Gene therapy improves vision

November 23 2009, By Brian Schleter

From left to right: Albert M. Maguire, associate professor of Ophthalmology at Penn; Katherine High, director of the Center for Cellular and Molecular Therapeutics at Children's Hospital of Philadelphia; and Jean Bennett, professor of Ophthalmology at Penn. Photo credit: The Children's Hospital of Philadelphia

German scientist Paul Ehrlich found what he coined the "magic bullet" in the early 20th century upon developing the world's first effective treatment of syphilis.

Now for the first time, the most promising magic bullet yet—gene therapy—has been shown to safely improve vision in children and adults with rare retinal diseases that cause blindness.

Penn husband-and-wife research team Albert M. Maguire and Jean Bennett have been examining inherited retinal degenerations together for nearly 20 years. Their study sought to improve vision in five children and seven adults with Leber's congenital amaurosis (LCA), which affects

fewer than 2,000 people in the United States. The results even surprised them.

“Children who were treated with gene therapy are now able to walk and play just like any normally sighted child,” says Maguire, an associate professor of ophthalmology at Penn and a physician at the Children’s Hospital of Philadelphia. “They can also carry out classroom activities without visual aids.”

“It’s a dream come true, really. We hope it’s a cure. We’ll have to wait for time to pass by to see if it is,” says Bennett, the F.M. Kirby Professor of Ophthalmology at Penn’s School of Medicine.

Maguire and Bennett met when they were first-year medical students at Harvard. “We were dissecting partners in neuroanatomy. It was love over the hypothalamus,” Bennett says.

They’ve been married for 24 years. A shared desire to combine their unique skill sets in search of new cures for eye disease led them to begin collaborating professionally.

“It was really fun. He’d come to my lab a couple of hours once a week and we’d work together, taking advantage of his surgical skills and whatever I’d concocted in the lab,” Bennett says. “We tried really hard not to bring it home and make our kids listen to it over dinner. But I must confess—they had an unusual vocabulary when they were little, talking about things like electroretinograms.”

The roots of their scientific breakthrough reach back to the early 1990s, when scientists began unraveling the complex human genetic code and the idea of gene therapy moved from the realm of science fiction to the covers of medical journals.“Twenty years ago, gene therapy was a pipe dream ... The ability to deliver genes stably and safely to the tissue didn’t

evolve until the late 1990s," Bennett says.

The particular form of LCA they looked at is even more rare: Approximately five babies are born with it each year. But they had a very good understanding of the genetics involved and what the specific gene does that's been implicated in this form of the disease, thanks in part to years of animal research, Bennett says.

"It was pretty obvious when we treated the first puppies with this blinding disease that, before the treatment, they were timid and they were scared to take a step because they would bump into things," she says. "Their personality and demeanor would change when they could see."

Now children are experiencing the same thrill. In April 2008, the study team published encouraging preliminary results in the New England Journal of Medicine regarding three young adults, the first to receive gene therapy in this current clinical trial. Those subjects showed improvements in their visual function in both objective vision tests and subjective reports by the patients themselves. Patients who could only detect hand movements gained the ability to read lines on an eye chart.

Based on the results, the study team extended gene therapy to five children and four adults, testing the hypothesis that younger human subjects would receive greater benefits from the treatment.

In all, 12 patients received the gene therapy via a surgical procedure performed by Maguire starting in October 2007 at the Children's Hospital of Philadelphia. For each subject, Maguire injected the therapeutic genes into the eye with poorer function. Starting two weeks after the injections, all 12 subjects reported improved vision in dimly lit environments.

“This result is an exciting one for the entire field of gene therapy,” says Katherine A. High, the director of the Center for Cellular and Molecular Therapeutics, the facility that sponsored the clinical trial at the Children’s Hospital of Philadelphia. “These findings may expedite development of gene therapy for more common retinal diseases, such as age-related macular degeneration.”

Another result that surprised the team was that the vision of the first patients treated nearly two years ago continues to improve.

The study findings were published in The Lancet and instantly were reported by mainstream media around the globe. CBS Evening News showed video footage recorded by the team of a 9-year-old boy previously classified as legally blind navigating an obstacle course they designed for testing purposes.

Bennett says she’s received an avalanche of e-mails and calls from people with LCA and different forms of blindness. Even owners of blind dogs have inquired about the study.

“It is challenging but it’s also gratifying and heartwarming. The messages I get are so lovely. I don’t think people are fooling themselves into thinking that a cure is around the corner for them, but they have hope. It’s nice to be able to help spread that message,” she says.

“The problem is that when parents are told their babies are blind because of LCA, they’re often told ‘there is nothing we can do. All you can do is teach your child how to use a cane and read Braille.’ That’s really devastating,” she says. “Now I think there is something we can do ... I think it brings hope that there might actually be a treatment on the horizon for their particular disease.”

Source: University of Pennsylvania (news : web)