Justin Hanes, center, in the lab with Kunal Parikh and Laura Ensign-Hodges.

Future Suture

Spinning a solution to deliver infection-preventing drugs after eye surgery.

Wilmer's Justin Hanes, Ph.D., knows a thing or two about necessity and invention. As a chemical and biomedical engineer specializing in nanomedicine, he has developed numerous technologies that offer life-changing treatments to patients across the eye disease spectrum. He has co-founded two companies to commercialize his creations. And so, when Wilmer Director Peter McDonnell, M.D., wanted to develop a new sort of suture specifically for eye surgery, he knew exactly where to turn.

"Peter had identified this gap in the medical technology for a suture—specifically designed for eye surgery—that could be impregnated with antibiotics to prevent infections," Hanes says. "The challenge, engineeringwise, was huge."

Developing a drug-eluting suture for the eye is very complex, Hanes explains. The suture must be thin and very strong. Those used in slow-healing corneal transplants, for instance, often must last a year or more. With the added requirement that the suture must also retain its strength after incorporation of a drug, the challenges became trickier still.

The thinner the suture, the larger the surface area-to-volume ratio is, meaning the drugs tend to escape too fast, Hanes says. His team also discovered that incorporation of drugs can make sutures weaker—too weak to be useful for surgical applications.

For inspiration, the team looked to nature, exploring how spiders spin their resilient threads. They also examined the science of rope making and worked with civil engineers to produce computer models of various fiber structures they might want to try.

Laura Ensign-Hodges, Ph.D., an assistant professor at Wilmer and a chemical and biomedical engineer like Hanes, helped investigate various

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>
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electrospinning methods with a team of talented faculty members and students that also included biomedical engineering professor Hai-Quan Mao, Ph.D., and graduate student Kunal Parikh.

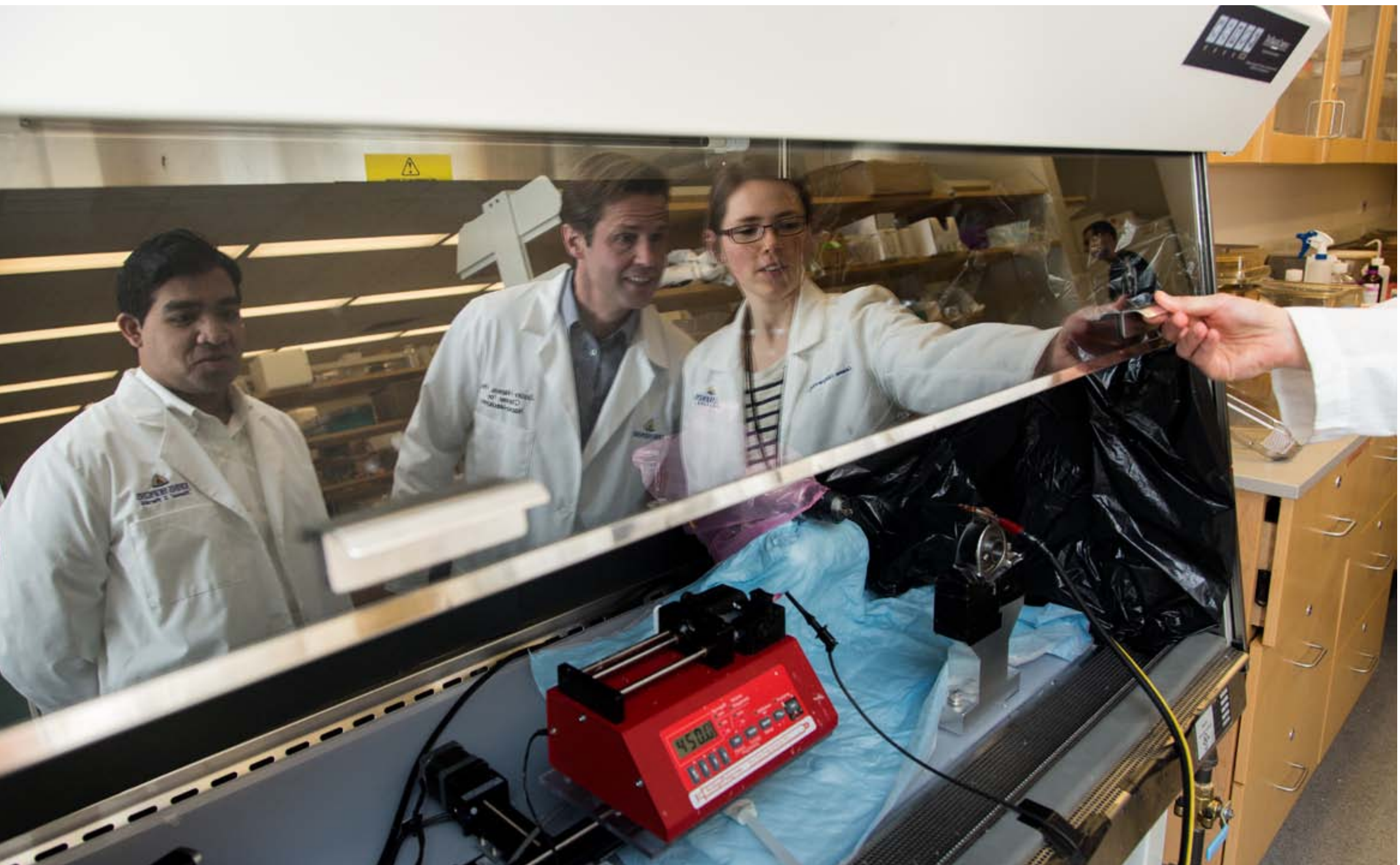
"Normal sutures are made of a single thread of polymer—a monofilament," Ensign-Hodges says. Though the team succeeded in using electrospinning to create drug-loaded polymeric monofilament structures, these were often one-third the strength necessary for clinical use.

