Validation of diagnostic and prognostic potential of PINK1, DLGAP5 and BUB1B expression patterns in adrenocortical tumors

Authors:
1. PhD Lidija Todorović - Vinca Institute of Nuclear Sciences - National Institute of the Republic of Serbia, University of Belgrade
2. PhD Bojana Kožik - Vinca Institute of Nuclear Sciences - National Institute of the Republic of Serbia, University of Belgrade
3. PhD Ana Božović - Vinca Institute of Nuclear Sciences - National Institute of the Republic of Serbia, University of Belgrade
4. PhD Vesna Mandušić - Vinca Institute of Nuclear Sciences - National Institute of the Republic of Serbia, University of Belgrade
5. PhD Boban Stanojević - Vinca Institute of Nuclear Sciences - National Institute of the Republic of Serbia, University of Belgrade
6. Prof. Vladan Živaljević - Center for Endocrine Surgery, Clinical Center of Serbia, Belgrade

School of Medicine, University of Belgrade, Belgrade
7. Prof. Ivan Paunović - Center for Endocrine Surgery, Clinical Center of Serbia, Belgrade

School of Medicine, University of Belgrade, Belgrade

Abstract:
Adrenocortical tumors (ACTs) are heterogeneous neoplasms with incompletely understood pathogenesis. Correct differential diagnosis between adrenocortical adenoma (ACA) and localized adrenocortical carcinoma (ACC), as well as improved prognostic stratification of ACC patients, are of great clinical importance. Alterations in gene expression patterns have been found in adrenocortical neoplasms compared to normal tissue. In addition to having a role in tumorigenesis, distinct gene expression signatures may help to distinguish different ACT types. The combined expression patterns of PINK1, DLGAP5 and BUB1B have been suggested as malignancy and outcome predictors in previous studies. In order to validate their diagnostic/prognostic potential, we investigated the expression levels of these three genes and their association with clinico-pathological parameters in a cohort of 47 ACC and 15 ACA patients from Serbia. In addition, we analyzed the association of their expression levels with survival data in an independent ACC cohort of 79 patients from The Cancer Genome Atlas (TCGA) database. The results showed that high expression levels of BUB1B and DLGAP5, and low expression levels of PINK1 significantly associated with ACC. Moreover, combined expression of both DLGAP5 and BUB1B with PINK1 were significantly higher in localized ACC compared with ACA. The results from the TCGA cohort showed that expression alterations of these genes were strong predictors of disease-free and overall survival in ACC patients. These results are consistent with the previously reported results and confirm that the expression patterns of PINK1, DLGAP5 and BUB1B might have value as molecular predictors of malignancy and/or survival in ACC patients.