

# It's about change ... regenerative medicine in the Obama era



## Regenerative Medicine talks to three opinion leaders about the prospects for stem cell research in the USA in light of the recent election

During his campaign, US President-elect Obama pledged to use an executive order to overturn federal-funding limits on research into human embryos that are created during fertility treatments imposed by President Bush. Robert Klein, Chairman of the Governing Board of California's stem cell funding agency, Governor Jim Doyle, and Bernard Siegel, Executive Director of the Genetics Policy Institute, discuss the implications of the new administration for regenerative medicine research in the USA.

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What impact has the restriction on federal funding for human embryonic stem cell (hESC) research had on research efforts in the USA?

► **Bernard Siegel (BS):** It has had a serious impact on hESC research in the USA. Essentially, researchers in the USA have only had federal funding for 21 stem cell lines, all of them created before 9th August 2001, when President Bush drew his arbitrary line in the sand. Since then there have been hundreds of new stem cell lines created, some of them disease-specific and free of animal proteins, and not a dollar of federal funding has been available. When you consider that the NIH is one of the great engines of scientific research in the history of man, with an annual budget of approximately \$28 billion, and in 8 years only \$200 million has been directed towards hESCs, it becomes abundantly clear that a change in policy is needed.

What has happened as a result of these restrictions is that states have become players in hESC research, most notably California, with \$3 billion available for stem cell research. Under current policy, utilizing equipment and supplies funded by NIH grants on non-approved hESC lines jeopardizes an institution's entire NIH funding. We have the peculiar situation where stem cell researchers are setting up separate laboratories, sometimes duplicating equipment in their original laboratory, to be able to carry out this work. It has been very frustrating and costly.

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In some instances it has caused US scientists to move abroad. Those countries that allow the research and are willing to fund it see it as a competitive advantage in hESC research and some have jumped in robustly, notably the UK, Israel, China, Singapore and Australia. Of course the California initiative has balanced the scales quite a bit. Nevertheless, other countries were spurred to act when the US government put these handcuffs on US researchers.

▶ **Robert Klein (RK):** The Bush administration's restriction of hESC research to a highly limited number of lines, corrupted by being maintained on mouse feeder cells, has made it very difficult for parts of the country to progress, but here in California, with the benefit of the vision of 7 million Californians who voted for Proposition 71, we have been advancing very well. There are also strong outposts in other states such as Wisconsin, which have maintained some momentum, but at a diminished level than where they would have been if they had not been subject to the ideological limits of the Bush administration.

▶ **Jim Doyle (JD):** The policies of the Bush administration have had two very major effects in Wisconsin. One is that we have had to set up a private stem cell institute, in addition to our public university, because of the Bush administration's restrictions on the use of federal funding. We have scientists who are engaged in research in one laboratory that is funded in part by federal money and they will have to leave that laboratory and go over to another privately funded laboratory in order to work with certain cell lines. It is a significant inconvenience. Second, most medical research in the USA is funded by the NIH, and the Bush administration has flat-out restricted the flow of resources to Wisconsin and other major research institutions around the country that are engaged in stem cell research. So it is both a major inconvenience and it has significantly restricted the flow of funding for stem cell research.

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What is the evidence for the American public's feelings on stem cell research, specifically hESCs?

▶ **BS:** The evidence shows that the public supports it. In this most recent election cycle, there was a referendum, a public vote, in the state of Michigan. Michigan had one of the most restrictive anti-hESC research laws on their books, and voters struck it off. The religious right and other social conservatives waged an incendiary campaign with misleading advertisements. They invested close to \$4 million in their failed effort to defeat the referendum. Voters were not persuaded by this propaganda, and supported the pro-hESC research position. The vote is evidence of the broad consumer ‘pro-cures’ movement. If you ask ordinary people whether they support stem cell research, by a large majority, approximately 70% in the USA will say ‘yes’. They do not see the research as a public health issue but a personal health issue. Something that might impact their own lives and the lives of their loved ones. That is a powerful force of public opinion.

