

Supporting Information

Drug Metabolism and Disposition

Simultaneous Quantification of the Abundance of Several Cytochrome P450 and Uridine 5'-Diphospho-Glucuronosyltransferase Enzymes in Human Liver Microsomes Using Multiplexed Targeted Proteomics.

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Cytochrome P450 liver enzyme pie chart

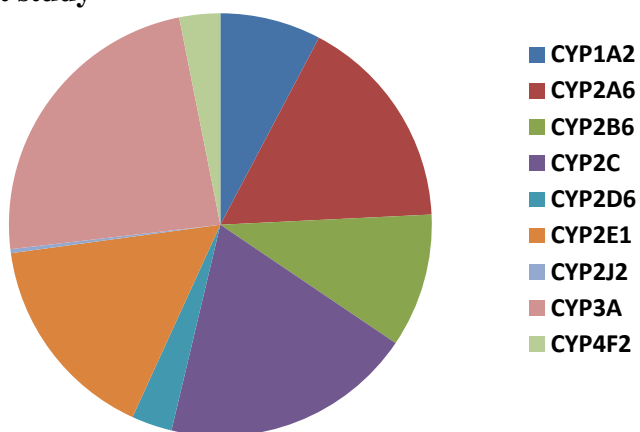
The P450 enzyme abundances obtained in this study were used to generate a pie chart of hepatic drug-metabolizing cytochrome P450 enzyme expression. In our study, two major enzymes (CYP2E1 and CYP2C9) were not quantified and the abundances of these enzymes were quoted from a meta-analysis carried out by Rowland-Yeo et al. (2004).

Pie charts of liver P450 enzyme abundances from this study, from Rowland-Yeo et al. (2004) and from Shimada et al. (1994) are shown in Supplementary Figure 1.

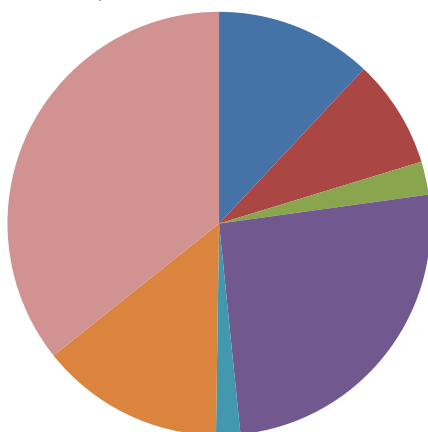
UGT liver enzyme pie chart

The UGT enzyme abundances obtained in this study were used to generate a pie chart of drug-metabolizing UGT enzyme expression in the liver. The pie chart for liver UGT enzyme abundances from this study is shown in Supplementary Figure 2.

