MOLECULAR PROFILING OF PROSTATE TUMORS

Gerashchenko G.V., Kashuba V.I.
Institute of Molecular Biology and Genetics, National Academy of Sciences of Ukraine, Ukraine

Prostate cancer is a very heterogeneous disease [1]. Upon cancerogenesis, not only prostate epithelial cells are altered, but also stromal elements. Growing tumors are capable to change their microenvironment to avoid immune surveillance and to grow and proliferate [2]. To understand cancer development, it is necessary to investigate both, the tumor cells and the composition and characteristics of the tumor microenvironment [3]. This is important for diagnostics, prognosis and for the choice of an effective patient treatment, making the basis of personalized medicine. Aim: To analyze an expression pattern of the prostate cancer-associated genes (PCAG) and genes - markers of tumor microenvironment (TM); and to examine a putative correlation between gene expression and clinical characteristics, to define the molecular subtypes of prostate cancer and form a basis for the molecular profiling of prostate cancer.

Materials and Methods. Relative gene expression (RE) of 56 PCAG and TM markers were analyzed by a quantitative PCR in 37 prostate cancer tissues (T) of different tumor stages and Gleason scores (GS), 37 corresponding (paired) conventionally normal prostate tissues (N) and in 20 samples of benign prostate tumors (adenomas (A).

Results. We have found 30 differentially expressed genes in T compared with A. Among them there were cancer-related and prostate specific genes (AR, KRT18, MMP9, PTEN, TMPRSS2/ERG, VIM, ESR1, GCR, PDL1, PRLR, SRD5A2, VDR), 3 genes of IncRNA (PCA3, SCLAP1, HOTAIR), several genes characterizing the state of tumor microenvironment (fibroblasts, lymphocytes, macrophages) (THY1, CXCL12, CXCL14, CTGF, HIF1A, FAP, IFNB1, CTLA4, IL1RL1, IL1R1, CD163, CCR4, CCL17, CCL22, NOS2A). It was found 29 of 56 genes with significant RE correlations in T with clinical and pathological characteristics (GS, stage, PSA level, age). We have found some specific RE changes in groups with the presence of TMPRSS2/ERG fusion and different expression of PTEN. For examples, KRT18, PCA3 and SCLAP1 genes showed significant differences in RE in adenocarcinomas with the fusion. In adenocarcinomas without the fusion, such properties were shown by the AR (2 isoform), MMP9, PRLR the HOTAIR genes. The ESR1 and SRD5A2 gene expression was altered in both types of adenocarcinomas Using the clustering procedures, we could cluster adenocarcinomas in three molecular subtypes, according to gene expression profiles of PCAG. A specific expression subtype of prostate tumors is characterized by the activated ERG signaling, due to the presence of TMPRSS2/ERG fusion, and also by high levels of the AR, PRLR, IGF, INSR and PCA3.

The obtained results make the basis for the molecular profiling of prostate tumors to stratify tumors on specific molecular subtypes. It could help in diagnostic and prognosis of a course of disease. Further experiments are needed to confirm these data in a larger patient cohort and to propose a panel of oncomarkers for prostate cancer.

References:

Key words: relative gene expression patterns, prostate cancer, tumor molecular characteristics, tumor microenvironment, oncomarkers.