Untargeted metabolomic analysis combined with multivariate statistics reveal distinct metabolic changes in GPR40 agonists-treated animals related to bile acid metabolism

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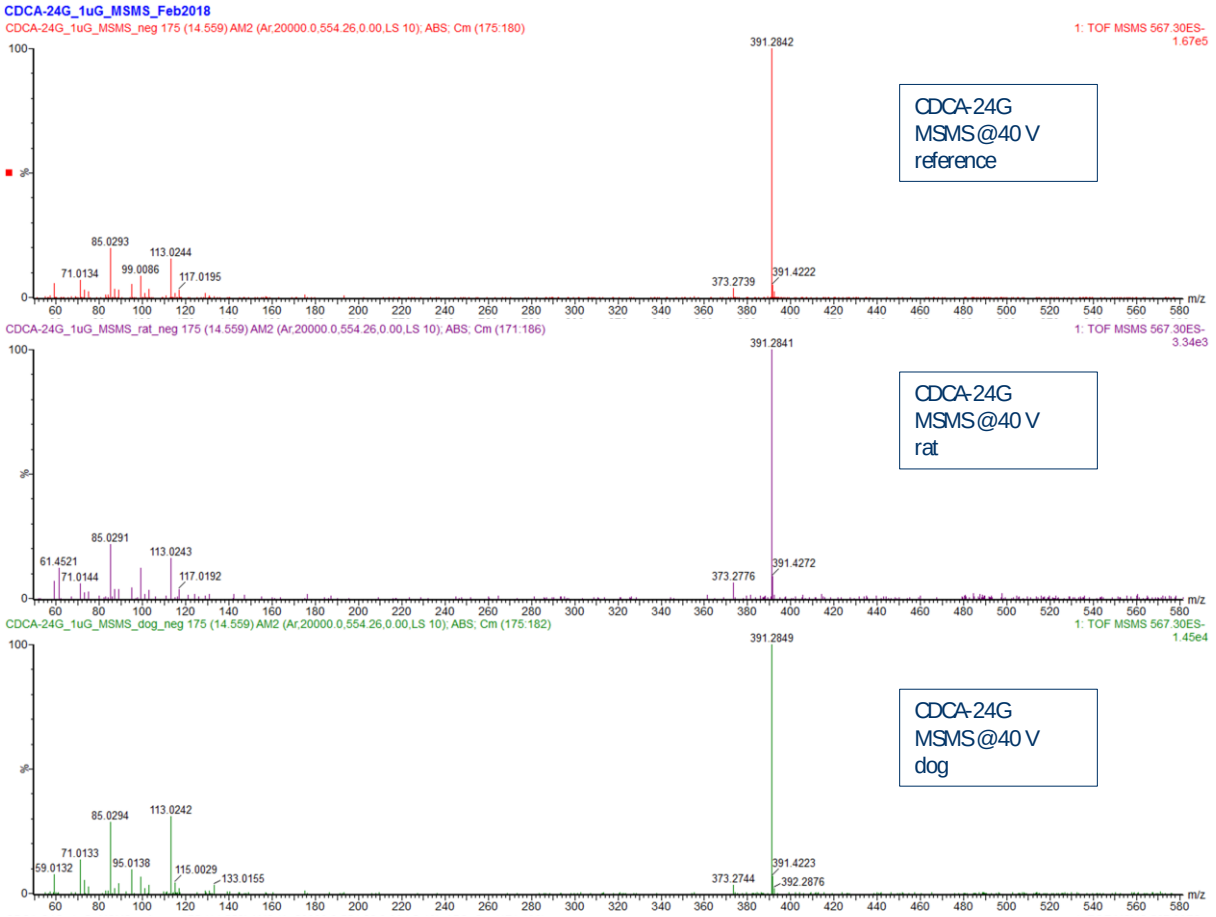
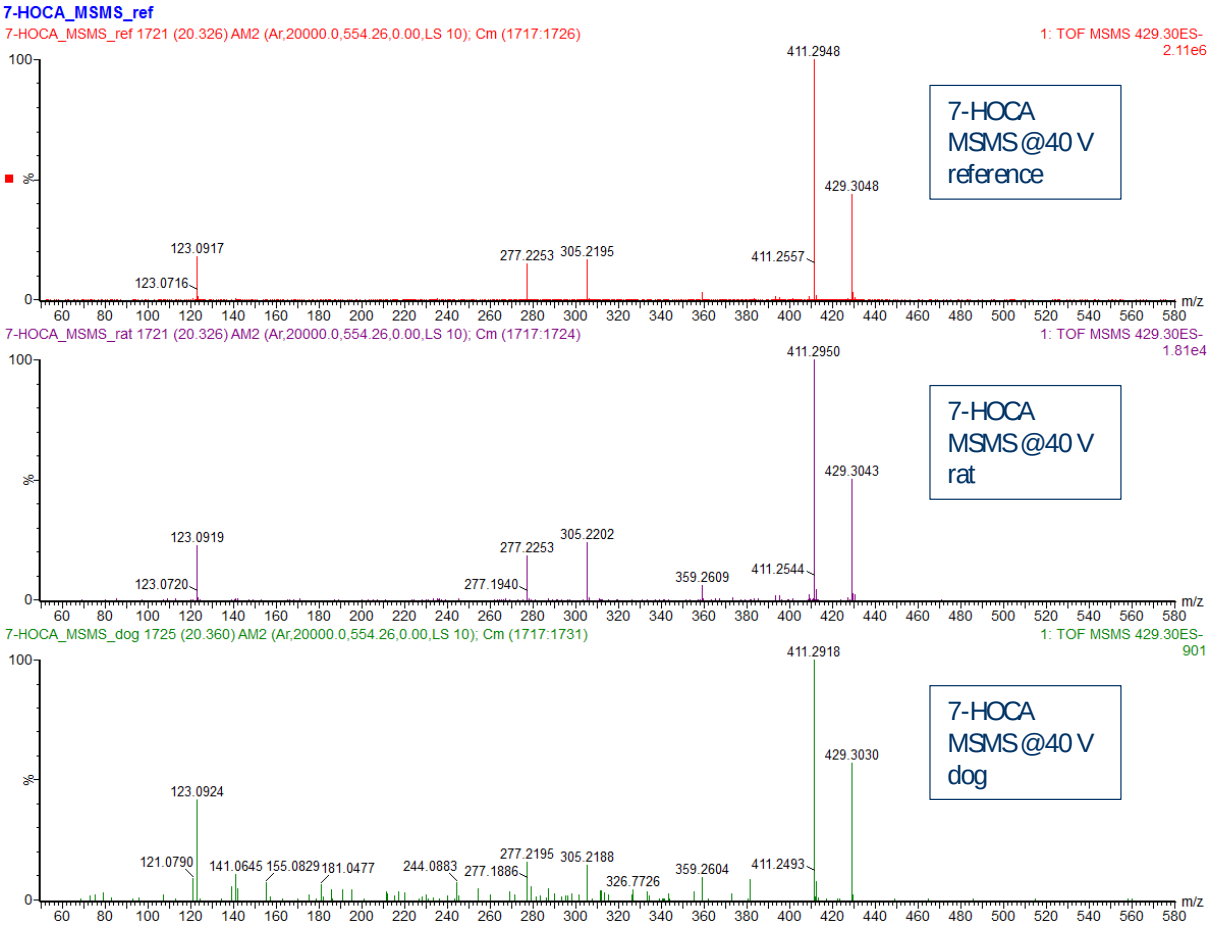
	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y	Z	AA
1	PrimaryId	Item descr	Gender	Group ID	Species	Dose	Study ID	Subject ID	Sample ty	346.0561	968.4745	968.1446	968.8124	783.3657	810.4007	832.3819	754.4349	427.1179	309.1079	274.0026	357.0822	411.1227	194.0455	411.0813	253.1189	430.1095	259.1293
2	m/z									346.0562	968.4746	968.1446	968.8124	783.3657	810.4007	832.3819	754.4349	427.118	309.108	274.0027	357.0822	411.1227	194.0456	411.0814	253.1189	430.1096	259.1293
3	RetentionTime									6.774	7.101	7.109	7.115	7.176	7.362	7.374	7.381	7.543	7.653	7.803	7.881	8.007	8.377	8.382	8.41	8.441	8.467
4	DriftTime									2.97	4.27	4.27	4.23	6.5	6.79	7.11	4.45	3.61	2.84	2.52	3.05	3.61	2.03	4.34	2.42	4.02	2.53
5	Comment																										
6	batch1	sample 102	1:1 A (50+50uL_ 35uL inj)		neg				Reference	0	0	0	0	0	0	0	0	0	0	0	236.33	720.72	0	0	0	0	0
7	batch1	sample 103	1:1 A (50+50uL_ 35uL inj)		neg				Reference	0	408.56	264.36	318.43	0	804.53	0	232.4	0	0	418.06	616.3	0	204.88	0	263.15	0	0
8	batch1	sample 104	1:1 A (50+50uL_ 35uL inj)		neg				Reference	0	0	0	0	0	0	0	0	0	0	0	276.22	0	0	0	0	0	0
