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Gene-therapy hope for rare, deadly disease

A RESEARCH TEAM based at University College Cork is attempting to apply the most cutting-edge of gene therapy techniques to one of the rarest genetic disorders known in Ireland. The medical charity Cystinosis Foundation Ireland and the Health Research Board (HRB) are jointly funding the research that will study cystinosis.

Just eight people in Ireland are affected by cystinosis, a condition caused by the absence of the gene encoding a protein called cystinosin. Patrick Harrison of UCC's Department of Physiology will receive more than €150,000 during the next three years to kick-start development of a gene therapy that could eventually be used in treatment.

Cystinosin normally transports the amino acid cystine into lysosomes, the cell's molecular recycling centres. Its absence leads to an accumulation of cystine crystals within cells, which can result in severe problems, including growth deficits, kidney failure, swallowing difficulties, light sensitivity and, eventually, blindness. Many children will require a kidney transplant at an early age. The drug cystagon, which has difficult side-effects, can help to slow progression, but life-expectancy remains tragically short for those born with the condition.

Using a cell culture model of cystinosis, Harrison and collaborator Martina Scallan from UCC's Department of Microbiology will build a rudimentary gene therapy system, recently developed by scientists at the Californian biotechnology firm Sangamo BioSciences, that attempts to mimic the cell's natural system for repairing breaks in the chromosomes.

Such a break can be introduced in a highly directed, site-specific manner using "zinc finger nucleases", which are artificially engineered proteins that can cut DNA at a predetermined location. A donor sequence of DNA can then be inserted into the damaged gene thereby "correcting" the inherited defect.

The approach circumvents several shortcomings associated with more conventional gene-therapy techniques, in which a functioning version of the damaged gene is delivered via a carrier system, such as a virus.

Harrison already has a similar project under way in the area of cystic fibrosis and restoring function in around 10 per cent of target cells might be enough to bring about a clinically meaningful effect. "In cystinosis, I would imagine it's quite a lot higher," he says.

The UCC initiative, which is part of a wider scheme co-funded by the Medical Research Charities Group and the HRB, represents Cystinosis Foundation Ireland's first Irish project. The small but highly effective charity is spending around €100,000 on research annually and is also sponsoring projects at Stanford University in California, US, and at the Robert Gordon University, in Aberdeen, Scotland.

The organisation is hosting the 5th International Cystinosis Conference in Dublin, which takes place tomorrow and on Saturday.

Information on donations at www.cystinosis.ie

Cormac Sheridan