

Summary

The study of signaling pathways that modulate multidrug resistance

The theme of cancer cell resistance to anti-cancer drugs including the common mechanisms of resistance development and the theory of cancer stem cells was introduced in the Introduction to the doctoral thesis. The theoretical part was focused more deeply on the two topics – the role of ATP-binding cassette (ABC) transport proteins and chromosomal abnormalities in the development of cancer chemoresistance. The possible therapeutic potential for the treatment of cancer was stressed for both topics. The Results were composed of the commentaries on the five published works, which the author of the thesis conducted as the main author. The first work brought the evidence supporting the hypothesis of the existence of ABC gene expression profiles (signatures), which are common to multiple types of tumors and are associated with significant clinical consequences. These general ABC gene expression profiles could possibly form a new hallmark of cancer. The second work studied more closely a group of acute myeloid leukemia patients, who did not achieve complete cytogenetic remission after two attempts to maintain remission of the malignant disease. The new entity, consisting of patients with the translocation $t(2;11)(p21;q23)$ without the rearrangement of the *MLL* gene, within the myelodysplastic syndromes could be recognized on the basis of the information, which was described in the third work. The authors of the third work also suggested that a good prognosis may be associated with the new entity. A comprehensive review of the theme - controlled discontinuation of the tyrosine kinase inhibitor therapy in chronic myeloid leukemia patients - was presented in the fourth work. A discussion about the unsolved questions from the laboratory as well as clinical point of view was the most important contribution. The main goal of the fifth work was to highlight the specific complex view and the ability to visualize small subclones maintained during the cytogenetic analysis of the cancer cell karyotype. The concept was demonstrated on a collection of childhood acute lymphoblastic leukemia samples. The main purpose for writing the presented doctoral thesis was to show the complex issue of cancer cell chemoresistance from different laboratory as well as clinical directions and bring new information, which could help with the treatment of oncology patients.