9	batch1	sample 105	1:1 A (50+50uL_ 35uL inj)		neg				Reference	0	0	0	0	0	0	0	0	0	0	0	355.49	534.99	0	0	0	0	0
10	batch1	sample 106	1:1 A (50+50uL_ 35uL inj)		neg				Reference	0	0	0	0	0	0	0	0	0	0	0	397.94	0	0	0	0	0	0
11	batch1	sample 107	1:1 A (50+50uL_ 35uL inj)		neg				Reference	0	0	0	0	0	0	0	0	266.63	0	0	240.57	770.92	0	0	0	0	0
12	batch1	sample 108	1:1 A (50+50uL_ 35uL inj)		neg				Reference	0	0	0	0	0	0	0	0	279.68	0	0	277.45	952.53	0	0	0	0	0
13	batch1	sample 109	1:1 A (50+50uL_ 35uL inj)		neg				Reference	0	0	0	0	0	0	0	0	0	0	0	469.14	0	0	0	0	0	0
14	batch1	sample 110	1:1 A (50+50uL_ 35uL inj)		neg				Reference	212.74	0	0	0	0	0	0	0	0	0	0	455.29	898.43	0	0	0	456.24	0
15	batch2	sample 501	1:1 A (50+50uL_ 35uL inj)		neg				Unknown	0	0	0	0	0	0	0	0	0	0	0	294.89	0	0	0	282.23	283.4	221.88
16	batch2	sample 504	1:1 A (50+50uL_ 35uL inj)		neg				Unknown	0	0	0	0	0	238.31	0	0	0	0	0	501.53	465.04	0	0	412.36	0	0
17	batch2	sample 506	1:1 A (50+50uL_ 35uL inj)		neg				Unknown	0	0	0	0	0	0	0	0	0	234.43	0	734.64	660.24	0	0	511.27	0	342.32
18	batch2	sample 507	1:1 A (50+50uL_ 35uL inj)		neg				Unknown	0	0	0	0	0	335.79	0	0	0	0	0	209.75	474.96	0	0	319.55	280.19	0
19	batch2	sample 508	1:1 A (50+50uL_ 35uL inj)		neg				Unknown	0	0	0	0	0	0	0	0	0	0	0	210.4	0	0	0	314.43	241.75	267.72
20	batch2	sample 510	1:1 A (50+50uL_ 35uL inj)		neg				Unknown	0	0	0	0	323.58	2706.65	255.51	0	0	0	0	225.46	0	272.31	246.41	0	327.8	0
21																											