▶ **RK:** The most recent polls that I have seen indicate around 74% of the American public is strongly supportive of ESC research. There is always going to be an opposition group based upon religious ideology. While I respect their religious views, this country is built upon religious tolerance required by our constitution. Whenever religion is used to suppress medical science, it is a very negative influence on society as a whole and medicine in particular.



President-elect Obama has said that he will lift President Bush's ban on federal funding for research on hESC lines derived after 9 August 2001. What impact do you think this will have on hESC research in the USA?

▶ **BS:** Unquestionably, President-elect Obama will be hugely more supportive of hESC research and the life sciences in general. He has always professed his support for this field. He realizes that there is a humanitarian side to it: that stem cell research has the potential



to relieve human suffering. We are hoping that he will issue an executive order early in his presidency to lift the restrictions on federal funding on new hESC lines. That will be a wonderful advancement for hESC research in the USA. hESC research is the gold standard for pluripotent cells: it is the missing component, because it has been so underfunded.

With the new administration, the Department of Health and Human Services and NIH, will undoubtedly implement detailed federal guidance or regulations pertaining to the research on the expanded lines. Currently, each funding body has its own rules and ethical guidelines pertaining to research grants for ESCs. There is a need for uniformity and we will now look to Washington for leadership. We do not want bureaucratic red tape holding back the timeline for potential treatments and clinical trials. There will be a lot of heavy lifting for lawyers, lawmakers and regulators to turn this promise into reality. It is beyond what researchers are accomplishing in the laboratory, we need to make sure we have the proper regulatory scheme.

► **RK:** The most important effect, in terms of the critical path to get treatments to patients, is that there will be a new US FDA commissioner, appointed by President Obama, who will be highly supportive of stem cell therapy, which will allow us to move to Phase I human safety and Phase IIA & B human efficacy trials. The Whitehouse pressure on the FDA not to allow hESC therapies to move forward has been extraordinary, so that will be critical. It will also be important to have Whitehouse leadership. When any new developments in induced pluripotent stem cell technology are announced, the Whitehouse, rather than trying to spin the news to indicate that hESCs are suddenly irrelevant, will be a leader in placing everything in context so it is clear that we need a whole range of stem cell research, because we cannot predict which cell development types will be needed across the many chronic diseases and injuries stem cell therapy might have applications for.

Given the financial crisis that the USA is going through, there may not be a substantial, sustainable source of funds to provide a major increase in NIH funding for stem cell research as a whole. However, the existing funding might be reallocated so that there is more proportional funding available for hESCs in comparison with cord blood, fetal and adult stem cells.

The lifting of restrictions will provide the opportunity for scientists to follow the best science, not dictated by these artificial divisions of funding by ideological boundaries. In addition, US nonprofit institutions have billions of dollars of equipment that was funded by prior grants from the NIH, previously off-limits to hESC researchers. Entire laboratories are separated by yellow lines on the floor, and staff working on hESC lines created after 9th August 2001 are not allowed to use surplus materials or equipment from NIH-funded studies. With the Obama administration reversing the executive order, that artificial ideological division should be removed from these laboratories and they will be able to access reserves of extraordinarily expensive equipment and supplies to help in their work on hESCs.



If federal funding is reintroduced, how will this affect state funding programs?

► **BS:** California Institute for Regenerative Medicine (CIRM) funding is already in place, and that funding is going to continue. There might be less incentive for new states to come in with separate funding mechanisms for this work because there will be a perception that the federal government is supplying the unmet need for hESC research funding. However, far-sighted lawmakers and states will still continue to promote the field. They are seeing this as an issue of economic development for their state. Stem cell research might eventually lead to a \$500 billion industry over the next 20 years. Why should California and a handful of other states reap all the benefits? Policymakers will continue to create legislative incentives to attract regenerative medicine companies to their state. There is room to grow. This is a burgeoning field. Stem cells have captured the public's imagination. The field is powered by consumer demand.

