6. CONCLUSIONS

The aims of our study were performed.

Twelve families with unrecognized type of MODY were collected.

Quite large cohorts of DM2 patients, direct offspring of DM2 patients, gestational diabetics and sufficiently large group of control subjects were completed. All the probands underwent a detailed anthropometric and biochemical characterisation. Data were filled in an electronic database.

The DNA bank was established and completed.

For *GCK* gene we adopted screening methods SSCP for all exons specific for β-cells (1a-10) and TGGE for exons 1a-7 and we confirmed their high sensitivity and the 100% concordance of both methods. Results were consequently confirmed by direct sequencing in both directions.

We found a novel heterozygous missense mutation V33A and a previously published mutation E40K in exon 2 of *GCK* gene in two differnent Czech MODY families. However, our study did not provide the evidence of *GC*K gene as a risk gene in the pathogenesis of diabetes mellitus type 2 or of the gestational diabetes in Czech population because we identified only one intronic mutation in a gestational diabetic and no differences in the frequencies of *GCK* polymorphisms between Czech diabetic and nondiabetic populations.

We assessed the frequency of common variant -30G>A in B-promoter of *GCK* gene. Although we did not detect the higher frequency of minor allele A in diabetic in comparison to nondiabetic population, we found out its influence in homozygote form to increased fasting and stimulated levels of glucose and to higher insulin resistance in healthy subjects without family history of DM2. We confirmed the dosage effect of the A allele.

We assessed the frequency of A98V polymorphism in *HNF-1α* gene that did not differ among diabetic and nondiabetic populations. We did not confirm the association of minor T allele (valin) with impaired insulin secretion. In opposite, in control population we identified increases of C-peptide and insulin secretions during the second phase of OGTT and the higher secretion of the β-cells.