

Table S4. The detailed information of the significant KEGG pathways. Three omics correlated information of genes in the selected key KEGG pathways. The fold change (FC), the direction (dir) and p value (p) of three omics information are shown. Meanwhile, the chromosomal localization (Chr), the strand of methylation (strand) and methylated positions (Gene_Info) are also shown in methylation information.

Table S4. The detailed information of the significant KEGG pathways.

KEGG pathway	Gene	Gene name	mRNA information				protein information				Methylation information					
			mRNA name	FC	dir	p value	protein	FC	dir	p value	FC	dir	chr	strand	Gene_Info	p value
Complement and coagulation cascades	C5	complement C5	ENSRNOT00000092736	0.92	down	0.44	A0A096P6L9	1.29	up	6.09E-17						
	C5	complement C5	ENSRNOT00000025534	1.01	up	0.34	A0A096P6L9	1.29	up	6.09E-17						
	Kng1	kininogen 1	ENSRNOT00000080562	1.02	up	0.47	A0A0G2KAY3	3.00	up	1.12E-18						
	Kng1	kininogen 1	ENSRNOT00000080949	0.9	down	0.34	A0A0G2KAY3	3.00	up	1.12E-18						
	Kng1	kininogen 1	ENSRNOT00000084867	1.52	up	0.11	A0A0G2KAY3	3.00	up	1.12E-18						
	C4bpb	complement component 4 binding protein, beta	ENSRNOT00000005505	0.97	down	0.86	A0A5C5	1.90	up	6.50E-16						
	C6	complement component 6	MSTRG.10628.1	2.8	up	0	F1M7F7	1.31	up	3.07E-17						
	C6	complement component 6	MSTRG.10628.4	2.28	up	0.06	F1M7F7	1.31	up	3.07E-17						
	C6	complement component 6	MSTRG.10628.2	1.04	up	0.04	F1M7F7	1.31	up	3.07E-17						
	C6	complement component 6	MSTRG.10628.3	1.33	up	0.08	F1M7F7	1.31	up	3.07E-17						
	C6	complement component 6	MSTRG.10628.6	2.15	up	0	F1M7F7	1.31	up	3.07E-17						
	C1qb	complement component 1, q subcomponent, B chain	ENSRNOT00000017060	1.2	up	0.7	G3V7N9	1.25	up	9.74E-13						
	C1qb	complement component 1, q subcomponent, B chain	MSTRG.16594.1	1.06	up	0.85	G3V7N9	1.25	up	9.74E-13						
	F13a1	coagulation factor XIII, A1 polypeptide	ENSRNOT00000021568	1.91	up	0.06	G3V811	1.27	up	1.99E-17						
	C3	complement component 3	ENSRNOT00000075494	1.68	up	0.25	M0RBJ7	1.26	up	7.42E-19						
	C3	complement component 3	MSTRG.20503.3	1.41	up	0.05	M0RBJ7	1.26	up	7.42E-19						
	C3	complement component 3	MSTRG.20503.1	1.22	up	0.46	M0RBJ7	1.26	up	7.42E-19						
	C3	complement component 3	ENSRNOT00000073042	1.69	up	0.24	M0RBJ7	1.26	up	7.42E-19						
	Thbd	thrombomodulin	ENSRNOT00000062000	0.57	down	0.75	O35370	0.60	down	5.77E-06						
	Fgg	fibrinogen gamma chain	ENSRNOT00000034521	1.27	up	0.41	P02680	1.57	up	3.22E-17						
	A2m	alpha-2-macroglobulin	ENSRNOT00000019346	2.78	up	0.26	P06238	1.93	up	1.94E-20						
	Fgb	fibrinogen beta chain	ENSRNOT00000009813	0.96	down	0.4	P14480	1.49	up	2.02E-21						
