Abstract

Chemotherapy is one of the basic therapeutic procedures of breast cancer (BC) which may precede and/or follow the surgical resection of a tumor as a part of neoadjuvant or adjuvant therapy. However, the selective pressure of chemotherapy on tumor cells may change their molecular and expression profile and thus also their chemosensitivity. The aim of our work was to document the expression changes of selected markers in BC after neoadjuvant chemotherapy, which may contribute to the understanding of the role of these proteins and genes in tumor response to chemotherapy and the development of chemoresistance.

Immunohistochemical analysis of expression of standard BC markers [estrogen (ER) and progesterone receptors (PR), HER2 and proliferation activity (Ki67)] and intercellular junction proteins (claudin 1, 3 and 4, E- and N-cadherin) before and after neoadjuvant chemotherapy revealed a decrease of PR, Ki67 and claudin 3 expression and an increase of claudin 1 expression. The expression of ER, HER2, claudin 4, E- and N-cadherin proved to be stable. Assessment of standard BC markers is performed routinely during a bioptic investigation as a necessary factor for therapy indication. Our results support the current recommendations for the re-examination before indication of adjuvant chemotherapy. Claudins and cadherins participate in the regulation of epithelial-mesenchymal transition (EMT), which affects tumor chemosensitivity. The changes of claudin 1 and 3 expression indicate their involvement in the response of BC to chemotherapy. Moreover, the expression of standard BC markers correlated with the expression of claudin 1 and N-cadherin.

Further, using real-time quantitative reverse transcription polymerase chain reaction (qRT-PCR), we evaluated the transcriptional profile of 84 genes associated with apoptosis, which serves a key role in tumor chemosensitivity. We proposed a panel of 13 genes with different expression before and after therapy *(MCL1*, *IGF1R*, *BCL2L10, BCL2A1, HRK, CASP8, CASP10, CASP14, FADD, TNFRSF25, TNFSF8, CD70* and *CIDEB)*, which can be employed in multigene assays to provide a more precise estimation of the patient's prognosis.

Our work presents changes of the expression profile of BC after chemotherapy that might affect further course of treatment. Our results expand knowledge about proteins and genes involved in tumor response to therapy.