Stem cell start-up

by Tim Stephens

UC Santa Cruz's programs in biomedical research have earned the campus a major role in one of the most exciting—and controversial—new areas of science.

Over the past two years, the California Institute for Regenerative Medicine (CIRM) has awarded UCSC nearly $5 million in grants for training programs, faculty research, and dedicated laboratory facilities for stem cell research.

Newly funded projects have potential applications for understanding and treating neurodegenerative conditions, such as Parkinson's and Lou Gehrig's disease, and spinal cord injuries. At the same time, as part of a new training program in stem cell biology, faculty and students on campus are exploring the ethical issues raised by research involving human embryonic stem cells.

CIRM was established in 2004 with the passage of Proposition 71, the California Stem Cell Research and Cures Initiative. After overcoming legal challenges, CIRM has distributed more than $200 million in funding for stem cell research at the state's universities and research institutions.

"The people of California have made an incredible commitment to support this kind of research, which will help us answer important questions in developmental biology," says Sofie Salama, a research biologist in UCSC's Center for Biomolecular Science and Engineering (CBSE).

The proposition that established CIRM was a direct response to restrictions on stem cell research imposed by the Bush administration. Currently, researchers using federal funding can study only the small number of human embryonic stem cell lines in laboratory use as of August 2001. Cell lines isolated after that date cannot be studied in laboratories built or equipped using federal funding.

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A $2.7 million CIRM grant announced in June is funding a shared stem cell research facility in UCSC's Sinsheimer Laboratories Building. Because it is entirely funded by the state, research at this facility is not subject to the federal restrictions, allowing UCSC researchers to work with new lines of human embryonic stem cells.

Lindsay Hinck, an associate professor of molecular, cell, and developmental biology who directs the facility, says the few lines of human embryonic stem cells approved under the federal policy have limited usefulness. "They don't grow well, many of them are contaminated, and they were derived in suboptimal conditions," she says. "So it is really important to be able to bring in new stem cell lines that can open up the potential for medical breakthroughs."

Growing and studying human embryonic stem cells in the laboratory is difficult and requires specialized equipment and expertise. The research is challenging, and it may take years to translate laboratory findings into medical advances. But the potential benefits are enormous. Hinck and her colleagues are thrilled about the new directions they can now pursue in their investigations.

"Most of us do basic research using model organisms, like fruit flies or mice, and incredible discoveries get made in simple organisms. But most scientists also want to do the next step, to see how their findings apply to human cells," Hinck says. "With a stem cell research facility at UCSC, we can follow up on our findings in a system where the results directly inform us about potential ways to improve human health."

Because stem cells are unspecialized, they are able to renew themselves indefinitely and can also differentiate into more specialized cell types. The ability to grow and manipulate human stem cells in the laboratory is already an extremely powerful tool for understanding human development and disease processes. Eventually, stem cells may be used therapeutically to replace damaged or dysfunctional cells in the body.

The use of human embryonic stem cells for research and, potentially, for medical therapies has raised ethical issues, mostly centering on how the stem cells are acquired. The process of taking stem cells from an embryo disrupts it; stem cells can be grown in culture dishes, but the embryo is no longer viable. Human stem cell lines are derived from embryos created in fertility clinics through in vitro fertilization and donated for research purposes with the informed consent of the donors.

Many people regard the destruction of human embryos as unethical, says Ellen Suckiel, professor of philosophy and provost of Stevenson College. "The moral issues surrounding stem cell research are among the deepest challenges we face today," she says.

Suckiel teaches an ethics course as part of the stem cell training program, which includes a broad range of courses designed to offer a comprehensive education in stem cell science and ethics. The training program also provides funding for three predoctoral fellows (graduate students) and three postdoctoral fellows engaged in stem cell research.

UCSC's proposals have fared well in every round of the competition for CIRM grants. The campus has won funding on a par with much larger institutions, such as UC Berkeley and UC San Francisco.

"We have an interdisciplinary group of biomedical researchers who really interact well together, and we have done a great job coalescing around the goal of bringing stem cell research to Santa Cruz," Hinck says.

David Feldheim and Bin Chen, both assistant professors of molecular, cell, and developmental biology, received CIRM research grants in March. Feldheim studies the development of neural circuits in the brain, while Chen focuses on the development of corticospinal motor neurons, which control voluntary muscle movements and are affected in neurodegenerative diseases and spinal cord injuries.

"In theory, if we can learn how to create pure populations of neurons from stem cells in the laboratory, they could be transplanted back into people with neurodegenerative diseases," Feldheim says.

According to Chen, humans have hundreds of thousands of different types of neurons, and in the cortex of the brain there are tens of thousands, all generated from the same stem cell population. "How do the same cells give rise to so many different kinds of neurons? That's the mystery," Chen says. "We are looking for genes that, when they are expressed in stem cells, drive them to become certain types of cortical neurons."

This is the kind of fundamental information needed before successful stem cell therapies can be developed, says David Haussler, professor of biomolecular engineering and a Howard Hughes Medical Institute investigator.

"The main thing missing is still basic knowledge about how human cells work," he says. "What happens in a cell as it differentiates from a stem cell into a liver cell or a neuron? We still don't understand how that process occurs. And UCSC is in as good a position as any other university in California to make important contributions in this area."

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UC Santa Cruz stem cell scientists (l–r) Armen Shamamian, stem cell laboratory manager; Lindsay Hinck, associate professor of molecular, cell, and developmental biology; Sofie Salama, staff research specialist in the Center for Biomolecular Science and Engineering; and David Feldheim and Bin Chen, both assistant professors of molecular, cell, and developmental biology