

Supplementary information

1

2

3 Multi-omics study of the anti-cancer effect of a ferulic acid derivative FA-30

4

5 Dongyao Wang^{†, a}, Dandan Guo^{†, a}, Yuxiao Tang^{†, b}, Minyu Qi^a, Jiahao Fang^a, Ying Zhang^a,
6 Yifeng Chai^{*, a}, Yan Cao^{*, a}, Diya Lv^{*, a}

7

8 a. Shanghai Key Laboratory for Pharmaceutical Metabolite Research, School of Pharmacy,
9 Second Military Medical University, Shanghai 200433, China

10 b. Department of nutrition, Second Military Medical University, Shanghai, China

11 Dongyao Wang: ORCID iD: 0000-0002-5852-2640

12 Diya Lv: ORCID iD: 0000-0002-6159-4311

13

14 **† These authors contributed equally.**

15 ***To whom correspondence should be addressed.**

16 Diya Lv, Ph.D. Address: No. 325, Guohe Road, Shanghai, China. E-mail:
17 lvdy2020@smmu.edu.cn. Correspondence may also be addressed to Yan Cao, Ph.D. No. 325,
18 Guohe Road, Shanghai, China. E-mail:caoyan@smmu.edu.cn; Yifeng Chai, Ph.D. No. 325,
19 Guohe Road, Shanghai, China. E-mail:yfchai@smmu.edu.cn.

20

21 Lead Contact: Diya Lv, Ph.D. E-mail: lvdy2020@smmu.edu.cn.

22

23 Author contributions

24

25 Dr. D.W: Conceptualization; Investigation; Writing – original draft; Writing – review & editing

26 Dr. D.G: Investigation; Formal analysis

27 Dr. Y. T: Investigation; Formal analysis

28 Miss M.Q: Investigation; Validation

29 Mr. J.F: Investigation;

30 Miss Y.Z: Investigation

31 Prof. Y.C (Yifeng Chai): Writing – review & editing

32 Prof. Y.C (Yan Cao): Funding acquisition; Writing – review & editing

33 Prof. D.L: Conceptualization; Funding acquisition; Writing – original draft; Writing – review &
34 editing.

35

36 Conflict of interest

37

38 There are no conflicts to declare.

39

40 Acknowledgement

41

42 This study was sponsored by the National Natural Science Foundation of China (82174092, to
43 Yan Cao; 82003711, to Dongyao Wang), the Science and Technology Commission of Shanghai

44 Municipality (21ZR1483000, to Yan Cao; 22ZR1476900, to Diya Lv), and the Shanghai Pujiang
45 Program (21PJD083, to Yan Cao).

46 **Data Availability**

47

48 The raw data of the metabolomics and proteomics studies has been uploaded into the Mendeley
49 Data repository (wang, dongyao (2022), “Metabolomics and Proteomics Research of FA-30”,
50 Mendeley Data, V1, doi: 10.17632/mkrzs2rsm4.1).

51 The contents are listed below:

52 metabonomic raw data-negative-hilic-blank-fa30.xlsx

53 metabonomic raw data-negative-reverse phase-blank-fa30.xlsx

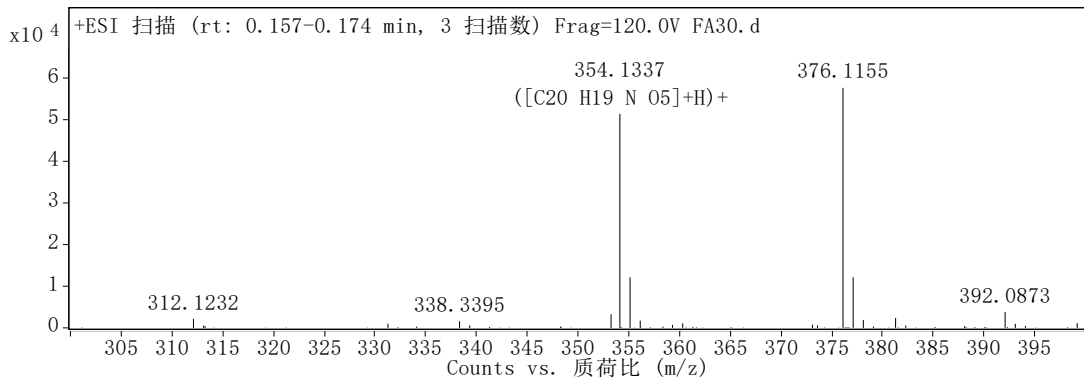
54 metabonomic raw data-positive-hilic-blank-fa30.xlsx

55 metabonomic raw data- positive -reverse phase-blank-fa30.xlsx

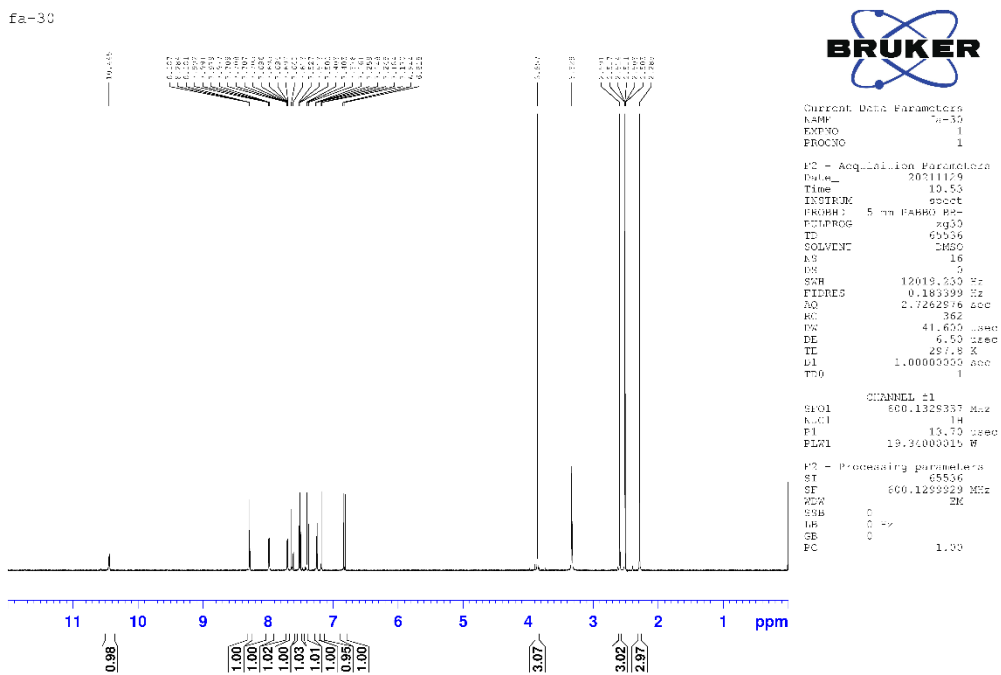
56 proteomics data-iTRAQ 8plex -blank-fa30.xlsx

