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Researchers develop gene therapy that could correct a common form of blindness

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A new gene therapy method developed by University of Florida researchers has the potential to treat a common form of blindness that strikes both youngsters and adults. The technique works by replacing a malfunctioning gene in the eye with a normal working copy that supplies a protein necessary for light-sensitive cells in the eye to function. The findings are published today (Monday, Jan. 23) in the *Proceedings of the National Academy of Sciences* online.

Several complex and costly steps remain before the gene therapy technique can be used in humans, but once at that stage, it has great potential to change lives.

"Imagine that you can't see or can just barely see, and that could be changed to function at some levels so that you could read, navigate, maybe even drive — it would change your life considerably," said study co-author William W. Hauswirth, Ph.D., the Rybaczki-Bullard professor of ophthalmology in the UF College of Medicine and a professor and eminent scholar in department of molecular genetics and microbiology and the UF Genetics Institute. "Providing the gene that's missing is one of the ultimate ways of treating disease and restoring significant visual function."

The researchers tackled a condition called X-linked retinitis pigmentosa, a genetic defect that is passed from mothers to sons. Girls carry the trait, but do not have the kind of vision loss seen among boys. About 100,000 people in the U.S. have a form of retinitis pigmentosa, which is

characterized by initial loss of peripheral vision and night vision, which eventually progresses to tunnel vision, then blindness. In some cases, loss of sight coincides with the appearance of dark-colored areas on the usually orange-colored retina.

The UF researchers previously had success pioneering the use of gene therapy in clinical trials to reverse a form of blindness known as Leber's congenital amaurosis. About 5 percent of people who have retinitis pigmentosa have this form, which affects the eye's inner lining.

"That was a great advance, which showed that gene therapy is safe and lasts for years in humans, but this new study has the potential for a bigger impact, because it is treating a form of the disease that affects many more people," said John G. Flannery, Ph.D., a professor of neurobiology at the University of California, Berkeley who is an expert in the design of viruses for delivering replacement genes. Flannery was not involved in the current study.

The X-linked form of retinitis pigmentosa addressed in the new study is the most common, and is caused by degeneration of light-sensitive cells in the eyes known as photoreceptor cells. It starts early in life, so though affected children are often born seeing, they gradually lose their vision.

"These children often go blind in the second decade of life, which is a very crucial period," said co-author Alfred S. Lewin, Ph.D., a professor in the UF College of Medicine department of molecular genetics and microbiology and a member of the UF Genetics Institute. "This is a compelling reason to try to develop a therapy, because this disease hinders people's ability to fully experience their world."

Both Lewin and Hauswirth are members of UF's Powell Gene Therapy Center.

The UF researchers and colleagues at the University of Pennsylvania performed the technically challenging task of cloning a working copy of the affected gene into a virus that served as a delivery vehicle to transport it to the appropriate part of the eye. They also cloned a genetic "switch" that would turn on the gene once it was in place, so it could start producing a protein needed for the damaged eye cells to function.

After laboratory tests proved successful, the researchers expanded their NIH-funded studies and were able to cure animals in which X-linked retinitis pigmentosa occurs naturally. The injected genes made their way only to the spot where they were needed, and not to any other places in the body. The study gave a good approximation of how the gene therapy might work in humans.

"The results are encouraging and the rescue of the damaged photoreceptor cells is quite convincing," said Flannery, who is on the scientific advisory board of the Foundation Fighting Blindness, which provided some funding for the study. "Since this type of study is often the step before applying a treatment to human patients, showing that it works is critical."

The researchers plan to repeat their studies on a larger scale over a longer term, and make a version of the virus that proves to be safe in humans. Once that is achieved, a pharmaceutical grade of the virus would have to be produced and tested before moving into clinical trials in humans. The researchers will be able to use much of the technology they have already developed and used successfully to restore vision.

Provided by University of Florida

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