# *PTEN* GENE MUTATIONS IN UTERINE SEROUS CARCINOMA AND THEIR RELEVANCE IN PERSONALISED CANCER TREATMENT

Lajos Gergely[1], Vanda Repiská[1], Vladimír Šišovský[2], Kristína Mosná[2], Petra Priščáková[1]

[1]*Institute of Medical Biology, Genetics and Clinical Genetics, Faculty of Medicine, Comenius University in Bratislava, Sasinkova 4, 811 08 Bratislava, SR*

[2]*Institute of Pathological Anatomy, Faculty of Medicine, Comenius University in Bratislava, Sasinkova 4, 811 08 Bratislava, SR*

**Introduction:** Uterine serous carcinoma (SC) is an aggressive variant of endometrial cancer with unfavourable prognosis. Mutations of the *TP53* tumour suppressor gene are characteristic in SC, while the mutations of the *PTEN* tumour suppressor gene are considered as atypical according to the literature. In contrast, mutations of the *PTEN* gene are the most frequent in the endometroid variant of endometrial cancer.

**Aim of the study:** To evaluate an association between the histomorphology of SC and the presence of *PTEN* mutations and in this way to determine if the sequencing analysis of the *PTEN* gene from SC tumour samples provides potentially useful information for therapeutic decision-making in patients from the Slovak population.

**Patients and methods:** In our study, the DNA was isolated from microdissections from eight formalin fixed paraffin embedded SC tissue samples of patients from the Slovak population. All (9) exons of the *PTEN* gene were amplified with PCR and then analysed with Sanger sequencing.

**Results:** We found more mutations than expected based on international standards, and we also found rare mutations in our study group. Of the eight analysed samples, three were found to have mutations in the *PTEN* gene, two of which contained two mutations in heterozygous state (c.389G>A + c.419T>G and c.19G>T + c.1021T>G), and one contained a single mutation in homozygous state (c.730C>T). All detected mutations can be found in the COSMIC (*Catalogue of Somatic Mutations in Cancer*) database and are classified as pathogenic, therefore are considered relevant in neoplastic context.

**Conclusion:** Comparing our results with the study of the TCGA (*The Cancer Genome Atlas*) Research Network and data from COSMIC, we suggest that in the population of the Slovak Republic, the frequency of *PTEN* gene mutations in SC is higher than the American (TCGA− approx. 2 %) or international (COSMIC −7 %) average. Thus, the sequencing analysis of this gene from tumour samples would be an effective, useful laboratory method with clinically relevant results. The protein encoded by the *PTEN* gene (PTEN) is the main negative regulator of the PI3K-Akt-mTOR signalling pathway, which alterations are important in the biology of many gynecologic malignancies such as gestational trophoblastic tumors. Loss of PTEN function leads to hyperactivity of this pathway, deregulating the cell cycle. Therefore, mutations of the *PTEN* gene can be exploited in the therapy as they increase the sensitivity of the tumour cells to PI3K and mTOR inhibitors. In this way, *PTEN* mutational analysis could be a relevant component useful in clinical practice.

**Acknowledgement:** The authors disclosed receipt of the following financial support for the research and/or authorship of this article: VEGA 1/0559/22 from The Ministry of Education, Science, Research and Sport of the Slovak Republic.