

Summary

Title: Epigenetic Regulation of Adhesive Molecules in High-grade Serous Ovarian Carcinoma

The lack of effective biomarkers for screening and early detection of ovarian cancer is currently considered as one of the most pressing problems in oncogynecology. Because epigenetic alterations occur early in the cancer development, they provide great potential to serve as such biomarkers. Epigenetic mechanisms have been implicated also in regulation of adhesion molecules that play a major role in cancer progression.

The main aim of this study was to investigate the methylation pattern of selected cadherin and catenin genes in ovarian cancer tissue by comparison with control tissue. The study group consisted of 68 patients with high-grade serous ovarian cancer (HGSOC) and 46 control patients. To determine the sites with the most significant methylation in selected genes next-generation sequencing was employed. For further confirmation of detected methylation of selected regions, methylation-sensitive high-resolution melting analysis and real-time methylation-specific polymerase chain reaction were used. In attempt to design potential biomarker panel for future screening of HGSOC as the secondary aim of our study, cadherins were evaluated together with transcription factors from our previous study.

Significant methylation-positive pattern was detected in *CDH13* and *PCDH17* genes. Simultaneous analysis of both genes together revealed methylation in 65.6 % of tumor samples, whereas control samples were methylation free. Four-gene methylation panel, that beside *CDH13* and *PCDH17* included also *HNF1B* and *GATA4* genes, reached sensitivity of 88.5 % with 100% specificity and 93.3% efficiency.

Our results indicate that methylation of the *CDH13* and *PCDH17* genes could play an important role in development and progression of HGSOC. With the right selection of the most relevant sites for methylation analysis these genes showed potential to become a target in search for new epigenetic biomarkers, especially as a part of a biomarker panel. However, further studies on more extensive group of patients are needed to confirm these novel results.