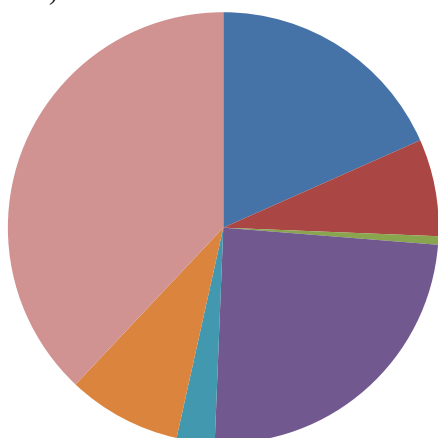
The present study



Rowland-Yeo et al., 2004

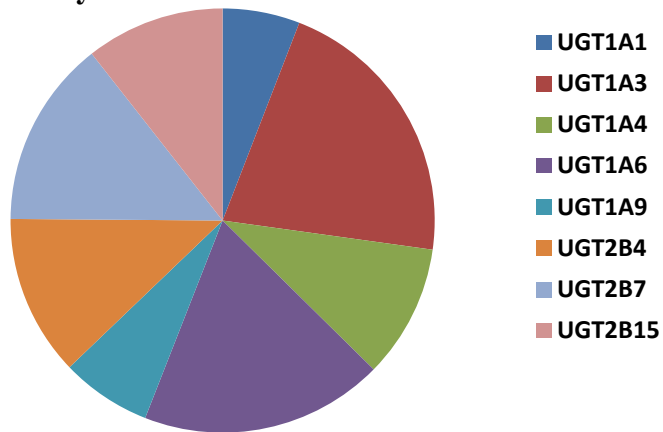


Shimada et al., 1994



Supplementary Figure 1. Pie charts of drug-metabolizing P450 enzyme abundances in the liver based on data from the present study and from two previous studies (Rowland-Yeo et al. and Shimada et al.). Higher relative abundance of CYP2B6 and lower relative abundance of CYP3A are observed in the present study. Two additional enzymes (CYP2J2 and CYP4F2) are added to the chart.

The present study



Supplementary Figure 2. Pie chart of drug-metabolizing UGT enzyme abundances in the liver using data from the present study.

Transitions for the quantification of the P450 and UGT surrogate peptides

Supplementary Table 1 shows details about the peptides used for the quantification of the 25 P450 and UGT enzymes, including sequences, transitions and collision energies (CE).

Supplementary Table 1. Sequences, transitions and collision energies of the P450 and UGT surrogate peptides.

Protein	Peptide sequence	Fragment ion	H or L	m/z (parent → fragment)		CE	
CYP1A2	YLPNPALQR	y7	L	536.300915	795.447162	19.1	
		y6	L	536.300915	698.394398	19.1	
		y5	L	536.300915	584.351471	19.1	
		y7	H	539.31098	801.467291	19.1	
		y6	H	539.31098	704.414527	19.1	
		y5	H	539.31098	590.3716	19.1	
	ASGNLIPQEK	y6	L	528.787838	727.434866	18.9	
		y5	L	528.787838	614.350802	18.9	
		y4	L	528.787838	501.266738	18.9	
		y6	H	531.797902	733.454995	18.9	
		y5	H	531.797902	620.370931	18.9	
		y4	H	531.797902	507.286867	18.9	
CYP2A6	GTGGANIDPTFFLSR	y9	L	776.891354	1095.583322	26.4	
		y8	L	776.891354	982.499258	26.4	
		y7	L	776.891354	867.472314	26.4	
		y9	H	779.901419	1101.603451	26.4	
		y8	H	779.901419	988.519387	26.4	
		y7	H	779.901419	873.492443	26.4	
	DPSFFSNPQDFNPQHFLNEK	y11	L	1204.550738	1388.65934	39.3	
		y10	L	1204.550738	1273.632397	39.3	
		y8	L	1204.550738	1012.521056	39.3	
		y11	H	1207.560803	1394.679469	39.3	
		y10	H	1207.560803	1279.652526	39.3	
		y8	H	1207.560803	1018.541185	39.3	
CYP2B6	GYGVIFANGNR	y7	L	584.298904	791.415862	20.6	
		y6	L	584.298904	678.331798	20.6	
		y7	H	587.308969	797.435991	20.6	
		y6	H	587.308969	684.351927	20.6	
	ETLDPSAPK	y7	L	479.248014	727.398481	17.4	
		y6	L	479.248014	614.314417	17.4	
		y5	L	479.248014	499.287474	17.4	
		y7	H	482.258079	733.41861	17.4	
		y6	H	482.258079	620.334546	17.4	
		y5	H	482.258079	505.307603	17.4	
	ETLDPSAPR	y7	L	493.251088	755.404629	17.8	
		y6	L	493.251088	642.320565	17.8	
		y5	L	493.251088	527.293622	17.8	
		y7	H	496.261153	761.424758	17.8	
		y6	H	496.261153	648.340694	17.8	
		y5	H	496.261153	533.313751	17.8	
	CYP2C8	SFTNFASK	y6	L	415.705785	743.372266	15.4
			y5	L	415.705785	596.303852	15.4
y4			L	415.705785	495.256174	15.4	
y6			H	418.71585	749.392395	15.4	
y5			H	418.71585	602.323981	15.4	
y4			H	418.71585	501.276303	15.4	
GNSPISQR		y6	L	429.725041	687.378414	15.9	
		y5	L	429.725041	600.346386	15.9	
		y4	L	429.725041	503.293622	15.9	
		y6	H	432.735105	693.398543	15.9	
		y5	H	432.735105	606.366515	15.9	
		y4	H	432.735105	509.313751	15.9	

Supplementary Table 1. Continued.

