital in Chicago and received his own stem cells in 2003. His MS symptoms disappeared in 4 months, and he continues to be symptom free today. Results were published last year by Burt and colleagues in Lancet.[16] Patients had what is known as relapsing-remitting MS. These were patients who were still having relapses despite interferon beta treatment. All of the treated patients did not show the normal progressive worsening associated with MS, and a significant functional improvement was noted in these patients. In a similar study published this year, they describe the 1-year fol-

[16] Burt RK, Y Loh, B Cohen, D. Stefosky et al., Autologous non-myeloablative haemopoietic stem cell transplantation in relapsing-remitting multiple sclerosis: a phase I/II study. The Lancet Neurology—1 March 2009 (Vol. 8, Issue 3, Pages 244—253.

lowup of six patients who showed improvement when their muscles were evaluated using electrophysiology.[17] Their condition either stayed the same or improved in a disease that is characterized with progressive decline in function.



The five pictures and their related clinical trials using adult stem cells show amazing progress for severe spinal cord injury, chronic heart failure, corneal blindness, sickle cell anemia, and multiple sclerosis. However, this is not an exhaustive list of the recent clinical trial findings using adult stem cells. I would just like to mention the amazing progress using adult stem cells in juvenile diabetes. A recent

[17] Rice, CM, E A Mallam, A L Whone, P Walsh, D J Brooks, N Kane, S R Butler, D I Marks and N J Scolding. Safety and feasibility of autologous bone marrow cellular therapy in relapsing-progressive multiple sclerosis. Clinical Pharmacology and Therapeutics, May 5, 2010 DOI: 10.1038/clpt.2010.44.

clinical trial report [18] in the Journal of the American Medical Association found that the majority of the 23 patients who received adult stem cells achieved insulin independence in the 2-year followup. Many may remember the news report of the person who received a new trachea using adult stem cells. An article published this year details the recovery of 20 patients with upper airway problems that received adult stem cells.[19] Another break-through article was published this year in Blood which calls the use of adult stem cells ". . . the gold standard in the frontline therapy of younger patients with multiple myeloma because it results in higher complete remission (CR) and longer event-free survival than conventional chemotherapy.[20]

Only with the help of NIH and the DOD Congressionally Directed Medical Research Programs, can these successful treatments reach all the people that desperately need them. I applaud Senator Harkin's efforts to increase the NIH budget in the past and ask all of the Senators and Representatives to make the people with diseases and injuries a major priority and put the patients first when considering funding stem cell research. These pioneers need to be joined by many other people to help those suffering from diseases and injuries. Adult stem cells aren't just showing great promise, but are treating people now. Much more of the limited funding needs to be directed at adult stem cells that are showing success right now.

Senator HARKIN. And now, Ms. Unser, welcome and please proceed.

STATEMENT OF CODY UNSER, FOUNDER, CODY UNSER FIRST STEP FOUNDATION, WASHINGTON, DC

Ms. UNSER. Thank you, Chairman Harkin, for allowing me to testify and use my voice on behalf of millions of Americans living with debilitating diseases. I feel very honored and, to be honest, frustrated as to why we are here today.

Ten years ago, my hero, my superman, Christopher Reeve, sat in his power wheelchair and using every breath he took, thanks to a machine, testified to Congress with the hope that embryonic stem cell research would be federally funded. Today in 2010 we are still fighting for this promising and hopeful research to continue.

Embryonic stem cells are science based on hope, hope for improving the quality of life of millions of Americans by providing better treatment and eventually cures.

My journey began 11 years ago. I was a healthy, 12-year-old kid who was very active and had big dreams. Everything changed on February 5, 1999. I cannot recall how it felt to put my feet on the floor, how I got dressed that morning, or what I had for breakfast, but what I do remember is that in a matter of 20 minutes my body became paralyzed and my life drastically changed. I was playing basketball at school and suddenly could not catch my breath and my head started pounding with sharp pain. The school I was attending called the ambulance and while laying down in the locker room, my left leg became numb and tingly. I picked it up, put it back down, and I could not feel the floor. I was scared out of my mind, but I thought that whatever was wrong the doctors could fix.

Transverse myelitis is an autoimmune disorder in which the immune system attacks the spinal cord causing inflammation that damages the cells that control sensory and movement of the body.

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[18] Couri CE, Oliveira MC, Stracieri AB, Moraes DA, Pieroni F, Barros GM, Madeira MI, Malmegrim KC, Foss-Freitas MC, Simoes BP, Martinez EZ, Foss MC, Burt RK, Voltarelli JC. C-peptide levels and insulin independence following autologous nonmyeloablative hematopoietic stem cell transplantation in newly diagnosed type 1 diabetes mellitus. JAMA. 2009 Apr 15;301(15):1573–9.

[19] Macchiarini P, Rovira I, Ferrarello S. Awake upper airway surgery. Ann Thorac Surg. 2010 Feb;89(2):387–90; discussion 390–1

[20] Bladé J, Rosiñol L, Cibeira MT, Rovira M, Carreras E. Hematopoietic stem cell transplantation for multiple myeloma beyond 2010. Blood. 2010 May 6; 115(18):3655–63.

After staying in the hospital for a couple of months, I went to rehabilitation where I learned how to do everything from a wheelchair, all the while having dreams of my feet imprinting in the sand.

Today I am a 23-year-old woman who has learned to adapt to a life in a wheelchair and in a paralyzed body. Even though I live life to the fullest and look as though I am just sitting down in a wheelchair, I don't have to always worry about pressure sores from constant sitting. I worry about my osteoporosis advancing in my bones from not standing and bearing weight, which led to a fracture of my left femur. I worry about my scoliosis getting worse, a curvature of the spine common in people with spinal cord injuries. I have bladder and bowel complications and advancing nerve pain. But I am just one out of millions of Americans living with various diseases and conditions that no matter how hard we try affect how we live our lives.

The first time hope actually meant something me to and became sort of my religion was when I saw what human embryonic stem cells can do. A year after I became paralyzed, my doctor and stem cell scientist, Doug Kerr, who was at Johns Hopkins at the time, showed me a mouse that was once paralyzed and now can bear its weight and take steps. At that moment, I realized that this is science I could not ignore, and it gave me a feeling of hope I wanted to fight for, which brings me to another point.

It is frustrating to hear critics of this research say this is a path we cannot go down and adult stem cells hold just as much promise as embryonic stem cells do. Science is the pursuit of discovery and possibility. We should explore every opportunity and not count anything out because I cannot wait. And I know millions of Americans now and in the future cannot wait.

In Christopher Reeve's testimony in 2000, he said, "No obstacle should stand in the way of responsible investigation of their possibilities." I am here today to remove yet another obstacle in the path of this research, this answer, this hope.

