

Table S1 Background of plasma samples in the discovery and validation sets.

Discovery Set			
No.	Age (year)	Gender	Disease
1	47	Female	Papillary Thyroid Carcinoma
2	28	Female	Papillary Thyroid Carcinoma
3	26	Female	Papillary Thyroid Carcinoma
4	37	Female	Papillary Thyroid Carcinoma
5	31	Female	Papillary Thyroid Carcinoma
6	46	Female	Papillary Thyroid Carcinoma
7	50	Female	Papillary Thyroid Carcinoma
8	32	Female	Papillary Thyroid Carcinoma
9	49	Female	Papillary Thyroid Carcinoma
10	30	Female	Papillary Thyroid Carcinoma
11	22	Female	Multinodular Goiter
12	23	Female	Multinodular Goiter
13	27	Female	Multinodular Goiter
14	31	Female	Multinodular Goiter
15	32	Female	Multinodular Goiter
16	36	Female	Multinodular Goiter
17	37	Female	Multinodular Goiter
18	43	Female	Multinodular Goiter
19	45	Female	Multinodular Goiter
20	47	Female	Multinodular Goiter
21	48	Female	Multinodular Goiter
22	49	Female	Multinodular Goiter
23	49	Female	Multinodular Goiter
24	49	Female	Multinodular Goiter
25	50	Female	Multinodular Goiter
Validation Set			
No.	Age	Gender	Disease
1	64	Female	Papillary Thyroid Carcinoma
2	31	Female	Papillary Thyroid Carcinoma
3	67	Female	Papillary Thyroid Carcinoma
4	56	Male	Papillary Thyroid Carcinoma
5	64	Female	Papillary Thyroid Carcinoma
6	28	Female	Papillary Thyroid Carcinoma
7	65	Male	Papillary Thyroid Carcinoma
8	46	Female	Papillary Thyroid Carcinoma
9	47	Female	Papillary Thyroid Carcinoma
10	48	Female	Papillary Thyroid Carcinoma
11	66	Female	Multinodular Goiter
12	58	Female	Multinodular Goiter
13	29	Female	Multinodular Goiter

14	31	Female	Multinodular Goiter
15	64	Female	Multinodular Goiter
16	46	Female	Multinodular Goiter
17	47	Female	Multinodular Goiter
18	69	Male	Multinodular Goiter
19	65	Female	Multinodular Goiter
20	49	Female	Multinodular Goiter

Table S2 Differentially expressed proteins.

UniProt ID	Symbol ID	Descriptions	p value	log2FC
P01024	C3	Complement C3	1.96E-02	0.24
P02533	KRT14	Keratin, type I cytoskeletal 14	1.73E-03	-1.67
P02741	CRP	C-reactive protein	4.36E-02	2.72
P02748	C9	Complement component C9	8.67E-03	0.57
P04180	LCAT	Phosphatidylcholine-sterol acyltransferase	3.32E-02	-0.30
P04264	KRT1	Keratin, type II cytoskeletal 1	4.47E-02	-1.28
P07360	C8G	Complement component C8 gamma chain	1.17E-02	-0.45
P12830	CDH1	Cadherin-1	4.29E-02	-0.37
P15144	ANPEP	Aminopeptidase N	4.13E-03	-0.53
P22352	GPX3	Glutathione peroxidase 3	3.09E-03	-0.39
P24158	PRTN3	Myeloblastin	1.88E-02	-0.80
P27169	PON1	Serum paraoxonase/arylesterase 1	3.92E-02	-0.29
P35527	KRT9	Keratin, type I cytoskeletal 9	1.33E-02	-2.02
Q03591	CFHR1	Complement factor H-related protein 1	2.71E-02	0.43
Q14623	IHH	Indian hedgehog protein	6.74E-03	-0.67
Q15848	ADIPOQ	Adiponectin	3.65E-02	0.72
Q6DHV5	CC2D2B	Protein CC2D2B	4.90E-02	-0.30
Q7Z794	KRT77	Keratin, type II cytoskeletal 1b	5.58E-04	-1.75
A0A125U0U6	NA	MS-A4 light chain variable region	1.28E-02	-0.64
A0A2U8J8H2	NA	Ig heavy chain variable region	4.23E-02	-0.78
A0A2U8J954	NA	Ig heavy chain variable region	2.77E-02	0.98

A0A5C2FVM9	NA	IGL c674_light_IGKV1D-13_IGKJ1	2.11E-02	-1.24
A0A5C2GBH4	NA	IGH c595_heavy_IGHV1-18_IGHD3-3_IGHJ6	7.19E-03	-0.53
A0A5C2GQG4	NA	IG c780_heavy_IGHV3-11_IGHD4-23_IGHJ4	3.06E-02	0.54
A2J1N0	NA	Rheumatoid factor RF-IP14	3.19E-02	0.44
A2J422	NA	Anti-HER3 scFv	3.19E-02	-0.47
A2N0U0	NA	VH6DJ protein	4.06E-02	-0.85
A2NB46	NA	Cold agglutinin FS-2 L-chain	3.93E-02	-0.36
A2NZ55	NA	Variable immunoglobulin anti-estradiol heavy chain	1.83E-02	-0.72
G3GAU4	NA	Anti-H1N1 influenza HA kappa chain variable region	1.45E-02	-0.70
Q56G89	NA	Serum albumin	1.13E-03	1.21
Q6DHW4	NA	Uncharacterized protein	3.70E-03	-2.09
Q6MZU6	NA	Uncharacterized protein DKFZp686C15213	4.84E-04	-2.35

Table S3 GO enrichment analysis results of biological process (qvalue < 0.05).

ID	Description	GeneRatio	BgRatio	pvalue	p.adjust	qvalue	geneID	Count
GO:0006956	complement activation	6/17	178/18866	7.36E-09	5.59E-06	3.23E-06	C3/CRP/C9/KRT1/C8G/CFHR1	6
GO:0006959	humoral immune response	7/17	377/18866	1.97E-08	7.49E-06	4.32E-06	C3/CRP/C9/KRT1/C8G/PRTN3/CFHR1	7
GO:0006957	complement activation, alternative pathway	3/17	17/18866	4.10E-07	1.04E-04	6.00E-05	C3/C9/C8G	3
GO:0019835	cytolysis	3/17	29/18866	2.19E-06	3.71E-04	2.15E-04	C9/C8G/CFHR1	3
GO:0070268	cornification	4/17	113/18866	2.73E-06	3.71E-04	2.15E-04	KRT14/KRT1/KRT9/KRT77	4
GO:0030449	regulation of complement activation	4/17	115/18866	2.93E-06	3.71E-04	2.15E-04	C3/C9/C8G/CFHR1	4
GO:0002920	regulation of humoral immune response	4/17	134/18866	5.39E-06	5.85E-04	3.38E-04	C3/C9/C8G/CFHR1	4
GO:0006958	complement activation, classical pathway	4/17	141/18866	6.60E-06	6.27E-04	3.62E-04	C3/CRP/C9/C8G	4
GO:0002455	humoral immune response mediated by circulating immunoglobulin	4/17	155/18866	9.60E-06	8.10E-04	4.68E-04	C3/CRP/C9/C8G	4
GO:1905952	regulation of lipid localization	4/17	171/18866	1.41E-05	1.07E-03	6.21E-04	C3/CRP/PON1/ADIPOQ	4
GO:0010876	lipid localization	5/17	440/18866	3.31E-05	2.29E-03	1.32E-03	C3/CRP/LCAT/PON1/ADIPOQ	5
GO:0031424	keratinization	4/17	225/18866	4.15E-05	2.45E-03	1.42E-03	KRT14/KRT1/KRT9/KRT77	4
GO:0016064	immunoglobulin mediated immune	4/17	227/18866	4.30E-05	2.45E-03	1.42E-03	C3/CRP/C9/C8G	4

