An artificial cornea is in sight, thanks to biomimetic hydrogels

If eyes are "the windows of the soul," corneas are the panes in those windows. They shield the eye from dust and germs. They also act as the eye's outermost lens, contributing up to 75 percent of the eye's focusing power. On Sept. 11 in San Francisco at the annual meeting of the American Chemical Society, chemical engineer Curtis W. Frank will present a novel biomimetic material that's finding its way into artificial corneas. It's a hydrogel, or polymer that holds a lot of water. That material may promise a new view for at least 10 million people worldwide who are blind due to damaged or diseased corneas or many millions more who are nearsighted or farsighted due to misshapen corneas.

Called Duoptix (TM), the material can swell to a water content of 80 percent--about the same as biological tissues. It's made of two interwoven networks of hydrogels. One network, made of polyethylene glycol molecules, resists the accumulation of surface proteins and inflammation. The other network is made of molecules of polyacrylic acid, a relative of the superabsorbent material in diapers.

"Think of a fishnet, but think of a 3-D fishnet," says Frank, the W. M. Keck, Sr. Professor in Engineering and a professor, by courtesy, of chemistry and of materials science and engineering. "It's a strong, stretchy material." That makes it able to survive suturing during surgery. The biocompatible hydrogel is transparent and permeable to nutrients, including glucose, the cornea's favorite food.

Collaborators on the hydrogel work that Frank is presenting at the chemists' meeting are Marianne E. Harmon, a former Stanford doctoral student now with GE Corporate Research Lab in Schenectady, N.Y.; Dirk Kucklung, an assistant professor at the Institute for Polymer Science in Dresden, Germany; Wolfgang Knoll, director of the Max Planck Institute for Polymer Research in Mainz, Germany; and David Myung, a medical student jointly working on a doctorate in chemical engineering in Frank's lab.

Myung's project, funded by Stanford's Bio-X interdisciplinary biosciences program, was to design, fabricate and characterize a bioengineered cornea based on the dual-network hydrogel. The result was a disc with a clear center and tiny pores populating the periphery. Myung calls the pores engineered into his artificial cornea the "homes" he built for cells that need to infiltrate the artificial lens and integrate it with surrounding natural tissue.

"If you build it, they will come," Myung says. "The cells move in, and they bring furniture too--meaning the collagen they secrete. They even 'remodel.'" Collagen binds to the edge of the synthetic disc and forms a junction between natural and synthetic tissues. Then a clear layer of epithelial cells grow over the disc.

'Broadly interdisciplinary'

Stanford's program to develop an artificial cornea is "broadly interdisciplinary," Frank says. Christopher Ta, an assistant professor of ophthalmology and ophthalmology residency director at the Stanford University Medical Center, leads the effort with Frank. Ta says scientists have tried to develop artificial corneas for half a century, but prototypes were not well tolerated. Infections developed around implants. Eyes extruded implants. A few years ago, in a pilot study for a Bio-X grant to show proof of concept, Ta began to test the hydrogel in assays to make sure it was not toxic to cells. Soon other experts joined the effort. Jaan Noolandi in Ophthalmology managed projects, worked with potential sponsors and provided insight into polymer physics. Nabeel Farooqui in Ophthalmology developed histology procedures. Won-Gun Koh, a former postdoctoral fellow in Chemical Engineering, first synthesized the polymer that Myung ultimately developed. Qi Liao, a graduate student in Chemical Engineering, contributed to a general understanding of the hydrogels. Jennifer Cochran, assistant professor in the Bioengineering Department, is investigating how to maximize epithelial adhesion to the material. Michael Carrasco, a peptide chemist at Santa Clara University, consulted about surface modifications for cellular adhesion.

The researchers are now testing the material for biocompatibility in animal models. Animals have tolerated artificial corneas with no problems in trials as long as eight weeks, Ta says. The material remains perfectly clear, he says. Longer trials are a next step.

The current source of tissue for corneal transplants is cadavers. Donor tissue has problems, Ta notes, including a rejection rate of about 20 percent and a period for visual recovery of six months to a year. "You get a more predictable shape with an artificial cornea," Ta says.

"In many countries, tissue availability is a problem," he says. "If the tissue is artificial, we don't have to rely on donor tissue." The high prevalence of laser-assisted in situ keratomileusis, or LASIK, eye surgery may contribute to the shortage of donor tissue in developed nations, he notes, as this surgery disqualifies donation. A tissue-engineered artificial cornea could lessen or eliminate the need for donor tissue.

At least a dozen groups worldwide are working to develop artificial corneas, Myung says. "Only two or three are on the market, but they are only used in last-ditch efforts [when transplants are rejected]," he notes. Stanford's artificial cornea is "the most biomimetic," he says, with a water concentration and mechanical properties that rival those of the natural cornea.

"The dream would be to have a corneal replacement that's sterilized and dehydrated and sent off to the hospital or battlefield, and rehydrated," Frank says.

Beyond blindness

Other ocular applications of the hydrogel include more comfortable contact lenses. Onlays of hydrogel lenses on the surface of the cornea could serve as extended-wear contact lenses.

Inlays are also possible. The cornea contains layers--a top layer of protective epithelial cells, a middle layer called stroma that provides the collagen matrix that gives the cornea its shape, and an innermost endothelial layer. With inlays, some of the epithelial layer can be scraped away and replaced with a hydrogel contact lens. The lens becomes biointegrated when clear epithelial cells grow over the top of the inlayed lens.

Inlays offer an advantage over LASIK surgery, which works but isn't reversible, Myung says. He envisions implantable contact lenses that can be replaced if the prescription changes.

Hydrogel lenses may even make their way deeper into the eye as replacements for inner-eye lenses damaged by cataracts.

The researchers have filed four patents for ocular applications of the hydrogel.

Source: Stanford University