After months of work, Parikh found success by building a state-of-the-art spinning system in-house. It begins with a solution of a quick-drying solvent in which molecules of antibiotic drugs are swirling alongside billions of tiny polymer chains. The solution is pressed through a tiny aperture, similar to the way medicine is dispensed from a syringe. As the solvent-drug-polymer cocktail travels through the opening, the polymer chains align into nanofibers—each 100 times thinner than a human hair.

The solution is electrically charged as it exits the aperture, and the now-charged solution gets attracted to two metal plates, thus forming a thin thread of drug-containing polymer. These nanofibers are then twisted together by the spinning system into a single thread—a multifilament suture. The nanosuture, as the team has dubbed it, is both strong and capable of releasing incorporated drugs over long periods of time, up to many months. The drug nestles comfortably within the fibers.

The next step was to test whether the antibiotic-eluting suture would reduce the rate of ocular infections in laboratory animals. The results showed that the technology was 100 percent effective in preventing ocular infections.

"The team could not be more excited about the potential of this technology," Hanes says. "We're now



Kunal Parikh's in-house spinning system produces a multifilament suture that is capable of releasing incorporated drugs over long periods of time.

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The scientists are also exploring the use of other medicines, including steroids, immune suppressants and drugs that prevent unwanted cell growth. The team working on this technology has grown from a few to more than 15 people, including engineers, ophthalmologists and vascular surgeons.

Of course, groundbreaking research like this does not happen simply because people wish it so. There is usually some forward-thinking donor who sees the promise and stakes the researchers with the considerable funding necessary to get their ideas off the ground. In this case, that donor was the Robert H. Smith Family Foundation.

The results to date have been due to a true team effort, Hanes says. McDonnell had the vision, and Hanes, Mao, Ensign-Hodges and Parikh brought the engineering skill. But it was the foundation's financial support that allowed the researchers to purchase critical equipment and build a team.

"Now it's time to push to make the first-generation, antibiotic-eluting nanosutures using a commercial process as we begin the hard work of preparing to test them in humans. But it is also time to go beyond sutures to medical devices with this technology. The possibilities are only limited by our imaginations in this next-generation stuff," Hanes says.

"It's really fun for me, personally," Ensign-Hodges says. "We're engineering unique solutions to real clinical problems that haven't been solved before." ■