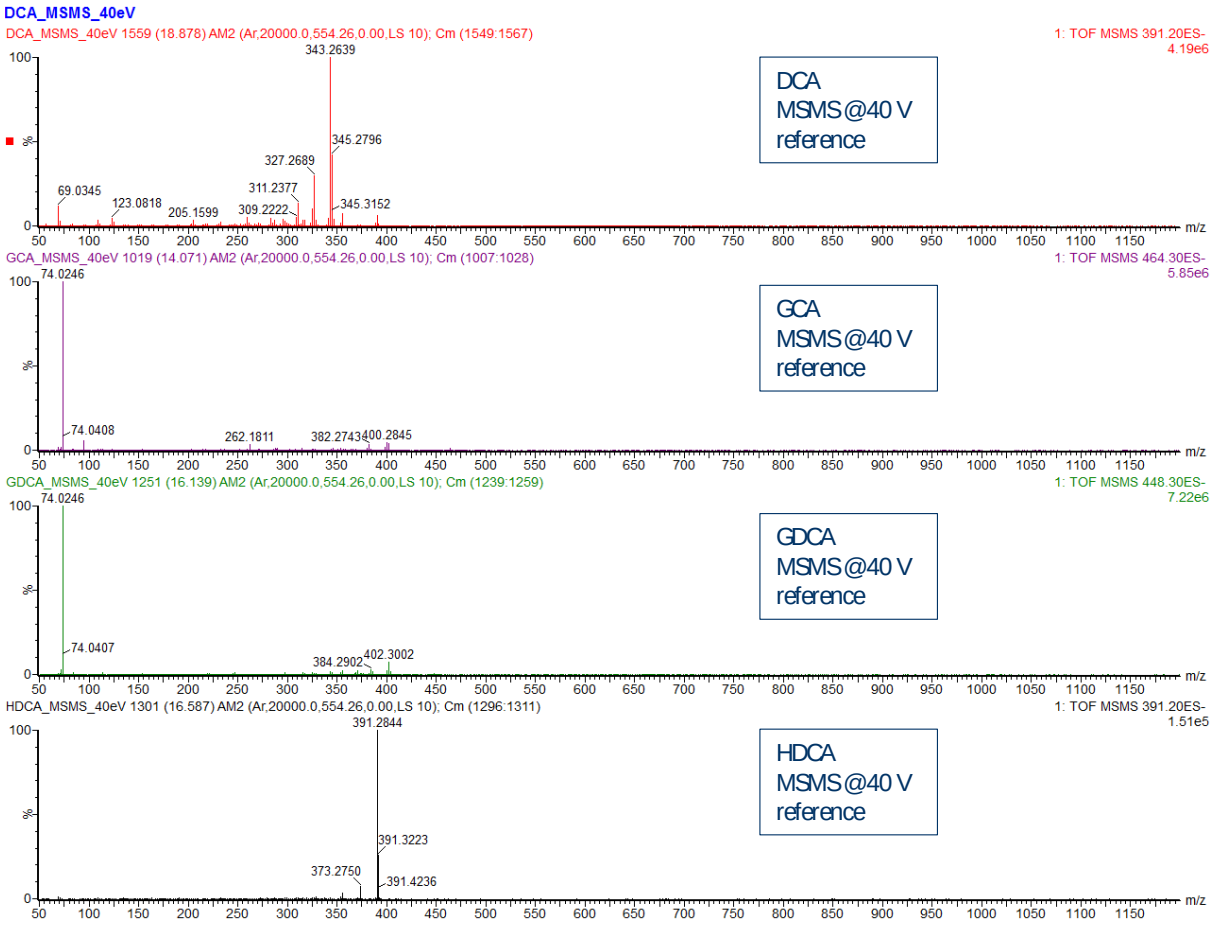
Supplementary Figure 1. A typical data sheet as example of a megavariate problem. The variables K (m/z features, in columns) are in excess compared to the observations, N (rows). In our case, the variables are singly charged precursor ions aligned by retention time (RT) and drift time (DT); one observation corresponds to one LC-MS run of a biological replicate.



