# Treatment breakthrough for rare disease linked to diabetes

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## University of Manchester scientists have led an international team to discover new treatments for a rare and potentially lethal childhood disease that is the clinical opposite of diabetes mellitus.

Congenital hyperinsulinism (CHI) is a condition where the body’s pancreas produces too much insulin – rather than too little as in diabetes – so understanding the disease has led to breakthroughs in diabetes treatment.

This latest study, published in the journal Diabetes today (Wednesday), was carried out with clinical colleagues at hospitals throughout Europe and at the two referral centres for hyperinsulinism in the UK, the Royal Manchester Children’s Hospital and Great Ormond Street Hospital, London.

“In healthy insulin-producing cells of the pancreas, a small group of proteins act as switches and regulate how much insulin is released,” said Dr Karen Cosgrove, who led the research with Professor Mark Dunne in Manchester’s Faculty of Life Sciences.

“When these proteins fail to function the cells can either release too little insulin – resulting in diabetes mellitus, or too much insulin – leading to congenital hyperinsulinism.”

She continued: “CHI causes dangerously low blood sugar levels which can lead to convulsions and brain damage if not treated promptly.

It is a complex condition caused by gene defects that keep the insulin-producing cells switched on when they should be switched off.

“Our group was the first to show how these gene defects led to uncontrolled insulin release in patients a number of years ago.

Now we have taken the cells from patients following surgery and proven that, in some cases, it is possible to correct defects in the rogue cells.”

Current drug treatments for CHI often fail in the most severe forms of the disease and the patient has to have some, or most, of their pancreas removed.

The Manchester researchers discovered that treating cells under specially modified conditions helped to recover the function of the internal switches that control insulin release.

Through these experiments the team have provided the first evidence that the outcomes of gene defects can be reversed in human insulin-producing cells.

One of the drugs used in their studies is currently in clinical trials to treat patients with cystic fibrosis but has not been tested in patients with CHI.

The team hope that their findings will pave the way for new or similar drugs to be used in clinical trials for hyperinsulinism.

“Although our results are really encouraging this is not a magic bullet for the treatment of this devastating condition, but it does offer real hope that in the future we may be able to use new drugs which can reverse the cellular defects,” added Dr Cosgrove.

The clinical service at Royal Manchester Children’s Hospital now includes state-of-the-art facilities for imaging the pancreas to detect hyperinsulinism.

The clinical and academic teams work closely together within NorCHI (Northern Congenital Hyperinsulinism in Infancy service) to learn more about causes and treatments for this disease.

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## Notes for editors

A copy of the paper is available on request.

Diabetes is an internationally renowned journal (impact factor 8.5) that publishes high calibre articles in the fields of diabetes and insulin-secreting cells.

For more information about congenital hyperinsulinism in infancy see <http://www.norchi.nhs.uk/> which also has details of a charitable fund set up to support research into disease.

Diabetes mellitus: affects around 2.5 million people in the UK (source Diabetes UK). Congenital hyperinsulinism: affects 1 in 20,000 to 1 in 40,000 live births in the UK.

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