57

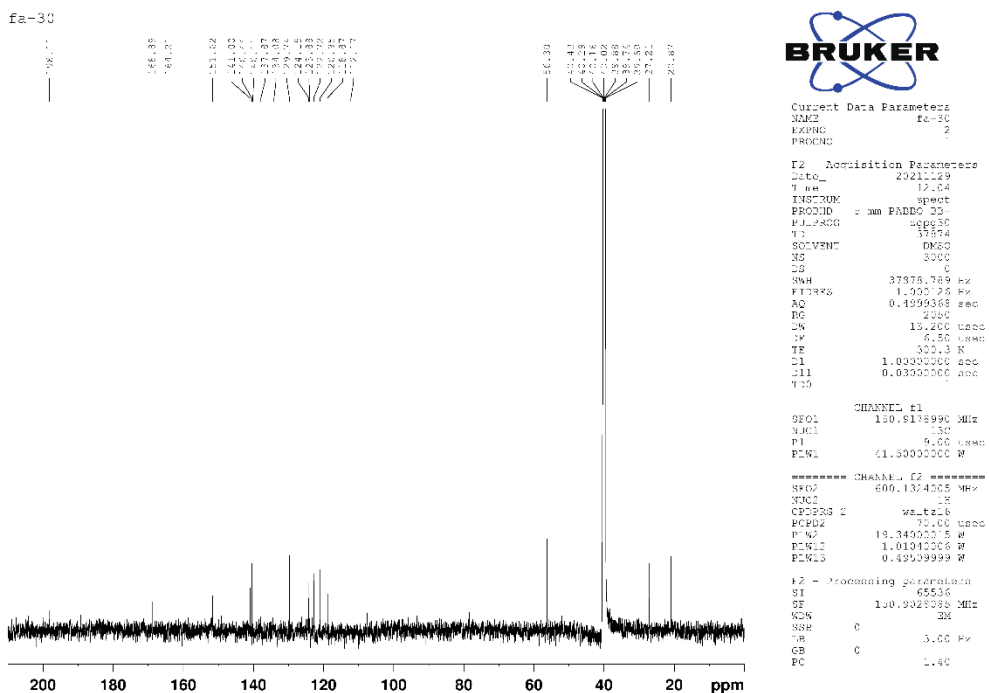
58



59



60



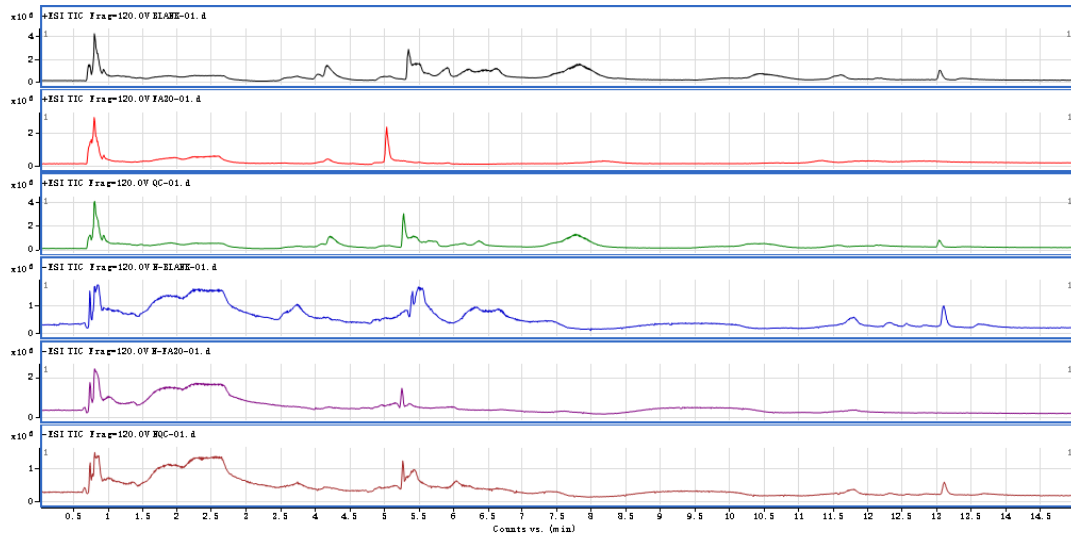
61

62

63 Fig S1 : The mass spectrometry and NMR spectrum of FA-30. Top, mass spectrum; middle, ¹H

64 NMR spectrum; bottom, ¹³C NMR spectrum.

65



66

67

68 Fig S2: The total ion chromatography spectrums of Blank, FA-30 and QC samples in Hilic
 69 separation mode. From top to bottom, Blank in positive, FA-30 in positive, QC in positive, Blank
 70 in negative, FA-30 in negative, QC in negative.

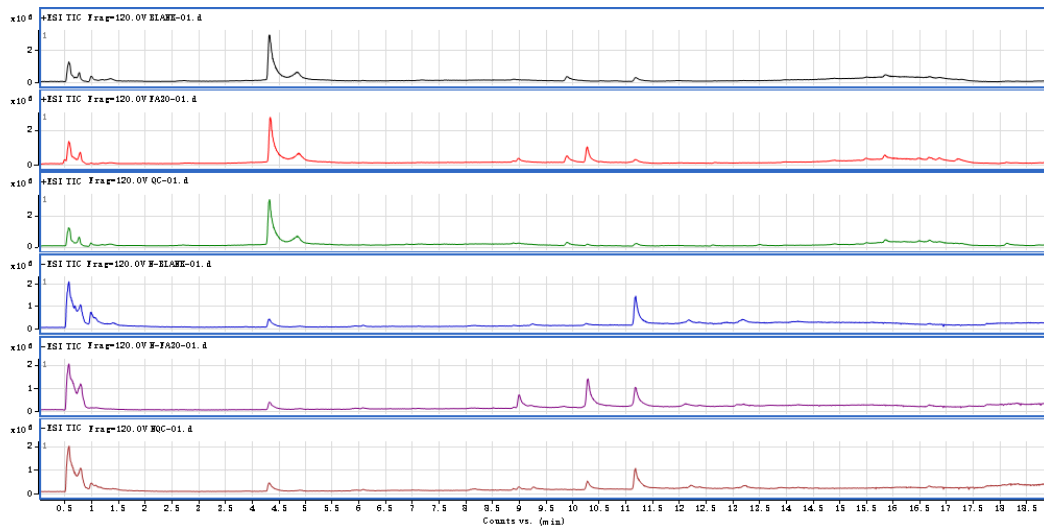


Fig S3: The total ion chromatography spectrums of Blank, FA-30 and QC samples in reversed-phase separation mode. From top to bottom, Blank in positive, FA-30 in positive, QC in positive, Blank in negative, FA-30 in negative, QC in negative.

