A de novo mutation causing type 2 MODY: a case report.

Background
Type 2 Maturity Onset Diabetes of the Young (MODY) is a monogenic and dominantly inherited form of diabetes characterized by an early age of onset that is featured by the development of mild hyperglycaemia. The cause of this disorder is the presence of mutations in the glucokinase (GCK) gene rendering an enzyme with decreased activity. More than 600 mutations have been reported for the GCK gene but only few de novo ones have been described. The molecular diagnosis of MODY is vital for the identification and classification and allows establishing the prognosis and treatment of this disease. The aim of this study was to analyze the presence of mutations in GCK gene in one family with only one symptomatic member.

Methods
A 17 years old adolescent with a medical history of mild hyperglycaemia and his parents and sister were studied. DNA was extracted from blood samples by the MagNA Pure system (Roche) followed by PCR employing specific primers and GCK gene sequencing (Sanger’s method). DNA sequences were analysed using the ChromasPro and BLAST softwares. Paternity was analysed by AmpFLSTR Identifier PCR Amplification Kit. At the moment of analysis the patient presented serum glucose levels of 7.1 mmol/l and HbA1c=7.4%. Anti-glutamic acid decarboxilase (GAD), tyrosine phosphatase antibodies (IA-2) and anti-insulin autoantibodies were negative. The patient did not present a family history of diabetes.

Results
Direct sequencing of the patient’s GCK gene revealed the presence of the heterozygous mutation 895G>C in the exon 8. This mutation has been previously described and it is known to cause a change in the codon 299 (G299R). This mutation was not detected in neither the parents nor his sister. Results obtained by the Identifier method allowed ruling out a case of false paternity. This result shows that the G299R mutation was generated de novo in this patient.

Conclusions
Family tree with affected proband, and their respective sequences of exon 8 showing that only affected individual had the described mutation.

This case highlights the importance of the molecular diagnosis of MODY in those patients without a family history of the disease but presenting several clinical signs and symptoms for this metabolic disorder. The performance of genetic tests is not only a useful tool in the diagnosis, prognosis and treatment of the MODY but also it allows future genetic counseling.