The political debate over this research is forcing many of our brilliant scientists to think twice about whether they should stay in this field. I know how dedicated and passionate they are about helping all of us find answers to our pain and suffering. If we keep dragging this debate back here to Washington, in Congress, and in the courts, more and more scientists will have no choice but to either find a different research avenue or move to another country where they can pursue the promise that embryonic stem cells possess. Once and for all, I urge Congress to pass unambiguous legislation that allows this research to move forward.

PREPARED STATEMENT

I grew up around racetracks, and my family has won the Indianapolis 500 a total of nine times. The goal of every driver is to pass under the black and white checkered flag first. The meaning of the checkered flag is winning. Right now, I can see the flag waiting for me to go by, but with this current court ruling, I feel that I have been driving under a long, yellow caution flag. Today I came here to say that this research is real, promising, and hopeful to me and to others as we want so much to take that checkered flag and win

our battles over diseases that constantly challenge our quality of life.

Thank you very much.

Senator HARKIN. Thank you, Ms. Unser.

[The statement follows:]

PREPARED STATEMENT OF CODY UNSER

Thank you Chairman Harkin for allowing me to testify and use my voice on behalf of millions of Americans living with debilitating diseases. I feel very honored and to be honest, frustrated as to why we are here today.

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have been driving under a long yellow caution flag. Today, I came here to say that this research is real, promising and hopeful to me and to others as we want so much to take that checkered flag and win our battles over diseases that constantly challenge our quality of life.

Thank you very much.

Senator HARKIN. We now have two more votes, which I did not anticipate. I will try to get in a few questions. How much time do we have left? Eight minutes left?

A couple of things. Dr. Morrison, in your statement, you alluded to claims made by some that adult stem cell research is more promising than embryonic stem cells because adult stem cells are already used to treat disease. We just heard a lot about that from Dr. Peduzzi Nelson. Could you expand on that? Should we be disappointed that embryonic stem cells have not yet yielded a cure? And how about all these pictures and things we just saw of people that have been cured by adult stem cells?

Dr. MORRISON. These arguments that you hear about focusing on adult stem cell research because they already treat people are meaningless arguments because human embryonic stem cells were first created in 1998. We have only had 12 years in which to work on them, whereas the adult stem cell therapies that are used clinically are related to bone marrow transplantation which was started in the 1950s. So we have had decades of work on adult stem cell therapies.

Now, let me tell a very quick story. The first attempt at bone marrow transplantation between an unrelated donor and recipient was in 1955 by Donnall Thomas and his team. All the patients died. He went back to the laboratory to try to figure out why it was that he could not just randomly transplant bone marrow cells from one donor into another recipient and learned that you had to match the immune systems of the donor and the recipient so they did not attack each other.

The first successful transplant from an unrelated donor and recipient was 1969, 14 years later.

So if we applied this criterion of abandoning any form of research that does not lead to cures within 10 or 12 years, as has been suggested by opponents of embryonic stem cell research, then none of these adult stem cell therapies would exist today and, frankly, most of the medicines that we benefit from would never have been possible to develop.

Senator HARKIN. Dr. Daley, one line in your testimony. You said iPS cells and embryonic stem cells are different in important ways. I understand you have an NIH grant to examine this very issue that could be endangered, I understand, if Judge Lamberth's injunction were upheld.

Again, tell me why this research is so important. What are the future discoveries that could be spurred by isolating the differences between these two types of cells?

Dr. DALEY. Yes. It is a major question to compare this new and very exciting and very powerful type of iPS cell against the embryonic stem cell, and we have one such grant. I am losing a lot of sleep over the future of that grant because when the injunction was in place, that grant was threatened. It was going to be pulled. It was not going to be renewed, and very promising projects that involve seven different institutions, the University of Miami, Boston

University, Johns Hopkins, as well as Harvard Medical School, were all at risk.

What our research has shown, our early research, primarily in mice and now also in humans, is that whereas our goal is to make iPS cells as close as possible to embryonic stem cells, despite our best efforts to date, there are still some differences. And understanding those differences is essential to understanding how those cells will behave in all of our research projects and ultimately for therapy.

What we found is that after we turned the skin cells or the blood cells back to their embryonic state, they remember where they came from. Now, that can be an advantage. For us we are interested in treating blood diseases, and so we are migrating our work to work with iPS cells that are derived from the blood. But if you are interested in treating Hirschsprung disease or in treating liver disease, this fact that that memory exists may actually thwart your research.

So fundamentally we are still so ignorant about how these new types of stem cells are going to function. We continue to depend on human embryonic stem cells.

AUTOLOGOUS STEM CELL TREATMENT

Senator HARKIN. Thank you very much.

I have got some more. There are two more votes. I cannot hold you here any longer.

Dr. Collins, Dr. Peduzzi's presentation see these people that have been cured—I have had people like that in my own office who have come in who have had autologous stem cell treatment in another country, and they come in and openly testified that whereas they could not walk, now they could a little bit. One person also had heart problems. What do I make of all this?

Dr. COLLINS. So Dr. Peduzzi Nelson's examples are, in fact, exciting to see the potential that is here.

Rob Califf who runs the clinical center at Duke once said something that I thought was kind of important, though, in all of this, that God gave us two gifts for understanding whether a treatment works or not: blinding and randomization. And if you have not applied those standards to an intervention, then you have to be skeptical because things happen that have nothing to do with the intervention. So the studies——

Senator HARKIN. What did you say again, Dr. Collins?

Dr. COLLINS. Blinding, that is, the patients and the investigators cannot know whether that individual received the new treatment or some other placebo approach. And randomization, that is, patients get randomized to one or the other arm so that you do not have a bias in the outcome just based on their not being well matched.

For all of us involved in medical research, until an effort has been put through that particular very stringent test, then one has to be a little concerned about whether what has happened is going to be generalizable. And that is what we want. We want things that you know will work for lots of people.

The exciting research reported by Dr. Peduzzi Nelson for the most part has not yet reached that standard in terms of the spinal

cords results that she talks about with these olfactory mucosal cells, although I think it is very exciting to see how that is. In fact, I understand there is an Australian study that has had difficulty replicating that. I am not, by this, saying that we should not be supporting that research. It is very exciting. We should be. But let us be clear about what we consider to be proof of success. Whether we are talking about human embryonic stem cells or iPS cells or adult stem cells, we have to be rigorous in our standards about when we are clear that we have established something confidently.

Dr. PEDUZZI NELSON. If I might make a comment.

Senator HARKIN. Dr. Peduzzi, I will give you a minute because I have got to go vote. I am sorry. Go ahead.

Dr. PEDUZZI NELSON. Just 1 minute. I would like to say that Dr. Collins is correct. And what I am saying is that we need the funds. We need funding from NIH and the Department of Defense, to bring these clinical trials to the next phase where there is blinding and there is randomization.

I would like to make the second point. There is some confusion with the study in Australia. They in no way replicated the work in Portugal. They were using a different cell type.

