The Golden Cells

July 25, 2008

UCSB researchers from a wide range of disciplines—biology, psychology, bioengineering and more—are getting into the stem cell field. They’re working in three general areas: regenerative medicine, basic biology, and bioengineering and biotechnology. These are a few of the stem cell projects underway on campus:

Regenerative Medicine

The great promise of stem cells is that they might be used to produce replacement parts for cells or tissue damaged by disease or injury.

Dennis Clegg, chair of the Department of Molecular, Cellular, and Developmental
Biology and co-director of the Center for Stem Cell Biology and Engineering, and other UCSB scientists are part of a group of researchers—the Southern California Consortium for Regenerative Eye Research—that’s working on stem cell treatments for eye disease.

Many devastating eye diseases like macular degeneration, the most common cause of blindness in older adults in the United States, rob people of their vision by killing cells in the eye. Scientists hope to treat those kinds of afflictions by replacing the lost ocular cells with new ones derived from stem cells.

Scientists at UCSB are studying how stem cells turn into eye cells. They’ve succeeded in coaxing stem cells to differentiate into retinal pigment epithelial cells, which nourish and support the eye’s vital photoreceptors, which respond to light. It’s these retinal pigment epithelial cells that are casualties of age-related macular degeneration. Clegg says this might be the first work out of UCSB to result in a clinical application. The prospects of being able to use stem cells to treat macular degeneration “look quite good,” he says.

Another UCSB researcher, Tod Kippin in the Department of Psychology, is focusing on stem cells in the brain. Until fairly recently, the adult brain was thought to be incapable of producing new cells to repair itself, but it’s now known that neural stem cells generate new brain cells—a phenomenon called neurogenesis—throughout our lives in the areas of the brain involved in memory and learning, and in processing odors.

UC Santa Barbara’s Dennis Clegg, James Thompson, and Tom Soh participated on a panel at a Town Hall at UC Santa Barbara in July. The event, which was open to the community, helped raise awareness and answer questions about stem cells and the research being done at UCSB.

Scientists don’t yet have a good understanding of the functioning and importance of adult neural stem cells, but there’s evidence that problems with neurogenesis may play a part in some brain diseases and disorders such as depression.

Kippin is studying neural stem cells in mice and looking at what happens to them when the animals have brain disorders. He’s looked at mice with Huntington’s disease, an inherited condition that destroys nerve cells in the brain, resulting in mental and physical decline. Kippin found that even as the disease kills off brain cells, the number of stem cells in the brains of the affected mice actually increases. He’s now working on ways of helping the brain repair itself and overcome the devastation of Huntington’s disease.

**Stem Cell Biology**

Stem cells have an amazing and potentially very useful ability to develop into specialized cells, but scientists don’t know exactly how they do it; how they can keep
dividing indefinitely and how they can produce muscle, liver, skin, or nearly any other type of tissue in the human body.

"We still don't know what makes a human embryonic stem cell a human embryonic stem cell," Clegg says. "It's an amazingly powerful cell, but we still don't understand how it works."

UCSB researchers are working on the problem by studying the basic biology of both embryonic and adult stem cells.

There are limitations, however, to the research that can be done on stem cells in humans, so "if you want to look at how stem cells act, it's often helpful to have an organism where you can grow it up and manipulate it and do genetic and biochemical studies," Clegg says.

"It's not enough if a patient loses brain cells to put stem cells in their brain. You need to be able to tell them to become nerve cells," says Rothman.

Joel Rothman in the Department of Molecular, Cellular, and Developmental Biology is looking at stem cells in the worm Caenorhabditis elegans—one of the most well-understood organisms, thanks to countless studies on everything from aging in the worm to the effects of alcohol. Most of the genes known in worms have the same function in humans, Rothman says.

He wants to know how stem cells become committed to developing into a particular cell type, because "one of the things we want to be able to do with stem cells in humans is tell them to become a particular kind of cell," Rothman says. "It's not enough if a patient loses brain cells to put stem cells in their brain. You need to be able to tell them to become nerve cells." Rothman has found that small pieces of RNA called microRNAs seem to control the "switch" that tells stem cells to develop into something more specialized.

He's also trying to figure out if it's possible to prompt a specialized cell to turn back into a stem cell by turning off certain genes. Thomson has converted human skin cells back into stem cells called induced pluripotent stem (iPS) cells by adding four genes, but Rothman hopes to do it without having to insert any genes.

Stem cells produced from a patient's own tissue could be used to supply replacement tissue that would be immunologically matched. That approach would also avoid the ethical issues associated by some of the use of stem cells taken from donated human embryos.
Bioengineering and Biotechnology

If stem cells are to become a routine treatment for disease and injury, there have to be efficient, effective and safe ways of growing and handling them, and making sure they get to the places in the body where they’re needed.

