NEWS

Tending Tender Tendons

What do a skate egg case and a tendon have in common? Cross-links that make them strong—an observation that propelled Thomas Koob on his quest to build a bionic tendon

Gazing at an aquarium tank almost 20 years ago, Thomas Koob made an observation that would eventually change the course of his research. While reflecting on the remarkable properties of a skate egg case, he realized it might hold the secret to an artificial tendon.

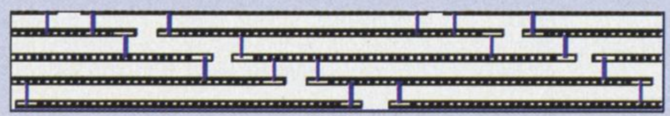
Bidding farewell to his studies of human and shark reproduction, Koob, a biochemist at Shriners Hospital for Children in Tampa, Florida, joined the then-very-small ranks of scientists trying to build a bionic tendon. He now has plenty of competition: The field is quite "huge," says Albert Banes, a cell biologist at the University of North Carolina, Chapel Hill, and another bionic-tendon pioneer.

If any of these contenders are successful, they will have a hot commodity. Tendons are the ropes that tie muscle to bone, enabling the former to maneuver the latter quickly and efficiently. Some, such as the Achilles' tendon, act as springs. Others get the body moving and, for example, help turn the open hand into a clenched fist. But when they break, "our ability to repair tendons is limited," laments Richard Gelberman, an orthopedic surgeon at Washington University School of Medicine in St. Louis, Missouri. He estimates that surgeons try to fix some 300,000 tendons a year—and that doesn't include those in the legs and feet. Recovery can take months, notes Adam Summers, a comparative physiologist at the University of California, Irvine, and at best the restored tendon is about 60% functional.

In their first attempts to create replacement tendons, researchers tried polyesters or other synthetic materials. But more recently, several research teams, including Koob's and Banes's, have gone after biologically based materials that might be less prone to immune rejection.

Koob and others are grappling with how to replicate the complex structure of the tendon. A substitute must be strong, stiff, and resilient, and it should be able to change its properties—such as its stiffness—as real tendons do. Contrary to the common view of them as elastic cables, "tendons are very much alive," explains Banes.

Viewed one way, the cells within a tendon look like boxcars along tracks of collagen. "But it's really more like a spider web. The cells are highly interactive and intertwined with the collagen," says Banes. This network includes molecular bridges that reach across and set up cross-links between nearby collagen strands, thereby preventing the collagen from slipping as the tendon is pulled by a contracting muscle.



Industrial strength. Cross-links between collagen strands impart strength to tendons.

Collagen helps make the tissue strong, but the tendon cells are equally important, because they react to loads, activate genes, and change the properties of the tendon itself. Any replacement tendon must either provide new cells or recruit new ones into the artificial tissue if it is to function as well as the original, says Banes, who thinks he has solved this problem.

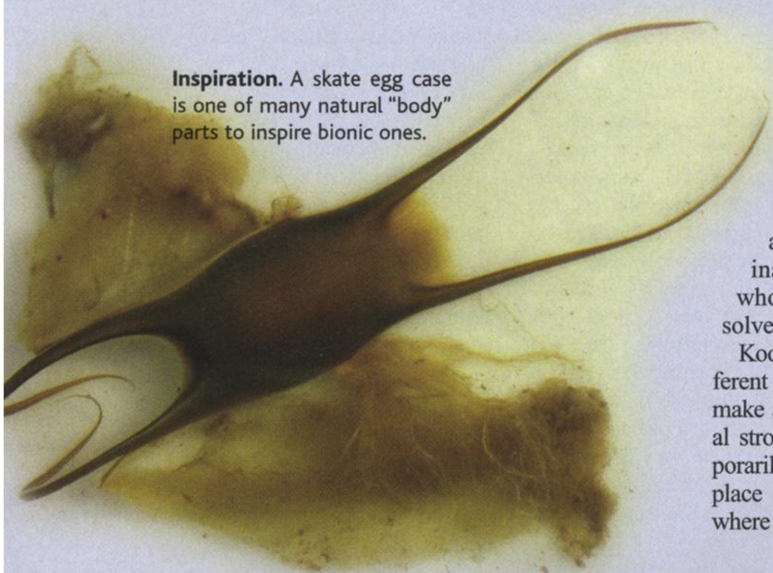
Koob is tackling a different issue first: how to make a biological material strong enough to temporarily take a tendon's place as it heals. That's where the egg cases came in. Skate eggs emerge white and pliable from a large gland in the reproductive tract; over the next few hours, they darken and become leathery. Made of collagenlike materials, the egg cases are tough enough to persist in the ocean for months, and so are its enzymes. Koob was intrigued by the chemistry underlying this transition and stability. Further study suggested that these enzymes form bonds that are the cross-links between the case's collagenlike fibers. He wondered whether that process could be mimicked to make biosynthetic tendons and began looking for a way to cross-link human collagen fibers.

After much searching, Koob found a chemical called NDGA, derived from a shrub called creosote, that could do just that in his lab. As he reported at a recent meeting,* the collagen-NDGA combination is very compatible with rabbit tissue and does not trigger immune reactions. (The Food and Drug Administration requires this test for biomaterials to be used in humans.) For that reason, notes Summers, this "natural" tendon material might be safer than a synthetic.

Not that this new tendon material is ready for use. Koob still needs to find a way to glue in the artificial tendon—something that can already be done with a woven polyester tendon material, notes Bahaa Seedhom, a bioengineer at the University of Leeds, U.K., who helped develop the polyester substitute. And even though Koob's material has the necessary strength and stiffness, he needs to demonstrate that it can withstand the multiple stresses to which it will be subjected, notes Robert Ker, another Leeds tendon expert.

The ideal tendon material, all these tendon contenders recognize, would need to contain or recruit cells that could help the tendon develop the right set of properties and repair small tears as needed. Because his material accumulates cells only on the outside, Koob is now working on making it less dense and more like a real tendon. Meanwhile, Banes and those working on gel-based substitutes have materials that already come with their own tendon cells or, in one case, stem cells. These groups plan to add genes to these cells that would enhance their ability to work like natural tendon cells. At this stage, however, no one can predict which approach will yield a tendon that is almost as good as the real thing.

–ELIZABETH PENNISI



Inspiration. A skate egg case is one of many natural "body" parts to inspire bionic ones.

CREDITS: THOMAS J. KOOB

* Society for Integrative and Comparative Biology 2002 Annual Meeting, 2–6 January, Anaheim, CA.