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Quantitative mRNA expression analysis of membrane bound uptake and efflux transporters in rodent tissues

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This study focussed on the interspecies differences between the membrane transporter Organic Anion Transporting Polypeptide 2B1 (OATP2B1) expressed in humans and rodents. In recent years the relevance of this uptake transporter in the context of drug-drug- and food-drug interaction gained attention. Since, OATP2B1 is ubiquitously expressed and many endogenous and exogenous compounds are described as substrates, the uptake transporter may have an essential role in pharmacokinetics. However, little is known about the orthologue in rats. Former studies indicated similar expression patterns for the transport protein in human and rat, but revealed differences in substrate specificity – namely steroid sulfates like estrone-3-sulfate and dehydroepiandrosterone sulfate. Whereas the human orthologue seems to have a crucial role in steroid metabolism, these steroids were not transported by rat Oatp2b1 (rOatp) indicating different functions. With regard to a follow-up study, where the function of the human OATP2B1 (hOATP2B1) will be studied in a humanized rat model, a method for absolute quantification of transport proteins involved in uptake or efflux using SYBRTM Green quantitative real-time polymerase chain (real-time qPCR) reaction was evaluated. Therefore standard curves were generated and the mRNA expression of different transporters was quantified using the respective standard curve for each transporter. To further characterize the function of rOatp2b1 in vitro experiments with the model substrate atorvastatin were conducted. These experiments showed that atorvastatin was transported by the rOatp2b1 even with a much lower affinity as it is reported for the human orthologue. In addition, the atorvastatin uptake was studied in the presence of eight different compounds previously reported as hOATP2B1 substrates or inhibitors. The intracellular atorvastatin concentration was significantly inhibition by celiprolol and BSP.