ABSTRACT

The Breast cancer gene 1 (BRCA1) codes for nuclear phosphoprotein with a key function in the regulation of DNA damage response. The BRCA1 protein contributes to the formation and regulation of protein supercomplexes that participates on the DNA double-strand break repair. These protein supercomplexes are formed by the protein-protein interactions between highly conservative protein motives in BRCA1 and its binding partners. Except to the wild type form of BRCA1 mRNA containing entire set of 22 exons coding for the 220 kD protein, numerous alternative splicing variants (ASVs) BRCA1 mRNA has been described. These ASVs code for BRCA1 isoforms lacking several critical functional domains. It has been proposed, that formation of BRCA1's ASVs represent a tool for regulation of BRCA1 function.

Only poorly has been characterized a complex catalogue of in various human tissues and their expression. This study aims to address these questions.

We optimized the identification of BRCA1's ASVs including those covering the entire transcripts of the wt BRCA1 mRNA with length exceeding 5.5 kb. In further analysis, we characterized 13 BRCA1's ASVs in RNA samples isolated from peripheral blood mononuclear cells (PBMNC) obtained from patients with breast cancer (BC) and control subjects. The majority of the identified ASVs (9/13) retained the original ORF of BRCA1. The expressions of five selected ASVs were quantified in PBMNC and non-tumor mammary and adipose tissues obtained from BC patients and controls using qPCR. The results of qPCR analyses show the low expression of analyzed BRCA1's ASVs with the exception of BRCA1Δ8-9. The ratio of mRNA ASVs was below 5 % of total BRCA1 mRNA expression.

Our results indicate that numerous ASVs of BRCA1 mRNA occur in analyzed samples, but their expression is extremely low. Further, we are planning to analyze the dynamics of BRCA1's ASVs changes, especially following the genotoxic insults.