	Proc	protein C	ENSRNOT00000019596	0.94	down	0.4	P31394	0.79	down	7.53E-11						
	F3	coagulation factor III (thromboplastin, tissue factor)	ENSRNOT00000015836	2.53	up	0.48	P42533	0.71	down	4.47E-19						
	F3	coagulation factor III (thromboplastin, tissue factor)	MSTRG.11600.1	0.23	down	0.45	P42533	0.71	down	4.47E-19						
	F3	coagulation factor III (thromboplastin, tissue factor)	MSTRG.11600.3	0.67	down	0.46	P42533	0.71	down	4.47E-19						
	C5ar1	complement component 5a receptor 1	MSTRG.545.1	1.72	up	0.49	P97520	1.47	up	9.88E-13						
	C5ar1	complement component 5a receptor 1	ENSRNOT00000073034	1.05	up	0.6	P97520	1.47	up	9.88E-13						
	C9	complement component 9	ENSRNOT00000018545	0.97	down	0.59	Q62930	1.44	up	6.93E-18						
	F10	coagulation factor X	ENSRNOT00000026677	1.26	up	0.42	Q63207	1.32	up	1.70E-14						
C4bpa	complement component 4 binding protein, alpha	ENSRNOT00000005461	1.46	up	0.07	Q63514	1.64	up	6.23E-17							
Mgst2	microsomal glutathione S-transferase 2	MSTRG.10921.1	0.97	down	0.2	A0A0G2JU12	1.49	up	4.54E-11							
Mgst2	microsomal glutathione S-transferase 2	MSTRG.10921.2	1.07	up	0.88	A0A0G2JU12	1.49	up	4.54E-11							
Mgst2	microsomal glutathione S-transferase 2	ENSRNOT00000088846	1.09	up	0.66	A0A0G2JU12	1.49	up	4.54E-11							
Aox3	aldehyde oxidase 3	ENSRNOT00000081146	1.28	up	0.44	A0A0G2K1Z5	0.73	down	6.67E-16							
Aox3	aldehyde oxidase 3	ENSRNOT00000093062	1	down	0.47	A0A0G2K1Z5	0.73	down	6.67E-16							
Aox3	aldehyde oxidase 3	ENSRNOT00000092841	1.07	up	0.17	A0A0G2K1Z5	0.73	down	6.67E-16							
Aox3	aldehyde oxidase 3	ENSRNOT00000092786	1.11	up	0.7	A0A0G2K1Z5	0.73	down	6.67E-16							
Aox3	aldehyde oxidase 3	ENSRNOT00000093120	0.8	down	0.48	A0A0G2K1Z5	0.73	down	6.67E-16							
Aox1	aldehyde oxidase 1	MSTRG.20927.3	0.76	down	0.15	F1LRQ1	0.73	down	3.54E-17	0.36	hypo-methylated	9	"+"	intron	1.54E-07	
Aox1	aldehyde oxidase 1	ENSRNOT00000092805	0.98	down	0.5	F1LRQ1	0.73	down	3.54E-17	0.36	hypo-methylated	9	"+"	intron	1.54E-07	
Aox1	aldehyde oxidase 1	MSTRG.20927.1	0.71	down	0.43	F1LRQ1	0.73	down	3.54E-17	0.36	hypo-methylated	9	"+"	intron	1.54E-07	
Aox1	aldehyde oxidase 1	MSTRG.20927.4	0.9	down	0.81	F1LRQ1	0.73	down	3.54E-17	0.36	hypo-methylated	9	"+"	intron	1.54E-07	
Aox1	aldehyde oxidase 1	ENSRNOT00000068633	1.13	up	0.8	F1LRQ1	0.73	down	3.54E-17	0.36	hypo-methylated	9	"+"	intron	1.54E-07	
Aox1	aldehyde oxidase 1	MSTRG.20927.2	0.98	down	0.92	F1LRQ1	0.73	down	3.54E-17	0.36	hypo-methylated	9	"+"	intron	1.54E-07	
Aox1	aldehyde oxidase 1	MSTRG.20927.5	0.66	down	0.37	F1LRQ1	0.73	down	3.54E-17	0.36	hypo-methylated	9	"+"	intron	1.54E-07	
Aox1	aldehyde oxidase 1	ENSRNOT00000092872	1	down	0.6	F1LRQ1	0.73	down	3.54E-17	0.36	hypo-methylated	9	"+"	intron	1.54E-07	
