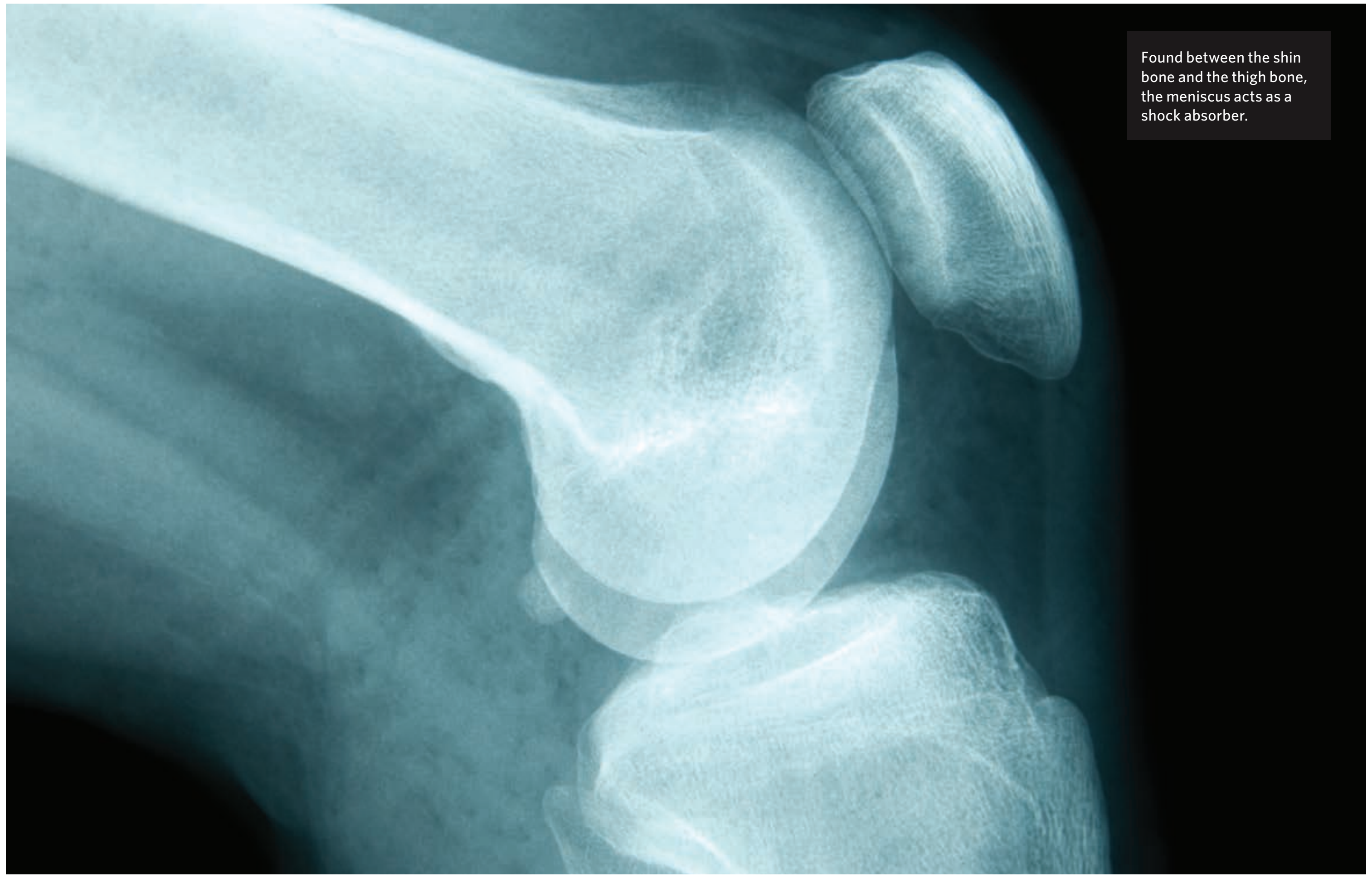
Preventing osteoarthritis with artificial proteins

MENISCUS REGENERATION with silk-elastin shows promise in preventing permanent knee damage.


Found between the shin bone and the thigh bone, the meniscus acts as a shock absorber.

To find treatment for knee pain, researchers are using an innovative artificial protein to regenerate the meniscus, a soft half-moon-shaped cartilage that cushions the shin and thigh bones.

