Study: Complex analysis of molecular characteristics of female genital tract lesions.

Project MZ ČR RVO – VFN 641
Institute of Pathology, First Faculty of Medicine of Charles University and General Teaching Hospital

This study extends our last pilot study dedicated to the analysis of somatic gene variants and epigenetic changes of the HNF1B gene in endometrial lesions.
Lesions of the female genital tract encompases heterogeneous group of tumors. Most commonly are diagnosed carcinomas of endometrium or ovary classified as endometrioid, mucinous, serous or clear cell carcinoma. The various histological types have different precursors, response to the therapy, prognosis and different spectrum of genetic and epigenetic changes.
Across subtypes the female genital tract carcinomas occures with different frequency, for example somatic mutations in the genes *BRCA1*, *BRCA2*, *PTEN*, *TP53*, *AKT*, *ARID1A*, *KRAS*, *BRAF* and *HER2*. It is supposed that somatic alterations of the aforementioned genes are involved in the pathogenesis of female genital tract lesions. However, there are still missing data and complex molecular characterization of different subtypes of these lesions. Description of genetic variations and expression profiles of selected genes and correlation of such data with clinicopathological characteristics can contribute to improvement of differential diagnostics, which has in deed an impact on patient care. Further, the results of this study can contribute to understanding of different biological behavior of different subtypes of female genital tract lesions.

Somatic alterations in chosen genes, including genes that code proteins involved in regulation of cell cycle, DNA reparation and epithelial-mezenchymal transition (e.g.: *BRCA1/2*, *PTEN*, *TP53*, *AKT*, *ARID1A*, *KRAS*, *BRAF*, *SNAI1*, *SNAI2*, *SNAI3*, ESR1/2, *JAM-1*, *JAM-2*, *JAM-3* and others). Sequence capture DNA library will be sequenced by Illumina MiSeq instrument. The results from NGS analysis can be supplemented by investigation of epigenetic alterations (especially promoter methylations), and expression profiles at RNA (qPCR) or protein level (immunohistochemistry) in relevant cases
The aim of this study is comprehensive characterization of somatic genetic and epigenetic alterations, expression profiles and immunohistochemical features in selected subtypes of female genital lesions, focused especially on genes and gene products associated with neoplastic transformation.
Extension of the study to a larger set of well-characterized and classified endometrial or ovarian tumors, enables searching for suitable factors (mutation profile) to be used in differential diagnostics, and the collection of clinical data allow us to investigate their prognostic and predictive significance.