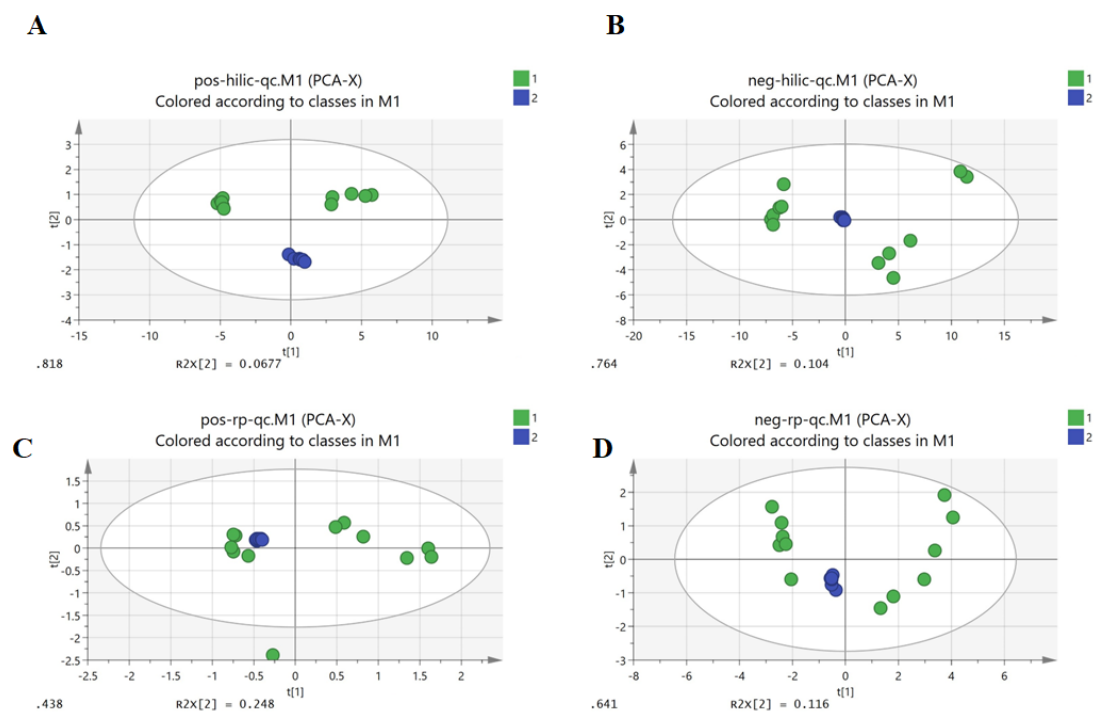


Fig S4: The score plot of the principal component analysis model for the sample group and QC group based on liquid chromatography–tandem mass spectrometry data. (A) Hilic chromatography in positive mode. (B) Hilic chromatography in negative mode. (C) Reverse phase chromatography in positive mode. (D) Reverse phase chromatography in negative mode. $n=6$ in each group, green represented samples, blue represented QC.

Table S1: The parameters of OPLS-DA models

No.	Separation mode	Detection mode	Type	R2X(cum)	R2Y(cum)	Q2(cum)
1	Hilic	positive	OPLS-DA	0.918	0.991	0.975
2	Hilic	negative	OPLS-DA	0.91	0.991	0.984
3	Reverse phase	positive	OPLS-DA	0.63	0.982	0.965
4	Reverse phase	negative	OPLS-DA	0.792	0.99	0.977

Table S2 : The potential biomarkers based on metabolome profiling

Var ID	mzme d	rtmed	Metabolite	Formula	Adduct	VIP value	P value
M116T3 43	116.0 708	5.714	L-Proline	C5H9NO2	M+H	1.1360 7	1.92E- 05
M130T3 68	130.0 5	6.141 5	N-Acryloylglycine	C5H7NO3	M+H	1.2842 9	0.00138 9
M200T2 51	200.0 483	4.187	1-Isothiocyanato-3-phenylpropane	C10H11NS	M+Na	1.4893 8	0.00232 8
M308T3 61	308.0 927	6.009 5	Glutathione	C10H17N3 O6S	M+H	1.1521 6	4.5E-06
M130T2 92	130.1 59	4.868	4-Trimethylammonio butanal	C7H16NO	M+H	1.1376 4	0.00142 9
M132T1 14	132.1 017	1.908	L-Isoleucine	C6H13NO2	M+H	1.1198 9	0.00033 7
M132T8 0	132.1 018	1.34	D-Leucine	C6H13NO2	M+H	1.2835 3	3.57E- 05
M143T4 1	142.9 484	0.685	3-Mercaptopyruvic acid	C3H4O3S	M+Na	1.1800 2	0.01028
M158T5 94	158.1 543	9.906	Tranexamic Acid	C8H15NO2	M+H	4.8712 2	0.01478 2
M159T3 3	158.9 641	0.556	Dimethyldithiophosphate	C2H7O2PS 2	M+H	1.1949	0.01701 2
M159T5 94	159.1 573	9.906	Decyl alcohol	C10H22O	M+H	1.5904 7	0.01605 4
M199T2 53	199.1 442	4.208 5	1-Methyl-2-n-hexylbenzene	C13H20	M+Na	1.0072 7	0.03102 8
M202T2 92	202.0 447	4.866	Thiabendazole	C10H7N3S	M+H	1.1156 2	0.01333 8
M227T3 3	226.9 524	0.551	Oltipraz	C8H6N2S3	M+H	2.3800 6	0.01677 7
M256T9 30	256.2 647	15.50 6	Palmitic amide	C16H33NO	M+H	2.0904 1	0.03675 9
M308T6 1	308.0 919	1.011	Glutathione	C10H17N3 O6S	M+H	1.0902 2	1.25E- 10
M312T5 40	312.1 238	9.002	Aspartyl-Arginine	C10H19N5 O5	M+Na	1.9200 3	4.2E-05
M315T5 94	315.3 016	9.906	3-hydroxypristanic acid	C19H38O3	M+H	1.0112	0.01269 4
M354T6 17	354.1 349	10.28 45	Honyumine	C20H19NO 5	M+H	3.7422 4	0.00066 9
M355T6 17	355.1 379	10.28 5	Tryptophyl-Glutamine	C16H20N4 O4	M+Na	1.6903 3	0.00052 6
M363T3 3	362.9 274	0.549	Fructose 1,6-bisphosphate	C6H14O12P 2	M+Na	1.3241 4	0.02286 2
M376T6 17	376.1 164	10.28 6	Honyumine	C20H19NO 5	M+H	1.2016 1	0.00060 2
M551T1 036	550.6 313	17.26 7	Octadecane	C18H38	2M+AC N+H	2.2920 1	0.03992 7
M566T1 137	565.5 693	18.95 4	FAHFA(18:1(9Z)/9-O-18:0)	C36H68O4	M+H	1.2479 7	0.03786 2
M707T6 17	707.2 618	10.27 8	Citbismine C	C37H36N2 O11	M+Na	1.3775 1	0.00794 5

M729T6 17	729.2 44	10.27 8	N- Desmethylritonavir	C36H46N6 O5S2	M+Na	1.2500 4	0.00507 8
M839T3 3	838.8 404	0.547	TG(14:0/O- 18:0/18:0)	C53H104O5	M+NH4	1.0606 3	0.03999
M91T33	90.97 677	0.551	Oxalic acid	C2H2O4	M+H	1.1482 3	0.01658 3
M113T3 11	112.9 857	5.182	Dimethyl sulfoxide	C2H6OS	M+Cl	1.7930 7	0.03009 2
M113T8 2	112.9 862	1.365	Parabanic Acid	C3H2N2O3	M-H	1.1892 5	0.00479 3
M132T3 24	132.0 302	5.404	L-Aspartic acid	C4H7NO4	M-H	1.2525 2	2.91E- 09
M135T7 0	134.8 954	1.166	Sulfate	H2O4S	M+K- 2H	2.0255 9	0.04507 2
M147T3 7	146.9 66	0.613	Benzenethiol	C6H6S	M+K- 2H	1.0288 3	0.00884 9
M147T6	146.9 661	0.095	Methylphosphate	CH5O4P	M+Cl	2.4946 9	0.04743 8
M215T9 2	215.0 334	1.529 5	L-Gulose	C6H12O6	M+Cl	1.1092 6	0.01127 6
M249T3 08	248.9 604	5.127 5	2,5-Dimethyl-3- furanthiol acetate	C8H10O2S	M+Br	1.1358 9	0.03329 5
M271T2 25	271.0 041	3.742	2-Propenyl 1-(2- propenylsulfanyl)pr opyl disulfide	C9H16OS3	M+Cl	1.0813 7	2.3E-06
M310T5 1	310.1 74	0.856	Pipertipine	C20H27NO 3	M-H20- H	1.0920 3	7.06E- 05
M318T3 24	318.0 769	5.403	gamma- Glutamylcysteinylse rine	C11H19N3 O7S	M-H20- H	1.3984 9	1.6E-10
M373T4 7	373.1 055	0.783	Acetyldeoxynivalen ol	C17H22O7	M+Cl	1.0731	0.00011 8
M385T3 08	384.9 355	5.135	Uridine 2',3'-cyclic phosphate	C9H11N2O 8P	M+Br	1.0036 7	0.00809 7
M388T4 4	388.1 555	0.74	Trifluoperazine	C21H24F3N 3S	M-H20- H	1.0381 6	0.00548
M415T4 6	415.1 154	0.773	(S)-Bitalin A 12- glucoside	C19H24O8	M+Cl	1.5826 7	0.00105 4
M62T48	61.98 912	0.794	Peroxynitrite	HNO3	M-H	1.9355 8	0.00849
M748T6 86	747.5 651	11.42 7	TG(14:1(9Z)/18:4(6 Z,9Z,12Z,15Z)/14:1 (9Z))	C42H80O6	M- H+HCO ONa	1.0021 3	0.01270 7
M310T5 40	310.1 092	9.004	Tryptophyl-Alanine	C14H17N3 O3	M+Cl	1.1806 2	0.00022 6
M415T6 17	415.1 154	10.28 9	(S)-Bitalin A 12- glucoside	C19H24O8	M+Cl	1.1313 6	0.00075 8
M398T6 17	398.1 252	10.28 9	Adlumidiceine	C21H21NO 7	M-H	1.6614 2	0.00294 2
M353T6 17	353.1 227	10.28 9	Methyl helianthoate F glucoside	C17H22O8	M-H	1.0560 1	0.00294 5
M352T6 17	352.1 198	10.28 9	Honyumine	C20H19NO 5	M-H	2.3442 9	0.00318 6
M445T6	444.9	11.18	Butoconazole	C19H17Cl3	M+Cl	1.0863	0.00427

