Supplementary Material

Integration network pharmacology, lipidomics, and transcriptomics analysis to reveal the mechanisms underlying amelioration of AKT-induced nonalcoholic fatty liver disease by total flavonoids in vine tea

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1. Supplementary figures

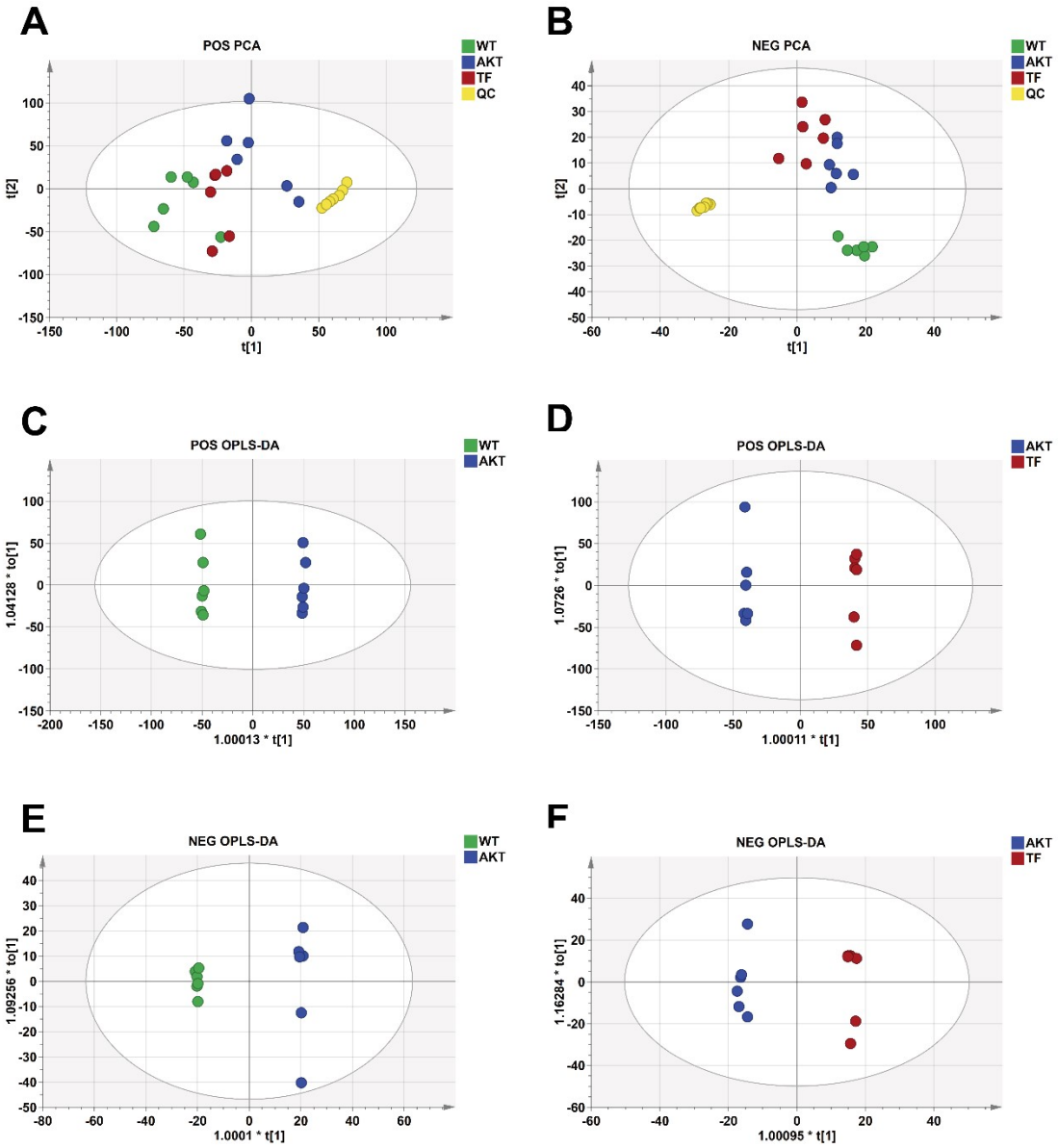

Fig. S1. The multivariate statistical analysis of the liver samples of lipidomics. PCA: principal component analysis; OPLS-DA: orthogonal partial least-squares discrimination analysis.