► **RK:** Because we are going to be going through a period of scarce federal resources, it is going to be vital not only for the California funding program to continue, but for

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other states to scale-up to California’s size in their programs or we will not have sufficient resources to seize the critical opportunities that are there and the responsibility to safely but aggressively pursue clinical treatments. We are going to need as much funding as we can identify among the states because the NIH budget has been fairly static for the last 5 years at \$26 billion and yet the cost of medical research has increased every year, so in real terms the federal budget is going down. It is going to be hard to get enough funds to even reverse that downward trend in the overall NIH budget on a sustainable basis, so it is very important that states be scaling up at a time when they are faced with very substantial financial difficulties of their own.

▶ **JD:** Reintroduction of federal funding will be enormously helpful to Wisconsin. We have a major research university (The University of Wisconsin ranks second among US public universities in total research spending) and we also have a very significant stem cell research capacity, well ahead of most other institutions in the country. Therefore, we hope that when the restriction is lifted and the federal funding starts flowing, a significant proportion of those funds will come to Wisconsin. We are planning to maintain our state commitment to stem cell research. It has become a very important part of our efforts to build a strong biosciences and biotech sector in Wisconsin. Even more importantly, this research has the potential to save lives and improve people’s health. This is an area of great expertise in Wisconsin and we are going to continue to fund it in a strong manner.



What other policy changes do you think are needed to promote the activities of biotech companies and academic researchers in stem cell research?

▶ **BS:** In hESC research, part of the reason why it has been so challenging to get funding for this field is that there is an annual Appropriations Bill to fund the department of Health and Human Services, which administers the NIH. In that Bill there is an amendment which passes without debate every year: the Dickey-Wicker Amendment, which forbids any research that would harm a human embryo. Even if the restriction on federal funding for work on stem cell lines created after 9 August 2001 is lifted, you cannot spend federal money to derive new hESC lines. The consumer movement will want to address that discrepancy and perhaps modify the Dickey-Wicker amendment so that federal money can also be spent on producing brand new stem cell lines.

▶ **JD:** There are a number of states that are restricted by their state laws from being able to participate in stem cell research. Some of those laws were put on the books long before anyone knew anything about stem cell research: they are anticloning laws put in place 30 years ago. Fortunately, Wisconsin has no such laws and we can move full-steam ahead, but there are a number of states that will have to overturn such laws. In addition, I believe that scientists in a lot of states have stayed away from stem cell research because of the Bush restrictions, so many states will need to work on building the capacity for stem cell research: they are going to be starting from point zero. I believe that we are going to see a real resurgence in stem cell research in the USA. Hopefully, even some of the great US scientists that have moved over to the UK will return now that the restrictions are to be lifted.

▶ **RK:** Beyond the nonprofit sector, the biotech sector is under very high stress. Around 40% of public companies in the biotech sector have 6 months or less of working capital. It is a difficult situation with an economy like this, because banks and even venture capitalists are pulling back from committing additional funds. This is an area where there will need to be focused, sustained efforts. CIRM has requests for applications going out early next year that will invite the creation of disease teams, and those teams will almost always include private companies in partnership with nonprofit groups. It is going to be very important that the federal government enhance their small business lending practices for biotech companies and provide loan guarantees to keep that sector viable during this period of extreme capital conservatism because the private sector is

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going to be a critical link in therapy development and commercialization. In addition, the government need to create vehicles to access the very large source of funds required once companies get past Phase I–II trials and need to scale-up to large-scale efficacy trials. It is clear that President-elect Obama's team recognizes the challenges to the biotech sector, although they have not made any statements yet about how they will address this area.

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Now that the restrictions on federal funding are to be lifted, do you think the political battle has been won in favor of stem cell research?

▶ **JD:** I think the battle has been won. In Wisconsin, when I ran for re-election 2 years ago, stem cell research was one of the central issues. My opponent was very much opposed to stem cell research and had voted against it on numerous occasions, while I am very much in favor. Before that election, it was a constant political battle in Wisconsin, but after that election the political fight has ended. I think you are going to see the same dynamic at the national level: President-elect Obama will remove restrictions, stem cell research will move forward, and once it has progressed, it will not be possible to go back. I really do believe that this political fight is over, and now it is up to scientists to move forward with the research.

