

Supporting information

Classification of inhibitors of hepatic organic anion transporting polypeptides (OATPs) – influence of protein expression on drug-drug interactions

Maria Karlgren, Anna Vildhede, Ulf Norinder, Jacek R. Wisniewski, Emi Kimoto, Yurong Lai, Ulf Haglund and Per Artursson

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Supplementary Table 2. Hill slopes \pm standard errors for the IC₅₀ curves shown in Figure 10.

	OATP1B1	OATP1B3	OATP2B1
Atazanavir	-2.25 \pm 0.14	-0.86 \pm 0.10	-1.20 \pm 0.30
Cyclosporin	-1.13 \pm 0.24	-2.96 \pm 0.32	-1.1 \pm 0.43
Doxorubicin	-1.34 \pm 0.12	-0.51 \pm 0.07	-0.46 \pm 0.09
Erlotinib	-0.87 \pm 0.08	-1.25 \pm 0.41	-1.16 \pm 0.25
Hoechst 3334	-0.92 \pm 0.20	-0.95 \pm 0.18	-0.51 \pm 0.06
Indomethacin	-2.04 \pm 0.56	-0.90 \pm 0.08	-2.29 \pm 0.35
KO143	-	-	-
MK571	-1.42 \pm 0.24	-0.94 \pm 0.22	-0.89 \pm 0.07
Pravastatin	-0.48 \pm 0.10	-0.66 \pm 0.12	-1.25 \pm 0.15
Rifampicin	-0.86 \pm 0.09	-1.53 \pm 0.13	-0.49 \pm 0.05
Ritonavir	-0.68 \pm 0.20	-1.19 \pm 0.34	-1.38 \pm 0.35
Sulfasalazine	-0.55 \pm 0.04	-0.98 \pm 0.17	-1.19 \pm 0.13
Vincristine	-1.04 \pm 0.23	-0.83 \pm 0.14	-

Supplementary Table 3. Gene specific primer pairs for amplification and cloning of OATP1B3 and OATP2B1. Restriction sites introduced by the primers are underlined.

Gene	Primer sequences
SLCO1B3	5'-CTAG <u>GGATCC</u> ATGGACCAACATCAACATTT -3' / '5'-CTAG <u>CTCGAG</u> TTAGTTGGCAGCAGCATTGT-3'
SLCO2B1	5'-CTAGA <u>AAGCTT</u> ATGGGACCCAGGATAGGGCC-3' /5'-CTAG <u>GATATCT</u> CACACTCGGGAATCCTCTG-3'

Supplementary Table 4. SMILES for the 225 investigated compounds.

Compound	Smiles
17β-estradiol	<chem>Oc1ccc2c(c1)CC[C@@H]1[C@@H]2CC[C@]2([C@H]1CC[C@H]2O)C</chem>
1-methyl-4-phenylpyridinium	<chem>C[n+]1ccc(cc1)c1ccccc1</chem>
5-Carboxyfluorescein diacetate	<chem>Oc1ccc2c(c1)Oc1c([C@@]32OC(=O)c2c3ccc(c2)C(=O)O)ccc(c1)O</chem> <chem>OC[C@H]1O[C@H](O[C@@H]2[C@@H](CO)O[C@H]([C@@H]([C@H]2O)O)O)[C@@H]([C@H]([C@@H]1O[C@H]1O[C@H](C)[C@H]([C@@H]([C@H]1O)O)N[C@H]1C=C(CO)[C@@H]([C@@H]([C@H]1O)O)O)O)</chem>
Acarbose	<chem>O=C1C=CC(=O)N[C@@H](C1)C(=O)O</chem>
Aciclovir	<chem>Nc1nc(=O)c2c([nH]1)n(COCCO)cn2</chem>
Allopurinol	<chem>O=c1ncnc2c1c[nH][nH]2</chem>
Amantadine	<chem>N[C@]12C[C@H]3C[C@@H](C2)C[C@@H](C1)C3</chem>
Amitriptyline	<chem>CN(CC/C=C/1\c2ccccc2CCc2c1cccc2)C</chem>
Amodiaquine	<chem>CCN(Cc1cc(ccc1O)Nc1ccnc2c1ccc(c2)Cl)CC</chem>
Amprenavir	<chem>CC(CN(S(=O)(=O)c1ccc(cc1)N)C[C@H]([C@H](Cc1ccccc1)NC(=O)O[C@H]1CCOC1)O)C</chem>
Astemizole	<chem>COc1ccc(cc1)CCN1CC[C@H](CC1)Nc1nc2c(n1Cc1ccc(cc1)F)cccc2</chem>
Atazanavir	<chem>COC(=O)N[C@@H](C(C)(C)C)C(=O)NN(Cc1ccc(cc1)c1ccccc1)C[C@@H]([C@H](Cc1ccccc1)NC(=O)[C@H](C(C)(C)C)NC(=O)OC)O</chem>
Atenolol	<chem>O[C@@H](COc1ccc(cc1)CC(=O)N)CNC(C)C</chem>
Atomoxetine	<chem>CNCC[C@H](c1ccccc1)Oc1ccccc1C</chem>
Atorvastatin	<chem>O[C@@H](C[C@H](CC(=O)O)O)CCn1c(C(C)C)c(c1c1ccc(cc1)F)c1ccccc1C(=O)Nc1cccc1</chem>
Baicalin	<chem>OC(=O)[C@H]1O[C@@H](Oc2cc3oc(cc(=O)c3c(2O)O)c2ccccc2)[C@@H]([C@H]([C@@H]1O)O)O</chem>
Benzbromarone	<chem>CCc1oc2c(c1C(=O)c1cc(Br)c(c(c1)Br)O)cccc2</chem>
Berberine	<chem>COc1c(OC)ccc2c1c[n+]1CCc3c(c1c2)cc1c(c3)OCO1</chem>
Bestatin	<chem>O[C@H](C(=O)N[C@@H](C(=O)O)CC(C)C)[C@@H](Cc1ccccc1)N</chem>
Bromsulfalein	<chem>Brc1c(Br)c(Br)c2c(c1Br)C(=O)O[C@@]2(c1ccc(c(c1)S(=O)(=O)[O-])O)c1ccc(c(c1)S(=O)(=O)[O-])O</chem>
Budesonide	<chem>CCC[C@H]1O[C@H]2[C@](O1)(C(=O)CO)[C@@]1([C@@H](C2)[C@@H]2CCC3=CC(=O)C=C[C@@]3([C@H]2[C@H](C1)O)C)C</chem>
Bufuralol	<chem>CCc1cccc2c1oc(c2)[C@H](CNC(C)(C)C)O</chem>
Bupropion	<chem>Clc1cccc(c1)C(=O)[C@H](NC(C)(C)C)C</chem>
Buspirone	<chem>O=C1CC2(CCCC2)CC(=O)N1CCCCN1CCN(CC1)c1ncccc1</chem>
Caffeine	<chem>Cn1cnc2c1c(=O)n(C)c(=O)n2C</chem>
Candesartan	<chem>CCOc1nc2c(n1Cc1ccc(cc1)c1ccccc1c1n[nH]nn1)c(ccc2)C(=O)O</chem>
Captopril	<chem>SC[C@H](C(=O)N1CCC[C@H]1C(=O)O)C</chem>
Carbamazepine	<chem>NC(=O)N1c2ccccc2C=Cc2c1cccc2</chem>
Carnitine	<chem>O[C@@H](C[N+](C)(C)C)CC(=O)[O-]</chem>
Cefadroxil	<chem>O=C([C@H](c1ccc(cc1)O)N)N[C@H]1C(=O)N2[C@H]1SCC(=C2C(=O)O)C</chem>
Cefamandole	<chem>O[C@@H](C(=O)N[C@@H]1C(=O)N2[C@@H]1SCC(=C2C(=O)O)CSc1nnnn1C)c1ccccc1</chem>
Celecoxib	<chem>Cc1ccc(cc1)c1cc(nn1c1ccc(cc1)S(=O)(=O)N)C(F)(F)F</chem>
Cerivastatin	<chem>COc1c(c2ccc(cc2)F)c(/C=C/[C@H](C[C@H](CC(=O)O)O)c(nc1C(C)C)C(C)C</chem>

