ABSTRACT

Changes in the regulation of apoptosis and cell cycle are involved in tumor development, progression, and resistance to antitumor therapy. The aim of this work was to evaluate the importance of apoptotic caspases and regulators of cytokineses as possible prognostic and predictive markers in breast carcinoma patients.

In addition to determining the transcript levels of selected genes in tumor and control tissues obtained from breast carcinoma patients, we have also focused on the importance of alternative splice variants of caspases and their potential genetially determined regulation. We analysed the obtained data in relation to the clinical-pathological characteristics of the tumors, the progression-free survival of patients and to the response of the patients to the neoadjuvant chemotherapeutic treatment. Part of the work was determination of protein expression levels and verification of the importance of selected candidates for the effect of chemotherapy by functional study.

The transcript levels of caspase 2, 3, 7, 8, 9, 10, the specifically detected splice variants caspase 2S, 2L, 3A and B, 3S, 9A, 9B, 8L, and the transcript levels of KIF14 and CIT in breast carcinomas were unrelated to the progression-free survival of patients, or to the response of patients to neoadjuvant treatment. The increased expression of caspase 9B, the alternative antiapoptic variant of caspase 9, and downregulation of major proapoptic variant 9A, evaluated as the ratio of these variants, was associated with a shorter progression-free survival of patients treated subsequently with adjuvant chemotherapy. Moreover, the haplotype of polymorphisms rs4645978-rs2020903-rs4646034 in the *CASP9* gene was associated with caspase 9 transcript levels and expression of recetors for progesterone and HER2 in breast carcinomas. High expression of PRC1 in breast carcinomas was associated with progression-free survival of non-selected patients. However, PRC1 most likely does not play significant role in the effect of taxane-based chemotherapy.

High expression of PRC1 in breast carcinomas is a factor of poor prognosis, independent of the carcinoma subtype or treatment of patients. The ratio of splice variants of caspase 9 should be further studied as potential prognostic and predictive factor in chemotherapy-treated patients.