

Supplementary table 1 Expression levels (ng/ml) of MOTS-c by ELISA in different groups

Groups	1	2	3	M	SD
CONTROL 1	200	192	198		
CONTROL 2	199	200	197		
CONTROL 3	192	200	200		
CONTROL 4	189	194	200	195.57	3.91
CONTROL 5	194	199	195		
CONTROL 6	195	196	191		
CONTROL 7	196	187	193		
TBI 1	159	147	162		
TBI 2	147	156	151		
TBI 3	167	161	158		
TBI 4	152	149	160	154.62	7.28
TBI 5	142	153	157		
TBI 6	163	154	155		
TBI 7	139	151	164		
MOTS-c 1	175	186	181		
MOTS-c 2	164	179	185		
MOTS-c 3	191	174	181		
MOTS-c 4	158	185	173	176.81	9.18
MOTS-c 5	166	188	171		
MOTS-c 6	184	176	163		
MOTS-c 7	169	187	177		

Notes: M: mean; SD: standard deviation.

Supplementary table 2 Time crossed the balance beam (s) & Score achieved on the balance beam

group	Day 3						M (time)	SD (time)	M (score)	SD (score)
	6am		10am		2pm					
	Time	Score	Time	Score	Time	Score				
CONTROL 1	22	3	16	4	9	4				
CONTROL 2	20	4	14	4	11	4				
CONTROL 3	18	4	15	3	12	3				
CONTROL 4	25	3	17	3	13	4	15.33	4.48	3.67	0.48
CONTROL 5	15	3	12	4	10	4				
CONTROL 6	23	4	15	4	10	4				
CONTROL 7	19	3	14	4	12	4				
MOTS-c 1	35	3	22	3	16	2				
MOTS-c 2	30	3	22	3	15	3				
MOTS-c 3	23	3	18	4	13	3				
MOTS-c 4	27	2	21	3	17	3	20.95	6.09	2.90	0.54
MOTS-c 5	30	3	23	3	15	3				
MOTS-c 6	22	2	18	3	11	3				

MOTS-c 7	25	2	21	3	16	4				
TBI 1	38	2	32	3	26	3				
TBI 2	42	2	34	3	28	2				
TBI 3	43	3	36	2	25	2				
TBI 4	26	2	22	2	18	3	31.62	7.73	2.33	0.48
TBI 5	44	2	35	2	27	3				
TBI 6	36	2	30	2	22	2				
TBI 7	42	2	35	2	23	3				

Notes: M: mean; SD: standard deviation.

Supplementary table 3 Time spent in the target quadrant (s)

Group	Day 5			M (day 5)	SD (day 5)
	8am	12am	4pm		
CONTROL 1	35	41	47		
CONTROL 2	33	48	46		
CONTROL 3	34	42	44	41.95	5.11
CONTROL 4	40	42	42		
CONTROL 5	48	45	49		
CONTROL 6	43	43	46		
CONTROL 7	31	39	43		
MOTS-c 1	22	20	25		
MOTS-c 2	21	32	43		
MOTS-c 3	22	28	33		
MOTS-c 4	20	28	34	28.90	6.88
MOTS-c 5	28	33	36		
MOTS-c 6	20	35	40		
MOTS-c 7	23	31	33		
TBI 1	18	12	21		
TBI 2	15	12	18		
TBI 3	8	14	16		
TBI 4	15	15	20	15.86	3.35
TBI 5	15	12	18		
TBI 6	17	15	19		
TBI 7	13	20	20		

Notes: M: mean; SD: standard deviation.

