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The modification of UGT1A10 isoenzyme activity by C-1305 and C-1311 antitumor agents in non-cellular system and in HCT-116 colon cell line

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Modern cancer treatment provides promising outcomes, thanks to the combined therapies. However, aiming to decrease resistance against individual drugs, treatment can intensify their adverse and toxic effects. Therefore, it is important to examine the influence that potential therapeutics have on cellular metabolism. Our group previously revealed that antitumor acridinone derivatives, C-1305 and C-1311, are metabolized to a great extent by UGT1A10. Thus, the aim of the present study is to test the ability of these compounds to modulate the activity of UGT1A10 isoenzyme both in non-cellular and cellular systems. The experiments were performed using human recombinant isoenzyme UGT1A10 and colon cancer line HCT-116 over expressing UGT1A10. Enzyme activity in both models were measured using UGT-specific reaction, 7-hydroxy-4-(trifluoromethyl)-coumarin glucuronidation in the presence of selected acridinone derivatives, as well as without the drug (control experiments) by RP-HPLC analysis. The results showed that, C-1305 and C-1311 act differently towards UGT1A10 activity in dependence on the applied model. Enzymatic activity of UGT1A10 was reduced by both acridinone derivatives in non-cellular system. By contrast, higher level of UGT1A10 activity was observed in HCT-116 cells treated with both studied compounds. It is supposed that C-1305 and C-1311 potentially applied in multidrug therapy might modulate the effectiveness of UGT1A10 on the protein and the transcriptional level. This finding provides new insights into potential pharmacokinetic drug-drug interactions between C-1305 and C-1311 and the substrates of UGT1A10.

Biography

Anna Bejrowska has graduated from Gdansk University of Technology (Poland) in the year 2013. She is a co-author of a paper about environmental tests based on nuclear receptors' activity changes. Her curiosity and desire for intellectual development is what led her to pursue her PhD in the field of Drug Development. Currently, she is a PhD candidate in the Department of Pharmaceutical Technology and Biochemistry at Gdansk University of Technology. She is consistently developing her experience of working with active compounds, enzyme fractions and cell cultures. Her interest is focused on modulations and differentiation of drugs' metabolism, including the role of nuclear receptors in those processes.

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