Protein	Peptide sequence	Fragment ion	H or L	m/z (parent → fragment)		CE
CYP2C9	LPPGPTPLPVIGNILQIGIK	y12	L	1019.127168	1264.798734	33.7
		y11	L	1019.127168	1167.74597	33.7
		y6	L	1019.127168	671.445037	33.7
		y12	H	1022.137232	1270.818863	33.7
		y11	H	1022.137232	1173.766099	33.7
		y6	H	1022.137232	677.465166	33.7
	GIFPLAER	y5	L	451.758352	585.335487	16.5
		y4	L	451.758352	488.282723	16.5
		y3	L	451.758352	375.198659	16.5
		y5	H	454.768417	591.355616	16.5
y4		H	454.768417	494.302852	16.5	
y3		H	454.768417	381.218788	16.5	
CYP2C18	SLTNFSK	y6	L	398.71361	709.387916	14.9
		y5	L	398.71361	596.303852	14.9
		y4	L	398.71361	495.256174	14.9
		y6	H	401.723675	715.408045	14.9
		y5	H	401.723675	602.323981	14.9
		y4	H	401.723675	501.276303	14.9
	GSFPVAEK	y6	L	417.721435	690.382102	15.5
		y5	L	417.721435	543.313689	15.5
		y4	L	417.721435	446.260925	15.5
		y6	H	420.7315	696.402231	15.5
y5		H	420.7315	549.333818	15.5	
y4		H	420.7315	452.281054	15.5	
CYP2C19	IYGPVFTLYFGLER	y11	L	837.948141	1341.720149	28.2
		y9	L	837.948141	1145.598972	28.2
		y8	L	837.948141	998.530558	28.2
		y7	L	837.948141	897.482879	28.2
		y11	H	840.958205	1347.740278	28.2
		y9	H	840.958205	1151.619101	28.2
		y8	H	840.958205	1004.550687	28.2
		y7	H	840.958205	903.503008	28.2
	GHFPLAER	y6	L	463.745776	732.403901	16.9
		y5	L	463.745776	585.335487	16.9
		y4	L	463.745776	488.282723	16.9
		y6	H	466.755841	738.42403	16.9
		y5	H	466.755841	591.355616	16.9
		y4	H	466.755841	494.302852	16.9
CYP2D6	DIEVQGFR	y6	L	482.248349	735.378414	17.5
		y4	L	482.248349	507.267407	17.5
		y3	L	482.248349	379.208829	17.5
		y6	H	485.258413	741.398543	17.5
		y4	H	485.258413	513.287536	17.5
		y3	H	485.258413	385.228958	17.5
	AFLTQLDELLTEHR	y5	L	562.633421	655.352199	20.4
		y4	L	562.633421	542.268135	20.4
		y2	L	562.633421	312.177864	20.4
		y5	H	564.640131	661.372328	20.4
		y4	H	564.640131	548.288264	20.4
		y2	H	564.640131	318.197993	20.4

Supplementary Table 1. Continued.