Supplementary table 4 Total distance (mm)

group	Day 1	Day 2	Day 3	M	SD
CONTROL 1	1586.60	1601.2	1633.9		
CONTROL 2	1675.40	1764.5	1745.7	1966.96	239.30
CONTROL 3	1879.60	1925.2	1967.4		
CONTROL 4	2372.70	2368.3	2378.0		

CONTROL 5	1994.50	2016.3	2021.2		
CONTROL 6	2096.70	2104.3	2137.6		
CONTROL 7	2021.30	2014.6	2001.1		
MOTS-c 1	1136.90	1201.8	1266.5		
MOTS-c 2	1299.40	1354.6	1501.8		
MOTS-c 3	1455.60	1577.1	1721.3		
MOTS-c 4	1476.40	1591.7	1658.3	1530.80	184.40
MOTS-c 5	1557.80	1642.3	1721.5		
MOTS-c 6	1601.50	1587.2	1714.2		
MOTS-c 7	1583.30	1696.4	1801.10		
TBI 1	1201.10	1125.40	1113.90		
TBI 2	1121.30	987.60	1002.40		
TBI 3	1214.70	1302.50	1217.30		
TBI 4	1502.80	1398.40	1402.30	1210.65	138.40
TBI 5	1292.70	1342.10	1320.10		
TBI 6	989.60	1134.30	1124.50		
TBI 7	1196.20	1237.40	1197.00		

Notes: M: mean; SD: standard deviation.

### Supplementary table 5 DEGs of MOTS-c VS TBI groups

Gene id	Gene	p	q	fc	log2(fc)	regulation	Significant
ENSMUSG00000078440	Dohh	1.57598E-19	5.2961E-15	0.23980458	-2.060068836	down	yes
ENSMUSG00000047976	Kcna1	6.62068E-17	1.11244E-12	0.24885454	-2.00662539	down	yes
ENSMUSG00000057036	Gm7536	9.99935E-16	8.4007E-12	0.13963307	-2.84028737	down	yes
ENSMUSG00000033307	Mif	2.3914E-11	5.74021E-08	0.29396922	-1.766262987	down	yes
ENSMUSG00000107705	Gm45062	6.06134E-11	1.35794E-07	3.48685E-05	-14.80771481	down	yes
ENSMUSG00000004366	Sst	2.09084E-08	2.12917E-05	0.45726009	-1.128913069	down	yes
ENSMUSG00000070003	Ssbp4	2.15488E-08	2.12984E-05	0.34873847	-1.519782556	down	yes
ENSMUSG00000005268	Prlr	1.1037E-07	7.89145E-05	0.21182445	-2.239058966	down	yes
ENSMUSG00000109061	Gm49320	1.19879E-07	8.22151E-05	0.00059945	-10.70406213	down	yes
ENSMUSG00000014301	Pam16	1.32806E-07	8.92588E-05	0.46191688	-1.114294808	down	yes
ENSMUSG00000024907	Gal	1.37639E-07	9.06933E-05	0.00017937	-12.44470088	down	yes
ENSMUSG00000066278	Vps37b	1.5337E-07	9.75676E-05	0.36364626	-1.45939234	down	yes
ENSMUSG00000103770	Pcdha9	2.00964E-07	0.000116438	0.22700452	-2.139207045	down	yes
ENSMUSG00000092981	Mir5125	2.90935E-07	0.00016294	0.43084082	-1.214773143	down	yes
ENSMUSG00000032997	Chpf	4.7277E-07	0.00025624	0.29831640	-1.745084765	down	yes
ENSMUSG00000035835	Plppr3	5.33743E-07	0.00028470	0.44786356	-1.158868799	down	yes
ENSMUSG00000023266	Frs3	5.99063E-07	0.00030502	0.38850011	-1.364013061	down	yes
ENSMUSG00000030595	Nfkbib	6.57628E-07	0.00032391	0.38114214	-1.391598952	down	yes
ENSMUSG00000024011	Pi16	7.99717E-07	0.00037851	0.08572729	-3.544101638	down	yes
ENSMUSG00000060438	Rps10-ps1	8.33434E-07	0.00038899	0.16329979	-2.614405099	down	yes
ENSMUSG00000049086	Bmyc	2.7864E-06	0.001170461	0.29218886	-1.775026899	down	yes
ENSMUSG00000037692	Ahdc1	3.04512E-06	0.00122089	0.40141469	-1.316834675	down	yes
ENSMUSG00000110483	Gm45702	3.76819E-06	0.00145551	0.13247483	-2.916209781	down	yes
ENSMUSG00000022623	Shank3	4.15558E-06	0.00155164	0.44919354	-1.154590894	down	yes
ENSMUSG00000027327	1700037H04Ri	4.41537E-06	0.00159546	0.44499469	-1.168139958	down	yes
ENSMUSG00000022577	Ly6h	5.22579E-06	0.00186123	0.48301839	-1.049849949	down	yes
ENSMUSG00000019433	Gipc1	5.29801E-06	0.00186123	0.48117722	-1.055359729	down	yes
ENSMUSG00000028398	Dmac1	5.31703E-06	0.00186123	0.43325979	-1.206695715	down	yes
ENSMUSG00000033768	Nrxn2	7.67883E-06	0.00258047	0.47151756	-1.084616579	down	yes