GO:0019724	response B cell mediated immunity	4/17	230/18866	4.52E-05	2.45E-03	1.42E-03	C3/CRP/C9/C8G	4
GO:0010745	negative regulation of macrophage derived foam cell differentiation	2/17	13/18866	5.93E-05	3.00E-03	1.73E-03	CRP/ADIPOQ	2
GO:1905954	positive regulation of lipid localization	3/17	94/18866	7.74E-05	3.68E-03	2.12E-03	C3/PON1/ADIPOQ	3
GO:0050764	regulation of phagocytosis	3/17	97/18866	8.50E-05	3.80E-03	2.20E-03	C3/PRTN3/ADIPOQ	3
GO:0030301	cholesterol transport	3/17	105/18866	1.08E-04	4.54E-03	2.62E-03	LCAT/PON1/ADIPOQ	3
GO:0030216	keratinocyte differentiation	4/17	306/18866	1.37E-04	5.47E-03	3.16E-03	KRT14/KRT1/KRT9/KRT77	4
GO:0010875	positive regulation of cholesterol efflux	2/17	20/18866	1.44E-04	5.47E-03	3.16E-03	PON1/ADIPOQ	2
GO:0015918	sterol transport	3/17	118/18866	1.52E-04	5.51E-03	3.18E-03	LCAT/PON1/ADIPOQ	3
GO:0050765	negative regulation of phagocytosis	2/17	22/18866	1.75E-04	6.03E-03	3.49E-03	PRTN3/ADIPOQ	2
GO:0045109	intermediate filament organization	2/17	25/18866	2.26E-04	7.48E-03	4.32E-03	KRT14/KRT9	2
GO:0009913	epidermal cell differentiation	4/17	365/18866	2.69E-04	8.25E-03	4.77E-03	KRT14/KRT1/KRT9/KRT77	4
GO:0002449	lymphocyte mediated immunity	4/17	366/18866	2.71E-04	8.25E-03	4.77E-03	C3/CRP/C9/C8G	4
GO:0002460	adaptive immune response based on	4/17	370/18866	2.83E-04	8.27E-03	4.78E-03	C3/CRP/C9/C8G	4

	somatic recombination of immune receptors built from immunoglobulin superfamily domains								
GO:0032373	positive regulation of sterol transport	2/17	29/18866	3.06E-04	8.30E-03	4.80E-03	PON1/ADIPOQ		2
GO:0032376	positive regulation of cholesterol transport	2/17	29/18866	3.06E-04	8.30E-03	4.80E-03	PON1/ADIPOQ		2
GO:0006909	phagocytosis	4/17	382/18866	3.20E-04	8.37E-03	4.84E-03	C3/CRP/PRTN3/ADIPOQ		4
GO:0010743	regulation of macrophage derived foam cell differentiation	2/17	32/18866	3.73E-04	9.45E-03	5.46E-03	CRP/ADIPOQ		2
GO:0001906	cell killing	3/17	172/18866	4.61E-04	1.13E-02	6.53E-03	C3/C9/CFHR1		3
GO:0043588	skin development	4/17	425/18866	4.79E-04	1.14E-02	6.57E-03	KRT14/KRT1/KRT9/KRT77		4
GO:0010742	macrophage derived foam cell differentiation	2/17	38/18866	5.27E-04	1.18E-02	6.81E-03	CRP/ADIPOQ		2
GO:0090077	foam cell differentiation	2/17	38/18866	5.27E-04	1.18E-02	6.81E-03	CRP/ADIPOQ		2
GO:0022408	negative regulation of cell-cell adhesion	3/17	191/18866	6.26E-04	1.36E-02	7.85E-03	CDH1/IHH/ADIPOQ		3
GO:0002697	regulation of immune effector process	4/17	470/18866	6.99E-04	1.48E-02	8.53E-03	C3/C9/C8G/CFHR1		4
GO:0008544	epidermis development	4/17	477/18866	7.39E-04	1.48E-02	8.54E-03	KRT14/KRT1/KRT9/KRT77		4
GO:0010828	positive regulation of glucose transmembrane transport	2/17	45/18866	7.40E-04	1.48E-02	8.54E-03	C3/ADIPOQ		2
GO:0010874	regulation of cholesterol	2/17	46/18866	7.73E-04	1.51E-02	8.70E-03	PON1/ADIPOQ		2

	efflux								
GO:0043312	neutrophil degranulation	4/17	487/18866	7.99E-04	1.52E-02	8.75E-03	C3/KRT1/ANPEP/PRTN3	4	
GO:0002283	neutrophil activation involved in immune response	4/17	490/18866	8.17E-04	1.52E-02	8.75E-03	C3/KRT1/ANPEP/PRTN3	4	
GO:0045104	intermediate filament cytoskeleton organization	2/17	50/18866	9.13E-04	1.65E-02	9.54E-03	KRT14/KRT9	2	
GO:0045103	intermediate filament- based process	2/17	51/18866	9.49E-04	1.68E-02	9.69E-03	KRT14/KRT9	2	
GO:0010883	regulation of lipid storage	2/17	52/18866	9.87E-04	1.70E-02	9.85E-03	C3/CRP	2	
GO:0009636	response to toxic substance	3/17	250/18866	1.36E-03	2.30E-02	1.33E-02	CDH1/GPX3/PON1	3	
GO:0033344	cholesterol efflux	2/17	64/18866	1.49E-03	2.46E-02	1.42E-02	PON1/ADIPOQ	2	
GO:0015850	organic hydroxy compound transport	3/17	268/18866	1.66E-03	2.69E-02	1.55E-02	LCAT/PON1/ADIPOQ	3	
GO:0032370	positive regulation of lipid transport	2/17	70/18866	1.78E-03	2.76E-02	1.59E-02	PON1/ADIPOQ	2	
GO:0032374	regulation of cholesterol transport	2/17	70/18866	1.78E-03	2.76E-02	1.59E-02	PON1/ADIPOQ	2	
GO:0032371	regulation of sterol transport	2/17	71/18866	1.83E-03	2.78E-02	1.61E-02	PON1/ADIPOQ	2	
GO:0010827	regulation of glucose transmembrane transport	2/17	79/18866	2.26E-03	3.32E-02	1.92E-02	C3/ADIPOQ	2	
GO:0007162	negative regulation of cell adhesion	3/17	301/18866	2.32E-03	3.32E-02	1.92E-02	CDH1/IHH/ADIPOQ	3	

GO:0032945	negative regulation of mononuclear cell proliferation	2/17	80/18866	2.32E-03	3.32E-02	1.92E-02	CRP/IHH	2
GO:0019915	lipid storage	2/17	81/18866	2.37E-03	3.34E-02	1.93E-02	C3/CRP	2
GO:0070664	negative regulation of leukocyte proliferation	2/17	86/18866	2.67E-03	3.69E-02	2.13E-02	CRP/IHH	2
GO:0046470	phosphatidylcholine metabolic process	2/17	88/18866	2.80E-03	3.79E-02	2.19E-02	LCAT/PON1	2
GO:0070542	response to fatty acid	2/17	90/18866	2.92E-03	3.90E-02	2.25E-02	PON1/ADIPOQ	2
GO:0032677	regulation of interleukin-8 production	2/17	93/18866	3.12E-03	4.01E-02	2.32E-02	CRP/ADIPOQ	2
GO:0051702	interaction with symbiont	2/17	93/18866	3.12E-03	4.01E-02	2.32E-02	CRP/CFHR1	2
GO:0032637	interleukin-8 production	2/17	101/18866	3.66E-03	4.64E-02	2.68E-02	CRP/ADIPOQ	2
GO:0097006	regulation of plasma lipoprotein particle levels	2/17	105/18866	3.95E-03	4.81E-02	2.78E-02	LCAT/ADIPOQ	2
GO:1902106	negative regulation of leukocyte differentiation	2/17	105/18866	3.95E-03	4.81E-02	2.78E-02	IHH/ADIPOQ	2
GO:0032091	negative regulation of protein binding	2/17	106/18866	4.03E-03	4.81E-02	2.78E-02	CFHR1/ADIPOQ	2
GO:0051098	regulation of binding	3/17	367/18866	4.05E-03	4.81E-02	2.78E-02	PON1/CFHR1/ADIPOQ	3

Table S4 GO enrichment analysis results of cellular component.