71	737	3		N2S		2	1
M431T7	430.9	12.12		C16H16N2		1.0557	0.04273
28	743	6	Cefalotin	O6S2	M+Cl	7	6
M495T7	494.9	12.12	8-Hydroxyluteolin	C15H10O10	M+TFA	1.2078	0.04650
28	704	6	8-sulfate	S	-H	5	9

Table S3 : The KEGG enrichment analysis based on metabolome profiling

Term ID	Term description	RichFactor	p-value
hsa00270	Cysteine and methionine metabolism	0.06349	8E-05
hsa00970	Aminoacyl-tRNA biosynthesis	0.05769	0.00099
hsa02010	ABC transporters	0.03226	0.00527
hsa04974	Protein digestion and absorption	0.06897	0.00564
hsa05230	Central carbon metabolism in cancer	0.06667	0.00603
hsa00920	Sulfur metabolism	0.06061	0.00727
hsa05418	Fluid shear stress and atherosclerosis	0.16667	0.02378
hsa05010	Alzheimer disease	0.08333	0.04704
hsa00230	Purine metabolism	0.02105	0.05349
hsa05131	Shigellosis	0.07143	0.05467
hsa05014	Amyotrophic lateral sclerosis	0.07143	0.05467
hsa04071	Sphingolipid signaling pathway	0.06667	0.05847
hsa04918	Thyroid hormone synthesis	0.05	0.07725
hsa04976	Bile secretion	0.04545	0.08466
hsa00220	Arginine biosynthesis	0.04348	0.08835
hsa00290	Valine, leucine and isoleucine biosynthesis	0.04348	0.08835
hsa04216	Ferroptosis	0.03704	0.10296
hsa00250	Alanine, aspartate and glutamate metabolism	0.03571	0.10658
hsa00770	Pantothenate and CoA biosynthesis	0.03333	0.11377
hsa00010	Glycolysis / Gluconeogenesis	0.03226	0.11735
hsa00410	beta-Alanine metabolism	0.03125	0.12091
hsa00030	Pentose phosphate pathway	0.02857	0.13153
hsa00480	Glutathione metabolism	0.02632	0.14202
hsa04080	Neuroactive ligand-receptor interaction	0.025	0.14896
hsa00280	Valine, leucine and isoleucine degradation	0.02439	0.1524
hsa00340	Histidine metabolism	0.02128	0.17281
hsa00053	Ascorbate and aldarate metabolism	0.02041	0.17952
hsa00260	Glycine, serine and threonine metabolism	0.02	0.18285
hsa00310	Lysine degradation	0.02	0.18285
hsa00051	Fructose and mannose metabolism	0.01852	0.19605
hsa00760	Nicotinate and nicotinamide metabolism	0.01818	0.19932
hsa00630	Glyoxylate and dicarboxylate metabolism	0.01613	0.22187
hsa00240	Pyrimidine metabolism	0.01538	0.23136
hsa00330	Arginine and proline metabolism	0.01282	0.27123

Table S4 : The GO enrichment analysis based on proteome profiling

Term ID	Term description	p-value	Category
GO:0005829	cytosol	1.66E-15	cellular_component
GO:0070062	extracellular exosome	3.11E-15	cellular_component
GO:0003723	RNA binding	4.09E-10	molecular_function
GO:0016020	membrane	2.67E-09	cellular_component
GO:0006412	translation	5.07E-07	biological_process
GO:0045296	cadherin binding	1.65E-06	molecular_function
GO:0005737	cytoplasm	1.74E-06	cellular_component
GO:0006418	tRNA aminoacylation for protein translation	1.02E-05	biological_process
GO:0006564	L-serine biosynthetic process	7.13E-05	biological_process
GO:0042470	melanosome	9.19E-05	cellular_component
GO:0003735	structural constituent of ribosome	0.000140485	molecular_function
GO:0005730	nucleolus	0.000142928	cellular_component
GO:0043486	histone exchange translation factor	0.000289236	biological_process
GO:0008135	activity, RNA binding	0.000328415	molecular_function
GO:0005524	ATP binding	0.000389471	molecular_function
GO:0015175	neutral amino acid transmembrane transporter activity	0.000405643	molecular_function
GO:0006183	GTP biosynthetic process	0.000555235	biological_process
GO:0006413	translational initiation	0.000692411	biological_process
GO:0006796	phosphate-containing compound metabolic process	0.000940574	biological_process
GO:0003725	double-stranded RNA binding	0.001020628	molecular_function
GO:0051085	chaperone cofactor- dependent protein refolding	0.001183452	biological_process
GO:0031012	extracellular matrix	0.001371227	cellular_component
GO:0006913	nucleocytoplasmic transport	0.00146247	biological_process
GO:0051289	protein homotetramerization	0.001869677	biological_process
GO:0034976	response to endoplasmic reticulum stress	0.00202066	biological_process
GO:0030529	intracellular ribonucleoprotein complex	0.002081834	cellular_component
GO:0005925	focal adhesion	0.00218194	cellular_component
GO:0015186	L-glutamine transmembrane transporter activity	0.002316243	molecular_function
GO:0047134	protein-disulfide reductase activity	0.002316243	molecular_function

