I worked on the referred to dissertation thesis in the Department of Biology and Human Genetics in cooperation with the Department of Nephrology of General Teaching Hospital and the First School of Medicine at Charles University. I concentrated on the possible influence of gene polymorphisms on the progression of renal insufficiency of IgAN and ADPKD to ESRD. I investigated the gene polymorphisms of Endothelin and Megsin myself and I participated in examinations of other gene polymorphisms.

In our study we were concerned with the **gene polymorphisms of G198T, T-1370G a 3A/4A ET-1** and **we did not find any differences by comparing genotype frequencies** among the IgAN groups with normal renal function and ESRD. The haplotype analysis demonstrated **the negative influence of GG4A haplotype** (defined as G-198, G-1370 and 4 A allele). The association of GG4A haplotype with the progression of chronic glomerulonephritides, especially IgAN, might be explained by shared interaction of all ET-1 polymorphisms.

Then we dealt with the research of **C2093T, C2180T Megsin gene polymorphisms** on the progression of IgAN in Czech patients. **No obvious effect** of these polymorphisms **was found in single-gene or in haplotype analysis**. Nevertheless, the Megsin haplotype reconstruction revealed that the **TT haplotype (defined as T-2093, T-2180)** could be found **significantly in a higher frequency with a stable group of IgAN** in comparison with its proportion within the progressive group. These differences in TT haplotype distribution can be in favour with a **protective role of TT haplotype in the progression of IgAN**. However, our results are restricted by the limited number of patients compared with the Asian studies. We are planning to extend our group of IgAN patients concerned with intrarenal gene expressions: an analysis of histological patterns of renal biopsies and the detection of the serum´s protein or abnormal glycosylated circulating imunocomplexes in the urine.

We excluded the putative **influence of C1363T exon 8 EDNRA gene polymorphism on the progression of IgAN and ADPKD in men**. CC homozygous women with ADPKD achieved ESRD four years later compared with CT heterozygous women. **The CC genotype is supposed to be a predictor of a favourable clinical course in ADPKD women.**

Subsequently, **we excluded the effect of ECE-1b C-338A polymorphism in the progression of ADPKD to ESRD**. AA homozygous patients occurred less in slow progressors by comparison with other ADPKD groups. AA homozygous patients had younger age of ESRD compared with the other genotypes. We observed **a mild tendency to faster declining of renal functioning in AA homozygous patients.**

Then we concentrated on the research of **Glu298Asp polymorphism eNOS** and we found the Glu298Asp and Asp298Asp genotypes to be more frequent in ADPKD groups with rapid progression and ESRD between 40-63 ages compared to slow progressors and the control group. Thus, we confirmed **the negative prognostic influence of Asp carrier variants of eNOS polymorphism on the progression of ADPKD to ESRD**. We demonstrated a five year lower mean age of ESRD in Asp homozygous women compared to Glu homozygous women.

We did not confirm the influence of **ACE and α-adducin gene polymorphisms** on the progression of ADPKD to ESRD but **Trp and I/I genotype carriers had a significantly better prognosis** in comparison with Gly/Gly homozygous patients.

We examined four families with suspected **familial IgAN**. A total of 29 subjects were genotyped and were included in a genome-wide linkage analysis. By genome-wide linkage analysis (Merlin 1.1.1.) of four IgAN families we found out **new linkage of IgAN to chromosome 13q 32.3** under an autosomal dominant model of transmission with estimated penetrance of 75 % with LOD score 2,28. To date, genome-wide linkage studies of familial IgAN have found no persuasive candidates. Our results provide further evidence for genetic heterogeneity among families with IgAN.

The results of gene polymorphisms shown above could be limited by the lower number of patients (nevertheless, in context with the studies performed in Europe, this number of patients was relatively high). Although the precise etiology of both studied diseases has yet to be known, undoubtably the genetic factors play the significant role by their occurance.
Gene polymorphisms studied in our project certainly contributed to an assessment of the prognosis of the diseases. In the future, these results have undoubtably to be connected with intrarenal gene expression (in case of IgAN) and the assesment of the serum proteins: the gene´s products.

The aim of our study was to determine the possible affecting factors of the progression of the diseases IgAN and ADPKD, and to help the treatment which could improve not only the patient´s quality of life but also to reduce the economic cost associated with renal replacement therapy.