ID	Description	GeneRatio	BgRatio	pvalue	p.adjust	qvalue	geneID	Count
GO:0072562	blood microparticle	6/17	148/19559	1.96E-09	1.02E-07	5.98E-08	C3/C9/KRT1/C8G/PON1/CFHR1	6
GO:0005882	intermediate filament	4/17	215/19559	3.02E-05	7.85E-04	4.61E-04	KRT14/KRT1/KRT9/KRT77	4
GO:0045111	intermediate filament cytoskeleton	4/17	251/19559	5.53E-05	9.34E-04	5.48E-04	KRT14/KRT1/KRT9/KRT77	4
GO:0045095	keratin filament	3/17	95/19559	7.18E-05	9.34E-04	5.48E-04	KRT14/KRT1/KRT77	3
GO:0046930	pore complex	2/17	23/19559	1.78E-04	1.85E-03	1.09E-03	C9/C8G	2
GO:0034364	high-density lipoprotein particle	2/17	27/19559	2.46E-04	2.14E-03	1.25E-03	LCAT/PON1	2
GO:0034358	plasma lipoprotein particle	2/17	36/19559	4.40E-04	2.86E-03	1.68E-03	LCAT/PON1	2
GO:1990777	lipoprotein particle	2/17	36/19559	4.40E-04	2.86E-03	1.68E-03	LCAT/PON1	2
GO:0032994	protein-lipid complex	2/17	39/19559	5.17E-04	2.99E-03	1.75E-03	LCAT/PON1	2
GO:0035578	azurophil granule lumen	2/17	91/19559	2.78E-03	1.45E-02	8.49E-03	C3/PRTN3	2
GO:0044853	plasma membrane raft	2/17	113/19559	4.25E-03	2.01E-02	1.18E-02	CDH1/PRTN3	2
GO:0062023	collagen-containing extracellular matrix	3/17	427/19559	5.59E-03	2.42E-02	1.42E-02	KRT1/PRTN3/ADIPOQ	3
GO:0005766	primary lysosome	2/17	155/19559	7.85E-03	2.92E-02	1.71E-02	C3/PRTN3	2
GO:0042582	azurophil granule	2/17	155/19559	7.85E-03	2.92E-02	1.71E-02	C3/PRTN3	2
GO:0005775	vacuolar lumen	2/17	173/19559	9.69E-03	3.36E-02	1.97E-02	C3/PRTN3	2
GO:0016342	catenin complex	1/17	31/19559	2.66E-02	8.09E-02	4.75E-02	CDH1	1
GO:0034774	secretory granule lumen	2/17	322/19559	3.12E-02	8.09E-02	4.75E-02	C3/PRTN3	2
GO:0060205	cytoplasmic vesicle lumen	2/17	326/19559	3.19E-02	8.09E-02	4.75E-02	C3/PRTN3	2
GO:0031983	vesicle lumen	2/17	328/19559	3.23E-02	8.09E-02	4.75E-02	C3/PRTN3	2
GO:0045121	membrane raft	2/17	329/19559	3.25E-02	8.09E-02	4.75E-02	CDH1/PRTN3	2

GO:0098857	membrane microdomain	2/17	330/19559	3.27E-02	8.09E-02	4.75E-02	CDH1/PRTN3	2
GO:0098589	membrane region	2/17	343/19559	3.51E-02	8.29E-02	4.86E-02	CDH1/PRTN3	2
GO:0001533	cornified envelope	1/17	45/19559	3.84E-02	8.69E-02	5.10E-02	KRT1	1
GO:0016328	lateral plasma membrane	1/17	65/19559	5.50E-02	1.19E-01	7.00E-02	CDH1	1
GO:0045178	basal part of cell	1/17	69/19559	5.83E-02	1.21E-01	7.12E-02	KRT14	1
GO:0030864	cortical actin cytoskeleton	1/17	80/19559	6.73E-02	1.33E-01	7.80E-02	CDH1	1
GO:0005901	caveola	1/17	82/19559	6.90E-02	1.33E-01	7.80E-02	CDH1	1
GO:0005581	collagen trimer	1/17	87/19559	7.30E-02	1.36E-01	7.96E-02	ADIPOQ	1
GO:0030863	cortical cytoskeleton	1/17	106/19559	8.83E-02	1.58E-01	9.29E-02	CDH1	1
GO:0101002	ficolin-1-rich granule	1/17	124/19559	1.03E-01	1.72E-01	1.01E-01	KRT1	1
GO:1904813	ficolin-1-rich granule lumen	1/17	124/19559	1.03E-01	1.72E-01	1.01E-01	KRT1	1
GO:0005793	endoplasmic reticulum-Golgi intermediate compartment	1/17	130/19559	1.07E-01	1.74E-01	1.02E-01	ANPEP	1
GO:0043296	apical junction complex	1/17	143/19559	1.17E-01	1.85E-01	1.09E-01	CDH1	1
GO:0009898	cytoplasmic side of plasma membrane	1/17	164/19559	1.33E-01	2.00E-01	1.18E-01	CDH1	1
GO:0005912	adherens junction	1/17	166/19559	1.35E-01	2.00E-01	1.18E-01	CDH1	1
GO:0019897	extrinsic component of plasma membrane	1/17	172/19559	1.39E-01	2.01E-01	1.18E-01	CDH1	1
GO:0098562	cytoplasmic side of membrane	1/17	188/19559	1.51E-01	2.13E-01	1.25E-01	CDH1	1
GO:0030027	lamellipodium	1/17	201/19559	1.61E-01	2.20E-01	1.29E-01	CDH1	1
GO:0005802	trans-Golgi network	1/17	245/19559	1.93E-01	2.57E-01	1.51E-01	CDH1	1
GO:0005938	cell cortex	1/17	305/19559	2.35E-01	2.86E-01	1.68E-01	CDH1	1
GO:0019898	extrinsic component of membrane	1/17	306/19559	2.35E-01	2.86E-01	1.68E-01	CDH1	1
GO:0030667	secretory granule membrane	1/17	306/19559	2.35E-01	2.86E-01	1.68E-01	ANPEP	1

GO:0005788	endoplasmic reticulum lumen	1/17	308/19559	2.37E-01	2.86E-01	1.68E-01	C3	1
GO:0098978	glutamatergic synapse	1/17	361/19559	2.72E-01	3.10E-01	1.82E-01	CDH1	1
GO:0098791	Golgi apparatus subcompartment	1/17	368/19559	2.76E-01	3.10E-01	1.82E-01	CDH1	1
GO:0005765	lysosomal membrane	1/17	375/19559	2.81E-01	3.10E-01	1.82E-01	ANPEP	1
GO:0098852	lytic vacuole membrane	1/17	375/19559	2.81E-01	3.10E-01	1.82E-01	ANPEP	1
GO:0031984	organelle subcompartment	1/17	392/19559	2.91E-01	3.16E-01	1.85E-01	CDH1	1
GO:0009897	external side of plasma membrane	1/17	417/19559	3.07E-01	3.19E-01	1.87E-01	ANPEP	1
GO:0031252	cell leading edge	1/17	421/19559	3.09E-01	3.19E-01	1.87E-01	CDH1	1
GO:0005774	vacuolar membrane	1/17	427/19559	3.13E-01	3.19E-01	1.87E-01	ANPEP	1
GO:0005911	cell-cell junction	1/17	493/19559	3.52E-01	3.52E-01	2.07E-01	CDH1	1

Table S5 GO enrichment analysis results of molecular function.

ID	Description	GeneRatio	BgRatio	pvalue	p.adjust	qvalue	geneID	Count
GO:0001848	complement binding	2/16	21/18352	1.48E-04	9.49E-03	5.93E-03	CRP/C8G	2
GO:0005200	structural constituent of cytoskeleton	2/16	104/18352	3.62E-03	8.11E-02	5.07E-02	KRT14/KRT9	2
GO:0052689	carboxylic ester hydrolase activity	2/16	143/18352	6.74E-03	8.11E-02	5.07E-02	LCAT/PON1	2
GO:0045295	gamma-catenin binding	1/16	12/18352	1.04E-02	8.11E-02	5.07E-02	CDH1	1
GO:0030280	structural constituent of skin epidermis	1/16	14/18352	1.21E-02	8.11E-02	5.07E-02	KRT1	1
GO:0032794	GTPase activating protein binding	1/16	14/18352	1.21E-02	8.11E-02	5.07E-02	CDH1	1
GO:0001846	opsonin binding	1/16	15/18352	1.30E-02	8.11E-02	5.07E-02	CRP	1
GO:0019215	intermediate filament binding	1/16	15/18352	1.30E-02	8.11E-02	5.07E-02	KRT14	1
GO:0019841	retinol binding	1/16	16/18352	1.39E-02	8.11E-02	5.07E-02	C8G	1
GO:0030169	low-density lipoprotein particle binding	1/16	17/18352	1.47E-02	8.11E-02	5.07E-02	CRP	1
GO:0034185	apolipoprotein binding	1/16	17/18352	1.47E-02	8.11E-02	5.07E-02	LCAT	1
GO:0030506	ankyrin binding	1/16	20/18352	1.73E-02	8.11E-02	5.07E-02	CDH1	1
GO:0004602	glutathione peroxidase activity	1/16	21/18352	1.82E-02	8.11E-02	5.07E-02	GPX3	1
GO:0050750	low-density lipoprotein particle receptor binding	1/16	21/18352	1.82E-02	8.11E-02	5.07E-02	CRP	1
GO:0033691	sialic acid binding	1/16	22/18352	1.90E-02	8.11E-02	5.07E-02	ADIPOQ	1
GO:0070006	metalloaminopeptidase activity	1/16	24/18352	2.07E-02	8.29E-02	5.18E-02	ANPEP	1
GO:0070325	lipoprotein particle receptor binding	1/16	26/18352	2.24E-02	8.45E-02	5.28E-02	CRP	1
GO:0004806	triglyceride lipase activity	1/16	29/18352	2.50E-02	8.89E-02	5.55E-02	LCAT	1
GO:0071813	lipoprotein particle binding	1/16	34/18352	2.92E-02	9.25E-02	5.78E-02	CRP	1
GO:0071814	protein-lipid complex binding	1/16	34/18352	2.92E-02	9.25E-02	5.78E-02	CRP	1

