

U.S. Embryonic Stem Cell Research: Can Young Researchers Succeed?

Sarah Webb
United States
22 September 2006

Sharyn Rossi's entry into neuroscience research using human embryonic stem cells (hESCs) required a full year, a bit of luck, some persistence, and a difficult cross-country move. The New Jersey native applied to 20 graduate programs, including some in nearby New York, but she was unable to find a position close to home. Then in early 2005, she became interested in the work being done in Hans Keirstead's lab at the University of California (UC), Irvine.

Rossi was accepted into UC Irvine's graduate program, but Keirstead didn't have space for her in his lab initially. The move involved some sacrifice, and at first she wasn't sure she had made a good decision. "I wasn't very happy in California, not working [in Keirstead's lab]," she says. She did a summer lab rotation in the lab before starting graduate school, then worked in another lab for the fall quarter. But she continued to talk to Keirstead regularly as she waited for a spot to open. Her chance came in January, at the beginning of the winter quarter. "Now that I'm in his lab, I really love it out here," she says.

Now, just a few months later, her research (which is supported by a fellowship from California's bond-issue-supported California Institute for Regenerative Medicine, or CIRM) is progressing well, but she's nervous about her career in a field in which politics has created a difficult funding climate and an uncertain future.

In the United States, presidential mandates and legal hurdles are major obstacles to funding and carrying out research involving hESCs. State governments--especially California's--and a few private foundations are scrambling to fill the gap. Still, a new generation of stem-cell scientists is forced to contend with restrictions that go well beyond what other early-career scientists--and established stem-cell scientists--must face.

Beginners take nothing

National Institutes of Health (NIH) guidelines limit the use of federal funds to work done on hESC lines developed before the 9 August 2001 [presidential mandate](#). Those restrictions include the use of NIH infrastructure--incubators, petri dishes, culture media, and even office supplies. Many of the NIH cell lines are difficult to grow and were developed from mouse feeder cells, making them unusable for clinical applications. Despite those restrictions, NIH continues to play a dominant funding role even for trainees and researchers whose ultimate interests lie beyond research governed by NIH regulations. State funding is a boon to researchers in states such as California, and private funding offers other opportunities, but NIH funds still form the core of many stem-cell research programs.



Evan Snyder

Whether it comes from NIH or other sources, experts say the money that's available goes mostly to the few centers--such as the Burnham Institute in San Diego, California, Harvard's Stem Cell Institute, the University of Wisconsin, Madison, and the University of Georgia--that already have the resources needed to carry out large-scale stem-cell research--or to a few other labs that are already recognized for their work on stem cells. "If you are a recognized stem-cell lab, then that is where you either get federal funding or [where] companies or foundations funnel their funding. If you are recognized, you probably don't have as much trouble," says Evan Snyder of the Burnham Institute. Because he works at a major center, Snyder has a lot of discretion to fund trainees in his group to do work they are interested in--although a project must, of course, fall within NIH guidelines if NIH money or infrastructure is used.

For researchers just starting out, finding funding is much harder. "Where I think you're going to see a problem is the new lab that wants to get into stem-cell research that hasn't previously been doing it or a lab that may be doing stem-cell research but is in a state that really underfunds it," Snyder says. "They need to compete with NIH funding for that topic as they would for any other topic in this climate of not enough money for research." Without this support, he says, many of these researchers may decide that the challenges are insurmountable and choose another related field.

But restrictions on the use of NIH-funded infrastructure may present an even more serious problem for investigators just starting out in the field. New investigators outside the major stem-cell hubs might be able to get a small grant from a private foundation or a state government, but if the work falls outside the NIH-approved guidelines, she won't be able to use existing freezers, incubators, sequencers, or other equipment funded either wholly or in part by government research grants. To separate the work, institutions such as UC Irvine and the University of Wisconsin are constructing buildings to separate research activities that do not fall within NIH rules from those that do. Many researchers see the duplication as wasteful, but under the current regulations, it's necessary.

Funding from an NIH-sponsored training grant and the recognition of the University of Wisconsin's WiCell as a center for embryonic stem-cell research factored heavily into Tom Keenan's decision to take a postdoctoral position there. "I knew that Wisconsin was the place to go because it had WiCell and the access to the stem-cell lines and the stem-cell bank that was not available elsewhere," he says. "At Wisconsin, I knew that I could be successful."