"Responding to the great demand for restoring menisci, researchers and surgeons have made significant progress in treating meniscus tears in the past five years," says Nobuo Adachi, an orthopaedic professor at Hiroshima University.

Meniscus tears are one of the most common knee injuries. Before the meniscus' role was fully appreciated, entire menisci were typically removed to alleviate pain. Without the meniscus, however, the articular cartilage, a smooth tissue that covers the ends of bones, degrades. This eventually results in osteoarthritis, the permanent deformation of the knee joint. One study in 2011 found that, in Japan, as many as 42% of men and 62% of women above 40 have the condition.

REINFORCING SUTURES

The meniscus is an unusual cartilage, with blood flow in only the peripheral 10–25% of the tissue. "If tears occur in an area with blood flow, suture is an option since the cells will bond back using oxygen, nutrients, and wound-healing cells carried in blood," explains Adachi. "But for tears in other areas, removing the torn area is the only treatment available since the tissue doesn't heal after surgery."

With partial removal of the meniscus, however, 50% of patients experience osteoarthritis within 10 years of surgery. "Removing even a small portion of the meniscus can have deleterious long-term effects," says Adachi. "Suture is the preferred method, but it isn't an option in most cases. Roughly 70% of meniscus surgeries in Japan involve partial removal." In some cases, the sutured tissue does not bond together after surgery, Adachi notes.

COMBINING HUMAN ELASTIN WITH SILKWORM FIBROIN

Adachi is pioneering a method of making suture an option for more cases, using the artificial protein silk-elastin. "Originally developed for treating spinal injuries, silk-elastin is a combination of human elastin, the protein polymer that gives skin and other tissues its elasticity, and silkworm fibroin," explains Tsubasa Yamanaka of Sanyo Chemicals, a company that manufactures the protein. The defining benefits of silk-elastin include the transformation from liquid to gel at body temperature, and the ease at which cells migrate into scaffolds made with the protein. Sanyo Chemicals had previously demonstrated the utility of silk-elastin in treating chronic skin ulcers, where it helped promote the migration of fibroblasts and macrophages — cells crucial to wound healing — into the affected area.

"The idea is to apply silk-elastin solution over the sutured area, so that the torn part of the meniscus regenerates even without blood flow," says Adachi. "Silk-elastin promotes the migration of synovial cells. These cells are found in joints and are key to repairing the meniscus since they secrete viscous liquids that serve as lubricants and nutrients."

The team is verifying the effects in animal experiments and is targeting clinical application by 2026.


Silk-elastin takes many forms. It can be a gel at room temperature.


Silk-elastin can also have a cotton-like appearance and texture.

REGENERATING PARTS OF THE MENISCUS

Still, suture may remain out of reach for patients with severe tears. For cases in which partial meniscectomy is unavoidable, the team is refining a technique using a silk-elastin sponge. "Instead of replacing entire chunks of tissue with liquid silk-elastin, the sponge serves as a solid scaffold for new cells to grow on," says Adachi. In this technique, the team utilizes the patient's own meniscus tissue to facilitate regeneration. Meniscus tissues removed during surgery typically go to medical waste; in this case, however, the removed tissues are shredded and used as a cell source. The minced tissue is sandwiched inside the silk-elastin sponge, which is then sewn on to removed parts of the meniscus so that cells proliferate and regenerate. The sponge eventually turns into a hydrogel and biodegrades in about 8 weeks.

The silk-elastin sponge would lessen the physical and financial burden for patients, Adachi says. "The standard in regenerative medicine involves removing the tissue, culturing cells in the lab, and then returning the cells to the patient. That requires two operations, and culturing cells is very expensive," says Adachi. "With the new technique, we plan to shred the removed tissue during the same operation so we can begin regeneration in just one operation. Determining the right level of stiffness for the sponge remains challenging — we need something hard enough to withstand compression from body weight, but soft enough to serve as a scaffold."

These solutions should help more patients retain the integrity of their joints. "For patients with severe osteoarthritis, replacing the joint with artificial implants is effective at eliminating pain. In fact, the number of artificial joint replacement surgeries have continued to increase over the past two decades," says Adachi. "But the replacement limits patient mobility, and they permanently lose the freedom to engage in vigorous exercise."

"Healthy ageing is critical for maintaining quality of life," adds Yamanaka. "Treating the meniscus is only part of the story. In the long term, we aim to harness functional regeneration of the meniscus and cartilage to achieve a longer healthy lifespan; this strategy aims to prevent long-term damage to the knee bones before it occurs." ■

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