GO:0005501	retinoid binding	1/16	36/18352	3.09E-02	9.25E-02	5.78E-02	C8G	1
GO:0019840	isoprenoid binding	1/16	37/18352	3.18E-02	9.25E-02	5.78E-02	C8G	1
GO:0004177	aminopeptidase activity	1/16	46/18352	3.94E-02	1.10E-01	6.85E-02	ANPEP	1
GO:0008374	O-acyltransferase activity	1/16	50/18352	4.27E-02	1.14E-01	7.10E-02	LCAT	1
GO:0004601	peroxidase activity	1/16	52/18352	4.44E-02	1.14E-01	7.10E-02	GPX3	1
GO:0016684	oxidoreductase activity, acting on peroxide as acceptor	1/16	56/18352	4.77E-02	1.18E-01	7.34E-02	GPX3	1
GO:0008235	metalloexopeptidase activity	1/16	64/18352	5.44E-02	1.29E-01	8.06E-02	ANPEP	1
GO:0001618	virus receptor activity	1/16	74/18352	6.26E-02	1.38E-01	8.64E-02	ANPEP	1
GO:0140272	exogenous protein binding	1/16	74/18352	6.26E-02	1.38E-01	8.64E-02	ANPEP	1
GO:0008013	beta-catenin binding	1/16	85/18352	7.16E-02	1.45E-01	9.05E-02	CDH1	1
GO:0016209	antioxidant activity	1/16	86/18352	7.24E-02	1.45E-01	9.05E-02	GPX3	1
GO:0043178	alcohol binding	1/16	86/18352	7.24E-02	1.45E-01	9.05E-02	C8G	1
GO:0008238	exopeptidase activity	1/16	95/18352	7.97E-02	1.55E-01	9.66E-02	ANPEP	1
GO:0016407	acetyltransferase activity	1/16	105/18352	8.78E-02	1.65E-01	1.03E-01	LCAT	1
GO:0005179	hormone activity	1/16	122/18352	1.01E-01	1.85E-01	1.16E-01	ADIPOQ	1
GO:0016298	lipase activity	1/16	130/18352	1.08E-01	1.91E-01	1.20E-01	LCAT	1
GO:0019842	vitamin binding	1/16	144/18352	1.18E-01	2.05E-01	1.28E-01	C8G	1
GO:0004252	serine-type endopeptidase activity	1/16	169/18352	1.38E-01	2.20E-01	1.38E-01	PRTN3	1
GO:0005201	extracellular matrix structural constituent	1/16	169/18352	1.38E-01	2.20E-01	1.38E-01	ADIPOQ	1
GO:0004866	endopeptidase inhibitor activity	1/16	183/18352	1.48E-01	2.20E-01	1.38E-01	C3	1
GO:0008236	serine-type peptidase activity	1/16	187/18352	1.51E-01	2.20E-01	1.38E-01	PRTN3	1
GO:0008237	metallopeptidase activity	1/16	189/18352	1.53E-01	2.20E-01	1.38E-01	ANPEP	1
GO:0030414	peptidase inhibitor activity	1/16	189/18352	1.53E-01	2.20E-01	1.38E-01	C3	1
GO:0017171	serine hydrolase activity	1/16	191/18352	1.54E-01	2.20E-01	1.38E-01	PRTN3	1

GO:0061135	endopeptidase regulator activity	1/16	192/18352	1.55E-01	2.20E-01	1.38E-01	C3	1
GO:0031406	carboxylic acid binding	1/16	212/18352	1.70E-01	2.36E-01	1.48E-01	ADIPOQ	1
GO:0043177	organic acid binding	1/16	224/18352	1.78E-01	2.38E-01	1.49E-01	ADIPOQ	1
GO:0016747	transferase activity, transferring acyl groups other than amino-acyl groups	1/16	229/18352	1.82E-01	2.38E-01	1.49E-01	LCAT	1
GO:0061134	peptidase regulator activity	1/16	229/18352	1.82E-01	2.38E-01	1.49E-01	C3	1
GO:0005125	cytokine activity	1/16	235/18352	1.86E-01	2.39E-01	1.49E-01	ADIPOQ	1
GO:0016746	transferase activity, transferring acyl groups	1/16	259/18352	2.03E-01	2.55E-01	1.60E-01	LCAT	1
GO:0030246	carbohydrate binding	1/16	267/18352	2.09E-01	2.57E-01	1.61E-01	KRT1	1
GO:0016791	phosphatase activity	1/16	277/18352	2.16E-01	2.61E-01	1.63E-01	PON1	1
GO:0001664	G protein-coupled receptor binding	1/16	293/18352	2.27E-01	2.69E-01	1.68E-01	C3	1
GO:0042277	peptide binding	1/16	308/18352	2.37E-01	2.76E-01	1.73E-01	ANPEP	1
GO:0046982	protein heterodimerization activity	1/16	321/18352	2.46E-01	2.81E-01	1.76E-01	KRT1	1
GO:0045296	cadherin binding	1/16	332/18352	2.53E-01	2.85E-01	1.78E-01	CDH1	1
GO:0042578	phosphoric ester hydrolase activity	1/16	369/18352	2.78E-01	3.06E-01	1.91E-01	PON1	1
GO:0033218	amide binding	1/16	381/18352	2.85E-01	3.06E-01	1.91E-01	ANPEP	1
GO:0004857	enzyme inhibitor activity	1/16	383/18352	2.87E-01	3.06E-01	1.91E-01	C3	1
GO:0004175	endopeptidase activity	1/16	440/18352	3.22E-01	3.38E-01	2.11E-01	PRTN3	1
GO:0005543	phospholipid binding	1/16	454/18352	3.30E-01	3.41E-01	2.13E-01	PON1	1
GO:0048018	receptor ligand activity	1/16	487/18352	3.50E-01	3.53E-01	2.20E-01	ADIPOQ	1
GO:0030546	signaling receptor activator activity	1/16	492/18352	3.53E-01	3.53E-01	2.20E-01	ADIPOQ	1

Table S6 KEGG enrichment analysis results in proteomics.