ENSMUSG00000010205	Raver1	7.81094E-06	0.00259887	0.43740616	-1.192954545	down	yes
ENSMUSG00000027551	Zfp64	1.04541E-05	0.00331424	0.40148055	-1.316597987	down	yes
ENSMUSG00000058441	Panx2	1.17815E-05	0.00366589	0.43711963	-1.1938999	down	yes
ENSMUSG00000022705	Drd3	1.60874E-05	0.00482692	0.06113247	-4.031917235	down	yes
ENSMUSG00000028661	Epha8	1.707E-05	0.00498814	0.28023471	-1.835292428	down	yes
ENSMUSG00000020153	Ndufs7	2.02341E-05	0.00566639	0.43442767	-1.202812077	down	yes
ENSMUSG000000104318	Pcdha7	2.78222E-05	0.00730441	0.32059977	-1.641154677	down	yes
ENSMUSG00000021848	Otx2	2.86294E-05	0.00745805	0.09422551	-3.407738477	down	yes
ENSMUSG00000024330	Col11a2	3.40354E-05	0.00860553	0.44895938	-1.155343157	down	yes
ENSMUSG00000027570	Col9a3	3.61158E-05	0.00898532	0.32872079	-1.605065384	down	yes
ENSMUSG00000018821	Avp1	3.9389E-05	0.00932159	0.38964977	-1.359750095	down	yes
ENSMUSG00000040972	Igsf21	4.18718E-05	0.00970102	0.48263691	-1.050989839	down	yes
ENSMUSG00000031828	Klhl36	4.2147E-05	0.00970102	0.34892149	-1.519025613	down	yes
ENSMUSG00000057342	Sphk2	4.84777E-05	0.01056269	0.49821720	-1.005153252	down	yes
ENSMUSG00000087408	Cers1	4.81158E-05	0.01056269	0.46817806	-1.094870752	down	yes
ENSMUSG00000041351	Rap1gap	5.7278E-05	0.011684689	0.49675110	-1.009404925	down	yes
ENSMUSG00000052837	Junb	5.8403E-05	0.011684689	0.36121476	-1.469071227	down	yes
ENSMUSG00000039477	Tnrc18	7.8412E-05	0.01472087	0.48420003	-1.046324914	down	yes
ENSMUSG00000076614	Ighg1	8.99177E-05	0.01631366	0.00103469	-9.916578503	down	yes
ENSMUSG00000036622	Atp13a2	9.70782E-05	0.01681604	0.48962279	-1.030257367	down	yes
ENSMUSG00000067847	Romo1	0.00010811	0.01789674	0.29414644	-1.765393489	down	yes
ENSMUSG00000039195	1110008P14Rik	0.00012146	0.01954437	0.44719851	-1.161012701	down	yes
ENSMUSG00000023328	Ache	0.00012682	0.02010284	0.45989450	-1.120625124	down	yes
ENSMUSG000000115483	Gm9732	0.00013091	0.02055765	0.00077670	-10.33033912	down	yes
ENSMUSG00000093738	Al606473	0.00013225	0.02067218	0.03487586	-4.841627281	down	yes
ENSMUSG00000023009	Nckap5l	0.00013789	0.021159581	0.36820237	-1.441429163	down	yes
ENSMUSG00000078348	Sf3b5	0.00016238	0.02382981	0.34662183	-1.528565573	down	yes
ENSMUSG00000029755	Dlx5	0.00020977	0.02854061	0.18742649	-2.415603168	down	yes
ENSMUSG00000000120	Ngfr	0.00022032	0.02926490	0.13594458	-2.878909362	down	yes
ENSMUSG00000033427	downb1	0.00023286	0.03044993	0.15121554	-2.725321677	down	yes
