

A Visionary Database

Two sports figures help an HHMI researcher realize his big dream to treat a rare genetic eye disease.

DERREK LEE, STAR FIRST BASEMAN AND SLUGGER FOR THE CHICAGO CUBS, AND HIS wife Christina brought their daughter Jada Ryan into the doctor’s office in mid-September to check out the 3-year-old’s vague complaint about a pain in her eye. ¶ The parents were stunned when the diagnosis came in: Leber’s congenital amaurosis (LCA), a rare genetic cause of blindness. The doctors determined that Jada was nearly blind in one eye already and could expect, sooner or later, to lose vision in her other eye.



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DERREK LEE

“You walk in thinking your daughter is going to have something minor and you walk out with some of the most devastating news you’re ever going to hear,” says Lee.

Enter HHMI investigator Edwin M. Stone, ophthalmic geneticist and authority on LCA at the University of Iowa’s Carver College of Medicine, where Jada’s parents took her for genetic testing to try to confirm

the diagnosis. Her clinical information was also added to Stone’s ambitious database—a work in progress that aims to collect information on all of the approximately 3,000 people in the United States with LCA; it now contains data on more than 500. One of them is 14-year-old Campbell Grousbeck, a patient of Stone’s and son of another high-profile sports figure, Wycliffe “Wyc” Grousbeck, co-owner and CEO of the Boston Celtics.

Lee, Grousbeck, and other motivated parents and donors are supporting Stone’s landmark project, appropriately dubbed

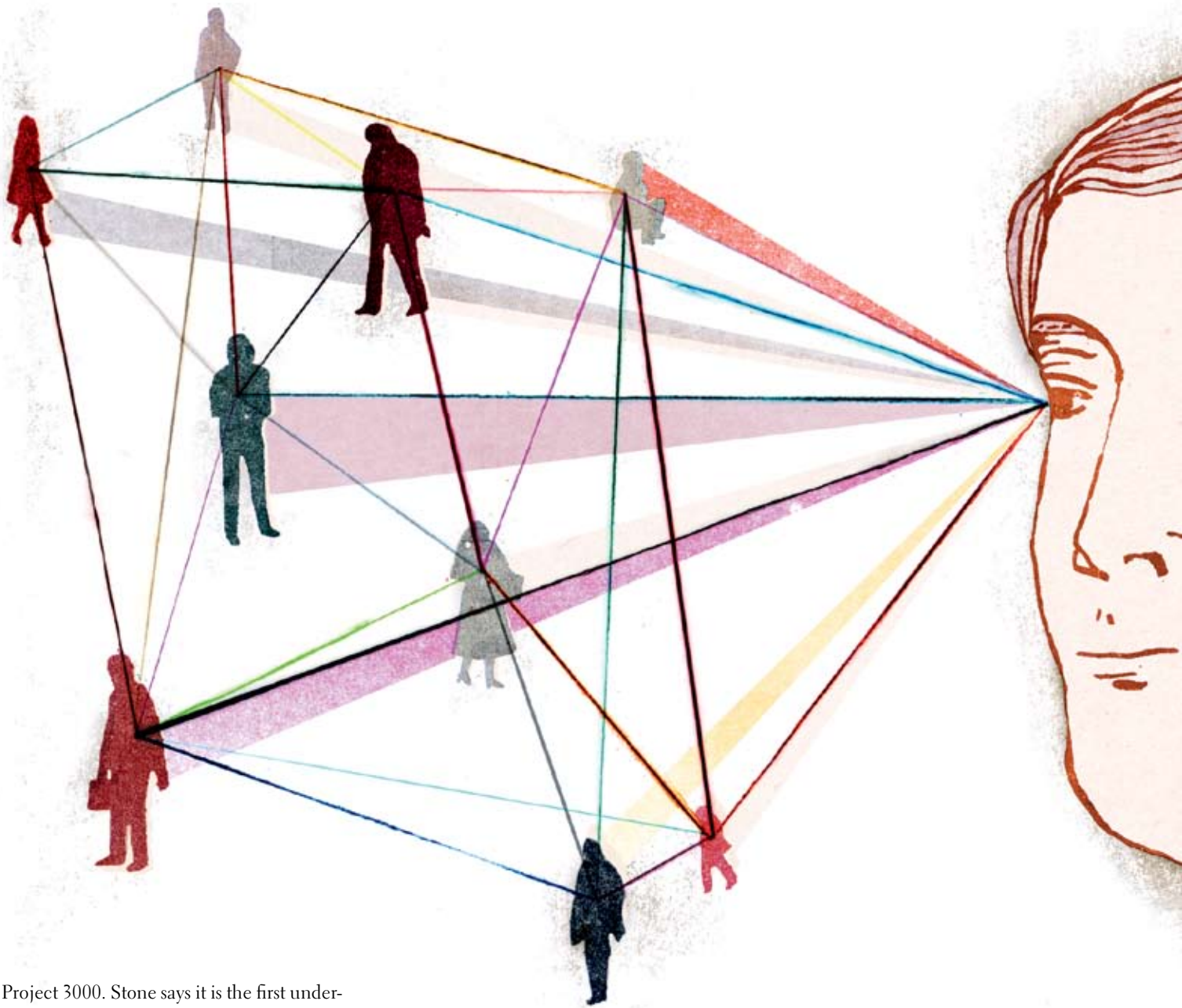
A New Meaning for “Seeing-Eye Dog”

