Introduction/Background In our previous microarray study we identified the 96-gene signature related to differential survival of patients with high-grade serous ovarian cancer (OC). Top differentially expressed genes were e.g. POSTN, COL11A1, SFRP2, MFAP5, ITGBL1, LOX. Similar mesenchymal signature has been observed also by others, but it has been ascribed to cancer associated fibroblasts, not epithelial cells. However, we postulate that these genes can be also expressed by cancer cells themselves.

Methodology For survival analysis we used Kaplan-Meier Plotter and Microarray Gene Expression Database of OC Subtype (CSIOVDB). Proteins expression was assessed by HeterogeneityAnalysis Portal (mdomics.org) [2]. Interaction networks were judged by STRING. Molecular cloning was performed using retroviral gene transfer; in vitro functional tests were done according to standard procedures; gene expression analyzed by PCR.

Results STRING algorithm applied to our prognostic signature showed interactions typical for proteins engaged in the function and structure of extracellular matrix. Our own qRT-PCR analysis, as well as Kaplan-Meier Plotter and CSIOVDB analysis confirmed that mRNA level of majority of genes from our negative prognostic signature is significantly related to survival of OC patients. Using HeterogeneityAnalysis Portal we analyzed 24 out of these genes and found that they are strongly expressed by tumor stromal cells, while weakly by epithelial cells. We analyzed ten of these genes in several OC cell lines by semi-quantitative RT-PCR, and we found that they are expressed by epithelial cells as well. By functional in vitro assays we observed that overexpression of these genes (ITGBL1, MFAP5, SFRP2) may affect OC cells phenotype (migration, invasiveness, proliferation, chemosensitivity).

Conclusion Mesenchymal signature with negative prognostic significance in OC is expressed mostly by stromal, but also by epithelial cells, and may affect phenotype of the latter. Exact role of these genes in OC cells remains to be assessed.

REFERENCE