Testimony by Sean J. Morrison, PhD

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My name is Sean Morrison and I'd like to begin by thanking Senator Harkin and the members of the Committee 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

ten 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 over 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 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 5000 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 non-functional because of the lack of nervous system in that segment. Surgery to remove the non-functional 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 non-functional 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 PhD 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 consequence, 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.