#Term	Database	ID	Input number	Background number	P-Value	Corrected P-Value	Input
Complement and coagulation cascades	KEGG PATHWAY	hsa04610	3	79	7.00E-06	3.15E-04	733 735 718
Systemic lupus erythematosus	KEGG PATHWAY	hsa05322	3	133	3.19E-05	7.18E-04	733 735 718
Prion diseases	KEGG PATHWAY	hsa05020	2	35	1.31E-04	1.96E-03	733 735
Glutathione metabolism	KEGG PATHWAY	hsa00480	2	56	3.23E-04	3.64E-03	2878 290
Amoebiasis	KEGG PATHWAY	hsa05146	2	95	9.01E-04	8.11E-03	733 735
Estrogen signaling pathway	KEGG PATHWAY	hsa04915	2	138	1.86E-03	1.40E-02	3857 3861
Renin-angiotensin system	KEGG PATHWAY	hsa04614	1	23	1.09E-02	6.25E-02	290
Thyroid cancer	KEGG PATHWAY	hsa05216	1	37	1.73E-02	6.25E-02	999
Bladder cancer	KEGG PATHWAY	hsa05219	1	41	1.91E-02	6.25E-02	999
Type II diabetes mellitus	KEGG PATHWAY	hsa04930	1	46	2.13E-02	6.25E-02	9370
Hedgehog signaling pathway	KEGG PATHWAY	hsa04340	1	47	2.18E-02	6.25E-02	3549
Cholesterol metabolism	KEGG PATHWAY	hsa04979	1	50	2.31E-02	6.25E-02	3931
Pathogenic Escherichia coli infection	KEGG PATHWAY	hsa05130	1	55	2.54E-02	6.25E-02	999
Legionellosis	KEGG PATHWAY	hsa05134	1	55	2.54E-02	6.25E-02	718
Endometrial cancer	KEGG PATHWAY	hsa05213	1	58	2.67E-02	6.25E-02	999
Arachidonic acid metabolism	KEGG PATHWAY	hsa00590	1	63	2.89E-02	6.25E-02	2878
Staphylococcus aureus infection	KEGG PATHWAY	hsa05150	1	68	3.12E-02	6.25E-02	718
Adipocytokine signaling pathway	KEGG PATHWAY	hsa04920	1	69	3.16E-02	6.25E-02	9370
Adherens junction	KEGG PATHWAY	hsa04520	1	72	3.30E-02	6.25E-02	999
Melanoma	KEGG PATHWAY	hsa05218	1	72	3.30E-02	6.25E-02	999
Bacterial invasion of epithelial cells	KEGG PATHWAY	hsa05100	1	74	3.38E-02	6.25E-02	999
Thyroid hormone synthesis	KEGG PATHWAY	hsa04918	1	74	3.38E-02	6.25E-02	2878

Leishmaniasis	KEGG PATHWAY	hsa05140	1	74	3.38E-02	6.25E-02	718
Pertussis	KEGG PATHWAY	hsa05133	1	76	3.47E-02	6.25E-02	718
PPAR signaling pathway	KEGG PATHWAY	hsa03320	1	76	3.47E-02	6.25E-02	9370
Longevity regulating pathway	KEGG PATHWAY	hsa04211	1	89	4.05E-02	7.01E-02	9370
Glycerophospholipid metabolism	KEGG PATHWAY	hsa00564	1	97	4.40E-02	7.07E-02	3931
Hematopoietic cell lineage	KEGG PATHWAY	hsa04640	1	97	4.40E-02	7.07E-02	290
Chagas disease (American trypanosomiasis)	KEGG PATHWAY	hsa05142	1	103	4.66E-02	7.24E-02	718
AMPK signaling pathway	KEGG PATHWAY	hsa04152	1	120	5.41E-02	8.11E-02	9370
Apelin signaling pathway	KEGG PATHWAY	hsa04371	1	137	6.14E-02	8.59E-02	999
Cell adhesion molecules (CAMs)	KEGG PATHWAY	hsa04514	1	146	6.53E-02	8.59E-02	999
Non-alcoholic fatty liver disease (NAFLD)	KEGG PATHWAY	hsa04932	1	149	6.66E-02	8.59E-02	9370
Gastric cancer	KEGG PATHWAY	hsa05226	1	149	6.66E-02	8.59E-02	999
Phagosome	KEGG PATHWAY	hsa04145	1	152	6.79E-02	8.59E-02	718
Hippo signaling pathway	KEGG PATHWAY	hsa04390	1	154	6.87E-02	8.59E-02	999
Tuberculosis	KEGG PATHWAY	hsa05152	1	179	7.94E-02	9.66E-02	718
Kaposi sarcoma-associated herpesvirus infection	KEGG PATHWAY	hsa05167	1	186	8.24E-02	9.75E-02	718
Viral carcinogenesis	KEGG PATHWAY	hsa05203	1	201	8.87E-02	1.01E-01	718
Proteoglycans in cancer	KEGG PATHWAY	hsa05205	1	203	8.95E-02	1.01E-01	3549
Rap1 signaling pathway	KEGG PATHWAY	hsa04015	1	210	9.25E-02	1.01E-01	999
Metabolic pathways	KEGG PATHWAY	hsa01100	2	1433	1.39E-01	1.49E-01	2878 290
Neuroactive ligand-receptor interaction	KEGG PATHWAY	hsa04080	1	338	1.45E-01	1.51E-01	718
Herpes simplex virus 1 infection	KEGG PATHWAY	hsa05168	1	492	2.03E-01	2.08E-01	718
Pathways in cancer	KEGG PATHWAY	hsa05200	1	530	2.17E-01	2.17E-01	999

Table S7 Differentially changed metabolites.

Name	Formula	Molecular Weight	RT	KEG G ID	HMDB ID	Endogenous/Exogenous	VI P	p value	p.adj ust
Octaethylene glycol	C16 H34 O9	370.22	4.4	null	HMDB00 94680	Exogenous	2. 52	4.93E -11	2.94E -08
Heptaethylene glycol	C14 H30 O8	326.19	4.1	null	HMDB00 61835	Exogenous	2. 51	1.08E -10	3.88E -08
Netilmicin	C21 H41 N5 O7	475.30	4.8	C0765 7	HMDB00 15090	Exogenous	2. 49	2.51E -10	6.42E -08
PA(22:6(4Z,7Z,10Z,13Z,16Z,19Z)/20:5(5Z,8Z,11Z,14Z,17Z))	C45 H67 O8 P	766.46	5.7	null	HMDB01 15418	Exogenous	2. 46	7.02E -10	1.16E -07
Ibutilide	C20 H36 N2 O3 S	384.25	5.6	C0775 3	HMDB00 14453	Exogenous	2. 44	1.28E -09	1.85E -07
Histidiny-Proline	C11 H16 N4 O3	252.12	3.5	null	HMDB00 28893	Endogenous	2. 44	3.31E -09	3.39E -07
PE(18:4(6Z,9Z,12Z,15Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z))	C45 H70 N O8 P	783.48	5.7	C0035 0	HMDB00 09210	Endogenous	2. 43	3.21E -09	3.38E -07
5'-(3',4'-Dihydroxyphenyl)-gamma-valerolactone sulfate	C11 H12 O7 S	288.03	3.2	null	HMDB00 29191	Endogenous	2. 39	1.06E -08	8.62E -07
Hexaethylene glycol	C12 H26 O7	282.17	3.9	null	HMDB00 61822	Exogenous	2. 38	1.50E -08	1.15E -06
Labetalol	C19 H24 N2 O3	328.18	5.4	C0706 0	HMDB00 14736	Exogenous	2. 29	1.83E -07	1.00E -05
5-(5,7-dihydroxy-4-oxo-3,4-dihydro-2h-chromen-2-yl)-2-hydroxyphenyl hydrogen sulfate	C15 H12 O9 S	368.02	5.2	null	HMDB01 33374	Exogenous	2. 20	2.57E -06	1.16E -04

4-ethylphenylsulfate	C8 H10 O4 S	202.03	3.0	null	HMDB00	Endogenous	2.	1.85E	8.62E
			8		62551		17	-06	-05
Dambonitol	C8 H16 O6	208.09	3.1	null	HMDB00	Exogenous	2.	2.89E	1.28E
			0		33942		17	-06	-04
hesperetin 3'-O-sulfate	C16 H14 O9 S	382.04	5.4	null	HMDB00	Exogenous	2.	1.06E	5.26E
			8		29202		16	-06	-05
Paraldehyde	C6 H12 O3	132.08	3.1	C0783	HMDB00	Exogenous	2.	7.81E	3.13E
			3	4	32456		11	-06	-04
3-Oxo-carbofuran	C12 H13 N O4	235.09	2.2	null	HMDB00	Endogenous	2.	6.74E	2.78E
			5		32776		10	-06	-04
Methyl dihydrojasmonate	C13 H22 O3	226.16	8.3	null	HMDB00	Exogenous	2.	1.82E	6.31E
			5		31740		06	-05	-04
Tetraethylene glycol	C8 H18 O5	194.12	3.1	null	HMDB00	Exogenous	2.	2.44E	7.89E
			4		94708		03	-05	-04
Ovalicin	C16 H24 O5	296.16	2.2	null	HMDB00	Exogenous	1.	4.54E	1.30E
			0		38120		97	-05	-03
(2e)-3-(6,7-dimethoxy-1,3-benzodioxol-5-yl)-2-propen-1-yl hydrogen sulfate	C12 H14 O8 S	318.04	3.5	null	HMDB01	Exogenous	1.	4.85E	1.36E
			3		28688		96	-05	-03
Losartan	C22 H23 Cl N6 O	422.16	8.4	C0707	HMDB00	Exogenous	1.	1.89E	6.52E
			5	2	14816		96	-05	-04
Methylgallic acid-O-sulphate	C8 H8 O8 S	263.99	3.7	null	HMDB00	Exogenous	1.	5.96E	1.61E
			7		60005		96	-05	-03
2-tert-Butyl-1,4-benzenediol	C10 H14 O2	166.10	4.9	null	HMDB00	Exogenous	1.	8.85E	2.08E
			6		32062		95	-05	-03
Tyrosyl-Phenylalanine	C18 H20 N2 O4	328.14	10.	null	HMDB00	Endogenous	1.	8.06E	1.98E
			08		29112		95	-05	-03