ENSMUSG00000043635	Adams3	0.00024090	0.031199678	0.44390586	-1.171674324	down	yes
ENSMUSG00000023911	Flywh2	0.00027211	0.03301205	0.36911253	-1.437867371	down	yes
ENSMUSG00000024112	Cacna1h	0.00027599	0.03325358	0.49524562	-1.013783868	down	yes
ENSMUSG00000041930	Fam222a	0.00027608	0.03325358	0.32399476	-1.625957599	down	yes
ENSMUSG00000030669	Calca	0.00029707	0.03442510	0.22681739	-2.140396836	down	yes
ENSMUSG00000040269	Mrps28	0.00031168	0.03538579	0.47472412	-1.074838713	down	yes
ENSMUSG00000027820	Mme	0.00037029	0.04027069	0.42079147	-1.248822622	down	yes
ENSMUSG0000002799	Jag2	0.00037926	0.04085043	0.47434926	-1.07597837	down	yes
ENSMUSG00000021453	Gadd45g	0.00038438	0.04126865	0.41158990	-1.280720483	down	yes
ENSMUSG00000099227	Mir8114	0.00041678	0.04390660	0.00238770	-8.710162283	down	yes
ENSMUSG00000034739	Mfrp	0.00045082	0.04661526	0.24066883	-2.054878734	down	yes
ENSMUSG00000020902	Ntn1	0.00048935	0.04953283	0.46409141	-1.107519082	down	yes
ENSMUSG00000096929	A330023F24Ri	7.29764E-16	8.17458E-12	3.10857099	1.636251529	up	yes
ENSMUSG00000028268	Gbp3	2.50829E-15	1.68582E-11	2.52179576	1.334451438	up	yes
ENSMUSG00000075602	Ly6a	2.16331E-14	1.21163E-10	2.31004084	1.207918363	up	yes
ENSMUSG00000074896	Ifit3	1.17788E-13	5.45639E-10	2.69571340	1.430667122	up	yes
ENSMUSG00000079363	Gbp4	1.29895E-13	5.45639E-10	2.62838551	1.394176896	up	yes
ENSMUSG00000027514	Zbp1	3.69667E-13	1.3803E-09	5.95237517	2.573465461	up	yes
ENSMUSG00000045868	Gvin1	1.23028E-12	4.13436E-09	2.71698305	1.442005568	up	yes
ENSMUSG00000078921	Tgtp2	4.69049E-12	1.43295E-08	3.62769483	1.859053099	up	yes
ENSMUSG00000069874	Irgm2	6.96883E-12	1.95156E-08	2.42416731	1.277489274	up	yes
ENSMUSG00000078606	Gm4070	7.7124E-12	1.99366E-08	2.61427415	1.386410444	up	yes
ENSMUSG00000029561	Oasl2	1.27763E-10	2.68342E-07	3.38335324	1.758453812	up	yes
ENSMUSG00000064215	Ifi27	4.43349E-10	8.76396E-07	2.02719954	1.019488104	up	yes
ENSMUSG00000070327	Rnf213	5.62872E-10	1.05085E-06	2.28393442	1.191521232	up	yes
ENSMUSG00000032690	Oas2	1.70365E-09	2.86256E-06	4.18442515	2.065029444	up	yes
ENSMUSG00000043263	Ifi209	3.08344E-09	4.93424E-06	4.99748971	2.321203598	up	yes
ENSMUSG000000105504	Gbp5	3.50501E-09	5.12112E-06	2.14861535	1.103407236	up	yes
ENSMUSG00000073491	Ifi213	3.96982E-09	5.55857E-06	6.83634575	2.773225364	up	yes
ENSMUSG00000073409	H2-Q6	5.96839E-09	7.71415E-06	4.95918462	2.310102937	up	yes
ENSMUSG00000037921	Ddx60	5.83274E-09	7.71415E-06	3.79936781	1.925759386	up	yes

