States step in for stem cell research

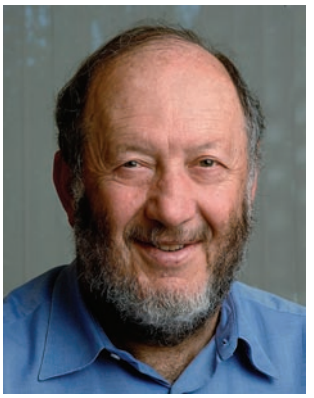
In the late 1930s, Joseph Stalin favored the neo-Lamarckian theories of Trofim Lysenko and created policies to suppress Mendelian genetic studies in the Soviet Union. This repressive situation caused many of the top Soviet geneticists to emigrate to other countries, including Theodosius Dobzhansky, one of the most influential geneticists of the twentieth century, who came to the United States. The Soviet Union, a previously world-renowned scientific center for genetics, was subsequently relegated to relative scientific obscurity for the next several decades.

In the 1980s, the Congress of the United States considered banning recombinant DNA technologies out of concern for their potential misuse. Ultimately, however, Congress decided to regulate rather than ban this area of research, and an entire new field of science developed that has resulted in uncounted new treatments and technologies.

In August, 2001, President George Bush signed into law a ban on embryonic stem cell (ESC) research that limited the use of federal funds to a small number of ESC lines that had already been created. How this ruling will ultimately affect US science and medicine will be a matter that is judged by future historians.

Several US states, however, are not content to wait to see if such federal restrictions will ultimately be harmful to the health of the citizens of the US and its scientific community and have passed laws, or are preparing laws, that allow the use of state funds for ESC research.

In September of last year, California was the first state to pass a bill specifically allowing the use of state funds for ESC research. New Jersey followed suit this year with its own ruling allowing the use of such funds. Additional states that are preparing similar legislation include Maryland, Massachusetts, Minnesota, New York, Pennsylvania, Rhode Island, Tennessee, and Washington. Other states, however, such as Arkansas, Iowa, Michigan, Nebraska, and North Dakota, have taken the opposite stance and have placed bans on several or all forms of ESC research within their jurisdictions. (The National Conference of State Legislatures website provides a detailed list of current allowed uses of ESCs in various states [http://www.ncsl.org/programs/health/genetics/embfet.htm].)



Irving Weissman feels that state support is now essential to maintain cutting-edge research.

Feelings among the public and among researchers vary considerably about the importance of such legislation and how it will affect the future of research.

Irving Weissman, of the University of California at San Francisco and head of the 2001 National Academy of Sciences panel on reproductive cloning and its effect on nuclear transfer legislation, works with adult stem cells but feels strongly that funding at all levels should be available for ESC research.

"Embryonic stem cell research allows the use of the technique of nuclear transfer to make new pluripotent cells," Weissman told the *JCI*. "This opens a whole new field that we can't get at with adult stem cells." Weissman pointed out that such techniques can provide essential means for studying both molecular and developmental aspects of disease by creating specific cell lines using nuclei from individuals with a disease.

Weissman noted by way of example that "we could have for the very first time an authentic Lou Gehrig's disease cell line, and then we can repair the genes one at a time and see which cell line can develop nerves that do not degenerate."

Martin Grumet, of Rutgers University, who works on spinal chord injury using rat embryonic stem cells, also shared his thoughts with the *JCI* concerning stem cell research. "The nuclear transfer technique is very powerful because it allows you to get around some of the problems in terms of histocompatibility if these cells are to be used therapeutically. Additionally, I don't think you want to restrict researchers from doing things that aren't blatantly unethical because you never know where a solution to a problem is going to come from."

Grumet does feel that, at least for the short term, it is okay to limit federal funding to the approved NIH embryonic stem cell lines. However, "in the long term," he added, "one can imagine that we will need to modify the existing legislation."

Although he has not been personally involved in the development of any of the legislation and currently is not directly affected by the funding restrictions, Grumet feels that state legislation supporting ESC research is important.

"Given that the federal government has taken its stand," he said, "if the states don't take a positive stand, we will lose research and researchers to foreign countries that allow and encourage this type of work. And I believe we've lost some already. If you consider that there is more money spent on health care in this country than probably almost all the outside world combined, then you are talking about a major force being handicapped. The efforts of New Jersey and California and other states to open up research in these areas are going to be very important."

Weissman agrees that bans on ESC research and lack of funding will have negative effects on attracting and keeping top researchers. As other state governments contemplate devising their own laws, he encourages them to consider how legislation in ESC research will affect their states. "If you ban this type of research, as

Martin Grumet believes that current restrictions may need to be revisited.

