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Stem cell agency's grants to UCLA help set stag for revolutionary medicine

Shaun Mason | January 29, 2014

Scientists from UCLA's Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research were today awarded grants totaling more than $3.5 million by California's stem cell agency for their ongoing efforts to advance revolutionary stem cell science in medicine.

Recipients of the awards from the California Institute of Regenerative Medicine (CIRM) included Lili Yang ($614,400), who researches how stem cells become rare immune cells; Denis Evseenko ($1,146,468), who is studying the biological niche in which stem cells grow into cartilage; Thomas Otis and Bennet Novitch ($1,148,758), who are using new techniques to study communication between nerve and muscle cells in spinal muscular atrophy; and Samantha Butler ($598,367), who is investigating the molecular elements that drive stem cells to become the neurons in charge of our sense of touch.

"These basic biology grants form the foundation of the revolutionary advances we are seeing in stem cell science," said Dr. Owen Witte, professor and director of the Broad Stem Cell Research Center. "Every cellular therapy that reaches patients must begin in the laboratory with ideas and experiments that will lead us to revolutionize medicine and ultimately improve human life. That makes these awards invaluable to our research effort."

The awards are part of CIRM's Basic Biology V grant program, which fosters cutting-edge research on significant unresolved issues in human stem cell biology, with a focus on unravelling the key mechanisms that determine how stem cells decide which cells they will become. By learning how such mechanisms work, scientists can develop therapies that drive stem cells to regenerate or replace damaged or diseased tissue.

Lili Yang: Tracking special immune cells

The various cells that make up human blood all arise from hematopoietic stem cells. These include

special white blood cells called T cells, the "foot soldiers" of the immune system that attack bacteria, viruses and other disease-causing invaders. Among these T cells is a smaller group, a kind of "special forces" unit known as invariant natural killer T cells, or iNKT cells, which have a remarkable capacity to mount immediate and powerful responses to disease when activated and are believed to be important to the immune system's regulation of infections, allergies, cancer and autoimmune diseases such as Type I diabetes and multiple sclerosis.

The iNKT cells develop in small numbers in the blood — generally accounting for less than 1 percent of blood cells — but can differ greatly in numbers among individuals. Very little is known about how blood stem cells produce iNKT cells.

Lili Yang, an assistant professor of microbiology, immunology and molecular genetics, aims to develop a model system to genetically program human blood stem cells to become iNKT cells. She and her colleagues will track the differentiation of human blood stem cells into iNKT cells, potentially providing answers to many critical questions about iNKT cell development.

With this knowledge, therapies can be created to increase the number of iNKT cells in the blood, creating more "special forces" cells and increasing the body's ability to fight off the diseases these cells affect.

Denis Evseenko: Finding the best environment for regenerating cartilage

In **recently published work**, Denis Evseenko, an assistant professor of orthopedic surgery, identified the origin cells of articular cartilage and tracked them at different stages of human growth, from the fifth week of fetal development to 60 years of age. The discovery is an important milestone toward a treatment that could help regenerate diseased or damaged joint cartilage. The development of such a therapy could delay, or for some patients eliminate, the need for joint-replacement surgery.

Another step along the path to this treatment is determining which molecular elements in the body create the environment, or niche, in which cartilage develops from stem cells. The niche aids the growth of healthy cartilage cells and helps them survive over time. Understanding the niche will help Evseenko create the best possible environment for regenerating healthy, long-lasting cartilage for therapeutic use in osteoarthritis and other diseases.

Thomas Otis and Bennet Novitch: Communication between nerve and muscle cells

Spinal muscular atrophy is an inherited disease that affects children very early in development, causing their muscles to waste away. Kids with SMA often can't walk or move well, and the progressive disease

eventually affects their ability to breathe. SMA often leads to death, usually before the age of 10. The disease is caused by a breakdown in communication between neurons and the muscles they signal to initiate movement, but researchers still don't know what part of the neuron-to-muscle communication pathway breaks down.

Scientists studying particular diseases commonly use stem cells' ability to become any cell in the body to grow disease models in the laboratory, and researchers have successfully grown neurons and muscle cells that communicate in a dish in the laboratory. The standard method of recording and measuring this communication is by connecting a tiny electrode to a neuron, which sends an electrical signal that is received by another electrode connected to a muscle cell. Although this system works, it is slow and has not been accurate enough to allow scientists to identify the causes of SMA.

Bennet Novitch, an assitant professor of neurobiology, and Thomas Otis, a professor of neurobiology and chair of the neurobiology department, are using a new technology called optigenetics to study the this neuron–muscle cell communication pathway. The technique uses light to stimulate genes in the neuron that send a message to the muscle cell to contract; the muscle cell can by infused with a special dye that lights up when signaled by the neuron, indicating a completed signal. This method is almost instantaneous and allows the researchers to determine where in the chain the breakdown happens in SMA.

With this knowledge, therapies can be designed that directly address what goes awry between the cells, making possible novel treatments for this devastating disease.

Samantha Butler: Regenerating spinal cord sensory function

The most obvious desire of those who suffer spinal cord injury is the recovery of motor function, such as the ability to walk. But these patients also lose the sense of touch in the affected parts of their body, effectively eliminating their ability to feel the pleasure of holding their child, for instance, or the pain being burned by a hot skillet. Important progress has been made toward rewiring motor circuits to permit paralyzed patients to walk, but very little progress has been made in reestablishing sensory circuits to enable them to experience their environment through the sense of touch.

In her research, Dr. Samantha Butler, an assistant professor of neurobiology, seeks to understand, and eventually apply, the fundamental mechanisms that direct stem cells to become spinal sensory neurons, the cells responsible for our sense of touch and ability to feel pleasure and pain. Successful determination of these cell types would make possible long-term studies on neuron implantation (now in progress with stem cell–derived motor neurons) and, potentially, the restoration of sensory function to

injured patients.

The Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research at UCLA was launched in 2005 with a UCLA commitment of $20 million over five years. A $20 million gift from the Eli and Edythe Broad Foundation in 2007 resulted in the renaming of the center. With more than 200 members, the Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research is committed to a multi-disciplinary, integrated collaboration of scientific, academic and medical disciplines for the purpose of understanding adult and human embryonic stem cells. The center supports innovation, excellence and the highest ethical standards focused on stem cell research with the intent of facilitating basic scientific inquiry directed towards future clinical applications to treat disease. The center is a collaboration of the David Geffen School of Medicine, UCLA's Jonsson Comprehensive Cancer Center, the Henry Samueli School of Engineering and Applied Science and the UCLA College of Letters and Science.

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