# Abstract

Diabetic nephropathy (DN) is induced by both type 1 and type 2 diabetes mellitus and it is one of the most serious complications associated with diabetes. Despite increasing incidence of diabetes, the exact pathogenesis remains unclear. Hypoxia is regarded as a crucial factor for the progression of renal disease. The responses to hypoxia are mainly regulated by hypoxia-inducible factor 1 (HIF1). We thus considered a possible link between HIF1-regulated pathways and the susceptibility to DN and the disease progression. We hypothesize that the exposure of renal tissue to diabetes causes gene expression changes in HIF1-regulated pathway and the altered expression profile is decisive for the development of DN. Using mouse model, we analyzed cellular and molecular changes in HIF1$\alpha$ heterozygous-null (*Hif1α*$^{+/-}$) and wild type (*wt*) littermates exposed to diabetic environment. Our histological analysis showed early pathological changes associated with DN in both diabetic *wt* and *Hif1α*$^{+/-}$ compared to non-diabetic controls. The morphological analysis did not demonstrate the effect of *Hif1α*$^{+/-}$ genotype in comparison to *wt*. For our molecular analysis with qRT-PCR method, we selected several genes, which were previously associated with pathological processes in kidney diseases. We identified statistically significant changes in gene expression of *Spp1* and *Cxcr4* in renal cortex and pulp. The relative expression of *Thbs1* was only increased in renal pulp. The differences in response to diabetic environment between *Hif1α*$^{+/-}$ heterozygotes mutants and *wt* were detected in *Spp1* and *Cxcr4* genes. These results confirm our original hypothesis that HIF1-regulated pathways are significantly influenced by diabetes mellitus and their target molecules participate in the development of DN.



**Key words:** diabetic nephropathy, gene profiling*, Cxcr4, Glut1, MIP-1α, Nphs2, Spp1, Thbs1, TNFα, Vcam1, HIF1α*


(in czech)