Cetirizine	<chem>OC(=O)COCCN1CCN(CC1)[C@H](c1ccc(cc1)Cl)c1ccccc1</chem>
Chelerythrine	<chem>COc1c(OC)ccc2c1c[n+](C)c1c2ccc2c1cc1OCOc1c2</chem>
Chloroquine	<chem>CCN(CCC[C@H](Nc1ccnc2c1ccc(c2)Cl)C)CC</chem>
Chlorpromazine	<chem>CN(CCCN1c2ccccc2Sc2c1cc(Cl)cc2)C</chem>
Chlorprothixene	<chem>CN(CC/C=C\1/c2ccccc2Sc2c1cc(Cl)cc2)C</chem>
Chlorzoxazone	<chem>Clc1ccc2c(c1)[nH]c(=O)o2</chem>
Cholecystokinin 8	<chem>CSCC[C@@H](C(=O)N(C(=O)[C@H](CC(=O)O)N)C(=O)[C@H](Cc1c[nH]c2c1cccc2)NC(=O)[C@H]([C@H](OS(=O)(=O)O)C)NC(=O)[C@@H](NC(=O)[C@H](Cc1ccc(cc1)O)N)CCSC)NCCCCC(=O)N[C@H](C(=O)N)Cc1ccccc1</chem>
Cholic acid	<chem>O[C@@H]1CC[C@]2([C@@H](C1)C[C@H]([C@@H]1[C@@H]2C[C@H](O)[C@]2([C@H]1)CC[C@@H]2[C@@H](CCC(=O)O)C)O)C</chem>
Cimetidine	<chem>N#CN/C(=N\C)/NCCSCc1nc[nH]c1C</chem>
Clarithromycin	<chem>CC[C@H]1OC(=O)[C@H](C)[C@@H](O[C@@H]2C[C@](C)(OC)[C@@H]([C@H](O2)C)O)[C@H](C)[C@@H](O[C@@H]2O[C@H](C)C[C@@H]([C@H]2O)N(C)C)[C@](C[C@H](C(=O)[C@@H]([C@H]([C@]1(C)O)O)C)C)C)OC</chem>
Clotrimazole	<chem>Clc1ccccc1[C@@](n1cncc1)(c1ccccc1)c1ccccc1</chem>
Colchicine	<chem>COc1c(OC)cc2c(c1OC)c1ccc(c(=O)cc1[C@H](CC2)NC(=O)C)OC</chem>
Coumarin	<chem>O=c1ccc2c(o1)cccc2</chem>
Coumestrol	<chem>Oc1ccc2c(c1)oc(=O)c1c2oc2c1ccc(c2)O</chem>
Cyclosporine A	<chem>C/C=C/C[C@H]([C@H]([C@H]1C(=O)N[C@@H](CC)C(=O)N(C)CC(=O)N(C)[C@@H](CC(C)C)C(=O)N[C@@H](C(C)C)C(=O)N(C)[C@@H](CC(C)C)C(=O)N[C@@H](C(=O)N[C@@H](C(=O)N[C@@H](C(=O)N1C)C(C)C)CC(C)C)CC(C)C)C)O)C</chem>
Daidzein	<chem>Oc1ccc(cc1)c1coc2c(c1=O)ccc(c2)O</chem>
Desipramine	<chem>CNCCCN1c2ccccc2CCc2c1cccc2</chem>
Dexamethasone	<chem>OCC(=O)[C@@]1(O)[C@H](C)[C@@H]2[C@]1(C)C[C@H](O)[C@]1([C@H]2CCC2=CC(=O)C=C[C@]12)C)F</chem>
Dextromethorphan	<chem>COc1ccc2c(c1)[C@@]13CCCC[C@@H]3[C@H](C2)N(CC1)C</chem>
Diazepam	<chem>Clc1ccc2c(c1)C(=NCC(=O)N2C)c1ccccc1</chem>
Diclofenac	<chem>OC(=O)Cc1ccccc1Nc1c(Cl)cccc1Cl</chem>
Diethylstilbestrol	<chem>CC/C(=C(\c1ccc(cc1)O)/CC)/c1ccc(cc1)O</chem>
Digoxin	<chem>O=C1OCC(=C1)[C@@H]1CC[C@]2([C@]1(C)[C@H](O)C[C@H]1[C@H]2CC[C@H]2[C@]1(C)CC[C@@H](C2)O[C@H]1C[C@H](O)[C@@H]([C@H](O1)C)O[C@H]1C[C@H](O)[C@@H]([C@H](O1)C)O[C@H]1C[C@H](O)[C@@H]([C@H](O1)C)O)O</chem>
Diltiazem	<chem>COc1ccc(cc1)[C@@H]1Sc2ccccc2N(C(=O)[C@@H]1OC(=O)C)CCN(C)C</chem>
Dipyridamole	<chem>OCCN(c1nc(N2CCCC2)c2c(n1)c(nc(n2)N(CCO)CCO)N1CCCC1)CCO</chem>
Disopyramide	<chem>CC(N(C(C)C)CC[C@](c1ccccc1)(c1ccccc1)C(=O)N)C</chem>
Disulfiram	<chem>CCN(C(=S)SSC(=S)N(CC)CC)CC</chem>
Dofetilide	<chem>CN(CCC1ccc(cc1)NS(=O)(=O)C)CCOc1ccc(cc1)NS(=O)(=O)C</chem>
Doxazosin	<chem>COc1cc2nc(nc2cc1OC)N)N1CCN(CC1)C(=O)[C@H]1COc2c(O1)cccc2</chem>
Doxorubicin	<chem>OCC(=O)[C@@]1(O)C[C@H](O[C@H]2C[C@H](N)[C@@H]([C@@H](O2)C)O)c2c(C1)c(O)c1c(c2O)C(=O)c2c(C1=O)cccc2OC</chem>
Efavirenz	<chem>FC([C@@]1(C#CC2CC2)OC(=O)Nc2c1cc(Cl)cc2)(F)F</chem>
Eletriptan	<chem>CN1CCC[C@@H]1Cc1c[nH]c2c1cc(cc2)CCS(=O)(=O)c1ccccc1</chem>
Emtricitabine	<chem>Nc1nc(=O)n(cc1F)[C@@H]1CS[C@@H](O1)CO</chem>
Enalapril	<chem>CCOC(=O)[C@H](N[C@H](C(=O)N1CCC[C@H]1C(=O)O)C)CCc1ccccc1</chem>

