The most common form of monogenic diabetes is MODY (Maturity-Onset Diabetes of the Young). It ranks among genetic defects of the β cell. It is clinically heterogenous group of disorders characterised with non insulin-dependent diabetes mellitus with autosomal dominant inheritance and age at diagnosis up to 40 years.
We specified the diagnosis of MODY in more than 240 Czech families using molecular-genetic approach. The most common subtype of MODY is GCK-MODY which was proved in 376 subjects from 175 families. The risk of macrovascular complications in patiens with GCK-MODY was not detected. Additionally, we tested the ancestral origin of 4 recurrent mutations in the GCK gene causing GCK-MODY using genetic and statistical methods. We showed that three mutations (p.Glu40Lys, p.Leu315His, p.Gly318Arg) spread approximately 82-110 generations ago due to a founder effect. We also dealed with the impact of the rs560887 polymorphism on the phenotype of the patients with GCK-MODY. The genotype GG was associated with higher level of glycated haemoglobin. Analysis of patients suspect for HNF1A- or HNF4A-MODY revealed the probably first evidence of patient with HNF1A-MODY present with macrosomia and recurring ketotic hypoglycaemias in the childhood. The rare MODY genes were investigated in patients fulfilling the clinical criteria of MODY but without detected mutation in the common MODY genes. We failed to find any Czech family with PAX4-MODY but we presented one family with ABCC8-MODY.
This work is a part of project focusing on complex study of MODY in the Czech Republic including search for new MODY families, genetic diagnostics, evaluation of clinical aspects, profound genetic analysis, investigation of rare forms and it is involved also in detection of novel genes causing MODY.