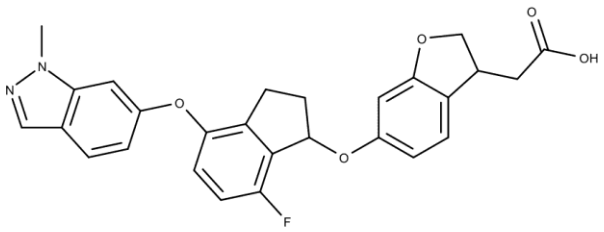
Supplementary Figure 2. MS/MS data of CDCA-24G: reference vs. signal in rat and dog



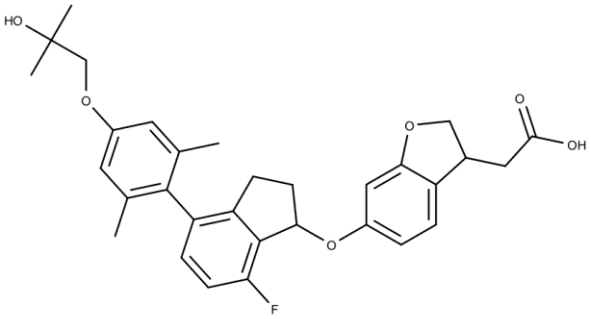
Supplementary Figure 3. MS/MS data of 7-HOCA: reference vs. signal in rat and dog