But beyond the fact about blinding and randomization, we do need that. In the case of the Portugal trial, there is a problem in that this is a surgical technique. They are actually putting the cells and tissue into the spinal cord. So you cannot go to the standard of having patients have a sham surgery. So that is part of the difficulty in verifying the technique.

But all of these other clinical trials that I presented need to be replicated in the United States and they need to be brought on to the clinical trial where you do blinding of the patients, meaning that the people doing the investigation do not know if they received the treatment or not and the patient does not know that. So we need to move in that direction, and it is terribly expensive.

Senator HARKIN. Do you think that funding for embryonic stem cell research should be prohibited?

Dr. PEDUZZI NELSON. This gets to—I am here as a scientist and not here giving a personal opinion. As a scientist, what I came here to say is that in this country and other countries, we have seen some results that are, frankly, amazing, that are published in major journals that are clinical trials, and we need the funding for adult stem cells so they can become standard of care. It does not do anyone any good to treat 5 or 10 patients.

ADDITIONAL COMMITTEE QUESTIONS

Senator HARKIN. I am sorry.

Ms. Unser, again, I thank you very much for being here today. You are a very courageous young woman and thank you for picking up Christopher Reeve's mantel and moving ahead with it. I compliment you very much on that.

I thank our whole panel. Thank you for being here. I am sorry. I could stay here and talk about this for another hour. I have got other things that I want to ask. I may submit questions to you in writing, and I would appreciate your responses to those.

Dr. Collins, again, thank you very much.

[The following questions were not asked at the hearing, but were submitted to the Department for response subsequent to the hearing:]

QUESTIONS SUBMITTED BY SENATOR THAD COCHRAN

SCIENTIFIC HURDLES

Question. In your testimony you said ". . . our best window into human development is using human embryonic stem cells." In July, the Food and Drug Administration (FDA) authorized the first test—in humans—of an embryonic stem cell therapy. When these cells were tested, partially paralyzed animals walked. Dr. Collins, what is the most significant hurdle in translating current stem cell research into treatments like the one recently approved by the FDA?

Answer. To use human embryonic stem cells (hESCs) for cell replacement and/or repair we must develop procedures that consistently produce a stem cell product that is appropriate for the specific use and safe for use in humans. Each particular disease or condition to be treated is likely to require a different cell therapy product. In some cases, scientists know the cell type required and the steps required for it to be produced. In others, they know the cell type required but not how to produce it and in yet others, investigators may not be sure what cell type would be most appropriate. Once the cell type has been identified and a protocol developed, scientists need to demonstrate the ability to produce enough of the desired cells consistently to allow comprehensive preclinical safety testing in animals, and support initiation of an early phase clinical trial in humans under FDA oversight. Significant hurdles during this stage of the process include manufacturing product of sufficient purity, tracking the cells inside the animal's body, and confirming that the cells integrate functionally into the target tissue. The timeframe for developing a stem cell therapeutic could easily be 10 years. For the few private companies making progress in the field of stem cell biology, such as Geron and ViaCyte, private sector funding has been consistent over a long period of time, while public funding has been unpredictable. If stem cell therapy is left to the private sector alone, development will likely be more restricted in breadth, access to research tools or results could be limited due to proprietary constraints, and innovative research may not be undertaken, thus hampering progress and threatening United States predominance in the field.

Question. In your testimony, you said that human embryonic stem cells are a better model for how humans will respond to drug treatment than the current method using animal models. Can you expand upon this and provide a few examples?

Answer. In the past, testing a drug or intervention on an animal model has been the best test that could be done before actually testing a drug on human beings in a clinical trial. In using an animal model, scientists are making an assumption that the human body is likely to respond to the drug or intervention being tested in a manner similar to that of the animal model's body, because humans and other animals are so similar in genetic makeup. However, scientists may now be one step closer to observing how the human body will respond to a therapy: we can use hESCs to generate the tissue of interest (heart, brain, skin, etc.) and then test the drug or intervention on those human cells for safety and effectiveness.

For example, in the area of diabetes, scientists have identified numerous therapies that "cure" Type 1 diabetes in mice. Many of those treatments, however, that seemed so promising in the mouse have not proven to be effective in treating human diabetes. So, although animal models such as mice are still useful, they cannot tell us exactly how humans will respond. Scientists are making significant progress in learning how to coax hESCs into becoming mature human beta cells—the cells that produce insulin. They hope that these cells will be more useful tools to test potential diabetes drugs or other interventions and better predict how the human body will respond.

In the area of heart disease, hESCs may also prove to be an invaluable tool. Although early stage clinical trials of drugs designed to improve heart function sometimes report positive results, the later stages are frequently halted due to unanticipated and negative side effects of the tested drug. Many of the drugs end up harming the very cells they were meant to help—the human heart cells, or cardiomyocytes. Scientists have now produced clinical grade cardiomyocytes from hESCs, and they hope that testing promising drugs on these cells prior to beginning clinical trials will speed safe and useful heart disease drugs to the many who need them.

FEDERAL FUNDING

Question. If Federal funding is no longer available to support hESC research, would private or State funding be able to maintain the current pace of research?

Answer. No. It would be extremely difficult for State or private funding in the United States to maintain the current pace of hESCs if Federal funds were no longer available.

Currently, less than a dozen States have implemented funding programs for hESC research and the amount of research funding varies from State to State. When State research funds are available, the funds are restricted to scientists who conduct research within those States. However, scientists from all States are eligible to apply to the National Institutes of Health (NIH) for research funding and NIH awards grants based on the scientific merit of the research proposed. In fiscal year 2009, NIH made hESC research awards to institutions in 22 different States.

In addition, although there is no hESC policy in the United States that applies to both the public and private sectors, the NIH Guidelines for Human Stem Cell Research provide ethical standards for the States to follow if they choose.

Without the central direction and coordinated research approach that the Federal Government can provide, many are concerned that the States' actions will result in duplication of research efforts among the States, variation in the level of ethics oversight, and ultimate loss of U.S. pre-eminence in basic hESC research, the foundation of translational and clinical hESC research.

Long-term investment in basic research is necessary before scientific findings can be translated into clinical applications. For example, research is needed to understand the basic biology of hESCs before scientists can determine how hESCs can be coaxed into a particular cell type before stem cells can be used for drug testing or use in regenerative medicine. NIH is more likely to support these fundamental studies. Basic research must produce evidence of clinical relevance and demonstrate a potential market before the private sector will take up the research.

INTERNATIONAL COMPETITIVENESS

Question. Medical research is projected to be one of the chief sectors for job growth over the next decade. What is the most significant hurdle for American scientists to remain competitive in the international stem cell arena?

