Researchers combine active proteins with material derived from fruit fly

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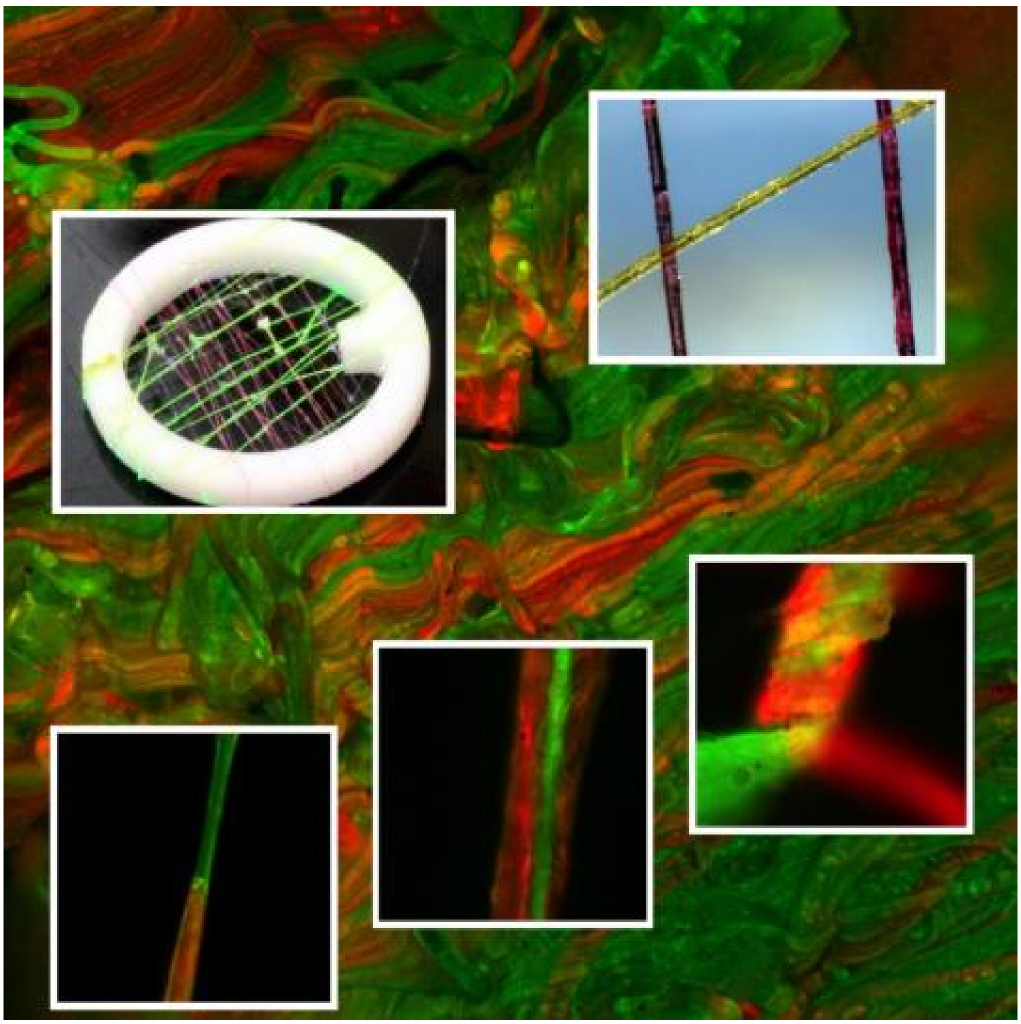

Strands of Ubx fiber patterned with fluorescent protein are the result of research by scientists at Rice University and Texas A&M. The strands can contain active proteins that may find use as chemical catalysts and biosensors and in tissue engineering. (Credit Zhao Huang/Rice University)

Researchers at Rice University and Texas A&M have discovered a way to pattern active proteins into bio-friendly fibers. The "eureka" moment came about because somebody forgot to clean up the lab one night.

The new work from the Rice lab of biochemist Kathleen Matthews, in collaboration with former Rice faculty fellow and current Texas A&M assistant professor Sarah Bondos, simplifies the process of making materials with fully functional proteins. Such materials could find extensive use as chemical catalysts and biosensors and in tissue engineering, for starters.

Their paper in today's online edition of Advanced Functional Materials details a method to combine proteins with a transcription factor derived from fruit flies and then draw it into fine, strong strands that can be woven into any configuration.