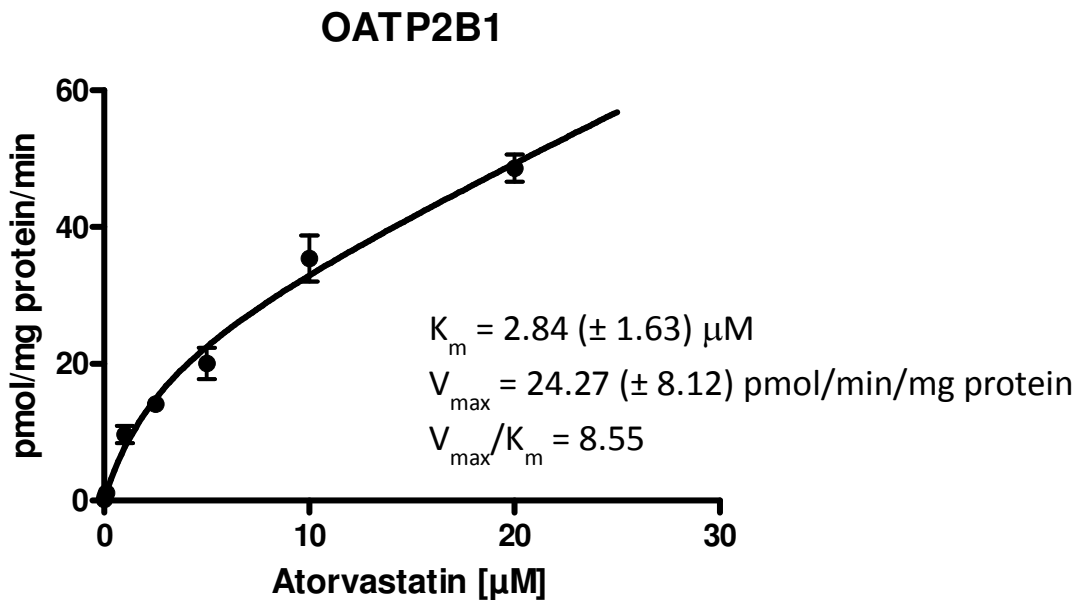
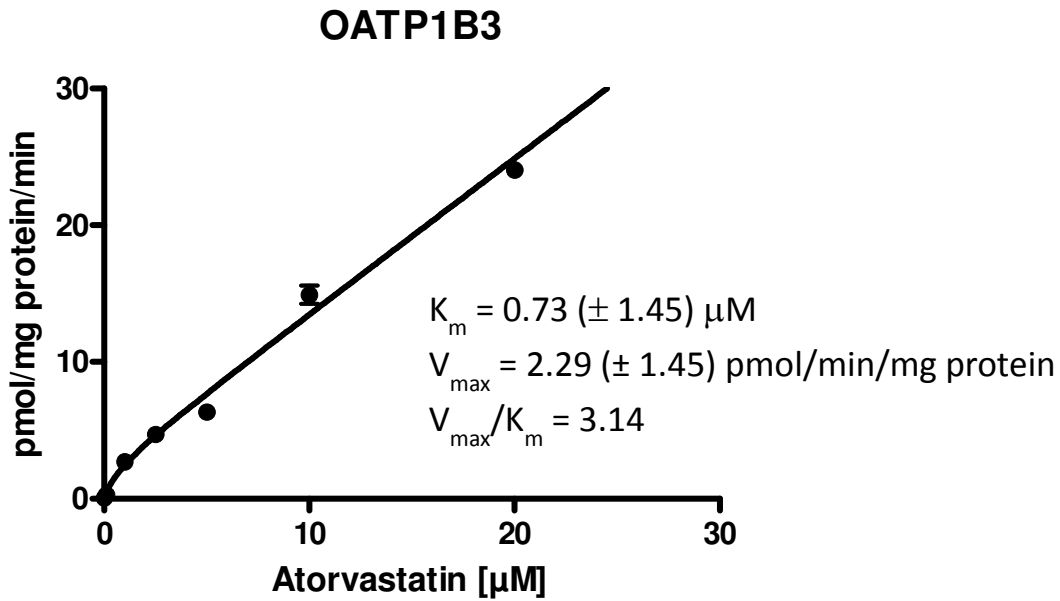
Erlotinib	<chem>COCCOc1cc2c(ncnc2cc1OCCOC)Nc1cccc(c1)C#C</chem>
Erythromycin	<chem>CC[C@H]1OC(=O)[C@H](C)[C@@H](O[C@@H]2O[C@@H](C)[C@@H]([C@](C2)(C)OC)O)[C@H](C)[C@@H](O[C@@H]2O[C@@H](C)C[C@@H]([C@H]2O)N(C)C)[C@](C[C@H](C(=O)[C@@H]([C@H]([C@]1(C)O)O)C)C)(C)O</chem>
Estradiol-17-β-glucuronide	<chem>[O-]C(=O)[C@@H]1O[C@@H](O[C@@H]2CC[C@H]3[C@@]2(C)CC[C@H]2[C@H]3CCc3c2ccc(c3)O)[C@@H]([C@@H]([C@@H]1O)O)O</chem>
Estrone-3-sulphate	<chem>O=C1CC[C@@H]2[C@]1(C)CC[C@H]1[C@H]2CCc2c1ccc(c2)OS(=O)(=O)O</chem>
Etoposide	<chem>COc1cc(cc(c1O)OC)[C@H]1[C@H]2C(=O)OC[C@@H]2[C@@H](c2c1cc1OCCOc1c2)O[C@@H]1O[C@@H]2CO[C@H](O[C@H]2[C@@H]([C@H]1O)O)C</chem>
Ezetimibe	<chem>Oc1ccc(cc1)[C@@H]1[C@@H](CC[C@@H](c2ccc(cc2)F)O)C(=O)N1c1ccc(cc1)F</chem>
Felodipine	<chem>CCOC(=O)C1=C(C)NC(=C([C@H]1c1cccc(c1Cl)Cl)C(=O)OC)C</chem>
Fendiline	<chem>C[C@@H](c1ccccc1)NCC[C@@H](c1ccccc1)c1ccccc1</chem>
Fenofibrate	<chem>CC(OC(=O)C(Oc1ccc(cc1)C(=O)c1ccc(cc1)Cl)(C)C)C</chem>
Fentanyl	<chem>CCC(=O)N(c1ccccc1)[C@@H]1CCN(CC1)CCc1ccccc1</chem>
Fexofenadine	<chem>OC(=O)C(c1ccc(cc1)[C@H](CCCN1CC[C@H](CC1)[C@@](c1ccccc1)(c1ccccc1)O)O)(C)C</chem>
Fluconazole	<chem>Fc1ccc(c(c1)F)[C@](Cn1cncn1)(Cn1cncn1)O</chem>
Fluo-3	<chem>OC(=O)CN(c1ccc(cc1OCCOc1cc(C)ccc1N(CC(=O)O)CC(=O)O)c1c2cc(Cl)c(=O)cc2oc2c1cc(Cl)c(c2)O)CC(=O)O</chem>
Fluoxetine	<chem>CNCC[C@H](c1ccccc1)Oc1ccc(cc1)C(F)(F)F</chem>
Flupenthixol	<chem>OCCN1CCN(CC1)CC/C=C\1/c2ccccc2Sc2c1cc(cc2)C(F)(F)F</chem>
Flutamide	<chem>O=C(C(C)C)Nc1ccc(c(c1)C(F)(F)F)[N+](=O)[O-]</chem>
Fluvastatin	<chem>OC(=O)C[C@H](C[C@H](/C=C/c1c(c2ccc(cc2)F)c2c(n1C(C)C)cccc2)O)O</chem>
Fluvoxamine	<chem>NCCO/N=C(\c1ccc(cc1)C(F)(F)F)/CCCCOC</chem>
Furafylline	<chem>Cc1[nH]c2c(n1)n(Cc1cccc1)c(=O)n(c2=O)C</chem>
Furosemide	<chem>OC(=O)c1cc(c(cc1NCc1cccc1)Cl)S(=O)(=O)N</chem>
Gemfibrozil	<chem>Cc1ccc(c(c1)OCCCC(C(=O)O)(C)C)C</chem>
Genistein	<chem>Oc1ccc(cc1)c1coc2c(c1=O)c(O)cc(c2)O</chem>
GF120918 (elacridar)	<chem>COc1cc2CN(CCc3ccc(cc3)NC(=O)c3ccccc3c4c3[nH]c3c(OC)cccc3c4=O)CCc2cc1OC</chem>
Glipizide	<chem>Cc1ncc(nc1)C(=O)NCCc1ccc(cc1)S(=O)(=O)NC(=O)NC1CCCCC1</chem>
Glibenclamide	<chem>COc1ccc(cc1C(=O)NCCc1ccc(cc1)S(=O)(=O)NC(=O)NC1CCCCC1)Cl</chem>
Glycochenodeoxycholate	<chem>O[C@@H]1CC[C@]2([C@@H](C1)C[C@H]([C@@H]1[C@@H]2CC[C@]2([C@H]1CC[C@@H]2[C@@H])(CCC(=O)NCC(=O)[O-])C)C)O)C</chem>
Glycocholic acid	<chem>O[C@@H]1CC[C@]2([C@@H](C1)C[C@H]([C@@H]1[C@@H]2C[C@H](O)[C@]2([C@H]1CC[C@@H]2[C@@H])(CCC(=O)NCC(=O)O)C)O)C</chem>
Glycodeoxycholate	<chem>O[C@@H]1CC[C@]2([C@@H](C1)CC[C@@H]1[C@@H]2C[C@H](O)[C@]2([C@H]1CC[C@@H]2[C@@H])(CCC(=O)NCC(=O)O)C)C)C</chem>
Glycyl proline	<chem>NCC(=O)N1CCC[C@@H]1C(=O)O</chem>
Glycyrrhizic acid	<chem>O[C@@H]1[C@@H](O[C@@H]2O[C@@H](C(=O)O)[C@H]([C@@H]([C@H]2O)O)O)[C@H](O[C@@H]([C@H]1O)C(=O)O)O[C@H]1CC[C@]2([C@H](C1(C)C)CC[C@@]1([C@@H]2C(=O)C=C2[C@@]1(C)CC[C@@]1([C@H]2C[C@](C)(CC1)C(=O)O)C)C)C</chem>
Hoechst 33342	<chem>CCOc1ccc(cc1)C1=NCc2c(N1)ccc(c2)C1=NCc2c(N1)ccc(c2)N1CCN(CC1)C</chem>
Hygromycin	<chem>CC(=O)[C@H]1O[C@H]([C@H]([C@@H]1O)O)Oc1ccc(cc1O)/C=C/C(=O)N[C@@H]1[C@H](O)[C@@H](O)[C@@H]2[C@H]([C@@H]1O)OCO2)\C</chem>
Ibuprofen	<chem>CC(Cc1ccc(cc1)[C@H](C(=O)O)C)C</chem>
Imipramine	<chem>CN(CCCN1c2ccccc2CCc2c1cccc2)C</chem>
Indinavir	<chem>O[C@H](CN1CCN(C[C@H]1C(=O)NC(C)(C)C)Cc1ccnc1)C[C@H](C(=O)N[C@@H]1[C@H</chem>

