In silico approaches, and in vitro and in vivo experiments to predict induction of drug metabolism

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Despite being described more than 40 years ago, the molecular mechanism that regulates hepatic induction of cytochromes P450 and other drug-metabolizing enzymes and drug transporters by xenobiotics has remained enigmatic until recently. A major breakthrough was the discovery of the orphan nuclear receptors pregnane X receptor and constitutive androstane receptor playing key roles as species-specific xenosensors in this induction response. Using this newly acquired knowledge, the human induction response can now be more accurately predicted. This is of considerable clinical importance, since induction of cytochrome P450s and other enzymes can lead to unwanted drug-drug interactions, adverse drug reactions and drug toxicity. In this review, in vitro, in vivo and in silico techniques are discussed that can identify troublesome compounds at an early stage and that can help to design new, safer medicines faster.
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