SUMMARY

Introduction
HNF-1β is a transcription factor that plays a crucial role in the ontogenesis, regulates expression of multiple genes involved in cell cycle modulation and seems to be involved in cancerogenesis of various tumors. HNF-1β protein is coded by the *HNF1B* gene. Genetic and epigenetic changes of *HNF1B* play role in tumorigenesis and these changes can be accompanied by loss of expression or increased protein expression as detected by immunohistochemistry. In gynecopathology, expression of HNF-1β was considered as specific marker of clear cell carcinomas of the ovary and endometrium. However, more recent studies described HNF-1β expression also in tumors of other histogenesis.

Aims:
Our study focused on the immunohistochemical and molecular analysis of HNF1B in the normal tissue, various types of tumors and non-neoplastic lesions of the female genital tract. The goals of our study were: 1. Analysis of HNF-1β expression in cervical carcinomas. 2 Analysis of HNF-1β expression in endometrial carcinomas and non-neoplastic tissues of the female genital tract. 3. Analysis of epigenetic and genetic changes of *HNF1B* in endometrioid carcinomas and ovarian clear cell carcinomas. 4. Comprehensive analysis of atypical polypoid adenomyomas.

Material and methods:
A total of 574 samples including 399 carcinomas of female genital tract (155 cervical, 225 endometrial and 19 ovarian carcinomas) and 175 non-neoplastic tissues were examined by immunohistochemistry with antibody directed against HNF-1β. Selected samples were examined immunohistochemically also with panel of other antibodies. Moreover, in selected cases we performed direct and bisulfite DNA sequence analysis and PCR analysis of the *HNF1B* gene. Cases of atypical polypoid adenomyomas were analyzed also by PCR and FISH.

Results:
1. We found that expression of HNF-1β is mostly restricted to adenocarcinomas, contrary to only rare expression in squamous cell carcinomas. 2. We found strong expression of HNF-1β in ovarial and endometrial clear cell carcinomas, compared to other tumor types. We observed different HNF-1β expression in endometrioid carcinomas depending on differentiation of tumor. 3. We detected relatively common methylation in promoter region of *HNF1B* gene in endometrioid carcinomas, but not in ovarial clear cell carcinomas. We have also found nonsense heterozygous mutations of *HNF1B* in 1 endometrioid carcinoma and 4 other single nucleotide variants (3 of them in endometrioid carcinomas and 1 in ovarial clear cell carcinoma). 4. We have shown that atypical polypoid adenomyomas exhibit consistent immunohistochemical and molecular features similar to those found in atypical hyperplasia and endometrioid carcinoma.

Conclusion:
In conclusion, expression of HNF-1-beta can be of use in the differential diagnosis of female genital tract tumors, either alone or in panel with other antibodies. Regarding epigenetic and genetic changes, we have found relatively common methylation of the *HNF1B* promotor in endometrioid carcinomas, but not in the ovarial clear cell carcinomas. We detected pathogenic mutation and three SNP in endometrioid carcinomas and one missense variant in ovarian clear cell carcinoma. Based on our results, we feel that, conceptually, atypical polypoid adenomyomas is best regarded as analogous to a localized form of atypical hyperplasia.