Gary Friedman thinks that private funding is the best way to stimulate ESC research.

Nebraska and Iowa have done, think about the biomedical institutes you have built, and what you are going to do when human cell lines become available, for example, for type 1 diabetes in another state, and you have just banned people from using those lines. Your best and brightest will go somewhere else."

Others are not quite so convinced that loss of funding at the federal and state level will necessarily impede research. Gary Friedman, head of Regenerative Medicine at Morristown Hospital, who is aiding in developing an endowment for stem cell research in New Jersey, told the *JCI* that it is important for people who are interested in pursuing stem cell research to "redirect their thinking from 'Great Society' type funding to the economic reality of the post–dot-com era. The days of quick investment and return on little substance are over. True economic connection to actual stem cell product will guide the success of this endeavor."

"Brain drain," Friedman stated, "is just a euphemism for failure to adapt. We are presumably all responsible adults involved in the stem cell endeavor and must consider the positions and concerns of all parties involved if we are to move forward in an effective manner. There are no superstars in this endeavor, and it is important to realize that the greatest contributions will come from the greatest team, not the almighty individual."

The two states that have passed legislation to allow ESC research have taken different approaches.

While the California bill, which was designed by Senator Debra Ortiz, approved the use of state funds for ESC research, it did not specifically put aside money in the state budget for such research. Many people therefore felt that this was a positive but ultimately empty piece of legislation. To remedy this, several researchers, funding institutions, and politicians have devised a ballot initiative for the November state election that, if approved, will specifically designate three billion dollars in state funds for ESC research. Ultimately, therefore, for California, the potential $295 million a year for the next ten years that this fund could provide is in the hands of its citizens.

In contrast to the California bill, the New Jersey bill, which passed this January by only a single vote, earmarked specific funds for ESC research. Assemblyman Neil Cohen, who sponsored the New Jersey bill, told the *JCI* that "the governor is using state funds for this research that are for the development of biotechnology and the development of businesses in New Jersey. He's utilizing those funds to create a stem cell center at Rutgers University. And he's also looking to be able to provide funds for biotech companies who want to do stem cell research in New Jersey." Cohen indicated that at least a dozen companies had already expressed a great deal of interest in the New Jersey program.

Additionally, Cohen said, "we have created a stem cell research endowment fund and are also creating a separate entity, a biomedical fund, which is going to be a cybersite that will have ongoing stem cell research projects listed on it."

"We are holding a stem cell summit on April 24th," Cohen said. "It will include all the major biotech companies, institutes, and hospitals, along with researchers and financial institutions. By contributing to the endowment fund, an institution will then be able to collaborate in ongoing research projects."

Assemblyman **Neil Cohen** sponsored the recent New Jersey ESC funding bill.

Gary Friedman has been playing a lead role in bringing the New Jersey stem cell summit to fruition and feels this initiative is one of the best ways to truly promote such research.

"There is no state in the union that has enough money to fund these kinds of projects," Friedman told the *JCI*. "You need a minimum of 250 million dollars per use of stem cells to really push this initiative. And that's after you have all the facilities up and built and ready to run."

The cybersite, known as the New Jersey BioMed Zone, is a for-profit site that Cohen and Friedman feel will best be able to generate the large amounts of money required for such research. Friedman explained that the BioMed Zone "creates a safe haven for research. Agreements are signed before the researchers ever post their information. All the work is proprietary, and if the work is hijacked in any way, there are significant penalties for the hijackers. Research cannot be viewed by anybody until they have anted up in support of the endowment fund in the BioMed Zone."

And that ante is between one and twenty million dollars. While that may seem a steep price to pay, Friedman looks at it this way: "If you look at a company that has its pipeline drying up, it is difficult for them to invest 250 million dollars, but to ante up between one to ten million dollars is insignificant in comparison. Especially if one of these cell lines leads to a treatment that will likely ultimately be worth a trillion dollars."

As other states come forward with their own directives and initiatives, the community will be better able to gauge which funding mechanisms work best to spur ESC research, whether the promise of such work plays out as viable treatments, and if certain past legislation requires revisiting sooner rather than later.

Irving Weissman identified the crux of the issue: "The states are the laboratories of democracy," he told the *JCI*, "With them we will see whether banning research is better than regulating research." Weissman further noted that this is the first instance in US history wherein a line of scientific research has been banned when there is no clear-cut medical or ethical reason to do so. While future historians will be able to reflect upon this decision dispassionately, individuals currently waiting for therapies and cures may not be so lucky.

Laurie Goodman