)(O)Cc2c1cccc2)Cc1cccc1
 Indocyanine green [O-]S(=O)(=O)CCCN1c2ccc3c(c2C(/C/1=C/C=C/C=C/C=C/C1=[N+](CCCCS(=O)(=O)[O-])c2c(C1(C)C)c1cccc1cc2)(C)C)cccc3
 Indomethacin COc1ccc2c(c1)c(CC(=O)O)c(n2C(=O)c1ccc(cc1)Cl)C
 Irinotecan CC[C@@]1(O)C(=O)OCc2c1cc1c3nc4ccc(cc4c(c3Cn1c2=O)CC)OC(=O)N1CC[C@H](CC1)N1CCCC1
 Isoniazid NNC(=O)c1ccncc1
 Isradipine COC(=O)C1=C(C)NC(=C([C@H]1c1cccc2c1non2)C(=O)OC(C)C)C
 Itraconazole CC[C@H](n1ncn(c1=O)c1ccc(cc1)N1CCN(CC1)c1ccc(cc1)OC[C@H]1CO[C@](O1)(Cn1cn1)c1ccc(cc1)Cl)Cl)C
 Ivermectin CO[C@H]1C[C@H](O[C@H]2[C@@H](C)/C=C/C=C/3\CO[C@H]4[C@]3(O)[C@@H](C=C([C@H]4O)C)C(=O)O[C@H]3[C@@H](C/C=C/2\CO[C@]2(C3)CC[C@@H]([C@H](O2)[C@H](CC)C)C)O[C@H]([C@@H]1O[C@H]1C[C@H](OC)[C@H]([C@@H](O1)C)O)C
 Ketoconazole Clc1ccc(c(c1)Cl)[C@@]1(OC[C@H](O1)COc1ccc(cc1)N1CCN(CC1)C(=O)C)Cn1cncc1
 KO143 COc1ccc2c(c1)[nH]c1c2C[C@@H]2N([C@H]1CC(C)C)C(=O)[C@@H](NC2=O)CCC(=O)OC(C)C
 Lamotrigine Nc1nnc(c(n1)N)c1cccc(c1)Cl)Cl
 Lansoprazole O=[S@](c1nc2c([nH]1)cccc2)Cc1nccc(c1C)OCC(F)(F)F
 Levothyroxin OC(=O)[C@H](Cc1cc(l)c(c(c1))O)c1cc(l)c(c(c1))O)N
 Lisinopril NCCCC[C@@H](C(=O)N1CCC[C@H]1C(=O)O)N[C@H](C(=O)O)CCc1cccc1
 Loperamide Clc1ccc(cc1)[C@]1(O)CCN(CC1)CC[C@](C(=O)N(C)C)(c1cccc1)c1cccc1
 Lopinavir O=C(N[C@H]([C@H](C[C@H](Cc1cccc1)NC(=O)[C@@H](N1CCCNC1=O)C(C)O)Cc1ccc1)COc1c(C)cccc1C
 Loratadine CCOC(=O)N1CCC(=C2c3ccc(cc3CCc3c2nccc3)Cl)CC1
 Lovastatin CC[C@@H](C(=O)O[C@H]1C[C@@H](C)C=C2[C@H]1[C@@H](CC[C@@H]1C[C@@H](O)CC(=O)O1)[C@H](C=C2)C)C
 Mephenytoin CC[C@]1(NC(=O)N(C1=O)C)c1cccc1
 Metformin CN(C(=N)NC(=N)N)C
 Methotrexate OC(=O)CC[C@@H](C(=O)O)NC(=O)c1ccc(cc1)N(Cc1cnc2c(n1)c(N)nc(n2)N)C
 Methoxsalen COc1c2oc(=O)ccc2cc2c1occ2
 Metoprolol COCCc1ccc(cc1)OC[C@H](CNC(C)C)O
 Midazolam Clc1ccc2c(c1)C(=NCc1n2c(C)nc1)c1cccc1F
 Mifepristone CC#C[C@]1(O)CC[C@H]2[C@]1(C)C[C@H](c1ccc(cc1)N(C)C)C1=C3CCC(=O)C=C3CC[C@@H]21
 Mitoxantrone OCCNCCNc1ccc(c2c1C(=O)c1c(C2=O)c(O)ccc1O)NCCNCCO
 MK571 OC(=O)CCS[C@H](c1cccc(c1)/C=C/c1ccc2c(n1)cc(cc2)Cl)SCCC(=O)N(C)C
 Moclobemide O=C(c1ccc(cc1)Cl)NCCN1CCOCC1
 Morin Oc1ccc(c(c1)O)c1oc2cc(O)cc(c2c(=O)c1O)O
 Naringenin Oc1ccc(cc1)[C@@H]1CC(=O)c2c(O1)cc(cc2O)O
 Naringin OC[C@H]1O[C@@H](Oc2cc(O)c3c(c2)O[C@@H](CC3=O)c2ccc(cc2)O)[C@@H]([C@H]([C@@H]1O)O)O[C@@H]1O[C@@H](C)[C@@H]([C@H]([C@H]1O)O)O
 Nefazodone CCc1nn(c(=O)n1CCOc1cccc1)CCCN1CCN(CC1)c1cccc(c1)Cl
 Nelfinavir O[C@@H]([C@@H](NC(=O)c1cccc(c1)O)CSc1cccc1)CN1C[C@H]2CCCC[C@H]2[C@H]1C(=O)NC(C)C)C
 Nicardipine COC(=O)C1=C(C)NC(=C([C@H]1c1cccc(c1)[N+](=O)[O-])C(=O)OCCN(Cc1cccc1)C)C
 Nicotine CN1CCC[C@H]1c1ccncc1
 Nifedipine COC(=O)C1=C(C)NC(=C([C@@H]1c1cccc1[N+](=O)[O-])C(=O)OC)C

