Abstract

Breast cancer is the most frequent malignancy in women population both in the Czech Republic and worldwide. Treatment of this disease involves surgical removal of the tumor, radiotherapy, chemotherapy and hormonal therapy. Recently, targeted biological treatment is also approached. Each patient reacts to the treatment individually and thus high variability in response is common.

Multidrug resistance (MDR) presents one of the most important obstacles to successful chemotherapy. MDR is often associated with a decreased intracellular accumulation of anticancer drugs and an increased expression of ABC transporters such asABCC1 of our interest.

The ABC family of membrane transport proteins includes the well-known mediators of resistance to anticancer drugs. In particular, ABCB1, ABCC1 and ABCG2 actively perform efflux of various types of drugs from cancer cells, thereby conferring resistance to those agents.

The main aim of this study was to asses the genetic variability of the *ABCC1* gene in 191 patients with breast cancer and to determinate the expression profile of *ABCC1* in 30 patients from this cohort who were treated preoperatively. We evaluated relations between *ABCC1* genotype, or phenotype and prognostic factors including the result of chemotherapy.

Gene expression was measured in preamplificated cDNA samples using real-time PCR with relative quantifiction and genetic variability (individual polymorphisms) was determined by direct sequencing and HRM analysis.

The study provided the insight into the *ABCC1* expression in patients with breast cancer. We managed to identify all selected SNPs in the NBD1 (nucleotide binding domain 1) of the *ABCC1* gene. Our statistical analysis also shows that due to the relation between SNPs and phenotype of *ABCC1* a different enzyme activity and thus a different risk of developing cancer when exposed to ABCC1 substrates during the life may be encountered. A protective allele can cause later onset of the disease. In conclusion, we did not find causal relation between ABCC1 and chemotherapy outcome but other interesting associations of *ABCC1* phenotype and genotype with prognostic factors were observed. These associations have to be confirmed by additional study.

Keywords: breast cancer, chemotherapy, multidrug resistance, single nucleotide polymorphism, expression, ATP-binding cassette transporter C1 (ABCC1), nucleotide binding domain 1(NBD1)