

### 7 Literaturverzeichnis

1. Ayrton A, Morgan P. Role of transport proteins in drug absorption, distribution and excretion. *Xenobiotica* 2001; **31**:469-497.
2. Kruijtzter CM, Beijnen JH, Schellens JH. Improvement of oral drug treatment by temporary inhibition of drug transporters and/or cytochrome P450 in the gastrointestinal tract and liver: an overview. *Oncologist*. 2002; **7**:516-530.
3. Stenberg P, Luthman K, Artursson P. Virtual screening of intestinal drug permeability. *J.Control Release* 2000; **65**:231-243.
4. Sellin JH. The pathophysiology of diarrhea. *Clin.Transplant*. 2001; **15 Suppl 4**:2-10.
5. Su SF, Huang JD. Inhibition of the intestinal digoxin absorption and exsorption by quinidine. *Drug Metab Dispos*. 1996; **24**:142-147.
6. Fricker G, Drewe J, Huwyler J, Gutmann H, Beglinger C. Relevance of p-glycoprotein for the enteral absorption of cyclosporin A: in vitro-in vivo correlation. *Br.J.Pharmacol*. 1996; **118**:1841-1847.
7. Girodon-Boulandet E, Cazeneuve C, Goossens M. Screening practices for mutations in the CFTR gene ABCC7. *Hum.Mutat*. 2000; **15**:135-149.
8. Kemp S, Pujol A, Waterham HR *et al*. ABCD1 mutations and the X-linked adrenoleukodystrophy mutation database: role in diagnosis and clinical correlations. *Hum.Mutat*. 2001; **18**:499-515.
9. Jansen PL, Strautnieks SS, Jacquemin E *et al*. Hepatocanalicular bile salt export pump deficiency in patients with progressive familial intrahepatic cholestasis. *Gastroenterology* 1999; **117**:1370-1379.
10. Allikmets R, Raskind WH, Hutchinson A, Schueck ND, Dean M, Koeller DM. Mutation of a putative mitochondrial iron transporter gene (ABC7) in X-linked sideroblastic anemia and ataxia (XLSA/A). *Hum.Mol.Genet*. 1999; **8**:743-749.

11. Dean M, Hamon Y, Chimini G. The human ATP-binding cassette (ABC) transporter superfamily. *J.Lipid Res.* 2001; **42**:1007-1017.
12. Gerloff T. Impact of genetic polymorphisms in transmembrane carrier-systems on drug and xenobiotic distribution. *Naunyn Schmiedebergs Arch.Pharmacol.* 2004; **369**:69-77.
13. Sakaeda T, Nakamura T, Okumura K. Pharmacogenetics of MDR1 and its impact on the pharmacokinetics and pharmacodynamics of drugs. *Pharmacogenomics.* 2003; **4**:397-410.
14. Schwab M, Eichelbaum M, Fromm MF. Genetic Polymorphisms of the Human MDR1 Drug Transporter. *Annu.Rev.Pharmacol.Toxicol.* 2002.
15. Juliano RL, Ling V. A surface glycoprotein modulating drug permeability in Chinese hamster ovary cell mutants. *Biochim.Biophys.Acta* 1976; **455**:152-162.
16. de Lannoy IA, Silverman M. The MDR1 gene product, P-glycoprotein, mediates the transport of the cardiac glycoside, digoxin. *Biochem.Biophys.Res.Commun.* 1992; **189**:551-557.
17. Yu DK. The contribution of P-glycoprotein to pharmacokinetic drug-drug interactions. *J.Clin.Pharmacol.* 1999; **39**:1203-1211.
18. Saeki T, Ueda K, Tanigawara Y, Hori R, Komano T. Human P-glycoprotein transports cyclosporin A and FK506. *J.Biol.Chem.* 1993; **268**:6077-6080.
19. Ambudkar SV, Dey S, Hrycyna CA, Ramachandra M, Pastan I, Gottesman MM. Biochemical, cellular, and pharmacological aspects of the multidrug transporter. *Annu.Rev.Pharmacol.Toxicol.* 1999; **39**:361-398.
20. Kim RB, Leake BF, Choo EF *et al.* Identification of functionally variant MDR1 alleles among European Americans and African Americans. *Clin.Pharmacol.Ther.* 2001; **70**:189-199.

