

## Interplay between breast cancer resistance protein (BCRP) and metabolizing enzymes in the intestine

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The intestine functions as a barrier against orally ingested xenobiotic compounds. Numerous drug metabolizing enzymes and transporters have been identified in the small intestine: as for drug metabolizing enzymes, cytochrome P-450 (CYP), carboxylesterase (CES), UDP-glucuronosyl transferase (UGT) and sulfotransferase (SULT), and as for efflux transporters, P-glycoprotein (P-gp), multi-drug resistance associated protein 2 (MRP2) and breast cancer resistance protein (BCRP). The recent findings suggest that these metabolizing enzymes and transporters work not only independently, but also form co-operative detoxification systems in the intestine. For instance, CES, UGT and SULT convert xenobiotics to the substrates of transporters such as MRP2 and BCRP, allowing the efficient removal into the lumen by these efflux transporters. This presentation will discuss the importance of such co-operation between drug metabolizing enzymes and transporters in the intestine. We will particularly focus on the interplay between BCRP and SULTs based on our recent results. BCRP, a member of ATP-binding cassette transporters, is localized in the apical membrane of the enterocytes, and excretes its substrates into the lumen. BCRP transports a wide variety of sulfoconjugates. *In vitro/in situ* studies using Bcrp knock-out mice revealed that BCRP plays major roles in the intestinal excretion of sulfoconjugates formed by SULTs in the enterocytes. In mice intestine, Bcrp and Sults exhibited overlapped distributions; Bcrp activity was high from the mid- to distal intestine and high sulfation activity was found in the distal intestine, especially the colon. This overlap will be important for co-operation of BCRP and SULTs in the intestine.