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APPROACH TO THE CREATION OF A GENE EXPRESSION PANEL FOR PROSTATE CANCER

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Biomarkers and panels of biomarkers are important for diagnostics of various human and animal diseases, and also for assessment of the risk and severity of disease, prediction of sensitivity and efficacy of drugs and response to treatment [1, 2]. Nowadays, several approaches are used to select the potential biomarkers or biomarker panels [3, 4]. However, the existing panels are not optimal yet. Aim: To develop a modified statistical approach to create the gene expression panel for a better diagnostics of prostate tumors .

Materials and Methods: Relative gene expression (RE) of 57 transcripts of cancer-associated genes were analyzed by quantitative PCR in 37 prostate cancer tissues (T) at various tumor stage and of Gleason score (GS), and also in 20 samples of benign prostate tumors, or adenomas (A). The STASISTICA 10 software was used to find possible "predictor" genes and rules for stratification of the sample groups. The MDR 3.0.2 was used to create the gene expression panelsand to analyze their applicability for diagnostics.

Results. In the result of a statistical analysis of RE, 31 out of 57 transcripts (from 5 functional groups [5-7]) were selected, based on significant differences in gene RE between A and T. Moreover, differences in gene RE in T group at different stages and of various GS were taking into account. The threshold in RE levels was chosen two for every gene (2-fold up or down) [5, 6], and A was the control group. Values of the fold change were transformed from continuous RE values to binary values. In result, we found 22 genes/transcripts with increased RE in T, compared with A; and 9 genes/transcripts with decreased RE in T. There were 15 transcripts of (epithelial-mesenchymal transition and prostate-cancer associated genes) and 16 transcripts of cancer-associated fibroblasts, tumor-associated macrophages, immune-associated genes) which have shown some datasets with high statistical parameters. The highest value for diagnostics showed panels, which contained the following gene groups: *PCA3, HOTAIR, ESR1, IL1R1*(Se=0.97, Sp=0.85, Ac= 0.93, OR=204) and *CDH2, KRT18, PCA3, HOTAIR, ESR1, IL1R1* (Se=1.0, Sp=0.8, Ac= 0.93, OR>500).

Conclusions/Perspectives: Modified statistical approach for gene expression data analysis was proposed to create the diagnostic panel for prostate tumor stratification in Ukrainian patients. Further estimation of the proposed method in a larger cohort of patients with prostate tumor is needed.

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Key words: *prostate tumors, gene expression panels, MDR analysis, prostate cancer biomarkers, cancer-associated genes.*

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MARKERS OF CHRONIC SYSTEMIC INFLAMMATION IN PATIENTS WITH ISCHEMIC HEART DISEASE IN COMBINATION WITH AUTOIMMUNE THYROIDITIS INFLUENCED BY RESVERATROL

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The incidence of coronary heart disease (CHD) is progressively increasing worldwide, despite active medical and preventive measures [1]. Furthermore, the proportion of endocrinopathies in the society is also increasing, more than 50% of which are diseases of the thyroid gland, primarily autoimmune thyroiditis (AIT) [2]. Recent studies have demonstated that chronic systemic inflammation (CSI) has importance in the development and progression of atherosclerosis, which forms the basis of coronary heart disease [3]. Apoptosis of thyrocytes in AIT also occurs with the participation of proinflammatory cytokines (CK) [4]. Further studies of markers of CSI in order to assess the course of these diseases and the effectiveness of therapeutic measures are in the focus of interest [5]. The aim of our research was to study the dynamics of CSI markers in patients with coronary heart disease concurrent with AIT under the influence of polyphenol resveratrol [6].

Materials and Methods. 115 patients of both sexes aged 48-69 participated in the study: 85 patients with coronary heart disease: stable exertional angina, FC II, CH 0-I and 30 patients with additional AIT diagnosis, euthyroid variant of the course, 5 of which – medically corrected subclinical hypothyroidism. 30 patients with coronary heart disease (study group 1) and 30 patients with concomitant AIT (study group 2) received standard resveratrol 100 mg daily for 2 months. 55 patients with CHD formed the comparison group. In all patients, the level of CK – tumor necrosis factor (TNFa), interleukin-1β (IL-1β) and IL-10 in blood serum was determined before the initiation of treatment and after 2 months by the immune enzyme method, the fibrinogen content (FG) in blood plasma by weight method, the content of circulating endothelial microparticles (CEM) with surface antigens CD32+ and CD40+ by flow cytofluorimetry using monoclonal antibodies and expression of the matrix ribonucleic acid gene (mRNA) of kappa B inhibitor (IkB) nuclear kappa B transcript (NF-kB) by real-time polymerase chain reaction (Real-time PCR) using a relative Ct method for data analysis [7, 8].

Results. In patients of all study groups, an increased content of CK was revealed, an increase in the number of CEM $CD32^{+}CD40^{+}$ ($p < 0.05$), indicating inflammatory activation and endothelium dysfunction. In 34% of patients with coronary heart disease and 25% of patients with coronary heart disease concurrent with AIT, an increase in the content of FG was observed. Expression of mRNA IkB ($2^{-\Delta C}$) in the study groups was not significantly different. Under the influence of resveratrol, the IL-1β content decreased (6.98 + 2.52 pg / ml versus 10.05 + 3.67 pg / ml, p = 0.0022), TNFa (7.28 + 2, 18 pg / ml versus 9.69 + 1.63 pg / ml, p = 0.013), there was a tendency to decrease in the content of IL-10 (p = 0.0546). In group 2, the content of IL-1β (6.87 + 2.13 pg / ml versus 10.06 + 2.79 pg / ml, p = 0.0011) and TNFa (7.94 + 3, 43 pg / ml versus 10.54 + 2.42 pg / ml, p = 0.00045) significantly decreased, while the content of IL-10 remained unchanged (p = 0.455). In the comparison group,