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Researchers awaken vision cells in blind mice

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University of Florida researchers used gene therapy to restore sight in mice with a form of hereditary blindness, a finding that has bearing on many of the most common blinding diseases.

Writing online in today's (May 21) edition of *Nature Medicine*, scientists describe how they used a harmless virus to deliver corrective genes to mice with a genetic impairment that robs them of vision.

The discovery shows that it is possible to target and rescue cone cells — the most important cells for visual sharpness and color vision in people.

"Cone vision defines whether someone is blind or not," said William W. Hauswirth, Ph.D., the Rybaczki-Bullard professor of ophthalmic molecular genetics in the College of Medicine and a member of the UF Genetics Institute. "If you can usefully deliver a gene specifically to cone cells, there are implications for all blinding diseases, not just inherited ones. Even in two very common types of blindness, age-related macular degeneration and diabetic retinopathy, if you can target cones you might be able to rescue that vision."

Scientists experimented with mice with a form of hereditary blindness called achromatopsia, which affects about 1 in 30,000 Americans by disabling cone photoreceptors in the retina. The disease results in nearly complete color blindness and extremely poor central vision.

Within two months of the gene therapy injection into the subretinal space of the mouse eyes, scientists measured the electrical activity in the

retinas, finding that 19 of the 21 treated eyes positively responded to therapy, and 17 of those 19 had electrical readings from their retinas on par with those taken in normal mice.

When the mice were between 6 and 7 months old, tests showed 18 of the 21 treated eyes continued to respond normally.

In addition, a separate, smaller group of treated mice were evaluated using an exam akin to an eye test at the doctor's office.

In experiments overseen by Robert B. Barlow, Ph.D., a professor of ophthalmology at State University of New York Upstate Medical University, the mice were surrounded by four computer monitors that simulated the appearance of being inside a moving drum that had vertical stripes on the walls.

Scientists knew the mice could see the stripes because sighted animals naturally move their heads in the same direction as the moving stripes. By making the stripes ever-narrower — similar to how the letters get smaller toward the bottom of an eye chart — researchers could assess the mice's visual abilities.

As a group, all of the mice displayed normal visual acuity in their treated eyes.

"People can talk and tell us what they see," said lead researcher John J. Alexander, Ph.D., a postdoctoral fellow in the department of ophthalmology at UF. "Animals are much more difficult. What makes this test so fantastic is that it involves an animal's natural response, and the results tell us that the animals' brains are involved in the process, that they are actually seeing something."

In addition to cones, which number about 6 million in the retina, the

eye's rod cells are important for low-light and peripheral vision and exist in much greater amounts, with populations of more 100 million.

But treating cones could play a role in diseases that begin with the destruction of rods, such as retinitis pigmentosa, which affects about 1 in 3,000 Americans.

"This is the first to my knowledge of a cone-targeted gene therapy that restores function in an animal model where cones are the primary defect," said Richard Weleber, Ph.D., a professor of molecular and medical genetics at Oregon Health & Science University who was not involved in the research. "This validates the concept that it is possible to deliver a gene therapy targeting the cone system, and that is incredibly important for a number of degenerative diseases."

Source: University of Florida