Important role of organic anion transporting polypeptide in disposition of flavonoid

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Background: Organic anion transporting polypeptides (OATP) 1B1 is an important transporter specifically expressed in human liver, which play important role in the trans-membrane transport of many substances. Flavonoids are the most common polyphenolic compounds in human diet, which are ubiquitously distributed in plants. Flavonoids are extensively metabolized by UGTs in the liver cells to corresponding glucuronides. However, the trans-membrane transport of flavonoid as well as the glucuronidation metabolites in the liver is largely unknown.

Methods: Transport of wogonin, scutellarein, baicalein, chrysin and the corresponding mono-glucuronides in CHO-OATP1B1 and CHO-K1 cells was determined. Further in vivo study using Oatp1b2 knock-out (Slco1b2(-/-)) and wildtype mice were conducted to confirm the transport of flavonoid glucuronide by OATPs.

Results: The transport of wogonin, scutellarein, baicalein and chrysin in CHO-OATP1B1 cell was similar to that in CHO-K1 cells. On the contrary, the mono-glucuronides of these flavonoids are all actively transported into the CHO-OATP1B1 cells and showed 2.5 to 5.3 times of that transported into CHO-K1 cells. After a single intravenous dose of the flavonoid glucuronide to the Oatp1b2 knock-out mice, the plasma AUC of the glucuronides significantly increased, whereas liver-to-plasma ratio was significantly reduced in Oatp1b2 knock-out mice.

Conclusions: OATP1B1 play important role in the transport of flavonoid glucuronide from the blood into the liver cells, which is pivotal in the disposition of both flavonoid and the glucuronidation metabolites.