GO:0005635	nuclear envelope	0.002322913	cellular_component
GO:0019509	L-methionine salvage from	0.00232632	biological_process
GO:0034394	methylthioadenosine protein localization to cell surface	0.002534352	biological_process
GO:1900026	positive regulation of substrate adhesion- dependent cell spreading	0.002975376	biological_process
GO:0016569	covalent chromatin modification	0.003239641	biological_process
GO:0003743	translation initiation factor activity	0.003302138	molecular_function
GO:0033327	Leydig cell differentiation	0.003453837	biological_process
GO:0035973	aggrephagy	0.003453837	biological_process
GO:0002039	p53 binding	0.003615452	molecular_function
GO:0008565	protein transporter activity	0.00376524	molecular_function
GO:0005694	chromosome	0.003949017	cellular_component
GO:0001933	negative regulation of protein phosphorylation	0.003983162	biological_process
GO:0051262	protein tetramerization	0.003991751	biological_process
GO:0015949	nucleobase- containing small molecule interconversion	0.003991751	biological_process
GO:0006606	protein import into nucleus	0.004339156	biological_process
GO:0061635	regulation of protein complex stability	0.004786043	biological_process
GO:0006307	DNA dealkylation involved in DNA repair	0.004786043	biological_process
GO:0042802	identical protein binding	0.005224064	molecular_function
GO:0005525	GTP binding	0.005869173	molecular_function
GO:0015935	small ribosomal subunit	0.005916819	cellular_component
GO:0030867	rough endoplasmic reticulum membrane	0.005916819	cellular_component
GO:0019215	intermediate filament binding	0.006289545	molecular_function
GO:0046686	response to cadmium ion	0.006316373	biological_process
GO:0009168	purine ribonucleoside monophosphate biosynthetic process	0.006316373	biological_process
GO:0006614	SRP-dependent cotranslational protein targeting to membrane	0.006931623	biological_process

GO:0008536	Ran GTPase binding	0.00732506	molecular_function
GO:0000502	proteasome complex	0.007617405	cellular_component
GO:0005975	carbohydrate metabolic process	0.007653679	biological_process
GO:0015804	neutral amino acid transport	0.008038412	biological_process
GO:0006414	translational elongation	0.008038412	biological_process
GO:0005643	nuclear pore	0.008144265	cellular_component
GO:0006986	response to unfolded protein	0.008199935	biological_process
GO:0051287	NAD binding	0.009023159	molecular_function
GO:0000049	tRNA binding	0.009055764	molecular_function
GO:0005721	pericentric heterochromatin	0.009322951	cellular_component
GO:0030496	midbody	0.009837765	cellular_component
GO:0015194	L-serine transmembrane transporter activity	0.009904208	molecular_function
GO:0006228	UTP biosynthetic process	0.009945896	biological_process
GO:0005741	mitochondrial outer membrane	0.01022074	cellular_component
GO:0042393	histone binding	0.010237212	molecular_function
GO:0005913	cell-cell adherens junction	0.010489108	cellular_component
GO:0000781	chromosome, telomeric region	0.011004128	cellular_component
GO:0030433	ubiquitin-dependent ERAD pathway	0.011050212	biological_process
GO:0006461	protein complex assembly	0.011902529	biological_process
GO:0030971	receptor tyrosine kinase binding	0.011968463	molecular_function
GO:0007004	telomere maintenance via telomerase	0.01203271	biological_process
GO:0061001	regulation of dendritic spine morphogenesis	0.01203271	biological_process
GO:1903076	regulation of protein localization to plasma membrane	0.01203271	biological_process
GO:0006241	CTP biosynthetic process	0.01203271	biological_process
GO:0006865	amino acid transport	0.012043139	biological_process
GO:0016235	aggresome	0.013067699	cellular_component
GO:0017101	aminoacyl-tRNA synthetase multienzyme complex	0.01340654	cellular_component
GO:0031966	mitochondrial membrane	0.013981792	cellular_component
GO:0098641	cadherin binding involved in cell-cell adhesion	0.014233759	molecular_function

GO:0008191	metalloendopeptidase inhibitor activity	0.014233759	molecular_function
GO:0010629	negative regulation of gene expression	0.014845851	biological_process
GO:0022627	cytosolic small ribosomal subunit	0.015337265	cellular_component
GO:0005840	ribosome	0.016550031	cellular_component
GO:0042288	MHC class I protein binding	0.016651868	molecular_function
GO:0019843	rRNA binding	0.016659593	molecular_function
GO:0005080	protein kinase C binding	0.016659593	molecular_function
GO:0040014	regulation of multicellular organism growth	0.016720571	biological_process
GO:0006259	DNA metabolic process	0.016720571	biological_process
GO:0021766	hippocampus development	0.016761297	biological_process
GO:0005813	centrosome	0.016835754	cellular_component
GO:0001618	virus receptor activity	0.01797108	molecular_function
GO:0043123	positive regulation of I-kappaB kinase/NF-kappaB signaling	0.018976918	biological_process
GO:0004033	aldo-keto reductase (NADP) activity	0.019231276	molecular_function
GO:0016779	nucleotidyltransferase activity	0.019231276	molecular_function
GO:0006488	dolichol-linked oligosaccharide biosynthetic process	0.019310091	biological_process
GO:0032092	positive regulation of protein binding	0.019455241	biological_process
GO:0002576	platelet degranulation	0.020228268	biological_process
GO:0005874	microtubule	0.020508567	cellular_component
GO:0034719	SMN-Sm protein complex	0.020708564	cellular_component
GO:0006334	nucleosome assembly	0.021300017	biological_process
GO:0035249	synaptic transmission, glutamatergic	0.022055879	biological_process
GO:0043113	receptor clustering	0.022055879	biological_process
GO:0097225	sperm midpiece	0.023435917	cellular_component
GO:0005720	nuclear heterochromatin	0.023435917	cellular_component
GO:0015171	amino acid transmembrane transporter activity	0.023777003	molecular_function
GO:0000723	telomere maintenance	0.024952507	biological_process
GO:0000060	protein import into nucleus, translocation	0.024952507	biological_process
GO:0042073	intraciliary transport	0.024952507	biological_process
GO:0006611	protein export from nucleus	0.024952507	biological_process
GO:1904813	ficolin-1-rich granule	0.026235921	cellular_component

GO:0000784	lumen nuclear chromosome, telomeric region	0.026508898	cellular_component
GO:0036498	IRE1-mediated unfolded protein response	0.027175107	biological_process
GO:0042803	protein homodimerization activity	0.027279515	molecular_function
GO:0071363	cellular response to growth factor stimulus	0.027994677	biological_process
GO:0043525	positive regulation of neuron apoptotic process	0.027994677	biological_process
GO:0035338	long-chain fatty-acyl- CoA biosynthetic process	0.027994677	biological_process
GO:0030170	pyridoxal phosphate binding	0.030479431	molecular_function
GO:0043022	ribosome binding	0.030479431	molecular_function
GO:1900034	regulation of cellular response to heat	0.030656471	biological_process
GO:0005634	nucleus nucleoside	0.030802305	cellular_component
GO:0004550	diphosphate kinase activity	0.031053339	molecular_function
GO:0042826	histone deacetylase binding	0.031491176	molecular_function
GO:0006890	retrograde vesicle- mediated transport, Golgi to ER	0.031726522	biological_process
GO:0000166	nucleotide binding	0.034164666	molecular_function
GO:0043015	gamma-tubulin binding	0.034358942	molecular_function
GO:0005487	nucleocytoplasmic transporter activity	0.034358942	molecular_function
GO:0030234	enzyme regulator activity	0.034358942	molecular_function
GO:0006325	chromatin organization	0.034360904	biological_process
GO:0048675	axon extension	0.034495081	biological_process
GO:0016049	cell growth	0.034495081	biological_process
GO:0015035	protein disulfide oxidoreductase activity	0.037794605	molecular_function
GO:0071889	14-3-3 protein binding	0.037794605	molecular_function
GO:0003924	GTPase activity	0.038600842	molecular_function
GO:0002931	response to ischemia	0.041517194	biological_process
GO:0071407	cellular response to organic cyclic compound	0.041517194	biological_process
GO:0006446	regulation of translational initiation	0.041517194	biological_process

