SUMMARY

Molecular biological changes in endometrial carcinoma

Endometrial cancer is the most common cancer of the female reproductive tract. The incidence has increased with lifestyle and environmental changes. Similar to other cancers, endometrial cancer has been shown to be a complex disease driven by different factors, including genetic and epigenetic alterations. Understanding these changes underlaying cancer development or progression is important for finding of new standards for both diagnosis and therapy of individual patients.

The aim of the study was to evaluate selected molecular biological changes in endometrial carcinoma comparing to non-neoplastic endometrium.

The first specific aim was to compare presence of K-ras mutation in early stages of endometrioid type of endometrial carcinoma with normal endometrium, and to evaluate association to clinical-pathological characteristics (tumor stage and grade). We analyzed 79 samples of endometrium (59 samples of endometrioid endometrial carcinoma stage I, and 20 samples of normal, non-neoplastic endometrium). Detection of K-ras mutation was made by using of K-ras StripAssay™ (ViennaLab Diagnostics GmbH). The frequency of K-ras mutation in the carcinoma group did not differ from the group of control samples (24% vs. 15%). No association between K-ras mutation and tumor stage and grade was observed for the patients with endometrioid carcinoma of endometrium.

The second specific aim was to compare promoter methylation in selected tumor suppressor genes in early stages of endometrioid type of endometrial carcinoma with normal endometrium, and to evaluate association to clinical-pathological characteristics (tumor stage and grade). MS-MLPA was used to analyze 79 samples of endometrium (59 samples of endometrioid endometrial carcinoma stage I, and 20 samples of normal, non-neoplastic endometrium). We observed higher methylation in CDH13 gene ($p<0.0001$) in the group of endometrioid carcinoma of endometrium compared to the group of control samples. MSP was used to analyze 72 samples of endometrium (54 samples of endometrioid endometrial carcinoma stage I, and 18 samples of normal, non-neoplastic endometrium). We observed higher methylation in GATA4 gene ($p<0.0001$) in the group of endometrioid carcinoma of endometrium compared to the group of control samples. Both WT1 ($p=0.002$) and GATA5 ($p=0.05$) genes showed a higher methylation in stage IB compared with stage IA of endometrial cancer samples. Methylation in GATA5 gene ($p=0.05$) was higher in grade 3 of endometrial cancer samples compared with the group of grade 1 and grade 2 tumors.

Whereas the role of K-ras mutation in endometrial carcinogenesis remains unclear, our finding suggests the importance of CDH13, WT1, GATA4 and GATA5 methylation in this process. Hypermethylation in WT1 and GATA5 genes could play an important role in tumor myometrial invasion and its aggressive behavior.