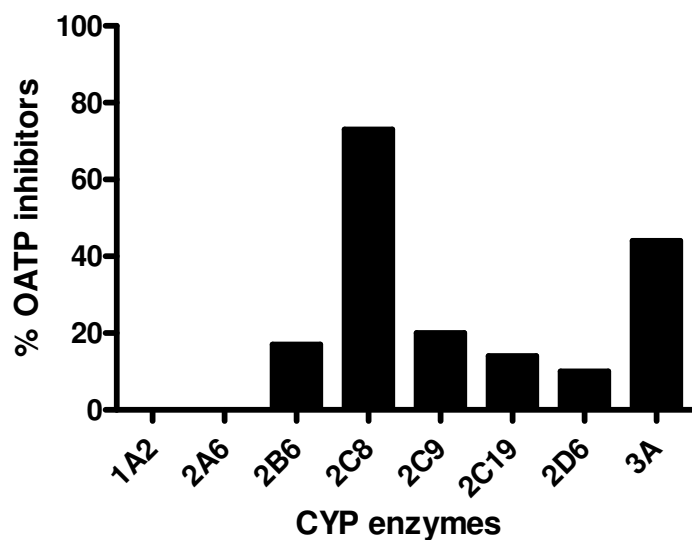
Nitrofurantoin	<chem>O=C1NC(=O)N(C1)/N=C\c1ccc(o1)[N+](=O)[O-]</chem>
N-methylnicotinamide	<chem>CNC(=O)c1cccnc1</chem>
N-methylpyridinium, ASP+	<chem>C[n+]1cccc1</chem>
N-methyl-quinidine	<chem>C=C[C@H]1C[N@+]2(C)CC[C@H]1C[C@@H]2[C@H](c1ccnc2c1cc(OC)cc2)O</chem>
Nootkatone	<chem>O=C1C[C@@H](C)[C@]2(C=C1)CC[C@H](C2)C(=C)C</chem>
Novobiocin	<chem>CO[C@@H]1[C@@H](OC(=O)N)[C@@H](O)[C@@H](OC1(C)C)Oc1ccc2c(c1C)oc(=O)c(2O)NC(=O)c1ccc(c(c1)CC=C(C)C)O</chem>
Nystatin	<chem>O[C@@H]1CC[C@H](O)[C@H](O)CC(=O)C[C@H](O)[C@@H](C(=O)O)[C@H](O)C[C@@H](/C=C/C=C/C=C/C=CC/C=C/C=C/[C@@H]([C@@H]([C@@H]([C@@H](OC(=O)C[C@@H](C[C@@H](C1)O)O)C)O)C)O[C@@H]1O[C@H](C)[C@H]([C@@H]([C@@H]1)O)N)O</chem>
Ofloxacin	<chem>CN1CCN(CC1)c1c(F)cc2c3c1OC[C@@H](n3cc(c2=O)C(=O)O)C</chem>
Olmesartan	<chem>CCCc1nc(c(n1Cc1ccc(cc1)c1ccccc1c1n[nH]nn1)C(=O)OCc1oc(=O)oc1C)C(O)(C)C</chem>
Omeprazole	<chem>COc1ccc2c(c1)[nH]c(n2)[S@](=O)Cc1ncc(c(c1C)OC)C</chem>
Ondansetron	<chem>O=C1[C@H](CCc2c1c1cccc1n2C)Cn1ccnc1C</chem>
Ouabain	<chem>OC[C@@]12[C@H](O)C[C@@H](C[C@@]2(O)CC[C@@H]2[C@@H]1[C@H](O)C[C@]1([C@]2(O)CC[C@@H]1C1=CC(=O)OC1)C)O[C@@H]1O[C@@H](C)[C@@H]([C@H]([C@H]1O)O)O</chem>
Oxaliplatin	<chem>O=C1O[Pt]2(OC1=O)N[C@H]1[C@H](N2)CCCC1</chem>
Paclitaxel	<chem>CC(=O)O[C@H]1C(=O)[C@]2(C)[C@@H](O)C[C@@H]3[C@]([C@H]2[C@@H]([C@]2(C)C1=C(C)[C@@H](OC(=O)[C@@H]([C@H](c1ccccc1)NC(=O)c1ccccc1)O)C2)(C)C)OC(=O)c1ccccc1)(CO3)OC(=O)C</chem>
P-aminohippuric acid	<chem>O=C(c1ccc(cc1)N)NCC(=O)O</chem>
Pantoprazole	<chem>COc1c(OC)ccnc1C[S@](=O)c1nc2c([nH]1)cc(cc2)OC(F)F</chem>
Paroxetine	<chem>Fc1ccc(cc1)[C@@H]1CCNC[C@H]1COc1ccc2c(c1)OCO2</chem>
Penicillin G	<chem>O=C(Cc1ccccc1)N[C@@H]1C(=O)N2[C@@H]1SC([C@@H]2C(=O)O)(C)C</chem>
Phalloidin	<chem>OC[C@](C)[C@@H]1NC(=O)[C@H]2NC(=O)[C@H](C)NC(=O)[C@@H]3C[C@H](CN3C(=O)[C@H](CSc3c(C2)c2ccccc2[nH]3)NC(=O)[C@@H](NC(=O)[C@@H](NC1=O)C)[C@H](O)C)O)O)C</chem>
Phenacetin	<chem>CCOc1ccc(cc1)NC(=O)C</chem>
Phenformin	<chem>N=C(NC(=N)N)NCCc1ccccc1</chem>
Phenobarbital	<chem>CCC1(C(=O)NC(=O)NC1=O)c1ccccc1</chem>
Phenylbutazone	<chem>CCCC[C@@H]1C(=O)N(N(C1=O)c1ccccc1)c1ccccc1</chem>
Phenylethyl isothiocyanate	<chem>S=C=NCCc1ccccc1</chem>
Phenytoin	<chem>O=C1NC(=O)N[C@@]1(c1ccccc1)c1ccccc1</chem>
Pilsicainide	<chem>O=C(C[C@]12CCCN2CCC1)Nc1c(C)cccc1C</chem>
Pindolol	<chem>O[C@@H](COc1ccc2c1cc[nH]2)CNC(C)C</chem>
Pioglitazone	<chem>CCc1ccc(nc1)CCOc1ccc(cc1)C[C@H]1SC(=O)NC1=O</chem>
Piroxicam	<chem>O/C(=C/1\C(=O)c2ccccc2S(=O)(=O)N1C)/Nc1cccn1</chem>
Pitavastatin	<chem>O[C@H](C[C@@H](/C=C/c1c(nc2c(c1c1ccc(cc1)F)cccc2)C1CC1)O)CC(=O)O</chem>
Pravastatin	<chem>CC[C@@H](C(=O)O)[C@H]1C[C@H](O)C=C2[C@H]1[C@@H](CC[C@H](C[C@H](CC(=O)O)O)O)[C@H](C=C2)C)C</chem>
Prazosin	<chem>COc1cc2nc(nc2cc1OC)N)N1CCN(CC1)C(=O)c1ccco1</chem>
Prednisolone	<chem>OCC(=O)[C@@]1(O)CC[C@@H]2[C@]1(C)C[C@H](O)[C@H]1[C@H]2CCC2=CC(=O)C=C[C@]12C</chem>
Probenecid	<chem>CCCN(S(=O)(=O)c1ccc(cc1)C(=O)O)CCC</chem>