2. Supplementary tables

Table S1. Mass spectrometric information of the flavonoid compounds in vine tea

No.	RT	MS	Compounds name	Molecular formula	Ion	MS/MS
1	1.069	305.0667	epigallocatechin	$C_{15}H_{14}O_7$	$[M-H]^-$	125. 0242 167. 0351 261. 0771
2	3.706	639. 0989	quercetin-3-(2-caffeoyl) glucuronide	$C_{30}H_{24}O_{16}$	$[M-H]^-$	193. 0152 301. 0357 319. 0465
3	5.045	319. 0472	ampeloptin	$C_{15}H_{12}O_8$	$[M-H]^-$	125. 0216 193. 0131 257. 0483
4	4.312	333. 0242	Hexahydroxyflavonol	$C_{15}H_{10}O_9$	$[M-H]^-$	151. 0008 289. 0359 334.0182
5	6.157	479. 0853	myricetin-3-O-galactoside	$C_{21}H_{20}O_{13}$	$[M-H]^-$	316. 0258 287. 0047 271. 0216
6	6.653	303. 0503	taxifolin	$C_{15}H_{12}O_7$	$[M-H]^-$	125. 0236 150.9998 285. 0409
7	7.198	449. 0714	myricetin-3-O-xyloside	$C_{20}H_{18}O_{12}$	$[M-H]^-$	316. 0217 271. 0250
8	7.380	463. 0893	myricitrin	$C_{21}H_{20}O_{12}$	$[M-H]^-$	316. 0223 271. 0302 151. 0034
9	4.718	609. 1468	rutin	$C_{27}H_{30}O_{16}$	$[M-H]^-$	301.0396 243.0262 179.0031
10	9.580	447. 0953	quercetin-3-rhamnoside	$C_{21}H_{20}O_{11}$	$[M-H]^-$	301. 0289 271. 0235 178. 9951
11	4.959	317. 0316	myricetin	$C_{15}H_{10}O_8$	$[M-H]^-$	151. 0018 178. 9983 151. 0034
12	10.029	471. 0580	5,7-dihydroxy-4-oxo-(3,4,5-trihydroxyphenyl) -3,4-dihydro-2H-chromen-3-yl-3,4,5-trihydroxybenzoate	$C_{22}H_{16}O_{12}$	$[M-H]^-$	137. 0234 319. 0418 301. 0313 193. 0143
13	9.202	579. 1744	naringin	$C_{28}H_{36}O_{13}$	$[M-H]^-$	125. 0225 270.7028 151. 0053

						564.8413
14	9. 334	609. 1850	hesperidin	$C_{28}H_{34}O_{15}$	$[M-H]^-$	01.0396
						175.0367
						432.0925
15	11.337	431. 0986	kaempferol-rhamnoside	$C_{21}H_{20}O_{10}$	$[M-H]^-$	285.0413
						152. 7543
						301.0264
16	13.535	301. 0364	quercetin	$C_{15}H_{10}O_7$	$[M-H]^-$	179.0003
						151.0037

Table S2. SMILE ID of 11 flavonoid components

No.	Component	Canonical SMLIES
1	ampeloptin	C1=C(C=C(C(=C1O)O)O)C2C(C(=O)C3=C(C=C(C=C3O2)O)O)O
2	myricetin-3-O-galactoside	C1=C(C=C(C(=C1O)O)O)C2=C(C(=O)C3=C(C=C(C=C3O2)O)O)OC4C(C(C(C(O4)CO)O)O)O
3	myricetin-3-O-xyloside	C1C(C(C(C(O1)OC2=C(OC3=CC(=CC(=C3C2=O)O)O)C4=CC(=C(C(=C4)O)O)O)O)O)O
4	myricitrin	CC1C(C(C(C(O1)OC2=C(OC3=CC(=CC(=C3C2=O)O)O)C4=CC(=C(C(=C4)O)O)O)O)O)O
5	rutin	CC1C(C(C(C(O1)OCC2C(C(C(C(O2)OC3=C(OC4=CC(=CC(=C4C3=O)O)O)C5=CC(=C(C=C5)O)O)O)O)O)O)O)O
6	quercetin-3-rhamnoside	CC1C(C(C(C(O1)OC2=C(OC3=CC(=CC(=C3C2=O)O)O)C4=CC(=C(C=C4)O)O)O)O)O
7	myricetin	C1=C(C=C(C(=C1O)O)O)C2=C(C(=O)C3=C(C=C(C=C3O2)O)O)O
8	naringin	CC1C(C(C(C(O1)OC2C(C(C(OC2OC3=CC(=C4C(=O)CC(OC4=C3)C5=CC=C(C=C5)O)O)CO)O)O)O)O)O
9	hesperidin	CC1C(C(C(C(O1)OCC2C(C(C(C(O2)OC3=CC(=C4C(=O)CC(OC4=C3)C5=CC(=C(C=C5)OC)O)O)O)O)O)O)O)O
10	kaempferol-rhamnoside	CC1C(C(C(C(O1)OC2=C(OC3=CC(=CC(=C3C2=O)O)O)C4=CC=C(C=C4)O)O)O)O
11	quercetin	C1=CC(=C(C=C1C2=C(C(=O)C3=C(C=C(C=C3O2)O)O)O)O)O

