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**PHILADELPHIA INTERNATIONAL MEDICINE® NEWS BUREAU**

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May 9, 2008

**For immediate release:**

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- 1. Gene Therapy Improves Vision in Patients with Congenital Retinal Disease**
- 2. Methodist Hospital Radiologist, Dr. Mark Cooper, Gets Own Exhibit at National Baseball Hall of Fame**

*Editors note: Research, new techniques and improved facilities by Philadelphia International Medicine hospitals and physicians may lead to new ways to treat some of our most challenging diseases. Below are just some examples from our hospitals.*

*Patients' Vision Improved from Detecting Hand Movements to Reading Lines on Eye Chart*

PHILADELPHIA – In a clinical trial at The Children's Hospital of Philadelphia, researchers from The University of Pennsylvania have used gene therapy to safely restore vision in three young adults with a rare form of congenital blindness. Although the patients have not achieved normal eyesight, the preliminary results set the stage for further studies of an innovative treatment for this and possibly other retinal diseases.

An international team led by The University of Pennsylvania, The Children's Hospital of Philadelphia, the Second University of Naples and the Telethon Institute of Genetics and Medicine (both in Italy), and several other American institutions reported their findings today in an online article in the *New England Journal of Medicine*.

"This is the first gene therapy trial for a nonlethal pediatric condition," said Albert M. Maguire, M.D., Associate Professor, Department of Ophthalmology, University of Pennsylvania School of Medicine and a physician at The Children's Hospital of Philadelphia. Maguire, together with his wife, Jean Bennett, M.D., Ph.D., Professor of Ophthalmology at Penn and Senior Investigator at the F.M. Kirby Center for Molecular Ophthalmology at Penn's Scheie Eye Institute, have been researching inherited retinal degenerations such as Leber congenital amaurosis (LCA), for 18 years. LCA is a group of inherited blinding diseases that damages light receptors in the retina. It usually begins stealing sight in early childhood and causes total blindness during a patient's twenties or thirties. Currently, there is no treatment for LCA.

"Patients' vision improved from detecting hand movements to reading lines on an eye chart," Maguire added. In 2001, Bennett and Maguire were part of a team which reported successfully

reversing blindness using gene therapy on dogs affected by the same naturally occurring form of congenital blindness.

The current study is sponsored by the Center for Cellular and Molecular Therapeutics at The Children's Hospital of Philadelphia, directed by Katherine A. High, M.D. High, a study leader and an Investigator of the Howard Hughes Medical Institute, has been a pioneer in translational and clinical studies of gene therapy for genetic disease, and in 2005 initiated a collaboration with Bennett and her group to translate their exciting animal findings into a clinical study.

The scientists used a vector, a genetically engineered adeno-associated virus, to carry a normal version of the gene, called *RPE65*, that is mutated in one form of LCA. Three patients, ages 19, 26 and 26, received the gene therapy via a surgical procedure performed by Maguire between October 2007 and January 2008 at The Children's Hospital of Philadelphia, where the gene vector was manufactured at the hospital's Center for Cellular and Molecular Therapeutics (CCMT).

Starting two weeks after the injections, all three patients reported improved vision in the injected eye. "Standard vision tests showed significantly improved vision in the patients," said Alberto Auricchio, M.D., a study leader from the Telethon Institute of Genetics and Medicine and University of Naples Federico II. The researchers also reported that each injected eye became approximately three times more sensitive to light, and each was improved compared to the uninjected, previously better functioning eye.

The LCA gene therapy vector showed no signs of causing inflammation in the retina or other toxic side effects. One of the three patients had an adverse event, a hole in the retina that did not affect eyesight and may have been surgery-related, rather than related to biological effects of the therapeutic gene or the vector used to carry it.

The patients enrolled in the study to date were identified at the Department of Ophthalmology at the Second University of Naples, an institution with long-standing experience in collecting and studying patients with inherited retinal diseases, under the supervision of Francesca Simonelli, M.D.

Testing continued over a period of six months following the gene therapy vector administration. One patient was better able to navigate an obstacle course compared to before the injection. The patients also had less nystagmus, an involuntary movement of the eyes that is common in LCA. In the patient who experienced better vision even in the uninjected eye, the researchers suggest that the reduced nystagmus benefited both eyes.

"The current clinical trial will continue with more patients and with ongoing follow-up to monitor results," said Bennett. "We expect improvements to be more pronounced if treatment occurs in childhood, before the disease progresses."

"This result is important for the entire field of gene therapy," notes High, a past president of the American Society of Gene Therapy. "Gene transfer has been in clinical trials for over 15 years now, and although it has an excellent safety record, examples of therapeutic effect are still relatively few. The results in this study provide objective evidence of improvement in the ability to perceive light, and thus lay the groundwork for future studies in this and other retinal disorders," said High.

