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GENETIC EPIDEMIOLOGY OF MODY IN THE CZECH REPUBLIC: NOVEL MUTATIONS IN THE MODY GENES HNF-4ALPHA, GCK, HNF-1ALPHA AND NEUROD1

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Maturity-onset diabetes of the young (MODY) is a form of diabetes characterised by autosomal dominant inheritance, an early onset (≤ 25 years of age), and a primary defect in beta-cell function. MODY is caused by mutations in genes encoding the hepatocyte nuclear factor-4α (HNF-4α), glucokinase (GCK), HNF-1α, insulin promoter factor-1 (IPF-1), HNF-1β and NeuroD1, respectively. In 61 unrelated subjects of Czech origin (28 males, 33 females) with clinical diagnosis of MODY and no kidney disease at onset of diabetes, mean age of probands was 22.7 ± 12.0 years (range, 6–62), mean age at the first recognition of hyperglycaemia was 14.7 ± 6.0 years (range, 1–29), we studied the promotor and coding regions of HNF-4α, GCK, HNF-1α , IPF-I and NeuroD1 by PCR-dHPLC and/or direct sequencing. We identified 22 different mutations in 32 families (52 % of all families studied). Six mutations were found in the HNF-1α gene, 11 mutations (10 novel) were detected in the GCK gene in 19 families. Furthermore, four novel mutations (including a –181G-A P2 promoter mutation) were found in the HNF-4α gene and one novel mutation in the NeuroD1 gene. In the remaining 48 % of families with clinical characteristics of MODY diabetes, no mutation was found in the examined genes. This finding supports the hypothesis that others candidate genes might be involved in families with autosomal dominant transmission of diabetes mellitus.