GO:0016607	nuclear speck	0.041715635	cellular_component
GO:0035064	methylated histone binding	0.042193478	molecular_function
GO:0000794	condensed nuclear chromosome	0.042546738	cellular_component
GO:0046540	U4/U6 x U5 tri- snRNP complex	0.042546738	cellular_component
GO:0006364	rRNA processing	0.044951812	biological_process
GO:0042169	SH2 domain binding	0.045037109	molecular_function
GO:0005507	copper ion binding	0.045037109	molecular_function
GO:0002376	immune system process	0.045211946	biological_process
GO:0009060	aerobic respiration	0.045211946	biological_process
GO:0022625	cytosolic large ribosomal subunit	0.047313886	cellular_component
GO:0005815	microtubule organizing center	0.047544031	cellular_component
GO:0002020	protease binding	0.048780132	molecular_function
GO:0090314	positive regulation of protein targeting to membrane	0.049023022	biological_process
GO:0030334	regulation of cell migration	0.049049454	biological_process

Table S5 : The KEGG enrichment analysis based on proteome profiling

Term_ID	Term_description	Enrichment_score	GeneSymbols	p-value
path:hsa03013	RNA transport	3.423 577	EIF2B5;UBE2I;EIF5;EIF2S2;EIF4EBP1;EIF2B1;XPOT;EIF1;EIF1AX;GEMIN4;RAN;EIF3F	0.000189
path:hsa00970	Aminoacyl-tRNA biosynthesis	6.458 111	GARS;EPRS;NARS;YARS;WARS;TARS	0.000292
path:hsa03010	Ribosome	3.534 289	RPLP1;RPS4X;RPS12;MRPL9;RPS18;RPL11;RPL24;RPL27A;RPL23;RPSA	0.000509
path:hsa00230	Purine metabolism	2.993 99	IMPDH2;POLR2L;ADK;PNP;AK1;HPRT1;ADSSL1;ITPA;NME1;NME7;APRT	0.001087
path:hsa00983	Drug metabolism - other enzymes	4.305 407	IMPDH2;TK1;CDA;HPRT1;ITPA;NME1;NME7	0.001138
path:hsa04216	Ferroptosis	5.919 935	ACSL5;TFRC;HMOX1;FTH1;SLC3A2	0.001425
path:hsa00270	Cysteine and methionine metabolism	5.038 242	MRI1;CTH;LDHB;AHCY;ADI1	0.002951
path:hsa00240	Pyrimidine metabolism	3.282 34	DTYMK;TK1;POLR2L;PNP;CDA;NME1;NME7	0.00535
path:hsa00260	Glycine, serine and threonine metabolism	4.735 948	SHMT2;PHGDH;CTH;PSAT1	0.009679
path:hsa03060	Protein export	6.177 323	SEC63;OXA1L;SRPRB	0.011992
path:hsa00450	Selenocompound metabolism	5.571 703	TXNRD1;CTH	0.048962
path:hsa00620	Pyruvate metabolism	3.551 961	GLO1;ACYP1;LDHB	0.051657
path:hsa05012	Parkinson disease	2.202 766	NDUFS7;HTRA2;PARK7;NDUFAB1;SLC25A6;CYCS	0.055019
path:hsa00565	Ether lipid metabolism	3.022 945	PAFAH1B2;PLPP2;PAFAH1B3	0.076325
path:hsa00900	Terpenoid backbone biosynthesis	4.305 407	PMVK;FNTA	0.077701
path:hsa00520	Amino sugar and nucleotide sugar metabolism	2.959 967	UAP1L1;GMPPA;GNPDA1	0.080207
path:hsa00510	N-Glycan biosynthesis	2.899 56	MGAT1;FUT8;ALG3	0.084172
path:hsa05110	Vibrio cholerae infection	2.841 569	SLC12A2;KDEL3;ATP6V1E1	0.088221
path:hsa05014	Amyotrophic lateral sclerosis (ALS)	2.841 569	DERL1;CCS;CYCS	0.088221
path:hsa04978	Mineral absorption	2.785 852	FTH1;MT2A;HMOX1	0.09235
path:hsa04146	Peroxisome	2.282 384	MPV17L2;PMVK;IDH1;ACSL5	0.097991

path:hsa 05134	Legionellosis	2.583 244	C3;CYCS;HSPA8	0.109636
path:hsa 00750	Vitamin B6 metabolism	7.893 246	PSAT1	0.120228
path:hsa 01523	Antifolate resistance	3.055 45	SHMT2;GGH	0.138627
path:hsa 00020	Citrate cycle (TCA cycle)	3.055 45	IDH1;SUCLA2	0.138627
path:hsa 05146	Amoebiasis	1.994 083	VCL;COL4A2;HSPB1;SERPINB6	0.140794
path:hsa 00640	Propanoate metabolism	2.959 967	LDHB;SUCLA2	0.145917
path:hsa 04215	Apoptosis - multiple species	2.870 271	HTRA2;CYCS	0.153285
path:hsa 05230	Central carbon metabolism in cancer	2.185 822	IDH1;SLC1A5;SLC7A5	0.15757
path:hsa 05131	Shigellosis	2.185 822	VCL;U2AF1L5;CRKL	0.15757
path:hsa 00250	Alanine, aspartate and glutamate metabolism	2.706 256	ADSSL1;ASNS	0.168229
path:hsa 04145	Phagosome	1.599 982	TUBB;C3;TUBB4B;ATP6V1E1;TFRC	0.202883
path:hsa 00130	Ubiquinone and other terpenoid- quinone biosynthesis	4.305 407	GGCX	0.209364
path:hsa 00860	Porphyrin and chlorophyll metabolism	2.255 213	HMOX1;EPRS	0.222099
path:hsa 00061	Fatty acid biosynthesis	3.643 037	ACSL5	0.242452
path:hsa 00190	Oxidative phosphorylation	1.578 649	NDUFAB1;NDUFS7;PPA1;ATP6V1E1	0.247698
path:hsa 00533	Glycosaminoglyca n biosynthesis - keratan sulfate	3.382 82	FUT8	0.258476
path:hsa 00600	Sphingolipid metabolism	2.015 297	PLPP2;SGPL1	0.261369
path:hsa 04012	ErbB signaling pathway	1.671 511	CRKL;PAK4;EIF4EBP1	0.267017
path:hsa 05164	Influenza A	1.401 168	STAT2;SLC25A6;CYCS;HSPA8;KPN A2	0.285607
path:hsa 05170	Human immunodeficiency virus 1 infection	1.346 715	CRKL;PAK4;APOBEC3B;CYCS;BST 2;CFL1	0.286994
path:hsa 00730	Thiamine metabolism	2.959 967	AK1	0.289522
path:hsa 04974	Protein digestion and absorption	1.578 649	COL4A2;SLC3A2;SLC1A5	0.295867
path:hsa 04666	Fc gamma R- mediated phagocytosis	1.578 649	PLPP2;CFL1;CRKL	0.295867
path:hsa	Phenylalanine	2.785	MIF	0.304557

