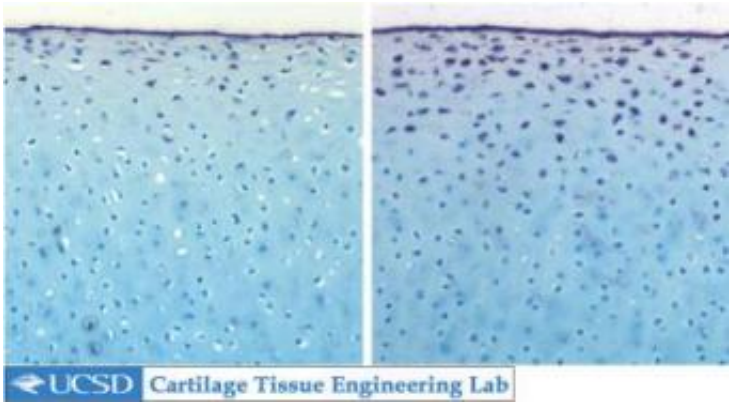
How movement lubricates bone joints

December 5 2006



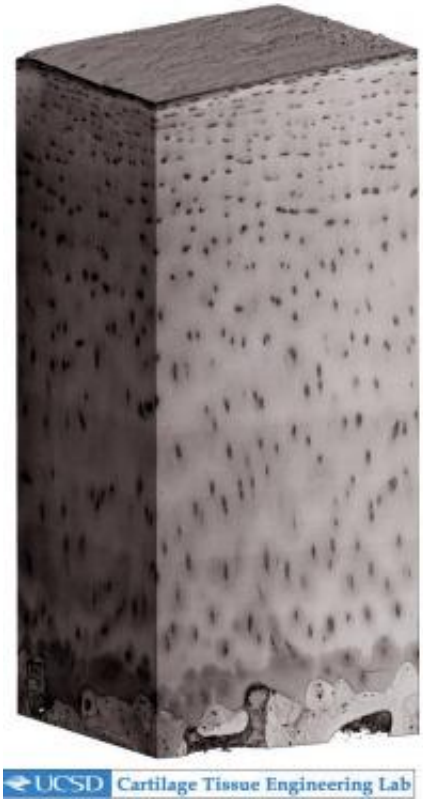
When the knee joint is not subjected to continuous passive motion (left), less proteoglycan 4 is produced by chondrocyte cells than when the knee joint is continuously moved (right). The dark purple stain is a specific visualization tool to identify chondrocyte cells in cartilage that are producing proteoglycan 4. Credit: UC San Diego

Taking a cue from machines that gently flex patients' knees to help them recover faster from joint surgery, bioengineering researchers at UC San Diego have shown that sliding forces applied to cartilage surfaces prompt cells in that tissue to produce molecules that lubricate and protect joints.

The results reported in *Osteoarthritis and Cartilage* are important in the ongoing efforts of the group led by Robert Sah, a Howard Hughes Medical Institute (HHMI) professor at UCSD's Jacobs School of Engineering, to grow cartilage in the laboratory that can be used to

replace patients' injured or diseased joint surfaces.

"We have shown that shear forces on cartilage prompt chondrocyte cells in it to produce proteoglycan 4," said Sah. "This is an important step toward our goal of eventually growing joint tissue for transplantation."



The surface (top) of joint cartilage has the highest concentration of chondrocyte cells, which are crucial to maintenance of a wear-resistant, frictionless, load-bearing surface for joint articulation. Credit: UC San Diego

Proteoglycan, a name that reflects its protein and polysaccharide components, is a basic building block of connective tissue throughout the body. The chondrocyte cells of cartilage make several forms of proteoglycans, including several that build up in cartilage and contribute to its stiffness. However, proteoglycan-4 is primarily secreted into the

joint fluid where it coats and lubricates cartilage surfaces.

Unfortunately, the smooth surface of the articular cartilage at the ends of bones located at joints often deteriorates with aging, becoming increasingly roughened and eroded. Those joints become painful and progress to osteoarthritis. Surgeons can replace damaged and diseased joints with artificial joints, but they would like to be able to simply resurface patients' existing joints with cartilage.

In a series of experiments, Sah's team attached bovine stifle joints, which are similar to human knee joints, to a bio-reactor that provided continuous irrigation with sterile nutritional fluids under normal physiological conditions. Immobile joints were compared to joints that were flexed 24 hours in a way that mimicked walking motions. The flexing was provided by a specially designed continuous passive motion device.

The team measured up to a three-fold increase in chondrocytes secreting proteoglycan 4 in continuously flexed joints compared to immobile controls. The flexing motion caused cartilage on the surfaces of opposing bones to slide against each other, creating so-called shear forces. In one large surface region of continuously sliding cartilage, 40 percent of the chondrocytes were secreting proteoglycan 4, whereas in the same areas of cartilage in immobilized joints only 13 percent of the chondrocytes were secreting proteoglycan 4. In areas of the joints exposed to only intermittent cartilage sliding, the effect on proteoglycan 4 production was intermediate between continuously sliding and immobilized regions of the joints.

"A challenge for us is to create large tissue grafts for transplantation," said Sah. "We are systematically addressing the technical challenges to maintain and grow healthy fragments of bone and cartilage in the laboratory and now we can use nature's self-regulating system, whereby

application of shear forces to this tissue increases its synthesis of proteoglycan 4."

Scientists have known for years that defects in a gene for proteoglycan 4 result in a type of childhood joint failure that resembles osteoarthritis in the elderly. Sah's goal is to stimulate healthy chondrocytes in cartilage tissue grown in the laboratory to form robust tissue that makes proteoglycan 4 and has a smooth, well-lubricated surface.

Source: University of California - San Diego