

Differences in the effect of cisplatin on the transcriptional profile of tumor-associated macrophages of breast cancer and colon cancer in vitro

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Introduction. Contribution of tumor-associated macrophages (TAM) in chemotherapy efficacy is one of the main reasons of tumor chemoresistance. However, the mechanisms of interaction of chemotherapeutic (CT) agents and macrophages, as well as the mechanisms of chemoresistance caused by the effect of CT on TAM in tumors, have not been fully studied.

Materials and methods. Full-transcriptome next-generation sequencing (NGS) of modeled TAM differentiated in vitro in the presence of supernatants from tumor cell lines of MCF-7 (breast adenocarcinoma) and Colo206F (colorectal cancer) was performed. All genes were ranked according to the p value ($p < 0.05$) and log₂FoldChange (at least 0.75). Venn diagrams for transcripts with up-regulation and down-regulation were obtained. REACTOM database was used.

Results. Different tumor cell lines showed the distinct numbers of up- and down-regulated transcripts. We showed that samples with MCF-7 supernatants have 150 unique down-regulated transcripts responsible for the process of ribosomal biogenesis, peptide metabolic process, translation, RNA metabolic process and biosynthesis. At the same time up-regulated transcripts (n=97) were more related to trans-membrane transport activity, receptor activity. The samples with Colo206F supernatants had 690 down-regulated and 818 up-regulated unique transcripts. Many down-regulated genes were related to epithelial-mesenchymal transition, angiogenesis, hypoxia, while activated genes participate most specifically in regulation of cell cycle.

Conclusions. We have shown that cisplatin may affect the transcriptional program of TAM, and that in tumors of different localization the effect of the CT agent on the macrophage functions may be different, that requires further validation on clinical material.

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Keywords : cisplatin, tumor-associated macrophages, chemotherapy, cancer

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