Scientists Restore Sight to Chickens with Blinding Disease

May 23 2006

Neuroscientist Sue Semple-Rowland of the University of Florida&acutes McKnight Brain Institute poses with a type of Rhode Island Red chicken born blind. Rowland has developed a gene therapy that enables these animals to hatch with their sight intact, which proves in principle that a similar treatment can be developed for an incurable form of blindness in children. Credit: Kristen Bartlett/University of Florida

University of Florida scientists have delivered a gene through an eggshell to give sight to a type of chicken normally born blind. The finding, reported Tuesday (May 23) in the online journal *Public Library of Science-Medicine*, proves in principle that a similar treatment can be

developed for an incurable form of childhood blindness.

“We were able to restore function to the photoreceptor cells in the retinas of an avian model of a disease that is one of the more common causes of inherited blindness in human infants,” said Sue Semple-Rowland, Ph.D., an associate professor of neuroscience with UF’s Evelyn F. and William L. McKnight Brain Institute. “The vision capabilities of the treated animals far exceeded our expectations.”

The bird — a type of Rhode Island Red chicken — carries a genetic defect that prevents it from producing an enzyme essential for sight. The condition closely models a genetic disease in humans that causes Leber congenital amaurosis type 1, or LCA1. About 2,000 people in the United States are blind because they have a disease that falls in the LCA family.

“Enabling chickens that can’t see to peck and eat after treatment is stunning,” said Dr. Jean Bennett, a professor of ophthalmology and cell and developmental biology at the University of Pennsylvania who was not involved in the study but who participated in a landmark gene transfer experiment five years ago that restored vision to blind Briard dogs. “This is proof of concept using a unique vector, animal model and approach. One would hope this could happen in a human.”

Semple-Rowland, a College of Medicine faculty member, has worked since 1986 to first discover the malfunctioning gene, known as GC1, and then to develop a viral therapy to treat it.

“I will always remember the first animal that we successfully treated,” said Semple-Rowland, who is also a member of the UF Center for Vision Research and the UF Genetics Institute. “I thought I saw signs that the chick was responding visually to the environment, but I didn’t want to believe it. Scientists always doubt what they see — it’s intrinsic to how we operate. So I did this simple little test, drawing little dots on a

piece of paper. The chick, which was standing on the table, came over to the paper and started pecking at all of them. It was so exciting."

Later, more precise tests showed that of the seven treated chickens, five displayed near-normal visual behavior. Measurement of electrical activity in the retinas of the same five animals showed they responded to light. In comparison, tests on three untreated chickens showed no meaningful responses.

"This is an interesting gene-transfer technique that appears to restore function to light-sensitive cells in the retina," said Dr. Paul A. Sieving, director of the National Eye Institute of the National Institutes of Health, which partially funded the study. "An approach such as this could lead eventually to a vision-restoring therapy for children who suffer from blinding retinal diseases."

Like people, chickens possess color vision and function best in daylight. The predominant photoreceptor cell type in the chicken retina, the cone cell, is the same cell type that is essential for normal human vision.

To develop the treatment, UF scientists constructed a virus able to infect photoreceptors, delivering a normal copy of the GC1 gene to these cells. Using a very fine glass needle, they injected the viral vector into the developing nervous system of a chicken embryo through a tiny hole in the eggshell. The shell was resealed and the egg was incubated to hatching to produce a live chick.

"The process sounds straightforward but it really isn't," Semple-Rowland said. "It took quite a long time to build the vector, develop the injection procedure and figure out how to hatch the eggs. By doing the injection early during development, we actually treat the cells before they become photoreceptors."

Infants with LCA1 would receive an injection of the gene transfer agents directly into the eyeball during the first couple of years of life, bypassing embryonic treatment. That's important, researchers say, because a diagnosis of LCA1 is often not made until months after a child is born.

"There are only a few clues that an infant may have this disease," Semple-Rowland said. "Often parents will notice that their child doesn't seem to be smiling at or looking at faces. Children may also poke or rub their eyes, behaviors clinically known as oculo-digital signs that may produce sensations of sight."

Work remains to refine the viral delivery system that transfers the healthy genes to the photoreceptor cells. In addition, solutions have to be found to make the treatment long-lasting — scientists have restored sight and slowed degeneration, but the retinal cells still degenerate.

But Semple-Rowland thinks the time necessary to turn these research results into a treatment for patients will be a fraction of the 20 years that have gone into discovering the genetic defect and developing a therapy for it.

"We can do amazing things in animal models," Semple-Rowland said, "but this work can't be done quickly. That's the hardest thing — knowing there are people who need these treatments now. But we work as fast as we can. You'll see the first treatments for some of these genetic eye diseases soon, especially after the groundwork for an approved therapy is laid and the therapy works."

Source: University of Florida