Table S3. Differential lipids in liver by UHPLC-QTOF-MS/MS

No.	Class	Lipid ID	m/z	RT (min)	Ion	Link	MS/MS	AKT vs. WT			TF vs. AKT		
								FC	Trend	VIP	FC	Trend	VIP
1	CER	Cer(d18:1/22:1)	619.5895	20.55	$[M+H]^+$	HMDB0011775	602.5866 620.5857	2.88	↑*	1.3915	-2.16	↓	1.05273
2	SP	SM(d18:2/22:0)	784.6455	19.27	$[M+Na]^+$	HMDB0240633	8624.5635 748.5617 807.6311	4.59	↑*	1.44602	-4.09	↓*	2.07999
3	DG	DG(16:0/22:2/0:0)	648.5694	21.10	$[M+NH4]^+$	LMGL02010127	393.3302 631.5695 666.6066	17.94	↑***	1.68369	-2.99	↓*	1.43746
4	DG	DG(18:0/22:6/0:0)	668.5369	18.95	$[M+NH4]^+$	LMGL02010216	1.3056 385.2729 65.556	3.00	↑*	1.53441	-3.5	↓**	1.87118
5	DG	DG(18:1/18:2/0:0)	618.5238	18.93	$[M+NH4]^+$	HMDB0007247	686.5723 337.2758 339.2885	3.89	↑**	1.82641	-2.6	↓	1.73031
6	DG	DG(18:1/22:6/0:0)	666.522	18.36	$[M+H]^+$	HMDB0007237	536.5542 385.2761 667.5301	2.54	↑**	1.9018	-3.85	↓*	1.10553
7	DG	DG(18:2/18:2/0:0)	616.5071	18.11	$[M+H]^+$	LMGL02010063	337.2739 634.5466	2.42	↑*	1.36322	-4.7	↓*	1.43261
8	TG	TG(18:3/18:1/22:6)	926.735	26.72	$[M+H]^+$	HMDB0052983	617.5145 944.7786	2.80	↑***	1.93927	0.409966	↓**	2.61636

9	CL	CL(18:2_18:2_18:2_18:2)	1448.971	24.64	$[M+NH4]^+$	LMGP12010001, HMDB0010692	599.5064 1449.972 1467.0109	-2.24	↓**	1.39174	-2.09	↑*	1.20613
10	PE	PE(15:0/24:1)	787.6103	19.10	$[M+H]^+$	HMDB0008915	788.6164	2.40	↑**	1.80576	-2	↓	1.52323
11	PE	PE(16:0/18:0)	719.5511	17.59	$[M+H]^+$	LMGP02011225	720.5572	2.31	↑	1.26425	-2.43	↓	1.2863
12	PE	PE(16:1/24:1)	799.6118	18.74	$[M+H]^+$	HMDB0009749	800.6194	2.20	↑**	1.57645	-4.28	↓**	2.23853
13	PE	PE(18:0/22:6)	791.55	17.63	$[M-H]^-$	LMGP02010094	283.2347 327.2337	2.43	↑**	1.10175	-2.07	↓***	1.88866
14	PE	PE(19:0/22:2)	813.6256	19.19	$[M+H]^+$	LMGP02010790	790.5343 814.6326	4.46	↑**	2.00892	-2.36	↓*	1.93712
15	PE	PE(24:1/16:0)	801.6259	19.69	$[M+H]^+$	HMDB0009748	802.6349	6.15	↑***	1.69752	-3.79	↓***	1.91773
16	PE	PE(O-18:0/20:5)	751.5533	18.60	$[M+H]^+$	LMGP02020008	611.5405 752.5603	4.07	↑***	1.77163	-3.09	↓**	2.203
17	PC	PC(16:1/20:2)	783.5794	17.81	$[M+H]^+$	LMGP01011490 HMDB0008012	184.0735 784.5872	2.34	↑**	1.01941	-2.23	↓*	1.18089
18	PC	PC(18:0/18:4)	781.5619	18.78	$[M+H]^+$	LMGP01010773	184.0733 782.5712	2.90	↑**	1.71183	-2.41	↓*	1.94402
19	PC	PC(18:2/20:5)	803.5452	16.15	$[M+H]^+$	LMGP01011634 HMDB0008149	184.0732 804.5583	11.85	↑***	1.77839	-2.37	↓*	1.28337
20	PC	PC(19:1/18:4)	793.5633	16.72	$[M+H]^+$	HMDB0009011	653.5572 794.5673	2.17	↑*	1.83393	-2.73	↓*	2.09641
21	PC	PC(20:2/20:2)	837.6263	18.70	$[M+H]^+$	LMGP01011856 HMDB0008342	184.0721 538.6312	2.30	↑**	1.73932	-2.02	↓	1.38986
22	PC	PC(O-18:1/16:0)	745.5999	18.70	$[M+H]^+$	LMGP01020152 HMDB0013424	184.0725 746.6009	2.19	↑**	1.47636	-2.12	↓*	1.18087

