

DMD # 62034 - Supplemental Data**Meta-analysis of expression of hepatic organic anion transporting polypeptide (OATP) transporters in cellular systems relative to human liver tissue**

Justine Badée, Brahim Achour, Amin Rostami-Hodjegan and Aleksandra Galetin – Drug Metabolism and Disposition

TABLE 1

Plasma membrane protein expression levels of OATP transporters in human liver tissue, SCHH and human cryopreserved hepatocytes in suspension. Data represent the mean \pm S.D. protein expression levels of OATP transporters determined using the plasma membrane fraction.

| OATP1B1 | | OATP1B3 | | OATP2B1 | | No. of samples | Reference |
|---|---------|---------------|---------|----------------------------|---------|----------------|-------------------------|
| Mean \pm SD | Max/Min | Mean \pm SD | Max/Min | Mean \pm SD | Max/Min | | |
| <i>Human liver tissue (fmol/μg protein)</i> | | | | | | | |
| 5.8 \pm 3.2 ^a | 3.8 | 1.7 \pm 0.5 | 2.6 | 1.7 \pm 1.1 ^b | 3.8 | 17 | (Ohtsuki et al., 2012) |
| <i>Sandwich-cultured human hepatocytes (fmol/μg protein)</i> | | | | | | | |
| 5.4 \pm 1.2 | 1.5 | 4.3 \pm 0.3 | 1.1 | 2.9 \pm 3.1 | 2.3 | 2 | (Schaefer et al., 2012) |
| <i>Human cryopreserved hepatocytes in suspension (fmol/μg protein)</i> | | | | | | | |
| 15.9 | - | 0.4 | - | 1.6 | - | 1 | (Kunze et al., 2014) |

^a Protein expression levels detected in only 8 out of 17 human liver tissue samples.^b Protein expression levels detected in only 4 out of 17 human liver tissue samples.

-, Individual data reported

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TABLE 2

Sample preparation and LC-MS/MS conditions used in the selected studies

| Membrane extraction | Sample preparation | | LC-MS/MS analysis | | | Study |
|---------------------------------|--------------------------------------|--------------------------------------|-----------------------|---|-------------------------------------|--|
| | Solubilizing/ Digestion enhancing | Proteolytic conditions | Calibration standards | Internal peptide standards | Type of quantification | |
| Extraction kit | Deoxycholate | Trypsin (20:1,37°C, overnight) | Peptides | 1B1 (NVTGFFQSFK); 1B3 (IYNSVFFGR, NVTGFFQSLK); 2B1 (VLAVTDSPAR, SSPAVEQQLLVSGPGK) | Absolute | (Balogh et al., 2012) (Kimoto et al., 2012) |
| Extraction kit | Deoxycholate | Trypsin (20:1,37°C, overnight) | Peptides | 1B1 (NVTGFFQSFK); 1B3 (NVTGFFQSLK); 2B1 (SSPAVEQQLLVSGPGK) | Absolute | (Bi et al., 2012) |
| Differential centrifugation | Guanidine HCl, Urea | Trypsin (100:1,37°C,16h) | Peptides | 1B1(LNTVGIK), 1B3(IYNSVFFGR), 2B1(VLLQTLR) | Absolute | (Ohtsuki et al., 2012) ^a (Schaefer et al., 2012) ^a (Kunze et al., 2014) ^a |
| Filter aided preparation (FASP) | SDS | LysC, trypsin (37°C,overnight) | - | NA (Label free method) | Relative to one sample ^b | Karlgren et al., 2012 Vildhede et al., 2014 |
| Extraction kit | Rapigest | Trypsin (20:1,37°C,16h) | Purified proteins | 1B1 (SSIIHIER, NVTGFFQSFK); 1B3 (NVTGFFQSLK); 2B1 (YYNNDLLR, SSPAVEQQLLVSGPGK) | Absolute | (Ji et al., 2012) |
| Extraction kit | - | Trypsin (25:1,37°C,24h) | Peptides | 1B1 (NVTGFFQSFK, YVEQQYGQPSSK), 1B3 (NVTGFFQSLK, IYNSVFFGR), 2B1 (VLAVTDSPAR, SSPAVEQQLLVSGPGK) | Absolute | (Prasad et al., 2014) |

^a Studies based on plasma membrane

^b The reference sample was processed as per Balogh et al., 2012

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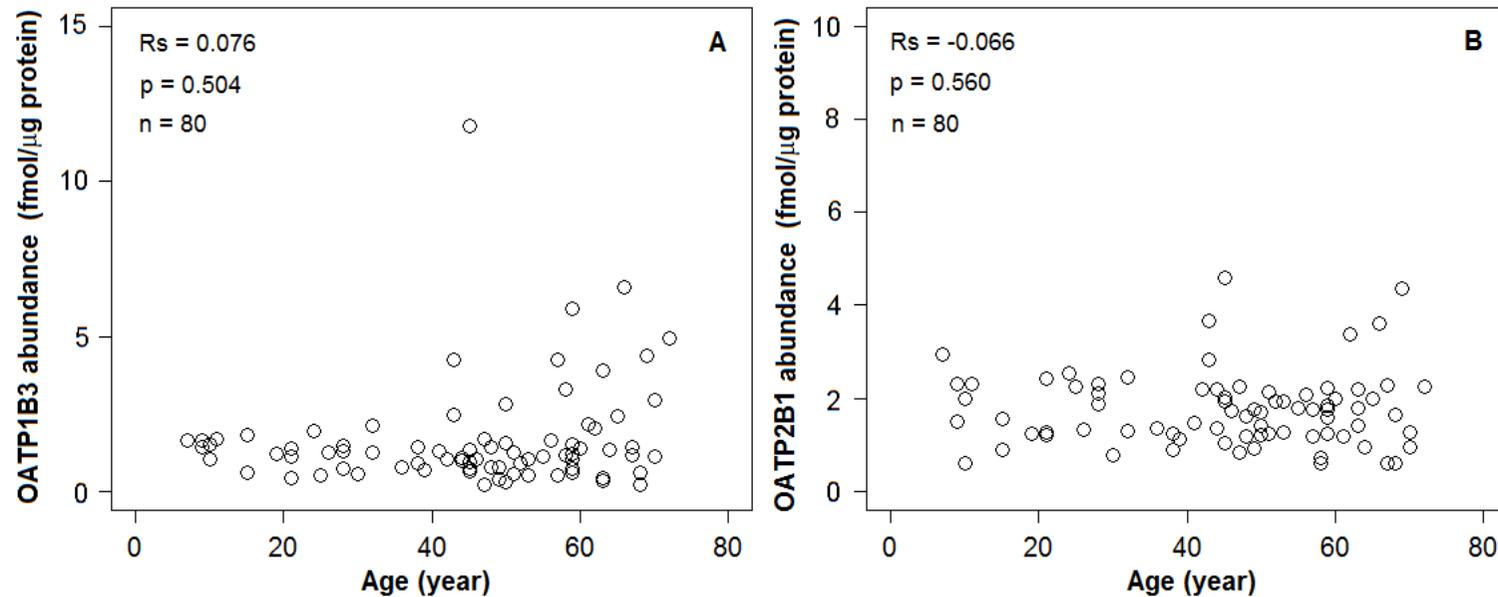


Figure 1. Age-related differences in hepatic tissue expression levels of OATP transporters. No significant correlation of OATP1B3 (A) and OATP2B1 (B) transporters expression levels and age of donors was detected (Spearman's rank test, $R_s < 0.10$, $p > 0.05$, $n = 80$).

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