Scientists discover new causes of diabetes

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Research by the University of Exeter Medical School has revealed two new genetic causes of neonatal diabetes.

The research, published today in the journal *Cell Metabolism*, provides further insights on how the insulin-producing beta cells are formed in the pancreas. The team discovered that mutations in two specific genes which are important for development of the pancreas can cause the disease. These findings increase the number of known genetic causes of neonatal diabetes to 20.The study was funded by the Wellcome Trust, Diabetes UK , European Community's Seventh Framework Programme and the National Institute for Health Research (NIHR).

Dr Sarah Flanagan, lead author on the paper, said: "We are very proud to be able to give answers to the families involved on why their child has diabetes. Neonatal diabetes is diagnosed when a child is less than six months old, and some of these patients have added complications such as muscle weakness and learning difficulties with or without epilepsy.

"Our genetic discovery is critical to the advancement of knowledge on how insulin-producing beta cells are formed in the pancreas, which has implications for research into manipulating stem cells, which could one day lead to a cure."

Dr Alasdair Rankin, Diabetes UK Director of Research, said: "As well as shedding further light on the genetic causes of neonatal diabetes and providing answers for parents of children with this rare condition, this work helps us understand how the pancreas develops. Many people with

diabetes can no longer make insulin and would benefit from therapies that replace the insulin producing beta cells of the pancreas. The results of this study are critical to bringing the day closer when this type of treatment is possible."

Neonatal diabetes is caused by a change in a gene which affects insulin production. This means that levels of blood glucose (sugar) in the body rise dangerously high.

The Exeter team is the leading centre for neonatal diabetes having recruited over 1200 patients from more than 80 countries. This specific study focussed on 147 young people with neonatal diabetes, a rare condition which affects approximately 1 in 100,000 births. Following a systematic screen, 110 patients received a genetic diagnosis. For the remaining 37 patients, mutations in genes important for human pancreatic development were screened. Mutations were found in 11 patients, four of which were in one of two genes not previously known to cause neonatal diabetes (NKX2-2 and MNX1).

For many of the 121 (82%) patients who received a genetic diagnosis, knowing the cause of the diabetes will result in improved treatment, and for all the patients it will provide important information on risk of neonatal diabetes in future pregnancies. These patients also provide important scientific insights into pancreatic development.

Provided by University of Exeter