Procainamide	<chem>CCN(CCNC(=O)c1ccc(cc1)N)CC</chem>
Progesterone	<chem>O=C1CC[C@]2(C(=C1)CC[C@@H]1[C@@H]2CC[C@]2([C@H]1CC[C@@H]2C(=O)C)C)C</chem>
Propranolol	<chem>O[C@@H](COc1cccc2c1cccc2)CNC(C)C</chem>
PSC833	<chem>C/C=C/C[C@H](C(=O)[C@H]1C(=O)N[C@@H](C(C)C)C(=O)N(C)CC(=O)N(C)[C@@H](CC(C)C)C(=O)N[C@@H](C(C)C)C(=O)N(C)[C@@H](CC(C)C)C(=O)N[C@@H](C(=O)N([C@H](C(=O)N([C@H](C(=O)N([C@H](C(=O)N1C)C(C)C)CC(C)C)CC(C)C)C)C)C)C</chem>
Quercetin	<chem>Oc1cc(O)c2c(c1)oc(c(c2=O)O)c1ccc(c(c1)O)O</chem>
Quinidine	<chem>C=C[C@H]1CN2CC[C@H]1C[C@@H]2[C@H](c1ccnc2c1cc(OC)cc2)O</chem>
Quinine	<chem>C=C[C@H]1CN2CC[C@H]1C[C@@H]2[C@H](c1ccnc2c1cc(OC)cc2)O</chem>
Ranolazine	<chem>COc1cccc1OC[C@H](CN1CCN(CC1)CC(=O)Nc1c(C)cccc1C)O</chem>
Repaglinide	<chem>CCOc1cc(ccc1C(=O)O)CC(=O)N[C@H](c1cccc1N1CCCC1)CC(C)C</chem>
Reserpine	<chem>COc1ccc2c(c1)[nH]c1c2CCN2[C@@H]1C[C@H]1[C@@H](C2)C[C@H]([C@@H]([C@H]1C(=O)OC)OC)OC(=O)c1cc(OC)c(c1)OC)OC</chem>
Rifampin	<chem>CO[C@H]1/C=C/O[C@@]2(C)Oc3c(C2=O)c2c(=O)/C(=C/NN4CCN(CC4)C)/C(=C(c2c(c3C)O)O)NC(=O)/C(=C\C=C\C[C@@H]([C@@H]([C@H]([C@H]([C@H]([C@@H]1C)OC(=O)C)O)C)O)C)/C</chem>
Rifamycin SV	<chem>CO[C@H]1/C=C/O[C@@]2(C)Oc3c(C2=O)c2c(O)cc(c(c2c(c3C)O)O)NC(=O)/C(=C/C=C/[C@@H]([C@@H]([C@H]([C@H]([C@H]([C@H]1C)OC(=O)C)O)C)O)C)/C</chem>
Ritonavir	<chem>O=C(N[C@H]([C@H](C[C@H](Cc1cccc1)NC(=O)[C@H](C(C)C)NC(=O)N(Cc1csc(n1)C(C)C)O)Cc1cccc1)OCc1cnsc1</chem>
Rosiglitazone	<chem>O=C1NC(=O)[C@H](S1)Cc1ccc(cc1)OCCN(c1ccccn1)C</chem>
Rosuvastatin	<chem>O[C@H](C[C@H](CC(=O)O)O)/C=C/c1c(nc(nc1c1ccc(cc1)F)N(S(=O)(=O)C)C)C(C)C</chem>
Sanguinarine	<chem>C[n+]1cc2c3OCOC3ccc2c2c1c1cc3OCOC3cc1cc2</chem>
Saquinavir	<chem>NC(=O)C[C@@H](C(=O)N[C@H]([C@@H](CN1C[C@@H]2CCCC[C@H]2C[C@H]1C(=O)NC(C)C)O)Cc1cccc1)NC(=O)c1ccc2c(n1)cccc2</chem>
Sildenafil	<chem>CCCc1nn(c2c1[nH]c(nc2=O)c1cc(ccc1OCC)S(=O)(=O)N1CCN(CC1)C)C</chem>
Silymarin	<chem>OC[C@H]1Oc2ccc(cc2O[C@@H]1c1ccc(c(c1)OC)O)[C@H]1Oc2cc(O)cc(c2C(=O)[C@@H]1)O</chem>
Simvastatin	<chem>CCC(C(=O)O[C@H]1C[C@@H](C)C=C2[C@H]1[C@@H](CC[C@H]1C[C@@H](O)CC(=O)O1)[C@H](C=C2)C)C(C)C</chem>
Sotalol	<chem>CC(NC[C@H](c1ccc(cc1)NS(=O)(=O)C)O)C</chem>
Spirolactone	<chem>CC(=O)S[C@@H]1CC2=CC(=O)CC[C@@]2([C@@H]2[C@@H]1[C@@H]1CC[C@]3([C@]1(CC2)C)CCC(=O)O3)C</chem>
Sulfaphenazole	<chem>Nc1ccc(cc1)S(=O)(=O)Nc1ccnn1c1cccc1</chem>
Sulfasalazine	<chem>OC(=O)c1cc(/N=N/c2ccc(cc2)S(=O)(=O)Nc2cccn2)ccc1O</chem>
Tamoxifen	<chem>CC/C(=C(\c1cccc1)/c1ccc(cc1)OCCN(C)C)/c1cccc1</chem>
Taurochenodeoxycholate	<chem>O[C@@H]1CC[C@]2([C@@H](C1)C[C@H]([C@@H]1[C@@H]2CC[C@]2([C@H]1CC[C@@H]2[C@@H](CCC(=O)NCCS(=O)(=O)[O-])C)O)C</chem>
Taurocholate	<chem>O[C@@H]1CC[C@]2([C@@H](C1)C[C@H]([C@@H]1[C@@H]2C[C@H](O)[C@]2([C@H]1CC[C@@H]2[C@@H](CCC(=O)NCCS(=O)(=O)O)C)O)C</chem>
Taurodeoxycholate	<chem>O[C@@H]1CC[C@]2([C@@H](C1)CC[C@@H]1[C@@H]2C[C@H](O)[C@]2([C@H]1CC[C@@H]2[C@@H](CCC(=O)NCCS(=O)(=O)O)C)C</chem>
Taurolithocholate	<chem>O[C@@H]1CC[C@]2([C@@H](C1)CC[C@@H]1[C@@H]2CC[C@]2([C@H]1CC[C@@H]2[C@@H](CCC(=O)NCCS(=O)(=O)[O-])C)C</chem>
Telmisartan	<chem>CCCc1nc2c(n1Cc1ccc(cc1)c1cccc1C(=O)O)cc(cc2C)c1nc2c(n1C)cccc2</chem>
Tenofovir	<chem>C[C@H](Cn1cnc2c1ncnc2N)OCP(=O)(O)O</chem>
Terfenadine	<chem>O[C@H](c1ccc(cc1)C(C)C)CCCN1CC[C@H](CC1)[C@@](c1cccc1)(c1cccc1)O</chem>