Raj Rao

Hedging their bets

Because Virginia is not among the states providing substantial funding for stem-cell research, Raj Rao, an assistant professor at Virginia Commonwealth University in Richmond, is seeking funding from private foundations, even though currently all of his lab's work falls within the NIH guidelines. He hopes the future will bring changes to NIH policy, but in the meantime he thinks it's a good idea to "not be totally dependent on NIH funding." Other researchers share Raj Rao's view: They're optimistic that NIH restrictions will be loosened in the near future, but they see wisdom in diversifying their funding portfolios--even in California, where, despite continuing legal challenges, Governor Arnold Schwarzenegger has already advanced \$150 million of the promised \$3 billion over 10 years to CIRM. The process of disbursing state money to California investigators is moving forward.

Almost all U.S. researchers work on adult stem cells or mouse stem cells instead of or in addition to hESCs. Senior researchers often advise trainees to have a backup plan and not to work exclusively with embryonic stem cell lines. In some cases, the alternatives are well suited to the research problem or may serve at least as a useful model--but not always. In "my lab, it was always 50% of the people worked on adult stem cells or embryonic stem cells part of the time," says Mahendra Rao. "Almost everyone did stem-cell work, but we mixed and matched so that you were asking a question and that question could be answered with the mouse cells and human cells, or it could be answered with human embryonic cells and adult stem cells." Many students, he says, refused to work with only embryonic stem cells.

Public engagement

In addition to the practical issues of day-to-day research, many researchers who work with embryonic stem cells deal with the public more than their colleagues in other fields do. "I'm in a field where I sometimes have to keep justifying what I'm doing because there are a lot of public misconceptions," says Raj Rao. "Technically, it is a distraction, but I feel as if it's part of my civic duty as a scientist to get involved in these kinds of issues," says Snyder. Still, "I'm resentful that it's required."

"Even when we have these debates, people are surprisingly open to looking at possibilities," says Mahendra Rao. "I've never had someone in the audience come up to me and tell me that I'm going to die and go to hell because what you're doing is morally and ethically wrong. I've had people come up and tell me that they personally would not want to do this sort of experiment, but they understand our rationale and why they don't think that what we're doing is criminally wrong," he says. The debate has been surprisingly open-minded across the board, he says, even with religious leaders. The sharpest disagreements about the policies result from conversations with U.S. government officials, he says.

For some graduate students, concern about the difficult funding climate and about public understanding of embryonic stem-cell research have catalyzed advocacy work. In 2003, Marion Riggs, now a graduate student in Raj Rao's lab, started the Student Society for Stem Cell Research ([SSSCR](#)), which now has more

than 100 chapters around the United States. Rossi recently founded an SSSCR chapter at UC Irvine.

Stem-cell funding sources--from a [28 July 2006 article](#) in *Science* (subscription req.)

State funding:

- California: \$3 billion over 10 years
- Connecticut: \$100 million over 10 years
- Illinois: \$15 million via executive order
- Maryland: \$15 million this year, as a start
- New Jersey: \$5 million this year
- Wisconsin: \$5 million to attract companies--also involved in building a \$375 million facility at WiCell

Private funding:

- Michael Bloomberg: \$100 million to Johns Hopkins University
- Starr Foundation: \$50 million to Rockefeller University, Cornell University, and Memorial Sloan-Kettering Cancer Center
- Broad Foundation: \$25 million to the University of Southern California
- Ray and Dagmar Dolby: \$16 million to UC San Francisco
- Stowers Medical Institute: \$10 million to Kevin Eggan and Chad Cowan at Harvard
- Leon D. Black: \$10 million to Mt. Sinai School of Medicine
- Private donors: almost \$40 million to Harvard Stem Cell Institute

NIH funding (estimated FY 2006)

- \$609 million for stem cells--all types
- \$38 million for hESC research

Standing on the sidelines

Despite the funding obstacles and the political challenges, researchers encourage trainees to enter the field if they're passionate about the science and they've found an interesting question that they want to address. These scientists are optimistic that the political climate will change with future elections and the evolution of public opinion--or that scientific progress will make some of the ethical objections obsolete.

But even with this optimism, many of the cutting-edge innovations in embryonic stem-cell research are coming from projects that are not funded by the U.S. government and that fall outside the NIH guidelines, leaving many federally funded researchers watching from the sidelines--and waiting. In the meantime, says Keenan, stem-cell researchers are doing the best they can with what they have: "But I guess in some sense, everyone is looking for a brighter day, trying to hold on until we have full freedom to do what the science tells us we need to be doing."