

## Stem Cells: Progress and Controversy

A NextGen *Free Standing Perspective*

The words "embryonic stem cell research" can trigger any number of reactions from a crowd of people. Some will immediately pose scientific questions (i.e. What are the underlying mechanisms of pluripotency?). Others, however, will raise their voice in sharp opposition or support. Supporters will tout the potential benefits of stem cell therapies, while the opposition will denounce it as unethical. Despite the wide coverage in the media of the political issues involved, too often people are unaware of the underlying scientific facts or of the opinions of the doctors and scientists involved in the research.

Douglas Melton, a Harvard University professor and a Howard Hughes Medical Institute Investigator, is one of these scientists who has regularly been in the media and at the forefront of the research and the controversy. He made headlines in 2003 for his derivation of 17 new embryonic stem cell lines (which is currently at a total of about 30 cell lines) of which he freely offers to scientists and researchers for research purposes. When asked what potential therapies he could envision, Professor Melton replied, "As for what's being envisioned, a significant number of diseases are caused by cell defects or deficiencies including all neurodegenerative disorders, cardiovascular diseases, and diabetes. So if you take that on one hand a particular cell type is defective or deficient and on the other hand that stem cells can make other types of cells, it's not difficult to envision the use of stem cells to treat these cellular deficiencies."

The opposition, however, does not seem to notice. Instead, because embryonic stem cells are derived from blastocysts (very early stage embryos), many religious leaders and conservatives view it as tantamount to murder. Melton, however, disagrees: "I don't think there are any compelling ethical arguments against the use of embryonic stem cells. What many people don't understand is that embryonic stem cells are derived from leftover material that is going to be destroyed anyways (ie from in vitro fertilization clinics)." He went on to point out that the research was conducted only after ethical board reviews were conducted and full consent was received from the couples involved.



**Douglas Melton, Ph.D.**

To Melton, the need to do embryonic stem cell research is especially compelling as alternative methods to derive embryonic stem cells have fallen short. With regards to the work done by Rudolf Jaenisch and Alexander Meissner at MIT to "more ethically" derive embryonic stem cells through

creating mouse embryos deficient in a gene called Cdx2 (a gene only expressed in embryos), Melton noted that "If you inactivate Cdx2, you are essentially creating a defective embryo," something Melton believed to be avoiding the real ethical issue by making "a convoluted ethical argument." The steps required to inactivate Cdx2 also greatly complicate the procedure and slow the progress of research unnecessarily. Moreover, without fully understanding how Cdx2 functions in humans and embryonic stem cell development, the prospects of using this methodology do not appear good.

Some critics have argued that the research ought to focus primarily on the ethically uncontroversial adult stem cells. On the subject, Melton seemed somewhat shocked. "No scientist, at least none that I know, would seriously argue to focus only on one or the other. The scientific facts are very simple. There are adult stems only for certain systems in the body. One example is the hematopoietic stem cell which has been in use for years in bone marrow transplants. But, for some systems, such as the pancreatic beta cells that I study which have no adult stem cells, the option is not available. For a scientist, there is no 'either/or' distinction, only a need to look at the cells that are most applicable for the tissues and diseases that one is studying. This 'one or the other' distinction is a political distinction, not a scientific one."

When asked about his own views on the matter, Melton simply replied, "I think its difficult to justify on ethical grounds the failure to help treat persons who are suffering from such diseases [as neurodegenerative disorders]. If anything, I think there is only an ethically compelling argument to conduct such research and to make those therapies possible to treat those people."

On the subject of the Bush administration federal restrictions on embryonic stem cell research funding and the general confusion as to what that policy entails, Melton noted, "I think the main reason it's confusing to people is because the policy is a political compromise and not an ethical compromise. What it says is that embryonic stem cells in existence before August 2001 – which was when the Bush administration established a position on embryonic stem cell research – can be studied with federal funds. Any cell line made after August 2001, however was unethical."

As to why such a decision was so paralyzing, Melton commented that "the truth is that the vast majority, possibly over 99%, of medical advances come from federal funding through organizations like the NIH and the NSF – so this policy had a dramatic effect on research because of federal restrictions on mixing funding, excessive red tape – effectively dissuading many researchers, especially young people, from going into this research."

This is especially true given that the federal funding restriction essentially restricted research to a few cell lines, many of which have been verified as unsuitable for medical research. Moreover, the "federal restrictions on mixing funding" alluded to by Melton effectively prohibit the use of ANY equipment or facilities paid for by the federal government in conducting research on federally unapproved lines. Melton's group, for instance, had to acquire its funding "from scratch" from philanthropic and private avenues, something which Melton only described as "very difficult."

It is for this reason that Harvard has decided to start the Harvard Stem Cell Institute, appointing Professor Melton as co-director along with Dr. David Scadden, Professor of Medicine at Harvard Medical School and Director of the Center for Regenerative Medicine at Massachusetts General Hospital. Functioning as "a community of over 200 researchers spread over multiple campuses and teaching hospitals," the Harvard Stem Cell Institute unites a diverse set of scholars at institutions including Harvard's Faculty of Arts and Sciences, John F. Kennedy School of Government, Harvard Business School and Harvard Law School as well as the Dana Farber Institute and Massachusetts General Hospital, all for the goal of researching stem cells, the political and ethical issues surrounding them, and the means to transform them into viable therapeutic options.

When asked when such therapies would be available for use, Melton noted "[That is a] difficult question to answer because it depends on discovery. So in essence you're asking when will that discovery happen . . . and to tell the truth, I can't really answer that question. But, I can address it in a negative sense in that it's not going to happen in the next year or two, but it's possible it can happen in the next decade."

When asked if he had any advice to any pre-medical students or doctor-scientists eager to make a contribution to the field, Professor Melton's voice simply brightened up and noted: "That's easy. Come join us at Harvard Stem Cell Institute!" □

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