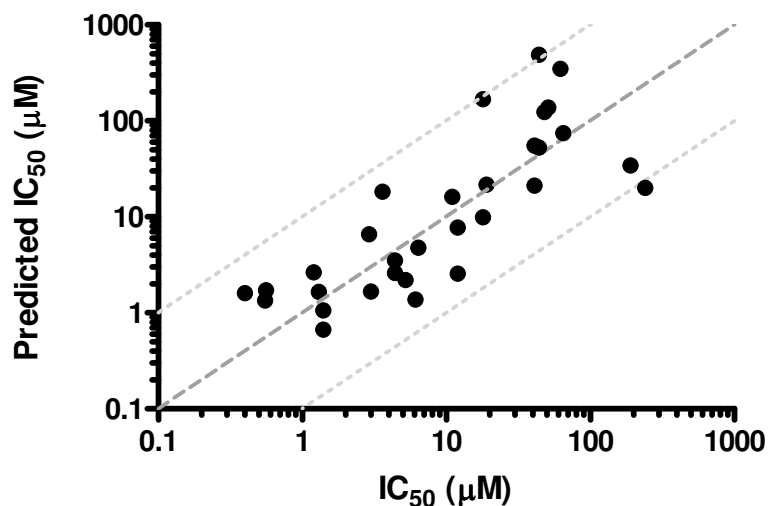
Testosterone	<chem>O=C1CC[C@]2(C=C1)CC[C@@H]1[C@@H]2CC[C@]2([C@H]1CC[C@@H]2O)C</chem>
Tetracycline	<chem>CN([C@@H]1C(=C(C(=O)N)C(=O)[C@@]2([C@H]1C[C@H]1C(=C2O)C(=O)c2c([C@@]1(C)O)cccc2O)O)C</chem>
Tetraethylammonium	<chem>CC[N+](CC)(CC)CC</chem>
Theophylline	<chem>Cn1c(=O)n(C)c2c(c1=O)[nH]cn2</chem>
Thioridazine	<chem>CSc1ccc2c(c1)N(CC[C@H]1CCCCN1C)c1c(S2)cccc1</chem>
Thiotepa	<chem>S=P(N1CC1)(N1CC1)N1CC1</chem>
Ticlopidine	<chem>Clc1cccc1CN1CCc2c(C1)ccs2</chem>
Tipranavir	<chem>CCC[C@@]1(CCc2cccc2)CC(=O)C(=C(O1)O)[C@@H](c1cccc(c1)NS(=O)(=O)c1ccc(cn1)C(F)(F)F)CC</chem>
Tolbutamide	<chem>CCCCNC(=O)NS(=O)(=O)c1ccc(cc1)C</chem>
Topotecan	<chem>CC[C@@]1(O)C(=O)OCc2c1cc1c3nc4ccc(c(c4cc3Cn1c2=O)CN(C)C)O</chem>
Tranlycypromine	<chem>N[C@@H]1C[C@H]1c1cccc1</chem>
Triazolam	<chem>Clc1ccc2c(c1)C(=NCc1n2c(C)nn1)c1cccc1Cl</chem>
Trimethoprim	<chem>COc1cc(Cc2cnc(nc2N)N)cc(c1OC)OC</chem>
Valaciclovir	<chem>CC([C@@H](C(=O)OCCOCn1cnc2c1[nH]c(N)nc2=O)N)C</chem>
Valproic acid	<chem>CCCC(C(=O)O)CCC</chem>
Valsartan	<chem>CCCCC(=O)N([C@H](C(=O)O)C(C)C)Cc1ccc(cc1)c1cccc1c1n[nH]nn1</chem>
Varenicline	<chem>N1C[C@@H]2C[C@H](C1)c1c2cc2c(c1)nccn2</chem>
Warfarin	<chem>CC(=O)C[C@H](c1c(O)oc2c(c1=O)cccc2)c1cccc1</chem>
Verapamil	<chem>COc1ccc(cc1OC)CCN(CCC[C@](c1ccc(c(c1)OC)OC)(C(C)C)C#N)C</chem>
Vinblastine	<chem>COc1cc2N(C)[C@@H]3[C@@]4(c2cc1[C@]1(C[C@@H]2CN(CCc5c1[nH]c1c5cccc1)C[C@@](C2)(O)CC)C(=O)OC)CCN1[C@H]4[C@@]([C@H]([C@]3(O)C(=O)OC)OC(=O)C)(CC)C=CC1</chem>
Vincristine	<chem>O=CN1c2cc(OC)c(cc2[C@]23[C@@H]1[C@@](O)(C(=O)OC)[C@H](OC(=O)C)[C@]1([C@@H]3N(CC2)CC=C1)CC)[C@]1(C[C@@H]2CN(CCc3c1[nH]c1c3cccc1)C[C@@](C2)(O)CC)C(=O)OC</chem>
Zidovudine	<chem>OC[C@H]1O[C@H](C[C@@H]1N=[N+]=[N-])n1cc(C)c(=O)[nH]c1=O</chem>



