**SUMMARY**

**Introduction**

HNF1B is a tissue-specific transcription factor, which plays a crucial role in the embryological development of a number of organs, especially kidneys, gastrointestinal system, pancreas and billiary system. While the significance of HNF1B in the development of urinary tract malformations has already been well described, its role in the pathogenesis of solid tumors has not yet been elucidated. Based on the current data it seems that depending on the type of individual tumor HNF1B can either act as an oncogene or a tumor suppressor. However, the precise mechanism of how it exerts its influence is still unclear.

**Aims:**

The thesis focuses on expanding the knowledge of the significance of HNF1B changes in selected solid tumors and non-neoplastic lesions. The individual goals include: 1) determining the role which HNF1B plays in the pathogenesis of these lesions, 2) evaluating the significance of HNF1B for differential diagnosis, 3) analysis of the prognostic and predictive meaning of HNF1B, 4) mutation analysis of the *HNF1B* gene in all the tumor and non-tumor tissues with the aim to identify novel pathogenic mutations, 5) methylation analysis of the *HNF1B* promoter.

**Material and methods:**

Immunohistochemical examination with the antibody against HNF1B was performed on 516 samples of tumor and non-tumor tissues. The mutation analyses included new generation amplicon sequencing or capture-based sequencing and were successfully performed on 400 samples. The mutation analysis was performed on 321 samples. Our data was also compared to the data available from The Cancer Genome Atlas.

**Results:**

1) The expression of HNF1B is significantly higher in colon adenomas than in carcinomas. 2) Low expression of HNF1B in colorectal carcinomas correlated with recurrence and shorter DFS. 3) There were significant differences in HNF1B expression across all 4 groups of renal tumors. 4) The highest expression of HNF1B in clear cell renal cell carcinoma (ccRCC) was observed in grade 1 tumors and was decreased with increasing grade. 5) In high grade serous carcinoma (HGSC) of the ovary the expression of HNF1B is generally low and higher expression was associated with lymphovascular invasion. 6) In prostate carcinoma, promoter methylation was associated with tumors of higher T stage and higher Gleason score. 7) 5 variants of *HNF1B* gene class 3-5 were found: 3 in colorectal carcinoma, 1 in HGSC and 1 in prostate carcinoma.

**Conclusion:**

Concerning differential diagnosis, the main significance of IHC expression of HNF1B could be in the tumors of the kidney, especially when differentiating between chRCC and renal oncocytoma. Another use could be in the tumors of the female genital system, however, the rather high percentage of expression found in our group of HGSCs may limit its use in this area. From the prognostic point of view the expression of HNF1B was significant especially in colorectal carcinoma, where decreased expression correlated with recurrence and worse prognosis. When considering the involvement of HNF1B in the pathogenesis of tumors, our data showed that in colorectal carcinoma, HGSC of the ovary, prostate carcinoma, ccRCC and chRCC HNF1B may act as a tumor suppressor, while in papRCC it could work as a protooncogene. The part of our work dealing with epigenetic alterations is significant especially for HGSC, where the confirmed high levels of methylation (in accordance with literature) suggest that methylation could represent a promising marker for early detection of HGSC.