Aox1	aldehyde oxidase 1	MSTRG.20927.7	1.37	up	0.03	F1LRQ1	0.73	down	3.54E-17	0.36	hypo-methylated	9	"+"	intron	1.54E-07	
Gsta3	glutathione S-transferase alpha 3	ENSRNOT00000088416	0.76	down	0.31	P04904	0.64	down	2.87E-15	2.74	hyper-methylated	9	"+"	exon	2.28E-04	
Gsta3	glutathione S-transferase alpha 3	MSTRG.10921.1	1.01	up	0.84	P04904	0.64	down	2.87E-15	2.74	hyper-methylated	9	"+"	exon	2.28E-04	
Adh1	alcohol dehydrogenase 1 (class I)	ENSRNOT00000083682	0.89	down	0.64	P06757	0.78	down	2.84E-16							
Adh1	alcohol dehydrogenase 1 (class I)	MSTRG.11708.1	1	down	0.97	P06757	0.78	down	2.84E-16							
Adh1	alcohol dehydrogenase 1 (class I)	ENSRNOT00000085067	0.99	down	0.97	P06757	0.78	down	2.84E-16							
Gstm3	glutathione S-transferase mu 3	ENSRNOT00000025800	1.01	up	0.91	P08009	0.59	down	2.02E-20							
Aldh3a1	aldehyde dehydrogenase 3 family, member A1	ENSRNOT00000003182	0.45	down	0.25	P11883	0.72	down	6.70E-23							
Gsta4	glutathione S-transferase alpha 4	MSTRG.20020.1	0.78	down	0.48	P14942	0.76	down	4.34E-13							
Gsta4	glutathione S-transferase alpha 4	ENSRNOT00000090146	0.88	down	0.55	P14942	0.76	down	4.34E-13							
Gsta4	glutathione S-transferase alpha 4	ENSRNOT00000012348	1.17	up	0.76	P14942	0.76	down	4.34E-13							
Gstt1	glutathione S-transferase theta 1	ENSRNOT00000001669	0.92	down	0.8	Q01579	0.80	down	1.36E-15	0.44	hypo-methylated	20	"+"	exon	5.43E-04	
Gstt1	glutathione S-transferase theta 1	MSTRG.12200.2	0.67	down	0.23	Q01579	0.80	down	1.36E-15	0.44	hypo-methylated	20	"+"	exon	5.43E-04	
Fmo5	flavin containing monooxygenase 5	ENSRNOT00000024423	1.49	up	0.37	Q8K4C0	1.26	up	1.37E-07							
Mgst2	microsomal glutathione S-transferase 2	MSTRG.10921.1	0.97	down	0.2	A0A0G2JU12	1.49	up	4.54E-11							
Mgst2	microsomal glutathione S-transferase 2	MSTRG.10921.2	1.07	up	0.88	A0A0G2JU12	1.49	up	4.54E-11							
Gsta3	glutathione S-transferase alpha 3	ENSRNOT00000088416	0.76	down	0.31	P04904	0.64	down	2.87E-15	2.74	hyper-methylated	9	"+"	exon	2.28E-04	
Gsta3	glutathione S-transferase alpha 3	ENSRNOT00000077372	1.01	up	0.84	P04904	0.64	down	2.87E-15	2.74	hyper-methylated	9	"+"	exon	2.28E-04	
Adh1	alcohol dehydrogenase 1 (class I)	ENSRNOT00000083682	0.89	down	0.64	P06757	0.78	down	2.84E-16							
Adh1	alcohol dehydrogenase 1 (class I)	MSTRG.11708.1	1	down	0.97	P06757	0.78	down	2.84E-16							
Adh1	alcohol dehydrogenase 1 (class I)	ENSRNOT00000085067	0.99	down	0.97	P06757	0.78	down	2.84E-16							
Ephx1	epoxide hydrolase 1, microsomal (xenobiotic)	ENSRNOT00000085279	0.89	down	0.77	P07687	0.69	down	5.24E-14	0.19	hypo-methylated	13	"-"	promoter	2.92E-07	
Ephx1	epoxide hydrolase 1, microsomal (xenobiotic)	ENSRNOT0000004780	0.92	down	0.69	P07687	0.69	down	5.24E-14	0.19	hypo-methylated	13	"-"	promoter	2.92E-07	
