MS05-4 **Role of MRP3/ABCC3 in the folate absorption**

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Background: Mrp3/*Abcc3* is an ABC transporter accepting glucuronide conjugates, bile acids, folates, and methotrexate (MTX) as substrate. Mrp3 is expressed in the basolateral membrane of the epithelial cells in the intestine and liver. We investigated the significance of Mrp3 in the disposition of MTX and folates. **Methods:** The disposition of MTX and folates was compared between wild-type and $Mrp3^{-/-}$ mice. Mucosal-to-serosal (MtoS) transport was determined in vitro using everted duodenum sacs. **Results:** The systemic exposure of MTX was significantly lower in $Mrp3^{-/-}$ mice following oral administration, because of enhanced biliary excretion and lower oral absorption. The intrinsic efflux clearance of MTX across the serosal membrane ($PS_{serosal}$) of MTX was decreased in the everted sacs from *MRP3*$^{-/-}$ mice to 23% compared with wild-type mice. The plasma concentrations of folic acid (FA) given orally were significantly lower in *MRP3*$^{-/-}$ mice whereas the systemic clearance was similar to wild-type mice. Oral absorption of leucovorin was significantly delayed. $PS_{serosal}$ of FA and leucovorin were decreased to 5 and 22% in *MRP3*$^{-/-}$ mice, while that of 5-methyltetrahydrofolate (5MeTHF) was to 50%. There was no change in plasma 5MeTHF level, and mRNA levels of folate-metabolizing enzymes in the liver and intestine. **Conclusion:** Mrp3, together with unknown transporter, mediates the intestinal absorption of MTX and folates, but the functional impairment of Mrp3 alone did not disturb folate homeostasis.