Individualization of treatments with drugs metabolized by CES1: combining genetics and metabolomics

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CES1 is involved in the hydrolysis of ester group-containing xenobiotic and endobiotic compounds including several essential and commonly used drugs. The individual variation in the efficacy and tolerability of many drugs metabolized by CES1 is considerable. Hence, there is a large interest in individualizing the treatment with these drugs. The present review addresses the issue of individualized treatment with drugs metabolized by CES1. It describes the composition of the gene encoding CES1, reports variants of this gene with focus upon those with a potential effect on drug metabolism and provides an overview of the protein structure of this enzyme bringing notice to mechanisms involved in the regulation of enzyme activity. Subsequently, the review highlights drugs metabolized by CES1 and argues that individual differences in the pharmacokinetics of these drugs play an important role in determining drug response and tolerability suggesting prospects for individualized drug therapies. Our review also discusses endogenous substrates of CES1 and assesses the potential of using metabolomic profiling of blood to identify proxies for the hepatic activity of CES1 that predict the rate of drug metabolism. Finally, the combination of genetics and metabolomics to obtain an accurate prediction of the individual response to CES1-dependent drugs is discussed.

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