Leukotriene B4	C20 H32 O4	336.23	7.9	C0216	HMDB00	Endogenous	1.	8.72E	2.06E
			0	5	01085		93	-05	-03
Sulfoxone	C14 H16 N2	404.02	5.4	null	HMDB00	Exogenous	1.	5.25E	1.45E
	O6 S3		8		15276		90	-05	-03
beta-Boswellic acid acetate	C32 H50 O4	498.37	10.	null	HMDB00	Exogenous	1.	8.44E	2.03E
			17		35160		89	-05	-03
Traumatic acid	C12 H20 O4	228.14	5.6	C1630	HMDB00	Exogenous	1.	1.04E	2.42E
			8	8	00933		89	-04	-03
2-sulfosuccinic acid	C4 H6 O7 S	197.98	0.6	null	HMDB00	Exogenous	1.	1.12E	2.56E
			1		40585		89	-04	-03
Paraxanthine	C7 H8 N4 O2	180.07	3.4	C1374	HMDB00	Endogenous	1.	1.26E	2.82E
			2	7	01860		86	-04	-03
Dimethylphosphate	C2 H7 O4 P	126.01	0.6	null	HMDB00	Exogenous	1.	2.81E	5.21E
			9		61734		85	-04	-03
3,3'-Thiobispropanoic acid	C6 H10 O4 S	178.03	1.0	null	HMDB00	Exogenous	1.	2.25E	4.51E
			9		31162		83	-04	-03
Ethylene brassylate	C15 H26 O4	270.18	7.6	null	HMDB00	Exogenous	1.	2.86E	5.24E
			5		40459		83	-04	-03
(2E)-2-methyl-3-phenyl-2-propen-1-yl hydrogen sulfate	C10 H12 O4	228.05	6.1	null	HMDB01	Exogenous	1.	2.11E	4.36E
	S		7		33620		83	-04	-03
Indolylacryloylglycine	C13 H12 N2	244.08	3.5	null	HMDB00	Exogenous	1.	3.79E	6.36E
	O3		4		06005		83	-04	-03
Pregnanetriol	C21 H36 O3	336.27	9.2	null	HMDB00	Endogenous	1.	3.63E	6.16E
			4		06070		81	-04	-03
Tripropylamine	C9 H21 N	143.17	3.2	null	HMDB00	Exogenous	1.	3.20E	5.62E
			8		32545		80	-04	-03

Theophylline	C7 H8 N4 O2	180.06	3.5	C0713	HMDB00	Exogenous	1.	2.50E	4.89E
			8	0	01889		80	-04	-03
1,4-dihydroxy-1-(1-oxo-1h-isochromen-3-yl)-2-butanyl hydrogen sulfate	C13 H14 O8 S	330.04	2.1	null	HMDB01	Exogenous	1.	3.86E	6.45E
			8		30090		79	-04	-03
Sulcatone	C8 H14 O	126.10	5.4	C0728	HMDB00	Exogenous	1.	3.79E	6.36E
			0	7	35915		79	-04	-03
4-vinylguaiacol sulfate	C9 H10 O5 S	230.02	4.8	null	HMDB01	Exogenous	1.	7.52E	1.08E
			6		27980		79	-04	-02
4-(1,2-dihydroxy-2-propanyl)-1-methyl-1,2- cyclohexanediol	C10 H20 O4	204.14	4.9	null	HMDB00	Exogenous	1.	2.81E	5.21E
			7		39974		78	-04	-03
3-Acetyl-2,5-dimethylfuran	C8 H10 O2	138.07	5.0	null	HMDB00	Exogenous	1.	6.82E	1.01E
			4		29563		78	-04	-02
1,7-Dimethyluric acid	C7 H8 N4 O3	196.06	2.3	C1635	HMDB00	Endogenous	1.	3.12E	5.55E
			9	6	11103		78	-04	-03
10-Hydroxy-octadec-12Z-enoate-9-beta-D-glucuronide	C24 H42 O10	490.28	7.6	null	HMDB00	Endogenous	1.	3.99E	3.49E
			9		60120		77	-03	-02
2,4,12-Octadecatrienoic acid isobutylamide	C22 H39 N O	333.30	9.1	null	HMDB00	Exogenous	1.	3.73E	3.35E
			9		32033		77	-03	-02
Ethyl 3-oxohexanoate	C8 H14 O3	158.09	5.2	C0297	HMDB00	Exogenous	1.	7.46E	1.07E
			3	5	31307		76	-04	-02
Hesperetin	C16 H14 O6	302.08	5.6	C0170	HMDB00	Exogenous	1.	2.31E	4.59E
			3	9	05782		76	-04	-03
Gamma-Linolenic acid	C18 H30 O2	278.22	8.8	C0642	HMDB00	Endogenous	1.	6.62E	9.87E
			4	6	03073		76	-04	-03
2-hydroxypropanoic acid	C3 H6 O3	90.03	0.7	C0143	HMDB01	Endogenous	1.	4.93E	7.80E
			0	2	44295		76	-04	-03

Pentadecanoic acid	C15 H30 O2	242.22	9.9	C1653	HMDB00	Endogenous	1.	5.07E	7.91E
			9	7	00826		75	-04	-03
anhydroretinol	C20 H28	268.22	7.6	null	HMDB00	Exogenous	1.	2.25E	4.51E
			3		62447		74	-04	-03
Thiomorpholine 3-carboxylate	C5 H9 N O2	147.04	1.1	C0390	HMDB00	Exogenous	1.	9.63E	1.30E
	S		0	1	59611		73	-04	-02
(2XI)-d-gluco-heptonic acid	C7 H14 O8	226.07	0.7	null	HMDB02	Endogenous	1.	1.24E	1.55E
			1		40292		71	-03	-02
Persin	C23 H40 O4	380.29	9.6	null	HMDB00	Exogenous	1.	7.00E	1.02E
			3		41103		71	-04	-02
Isobutyric acid	C4 H8 O2	88.05	3.5	C0263	HMDB00	Exogenous	1.	2.42E	4.76E
			6	2	01873		71	-04	-03
Momordol	C26 H48 O5	440.35	10.	null	HMDB00	Exogenous	1.	6.21E	9.42E
			03		29804		71	-04	-03
Caproic acid	C6 H12 O2	116.08	5.5	C0158	HMDB00	Endogenous	1.	1.09E	1.41E
			8	5	00535		69	-03	-02
Methyprylon	C10 H17 N O2	183.13	4.5	null	HMDB00	Exogenous	1.	8.83E	1.21E
			1		15239		69	-04	-02
Erythrasinate A	C38 H66 O4	586.49	10.	null	HMDB00	Exogenous	1.	7.86E	1.11E
			34		38713		69	-04	-02
Nifedipine	C17 H18 N2 O6	346.12	4.6	C0726	HMDB00	Exogenous	1.	9.87E	1.32E
			1	6	15247		69	-04	-02
Trihydroxycoprostanic acid	C28 H48 O5	464.35	9.3	null	HMDB00	Exogenous	1.	7.81E	1.11E
			9		02163		68	-04	-02
Valyl-Valine	C10 H20 N2 O3	216.15	5.2	null	HMDB00	Exogenous	1.	1.23E	1.55E
			9		29140		68	-03	-02

