Medical Xpress

Researchers Convert Stem Cells into Cartilage

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Dr. Caroline Dealy. Photo by Al Ferreira

(PhysOrg.com) -- The ultimate goal is to grow replacement cartilage in a lab that can be used to repair human joints and treat osteoarthritis.

For the millions of aging Americans who suffer from joint pain, stem cells may be riding to the rescue. Scientists at the University of Connecticut Health Center have recently developed a technique that reliably converts stem cells into cartilage cells. Someday, that might allow doctors to grow replacement cartilage in a laboratory for the surgical repair of joints lost to injury or impaired by degenerative diseases such as arthritis.

Now UConn's Center for Science and Technology Commercialization (CSTC) has stepped in with a $75,000 prototype project - financed by royalties generated from other UConn inventions - to help determine whether the cells can function to repair living cartilage tissue in animal joints. The Center - part of UConn's primary economic development arm, the Office of Technology Commercialization (OTC) - makes "prototype" funds available to faculty so they can demonstrate the commercial potential of their lab discoveries.

"The future of healthcare depends on expanding the knowledge base of basic biological science as well as integrating new scientific discoveries with personalized medicine and regenerative medicine, even if such cures are still far in the future," says Rita Zangari, OTC's interim director. "This research offers an opportunity to address an unmet medical need that could transform the healthcare industry. Moving discoveries like this from our labs to safer and more effective therapeutics is our ultimate goal."

Cartilage is the dense connective tissue found between bones that allows for smooth movement of joints. The breakdown and loss of this tissue by injury or age-related "wear and tear" ultimately leads to osteoarthritis. One of the most prevalent health problems in the U.S., osteoarthritis is a major cause of decreased quality of life in adults. Yet treatment remains a challenge because cartilage lacks the ability to repair and renew itself.

Stem cells have an unlimited capacity for self-renewal, as well as the ability to become any type of cell in the human body, so they are ideal for generating replacement cartilage tissue to repair damaged cartilage. Developmental biologists, like Dr. Caroline Dealy, an associate professor at UConn's Center for Regenerative Medicine and Skeletal

Development, are attempting to understand the signals and conditions that regulate how stem cells differentiate into articular chondrocytes - which make up the unique type of cartilage present at the surface of joints.

Research published in the *Journal of Cellular Physiology* in April details how Dealy and her colleague, Dr. Robert Kosher, a former professor at the Health Center, successfully developed a methodology to direct "substantially uniform and progressive in vitro differentiation of human embryonic stem cells (hESC) and induced pluripotent stem cells (iPSC) into the chondrogenic lineage."

Converting stem cells into chondrocytes in culture involves using a mix of stimuli that replicate how cells normally undergo differentiation into cartilage during embryonic development. Dealy's team experimented with a series of culture conditions and signaling molecules in the laboratory and eventually created a specialized culture that encouraged the stem cells to convert into the chondrogenic lineage.

Achieving uniform chondrogenic differentiation by the cells is important so that all of the cells will be able to potentially participate in cartilage repair. Significantly, Dealy's team focused on both human embryonic stem cells (hESC) and induced pluripotent stem cells (iPSC), which are adult somatic cells redirected back into stem cells, and which hold exciting promise for patient-specific therapy.

The team was also able to obtain cells at early and later stages of chondrogenic differentiation, and their plan is to compare their efficacy for cartilage repair. Since earlier stage cells may be particularly responsive to local signals present in the joint that promote their ability to repair cartilage damage, they may yield superior repair compared to later stage cells, Dealy suggests.

Dealy notes that the research would not have been possible without the support of the State of Connecticut and its stem cell initiative. "That support has laid the foundation for ongoing work by this team to fulfill the potential of human stem cell-derived chondrogenic cells for articular cartilage repair," she says.

UConn's CSTC filed a patent application for the methodology developed by Drs. Dealy and Kosher to produce the hESC and iPSC derived chondrogenic cells, and for their use in articular cartilage repair.

The essential next step in translating the research into a future potential therapy is to determine whether the cells can function to repair living cartilage tissue in the joint. This is the intent of the CSTC's prototype project grant that will give Dealy's team a "first-look" at the ability of the stem cell-derived chondrogenic cells to repair damaged articular cartilage in an animal model of osteoarthritis. The cells will be introduced into the joints of mice with osteoarthritis to learn whether they can form new cartilage and repair the damage.

"Our long-term goal is to one day develop a new cell-based strategy for treatment of human articular cartilage injury and degenerative joint disease," Dealy says.

UConn's Research & Development Corp., which initiates new business start-ups based on innovative technologies developed by UConn researchers, has helped Dealy and Kosher form a company to seek additional capital to further commercialize this novel stem cell technology.

Formation of the company, Chondrogenics Inc., has enabled them to apply for a federal Small Business Innovation Research grant to conduct further studies evaluating and comparing the efficacies of the stem cell-derived chondrogenic cells for repair, in order to identify the cells with the best potential for articular cartilage repair and to optimize their repair abilities.

Some of these studies are planned to be conducted in the Technology Incubator laboratories in the new Cell and Genome Sciences Building scheduled to open in July near the UConn Health Center in Farmington. The Technology Incubator facilitates access by new companies such as Chondrogenics Inc., which have a technology link or synergistic relationship with the University, to resources that can accelerate the success and viability of the technology endeavor.

Says Dealy: "The common goal of all of these efforts is to one day realize the potential of human stem cell-derived chondrocytes in providing a new cell-based strategy for human articular cartilage repair and treatment of osteoarthritis."

More information: Research paper: www3.interscience.wiley.com/jo … l/123355925/abstract

Provided by University of Connecticut