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Drug Metab Dispos

Characterization of Enzymes Involved in Nintedanib Metabolism in Humans

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Supplemental Table 1. Characteristics of 30 donors of liver used in the present study.

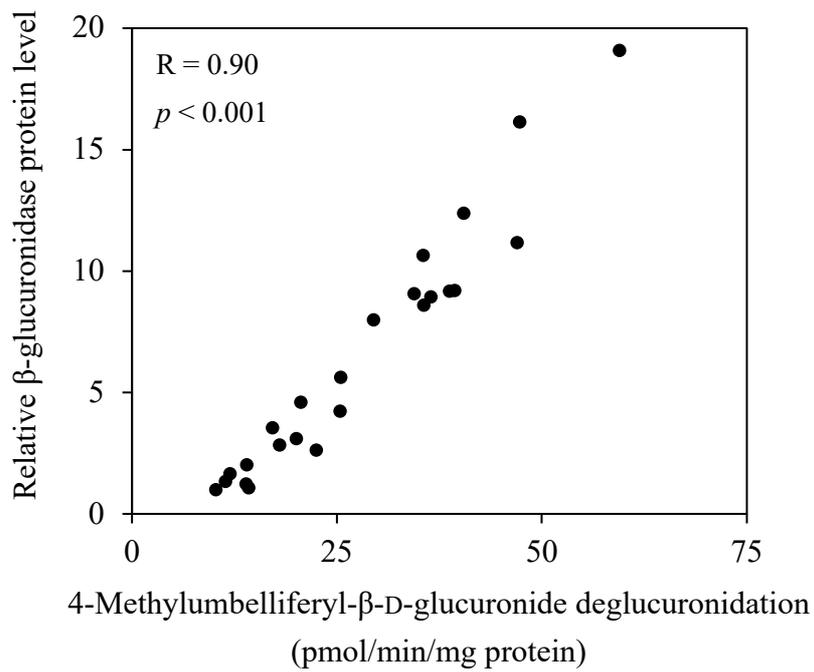
No.	Sex	Age (yr)	Ethnicity	Cause of death	Western blotting or Genotyping	Untargeted proteomics
1	M	33	C	Head trauma	✓	✓
2	F	47	C	Cerebrovascular accident	✓	✓
3	F	32	H	Subarachnoid hemorrhage	✓	✓
4	F	33	H	Intracerebral hematoma	✓	✓
5	F	41	C	Intracerebral hematoma	✓	✓
6	M	38	C	Head trauma	✓	✓
7	F	34	B	Cerebrovascular accident	✓	✓
8	F	35	H	Cerebral hemorrhage	✓	
9	M	36	C	Intracerebral hematoma	✓	
10	M	46	C	Oxygen deficiency	✓	✓
11	M	68	C	Cerebrovascular accident	✓	✓
12	F	59	C	Traffic accident	✓	✓
13	F	52	A	Cerebrovascular accident	✓	✓
14	F	35	H	Intracerebral hematoma	✓	
15	M	51	C	Cerebrovascular accident	✓	✓
16	M	36	C	Suicide	✓	✓
17	M	53	C	Rupture of aneurysm	✓	✓
18	M	54	C	Cerebrovascular accident	✓	
19	M	16	C	Head trauma	✓	✓
20	M	62	A	Rupture of aneurysm	✓	✓
21	F	33	C	Primary brain tumor	✓	
22	M	52	C	Cerebrovascular accident	✓	✓
23	F	47	C	Cerebrovascular accident	✓	✓
24	M	60	H	Cerebrovascular accident	✓	✓
25	M	46	C	Oxygen deficiency		✓
26	M	53	C	Rupture of aneurysm		✓
27	M	57	A	Cerebrovascular accident		✓
28	F	47	C	S/P code		✓
29	F	51	A	Cerebrovascular accident		✓
30	M	43	C	Cerebrovascular accident		✓

