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VMD-PhD Student Sylvia Qu

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Like many veterinary students, Feini (Sylvia) Qu grew up with a love for animals and zoology. In college, she volunteered at a lemur research center and traveled to Paraguay to study tropical birds. She also shadowed veterinarians as they worked in clinics seeing patients.

But unlike many traditional vet students, the tools and technology the clinicians used fascinated Qu almost as much as the practice of medicine itself.

“I was so excited by the instrumentation,” Qu says. “I always wanted to know how a probe or any given piece of equipment does what it does.”

That fascination led her to Penn Vet’s VMD-PhD Program, and to pursue interdisciplinary research into tissue engineering to create a better approach to connective tissue repair surgeries—for both people and pets.

Qu majored in biomedical engineering as an undergraduate at Duke University and entered Penn Vet’s dual-degree program with a good sense of what she wanted to pursue for her PhD. While some combined-degree students rotate through different labs during the summers between their first years of veterinary school, she spent much of her time in the lab of Dr. Robert Mauck, Associate Professor of Orthopaedic Surgery and Bioengineering, with appointments in the Perelman School of Medicine and the School of Engineering and Applied Science.

“I came in with an interest in tissue engineering and orthopedics,” she says. “I wanted to be the person with a knowledge of both the engineering side and the veterinary side to help with making the bench-to-bedside transition.”

To do so, preclinical studies in large animal models are typically a necessary step, and were a major part of Qu’s dissertation research, which focused on strategies to repair injuries to connective tissues such as tendons, ligaments, and cartilage.

In particular, Qu zeroed in on attempts to repair the meniscus, a rubbery, C-shaped piece of dense tissue known as fibrocartilage that cushions the knee joint. Meniscus tears
are a common injury, but very difficult to repair because only the outer third of the tissue receives significant blood flow. Injuries that are complex or that affect the inner part of the meniscus are treated by surgery to cut out and remove the torn portion, rather than attempt a repair.

For decades, researchers have attempted to encourage better healing by designing scaffolds on which new cells could accumulate, but efforts have fallen short. Qu, collaborating with Mauck and postdoctoral researcher Dr. Matthew Fisher, worked on an innovative approach to build a nanoscale scaffold that would not only direct cells where to go and how to be structured appropriately, but would also influence tissue at the repair site to increase the odds of a successful healing process.

Her work was based on the recognition that fetal connective tissue is better at healing than adult tissue. Using advanced imaging technology, Qu found that this enhanced healing capability may be due to the fact that, whereas adult connective tissues such as the meniscus are stiff and dense so as to bear up under heavy loads, fetal tissue is less dense and softer. This “looser” structure is more conducive to allowing cells to migrate through a tissue to a wound site and promote healing.

What if, the researchers wondered, they could somehow revert adult tissue to a more fetal-like state to improve healing?

“The idea is to degrade the tissue next to the wound site so it’s looser and easier for cells to migrate in,” Qu says.

Qu and colleagues first worked in vitro to examine whether the collagen-degrading enzyme collagenase effectively digested the extracellular matrix of adult cow meniscus tissue. They found that, indeed, the matrix density decreased and the number of cells increased when incubated with the enzyme.

But the researchers didn’t want to have to soak damaged meniscus tissue with an enzyme, because it could also degrade healthy tissues. A more targeted approach involved using a nanofiber-crafted scaffold embedded with the enzyme, which could be implanted into the wound site and would release the enzyme selectively into the adjacent tissue.

They did an initial in vivo test of the scaffold construct in a rat model to evaluate its activity and safety. They again took cow meniscal tissue, placed the scaffold inside to replicate a wound closure, and implanted the tissue in the rats subcutaneously. After four weeks, they found signs that matrix density was reduced and cells were migrating into the repair site, just as they had in the in vitro experiments.

With confidence in the approach, the researchers moved into a pilot study with a large animal model: sheep, which Qu says provide an excellent model for human knee surgeries.

“Size matters,” she says. “It’s hard to do these kinds of surgeries in an animal as small as a rat or mouse. Also, the loading patterns in sheep knees are similar to those of humans.”

Dr. Thomas Schaer, Director of Penn Vet’s Translational Orthopaedic Research & Preclinical Studies program at New Bolton Center, performed the surgeries in sheep with an injury to their menisci to introduce the construct—a challenging task because the meniscus can be difficult to visualize.

The result was encouraging: those sheep who had the enzyme-treated scaffold embedded in the repair site had evidence of a robust healing response, with no evidence that other tissues were affected by the enzyme treatment.

In future studies, Qu and her colleagues hope to expand the investigation to evaluate longer-term efficacy of the scaffold-aided repair. She is also exploring a strategy to deliver an additional drug that could work in conjunction with collagenase to promote healing.

And because the meniscus tissue resembles that of many other dense connective tissues in the body, the work could be applied broadly—even in companion animals. Dogs, for example, commonly injure their meniscus when they experience a cranial cruciate ligament tear, akin to an ACL tear in humans.

“I see this as a treatment that could help a lot of injured canine companions,” Qu says.

As a side project, Qu is working with a graduate student in Penn’s Computer and Information Science Department to design a wearable wireless electronic device that would measure how well a joint returns to function after a surgery, looking at its ability to bear weight and achieve a wide range of motion.

Qu is hopeful that her work contributes to more overlap and exchange between the engineering and veterinary fields.

“We’ve started building this bridge between these two disparate worlds that really shouldn’t be disparate,” she says.