▶ **BS:** In the USA, the battle over hESC research has been a proxy for the abortion debate that has been going on since the early 1970s, and we can expect the foes of this research to continue attempting to put legal roadblocks in the way. Those of us who labor every day to have progressive legislation to advance this field are still going to have to be vigilant and work very hard to ensure that stem cell research continues and grows in the USA.

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### Robert N Klein



Robert N Klein's commitment to advancing medical research originated in his younger son Jordan's diagnosis with juvenile diabetes in 2001. Bob served as the author and Chairman of California's Proposition 71, the 'California Stem Cell Research and Cures' ballot initiative. It passed in November 2004, and was approved by 59% of the California voters. It supports research with a focus on pluripotent and progenitor stem cell research. Time Magazine honored Bob as "one of the World's 100 Most Influential People of the Year" for 2005. Soon after, Scientific American named Bob one of "The Scientific American 50" as a leader shaping the future of science. Bob serves as the Chairman of the Governing Board of California's \$3 billion stem cell funding agency, CIRM, created by Proposition 71. He has served as a board member on Genome Canada's governing body, which has funded approximately \$1.8 billion over the last 9 years in genome research. Bob currently serves on the international

board of the Juvenile Diabetes Research Foundation (JDRF). Bob has a Bachelor of Arts in History with Honors from Stanford University and a Juris Doctorate from Stanford Law School. Bob Klein is a member of both the California Bar Association and the American Bar Association.

### Governor Jim Doyle



Governor of Wisconsin, Jim Doyle, has long been an outspoken supporter of stem cell research. Wisconsin is the birthplace of human embryonic stem cell research, where James Thomson announced the first isolation and culturing of hESC lines in 1998. Governor Doyle is strongly committed to promoting stem cell research in Wisconsin. He received the National Leadership award at the 2008 World Stem Cell Summit in Madison, in recognition of his long-term advocacy for stem cell research and his promotion of Wisconsin's strategic goal to invest \$750 million in biotechnology and stem cell research. Governor Jim Doyle attended Stanford University for 3 years, then finished his senior year at UW-Madison. He is a 1972 graduate of Harvard Law School. After he graduated from law school, the Governor moved to the Navajo Indian Reservation in Chinle, Arizona to work as an attorney in a federal legal services office. In 1976, Governor Doyle was elected Dane County District Attorney and served three terms from 1977–1982. When he left that office, he spent 8 years building his own private law practice until he was elected Wisconsin Attorney General in 1990. Governor Doyle was re-elected as Attorney General in 1994 and 1998. Between 1997 and 1998, he served as the president of the National Association of Attorneys General. He was elected as Wisconsin's Governor in 2002 and re-elected in 2006.



### Bernard Siegel



Bernard Siegel is the founder and full-time executive director of the nonprofit Genetics Policy Institute based in Palm Beach Gardens, Florida. He is the creator and co-chair of the World Stem Cell Summit that took place in Madison, Wisconsin in September 2008. He serves as the co-chair of the Governmental Affairs Committee of the International Society for Stem Cell Research. He received his undergraduate and law degrees from the University of Miami (BA 1972, JD 1975), and he is a member of the Florida Bar since 1975. In

2003, he traded his 30-year courtroom career to found Genetics Policy Institute, which leads the global 'pro-cures movement' in support of stem cell research. He is a recognized policy expert relating to stem cell research, regenerative medicine and cloning. Working with the world's leading stem cell researchers, Mr Siegel played a pivotal role in protecting nuclear transfer research in the United Nations, which was under the threat of being banned by world treaty. He also works with grassroots activists throughout the USA, educating lawmakers and formulating effective strategies supporting research for cures. He is a frequent lecturer, panelist and keynote speaker on the subject of stem cells and public policy.

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