Supplementary Figure 1. Michaelis-Menten kinetics of uptake in HEK293 cells stably expressing OATP1B3 (a) or OATP2B1 (b) transporter. For both cell lines cells grown in 24-well plates were incubated with 0.01-20 μM atorvastatin at 37°C. The intracellular accumulation of atorvastatin was measured using LC-MS/MS and the results are presented as the uptake in pmol per minute and per mg total protein. Each data point represents the mean uptake \pm standard deviation (n=2). A corresponding curve for OATP1B1 can be found elsewhere (OATP1B1: $K_m = 0.77 \mu\text{M}$, $V_{\max} = 6.61 \text{ pmol/min}/\mu\text{g protein}$ and $V_{\max}/K_m = 8.58$).¹



Supplementary Figure 2. Overlap between OATP inhibitors and compounds interacting with cytochrome P450 (CYP) enzymes. Out of a subset of 67 compounds, recommended as CYP substrates, inhibitors and/or inducers by the FDA and EMA,¹³ 21 compounds were identified as OATP inhibitors in our screens. The bars represent the frequency (in percent) of OATP inhibitors identified among the interacting drugs of each individual CYP enzyme.



Supplementary Figure 3. Predicted vs experimental IC_{50} values for the 13 selected compounds and for all three OATP transporters. Predicted IC_{50} values were calculated based on the obtained single point inhibition results using Equation 6 and compared to the experimentally determined IC_{50} values. The dashed dark grey line is the unity line whereas the dotted light grey lines indicate 10-fold differences. Compounds inhibiting the transport to >100 % or <0 % in the single point inhibition studies as well as compounds where no experimentally IC_{50} could be determined were excluded. In total, 31 data points were included in the correlation.

References

1. Karlgren, M.; Ahlin, G.; Bergstrom, C. A.; Svensson, R.; Palm, J.; Artursson, P., In Vitro and In Silico Strategies to Identify OATP1B1 Inhibitors and Predict Clinical Drug-Drug Interactions. *Pharm Res* **2011**.