

Strictly embargoed to Sunday 27th April 2008 at 22.15 GMT (17.15 Eastern)

Results of world's first gene therapy for inherited blindness show sight improvement

UK researchers from the UCL Institute of Ophthalmology and Moorfields Eye Hospital have announced results from the world's first clinical trial to test a revolutionary gene therapy treatment for a type of inherited blindness. The results, published today in the *New England Journal of Medicine*, show that the experimental treatment is safe and can improve sight. The findings are a landmark for gene therapy technology and could have a significant impact on future treatments for eye disease.

The trial, which received funding from the Department of Health, represented a world first when it began in February 2007. It involves young patients with a condition called Leber's congenital amaurosis (LCA), a rare inherited eye disease caused by an abnormality in a gene called RPE65. The condition appears at birth or in the first few months of life and causes progressive deterioration and loss of vision. There are currently no effective treatments available. The trial's purpose was firstly to find out whether gene therapy for retinal disease is safe, and secondly to find out if it can benefit vision in young adults who already have advanced retinal disease.

Crucially, the experimental treatment was found to cause no side effects in this trial. Following the treatment, the three patients involved underwent a series of tests designed to establish the effects of the therapy on vision. They all achieved levels of vision at least equivalent to before the operation, but one patient (Steven Howarth, 18) benefited from significantly improved night vision. This was demonstrated by his ability to negotiate a specially constructed simulation of a night-time street scene. Before the operation he completed the task slowly and made several mistakes, but following the surgery he was able to navigate quickly and without mistakes. (Video available for media release – please see Notes to Editors.)

The researchers believe the operation's success for this particular patient could be because his disease had not progressed to the same extent as the others. The other two patients may also still benefit from the new treatment in the future, but it will be some time before this becomes apparent. The team have already begun to trial the technique in younger patients, where they hope to achieve even better results.

The team conducting the trial, from the joint Moorfields Eye Hospital/UCL Institute of Ophthalmology NIHR Biomedical Research Centre, is led by Professor Robin Ali and includes eye surgeon Mr James Bainbridge and retinal specialist Professor Tony Moore. The technique used in the trial involved inserting healthy copies of the missing RPE65 gene into the cells of the retina to help them to function normally. This involved an operation which delivered the normal genes to the retina, using a harmless virus or 'vector' to carry the gene into the cells – the vector was manufactured by US company Targeted Genetics.

Commenting on the findings, Professor Ali said: "Showing for the first time that gene therapy can work in patients with eye disease is a very significant milestone. This trial establishes proof of principle of gene therapy for inherited retinal disease and paves the way for the development of gene therapy approaches for a broad range of eye disorders."

Explaining the technique, Mr James Bainbridge, who leads the surgical team, said: "We developed surgical techniques to enable access to the cells beneath the retinas of patients, using a very fine needle to deliver the modified virus in a controlled retinal detachment that resolves as the vector is absorbed. It is tremendously exciting to see that this technique is safe in an extremely fragile tissue and can improve vision in a condition previously considered wholly untreatable."

Professor Moore said: "It is very encouraging to see that this treatment can work, even in young adults who have severely advanced disease. We anticipate an even better outcome in the younger patients we are now beginning to involve as the trial proceeds, as we will be treating the disease in the early stages of its development."

Professor Ali added: "These results give us great confidence that this technique is safe and can bring real benefit to patients with impaired vision. While we're very excited about the improvement in Steven's vision, it's important to emphasise that gene therapy is still an experimental treatment not yet generally available to patients. The technique will be tested in other patients with LCA and we also hope to begin trials for other forms of retinal disease in the future."

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Notes for Editors

1. For further information, or to arrange an interview with Professor Robin Ali or Mr James Bainbridge, please contact Ruth Metcalfe in the UCL Media Relations Office on tel: +44 (0)20 7679 9739, mobile: +44 (0)7990 675 947, out of hours: +44 (0)7917 271 364, e-mail: r.metcalfe@ucl.ac.uk
2. Video and images from the trial, along with a background document, are available from UCL Media Relations using the contact information above.
3. The paper 'Effect of Gene Therapy on Visual Function in Leber Congenital Amaurosis' is published online ahead of print in the New England Journal of Medicine on April 28th 2008. Copies of the paper can be obtained by journalists from UCL Media Relations.
4. Professor John Marshall, Chairman of the Medical Board at the British Retinitis Pigmentosa Society and Professor of Ophthalmology at King's College London, can be contacted for comment on mobile: +44 (0)7802 157156, email: marshall-eye@kcl.ac.uk
5. The vector used in this trial was manufactured by Targeted Genetics, Seattle, USA. For further information about Targeted Genetics, please contact Stacie D. Byars, Director of Communications, on tel: +1 206 521 7392, email: sdbyars@wcpglobal.com
6. The team is supported by funding from the Department of Health, British Retinitis Pigmentosa Society, Sir Jules Thorn Charitable Trust, The Wellcome Trust, The European Union (EVI Genoret and Clinigene programmes), The Special Trustees of Moorfields Eye Hospital, The Medical Research Council, Foundation Fighting Blindness USA, Fight for Sight and the Ulverscroft Foundation, Fighting Blindness Ireland
7. Robin Ali is Professor of Human Molecular Genetics at UCL Institute of Ophthalmology and Head of Division of Molecular Therapy. James Bainbridge is a Wellcome Trust Advanced Fellow at UCL Institute of Ophthalmology and Consultant Ophthalmologist at Moorfields Eye Hospital. Tony Moore is Professor of Ophthalmology at UCL Institute of Ophthalmology and Consultant Ophthalmologist at Moorfields Eye Hospital and Great Ormond Street Hospital for Children.

About Moorfields Eye Hospital/UCL Institute of Ophthalmology NIHR Biomedical Research Centre

The Centre was established in April 2007, funded by the Department of Health through the National Institute for Health Research (NIHR). It is one of 12 NHS-university partnerships that have been awarded Biomedical Research Centre status, following an international peer reviewed competition based on an outstanding international reputation for medical research and expertise, and experience of translating that research into the clinical setting.

The results from this gene therapy trial are the first significant outcome from the establishment of the centre, and strongly demonstrate its purpose - to conduct translational research designed to take advances in basic medical research from the laboratory to the clinic, enabling patients to benefit more quickly from new scientific breakthroughs.

About UCL Institute of Ophthalmology

UCL Institute of Ophthalmology is one of a number of specialised research centres linked to UCL (University College London) and is, together with Moorfields Eye Hospital, one of the leading centres for eye research. The Institute scored 5*A (the highest possible rating) in the last Research Assessment Exercise and is committed to a multi-disciplinary research portfolio that furthers an understanding of the eye and visual system, linked with clinical investigations targeted to specific problems in the prevention and treatment of eye disease. The combination of the Institute's research resource with the resources of Moorfields Eye Hospital, which has the largest ophthalmic patient population in the Western World, opens the way for advances at the forefront of vision research.

About Moorfields Eye Hospital NHS Foundation Trust

Founded in 1804 and opened in 1805, Moorfields Eye Hospital is one of the world's leading centres for ophthalmic treatment, teaching, and research. It is the oldest and largest specialist eye hospital in the world, and became one of the UK's first NHS Foundation Trusts in 2004. More than half the ophthalmologists practicing in the UK, and many more overseas, have received specialist training at Moorfields. As well as its main site based on City Road, EC2 the Trust has over 1,300 staff spread over ten sites in Greater London. They are able to treat the entire range of eye diseases from cataracts, to more complex conditions, and patients come to them from all over the UK and the world.