The Achilles' heel of tendons

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Tendons are the body's marionette strings, connecting bones to muscles that raise an eyebrow or propel us into a full run. That is, until an unusually forceful or awkward pull on the strings leaves us with a sprain, strain or tear. Surgeons attempt to repair over 300,000 of these injuries every year, and doctors visits for sore tendons run into the millions.

Using a combination of nanoscience and biomedical and civil engineering to explore tendon structure from atoms on up, researchers have unraveled part of the mystery behind why we have problems with our tendons.

A new study led by scientists at Case Western Reserve University examines single threads of these essential connectors and found the weakest links - potential targets for imaging techniques to detect problems before a tendon fails and for drugs to increase flexibility and heal damage. Their work is published in the September issue of *Biophysical Journal*.

The threads are fibrils of collagen, a tougher form of the soft tissue implanted in models' pouty lips.

"The fibrils are about five times stronger and can strain about five times farther than a tendon," said Steven Eppell, a professor of biomedical engineering and senior author of the study.

"About 80 to 90 percent of a tendon is collagen but mechanical properties like strength are probably controlled by the other stuff."

The other stuff is a cement that holds the bundles of fibrils together; it's made of molecules called proteoglycans. This cement or the interface between collagen fibrils and proteoglycans, is most likely the weakest link in the system, the researchers say.

The scientists suspected that's the case but direct testing of cement, which is more complex and less available than fibrils, was difficult. So, they decided to test the strength of just the collagen fibrils and then compare this with the strength of whole tendons.

To test the tensile strength of fibrils, which have a diameter 100 times smaller than the diameter of a human hair, Eppell's team used what is essentially a structural testing lab on a microchip. This allowed them to measure how far fibrils stretch and the pressures they withstand before breaking.

"It's the equivalent of what civil engineers use to test a steel beam under 100,000 pounds of pressure, shrunk to the micro level," said co-author Roberto Ballarini, a professor of civil engineering formerly at Case Western Reserve and now chairman of civil engineering at the University of Minnesota. Ballarini is one of the inventors of the device to test the fibrils' strength.

In the first tests of their kind, the scientists glued one end of fibrils taken from a sea cucumber to a stationary base and the other end to a movable pad. When pulled apart, the fibrils stretched up to 100 percent of their resting length before breaking. A tendon stretches only 10 to 20 percent before breaking.

The new technology, developed by Zhilei Shen during her Ph.D. dissertation work, allowed her to keep the fibrils hydrated in saline to mimic their condition in the body. Earlier testing on dehydrated fibrils and tendons gave her different results.

The investigators believe water actually toughens fibrils and tendons as a whole. Since the proteoglycans in the cement largely control the degree of hydration around the fibrils, the team suspects they may be useful targets when designing drugs to control tendon strength.

In collaborations with nanoscientists at Yeshiva University and multi-scale modeling experts at MIT, the researchers took the lead in applying for funding to continue their work.

Their next steps include more detailed testing of bundles of fibrils and whole tendons as well as computer modeling that connects behavior of individual atoms and their bonds to molecular behavior and finally to mechanics of simulated fibrils and tendons. The models will be tested against experimental data collected here in the biomedical engineering department at Case Western Reserve.

Although the work focuses on tendons, the investigation will also provide insight into the workings of collagen in ligaments, skin and even mineralized collagen in bone.

Provided by Case Western Reserve University

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