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Finding a cure for Best Disease – how understanding the effects of a single genetic mutation could hold the key

Dr Michael O'Connor from the School of Medicine and a leading research team* have been granted funding to investigate the role of a specific genetic mutation in the development of the blinding disorder Best Disease. The aim of the research is to establish how a mutation in the BEST1 gene might lead to key Best Disease symptoms such as fluid and waste-product build-up in the retina. The project will provide postdoctoral funding for a current PhD student, Melissa Mangala.

'Best Disease is an inherited eye disorder that causes accumulation of fluid and a fatty yellow pigment within the retina, resulting in eventual blindness' Dr O'Connor explains. 'It affects children, and unfortunately there is no cure. Other researchers previously found that a specific mutation in the BEST1 gene, the F305S mutation, is linked with progression of Best Disease. We have now started to uncover the cellular pathways affected by this mutation. It is hoped that by further investigating the mutation's effects on these pathways we might identify targeted interventions which could be administered to children before their vision is lost.'

Many different mutations within the BEST1 gene have been implicated in the disease, and this research will focus on the F305S mutation. Researchers will generate retinal pigment epithelium (RPE) from human embryonic stem cells that contain the F305S mutation, and compare it to RPE without the mutation. Various molecular biology, proteomic and electrophysiology measures will be used to define the intracellular pathways affected by the F305S mutation and how they lead to impaired RPE function. In particular, the downstream effects of altered chloride and calcium-homeostasis that result from BEST1 mutation will be defined.

This research will contribute to the ongoing search for a Best Disease cure, and could provide new biological targets for future medical trials. The research may also provide new insights into age-related macular degeneration.

Project Title: Defining the molecular pathways regulated by endogenous BEST1 in Best Disease
Funding has been set at: $2oo,ooo USD
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