The science of producing stem cells “is really in its infancy,” Clegg says, and “we don’t understand all the factors that are significant.”

Human embryonic stem cells are currently grown on material derived from mice. That might be fine for experimental work, but “if you want to use stem cells for human therapies, you’ll have to have cleaner ways of growing them,” Clegg says, “because if you’re growing them on animal products you might have an animal virus and the Food and Drug Administration just wouldn’t approve it.”

Biotechnologists and bioengineers at UCSB are working on ways of producing stem cells using new, synthetic materials. An improved method of growing stem cells “could be applied very rapidly in the field,” Clegg says.

When embryonic stem cells are used to produce specialized cells, the result is a mixture that includes some of the desired target cells, and “other cells that didn’t take that lineage,” explains Hyongsok (Tom) Soh, an associate professor in the Department of Mechanical Engineering and co-director of the Center for Stem Cell Biology and Engineering. “It’s very important to purify at almost every step.”

To do that, two different technologies are needed: “affinity reagents” that specifically label the target cells, and instrumentation that can sort out those cells. Soh’s laboratory works in both research areas, labeling target cells so they react differently to electrical or magnetic fields, allowing the cells to be sorted accurately and rapidly. Such technologies are invaluable for stem cell research and cell-based therapeutics.

“We’re developing the technology that’s needed to bring stem cell technology to a point where it’s economically viable,” Soh says.

Relevant links:
UCSB Center for Stem Cell Biology and Engineering:
stemcell.ucsb.edu

UCSB Department of Molecular, Cellular, and Developmental Biology:
mcdb.ucsb.edu
Stem Cell Pioneer Jamie Thomson

When University of Wisconsin researcher James “Jamie” Thomson, widely recognized as the “father of stem cell research,” visited UC Santa Barbara a few years ago, his interest was piqued by several of the university’s researchers and their work. Those encounters and UCSB’s strength in engineering prompted Thomson to seek out an affiliation here.

Now Thomson has a new laboratory here and is a co-director of UCSB’s Center for Stem Cell Biology and Engineering. He was appointed an adjunct professor in Molecular, Cellular, and Developmental Biology (MCDB) last year; while he still has a full time faculty appointment in Wisconsin, Thomson visits UCSB every month and otherwise maintains a steady exchange of ideas and advice between Wisconsin and Santa Barbara.

“There is a lot of back and forth,” he says, “not just me, but postdocs as well.”
Thomson says UCSB’s excellence in engineering means the university has a lot to offer him, and the stem cell field in general, since the ability to efficiently and effectively produce, sort and deliver stem cell products is what will make them useful on a large scale for research and potentially clinical applications.

Santa Barbara’s coastal location is also a factor—it not only provides Thomson with a respite from harsh Wisconsin winters, but also gives him easy access to marine organisms that he can use for research.

Thomson’s primary collaboration here is with Hyongsok (Tom) Soh of the Department of Mechanical Engineering. Soh, also a co-director of the Center for Stem Cell Biology and Engineering, is developing methods of quickly and accurately sorting cells. That collaboration, Thomson says, is “the one that’s exciting me currently. That’s something that I can’t do elsewhere.”

Thomson is also working with Dennis Clegg, chair of MCDB and the third co-director of the Center for Stem Cell Biology and Engineering, and other researchers on using stem cells to produce eye cells that could perhaps replace those lost in diseases such as macular degeneration, the leading cause of blindness among older people in the United States.

The stem cell pioneer’s association with UCSB has energized research here and helped push the university further up the ranks of the many institutions where stem cell research is underway.

In 1998, Thomson was the first person to isolate human embryonic stem cells—an achievement that opened up an exciting new field of research that scientists believe is leading to a greater understanding of our biology, and toward treatments or even cures for a litany of human diseases, from diabetes to Parkinson’s. Because embryonic stem cells can develop into nearly any kind of cell found in the human body, they can potentially be used to produce replacement parts for cells or tissues damaged or destroyed by disease or injury.

Thomson chalked up another milestone contribution to the stem cell field last year,
when he succeeded in transforming human skin cells into stem cells by adding four genes, a feat also reported at the same time by Shinya Yamanaka of the University of Kyoto in Japan. Thomson says the resulting stem cells are indistinguishable from embryonic stem cells. The achievement won him a spot in Time magazine’s list of the “World’s Most Influential People” of 2008.

If stem cells can be obtained that way, cells or tissues derived from them will be an immunological match to a patient, overcoming the problem of the body rejecting foreign cells. The approach could also avoid some of the issues associated with the use of human embryonic stem cells.

Relevant links: