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A Conversation With Douglas Melton

At Harvard's Stem Cell Center, the Barriers Run Deep and Wide

By CLAUDIA DREIFUS

CAMBRIDGE, Mass. - To enter his laboratory at the Harvard Stem Cell Institute here, Douglas Melton must use a special key card that electronically checks his identity.

Even before President Bush barred federal financing for most human embryonic <u>stem cell</u> research in August 2001, the work of Dr. Melton was mired in controversy.

And once the ban was enacted, a new set of barriers rose, extending the scientists' challenges far beyond the test tube.

At Dr. Melton's lab, embryonic stem cells from fertilized human eggs are part of a search for a cure to Type 1 diabetes.

Though Dr. Melton's research is privately financed, he must certify that no federal money supports any of his efforts. Hence the key cards. They provide a kind of barrier against people and things that have a federal tie.

"Running a stem cell lab is a little like keeping a kosher kitchen: you've got to really keep things separate," said Dr. Melton, who is 52. "Actually, a kosher kitchen is probably easier."

Q. Last month, after the Korean stem cell cloning scandal broke, a Roman Catholic scientist-theologian, the Rev. Tadeusz Pacholczyk, told The Boston Globe that too many researchers in this renegade branch of science had been playing down the grave ethical concerns for much too long. What is your response?

A. My first response is, There's nothing unethical about what we're doing here. We think embryonic stem cells can be made to become pancreatic beta cells and that they will be able to help diabetics produce their own insulin. I've never once doubted the morality of this work.

This is all about differing religious beliefs. I don't believe I have the right to tell others when life begins. Science doesn't have the answer to that question; it's metaphysical.

Now it's true, we use fertilized human eggs to derive embryonic stem cells. And those fertilized eggs have the potential, under certain circumstances, to become a living person. There are many who believe that there's a moral imperative to use that potential to try to help living sick people.

I hold with them.

Q. You have a child at home with diabetes, right?

A. It's a little bit uncomfortable to talk about this. But it's not a secret. My interest was, for many years, in basic embryology.

When my son, Samuel, was about 6 months old, he came down with Type 1 diabetes, which means that his pancreas couldn't make insulin. About four years ago, my daughter came down with this same disease.

Like any parent, I asked myself, What can I do? The answer was to shift my research to an area that might help them.

I wanted my children to know I was doing everything I could for them.

Q. Does the Korean stem call scandal surrounding the stem cell research of Hwang Woo Suk make your work harder?

A. It has to raise, in the public's mind, the question as to whether there's legitimacy to this kind of science. Fortunately, stem cell research is not dependent on one discovery. Even though Hwang's findings turned out to be fraudulent, nothing he claimed was a fundamental challenge to the principles of embryonic stem cell research.

Hwang claimed to have successfully cloned human embryos, which was only a technical accomplishment. It's something that's already been done in animals.

If you ask me what really holds this research back, I'd say that the policies of the Bush administration have affected us more significantly than

the Hwang debacle. The lack of federal support keeps many of America's brightest young scientists from working in this area.

Q. Were you ever skeptical of Dr. Hwang as he reported a succession of breakthroughs in human stem cell research?

A. I'd like to tell you I suspected something. I didn't. When his papers were published, I read them carefully. I was impressed by the speed and the efficiency by which he'd cloned a human embryo. We hadn't done those experiments ourselves. So I didn't know how difficult it would be in humans.

I met Dr. Hwang and his colleagues several times. He didn't seem nutty, squirrely or deceptive or anything like that.

O. How exactly has President Bush's ban on federal financing for most embryonic stem cell study affected your research?

A. It made it more difficult, to say the least. Long before Bush's speech, we had planned stem cell experiments. Afterward, we were able to go forward because the Howard Hughes Medical Institute, the Juvenile Diabetes Association and Harvard alumni provided private funding.

However, because of administration policy, we had to set up this whole new laboratory that was separate from everything else here at Harvard.

And we had to separate the money in a really scrupulous way. We have an accountant who makes sure that not a penny of federal funds goes to embryonic stem cell research. We have separate everything - light bulbs, computers, centrifuges.

This can be burdensome. Most of the activities at this university receive federal money in some indirect way. So you have to ask yourself, "How can you do the research without any imprint of federal funding?"

And we're not just talking about equipment and real estate; it's people. Let's suppose there's a graduate student who's receiving a federally funded fellowship, can he or she participate in thinking about this research or even look at the data? The answer is no.

Q. Some say that your laboratory's existence proves that the Bush administration's directive didn't stop research in this controversial area. Are they right?

A. Listen, I'm a tenured professor at Harvard, where I have a president who backs my freedom of inquiry - and puts money behind it. If I'd been at a state college, it would have been a different story. Though some states are now keen to support stem cell research, state governments, at first, were very worried.

The bottom line here is that it's unlikely that one person or one lab will solve a problem as big as degenerative diseases, which is what stem cell researchers are trying to do.

It takes a community of people in an area to solve a big problem. If you were trying to solve <u>cancer</u> at two places, no one would think that was enough.

Q. Your lab created 30 stem cell lines and offered them free to any scientist who wanted them. Why?

A. Because in his speech, President Bush said that he was going to permit federal funding for scientists to work with some 60 pre-existing stem cell lines and it turned out that there were probably only about 10 usable lines. Maybe a few more.

And many of those were problematic. Some had abnormal chromosomes, like a cancer cell might. If you're using stem cells to create pancreatic beta or muscle or nerve cells, you want to begin with high-quality normal cells.

All the pre-existing lines were grown with mouse cells - which probably means you can't ever use them with human patients to treat diseases. Some of the lines, when researchers asked for them, came from a biotech company or some investigator who wanted to impose onerous restrictions on their use.

So we made our cell lines because we thought there aren't enough human stem cell lines around for researchers to really explore their properties.

We offered them free of charge because there's a long scientific tradition of making the fruits of one's research available to others.

Q. How far have you gotten in your quest to find a way to make pancreatic cells that will produce insulin for patients?

A. I'd say we've made progress. We don't know exactly how much because we don't yet know how many pieces there are in the puzzle we're trying to solve. I'm an optimist, though. I don't think we'll fail.

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