21. Marzolini C, Paus E, Buclin T, Kim RB. Polymorphisms in human MDR1 (P-glycoprotein): recent advances and clinical relevance. *Clin.Pharmacol.Ther.* 2004; **75**:13-33.
22. Zhou S, Lim LY, Chowbay B. Herbal modulation of P-glycoprotein. *Drug Metab Rev.* 2004; **36**:57-104.
23. Kivisto KT, Niemi M, Fromm MF. Functional interaction of intestinal CYP3A4 and P-glycoprotein. *Fundam.Clin.Pharmacol.* 2004; **18**:621-626.
24. Schuetz EG, Umbenhauer DR, Yasuda K *et al.* Altered expression of hepatic cytochromes P-450 in mice deficient in one or more *mdr1* genes. *Mol.Pharmacol.* 2000; **57**:188-197.
25. Chawla A, Repa JJ, Evans RM, Mangelsdorf DJ. Nuclear receptors and lipid physiology: opening the X-files. *Science* 2001; **294**:1866-1870.
26. Higgins CF, Callaghan R, Linton KJ, Rosenberg MF, Ford RC. Structure of the multidrug resistance P-glycoprotein. *Semin.Cancer Biol.* 1997; **8**:135-142.
27. Cordon-Cardo C, O'Brien JP, Casals D *et al.* Multidrug-resistance gene (P-glycoprotein) is expressed by endothelial cells at blood-brain barrier sites. *Proc.Natl.Acad.Sci.U.S.A* 1989; **86**:695-698.
28. Tanigawara Y. Role of P-glycoprotein in drug disposition. *Ther.Drug Monit.* 2000; **22**:137-140.
29. Thiebaut F, Tsuruo T, Hamada H, Gottesman MM, Pastan I, Willingham MC. Cellular localization of the multidrug-resistance gene product P-glycoprotein in normal human tissues. *Proc.Natl.Acad.Sci.U.S.A* 1987; **84**:7735-7738.
30. Brinkmann U, Roots I, Eichelbaum M. Pharmacogenetics of the human drug-transporter gene MDR1: impact of polymorphisms on pharmacotherapy. *Drug Discov.Today* 2001; **6**:835-839.

31. Rao VV, Dahlheimer JL, Bardgett ME *et al.* Choroid plexus epithelial expression of MDR1 P glycoprotein and multidrug resistance-associated protein contribute to the blood-cerebrospinal-fluid drug-permeability barrier. *Proc.Natl.Acad.Sci.U.S.A* 1999; **96**:3900-3905.
32. Arceci RJ, Croop JM, Horwitz SB, Housman D. The gene encoding multidrug resistance is induced and expressed at high levels during pregnancy in the secretory epithelium of the uterus. *Proc.Natl.Acad.Sci.U.S.A* 1988; **85**:4350-4354.
33. Schinkel AH. The physiological function of drug-transporting P-glycoproteins. *Semin.Cancer Biol.* 1997; **8**:161-170.
34. Andreana A, Aggarwal S, Gollapudi S, Wien D, Tsuruo T, Gupta S. Abnormal expression of a 170-kilodalton P-glycoprotein encoded by MDR1 gene, a metabolically active efflux pump, in CD4+ and CD8+ T cells from patients with human immunodeficiency virus type 1 infection. *AIDS Res.Hum.Retroviruses* 1996; **12**:1457-1462.
35. Chaudhary PM, Roninson IB. Expression and activity of P-glycoprotein, a multidrug efflux pump, in human hematopoietic stem cells. *Cell* 1991; **66**:85-94.
36. Johnstone RW, Ruefli AA, Smyth MJ. Multiple physiological functions for multidrug transporter P-glycoprotein? *Trends Biochem.Sci.* 2000; **25**:1-6.
37. Schinkel AH, Wagenaar E, van Deemter L, Mol CA, Borst P. Absence of the mdr1a P-Glycoprotein in mice affects tissue distribution and pharmacokinetics of dexamethasone, digoxin, and cyclosporin A. *J.Clin.Invest* 1995; **96**:1698-1705.
38. Kim RB, Fromm MF, Wandel C *et al.* The drug transporter P-glycoprotein limits oral absorption and brain entry of HIV-1 protease inhibitors. *J.Clin.Invest* 1998; **101**:289-294.