The pace of moving from pre-clinical discoveries into clinical trials has typically been slow in the field of gene therapy due to the breadth of expertise required, ranging from in-depth knowledge of

the disorder to detailed understanding of vector design, manufacture, and pre-clinical evaluation. The complexities of regulatory oversight at both the federal and local levels also present challenges. Through the Center for Cellular and Molecular Therapeutics, The Children's Hospital of Philadelphia has developed concentrated expertise and substantial resources to facilitate the "bench to bedside" translation of gene therapy.

The scientists at the Clinical Vector Core at CCMT have over 30 years experience in the biopharmaceutical industry and in 2007 were awarded a National Institutes of Health contract for clinical grade vector production for trials throughout the United States, attesting to the quality of their vector manufacture. The CCMT's dedicated regulatory affairs support has specialized expertise in clinical gene therapy and coordinates trial approvals from multiple scientific and ethic review committees, manages the study activities at all clinical sites, and ensures compliance with international quality standards for conducting, monitoring, and reporting clinical trials.

The clinical trial was sponsored and primarily funded by the Center for Cellular and Molecular Therapeutics at The Children's Hospital of Philadelphia. Research support was received from The Department of Ophthalmology at the University of Pennsylvania, the F.M. Kirby Foundation, the Foundation Fighting Blindness, Research to Prevent Blindness, the Macula Vision Foundation, the Paul and Evanina Mackall Foundation Trust at the Scheie Eye Institute, the Rosanne H. Silbermann Foundation, the Italian Telethon Foundation, the Associazione Italiana Amaurosi Congenita di Leber, the National Center for Research Resources, the Howard Hughes Medical Institute, the National Eye Institute of the National Institutes of Health, private philanthropy, and an anonymous donor who is committed to advancing pediatric medicine through maximizing the potential of gene therapy.

(PHILADELPHIA)For only the third time ever, the National Baseball Hall of Fame has dedicated an exhibit to the collection of one person—and that person is Philadelphia native and Methodist Hospital radiologist Mark Cooper, M.D., M.B.A. The exhibit, which opened on April 12 in Cooperstown, NY, is called *Home Games: A Century of Baseball Games from the Collection of Dr. Mark Cooper*. It features more than 50 games over a 100 year period from 1860 to 1960, and is on display through the end of the 2008 baseball season.

Dr. Cooper, who is also a clinical assistant professor of Radiology at Jefferson Medical College of Thomas Jefferson University, was raised in North Philadelphia at 15<sup>th</sup> and Clearfield Streets, close to where the Philadelphia Phillies played ball prior to the opening of Veterans Stadium. He developed a strong passion for the national pastime early on, growing up in the 1950s and '60s, and enjoyed countless hours playing baseball board games. With the roll of the dice or the flick of a spinner, Dr. Cooper brought to life a wealth of players and plays in the field of his imagination. It wasn't until Dr. Cooper was at a flea market in Adamstown in 1983 with his wife, Lynne, that he started collecting the games of his youth and recapturing the past. Now, with a collection

numbering over 500, he's built a special room in his Wynnewood, PA home to showcase the board games and other memorabilia that he has amassed over a lifetime. A national expert on the subject, Dr. Cooper co-authored *Baseball Games: Home Versions of the National Pastime, 1860's – 1960's* in 1995, a copy of which is proudly displayed in the radiologist's Methodist Hospital office. (The book is sold internationally.) The Smithsonian Institute has even recognized his collection by including it in their book, *Smithsonian Baseball: Inside the World's Finest Private Collections*. "Baseball is the only game without a clock. And board games don't have clocks either. So for me, these games represent the timelessness of childhood," says Dr. Cooper.

"I like to say that I collected the games as I moved South on Broad over the years -- from Central High, to Temple (University), to Jefferson (Medical College), to Methodist (Hospital)," says Dr. Cooper with an obvious sense of nostalgia and pride for his hometown heritage and love of baseball. "I guess you could say that as I moved forward in my life these games took me back to a time when baseball was truly a game – prior to free agency, when baseball was not as dependent on salary caps and T.V. revenue."

Dr. Cooper's collection stops at the point when games became electronic, between the 1960s and '70s.

Among the games featured in the Hall of Fame exhibit: *The New Parlor Game of Base Ball* from 1869, the oldest existing game, dating back to the first year of professional baseball; *League Parlor Base Ball* of 1884, the first baseball game to use dice; *The Professional Game of Base Ball* of 1890, the first baseball game produced by Parker Brothers; and *The Champion Game of Base Ball* from 1889, featuring the likenesses of Hall of Famers Dan Brouthers and John Clarkson.

Dr. Cooper graduated from Central High School in 1969 and Temple University, with a B.A. in biology, in 1973. He received his doctor of medicine degree from Jefferson Medical College in 1977, and completed a residency in diagnostic radiology and fellowship in angiography at Thomas Jefferson University Hospital in 1981. Since 1981 he has been with Methodist Hospital Division of Thomas Jefferson University Hospital.

To read more about Dr. Mark Cooper's Hall of Fame exhibit, go to:

<http://web.baseballhalloffame.org/museum/homegames.jsp>

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