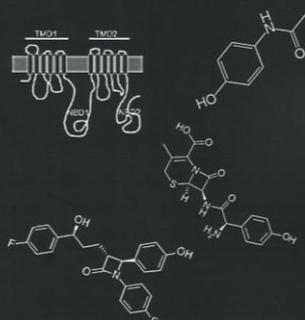




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Basolateral and apical ABC transporters in liver and intestine



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Samenvatting proefschrift Dirk R. de Waart

‘Basolateral and apical ABC transporters in liver and intestine’

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ABC-transporters are essential transport systems in many organ barriers i.e liver and intestine. These transporters are able to transport substrates against steep concentration gradients and have a very broad substrate specificity. Many ABC transporters have been associated with inherited human diseases. The focus of this thesis is on ABC-transporters expressed in the human intestine and liver. The intestine is a highly important gate-keeper controlling the uptake of substances into the human body. It does so by uptake of substances from the intestinal lumen or by excreting substance back into the intestinal lumen. As such, it is an organ, which is highly relevant both in the disposition of drugs as well as of toxins. The liver is the second barrier for substances to pass to get access to the systemic circulation. It fulfills this function by eliminating toxic substances into bile and/or by extensive metabolism of endo- and xenobiotics.

The thesis describes research on the importance of ABC transporters in the barrier function of the liver and intestine towards the heterocyclic amine PhIP (a food-derived toxin) and the hepatotoxicant acetaminophen (better known as paracetamol). In addition, we have studied the enterohepatic circulation of the cholesterol lowering drug ezetimibe and the oral availability of the antibiotic cefadroxil. Furthermore, the thesis presents data to support the use of Cholyl-L-Lysyl-Fluorescein as a diagnostic marker in a liver function test. Finally, the influence of plasma membrane cholesterol on the activity of ABC transporters is investigated.

The data presented in this thesis underscore the importance of hepatic and intestinal ABC transporters in the elimination and oral availability of toxic waste products and clinically relevant drugs. ◀

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