4. CONCLUSIONS

The postulated aim of the work was fulfilled:

1) Quite a large cohorts of DM2 patients, direct offspring of DM2 patients, and obese subjects as well as a group of women suffering from PCOS, and sufficiently large group of control subjects were completed
    a. All the probands underwent a detailed anthropometric and biochemical characeterization
    b. The DNA bank was established and completed
2) An electronic database was established
3) Molecular genetic methods PCR, RFLP, and SSCP were established and optimized
4) Specific polymorphisms in the selected candidate genes were genotyped and unique data regarding genotypic frequencies of these polymorphisms in Czech population were obtained
5) Genetic, biochemical and anthropometric data underwent statistical analysis. Especially associations between genetic polymorphisms/adipocytokine concentrations and anthropometric/biochemical parameters were tested
6) Final results were evaluated and possible effect of the studied genetic polymorphisms and/or adipocytokines on body composition and/or biochemical status was assessed. Also an eventual involvement of the studied genetic and hormonal factors in aethiopathogenesis of obesity, DM2, metabolic syndrome, and PCOS was considered
7) Main results and conclusions of the research were published in scientific journals. The publications represent the pivotal part of the submitted Ph.D. thesis.

During the six years of research, interesting new observations were made regarding selected adipocytokines and their relations to biochemical metabolic markers and certain somatometric parameters. In case of leptin, its reaction to the intense changes in energy balance was followed. Furthermore, an association of several studied polymorphisms in candidate genes PPARgamma2, UCP1, and KCNJ11 with some anthropometric and clinical/biochemical parameters were described in Czech population.

These results indicate that selected genetic polymorphisms play a minor role in the aethiopathogenesis of DM2, obesity, and metabolic syndrome in the Czech population. Nevertheless, these observations contribute to a better understanding of the complex pathogenesis of these disorders, where genetic as well as environmental factors are involved. A lot of patience and time is needed to uncover a little part of so-called „genetic background" of these complex metabolic disorders. Because the effect of a particular genetic polymorphism on biochemical markers and/or on body composition is usually weak, very large cohorts of subjects are necessary to prove statistical significance.

In spite of the relatively slow progress, it is essential to map genetic factors involved in pathogenesis of diseases such as obesity, DM2, and metabolic syndrome, that are increasing world-wide and have reached epidemic proportions in both developed and developing countries. Better understanding of genetic background may lead to a development of more effective and accurately targeted drugs (pharmacogenomic). Pharmacotherapy should be an integral part of the comprehensive management of these disorders together with diet, physical activity, and cognitive behavioral modification of lifestyle. Identification of genetic predisposing markers could increase a chance of successful prevention, since motivation and ability of the informed high risk subjects to follow the advised changes in lifestyle could strengthen.