OATP1B3-1B7 a novel Organic Anion Transporting Polypeptide is modulated by FXR ligands and transports bile acids

JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)

ID 4515762
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Year 2019
Title OATP1B3-1B7 a novel Organic Anion Transporting Polypeptide is modulated by FXR ligands and transports bile acids
Journal American journal of physiology. Gastrointestinal and liver physiology
Volume 317
Number 6
Pages / **Article-Number** G751-G762
Keywords LST-3TM12; OATP1B3-1B7; SLCO1B3; SLCO1B7; farnesoid X receptor
Mesh terms Antineoplastic Agents, pharmacology; Bile Acids and Salts, physiology; Biological Transport, physiology; Gene Expression Regulation; Gene Regulatory Networks, physiology; HeLa Cells; Hep G2 Cells; Humans; Isoxazoles, pharmacology; Organic Anion Transporters, metabolism; Receptors, Cytoplasmic and Nuclear, genetics; Solute Carrier Organic Anion Transporter Family Member 1B3, metabolism; Solute Carrier Proteins, metabolism; Transcription Factors; Transcriptional Activation
OATP1B3-1B7 (LST-3TM12) is a member of the OATP1B (; SLCO1B;)-family. This transporter is not only functional, but also expressed in the membrane of the smooth endoplasmic reticulum of hepatocytes and enterocytes. OATP1B3-1B7 is a splice variant of; SLCO1B3; where the initial part is encoded by; SLCO1B3; , whereas the rest of the mRNA originates from the gene locus of; SLCO1B7; . In this study we not only showed that; SLCO1B3; and the mRNA encoding for OATP1B3-1B7 share the 5' untranslated region, but also that silencing of an initial; SLCO1B3; exon lowered the amount of; SLCO1B3; and of; SLCO1B7; mRNA in Huh-7 cells. To validate the assumption that both transcripts are regulated by the same promoter we tested the influence of the bile acid sensor farnesoid X receptor (FXR) on their transcription. Treatment of Huh-7 and HepaRG cells with activators of this known regulator of OATP1B3 not only increased; SLCO1B3,; but also OATP1B3-1B7 mRNA transcription. Applying a heterologous expression system we showed that several bile acids interact with OATP1B3-1B7 and that taurocholic acid and lithocholic acid are OATP1B3-1B7 substrates. As OATP1B3-1B7 is located in the smooth endoplasmic reticulum it may grant access to metabolizing enzymes. In accordance are our findings showing that the OATP1B3-1B7 inhibitor bromsulphthalein significantly reduced uptake of bile acids into human liver microsomes. Taken together we report that OATP1B3-1B7 transcription can be modulated with FXR agonists and antagonists and that OATP1B3-1B7 transports bile acids.
Publisher AMER PHYSIOLOGICAL SOC
ISSN/ISBN 1522-1547
edoc-URL https://edoc.unibas.ch/73635/
Full Text on edoc No;
Digital Object Identifier DOI 10.1152/ajpgi.00330.2018
PubMed ID http://www.ncbi.nlm.nih.gov/pubmed/31509437
ISI-Number WOS:000498689000001

Document type (ISI) Journal Article