39. Mayer U, Wagenaar E, Beijnen JH *et al.* Substantial excretion of digoxin via the intestinal mucosa and prevention of long-term digoxin accumulation in the brain by the mdr 1a P-glycoprotein. *Br.J.Pharmacol.* 1996; **119**:1038-1044.
40. Fromm MF. The influence of MDR1 polymorphisms on P-glycoprotein expression and function in humans. *Adv.Drug Deliv.Rev.* 2002; **54**:1295-1310.
41. Hoffmeyer S, Burk O, von Richter O *et al.* Functional polymorphisms of the human multidrug-resistance gene: multiple sequence variations and correlation of one allele with P-glycoprotein expression and activity in vivo. *Proc.Natl.Acad.Sci.U.S.A* 2000; **97**:3473-3478.
42. Lepper ER, Nooter K, Verweij J, Acharya MR, Figg WD, Sparreboom A. Mechanisms of resistance to anticancer drugs: the role of the polymorphic ABC transporters ABCB1 and ABCG2. *Pharmacogenomics.* 2005; **6**:115-138.
43. Pauli-Magnus C, Kroetz DL. Functional implications of genetic polymorphisms in the multidrug resistance gene MDR1 (ABCB1). *Pharm.Res.* 2004; **21**:904-913.
44. Kroetz DL, Pauli-Magnus C, Hodges LM *et al.* Sequence diversity and haplotype structure in the human ABCB1 (MDR1, multidrug resistance transporter) gene. *Pharmacogenetics* 2003; **13**:481-494.
45. Gerloff T, Schaefer M, Johne A *et al.* MDR1 genotypes do not influence the absorption of a single oral dose of 1 mg digoxin in healthy white males. *Br.J.Clin.Pharmacol.* 2002; **54**:610-616.
46. Siegmund W, Ludwig K, Giessmann T *et al.* The effects of the human MDR1 genotype on the expression of duodenal P-glycoprotein and disposition of the probe drug talinolol. *Clin.Pharmacol.Ther.* 2002; **72**:572-583.
47. Sakaeda T, Nakamura T, Horinouchi M *et al.* MDR1 genotype-related pharmacokinetics of digoxin after single oral administration in healthy Japanese subjects. *Pharm.Res.* 2001; **18**:1400-1404.

48. Horinouchi M, Sakaeda T, Nakamura T *et al.* Significant genetic linkage of MDR1 polymorphisms at positions 3435 and 2677: functional relevance to pharmacokinetics of digoxin. *Pharm.Res.* 2002; **19**:1581-1585.
49. Tanabe M, Ieiri I, Nagata N *et al.* Expression of P-glycoprotein in human placenta: relation to genetic polymorphism of the multidrug resistance (MDR)-1 gene. *J.Pharmacol.Exp.Ther.* 2001; **297**:1137-1143.
50. Johne A, Kopke K, Gerloff T *et al.* Modulation of steady-state kinetics of digoxin by haplotypes of the P-glycoprotein MDR1 gene. *Clin.Pharmacol.Ther.* 2002; **72**:584-594.
51. Yi SY, Hong KS, Lim HS *et al.* A variant 2677A allele of the MDR1 gene affects fexofenadine disposition. *Clin.Pharmacol.Ther.* 2004; **76**:418-427.
52. Ambudkar SV, Kimchi-Sarfaty C, Sauna ZE, Gottesman MM. P-glycoprotein: from genomics to mechanism. *Oncogene* 2003; **22**:7468-7485.
53. Oselin K, Nowakowski-Gashaw I, Mrozikiewicz PM, Wolbergs D, Pahkla R, Roots I. Quantitative determination of MDR1 mRNA expression in peripheral blood lymphocytes: a possible role of genetic polymorphisms in the MDR1 gene. *Eur.J.Clin.Invest* 2003; **33**:261-267.
54. van Aubel RA, Smeets PH, van den Heuvel JJ, Russel FG. Human organic anion transporter MRP4 (ABCC4) is an efflux pump for the purine end metabolite urate with multiple allosteric substrate binding sites. *Am.J.Physiol Renal Physiol* 2005; **288**:F327-F333.
55. Hooiveld GJ, Heegsma J, van Montfoort JE, Jansen PL, Meijer DK, Muller M. Stereoselective transport of hydrophilic quaternary drugs by human MDR1 and rat Mdr1b P-glycoproteins. *Br.J.Pharmacol.* 2002; **135**:1685-1694.
56. Gerloff T, Stieger B, Hagenbuch B *et al.* The sister of P-glycoprotein represents the canalicular bile salt export pump of mammalian liver. *J.Biol.Chem.* 1998; **273**:10046-10050.

