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OATP2B1 – Localisation and Influence of PDZK1

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The organic anion-transporting polypeptide 2B1 (OATP2B1) is a member of the influx transporting solute carrier superfamily. Only a small amount of substrates is known for OATP2B1, for example steroid sulfates and pharmacologically relevant compounds like statins. For its location in human intestine and heart it is most likely an important part of the uptake and distribution of these compounds. Therefore this transporter might be a promising target for research. PDZ domain-containing protein 1 (PDZK1) is a so called “scaffolding” protein, which is assumed to be part in the allocation of several proteins within the cells. Protein-protein interactions between OATP2B1 and PDZK1 were suggested by several research groups. As this kind of interaction requires close proximity of the proteins, the main focus of the present study was their localisation. Tissues investigated in immunofluorescence and immunohistochemistry were human liver, kidney and intestine, complemented with immunofluorescent staining of MDCKII cells. Additionally, transport studies as well as protein and mRNA expression analyses in Caco-2 cells in the setting of thyroid hormone treatment were conducted. In preparation of further experiments, creation of a mutant vector for OATP2B1 lacking the suggested interaction site was performed.
Staining for OATP2B1 was successful in liver, kidney and intestine, while PDZK1 was located in kidney and intestine. On basis of the localisations, however, interactions of the two proteins are solely suggested for intestine. Transport studies show a decline of influx transport rate after thyroid hormone treatment most likely caused by induction of efflux transporters like BCRP. Quantifications of protein and mRNA content lead to no significant results. Altogether the interaction of OATP2B1 and PDZK1 still remains to be proven. But the present work shows evidence that helps to clarify the possible role of PDZK1 in regulation of OATP2B1 in certain tissues.

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