23	PS	PS(18:1/20:2)	813.55	19.30	$[M-H]^-$	LMGP03010334	281.2492 812.5412	2.22	↑***	1.45578	-2.26	↓***	1.35931
24	PS	PS(19:0/22:6)	849.55	16.18	$M-H]^-$	LMGP03010479	283.2506 327.2308 848.5472	2.23	↑**	1.22955	-2.25	↓***	1.36956
25	PS	PS(20:1/21:0)	859.63	19.29	$[M-H]^-$	LMGP03010552	309.2774 858.621	2.31	↑***	1.68236	-2.26	↓***	1.20287
26	PI	PI(16:0/18:2)	834.52	16.66	$[M-H]^-$	LMGP06010959	152.9949 255.233 409.2322 833.5178	3.20	↑***	1.48985	-2.34	↓***	1.07798
27	LPC	LysoPC(17:0)	509.3488	6.94	$[M+H]^+$	LMGP01050024	184.0734 510.3558	3.96	↑**	1.37581	-2.25	↓	1.20769
28	LPC	LysoPC(18:1)	521.3492	5.04	$[M+H]^+$	HMDB0061701	184.0731 504.3462 5223564	3.59	↑***	1.86252	-2.09	↓*	1.52456
29	LPC	LysoPC(19:0)	537.3796	12.24	$[M+H]^+$	LMGP01050041	184.0746 520.3822 538.385	3.01	↑*	1.10935	-3.68	↓**	1.47399
30	LPE	LysoPE(16:0)	453.2859	5.01	$[M+H]^+$	HMDB0011473	313.2789 436.2806 454.2965	2.26	↑**	1.23619	-2.09	↓*	1.1344
31	LPE	LysoPE(18:1)	479.3048	5.12	$[M+H]^+$	HMDB0011475	198.0546 216.0602 339.2904 480.3104	3.23	↑***	1.65184	-2.4	↓	1.34276

32	LPE	LysoPE(22:6)	525.286	3.09	$[M+H]^+$	HMDB0011496	142.0275 216.0609 385.2729 526.2938	2.54	↑**	1.26637	-2.42	↓*	1.24282

↑ indicates increase; ↓ indicates decrease * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table S4. Primer sequences for RT-qPCR analysis

Gene	Forward primer sequence (5'-3')	Reverse primer sequence (5'-3')
GAPDH	GGCAAATTCAACGGCACAGTCAA	GACATACTCAGCACCGGCCTCAC
PPARG	TGTTCGCCAAGGTGCTCCAG	TGAAGGCTCATGTCTGTCTCTGTC
SCD1	GGTGAACAGTGCCGCGCATCTC	GTGTGGTGGTAGTTGTGGAAGCC
CHPT1	CATCAACCTGGTCACCACAC	CCCAGGGCACATAAAAGGTA
PLA2G12B	CCACTCAATCTGCTCCGACCTC	ACACGGTATCAGCCAGAGAATCAC
DGKZ	GGAGAACAGACAGCATTACCAGATG	GACAGGAATGTGGCAGTGAGATG