Hope for LCA patients comes in the form of a handsome long-haired French sheepdog known as a Briard. Briards are prone to developing a type of LCA caused by the inability of a layer of eye tissue beneath the retina—the retinal pigment epithelium (RPE)—to produce a normal version of the RPE65 protein, an enzyme that is vital to sight. A veterinary ophthalmologist at the University of Pennsylvania bred a colony of these dogs, some of which are born blind because of an RPE65 defect.

Penn scientists and their colleagues have shown that gene therapy—injecting viruses containing a normal RPE65 gene into the subretinal space—can restore vision in the Briards. Within weeks, the treated eyes are producing normal RPE65 protein.

HHMI investigator Edwin M. Stone is of course enthusiastic about these results: “Researchers took a blind dog—a dog that walked into walls and other obstacles—and changed it into one that could trot around, avoid chair legs, and catch a ball of socks in mid-air.” He says the results have held up for more than five years and that about 40 dogs have been successfully treated.

That’s potentially good news for people with the RPE65 defect, and human trials are in fact gearing up. But only a limited population of LCA patients—about 10 percent—have this subtype. Still, Stone says, Project 3000 will help find candidates for human trials with this therapy, as well as for other treatments as they become available.



Project 3000. Stone says it is the first undertaking in the visual sciences to build a database of information on everyone in the country with a specific genetic disease. The plan is to reach out to pediatric ophthalmologists, visual scientists, and others with a special interest in LCA who are likely to know patients with the condition. “We want to make it clear that a good molecular test is ready to go,” Stone says.

Now is an opportune time to find LCA patients because of advances in the genetic understanding of the disease and because of new prospects to treat and even cure the disease, he adds (see sidebar, page 8). Since the mid-1990s, nine genes for LCA have been identified, accounting for 65 percent

of the cases. Stone, whose research team identified one of those genes, estimates that four or five more culprit genes will be discovered. If all 3,000 LCA patients were identified, their histories taken, and their genes studied, Stone says, the disease would be better defined and, he hopes, new therapies devised.

Lee has been eager to help. “I needed to do something,” he says. “When they told me about treatment being a bit of a ways

away, my first question was ‘What can I do to speed this process?’” Within six weeks of launching Project 3000 more than a dozen LCA patients previously unknown to Stone had agreed to participate and donations started coming in from all over the world.

“I hope this pays off for my daughter,” Lee says. “But if not, if it helps someone else’s daughter, it would all be worth it. When you go into a game, you play to win.”

■ -HOWARD WOLINSKY

FOR MORE INFORMATION: The Website for Project 3000 is: www.carverlab.org.