Gene for rare form of diabetes found

In MODY, a defect in a single gene causes a rare form of the metabolic disease that is often misdiagnosed as Type 1-diabetes

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A team led by researchers in Chennai has isolated a gene that causes a rare form of diabetes, called Maturity-Onset Diabetes of the Young (MODY). This adds to the 14 known gene variants that cause MODY and could advance the emerging field of precision diabetes, by helping personalise diabetes care.

Diabetes involves a disruption of how blood sugar is kept in check by the hormone insulin. In Type-2 diabetes, which is the most common form of the disorder, many genes and environmental factors combine to cause this disruption. In MODY, any one of the 14 genes, if defective, can hamper the body's insulin usage and trigger Type-2 diabetes.

Some forms treatable

Many times non-obese children, with elevated blood sugars, are often misdiagnosed to have Type 1 diabetes and treated with insulin, leading to poor or no control of the blood sugar. "Some forms of MODY can easily be treated with sulphonylurea, an inexpensive drug. And it works very well on the patients. If you consider the age group – young adults [14-21 years] – it is a game changer. It dramatically improves quality of life," says V. Mohan, president, Madras Diabetes Research Foundation (MDRF), a partner in the study.

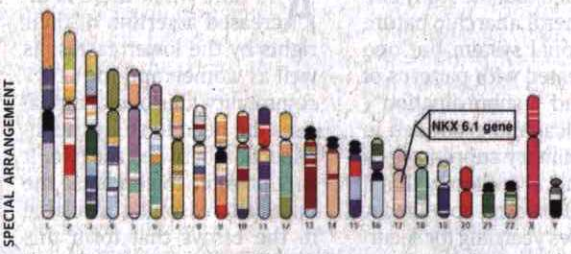
Type 1 diabetes, that MODY is usually mistaken for, is not gene-dependent, and therefore not inherited. "While it will not be cost effective to test everyone, you can look for signs such as the children are not obese, they have a family history, and the insulin they are being treated with does not seem to help. Running the MODY gene test, first for the more common forms, and if they are negative, testing for the rare ones would be the line to take," he adds.

In a paper published in the *BMC Medical Genetics* journal, researchers outlined that variants of the NKX6-1 gene found in MODY patients were "functionally impaired". The study was carried out by the MDRF in collaboration with scientists from Genentech, California, and MedGenome, India.

Of the 14 MODY genes already identified, largely from European studies, MODY 1-3 are the most common. Radha Venkatesan, who heads the molecular genetics wing at the MDRF, says: "I was testing for 1-3 and it was the causative factor in only 11% of the cases. Therefore, we figured that there must be others. We found four other variants in RFX6, WFS1, AKT2, NKX6-1 that may contribute to MODY. A further functional assessment of the NKX6-1 variants showed that they are impaired." She is hopeful that further evidence might emerge to fix the role of the three other variants also discovered, as more and more families come forward to be tested.

The study carried out was based on a comprehensive genomic analysis of 289 individuals from India that included 152 MODY cases and 137 patients without diabetes. The latter showed no genetic variants associated with MODY.

Position of the novel MODY gene(NKX6.1) in the entire set of human chromosomes



The costs

Currently, the costs of testing could be pretty high. "While the cost of testing each gene is about ₹3,000, the costs for the entire MODY genetic panel, come to about ₹18,000. However, we are trying to bring it to under ₹10,000, for the entire package," Dr. Mohan explains.

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