00360	metabolism	852		
path:hsa 00480	Glutathione metabolism	1.787 15	GGCT;IDH1	0.308544
path:hsa 03040	Spliceosome	1.424 345	U2AF1L5;SNRPE;LSM3;HSPA8	0.308993
path:hsa 04120	Ubiquitin mediated proteolysis	1.392 926	UBE3C;UBE2Q1;UBE4A;UBE2I	0.323396
path:hsa 05130	Pathogenic Escherichia coli infection	1.722 163	TUBB4B;TUBB	0.324166
path:hsa 00770	Pantothenate and CoA biosynthesis	2.492 604	PPCS	0.333685
path:hsa 00670	One carbon pool by folate	2.367 974	SHMT2	0.347791
path:hsa 04066	HIF-1 signaling pathway	1.420 784	TFRC;HMOX1;EIF4EBP1	0.353957
path:hsa 00310	Lysine degradation	1.605 406	NSD1;SETD7	0.355122
path:hsa 05016	Huntington disease	1.266 296	NDUFS7;POLR2L;NDUFAB1;SLC25 A6;CYCS	0.360793
path:hsa 00561	Glycerolipid metabolism	1.552 77	GK;PLPP2	0.370418
path:hsa 03430	Mismatch repair	2.059 108	LIG1	0.388355
path:hsa 05206	MicroRNAs in cancer	1.262 919	UBE2I;CRKL;HMOX1;PAK4	0.390917
path:hsa 04150	mTOR signaling pathway	1.254 556	SLC3A2;SLC7A5;ATP6V1E1;EIF4EB P1	0.395726
path:hsa 04510	Focal adhesion	1.189 937	FLNA;PAK4;COL4A2;VCL;CRKL	0.411444
path:hsa 00790	Folate biosynthesis	1.821 518	GGH	0.42641
path:hsa 04218	Cellular senescence	1.198 974	MCU;SLC25A6;SQSTM1;EIF4EBP1	0.429198
path:hsa 05211	Renal cell carcinoma	1.372 738	CRKL;PAK4	0.43003
path:hsa 04966	Collecting duct acid secretion	1.754 055	ATP6V1E1	0.438565
path:hsa 01040	Biosynthesis of unsaturated fatty acids	1.754 055	HSD17B12	0.438565
path:hsa 04217	Necroptosis	1.169 37	STAT2;SLC25A6;SQSTM1;FTH1	0.448121
path:hsa 04141	Protein processing in endoplasmic reticulum	1.155 109	DERL1;UBQLN1;HSPA8;SEC63	0.457512
path:hsa 05010	Alzheimer disease	1.155 109	NDUFS7;NDUFAB1;CDK5;CYCS	0.457512
path:hsa 05100	Bacterial invasion of epithelial cells	1.279 986	VCL;CRKL	0.465763
path:hsa 00562	Inositol phosphate metabolism	1.279 986	INPP1;PI4KB	0.465763
path:hsa 03320	PPAR signaling pathway	1.279 986	GK;ACSL5	0.465763

path:hsa 00062	Fatty acid elongation	1.578 649	HSD17B12	0.473516
path:hsa 00630	Glyoxylate and dicarboxylate metabolism	1.578 649	SHMT2	0.473516
path:hsa 00030	Pentose phosphate pathway	1.578 649	TALDO1	0.473516
path:hsa 00760	Nicotinate and nicotinamide metabolism	1.578 649	PNP	0.473516
path:hsa 05133	Pertussis	1.246 302	CFL1;C3	0.479686
path:hsa 03020	RNA polymerase	1.527 725	POLR2L	0.484679
path:hsa 03018	RNA degradation	1.198 974	DHX36;LSM3	0.500153
path:hsa 00051	Fructose and mannose metabolism	1.435 136	GMPPA	0.506305
path:hsa 03410	Base excision repair	1.435 136	LIG1	0.506305
path:hsa 03008	Ribosome biogenesis in eukaryotes	1.169 37	RAN;UTP4	0.51351
path:hsa 05143	African trypanosomiasis	1.392 926	HBB	0.516777
path:hsa 05162	Measles	1.084 568	STAT2;RACK1;HSPA8	0.526044
path:hsa 03030	DNA replication	1.315 541	LIG1	0.537063
path:hsa 00350	Tyrosine metabolism	1.315 541	MIF	0.537063
path:hsa 04210	Apoptosis	1.052 433	HTRA2;CTSD;CYCS	0.546492
path:hsa 05418	Fluid shear stress and atherosclerosis	1.044 694	TXN;SQSTM1;HMOX1	0.551524
path:hsa 04915	Estrogen signaling pathway	1.044 694	KRT17;CTSD;HSPA8	0.551524
path:hsa 04910	Insulin signaling pathway	1.037 069	PRKAR2A;CRKL;EIF4EBP1	0.556524
path:hsa 04540	Gap junction	1.076 352	TUBB4B;TUBB	0.558387
path:hsa 04975	Fat digestion and absorption	1.155 109	PLPP2	0.584154
path:hsa 05222	Small cell lung cancer	1.018 483	COL4A2;CYCS	0.588611
path:hsa 04932	Non-alcoholic fatty liver disease (NAFLD)	0.979 851	NDUFAB1;NDUFS7;CYCS	0.595308
path:hsa 00071	Fatty acid degradation	1.076 352	ACSL5	0.610091
path:hsa 03022	Basal transcription factors	1.076 352	TAF15	0.610091
path:hsa	Vasopressin-	1.076	DYNLL2	0.610091

04962	regulated water reabsorption	352		
path:hsa 03050	Proteasome	1.052 433	PSMF1	0.618374
path:hsa 05231	Choline metabolism in cancer	0.956 757	PLPP2;EIF4EBP1	0.622835
path:hsa 04070	Phosphatidylinositol signaling system	0.956 757	INPP1;PI4KB	0.622835
path:hsa 03420	Nucleotide excision repair	1.029 554	LIG1	0.626482
path:hsa 04330	Notch signaling pathway	0.986 656	NUMB	0.642189
path:hsa 05030	Cocaine addiction	0.966 52	CDK5	0.649795
path:hsa 05144	Malaria	0.966 52	HBB	0.649795
path:hsa 04810	Regulation of actin cytoskeleton	0.889 38	VCL;CRKL;CFL1;PAK4	0.663739
path:hsa 05150	Staphylococcus aureus infection	0.910 759	C3	0.671661
path:hsa 04714	Thermogenesis	0.877 027	NDUFAB1;NDUFS7;COX20;ACSL5	0.674508
path:hsa 05145	Toxoplasmosis	0.853 324	CYCS;HSPA8	0.684652
path:hsa 04621	NOD-like receptor signaling pathway	0.850 769	TXN;MCU;STAT2	0.690188
path:hsa 05416	Viral myocarditis	0.845 705	CYCS	0.69872
path:hsa 04071	Sphingolipid signaling pathway	0.802 703	CTSD;SGPL1	0.716754
path:hsa 04370	VEGF signaling pathway	0.802 703	HSPB1	0.71755
path:hsa 04360	Axon guidance	0.811 877	CDK5;CFL1;PAK4	0.720302
path:hsa 05152	Tuberculosis	0.811 877	C3;CYCS;CTSD	0.720302
path:hsa 00140	Steroid hormone biosynthesis	0.789 325	HSD17B12	0.723563
path:hsa 04152	AMPK signaling pathway	0.789 325	EEF2;EIF4EBP1	0.725411
path:hsa 04213	Longevity regulating pathway - multiple species	0.763 863	HSPA8	0.73521
path:hsa 04623	Cytosolic DNA-sensing pathway	0.763 863	POLR2L	0.73521
path:hsa 00590	Arachidonic acid metabolism	0.751 738	PTGES3	0.740849
path:hsa 04721	Synaptic vesicle cycle	0.751 738	ATP6V1E1	0.740849
path:hsa 04380	Osteoclast differentiation	0.757 752	STAT2;SQSTM1	0.746086
path:hsa	Herpes simplex	0.776	STAT2;C3;CYCS	0.748115

