Cartilage regeneration '20,000 Leagues Under the Sea'

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Bioengineers at Rice University have discovered that intense pressure -- similar to what someone would experience more than a half-mile beneath the ocean's surface -- stimulates cartilage cells to grow new tissue with nearly all of the properties of natural cartilage. The new method, which requires no stem cells, may eventually provide relief for thousands of arthritis sufferers.

"This tissue-engineering method holds promise not only for cartilage but also for tissues to repair bladders, blood vessels, kidneys, heart valves, bones and more," said lead researcher Kyriacos Athanasiou, Rice's Karl F. Hasselmann Professor of Bioengineering.

The findings appear this week in the journal PLoS ONE. They are the latest from the emerging field of tissue engineering, a new discipline that aims to capitalize on the body's innate healing abilities to develop new ways of growing tissues that can be used to surgically repair wounds without risk of rejection.

Cartilage, a tissue in the human body that cannot heal itself, has long been a target of tissue engineers. Cartilage is the skeleton's shock absorber, and its stiffness, strength and other mechanical properties derive not from living cartilage cells but from the densely woven matrix of collagen and proteoglycan that surrounds them. This extracellular matrix, or ECM, is produced during cartilage development in children, but cannot be repaired following injury in adulthood.

Injured cartilage often serves as the focal point for arthritis formation, so tissue engineers have long sought a means of growing new cartilage that can be transplanted into adults to repair damaged joints before arthritis can develop. Unfortunately, cartilage is difficult to engineer, in part because there are no natural healing processes to mimic.

Athanasiou's Musculoskeletal Bioengineering Laboratory has focused on cartilage for more than 10 years, and he said the new process is the first he has studied that produces cartilage that's almost identical to the body's own tissue.

"The combination of hydrostatic pressure and growth factors used in this process result in an engineered cartilage ECM with properties nearly identical to that of native cartilage," he said. "This research appears very promising for treating arthritis, as cartilage can now be produced in our lab that is almost identical in composition to native tissue."

So far, the process has been tried only with cells from cows and has yet to be tested in live animals. Athanasiou cautions that it will be several years before the process will be ready for clinical testing in humans.

The new findings are based on three years of data collected by graduate student Benjamin Elder, who is simultaneously earning a doctorate in bioengineering at Rice and a medical degree at Baylor College of Medicine under Rice and Baylor's Medical Scientist Training Program.

In the study, Elder took small samples of cartilage from calves' knees, dissolved the ECM and isolated the living cartilage cells, or chondrocytes. The calf chondrocytes were used to create tissue-engineered cartilage. The engineered cartilage was placed into a chemical bath of growth factors and sealed inside soft plastic containers that were placed inside a chamber connected to a hydraulic press. For one hour per day, the bags were squeezed at intense pressures.

"Our knees are filled with fluid, and when we walk or run the hydrostatic pressure on the cartilage cells in the knee approaches the pressures we used in our experiments," Elder said. "But in daily activities, these pressures are fleeting, just a second or so at a time."

Most of the prevailing strategies in tissue engineering attempt to reproduce the conditions that cells experience in the body. Athanasiou said the unconventional approach of using unnaturally high-pressure stemmed from insights gained during years of previous experiments.

Elder said, "By combining high pressure and growth factors, we were able to more than triple the biomechanical properties of the cartilage. We're not sure why they reinforce one another, but we do not get the same results when we apply them independently."

Elder, who earned both a bachelor's and master's degree from Yale in four years, has a 4.2 grade point average at Rice and is on track to earn his bioengineering doctorate in just three years. He's already finished two years of medical school and will resume his medical studies in the fall.

"Ben's an exceptional student and he embodies the future of this field," Athanasiou said. "He plans to pursue a career in neurosurgery, where he will be able to conduct future work in tissue engineering and translate it from the laboratory bench to the patient's bedside."

Source: Rice University