Linoleamide	C18 H33 N O	279.26	7.9	null	HMDB00	Endogenous	1.	1.40E	1.69E
			6		62656		66	-03	-02
Oleic acid	C18 H34 O2	282.26	9.9	C0071	HMDB00	Exogenous	1.	1.43E	1.71E
			8	2	00207		66	-03	-02
Perfluorooctanoic acid	C8 H F15 O2	413.97	7.8	null	HMDB00	Exogenous	1.	1.28E	1.57E
			3		59587		66	-03	-02
24-Epibrassinolide	C28 H48 O6	480.34	9.3	null	HMDB00	Exogenous	1.	1.09E	1.41E
			1		41130		66	-03	-02
Oleoyl glycine	C20 H37 N O3	339.28	8.8	null	HMDB00	Endogenous	1.	1.67E	1.94E
			5		13631		65	-03	-02
1-Methylxanthine	C6 H6 N4 O2	166.05	2.6	C1635	HMDB00	Endogenous	1.	1.03E	1.36E
			4	8	10738		64	-03	-02
Capryloylglycine	C10 H19 N O3	201.14	5.7	null	HMDB00	Endogenous	1.	1.32E	1.62E
			7		00832		64	-03	-02
LysoPE(18:2(9Z,12Z)/0:0)	C23 H44 N O7 P	477.28	9.7	null	HMDB00	Endogenous	1.	1.67E	1.94E
			5		11507		64	-03	-02
4-(8-hydroxy-7-methoxy-4-oxo-3,4-dihydro-2H-chromen-2-yl)phenyl hydrogen sulfate	C16 H14 O8 S	366.04	6.3	null	HMDB01	Exogenous	1.	1.73E	1.99E
			8		33303		64	-03	-02
Mitotane	C14 H10 Cl4	317.95	0.7	null	HMDB00	Exogenous	1.	1.24E	1.55E
			9		14786		64	-03	-02
Acetyl hexamethyl tetralin	C18 H26 O	258.20	9.4	null	HMDB00	Exogenous	1.	1.81E	2.04E
			0		61860		62	-03	-02
Pregnenolone	C21 H32 O2	316.24	8.1	C0195	HMDB00	Endogenous	1.	1.68E	1.96E
			6	3	00253		62	-03	-02
Butabarbital	C10 H16 N2 O3	212.12	3.6	C0782	HMDB00	Exogenous	1.	1.88E	2.11E
			4	7	14382		62	-03	-02

Cyclamic acid	C6H13NO3	179.06	3.5	C0282	HMDB00	Exogenous	1.	1.44E	1.71E
	S		8	4	31340		61	-03	-02
delta-Decalactone	C10H18O2	170.13	6.5	null	HMDB00	Exogenous	1.	2.34E	2.49E
			3		37116		61	-03	-02
LysoPE(0:0/20:2(11Z,14Z))	C25H48N	505.31	9.7	null	HMDB00	Endogenous	1.	2.20E	2.38E
	O7P		4		11483		61	-03	-02
Octadecyl fumarate	C22H40O4	368.29	9.6	null	HMDB00	Exogenous	1.	2.37E	2.49E
			5		38073		61	-03	-02
N6-Methyladenosine	C11H15N5	281.11	0.7	null	HMDB00	Endogenous	1.	1.92E	2.14E
	O4		7		04044		60	-03	-02
Nepitrin	C22H22	478.11	5.2	null	HMDB00	Exogenous	1.	1.19E	1.52E
	O12		8		30548		60	-03	-02
2-Hexyl-3-phenyl-2-propenal	C15H20O	216.15	8.8	null	HMDB00	Exogenous	1.	2.40E	2.52E
			3		31736		59	-03	-02
Pregabalin	C8H17NO2	159.13	6.6	null	HMDB00	Exogenous	1.	2.09E	2.29E
			4		14375		59	-03	-02
1,2,3-Tris(1-ethoxyethoxy)propane	C15H32O6	308.22	9.6	null	HMDB00	Exogenous	1.	2.27E	2.43E
			6		37162		59	-03	-02
LysoPE(0:0/18:2(9Z,12Z))	C23H44N	477.29	9.3	null	HMDB00	Endogenous	1.	2.87E	2.83E
	O7P		4		11477		59	-03	-02
12,13-DHOME	C18H34O4	314.25	10.	C1482	HMDB00	Endogenous	1.	2.72E	2.74E
			00	9	04705		58	-03	-02
Caffeine	C8H10N4	194.08	5.7	C0748	HMDB00	Exogenous	1.	2.56E	2.61E
	O2		9	1	01847		58	-03	-02
Quercitrin	C21H20	448.10	4.6	C0175	HMDB00	Exogenous	1.	3.12E	2.95E
	O11		4	0	33751		58	-03	-02

Butyl levulinate	C9 H16 O3	172.11	4.7	null	HMDB00	Exogenous	1.	2.28E	2.44E
			5				40165	58	-03
16-Acetylpriverogenin A	C32 H50 O5	514.36	9.6	null	HMDB00	Exogenous	1.	1.66E	1.94E
			5				34529	58	-03
3,6-Epoxy-5,5',6,6'-tetrahydro-b,b-carotene-3',5,5',6'-tetrol	C40 H58 O5	618.43	9.9	null	HMDB00	Exogenous	1.	2.55E	2.60E
			8				29654	58	-03
DG(18:4(6Z,9Z,12Z,15Z)/15:0/0:0)	C36 H62 O5	574.46	10.	null	HMDB00	Exogenous	1.	2.76E	2.75E
			13				07329	57	-03
Malondialdehyde	C3 H4 O2	72.02	0.7	C1944	HMDB00	Endogenous	1.	3.48E	3.19E
			2				0	06112	57
Glutaric acid	C5 H8 O4	132.04	0.6	C0048	HMDB00	Endogenous	1.	3.69E	3.34E
			5				9	00661	57
O-pentadecanoylcarnitine	C22 H43 N O4	385.32	8.4	null	HMDB00	Endogenous	1.	3.52E	3.22E
			7				62517	57	-03
Levetiracetam	C8 H14 N2 O2	170.11	3.5	null	HMDB00	Exogenous	1.	2.62E	2.66E
			5				15333	57	-03
9-Methyluric acid	C6 H6 N4 O3	182.04	1.1	null	HMDB00	Exogenous	1.	1.95E	2.16E
			9				01973	56	-03
Hexyl 2-furoate	C11 H16 O3	196.11	4.8	null	HMDB00	Exogenous	1.	2.53E	2.60E
			1				37725	56	-03
4alpha-hydroxymethyl-4beta-methylzymosterol	C29 H48 O2	428.37	10.	null	HMDB00	Endogenous	1.	4.09E	3.55E
			61				62390	55	-03
2,6-Di-tert-butyl-4-hydroxymethylphenol	C15 H24 O2	236.18	8.2	null	HMDB00	Exogenous	1.	3.01E	2.91E
			0				32048	55	-03
Dimethyl fumarate	C6 H8 O4	144.04	0.7	null	HMDB00	Exogenous	1.	4.38E	3.71E
			1				31257	54	-03

2-Hexaprenyl-3-methyl-5-hydroxy-6-methoxy-1,4-benzoquinol	C38 H58 O4	578.43	10.47	null	HMDB00	Exogenous	1.54	3.90E-03	3.45E-02
3-(3,4-dihydroxyphenyl)-2-(sulfoxy)propanoic acid	C9 H10 O8 S	278.01	0.61	null	HMDB01	Exogenous	1.53	3.24E-03	3.05E-02
Eucalyptol	C10 H18 O	154.14	8.02	C0984	HMDB00	Exogenous	1.53	3.71E-03	3.35E-02
Diethylhexyl adipate	C22 H42 O4	370.31	9.84	C1424	HMDB00	Exogenous	1.52	4.23E-03	3.65E-02
Geosmin	C12 H22 O	182.17	8.77	C1628	HMDB00	Exogenous	1.52	4.43E-03	3.72E-02
3-Oxotetradecanoic acid	C14 H26 O3	242.19	8.82	null	HMDB00	Endogenous	1.52	4.30E-03	3.68E-02
Sebacic acid	C10 H18 O4	202.12	6.64	C0827	HMDB00	Endogenous	1.52	4.73E-03	3.85E-02
3-Oxododecanoic acid	C12 H22 O3	214.16	7.71	C0236	HMDB00	Endogenous	1.52	5.02E-03	4.01E-02
3-Oxohexadecanoic acid	C16 H30 O3	270.22	9.23	null	HMDB00	Endogenous	1.52	4.18E-03	3.61E-02
p-Cresol sulfate	C7 H8 O4 S	188.01	4.01	null	HMDB00	Endogenous	1.52	6.13E-03	4.53E-02
27-Nor-5b-cholestane-3a,7a,12a,24,25-pentol	C26 H46 O5	438.33	9.21	null	HMDB00	Endogenous	1.52	3.54E-03	3.23E-02
L-Norleucine	C6 H13 N O2	131.09	1.75	C0193	HMDB00	Endogenous	1.52	3.64E-03	3.30E-02
Ibuprofen	C13 H18 O2	206.13	4.87	C0158	HMDB00	Exogenous	1.51	4.75E-03	3.87E-02