Answer. The most significant hurdle for American scientists to remain competitive in the international stem cell arena is the uncertainty of Federal funding for hESCs. In contrast, there is strong government support and investment in hESC in countries such as Singapore, India, China, and the United Kingdom. A 2008 study ranked the United States as a low performer in hESC research as compared to its leadership in other areas of emerging, but noncontroversial, biomedical research.[1] Notably, the top four high-performing countries in hESC-related research (United Kingdom, Israel, China, and Singapore) all have supportive government policies for this field. The uncertainty in Federal funding for hESC research discourages established investigators from pursuing promising leads since they cannot count on stable funding for their best projects. Outstanding young scientists are reluctant to focus their efforts on promising hESC research when they may not be able to continue because of changes in funding policy.

QUESTION SUBMITTED BY SENATOR PATTY MURRAY

RESEARCH FUNDING

Question. In your testimony, you mentioned that the National Institutes of Health (NIH) has invested more than $500 million in human embryonic stem cell (hESC) research since 1998. You also mentioned that stopping Federal investment of this research mid-stream would result in wasting the funds that have been put in accounts or already drawn down. You stated this wasted amount will amount to $270 million. This inconsistent policy of Federal support has effects on research budgets and planning. As a researcher, have you seen how this policy has affected budgets for promising research? Could you expand a little bit on how looking for other types of funding when Federal support stops and starts affects the continuation of research?

Answer. Speaking as both NIH Director and a researcher with my own laboratory, even a temporary suspension of funds can jeopardize ongoing research projects.

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[1] Levine, A.D. "Identifying Under- and Overperforming Countries in Research Related to Human Embryonic Stem Cells" Cell Stem Cell 2, June 2008, pp. 521–524.

When a laboratory experiment or clinical study is interrupted, it cannot be easily restarted. Such experiments may involve biological materials such as cell lines growing in lab incubators that must be managed daily to encourage growth and prevent contamination. Valuable laboratory animals serving as models of a wide range of human diseases and disorders that are being used to test new therapies could be lost due to the lack of funds to pay personnel to care for them. Once critical research tools and reagents—including unique materials that have taken years to develop—have been lost for lack of funding, it may take months or years to recreate them, if that is even possible. In clinical research projects, it can be very difficult to maintain the willingness of participants to stay involved with research. In cases where clinical interventions are being tested, this could pose severe ethical concerns about benefits and risks to those who have received only part of the scheduled protocol. In addition, laboratory personnel whose jobs depend on grant funds may be let go and the best investigators, including promising young investigators, may abandon that particular line of research or possibly move to other countries that have more predictable support for hESC research.

CONCLUSION OF HEARING

Senator HARKIN. Thank you all for being here. I am sorry I have to run.

[Whereupon, at 12:17 p.m., Thursday, September 16, the hearing was concluded, and the subcommittee was recessed, to reconvene subject to the call of the Chair.]

MATERIAL SUBMITTED SUBSEQUENT TO THE HEARING

[CLERK'S NOTE.—The following testimonies were received by the Subcommittee on Labor, Health and Human Services, and Education, and Related Agencies for inclusion in the record.

PREPARED STATEMENT OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH

The American Association for Cancer Research (AACR), the world's oldest and largest professional organization dedicated to advancing cancer research, represents more than 32,000 cancer researchers, physician-scientists, other healthcare professionals, and survivors and patient advocates. On behalf of AACR, I thank you, Chairman Harkin and members of the Senate Appropriations Subcommittee on Labor, Health and Human Services, and Education, and Related Agencies, for holding this important hearing on the future and promise of human embryonic stem cell research. The AACR appreciates the opportunity to share its views on this issue.

There is vast potential for stem cell research to improve the prevention, diagnosis, and treatment of cancer and many other diseases. Human embryonic stem cell research, in particular, may lead to new biological insights that offer previously unknown avenues for the development of promising new therapies for cancer patients. As stated in our 2005 policy statement on stem cell research,[1] the AACR believes that reasonable, ethical exploration of the full spectrum of stem cell biology is a crucial component of scientific discovery.

THE COURT INJUNCTION IS A SETBACK FOR SCIENTIFIC DISCOVERY AND CANCER RESEARCH

Scientists who were recently given new opportunities under President Obama's Executive order[2] to pursue important research questions using human embryonic stem cell lines could now be stopped in their tracks. The recent decision by the Federal District Court of the District of Columbia to block Federal funding for human embryonic stem cell research underscored the instability faced by scientists working in this promising field. The injunction created mayhem for scientists, who in the blink of an eye became unsure whether they could legally continue their experiments funded by the National Institutes of Health (NIH). A whole cadre of young scientists interested in pursuing this area of science may be discouraged from doing so due to concerns about funding stability. The AACR is deeply concerned that the lack of clarity on Federal funding for human embryonic stem cell research will significantly affect the ability of the United States to be a leader in this cutting-edge field of science that has real potential to save lives. United States scientists already face a distinct disadvantage in this field compared to their colleagues in countries such as Great Britain and Australia with more progressive, yet still ethically responsible, policies. While the injunction temporarily was lifted, great uncertainty remains as the case goes to the appellate court.

HUMAN EMBRYONIC STEM CELL RESEARCH HOLDS MUCH PROMISE FOR CANCER PATIENTS

Stem cell research is part of a multi-faceted approach to understanding the biology of cancer and developing new ways to combat the 200 diseases collectively called "cancer." Potentially paradigm-shifting research may be developed from embryonic

[1] American Association for Cancer Research. *Responsible Exploration of the Full Spectrum of Stem Cell Biology is Essential to the Advancement of Cancer Research*. Position Statement, 2005. http://www.aacr.org/home/public-media/aacr-press-releases/press-releases-2005.aspx?d=482.

[2] On March 9, 2009, President Barack H. Obama issued Executive Order 13505 Removing Barriers to Responsible Scientific Research Involving Human Stem Cells.

stem cell research, as scientists are just now learning what potential these stem cells hold and how they differ from the less-controversial adult stem cells.

For example, recent scientific discoveries have shown that human cancer cells often display features that are reminiscent of human embryonic stem cells and that the more a cancer cell resembles an embryonic stem cell, the more aggressive its behavior. Indeed, it is only now being appreciated that the initiation and progression of many, if not all human cancers, involves deregulation of the very same genes and pathways that are necessary and responsible for normal human embryonic development. Inappropriate activation of these pathways in an adult cell can overtake its development and drive creation of a tumor.

Early studies in the laboratories of numerous cancer researchers are showing that if these genetic and epigenetic errors are corrected, the growth of the cancer can be slowed or even reversed. However, successful translation of these exciting laboratory discoveries into advances for patient care requires that we better understand the differences between normal embryonic stem cell and cancer biology. To achieve this, it is absolutely imperative that this fundamental research, which has already led to so many significant discoveries, be allowed to continue. This research de facto depends on laboratory-based investigations of human embryonic stem cells.