Bondos and Matthews led the team that included primary author Zhao Huang and research technician Taha Salim, both of Rice, and research assistants Autumn Brawley and Jan Patterson, both of Texas A&M.

The research had its genesis while Bondos was in Matthews' Rice lab studying Ultrabithorax (Ubx), a recombinant transcription factor protein found in Drosophila melanogaster (the common fruit fly). This protein regulates the development of wings and legs.

"It's biodegradable, nontoxic and made of naturally occurring proteins -- though we have no reason to believe that fruit flies ever produce enough of these proteins to actually make fibers," Bondos said.

It was a surprise, then, to find that Ubx self-assembles into a film under relatively mild conditions.

"I was cleaning up in the lab one morning and I noticed what appeared to be a drop of water suspended in midair beneath a piece of equipment I was using the previous night," Bondos recalled.

It turned out the droplet was water encased in a sac of Ubx film. The sac was hanging by a Ubx fiber so thin that it was more difficult to see than a strand of a spider's web, Bondos said.

"It clued us in that this was making materials," said Matthews, Rice's Stewart Memorial Professor of Biochemistry and Cell Biology and former dean of the Wiess School of Natural Sciences.

The chance discovery prompted a 2009 paper in the journal *Biomacromolecules* about the material they dubbed "ultrax," a superstrong and highly elastic natural fiber.

"We found that if you put a little drop of this protein solution on a slide, the Ubx forms a film. And if you touch a needle to that film, you can draw a fiber," Matthews said. "Then we asked, What if we could incorporate other functions into these materials? Can we make chimeras?" The answer was yes, though it took ingenuity to prove.

Chimeras in the biological world contain genetically distinct cells from two or more sources. In Greek mythology, chimeras are beings with parts from multiple animals; a pig with wings, for instance, would qualify. But real chimeras are usually more subtle. On the molecular level, chimeras are proteins that are fused into a single polypeptide and can be purified as a single molecular entity.

As a proof of principle, the team used gene-fusion techniques to create chimeras by combining Ubx with fluorescent and luminescent proteins to see if they remained functional. They did. The combined materials still formed a film on water. Drawn into fibers and put under a microscope, Ubx combined with enhanced green fluorescent protein

(EGFP) kept its bright green color. Ubx-mCherry was bright red, the brown protein myoglobin (from sperm whales) was brown, and luciferase glowed.

Huang was able to make patterns with strands generated by the chimeras by twisting red and green fluorescent proteins into candy cane-like tubes, or lacing them on a frame. "This patterning technique is pretty unique and very simple," said Huang, who recently defended his thesis on the subject. He said making solid materials with functional proteins often requires harsh chemical or physical processing that damages the proteins' effectiveness. But creating complex three-dimensional structures with Ubx is efficient and requires no specialized equipment.

Bondos is studying how many proteins are amenable to fusion with Ubx. "It looks like it's a fairly wide range, and even though Ubx is positively charged, both positively and negatively charged proteins can be incorporated." She said even proteins that don't directly fuse with Ubx may be able to connect through intermediary binding partners.

Bondos said the 2009 paper "showed we could make three-dimensional scaffolds. We can basically make rods and sheets and meld them together; anything you can build with Legos, we can build with Ubx."

Ubx-based materials can match the natural properties of elastin, the protein that makes skin and other tissues pliable, Bondos said. "You don't want to make a heart out of something hard, and you don't want to make a bone out of something soft," she said. "We can tune the mechanical properties by changing the diameter of the fibers."

She said functionalized Ubx offers a path to growing three-dimensional organs layer by layer. "We should be able to build something shaped like a heart, and because we can pattern the chimeras within fibers and films, we can build instructions into the material that cause cells to differentiate as muscle, nerves, vasculature and other things."

Bondos suggested the material might also be useful for replacing damaged nerves. "We should be able to stimulate cell attachment and nerve growth along the middle and factors on the ends to enhance attachment to existing nerve cells, to tie it into the patient. It really is pretty exciting."

Matthews said the ability to characterize and pattern fibers for different functions should find many uses, because enzymes, antibodies, growth factors and peptide recognition sequences can now be incorporated into biomaterials. She said sequential arrays of functional fibers for step-by-step catalysis of materials is also possible.

"You're only limited by your mechanical imagination," she said.

More information: onlinelibrary.wiley.com/doi/10 … m.201100067/abstract

Provided by Rice University