Gstm3	glutathione S-transferase mu 3	ENSRNOT00000025800	1.01	up	0.91	P08009	0.59	down	2.02E-20							
Aldh3a1	aldehyde dehydrogenase 3 family, member A1	ENSRNOT00000003182	0.45	down	0.25	P11883	0.72	down	6.70E-23							
Gsta4	glutathione S-transferase alpha 4	MSTRG.20020.1	0.78	down	0.48	P14942	0.76	down	4.34E-13							
Gsta4	glutathione S-transferase alpha 4	ENSRNOT00000090146	0.88	down	0.55	P14942	0.76	down	4.34E-13							
Gsta4	glutathione S-transferase alpha 4	ENSRNOT00000012348	1.17	up	0.76	P14942	0.76	down	4.34E-13							
Gstt1	glutathione S-transferase theta 1	ENSRNOT00000001669	0.92	down	0.8	Q01579	0.80	down	1.36E-15	0.44	hypo-methylated	20	"+"	exon	5.43E-04	
Gstt1	glutathione S-transferase theta 1	MSTRG.12200.2	0.67	down	0.23	Q01579	0.80	down	1.36E-15	0.44	hypo-methylated	20	"+"	exon	5.43E-04	
Col6a5	collagen, type VI, alpha 5	ENSRNOT00000038160	0.84	down	0.15	A0A0G2JTX7	0.69	down	9.0							

	Fln	filamin C, gamma	ENSRNOT00000027237	1.11	up	0.35	A0A0H2UHR7	0.75	down	1.10E-19							
	Fln	filamin C, gamma	ENSRNOT00000088149	0.84	down	0.49	A0A0H2UHR7	0.75	down	1.10E-19							
	Mapk10	mitogen activated protein kinase 10	ENSRNOT00000092542	1	down	0.4	A0A0U1RRS7	0.56	down	6.75E-04	6.77	hyper-methylated	14	"+"	intron		5.13E-18
	Mapk10	mitogen activated protein kinase 10	ENSRNOT00000065965	0.99	down	0.41	A0A0U1RRS7	0.56	down	6.75E-04	6.77	hyper-methylated	14	"+"	intron		5.13E-18
	Mapk10	mitogen activated protein kinase 10	ENSRNOT00000092395	0.99	down	0.45	A0A0U1RRS7	0.56	down	6.75E-04	6.77	hyper-methylated	14	"+"	intron		5.13E-18
	Cav1	caveolin 1	ENSRNOT00000078250	0.54	down	0.07	B1WBN8	0.73	down	8.89E-14							
	Cav1	caveolin 1	MSTRG.14338.1	0.99	down	0.53	B1WBN8	0.73	down	8.89E-14							
	Myl10	myosin, light chain 10, regulatory	ENSRNOT00000041654	1.05	up	0.09	D3ZC19	0.76	down	1.15E-16							
	Col6a6	collagen, type VI, alpha 6	ENSRNOT00000056414	0.54	down	0.06	D3ZL10	0.72	down	2.01E-20							
	Lamb1	laminin, beta 1	ENSRNOT00000008321	2.02	up	0.49	D3ZQN7	1.31	up	5.36E-17	3.86	hyper-methylated	6	"+"	intron		8.86E-05
	Lamb1	laminin, beta 1	MSTRG.17232.1	1.22	up	0.71	D3ZQN7	1.31	up	5.36E-17	3.86	hyper-methylated	6	"+"	intron		8.86E-05
	Lamb1	laminin, beta 1	MSTRG.17232.2	3.85	up	0.02	D3ZQN7	1.31	up	5.36E-17	3.86	hyper-methylated	6	"+"	intron		8.86E-05
Focal adhesion	Thbs4	thrombospondin 4	MSTRG.10411.3	1.07	up	0.47	FILMS5	1.25	up	3.66E-10	0.15	hypo-methylated	2	"-"	intron		3.98E-04
	Thbs4	thrombospondin 4	MSTRG.10411.2	0.99	down	0.45	FILMS5	1.25	up	3.66E-10	0.15	hypo-methylated	2	"-"	intron		3.98E-04
	Thbs4	thrombospondin 4	ENSRNOT00000065224	2.16	up	0.08	FILMS5	1.25	up	3.66E-10	0.15	hypo-methylated	2	"-"	intron		3.98E-04