Protein	Peptide sequence	Fragment ion	H or L	m/z (parent → fragment)		CE
CYP2E1	GIIFNNGPTWK	y8	L	623.83258	963.468292	21.8
		y7	L	623.83258	816.399878	21.8
		y5	L	623.83258	588.314023	21.8
		y8	H	626.842644	969.488421	21.8
		y7	H	626.842644	822.420007	21.8
		y5	H	626.842644	594.334152	21.8
	FITLVPSNLPHEATR	y11	L	847.964854	1220.638211	28.5
		y10	L	847.964854	1121.569797	28.5
		y6	L	847.964854	710.358013	28.5
		y11	H	850.974918	1226.65834	28.5
		y10	H	850.974918	1127.589926	28.5
		y6	H	850.974918	716.378142	28.5
CYP2J2	VIGQQQPSTAAR	y9	L	656.852032	915.464269	22.8
		y7	L	656.852032	730.384228	22.8
		y6	L	656.852032	602.32565	22.8
		y9	H	659.862097	921.484398	22.8
		y7	H	659.862097	736.404357	22.8
		y6	H	659.862097	608.345779	22.8
	FEYQDSWFQQLLK	y9	L	866.422487	1164.604785	29.1
		y8	L	866.422487	1049.577842	29.1
		y9	H	869.432552	1170.624914	29.1
		y8	H	869.432552	1055.597971	29.1
CYP3A4	EVTNFLR	y6	L	439.740159	749.43045	16.2
		y5	L	439.740159	650.362036	16.2
		y4	L	439.740159	549.314357	16.2
		y6	H	442.750224	755.450579	16.2
		y5	H	442.750224	656.382165	16.2
		y4	H	442.750224	555.334486	16.2
	LSLGLLQPEKPVVLK	y10	L	846.026923	1150.719421	28.5
		y8	L	846.026923	909.57678	28.5
		y5	L	846.026923	555.38646	28.5
		y10	H	849.036987	1156.73955	28.5
		y8	H	849.036987	915.596909	28.5
		y5	H	849.036987	561.406589	28.5
CYP3A5	DTINFLSK	y6	L	469.2531	721.424302	17.1
		y5	L	469.2531	608.340238	17.1
		y2	L	469.2531	234.144832	17.1
		y6	H	472.263164	727.444431	17.1
		y5	H	472.263164	614.360367	17.1
		y2	H	472.263164	240.164961	17.1
		YWTEPEEFRPER	y8	L	819.880987	1059.521784
	y7		L	819.880987	962.46902	27.7
	y6		L	819.880987	833.426427	27.7
	y3		L	819.880987	401.214309	27.7
	y8		H	822.891051	1065.541913	27.7
	y7		H	822.891051	968.489149	27.7
	y6		H	822.891051	839.446556	27.7
	y3	H	822.891051	407.234438	27.7	

Supplementary Table 1. Continued.

Protein	Peptide sequence	Fragment ion	H or L	m/z (parent → fragment)		CE
CYP3A7	FGLLLLTEKPIVLK	y9	L	764.479077	1040.671408	26
		y8	L	764.479077	927.587344	26
		y9	H	767.489141	1046.691537	26
		y8	H	767.489141	933.607473	26
	FNPLDPFVLSIK	y10	L	695.39247	1128.666323	23.9
		y8	L	695.39247	918.529495	23.9
		y7	L	695.39247	803.502552	23.9
		y10	H	698.402535	1134.686452	23.9
		y8	H	698.402535	924.549624	23.9
		y7	H	698.402535	809.522681	23.9
CYP3A43	DVTHFLK	y5	L	430.237253	645.371872	15.9
		y4	L	430.237253	544.324194	15.9
		y5	H	433.247317	651.392001	15.9
		y4	H	433.247317	550.344323	15.9
	YIPFGAGPR	y7	L	489.263802	701.372935	17.7
		y6	L	489.263802	604.320171	17.7
		y7	H	492.273866	707.393064	17.7
		y6	H	492.273866	610.3403	17.7
CYP4F2	HVTQDIVLPDGR	y10	L	675.362233	1113.589864	23.3
		y6	L	675.362233	656.3726	23.3
		y4	L	675.362233	444.220122	23.3
		y10	H	678.372297	1119.609993	23.3
		y6	H	678.372297	662.392729	23.3
		y4	H	678.372297	450.240251	23.3
	FDPENIK	y6	L	431.718893	715.362095	15.9
		y5	L	431.718893	600.335152	15.9
		y4	L	431.718893	503.282388	15.9
		y6	H	434.728957	721.382224	15.9
		y5	H	434.728957	606.355281	15.9
		y4	H	434.728957	509.302517	15.9
UGT1A1	TYPVPFQR	y6	L	504.269084	743.419885	18.1
		y5	L	504.269084	646.367121	18.1
		y4	L	504.269084	547.298707	18.1
		y6	H	507.279149	749.440014	18.1
		y5	H	507.279149	652.38725	18.1
		y4	H	507.279149	553.318836	18.1
	DGAFYTLK	y6	L	457.734543	742.413403	16.7
		y5	L	457.734543	671.376289	16.7
		y4	L	457.734543	524.307875	16.7
		y6	H	460.744607	748.433532	16.7
		y5	H	460.744607	677.396418	16.7
		y4	H	460.744607	530.328004	16.7

