



Breaking new ground with gene therapy

The cutting-edge laboratory work we do with our partners at the UCL Institute of Ophthalmology (IoO) is breaking new ground in vision research – identifying promising new avenues of treatment for people with genetic eye diseases for which there are currently no treatments or cure.

Fighting inherited eye disorders

One of these genetically inherited eye disorders is leber congenital amaurosis (LCA), which causes impaired night vision and variable loss of day vision in patients. Vision impairment often starts in early childhood and can progress to blindness in later life. LCA is estimated to affect one in 80,000 people worldwide and is caused by defects in at least 19 different genes that lead to degeneration of the light-sensitive layer of cells at the back of the eye called the retina.

One of the most common forms of the condition, LCA type 2 (LCA2), is caused by a defect in the RPE65 gene. This gene encodes an important protein found in the retinal pigment epithelium (RPE) layer of the retina and is needed to help the light-sensing photoreceptor cells of the eye detect light.

At the UCL IoO, the team, led by Professor Robin Ali and Professor James Bainbridge, has been working for a number of years at the forefront of translational research to develop a novel way to deliver a treatment to the back of the eye to prevent or reverse this degeneration.

A new way of thinking

This world-leading research team decided to tackle this problem from inside the cells themselves. Rather than using pharmaceuticals or surgery to treat the symptoms of the condition, they decided to use DNA to repair the genetic defect, an approach called gene therapy.

Their aim was to inject a new copy of the RPE65 gene directly in to the retina (to replace the defective version), with the aim of helping the cells to function more normally. After a number of years of laboratory-based research using different models of disease the team were able to move this investigational therapy into the clinic where they began the world's first-in-human trial of gene therapy for inherited blindness at Moorfields.



Moving on: optimising gene therapy

While these latest results provide confirmation of the efficacy of the gene therapy, the effect is not long lasting. It appears that the demand for RPE65 in the eye is not fully met with the current generation of gene therapy vectors, which is consistent with the published findings of other groups.

The team believe that by treating patients earlier and using a more efficient gene therapy they may be able to generate greater benefits, including protecting daytime vision and reducing progressive retinal degeneration in people with LCA2.

Back in the lab, the team has used this knowledge to design and produce a new more potent gene therapy, which they believe has the potential to offer greater improvements in visual function than other therapies currently in development. From spring 2015, this groundbreaking work has received a major grant from the Medical Research Council to support a new clinical trial.

“Our new clinical trial will be an exciting next step in the development of our gene therapy programme. We believe that earlier intervention with our more efficient RPE65 gene therapy is likely to provide greater benefit and protection for patients. Our partnership with Moorfields enables us to accelerate this development into the clinic.”

Professor Robin Ali – Professor of human molecular genetics, UCL Institute of Ophthalmology, NIHR senior investigator and gene therapy theme lead, NIHR Moorfields Biomedical Research Centre

“We are encouraged by the results from our first clinical trial for gene therapy. Our findings not only have implications for the future of RPE65 gene therapy but have also been essential in establishing a framework that will help us in expanding the application of gene therapy to potentially benefit more patients with other inherited retinal conditions.”

Professor James Bainbridge – Professor of retinal studies, UCL Institute of Ophthalmology and NIHR research professor and consultant ophthalmologist, NIHR Moorfields Biomedical Research Centre