Another important advancement in cancer research has been the discovery that certain tumors arise as a consequence of genetic mutations in normal adult stem cells. For example, leukemia can arise when mutations occur in normal hematopoietic (blood) stem cells, and brain tumors can arise as a consequence of mutations in normal neural stem cells. The ability to isolate normal hematopoietic stem cells from bone marrow has fueled discovery into the origins of leukemia and is leading to the development of novel therapies to target leukemia stem cells. However, because of the relative rarity and inaccessibility of other adult stem cells, very little is yet known about their normal biology or how they morph into cancer cells. Cancer researchers are harnessing the pluripotency and regenerative power of embryonic stem cells to generate these rare adult stem cells in the laboratory.

As a renewable source of neural, neural crest, pancreatic, liver, and other tissue-specific stem cells, embryonic stem cells are—for the first time—providing cancer researchers with the tools to study differences between normal adult stem cells and cancer stem cells. Already these studies are generating novel insights into tumor biology and identifying potential therapeutic targets that could be exploited to selectively kill cancerous stem cells.

The benefits of this research are applicable especially to the pediatric population. Given that fully two-thirds of childhood cancer survivors are afflicted with long-term side effects from cancer treatments that negatively impact their health and well being, it is imperative that we strive to develop new therapies for pediatric cancers that spare normal stem cells and developing tissues. The promise of human embryonic stem cells as tools for scientific discovery provides hope for these children and for all patients who are afflicted with brain tumors, bone and soft tissue sarcomas, neuroblastoma, malignant melanoma, pancreatic, liver, and other solid tumors that all too frequently resist current therapies.

AACR SUPPORTS SOUND, ETHICAL AND RESPONSIBLE STEM CELL RESEARCH POLICIES

The AACR believes that human embryonic stem cell research must be conducted in accordance with policies that are sound, ethical, and responsible. As with any scientific investigation, explorations of stem cell biology must be pursued in strict accordance with such policies to safeguard the welfare of research donors and recipients. Individuals donating biological materials for research—including somatic cells, gametes and embryos—need to give their fully informed and voluntary consent through a mechanism uncompromised by financial incentive.

The NIH has exerted significant effort to ensure that this promising research, like all NIH research, is conducted in a manner consistent with established ethical principles. After a thorough and transparent process involving extensive public input, the NIH put forth guidelines last July that stipulate the assurances and supporting documentation that must accompany requests for NIH funding for research using human embryonic stem cells. The guidelines also expressly prohibit funding for research projects using lines derived for the purpose of research through processes such as somatic cell nuclear transfer, in vitro fertilization or parthenogenesis. Neither Obama's Executive order nor the NIH guidelines permit Federal funding to be used for the generation of new stem cell lines.

In considering its support for research utilizing human embryonic stem cells, the AACR recognizes and shares the universal sentiment that the human embryo deserves respect. Research involving human embryonic stem cells must serve important research aims that cannot be reached by other means. Moreover, we agree with

the internationally accepted 14-day limit on the developmental age of blastocysts from which the embryonic stem cells are derived.

Although research using human embryonic stem cells raises many important ethical considerations, the majority of Americans believe that the potential for research to yield significant advances in patient care warrants responsible conduct of research. A 2008 Time magazine poll showed that nearly three-quarters of Americans support embryonic stem cell research using cells derived from embryos that will be discarded following in vitro fertilization procedures.[3] Enforcing strict guidelines with appropriate oversight will ensure that such research is conducted according to the highest ethical standards.

CONCLUSION

The AACR believes that stem cell research can be conducted in a manner consistent with established ethical principles, and strongly supports responsible explorations of the full spectrum of stem cell biology, including the use of human embryonic stem cells, for meritorious scientific research and therapy development.

The AACR has been moving cancer research forward since its founding in 1907. The AACR and its more than 32,000 members worldwide strive tirelessly to carry out its important mission to prevent and cure cancer through research, education, and communication. Responsible embryonic stem cell research holds tremendous promise to deliver new therapies to patients suffering from cancer, as well as many other diseases such as heart disease, Parkinson's, diabetes, Alzheimer's, HIV/AIDS, and spinal paralysis.

PREPARED STATEMENT OF THE AMERICANS FOR CURES FOUNDATION

Honorable Senators Tom Harkin and Thad Cochran, members: Thank you for this opportunity to provide testimony on a subject which affects 100 million Americans with a chronic (incurable) disease or disability—and everybody who pays the medical bills.

The costs are staggering: last year, chronic illness cost America $1.65 trillion, more than all Federal income taxes ($1.2 trillion) combined. The suffering is incalculable.

These are not empty statistics, but members of your family and mine: people like my son.

On September 10, 1994, Roman Reed was playing college football. At middle linebacker he was having a great game: 11 solo tackles, a diving one-hand interception, a forced and recovered fumble.

And then, the accident. There was a hideous sound, like an axe handle breaking on a rock. In an instant our son was paralyzed from the shoulders down. He was 19.

The doctors gave us no hope.

"He will never walk again, nor close his fingers; almost certainly no children", they said.

We would not accept that diagnosis then, and we do not accept it now. We worked to find a cure.

With the leadership of Fremont Assemblyman John Dutra, we passed a California law, Assembly Bill 750, the Roman Reed Spinal Cord Injury Research Act of 1999.

On March 1, 2002, I held in my hands a rat which had been paralyzed, but which walked again, thanks to embryonic stem cells—as my son watched from his wheelchair.

This was the famous experiment to re-insulate damaged nerves in the spine. Geron is taking it to the world's first human trials of embryonic stem cells, recently approved by the Food and Drug Administration (FDA). Ten newly paralyzed young men or women will be offered a chance my son did not: to maybe get better, through embryonic stem cell research.

"Roman's law" funded the first use of the Presidentially approved embryonic stem cell lines. And, importantly, the Federal Government backed us up. For our total expenditure of $14 million over 9 years, we brought in an additional $60 million in follow-up grants and matching funds from the National Institutes of Health (NIH), new jobs and revenue. But it was not enough.

For a cure to come, not only for paralysis, but also the dozens of incurable diseases afflicting so many, the entire field of regenerative medicine had to advance.

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[3] SBIR Research poll for Time magazine. June 2008. http://www.pollingreport.com/science.htm. Accessed September 8, 2010.

In 1942, research connected with the medical aspects of radiation sickness from the atomic bomb revealed that bone marrow transplants had healing properties. That was the beginning of adult stem cell research, which has proved extremely useful in the treatment of forms of cancer and blood disease.

But it is not the exclusive answer to all chronic illness and injury.

Embryonic stem cells which build every portion of the body are also important.

The difference between adult and embryonic stem cells is like the difference between gift certificates and cash money—one can only be spent in certain places, the other is acceptable everywhere.