Supplementary Table 1. Continued.

Protein	Peptide sequence	Fragment ion	H or L	m/z (parent → fragment)		CE
UGT1A3	HVLGHTQLYFETEHFLK	y10	L	1050.038935	1326.672865	34.7
		y9	L	1050.038935	1213.588801	34.7
		y8	L	1050.038935	1050.525472	34.7
		y10	H	1053.049146	1332.692994	34.7
		y9	H	1053.049146	1219.60893	34.7
		y8	H	1053.049146	1056.545601	34.7
	YLSIPTVFFLR	y7	L	678.389731	879.5087	23.4
		y6	L	678.389731	782.455936	23.4
		y5	L	678.389731	681.408258	23.4
		y7	H	681.399795	885.528829	23.4
		y6	H	681.399795	788.476065	23.4
		y5	H	681.399795	687.428387	23.4
UGT1A4	YIPCDDLFK	y7	L	585.778624	894.40258	20.6
		y6	L	585.778624	797.349816	20.6
		y5	L	585.778624	637.319168	20.6
		y7	H	588.788689	900.422709	20.6
		y6	H	588.788689	803.369945	20.6
		y5	H	588.788689	643.339297	20.6
	GTQCPNPSSYIPK	y9	L	724.845558	1002.525472	24.8
		y8	L	724.845558	905.472708	24.8
		y7	L	724.845558	791.429781	24.8
		y9	H	727.855623	1008.545601	24.8
		y8	H	727.855623	911.492837	24.8
		y7	H	727.855623	797.44991	24.8
UDP1A6	VSVWLLR	y6	L	436.771263	773.466835	16.1
		y5	L	436.771263	686.434807	16.1
		y4	L	436.771263	587.366393	16.1
		y6	H	439.781327	779.486964	16.1
		y4	H	439.781327	593.386522	16.1
		y3	H	439.781327	407.307209	16.1
	SFLTAPQTEYR	y8	L	656.830234	965.468686	22.8
		y7	L	656.830234	864.421007	22.8
		y6	L	656.830234	793.383893	22.8
		y8	H	659.840299	971.488815	22.8
		y7	H	659.840299	870.441136	22.8
		y6	H	659.840299	799.404022	22.8
UDP1A9	AFAHAQWK	y6	L	479.748319	740.383834	17.4
		y5	L	479.748319	669.34672	17.4
		y4	L	479.748319	532.287808	17.4
		y6	H	482.758383	746.403963	17.4
		y5	H	482.758383	675.366849	17.4
		y4	H	482.758383	538.307937	17.4
	ESSFDAVFLDPFDNCGLIVAK	y13	L	1172.561926	1461.740627	38.4
		y12	L	1172.561926	1348.656563	38.4
		y11	L	1172.561926	1233.62962	38.4
		y13	H	1175.57199	1467.760756	38.4
		y12	H	1175.57199	1354.676692	38.4
		y11	H	1175.57199	1239.649749	38.4

Supplementary Table 1. Continued.