	Thbs4	thrombospondin 4	ENSRNOT00000083531	2.15	up	0.1	FILMS5	1.25	up	3.66E-10	0.15	hypo-methylated	2	"-"	intron		3.98E-04
	Col2a1	collagen, type II, alpha 1	ENSRNOT00000086062	0.98	down	0.33	FILRM7	0.58	down	9.54E-17							
	Fn1	fibronectin 1	MSTRG.21023.11	8.43	up	0.01	FILST1	1.27	up	4.07E-20	0.11	hypo-methylated	9	"-"	intron		2.24E-04
	Fn1	fibronectin 1	MSTRG.21023.6	7.56	up	0.49	FILST1	1.27	up	4.07E-20	0.11	hypo-methylated	9	"-"	intron		2.24E-04
	Fn1	fibronectin 1	MSTRG.21023.9	0.17	down	0.09	FILST1	1.27	up	4.07E-20	0.11	hypo-methylated	9	"-"	intron		2.24E-04
	Fn1	fibronectin 1	ENSRNOT00000019772	0.52	down	0.62	FILST1	1.27	up	4.07E-20	0.11	hypo-methylated	9	"-"	intron		2.24E-04
	Fn1	fibronectin 1	MSTRG.21023.8	9.19	up	0.42	FILST1	1.27	up	4.07E-20	0.11	hypo-methylated	9	"-"	intron		2.24E-04
	Fn1	fibronectin 1	MSTRG.21023.4	1.68	up	0.61	FILST1	1.27	up	4.07E-20	0.11	hypo-methylated	9	"-"	intron		2.24E-04
	Fn1	fibronectin 1	ENSRNOT00000057585	1.31	up	0.79	FILST1	1.27	up	4.07E-20	0.11	hypo-methylated	9	"-"	intron		2.24E-04
	Fn1	fibronectin 1	MSTRG.21023.2	1.2	up	0.84	FILST1	1.27	up	4.07E-20	0.11	hypo-methylated	9	"-"	intron		2.24E-04
	Fn1	fibronectin 1	MSTRG.21023.3	1.42	up	0.73	FILST1	1.27	up	4.07E-20	0.11	hypo-methylated	9	"-"	intron		2.24E-04
	Fn1	fibronectin 1	MSTRG.21023.5	8.58	up	0.48	FILST1	1.27	up	4.07E-20	0.11	hypo-methylated	9	"-"	intron		2.24E-04
	Fn1	fibronectin 1	MSTRG.21023.10	9.31	up	0.44	FILST1	1.27	up	4.07E-20	0.11	hypo-methylated	9	"-"	intron		2.24E-04
	Spp1	secreted phosphoprotein 1	ENSRNOT00000075989	5.34	up	0.17	P08721	1.32	up	5.17E-14	29.54	hyper-methylated	14	"+"	exon		1.81E-44
	Spp1	secreted phosphoprotein 1	MSTRG.6515.2	4.8	up	0.11	P08721	1.32	up	5.17E-14	29.54	hyper-methylated	14	"+"	exon		1.81E-44
	Spp1	secreted phosphoprotein 1	ENSRNOT00000067875	7.36	up	0.06	P08721	1.32	up	5.17E-14	29.54	hyper-methylated	14	"+"	exon		1.81E-44
	Ppp1cc	protein phosphatase 1 catalytic subunit gamma	ENSRNOT00000078761	1.05	up	0.47	P63088	0.69	down	9.22E-05							
	Ppp1cc	protein phosphatase 1 catalytic subunit gamma	MSTRG.5563.2	1	down	0.99	P63088	0.69	down	9.22E-05							
	Ppp1cc	protein phosphatase 1 catalytic subunit gamma	ENSRNOT00000048851	1.05	up	0.59	P63088	0.69	down	9.22E-05							
	Ppp1cc	protein phosphatase 1 catalytic subunit gamma	ENSRNOT00000083296	1.19	up	0.26	P63088	0.69	down	9.22E-05							
	Vtn	vitronectin	ENSRNOT00000078897	1.01	up	0.76	Q3KR94	1.27	up	2.27E-07							
	Vtn	vitronectin	ENSRNOT00000039954	1.2	up	0.41	Q3KR94	1.27	up	2.27E-07							
	Col4a1	collagen, type IV, alpha 1	MSTRG.8454.1	2.88	up	0.52	Q5FWY9	1.87	up	1.30E-15							
	Col4a1	collagen, type IV, alpha 1	ENSRNOT00000057386	1.58	up	0.25	Q5FWY9	1.87	up	1.30E-15							