For example, adult stem cells heal surface wounds slowly, leaving a scar. Embryonic stem cells build the entire human body. The difference is power is extraordinary.

For the field of regenerative medicine to advance, both types of cells are needed. Each is different and has different powers and purposes.

But there are subtle dangers to be aware of with adult stem cells. They cannot always do what embryonic stem cells can. Sometimes adult cells which have been experimentally turned into useful cells revert to their original adult stem cell state. One attempt to turn adult stem cells into nerve cells did not last, and after a few days, the rats which had the cells implanted developed excruciating pain, so they gnawed off their paws. (A replication of this study was done by Dr. Candace Floyd, UC Davis.)

An approach I regard as a failure is the attempt to use Olfactory Epithelial Glia (OEGs) to restore spinal cord function, basically reaching a scalpel up into the nose and scraping off part of the brain, which is then spread like jelly on the injured spine. I have spoken with a recipient of that treatment who described (after an expenditure of approximately $40,000) the essential failure of it: the paralyzed person regained a patch of skin sensation on his elbow, so that he could feel his sleeve go on, when they dressed him in the morning.

Much has been said about "adult stem cell treatments for 70 diseases", but this is misleading at best. Prescribing aspirin for cancer may be a treatment, but it is not a cure.

The ancient scientist Galen spread pigeon dung on the spines of paralyzed gladiators. It was a treatment, but hardly a successful one.

The idea of adult stem cells being ready to be the sole standard of treatment is not only unwise but cruel, imposing something unreliable in place of the possibility of actual cure.

California's Bob Klein began an initiative, Proposition 71, the Stem Cells for Research and Cures Act. I was proud to serve on the board of directors of that successful effort.

But even when 7 million voters approved the $3 billion stem cell program, lawsuits were hurled against us: frivolous in their grounds, but devastating in their consequences.

For almost 2 years the full program was held up. Research delayed is research denied. Who knows what might have been discovered during that time, if we had our program fully operational?

But we prevailed, and today the California Institute for Regenerative Medicine (CIRM) is the pride of our State and a friend to all the world.

Recently, four major grants, $20 million each, were awarded by the CIRM for embryonic stem cell research: Lou Gehrig's disease, stroke, juvenile diabetes, and age-related blindness were chosen. Each is an attempt to do the impossible with the invisible: to try and heal a malady incurable since the dawn of time.

Cures the CIRM develops will benefit everyone; not only the individual families whose suffering will end, but also the economies of every nation, struggling to pay mountains of medical debt. All will benefit.

But we need the Federal Government to help with the enormous costs which wait beyond initial research: the "valley of death" which faces all new medical discoveries: the costs of turning theory into therapy, all the way from bench to bedside, may approach $1 billion. California's program has a budget of approximately $300 million a year: we can't do it alone.

March 9, 2009, a day of joy. Roman, Gloria and I were in the room when President Barack Obama reversed the Bush restrictions. Now, at last, the Federal Government would take its rightful place, leading in the quest for cure.

But another obstacle arose. The case of *Sherley* v. *Sebelius* may shut down Federal funding of the research so many patients and families have worked to advance.

The argument is often made by ideological opponents that embryonic stem cell research is a form of abortion.

This is false. How can there be an abortion, when there is no baby?

There is no pregnancy in embryonic stem cell research. Nothing is placed in the womb. It is biologically impossible for an unemplanted blastocyst to become a child. It is living tissue, like a wiggling sperm, but not a life. It cannot possibly become a child without the nurturing protection of a mother's womb. No mother, no baby: this is unarguable fact.

Congress had a full and vigorous debate on Federal funding for the research: and approved it twice. The Stem Cell Research Enhancement Acts of 2005 and 2007 passed both houses with strong majorities. President Bush exercised his prerogative and vetoed both bills, but the will of Congress was crystal clear.

The Senate, the House of Representatives, and the President of the United States support Federal funding of embryonic stem cell research.

If research funding is blocked for ideological reasons, we abandon a principle: that every American family deserves the best medical treatment science can provide.

Denying cure condemns 2 million paralyzed Americans like my paralyzed friend Karen Miner to a life sentenced incarcerated in a chair; it diminishes hope for those who suffer cancer and leukemia, which killed my mother and my sister Patty; and it slows the growth of jobs in America's shining new industry: biomedicine. Nine years ago, September 5, 2001, I provided testimony for Senator Edward Kennedy's similar hearings on scientific freedom for stem cell research. I conveyed my son Roman Reed's request, asking that the Senate:

"Take a stand: take a stand in favor of medical research; take a stand-so one day everybody can."

Roman and his wife Terri, and their three children, Roman Jr., Jason, and Katie—send that message again.

Finally, I would be remiss if I did not cite one of America's greatest advocates.

The late Christopher Reeve sent a dictated letter to our family. It said: "One day, Roman and I will stand up from our wheelchairs, and walk away from them forever."

Cure did not come in time for the paralyzed Superman, but we still believe in his great dream. Our champion has fallen, but the flame of his faith still lights our way. He always said, we must "go forward". And we will go forward: because America has picked up the torch.

PREPARED STATEMENT OF THE CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

In 2004, 7 million Californians, accounting for 59 percent of the electorate, approved Proposition 71, The Stem Cell Research and Cures Initiative; creating the California Institute for Regenerative Medicine (CIRM), the State stem cell institute. In the ensuing 5 years, scientists and clinicians empowered by CIRM have made extraordinary advances in medical research.

As the largest United States based funder of human embryonic stem cell research during the Bush administration, CIRM has a unique understanding of the importance of stable funding for therapies derived from human embryonic stem cell research. At least four grants for therapies derived from human embryonic stem cells are currently headed towards human clinical trials, including: Type 1 Diabetes, Stroke, Macular Degeneration (age-related vision impairment or blindness), and Amyotrophic Lateral Sclerosis (ALS—Lou Gehrig's Disease).

NATIONAL INSTITUTES OF HEALTH (NIH) GRANTS FOR HUMAN EMBRYONIC STEM CELL RESEARCH COVER CRITICAL WORK ON WHICH CIRM/CALIFORNIA RESEARCH IS DEPENDENT

Although California-based embryonic researchers receive substantial financial commitments from CIRM, the NIH's backing is crucial for many of our grantees. If the Federal Government stopped funding embryonic stem cell research, many of our grantees most promising work would be in jeopardy. With 50 percent of our stem cell researchers responding, more than 31 of our grantees that perform embryonic stem cell research have indicated that they also received NIH funding covered by NIH regulations. The reported total value of these grants is $45.5 million. Virtually all reported there would be negative impact on their research if NIH funds were cut.

More importantly, halting this research will have a devastating impact on the future of the field and the United States' leadership position in biomedical research. With a 50 percent response rate, 16 of our grantees reported the need to eliminate or reduce postdoctoral positions, if NIH funding is not permanently restored. America's best and brightest scientists are unlikely to enter this promising field if Federal funding is cut off or stagnant.