57. Germann UA, Willingham MC, Pastan I, Gottesman MM. Expression of the human multidrug transporter in insect cells by a recombinant baculovirus. *Biochemistry* 1990; **29**:2295-2303.
58. Mickley LA, Lee JS, Weng Z *et al.* Genetic polymorphism in MDR-1: a tool for examining allelic expression in normal cells, unselected and drug-selected cell lines, and human tumors. *Blood* 1998; **91**:1749-1756.
59. Lin JH, Yamazaki M. Role of P-glycoprotein in pharmacokinetics: clinical implications. *Clin.Pharmacokinet.* 2003; **42**:59-98.
60. Kimchi-Sarfaty C, Gripar JJ, Gottesman MM. Functional characterization of coding polymorphisms in the human MDR1 gene using a vaccinia virus expression system. *Mol.Pharmacol.* 2002; **62**:1-6.
61. Morita N, Yasumori T, Nakayama K. Human MDR1 polymorphism: G2677T/A and C3435T have no effect on MDR1 transport activities. *Biochem.Pharmacol.* 2003; **65**:1843-1852.
62. Gottesman MM, Pastan I. Biochemistry of multidrug resistance mediated by the multidrug transporter. *Annu.Rev.Biochem.* 1993; **62**:385-427.
63. Shapiro AB, Corder AB, Ling V. P-glycoprotein-mediated Hoechst 33342 transport out of the lipid bilayer. *Eur.J.Biochem.* 1997; **250**:115-121.
64. Kurata Y, Ieiri I, Kimura M *et al.* Role of human MDR1 gene polymorphism in bioavailability and interaction of digoxin, a substrate of P-glycoprotein. *Clin.Pharmacol.Ther.* 2002; **72**:209-219.
65. Ishikawa T, Onishi Y, Hirano H, Oosumi K, Nagakura M, Tarui S. Pharmacogenomics of drug transporters: a new approach to functional analysis of the genetic polymorphisms of ABCB1 (P-glycoprotein/MDR1). *Biol.Pharm.Bull.* 2004; **27**:939-948.

66. Polli JW, Baughman TM, Humphreys JE *et al.* P-glycoprotein influences the brain concentrations of cetirizine (Zyrtec), a second-generation non-sedating antihistamine. *J.Pharm.Sci.* 2003; **92**:2082-2089.
67. Drescher S, Schaeffeler E, Hitzl M *et al.* MDR1 gene polymorphisms and disposition of the P-glycoprotein substrate fexofenadine. *Br.J.Clin.Pharmacol.* 2002; **53**:526-534.
68. Chiou WL, Chung SM, Wu TC, Ma C. A comprehensive account on the role of efflux transporters in the gastrointestinal absorption of 13 commonly used substrate drugs in humans. *Int.J.Clin.Pharmacol.Ther.* 2001; **39**:93-101.
69. Ford JM. Experimental reversal of P-glycoprotein-mediated multidrug resistance by pharmacological chemosensitisers. *Eur.J.Cancer* 1996; **32A**:991-1001.
70. Ramachandra M, Ambudkar SV, Chen D *et al.* Human P-glycoprotein exhibits reduced affinity for substrates during a catalytic transition state. *Biochemistry* 1998; **37**:5010-5019.
71. Litman T, Zeuthen T, Skovsgaard T, Stein WD. Competitive, non-competitive and cooperative interactions between substrates of P-glycoprotein as measured by its ATPase activity. *Biochim.Biophys.Acta* 1997; **1361**:169-176.
72. Pascaud C, Garrigos M, Orlowski S. Multidrug resistance transporter P-glycoprotein has distinct but interacting binding sites for cytotoxic drugs and reversing agents. *Biochem.J.* 1998; **333 ( Pt 2)**:351-358.
73. Stephens RH, O'Neill CA, Warhurst A, Carlson GL, Rowland M, Warhurst G. Kinetic profiling of P-glycoprotein-mediated drug efflux in rat and human intestinal epithelia. *J.Pharmacol.Exp.Ther.* 2001; **296**:584-591.
74. Makhey VD, Guo A, Norris DA, Hu P, Yan J, Sinko PJ. Characterization of the regional intestinal kinetics of drug efflux in rat and human intestine and in Caco-2 cells. *Pharm.Res.* 1998; **15**:1160-1167.



## Literaturverzeichnis

---

75. Kioka N, Tsubota J, Kakehi Y *et al.* P-glycoprotein gene (MDR1) cDNA from human adrenal: normal P-glycoprotein carries Gly185 with an altered pattern of multidrug resistance. *Biochem.Biophys.Res.Commun.* 1989; **162**:224-231.
76. Wang D, Johnson AD, Papp AC, Kroetz DL, Sadee W. Multidrug resistance polypeptide 1 (MDR1, ABCB1) variant 3435C>T affects mRNA stability. *Pharmacogenet.Genomics* 2005; **15**:693-704.