A material to rejuvenate aging and diseased human vocal cords

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A new made-in-the-lab material designed to rejuvenate the human voice, restoring the flexibility that vocal cords lose with age and disease, is emerging from a collaboration between scientists and physicians, a scientist heading the development team said here today.

That's just one of several innovations that Robert Langer, Sc.D., discussed in delivering the latest Kavli Foundation Innovations in Chemistry Lecture at the 244^{th} National Meeting & Exposition of the American Chemical Society (ACS).

Langer heads a team of almost 100 in laboratories at the Massachusetts Institute of Technology (MIT), one of the world's largest academic research laboratories. He holds, or has applied for, more than 800 patents, and has founded or co-founded numerous companies, with honors that include the ACS' 2012 Priestley Medal, the highest honor of the world's largest scientific society.

The artificial vocal cord material, the first designed to restore lost flexibility in human vocal cords, results from an ongoing effort to produce artificial tissues in the lab, Langer explained. Lost flexibility in the vocal cords, due to the effects of aging or disease, is a major factor in the voice loss that affects 18 million people in the United States alone.

"The synthetic vocal cord gel has similar properties as the material found in human vocal cords and flutters in response to air pressure changes, just like the real thing," explained Langer, who is the David H. Koch

Institute Professor at MIT.

The vocal cords are two folds in the "voice box" that vibrate, or come together and away from each other very quickly to produce puffs of air that help form sounds. They function in much the same way as a reed in a saxophone. The cords consist of layers of muscle, ligament and a membrane. A layer between the ligament and the membrane is very flexible, and that flexibility and pliability is critical for speech.

But when someone, such as a teacher, a politician or a performer, overuses their voice, scar tissue develops. The same thing happens when a person gets older, accounting for the lower volume and hoarseness often apparent in older people. Cancer or having a tube inserted in the throat for medical procedures also can damage the cords. Scar tissue is stiff, and scarring leaves a person with a hoarse, breathy voice.

"About 90 percent of human voice loss is because of lost pliability," said Steven Zeitels, M.D., F.A.C.S., Langer's collaborator on the project. Zeitels is the Eugene B. Casey Professor at Harvard Medical School and Director of the Massachusetts General Hospital Voice Center. His patients include singers Julie Andrews of *The Sound of Music* fame, who lost her full vocal range after surgery done elsewhere in 1997, Steven Tyler of Aerosmith and Adele. "I recognized this need in my practice over the years, after seeing many patients with voice problems. I went to Bob Langer because I knew he could help design a material that would ultimately help patients speak and sing again. Currently, no treatments exist to restore vocal cord flexibility."

The material had to be very flexible and be able to vibrate just like human vocal cords. After trying numerous candidates, Langer's team settled on polyethylene glycol 30 (PEG30), which is already used in personal care creams and in medical devices and drugs approved by the U.S. Food and Drug Administration (FDA), as a starting material and created polymers based on it. The PEG30 gel can flutter at a rate of 200 times per second, which is a normal rate for a woman speaking in a conversation. Watch a video of the artificial vocal cord gel in action here .

A physician would inject the gel into a patient's vocal cords. Patients would receive different formulations, depending on how they use their voices. The most stable version is highly "cross-linked," which means the molecules of PEG are more tightly stitched together than in other versions. That makes the material a little bit rigid, but it would still help restore someone's speaking voice. A singer, however, would likely receive a formulation that is more loosely stitched together, or less cross-linked, which is more flexible to allow the patient to hit high notes. The gel degrades over time, so patients would receive two to five injections per year, estimated Zeitels.

Tests in animals suggest that the material is safe, and human trials will hopefully begin in mid-2013. Some of Zeitels' patients, such as Andrews, have formed a nonprofit organization called The Voice Health Institute, which funds Langer and Zeitels' research on the vocal cord biomaterial.

Artificial vocal cords are just one artificial tissue in development in Langer's lab. He described work on building intestinal, spinal cord, pancreatic and heart tissue in the laboratory with many different types of materials. Among them: Nanowires (which are about a tenth the diameter of a human hair) and something called "biorubber."

"It's hard to know when they will be ready for clinical use," Langer said. "But In Vivo Therapeutics hopes to start clinical trials for the spinal cord tissue we've developed within the next year."

Langer also recently developed a pacemaker-sized microchip that delivers just the right amount of medication at just the right time, potentially allowing thousands of patients to ditch painful needles forever. A clinical trial of the device, implanted in women with osteoporosis, has just concluded and showed that it was safe to use. The device released osteoporosis medication when it received a signal from a computer. It worked just as well as daily shots of the drug. MicroCHIPS, Inc., a company that Langer co-founded, will commercialize the remote-controlled microchip.

Another way to make medicines more effective is to make sure they go exactly to the location where they are needed; this reduces harmful side effects. Langer's targeted nanoparticles can do just that. A clinical trial run by BIND Biosciences, another company co-founded by Langer, recently found that these nanoparticles are safe in humans. The particles have a homing molecule on them that targets them to prostate cancer cells or cancer blood vessels, and they deliver an anti-cancer medication called docetaxel. All of the materials, including the drug, are already approved by the FDA.

Langer said that the chemical engineering field, which marries chemistry and engineering to make useful devices and other substances, is booming. "There are all kinds of advances happening in drug delivery, new vaccines and immunotherapies, tissue engineering, nanotherapies and nanodiagnostics," he said.

Watch a video here for more information about Langer's innovations.

Langer acknowledged funding from the National Institutes of Health and the National Cancer Institute.

Sponsored by The Kavli Foundation, a philanthropic organization that supports basic scientific research, the lectures are designed to address the urgent need for vigorous, "outside the box" thinking by scientists as they tackle the world's mounting challenges, including climate change, emerging diseases and water and energy shortages.

"We are dedicated to advancing science for the benefit of humanity, promoting public understanding of scientific research and supporting scientists and their work," said Kavli Foundation President Robert W. Conn in a statement. "The Kavli Foundation Innovations in Chemistry Lecture program at the ACS national meetings fits perfectly with our commitment to support groundbreaking discovery and promote public understanding."

The Kavli lectures debuted at the Anaheim meeting in March 2011 and will continue through 2013. They will address the urgent need for vigorous, new, "outside-the-box"- thinking, as scientists tackle many of the world's mounting challenges like climate change, emerging diseases and water and energy shortages. The Kavli Foundation, an internationally recognized philanthropic organization known for its support of basic scientific innovation, agreed to sponsor the lectures in conjunction with ACS in 2010.

Provided by American Chemical Society