PHARMACOGENETIC MODELS OF ADVERSE REACTIONS TO FAC CHEMOTHERAPY IN BREAST CANCER PATIENTS.

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The differences in patients' response to the same medication are one of the major problems in breast cancer treatment. Chemotherapy's toxicities make a significant clinical problem due to decreased quality of life, prolongation of treatment and reinforcement of negative emotions associated with therapy.

In this study we evaluated the genetic and clinical risk factors of FAC chemotherapy-related toxicities in the group of 324 breast cancer patients. Selected genes and their polymorphisms were involved in FAC drugs transport (*ABCB1*, *ABCC2*, *ABCG2*, *SLC22A16*), metabolism (*ALDH3A1*, *CBR1*, *CYP1B1*, *CYP2C19*, *DPYD*, *GSTM1*, *GSTP1*, *GSTT1*, *MTHFR*, *TYMS*), DNA damage recognition, repair and cell cycle control (*ATM*, *ERCC1*, *ERCC2*, *TP53*, *XRCC1*).

The multifactorial risk models were constructed for 12 toxic symptoms, that combine genetic risk modifiers and clinical characteristics. The majority of toxicities was dependent on the modifications in components of more than one pathway of FAC drugs, while the impact level of clinical factors was comparable to the genetic ones. Furthermore, for the carriers of multiple high risk factors the chance of developing given symptom was significantly elevated. Our results therefore emphasize the complex nature of adverse effects during FAC breast cancer therapy, including the interplay among the polygenic inheritance and clinical risk factors.

It is hoped, that predictive models that engage multiple factors could be potentially useful in future personalized approach to cancer treatment. The tool that enable the separation of patients group in terms of expected toxicity and therefore allows the tailoring of treatment to the characteristics of given patients, could significantly improve its tolerance, patients' quality of life and also outcome.

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