1-Methyluric acid	C6H6N4O3	182.04	2.3	C1635	HMDB00	Exogenous	1.	3.93E	3.46E
			6	9	03099		51	-03	-02
Methyl 2-octynoate	C9H14O2	154.10	6.3	null	HMDB00	Exogenous	1.	5.12E	4.04E
			7		31302		51	-03	-02
Phenylmethyl butanoate	C11H14O2	178.10	6.3	null	HMDB00	Exogenous	1.	4.61E	3.80E
			1		33376		50	-03	-02
3-methyl-1-phenyl-2-butene	C11H14	146.11	7.7	null	HMDB00	Exogenous	1.	4.89E	3.93E
			7		61808		49	-03	-02
Myristic acid	C14H28O2	228.21	9.7	C0642	HMDB00	Endogenous	1.	5.51E	4.24E
			6	4	00806		49	-03	-02
Polyporusterone C	C28H44O6	476.31	8.9	null	HMDB00	Exogenous	1.	5.53E	4.24E
			9		38497		49	-03	-02
Sphingosine 1-phosphate	C18H38N O5P	379.25	9.5	C0612	HMDB00	Endogenous	1.	6.37E	4.65E
			5	4	00277		49	-03	-02
3-Methyl-5-pentyl-2-furannonanoic acid	C19H32O3	308.23	8.3	null	HMDB00	Exogenous	1.	5.51E	4.24E
			4		31091		49	-03	-02
2,5-Dimethyl-4-ethoxy-3(2H)-furanone	C8H12O3	156.08	3.8	null	HMDB00	Exogenous	1.	6.81E	4.82E
			2		32232		48	-03	-02
Carisoprodol	C12H24N2 O4	260.17	0.7	C0792	HMDB00	Exogenous	1.	6.70E	4.77E
			7	7	14539		46	-03	-02
Cyclopassifloic acid B	C31H52O6	520.38	9.6	null	HMDB00	Exogenous	1.	6.09E	4.51E
			2		38388		46	-03	-02
(9E)-10-nitrooctadecenoic Acid	C18H33N O4	327.24	7.0	null	HMDB00	Endogenous	1.	6.85E	4.84E
			9		62737		46	-03	-02
3,4-Dihydrocadalene	C15H20	200.16	7.8	null	HMDB00	Exogenous	1.	7.02E	4.92E
			2		36453		46	-03	-02

2,6 Dimethylheptanoyl carnitine	C16 H31 N O4	301.23	6.3	7	null	HMDB00 06320	Endogenous	1. 46	5.72E -03	4.35E -02
Lanthionine ketimine	C6 H7 N O4 S	189.01	2.5	3	null	HMDB00 04823	Endogenous	1. 46	6.30E -03	4.62E -02
Cysteinyl-Serine	C6 H12 N2 O4 S	208.05	4.9	5	null	HMDB00 28784	Endogenous	1. 45	5.43E -03	4.20E -02
2-Tetradecylcyclobutanone	C18 H34 O	266.26	10.	01	null	HMDB00 37517	Exogenous	1. 45	6.39E -03	4.66E -02
Anagrelide	C10 H7 Cl2 N3 O	255.00	5.5	6	null	HMDB00 14406	Exogenous	1. 45	4.79E -03	3.87E -02
Alpha-Tocopherol	C29 H50 O2	430.38	11.	19	C0247 7	HMDB00 01893	Endogenous	1. 44	4.95E -03	3.96E -02
Pyruvic acid	C3 H4 O3	88.02	0.6	5	C0002 2	HMDB00 00243	Endogenous	1. 44	6.18E -03	4.56E -02
Prostaglandin E1	C20 H34 O5	354.24	7.7	1	C0474 1	HMDB00 01442	Endogenous	1. 43	6.03E -03	4.49E -02
6-Thioxanthine 5'-monophosphate	C10 H13 N4 O8 P S	380.02	0.7	5	C1661 8	HMDB00 60418	Endogenous	1. 43	6.70E -03	4.77E -02
2-Phenylethyl octanoate	C16 H24 O2	248.18	7.9	7	null	HMDB00 37719	Exogenous	1. 42	7.13E -03	4.98E -02
PE(18:4(6Z,9Z,12Z,15Z)/24:1(15Z))	C47 H84 N O8 P	821.59	11.	25	C0035 0	HMDB00 09212	Endogenous	1. 42	6.80E -03	4.82E -02
Acrylamide	C3 H5 N O	71.04	9.6	2	C0165 9	HMDB00 04296	Exogenous	1. 41	7.02E -03	4.92E -02
Varanic acid	C26 H44 O5	436.32	9.6	3	null	HMDB00 02195	Endogenous	1. 40	6.63E -03	4.77E -02

TG(8:0/8:0/13:0)	C32 H60 O6	540.44	10.03	null	HMDB0072647	Exogenous	1.39	7.04E-03	4.92E-02
3-Hydroxybenzoic acid	C7 H6 O3	138.03	3.00	C00587	HMDB0002466	Endogenous	1.37	2.88E-03	2.83E-02

Table S8 KEGG enrichment analysis results in metabolomics.

Term	Total	Expected	Hits	Raw p	-log10(p)	Holm adjust	FDR	Impact
Caffeine metabolism	10	0.15	3	3.20E-04	3.49E+00	2.69E-02	2.69E-02	1.00
Glycosylphosphatidylinositol (GPI)-anchor biosynthesis	14	0.21	1	1.90E-01	7.22E-01	1.00E+00	1.00E+00	0.00
Citrate cycle (TCA cycle)	20	0.30	1	2.60E-01	5.85E-01	1.00E+00	1.00E+00	0.05
Sphingolipid metabolism	21	0.31	1	2.71E-01	5.67E-01	1.00E+00	1.00E+00	0.02
Pyruvate metabolism	22	0.33	1	2.82E-01	5.50E-01	1.00E+00	1.00E+00	0.21
Glycolysis / Gluconeogenesis	26	0.39	1	3.24E-01	4.89E-01	1.00E+00	1.00E+00	0.10
Alanine, aspartate and glutamate metabolism	28	0.42	1	3.44E-01	4.63E-01	1.00E+00	1.00E+00	0.00
Glyoxylate and dicarboxylate metabolism	32	0.47	1	3.83E-01	4.17E-01	1.00E+00	1.00E+00	0.00
Glycine, serine and threonine metabolism	33	0.49	1	3.93E-01	4.06E-01	1.00E+00	1.00E+00	0.00
Cysteine and methionine metabolism	33	0.49	1	3.93E-01	4.06E-01	1.00E+00	1.00E+00	0.00
Biosynthesis of unsaturated fatty acids	36	0.53	1	4.20E-01	3.77E-01	1.00E+00	1.00E+00	0.00
Arachidonic acid metabolism	36	0.53	1	4.20E-01	3.77E-01	1.00E+00	1.00E+00	0.02
Glycerophospholipid metabolism	36	0.53	1	4.20E-01	3.77E-01	1.00E+00	1.00E+00	0.10
Arginine and proline metabolism	38	0.56	1	4.37E-01	3.59E-01	1.00E+00	1.00E+00	0.00
Drug metabolism - other enzymes	39	0.58	1	4.46E-01	3.51E-01	1.00E+00	1.00E+00	0.05
Tyrosine metabolism	42	0.62	1	4.71E-01	3.27E-01	1.00E+00	1.00E+00	0.00
Fatty acid biosynthesis	47	0.70	1	5.10E-01	2.92E-01	1.00E+00	1.00E+00	0.00
Steroid hormone biosynthesis	85	1.26	1	7.29E-01	1.37E-01	1.00E+00	1.00E+00	0.03