Supplementary Figure 4. MS/MS data of DCA, GCA, GDCA and HDCA (see Table 1)

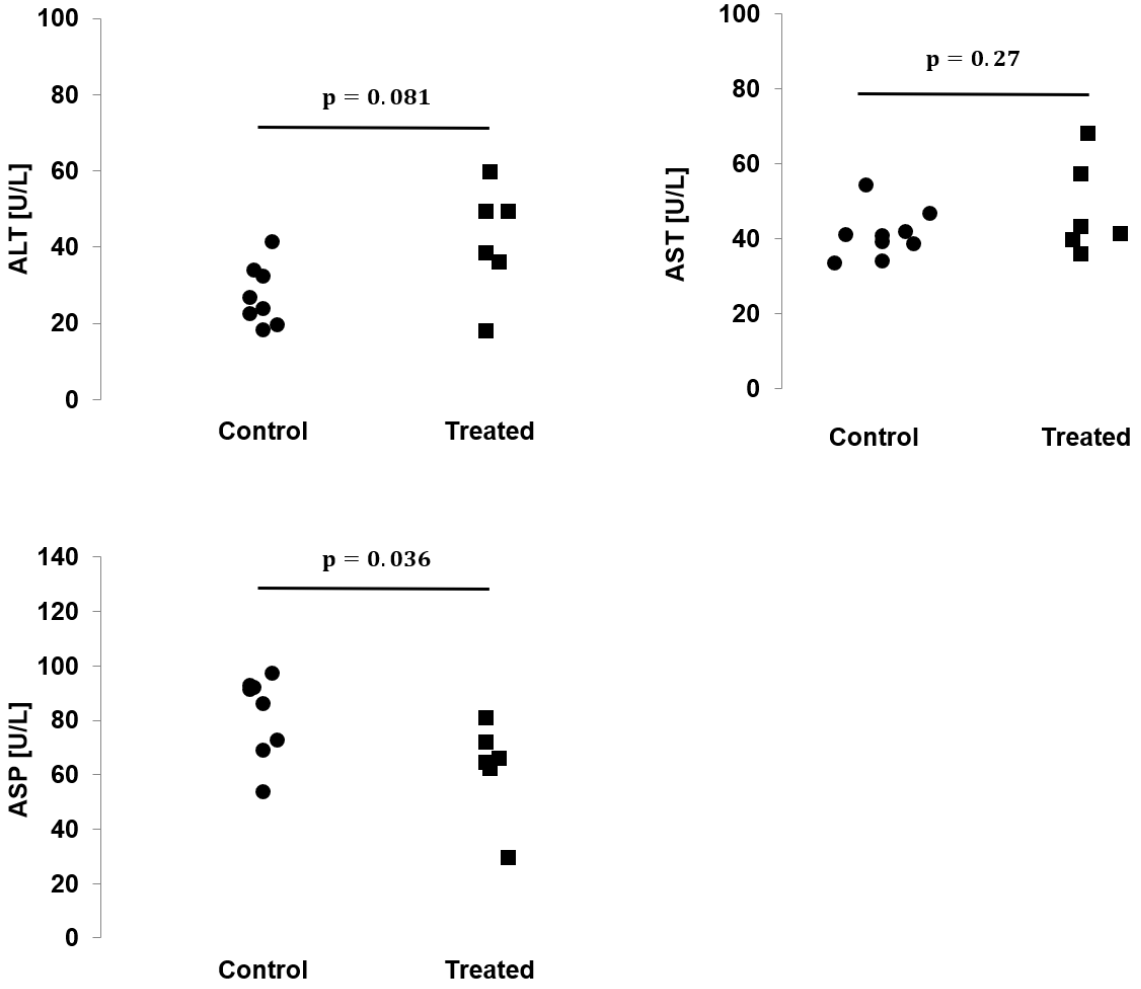


BI-1



BI-2

Supplementary Figure 5. Structures of BI-1 and BI-2



Supplementary Figure 6. ALT (panel A), AST (panel B) and ASP (panel C) enzyme levels in the control (N = 9) and treated (N = 6) mouse samples