LST-3TM12 is a member of the OATP1B family and a functional transporter

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Organic anion transporting polypeptides (OATPs) and particularly the two members of the OATP1B family are known for their role in pharmacokinetics. Both SLCO1B3 and SLCO1B1 are located on chromosome 12 encompassing the gene locus SLCO1B7. Hitherto, this particular gene has been assumed to be a pseudogene, even though there are published mRNA sequences linked to this chromosomal area. It was aim of this study to further investigate SLCO1B7 and the associated mRNA LST-3TM12. In a first step, we aligned all mRNAs linked to the chromosomal region of SLCO1B-transporters. This in silico analysis revealed that LST-3TM12 is a product of splicing of SLCO1B3 and SLCO1B7, and encodes for a protein with twelve transmembrane domains. The existence of LST-3TM12 mRNA was verified by polymerase chain reaction showing liver enriched expression. In addition, immunohistological staining showed that LST-3TM12 protein was expressed in the endoplasmic reticulum (ER) of hepatocytes. Localization in the ER was further verified by immunoblot analysis showing high amounts of LST-3TM12 in liver microsomes. Function of LST-3TM12 was assessed by transport studies after heterologous expression in HeLa cells, where the transporter was shown to be expressed not only in the ER but also in the plasma membrane. Overexpression of LST-3TM12 was associated with enhanced cellular accumulation of dehydroepiandrosterone sulfate (Vmax 300.2pmol mg-1 min-1; Km 34.2ţm) and estradiol 17β-glucuronide (Vmax 29.9mol mg-1 min-1 and Km 32.8ţM). In conclusion, LST-3TM12 is a functional splice variant of SLCO1B3 and SLCO1B7 expressed in the ER of human liver.
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