Protein	Peptide sequence	Fragment ion	H or L	m/z (parent → fragment)		CE
UDP2B4	ANVIASALAK	y8	L	479.290016	772.492716	17.4
		y7	L	479.290016	673.424302	17.4
		y6	L	479.290016	560.340238	17.4
		y8	H	482.300081	778.512845	17.4
		y7	H	482.300081	679.444431	17.4
		y6	H	482.300081	566.360367	17.4
	FSPGYAIEK	y7	L	506.260925	777.414131	18.2
		y6	L	506.260925	680.361367	18.2
		y5	L	506.260925	623.339903	18.2
		y7	H	509.270989	783.43426	18.2
		y6	H	509.270989	686.381496	18.2
		y5	H	509.270989	629.360032	18.2
UDP2B7	TILDELIQR	y7	L	550.819138	886.499258	19.5
		y6	L	550.819138	773.415194	19.5
		y5	L	550.819138	658.38825	19.5
		y7	H	553.829203	892.519387	19.5
		y6	H	553.829203	779.435323	19.5
		y5	H	553.829203	664.408379	19.5
	ADVWLIR	y6	L	436.75307	801.46175	16.1
		y5	L	436.75307	686.434807	16.1
		y4	L	436.75307	587.366393	16.1
		y5	H	439.763134	692.454936	16.1
		y4	H	439.763134	593.386522	16.1
		y3	H	439.763134	407.307209	16.1
UDP2B10	DTFWLPFSQEILWAINDIIR	y10	L	912.134027	1226.725569	29
		y9	L	912.134027	1113.641505	29
		y8	L	912.134027	1000.557441	29
		y8	H	914.140737	1006.57757	29
		y7	H	914.140737	820.498257	29
		y6	H	914.140737	749.461143	29
	GHEVTVLASSASILFDPNDSSTLK	y10	L	830.090376	1123.526595	26.9
		y9	L	830.090376	976.458181	26.9
		y8	L	830.090376	861.431238	26.9
		y10	H	832.097085	1129.546724	26.9
		y9	H	832.097085	982.47831	26.9
		y8	H	832.097085	867.451367	26.9

Supplementary Table 1. Continued.

Protein	Peptide sequence	Fragment ion	H or L	m/z (parent → fragment)		CE
UDP2B11	DSFWLYFSQEILWELYDIFR	y10	L	976.469075	1367.7358	30.5
		y9	L	976.469075	1254.651735	30.5
		y8	L	976.469075	1141.567671	30.5
		y10	H	978.475785	1373.755929	30.5
		y9	H	978.475785	1260.671864	30.5
		y8	H	978.475785	1147.5878	30.5
	GHEVTVLASSASILFDPNDASTLK	y10	L	824.758737	1107.53168	26.8
		y9	L	824.758737	960.463266	26.8
		y8	L	824.758737	845.436323	26.8
		y10	H	826.765447	1113.551809	26.8
		y9	H	826.765447	966.483395	26.8
		y8	H	826.765447	851.456452	26.8
UDP2B15	SVINDPVYK	y7	L	517.779482	848.451245	18.5
		y6	L	517.779482	735.367181	18.5
		y4	L	517.779482	506.29731	18.5
		y7	H	520.789546	854.471374	18.5
		y6	H	520.789546	741.38731	18.5
		y4	H	520.789546	512.317439	18.5
	WIYGVSK	y6	L	426.734346	666.382102	15.8
		y5	L	426.734346	553.298038	15.8
		y6	H	429.74441	672.402231	15.8
		y5	H	429.74441	559.318167	15.8

References

Rowland-Yeo K, Rostami-Hodjegan A, and Tucker GT (2004) Abundance of cytochrome P450 in human liver: a meta-analysis. *Br J Clin Pharmacol* **57**:687–688.

Shimada T, Yamazaki H, Mimura M, Inui Y, and Guengerich FP (1994) Interindividual variations in human liver cytochrome P-450 enzymes involved in the oxidation of drugs, carcinogens and toxic chemicals: studies with liver microsomes of 30 Japanese and 30 Caucasians. *J Pharmacol Exp Ther* **270**:414–423.