M, Male; F, Female; A, Asian; B, Black; C, Caucasian; H, Hispanic

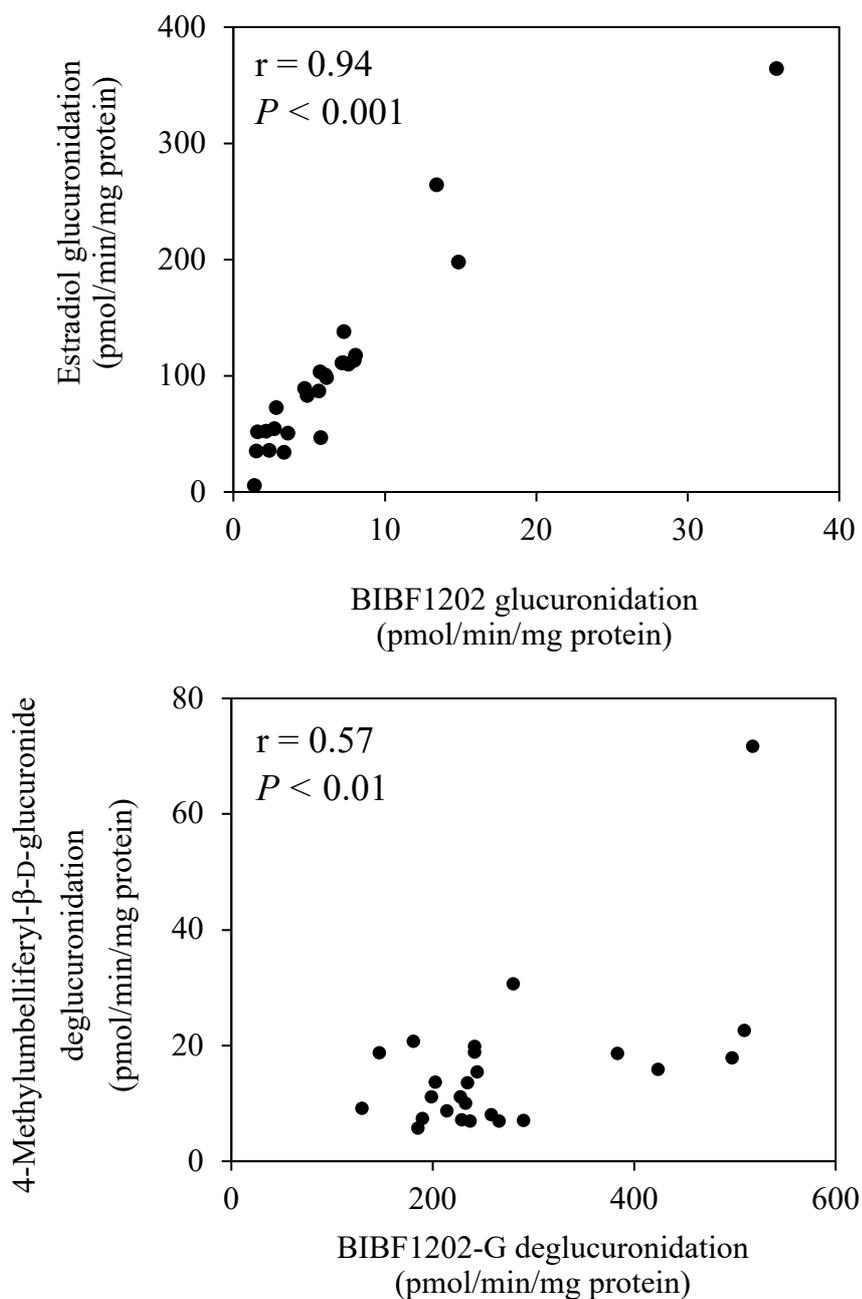
Supplemental Table 2. Peptide sequences used to quantify CES1, UGT1A1, and β -glucuronidase.

Peptide sequence	Position
CES1	
FTPPQPAEPWSFVK	65 - 78
AGQLISELFTNR	93 - 104
AGQLLSELFTRK	93 - 105
KENIPLK	105 - 111
LSEDCLYLNIYTPADLTK	112 - 129
LGIWGGFFSTGDEHSR	172 - 186
GNWGHLDQVAALR	187 - 199
WVQDNIAFSGGNPGSVTIFGESAGGESVSVLVLSPLAK	200 - 237
AISESGVALTSVLVK	243 - 257
KGDVKPLAEQIAITAGCK	258 - 275
GDVKPLAEQIAITAGCK	259 - 275
TTTSAVMVHCLR	276 - 287
QKTEEELLETTLK	288 - 300
TEEELLETTLK	290 - 300
FLSLDLQGDPR	303 - 313
ESQPLLGTVIDGMLLLK	314 - 330
TPEELQAER	331 - 339
TPEELQAERNFHTVPYMGINK	331 - 352
NFHTVPYMGINK	340 - 352
QFEGWLIPMQLMSYPLSEGQLDQK	353 - 376
TAMSLWK	377 - 384
SYPLVCIK	385 - 393
ELIPEATEK	394 - 402
YLGGTDDTVK	403 - 412
YLGGTDDTVKK	403 - 413
DAGAPTYMYEFQYRPSFSSDMKPK	439 - 462
TVIGDHGDELFSVFGAPFLK	463 - 482
EGASEEEIR	483 - 491
FWANFAR	499 - 505
NGNPNGEGLPHWPEYNQK	506 - 523
EGYLQIGANTQAAQK	524 - 538
LKDKEVAFWTNLFAK	539 - 553
DKEVAFWTNLFAK	541 - 553
EVAFWTNLFAK	543 - 550
KAVEKPPQTEHIEL	554 - 567

AVEKPPQTEHIEL	555 - 567
UGT1A1	
GHEIVVLAPDASLYIR	54 - 69
DGAFYTLK	70 - 77
TYPVVFQR	78 - 85
EDVKESFVSLGHNVFENDSFLQR	86 - 108
ESFVSLGHNVFENDSFLQR	90 - 108
KDSAMLLSGCSHLLHNK	118 - 134
DSAMLLSGCSHLLHNK	119 - 134
AMAIADALGK	319 - 328
WLPQNDLLGHPMTR	354 - 367
AFITHAGSHGVYESICNGVPMVMPLFGDQMDNAK	368 - 402
GAGVTLNVLEMTSEDLENALK	408 - 428
AVINDK	429 - 434
β-Glucuronidase	
GYFVQNTYFDFFFNYAGLQR	198 - 216
LLDAENK	262 - 268
SQFLINGKPFYFHGVNK	334 - 350
GFDWPLLVK	360 - 368
TSHYPYAEVVMQMCDR	383 - 398
NHPAVVMWSVANEPASHLESAGYYLK	439 - 464
MVIAHTK	465 - 471
SLDPSRPVTFVSNSNYAADK	472 - 491
YQKPIIQSEYGAETIAGFHQDPPLMFTEEYQK	532 - 563
SLLEQYHLGLDQK	564 - 576
SAAFLLR	617 - 623



Supplemental Figure 1. Correlation analysis between 4-methylumbelliferyl-β-D-glucuronide deglucuronidation and β-glucuronidase protein levels in a panel of 24 individual HLM samples. Each point represents the mean of duplicate determinations.



Supplemental Figure 2. Correlation analyses between BIBF1202 glucuronidation and estradiol glucuronidation (upper panel), and BIBF1202-G deglucuronidation and 4-methylumbelliferyl-β-D-glucuronide deglucuronidation (bottom panel) in a panel of 25 individual HLM samples. Each point represents the mean of duplicate determinations.