While we are thrilled California is among the worlds leaders in biomedical research, California cannot drive the field alone. It is imperative for the NIH, the leading funder of biomedical research in the world, to fund this vitally important field. Collaboration between scientists at different institutions around the world is imperative if we are going to develop therapies and cures to fight some of today's most debilitating diseases. The collaboration among many of these scientists depends on U.S. scientists receiving NIH funds.

VALIDATING THE POTENTIAL FOR THERAPIES DERIVED FROM HUMAN EMBRYONIC STEM CELLS

In October 2009, CIRM awarded $230 million for 14 unique multidisciplinary Disease Team Research Awards. The goal of these awards is to develop new medical therapies from stem cell research to reduce the suffering from chronic disease and injuries to cure these conditions, if possible. According to an international peer review panel of 15 scientists (all from outside of California) the Disease Team grants and loans, have all demonstrated "compelling and reproducible evidence" that "demonstrates that the proposed therapeutic has disease- (or injury-) modifying activity. The project is sufficiently mature, such that there is reasonable expectation that an Investigational New Drug (IND) filing" for a phase 1 human trial "can be achieved within 4 years of the project start date."

As previously stated, four of these projects utilize embryonic stem cell research to treat some of today's most harmful conditions, including: Type 1 Diabetes, stroke, macular degeneration, and amyotrophic lateral sclerosis (ALS—Lou Gehrig's Disease).

TYPE 1 DIABETES

This public-private disease team partnership between Novocell Inc. and the University of California San Francisco (UCSF) has developed methods to make large-scale batches of replacement beta cells from human embryonic stem cells (hESC). The team has demonstrated that these hESC-derived beta cells cure experimental diabetes in mice and rats. Additionally, they have devised strategies to reduce the risk that recipients will see these implanted hESC-derived beta cells as foreign cells and subsequently reject them. The team now plans to complete the manufacturing, efficacy, safety testing required to generate the necessary data for Food and Drug Administration approval to test in phase 1 clinical trials.

STROKE

Led by renowned Stanford and University of California Los Angeles (UCLA) researchers, this team has produced preliminary evidence on the use of cells derived from human embryonic stem cells as a poststroke treatment to improve recovery in the weeks and months following a stroke. The team has developed a technique that to restrict the potential of embryonic stem cells to neural stem cells that differentiate only into cell types that are normally found in the brain. When these neural stem cells are transplanted into the brains of mice or rats 1 week after a stroke, the animals are able to regain strength in their limbs. Based on these findings, the Stanford led team proposes to further develop these neural stem cells into a clinical development program for stroke in humans at the end of this grant period.

MACULAR DEGENERATION (AGE-RELATED VISION IMPAIRMENT OR BLINDNESS)

The multidisciplinary team led by researchers at the University of Southern California and the University of California—Santa Barbara have produced preliminary evidence on the use of human embryonic stem cells to replace dysfunctional or destroyed retinal pigment epithelial cells to slow or reverse the disease. They plan to coax human embryonic stem cells to differentiate into a monolayer of retinal pigment epithelial cells that can be transplanted into the eye. The replacement RPE cells will function normally to support and protect the light-sensitive cells of the retina and prevent further degeneration and vision loss.

ALS—LOU GEHRIG'S DISEASE

This San Diego based team (from the Salk Institute for Biological Studies, University of California San Diego, and the Ludwig Institute for Cancer Research) plans to protect surviving neurons in people diagnosed with ALS from further degeneration. The strategy involves targeting glial cells, which are neuroprotective cells that surround and support neurons. A type of glial cell called an astrocyte is found in both the brain and spinal cord and acts as a regulator of glutamate surrounding motor neurons. The team intends to grow human embryonic stem cell-derived

astrocyte precursors that will be transplanted directly into the spinal cord environment to prevent further neurodegeneration caused by ALS. The work, which is based on mouse experiments, should be effective in both familial and sporadic ALS.

ALZHEIMER'S DISEASE

Alzheimer's disease, the most common cause of dementia among the elderly and the third-leading cause of death, presently afflicts more than 5 million people in the United States, including more than 500,000 in California. University of California Irvine (UCI) received an early translational grant from CIRM aimed at developing a development candidate for treating Alzheimer's disease. Their proposed studies, utilizes embryonic stem cells to develop a novel and promising strategy for creating an effective therapeutic. Their preliminary studies indicate that stem cell biology may provide a significantly more effective therapy for the disease than any current pharmaceutical products. These results, however are preliminary, and will require years of additional research to confirm the potential.

We have a moral obligation as citizens of the United States to support the dedicated scientists, clinicians, and patient advocate organizations to pursue the best scientific approaches across the scientific field of stem cell research, including human embryonic stem cell research—to reduce the suffering of our families and friends and families around the world.

PREPARED STATEMENT OF THE STUDENT SOCIETY FOR STEM CELL RESEARCH

On behalf of the Student Society for Stem Cell Research (SSSCR), our chapters across this great Nation, and our membership worldwide, we urge Congress to act expeditiously to address recent events regarding Federal funding of human embryonic stem cell research. The recent preliminary injunction against human embryonic stem cell research in Judge Lamberth's district court is deeply disturbing and threatens the education and training of thousands of students. More specifically, graduate students working on human embryonic stem cell projects supported by the National Institutes of Health (NIH) are in danger of having their financial support entirely cut off. Our constituency is directly affected by the court's ruling. Many of us will not be able to continue our biomedical programs if the injunction holds and Congress fails to act. Simply stated, we will lose our means of financial support and potentially our careers. The impact on the American people will be devastating as our country risks losing scores of developing scientists working on the most promising medical science in human history.

On March 9, 2009, SSSCR and the more than 3,500 members of our network were elated when President Obama issued Executive Order 13505, entitled "Removing Barriers to Responsible Research Involving Human Stem Cells." It is our assertion that the order expressed the will of the American people, Congress, and in particular our generation. Medical research and clinical advances that would alleviate human suffering and restore quality of life is a humanitarian concern of greatest importance to us. Each year, at hundreds of U.S. institutions, students enter undergraduate, graduate, and medical school programs designed to fulfill the needs of the biomedical industry. The biomedical industry is one of the fastest-growing industries nationally and internationally. Within the biomedical industry, stem cell research has attracted the excitement of students, researchers, doctors, and companies. In 2009, the State of California passed Bill 471, "The Biomedical Training and Stem Cell Research Education Act" to ensure that enough workers would be trained to meet the growing demands of the regenerative medicine industry. Students believe that the medical promise of cellular regeneration using stem cells is unparalleled in human history. This excitement is demonstrated by our decision to choose medical research projects focusing on stem cell applications, in which the vast majority of graduate student stipends are funded by NIH grants. The accelerated development of this new field, unprecedented State bills to support the research and career training of scientists and doctors, and the influx of commercial investments are all indicative of a trajectory consistent with our intuitive assertion that stem cell research will revolutionize medicine. However, absent the temporary stay, the recent preliminary injunction turns the field on its head and is immediately devastating to career development in regenerative medicine, threatening our generation's long term objective of finding cures to intractable medical conditions. Federal funding of human embryonic stem cell research is the will of the people, necessary for biomedical advance, critical to America maintaining its competitive advantage, morally and ethically acceptable, and integral to the education and training of the next generation of scientists and doctors. Human embryonic stem cells (hESCs) are unique in their use as biomedical research tools and for their current and eventual clinical

application. HESCs are not supplanted by any other cell source, including adult stem cells or induced pluripotent stem cells. Therefore, SSSCR urges Congress to act swiftly and decisively to legislatively fix our current public policy debacle on funding hESC research

