Developing a therapeutic approach for collagen VI-related muscular dystrophy

In this project, Professor Muntoni will develop a novel therapeutic approach for people affected by Ullrich congenital muscular dystrophy caused by dominant mutations in one of the three collagen VI genes. It will use oligonucleotides, which are being developed for other conditions including Duchenne muscular dystrophy. The concept relies on the fact that only one healthy copy of the collagen VI gene is required for the gene to function properly. The potential therapy will be tested in skin cells from people with the condition.

What are the researchers aiming to do?

Ullrich muscular dystrophy is caused by a lack of collagen VI protein, which acts as a scaffold to hold and support muscle cells. Some mutations in the genes that carry the blueprint for collagen VI protein have no effect on the amount of protein that is produced, but stop the scaffold assembling correctly. These mutations are inherited in a dominant way; a single copy of a mutated gene is enough to cause the condition.

Studies have shown that one functional copy of the gene is able to produce sufficient collagen VI protein to build an effective scaffold. Professor Muntoni aims to develop techniques to switch off or 'silence' a gene with a dominant mutation, to allow the second, healthy copy of the gene, to function normally.

In this project, two methods of 'silencing' the gene will be tested: exon skipping and a new technique called RNA interference. Both use small molecules called oligonucleotides to prevent the mutated copy of the gene producing protein and have shown potential as a therapy for other conditions.

These approaches will be tested in skin cells taken from people with Ullrich congenital muscular dystrophy and grown in the laboratory. The researchers will apply oligonucleotides to the cells and check whether this stops the mutated copy of the gene producing protein. They will also investigate whether the techniques result in functional collagen VI being produced - something that could represent a therapeutic approach for Ullrich congenital muscular dystrophy.
How will the outcomes of the research benefit patients?

Approximately 50 percent of cases of Ullrich muscular dystrophy are caused by dominant mutations. If successful, this project will prove the concept that oligonucleotides could be used therapeutically for Ullrich congenital muscular dystrophy caused by these mutations. The next steps would be testing in an animal model to investigate the safety and effectiveness of this potential approach.

Grant information

Project leader: Professor Francesco Muntoni
Location: University College, London
Conditions: congenital muscular dystrophy, Ullrich muscular dystrophy
Duration: two years, starting 2014
Total project cost: £ 116,384
Official title: Allele-selective suppression by antisense oligonucleotide as a therapeutic strategy for collagen VI-related congenital muscular dystrophy

For further information

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