05168	infection	385		
path:hsa 04137	Mitophagy - animal	0.728 607	SQSTM1	0.751772
path:hsa 05202	Transcriptional misregulation in cancer	0.767 992	FUT8;MLLT1;TAF15	0.754716
path:hsa 05221	Acute myeloid leukemia	0.717 568	EIF4EBP1	0.757061
path:hsa 05167	Kaposi sarcoma- associated herpesvirus infection	0.763 863	STAT2;C3;CYCS	0.757965
path:hsa 05322	Systemic lupus erythematosus	0.728 607	C3;HIST3H2BB	0.765421
path:hsa 05120	Epithelial cell signaling in Helicobacter pylori infection	0.696 463	ATP6V1E1	0.767305
path:hsa 04920	Adipocytokine signaling pathway	0.686 369	ACSL5	0.772265
path:hsa 00010	Glycolysis / Gluconeogenesis	0.686 369	LDHB	0.772265
path:hsa 04612	Antigen processing and presentation	0.686 369	HSPA8	0.772265
path:hsa 05140	Leishmaniasis	0.676 564	C3	0.77712
path:hsa 01524	Platinum drug resistance	0.667 035	CYCS	0.781872
path:hsa 04115	p53 signaling pathway	0.657 771	CYCS	0.786523
path:hsa 04520	Adherens junction	0.657 771	VCL	0.786523
path:hsa 00980	Metabolism of xenobiotics by cytochrome P450	0.657 771	AKR7A2	0.786523
path:hsa 04723	Retrograde endocannabinoid signaling	0.671 766	NDUFAB1;NDUFS7	0.803529
path:hsa 05220	Chronic myeloid leukemia	0.623 151	CRKL	0.804164
path:hsa 05161	Hepatitis B	0.662 37	STAT2;CYCS	0.809841
path:hsa 01521	EGFR tyrosine kinase inhibitor resistance	0.599 487	EIF4EBP1	0.816437
path:hsa 04610	Complement and coagulation cascades	0.599 487	C3	0.816437
path:hsa 04512	ECM-receptor interaction	0.577 555	COL4A2	0.827945
path:hsa 05132	Salmonella infection	0.563 803	FLNA	0.835216
path:hsa 04911	Insulin secretion	0.557 17	GLP1R	0.838736

path:hsa 05323	Rheumatoid arthritis	0.550 692	ATP6V1E1	0.842182
path:hsa 05210	Colorectal cancer	0.550 692	CYCS	0.842182
path:hsa 04211	Longevity regulating pathway	0.532 129	EIF4EBP1	0.852086
path:hsa 04970	Salivary secretion	0.526 216	SLC12A2	0.855248
path:hsa 05163	Human cytomegalovirus infection	0.637 123	CRKL;CYCS;EIF4EBP1	0.855615
path:hsa 04064	NF-kappa B signaling pathway	0.509 242	UBE2I	0.864337
path:hsa 04640	Hematopoietic cell lineage	0.503 824	TFRC	0.867238
path:hsa 05225	Hepatocellular carcinoma	0.574 054	TXNRD1;HMOX1	0.868238
path:hsa 00564	Glycerophospholi pid metabolism	0.488 242	PLPP2	0.875579
path:hsa 04010	MAPK signaling pathway	0.642 162	HSPB1;CRKL;FLNA;HSPA8	0.876041
path:hsa 04972	Pancreatic secretion	0.483 26	SLC12A2	0.878242
path:hsa 04914	Progesterone- mediated oocyte maturation	0.478 379	KIF22	0.880848
path:hsa 04933	AGE-RAGE signaling pathway in diabetic complications	0.478 379	COL4A2	0.880848
path:hsa 05142	Chagas disease (American trypanosomiasis)	0.468 906	C3	0.885895
path:hsa 04660	T cell receptor signaling pathway	0.468 906	PAK4	0.885895
path:hsa 04922	Glucagon signaling pathway	0.459 801	LDHB	0.89073
path:hsa 04625	C-type lectin receptor signaling pathway	0.455 38	STAT2	0.89307
path:hsa 04144	Endocytosis	0.582 289	ARF3;TFRC;HSPA8	0.894214
path:hsa 04020	Calcium signaling pathway	0.520 434	MCU;SLC25A6	0.901611
path:hsa 05166	Human T-cell leukemia virus 1 infection	0.561 575	RAN;BUB1B;SLC25A6	0.907738
path:hsa 04062	Chemokine signaling pathway	0.506 518	STAT2;CRKL	0.909824
path:hsa 04670	Leukocyte transendothelial migration	0.422 852	VCL	0.910087
path:hsa 04722	Neurotrophin signaling pathway	0.397 979	CRKL	0.922752

path:hsa 05169	Epstein-Barr virus infection	0.478 379	STAT2;CYCS	0.925697
path:hsa 05203	Viral carcinogenesis	0.473 595	C3;HIST3H2BB	0.928286
path:hsa 04142	Lysosome	0.385 036	CTSD	0.929176
path:hsa 04110	Cell cycle	0.381 931	BUB1B	0.930698
path:hsa 05165	Human papillomavirus infection	0.558 814	STAT2;COL4A2;ATP6V1E1;EIF4EBP 1	0.932781
path:hsa 04140	Autophagy - animal	0.369 996	CTSD	0.936465
path:hsa 04926	Relaxin signaling pathway	0.364 304	COL4A2	0.939167
path:hsa 05160	Hepatitis C	0.361 523	STAT2	0.940475
path:hsa 04068	FoxO signaling pathway	0.358 784	SETD7	0.941755
path:hsa 04072	Phospholipase D signaling pathway	0.326 617	PLPP2	0.956106
path:hsa 04921	Oxytocin signaling pathway	0.311 576	EEF2	0.962316
path:hsa 05200	Pathways in cancer	0.543 321	STAT2;TXNRD1;COL4A2;HMOX1;C YCS;CRKL	0.969443
path:hsa 04630	Jak-STAT signaling pathway	0.292 342	STAT2	0.969703
path:hsa 04022	cGMP-PKG signaling pathway	0.290 549	SLC25A6	0.970357
path:hsa 05034	Alcoholism	0.263 108	HIST3H2BB	0.979559
path:hsa 05205	Proteoglycans in cancer	0.239 189	FLNA	0.986222
path:hsa 04024	cAMP signaling pathway	0.237 987	GLP1R	0.986521
path:hsa 04015	Rap1 signaling pathway	0.229 9	CRKL	0.988442
path:hsa 04014	Ras signaling pathway	0.204 136	PAK4	0.993479
path:hsa 04151	PI3K-Akt signaling pathway	0.268 326	COL4A2;EIF4EBP1	0.996019
path:hsa 04080	Neuroactive ligand-receptor interaction	0.155 277	GLP1R	0.998707

The raw data of metabolomics and proteomics were uploaded as well.

The contents are listed below:

metabonomic raw data-negative-hilic-blank-fa30.xlsx

metabonomic raw data-negative-reverse phase-blank-fa30.xlsx

metabonomic raw data-positive-hilic-blank-fa30.xlsx

metabonomic raw data- positive -reverse phase-blank-fa30.xlsx

proteomics data-iTRAQ 8plex -blank-fa30.xlsx

Mendeley Data repository (wang, dongyao (2022), “Metabolomics and Proteomics Research of FA-30”, Mendeley Data, V1, doi: 10.17632/mkrzs2rsm4.1).