In the interest of maintaining a strong, healthy, and competitive Nation we present to Congress the following arguments:

Federal Funding of Human Embryonic Stem Cell Research is the Will of the American People and Congress.—Poll after poll since the early 2000's has unanimously demonstrated a majority support for hESC research and Federal funding of the research. State led campaigns in California, Missouri, and Michigan have sided with the research. In the most recent poll on the subject conducted in August 2010 by Research!America, it was found that 70 percent of Americans favor expanded Federal funding of research using human embryonic stem cells. Gallup polls from 2005 to 2009 have shown support for fewer restrictions on hESC research to range between 52–60 percent. In 2006 and 2007, Congress passed Stem Cell Research Enhancement Acts in both the House and Senate specifically removing Federal funding restrictions on new stem cell lines. It has been the unambiguous interpretation of three administrations, the NIH in 1999, congressional votes in 2006 and 2007, and Senate appropriations since 2002, that Federal funding of hESC research does not violate the Dickey-Wicker amendment. Five hundred forty-six million dollars in Federal funds has been invested in hESC research, since 2002, and nearly a decade of scientific advance is in jeopardy. Projects may be lost forever and millions of taxpayer dollars wasted. The students engaged in these projects will very likely have to change their discipline or their careers entirely due to losing their research stipends.

HESC is Morally and Ethically Acceptable.—It is SSSCR's contention that a society's highest moral obligation is to treat the sick medically and with dignity. When a research path presents hope to millions of patients with debilitating conditions, the only dignified approach by society and government is to provide that hope by pursuing promising medical research in an expeditious and ethical manner. SSSCR feels that the reality of the potential for excess IVF embryos to generate offspring is often clouded by ideology from those opposing the research. Scientifically, many of the embryos that would be donated to research for the generation of new human embryonic stem cell lines are enviable for implantation and could never lead to a successful pregnancy. The supply of IVF embryos far exceeds the demand for reproductive purposes. In a famous RAND corporation study, it was found that more than 400,000 IVF embryos were still in storage, dating back to the 1970s. This fact underscores that hESC research does not necessitate the destruction of any embryo nor has the research prevented a single pregnancy. The generation of IVF embryos for reproductive purposes results in excess embryos that will be stored indefinitely or destroyed. The creation of stem cell lines for research is a subsequent, determining act that chooses humanitarian benefit over biomedical waste. Furthermore, prior congressional legislation and the "New Guidelines on Human Stem Cell Research" have carefully addressed ethical considerations by mandating approved lines to have been donated under informed consent, without financial incentive, and for the embryo to have been created with reproductive intent, but no longer desired for such purposes. Therefore, SSSCR feels that it is our society's moral obligation to conduct hESC research and that the Government has put in place an appropriate framework for students to ethically continue our research projects and to pursue our passion for finding cures.

NIH Funding is Critical to the Education and Training of the Next-generation of Scientists and Doctors.—The vast majority of biomedical research conducted at our universities is carried out by graduate and medical students who depend on a mentor's grant to fund their stipend, which covers living expenses while completing the biomedical research program. For fiscal year 2010, the NIH funded $131 million for hESC research. In total, there are 223 hESC NIH-funded research projects estimated to support 1,300 jobs. However, the impact can spread beyond these projects. One example is the UCSF Medical Scientists Training Programming involving 88 students earning joint M.D. and Ph.D. degrees. The entire program is in jeopardy of losing NIH funding, since mentors working with hESCs cannot be separated out based on the interdependency of the award and the applicant. Twenty-four NIH-funded projects that are up for $54 million in annual renewal on September 30, 2010, is in jeopardy if a stay in not continued at the projected September 27 hearing. In future fiscal years, projects up for annual renewal are also in danger of losing all funding. In all these cases, the immediate impact of an injunction on Federal funding of hESCs is the imminent loss of students' stipends. Current students will be financially forced out of the field to find alternative salary, while new students will be dissuaded from entering the field, and America will begin to lose its competi-

tive advantage in science and medicine. It is imperative that Congress takes action to establish the policy for hESC research funding, so that we never again jeopardize the future and training of our young scientists and doctors in this field.

HESCs are Unique in Their Medical Promise and are not Replaced by Other Types of Stem Cells.—Despite 50 years of research using adult stem cells, severe limitations have not been overcome, such as growing them in sufficient numbers for clinical use and continued failure to treat nonhematological tumors. Pluripotent cells offer a distinct advantage for neurological conditions where brain biopsies can only be used for diagnostic purposes and autopsies do not yield viable nerves. A recent medical advance in reprogramming adult cells back to a pluripotent state, called induced pluripotent stem cells (iPSCs), is very promising; however, iPSCs do not replace the need for hESCs in basic research and clinical application. The industry standard for iPSC cells is not well-established, resulting in a great deal of inter-lab variability, and characterization continues to be based on hESC comparison. Clinically, iPSC cells remain very hazardous and are unlikely for FDA approval anytime soon. The reprogramming process involves hazardous viral gene delivery methods and in some cases known cancer causing genes. While the field hopes to resolve these issues, it's too early to project confidently their use in the clinic. Much more basic research needs to be done on both iPSC and hESCs to understand their biological differences and similarities. Geron has received FDA approval for clinical trials using hESCs to treat spinal cord injury. Advanced Cell Technologies is expected to receive FDA approval to use hESC-derived retinal cells in clinical trials to treat eye disease. IPSCs do not replace hESCs. Clinical trials with hESCs have already received FDA approval, while iPSCs remain clinically hazardous with the current technology.

Our generation has a great responsibility to society to advance science and medicine. In order to realize the potential of regenerative medicine and maintain our global scientific leadership, our young scientists and doctors in training must receive the financial support to continue their programs. The NIH is critical in this aim and thusly Federal funding for hESC research must be safeguarded and maintained. We urge Congress to sort out the legal wrangling and provide our generation the chance to use hESCs in regenerative medicine to discover cures for devastating medical conditions.

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