

## Summary

### Cancer microenvironment as a target for personalized therapy

The tumor microenvironment (TME) consists not only of a heterogeneous population of tumor cells, but also of Mesenchymal Stem Cells (MSCs), Cancer-Associated Fibroblasts (CAFs) and many other cell types. It contains soluble mediators synthesized by cells in this area as well. Interactions between cancer cells and their microenvironment are involved in tumor growth, invasion, metastasis and treatment. At this stage, it is important to conduct basic research to increase knowledge of these interactions.

In the study, the prostate cancer cell line DU145 and bladder cancer cell line HB-CLS-1 were used. Conditioned medium (CM) representing TME was obtained from immortalized MSCs - ASCStelo, and primary prostate cancer-associated fibroblasts HC-6223. MTT, BrdU, CellEvast Caspase-3/7 Green staining and ELISA tests were used for the study. Cisplatin and ciprofloxacin were used to assess drug resistance, respectively for prostate cancer and bladder cancer.

Cancer-associated fibroblasts paracrinely increased the viability, proliferation and resistance of the studied cancer cells by regulating their secretome, Akt/ERK/p70 signaling pathways and p53 protein expression. It was also observed that MSCs paracrinely promote the growth and proliferation of the studied cancer cells. They can both promote resistance and sensitize cancer cells to the drugs used. The study demonstrated increased sensitivity of the DU145 and HB-CLS-1 cell lines cultured with CAF-CM to selected chemotherapeutic agents after FGF2 neutralization.

The study showed that there is a close relationship between factors secreted in the tumor microenvironment and prostate and bladder cancer cells. It has been observed that targeting single molecules in TME may reduce drug resistance caused by the paracrine effect of CAF.

**Keywords:** Tumor Microenvironment, Cancer-Associated Fibroblasts, Cell Secretome