Abstract

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Title of diploma thesis: **Study on the role of selected cytochrome P450 isoforms in cytostatic resistance at apoptosis level**

Cytostatic resistance is one of the most problematic obstacles in oncological treatment. Beside pharmacodynamic mechanisms, pharmacokinetic factors play an important role in drug resistance as well. Enzymatic transformation of active substance to inactive metabolite in tumor cells probably belongs to these mechanisms, however, evidences concerning the relevance of this phenomenon are predominantly either indirect and/or affected by interference elements. Using comparative experiments with HepG2 cell lines with/without CYP3A4 overexpression, we focused on the evaluation of the role of this clinically important enzyme in the resistance against docetaxel. Methodologically, it was the assessment of apoptosis induction (activation of caspases 3/7, 8 and 9) using commercial luminescent kits. Our results suggest significant participation of CYP3A4 enzyme on the reduction of docetaxel anticancer efficacy after 48 h from treatment, whereas this effect was not recorded in earlier intervals. These findings perfectly correlate with the results from our previous studies focusing on the level of changes in proliferation. Obtained knowledge could be beneficial for improvement of combination chemotherapy in future.