Expression of sodium-dependent phosphate transporter NaPi2b is downregulated in malignant ovarian tumors after neoadjuvant chemotherapy

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Background: The membrane protein NaPi2b (SLC34A2 gene) is overexpressed in ovarian cancer and other malignancies including thyroid, lung, breast, and others. Currently, NaPi2b-specific therapeutic monoclonal antibodies XMT-1536 and XMT-1592 are successfully undergoing clinical trials for the treatment of ovarian and non-small cell lung cancers, demonstrating safety and clinical efficacy. These humanized auristatin F (AF-HPA) conjugated antibodies are created on the dolaflexin and dolasynthen technology platforms respectively. We aimed to evaluate NaPi2b as a target for antibody therapy and molecular marker for diagnostics and predicting the course and outcome of ovarian cancer disease.

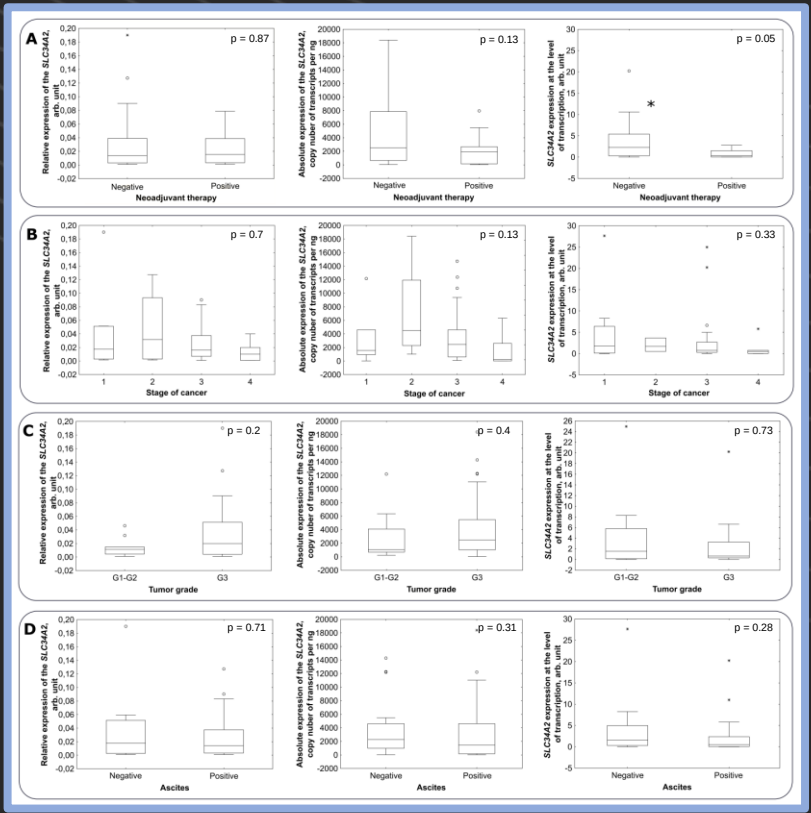

Fig.2. Box plots comparing the *SLC34A2* gene expression at the level of transcription and translation with considering the clinicopathological characteristics

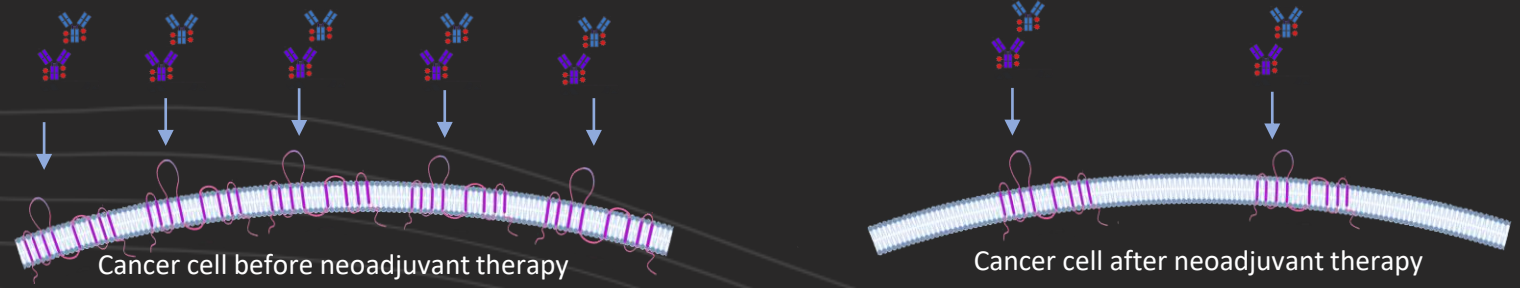

Fig.1. NaPi2b protein abundance is lower in tumor ovarian cells of patients who had received neoadjuvant therapy

Methods: The analysis of SLC34A2 gene expression in 48 ovarian tumors was performed using real-time PCR, droplet digital PCR, and Western blot analysis. Statistical analysis was performed taking into account various clinicopathological characteristics of the ovarian cancer patients, including the stage of the disease, the tumor grade, the presence of ascites and the applying of neoadjuvant chemotherapy which was predominantly carried out according to the TCb regimen (carboplatin and paclitaxel).

Results: It was shown that expression of the NaPi2b transporter is downregulated in tumors of patients who received neoadjuvant chemotherapy (Fig. 2). This fact allowed us to suggest that ovarian cancer patients after neoadjuvant therapy may be not sensitive to targeted drugs directed against the NaPi2b transporter due to the loss of its expression. We found no relationships in the expression level of the NaPi2b transporter with the survival rate of ovarian cancer patients, as well as with tumor grade, and presence of ascites. The NaPi2b showed also a tendency to be downregulated at late stage of disease most likely due to low degree of differentiation of tumor cells.

Conclusions: Thus, the NaPi2b protein abundance is lower in tumor ovarian cells of patients who had received neoadjuvant therapy. This study suggests that the level of expression of the NaPi2b transporter gene can serve as a potential marker for the monitoring and predicting responses to neoadjuvant and targeted therapy in patients with ovarian cancer.

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