

## Publication

### The scaffold protein PDZK1 modulates expression and function of the organic anion transporting polypeptide 2B1

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The protein family of Organic Anion Transporting Polypeptides (OATPs) summarizes various transporters known to facilitate cellular uptake of xenobiotics. One member of this family is OATP2B1. This transporter is ubiquitously expressed and possesses a PDZ-binding motif at the C-terminus. PDZK1 (PDZ domain-containing 1) is a scaffold protein that influences function of different membrane proteins by sorting/stabilization of their membrane localization. It was aim of the herein reported study to investigate whether there is an interaction between OATP2B1 and PDZK1, and to further characterize its impact on transport function. At first expression of both OATP2B1 and PDZK1 was evaluated in liver, kidney and intestine. Based on the existence of a C-terminal PDZ-class I binding motif in OATP2B1 and the co-expression in all tested tissues an interaction was likely. Testing the influence of PDZK1 on OATP2B1 transport function revealed enhanced transport capacity for estrone 3-sulfate, thereby suggesting a change in OATP2B1 amount in the membrane. This assumption was validated by Western blot analysis. Finally, deletion of the C-terminal PDZ-binding motif in OATP2B1 lowered the impact of PDZK1 on transport function. Taken together, we report an interaction of PDZK1 with OATP2B1, which influences localization and function of the transporter. Changes in PDZK1 expression may therefore be one factor contributing to interindividual differences in OATP2B1 mediated pharmacokinetic processes.

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