ENSMUSG00000100254	Trpc2	1.00622E-08	1.25237E-05	3083.65	11.59042331	up	yes
ENSMUSG00000024136	Dnase1l2	1.19509E-08	1.38486E-05	2.01275839	1.009174008	up	yes
ENSMUSG00000040483	Xaf1	1.24176E-08	1.39098E-05	2.34934699	1.232259813	up	yes
ENSMUSG00000029454	Mapkapk5	1.60929E-08	1.69001E-05	3.82424466	1.935174825	up	yes
ENSMUSG00000033355	Rtp4	1.607E-08	1.69001E-05	3.16773462	1.66345148	up	yes
ENSMUSG00000030653	Gm45837	2.40996E-08	2.30809E-05	347.634319	8.441426708	up	yes
ENSMUSG00000025492	Ifitm3	2.47258E-08	2.30809E-05	3.05644828	1.611856155	up	yes
ENSMUSG00000026222	Sp100	4.37994E-08	3.97805E-05	2.28628175	1.193003209	up	yes
ENSMUSG00000035692	lsg15	4.87692E-08	4.31286E-05	3.25005711	1.70046507	up	yes
ENSMUSG00000034459	Ifit1	5.03339E-08	4.33711E-05	3.41276187	1.770939754	up	yes
ENSMUSG00000062488	Ifit3b	5.27061E-08	4.42797E-05	2.23370553	1.159439009	up	yes
ENSMUSG00000087579	Hectd2os	5.9351E-08	4.74879E-05	6.24399590	2.642469591	up	yes
ENSMUSG00000025498	Irf7	6.21505E-08	4.85714E-05	3.82240437	1.934480409	up	yes
ENSMUSG00000066861	Oas1g	9.55967E-08	7.30119E-05	6.99293797	2.805898709	up	yes
ENSMUSG00000033880	Lgals3bp	1.02626E-07	7.50551E-05	2.2328699	1.158899194	up	yes
ENSMUSG00000024066	Xdh	1.02739E-07	7.50551E-05	2.15697846	1.109011774	up	yes
ENSMUSG00000035208	Slfn8	1.17335E-07	8.21467E-05	3.11489368	1.639182923	up	yes
ENSMUSG00000010358	Ifi35	1.53878E-07	9.75676E-05	2.17926185	1.123839556	up	yes
ENSMUSG00000030921	Trim30a	1.7246E-07	0.00010537	2.52243006	1.334814269	up	yes
ENSMUSG00000052776	Oas1a	2.15089E-07	0.00012251	3.58416017	1.841635112	up	yes
ENSMUSG00000034422	Parp14	5.55598E-07	0.00029173	2.38848283	1.256094508	up	yes
ENSMUSG00000026536	Ifi211	5.98563E-07	0.00030502	5.58796058	2.482321845	up	yes
ENSMUSG00000030107	Usp18	6.65088E-07	0.00032391	3.31917587	1.730825076	up	yes
ENSMUSG00000073490	Ifi207	7.32828E-07	0.00035181	5.59399937	2.483880091	up	yes
ENSMUSG00000017830	Dhx58	1.29673E-06	0.00059693	2.36457045	1.241578128	up	yes
ENSMUSG00000028270	Gbp2	1.36433E-06	0.00061957	2.59518475	1.375837248	up	yes
ENSMUSG00000078903	Gm14391	1.46682E-06	0.00065723	2.52250645	1.33485796	up	yes
ENSMUSG00000073489	Ifi204	1.58405E-06	0.00070042	4.32495303	2.112684465	up	yes
ENSMUSG00000056290	Ms4a4b	1.83175E-06	0.00077918	21.5260645	4.428012683	up	yes
ENSMUSG00000056144	Trim34a	2.83339E-06	0.001175509	2.19541618	1.134494458	up	yes
ENSMUSG00000026628	Atf3	3.05178E-06	0.00122089	3.49812492	1.806581811	up	yes
ENSMUSG00000090733	Rps27	3.00606E-06	0.00122089	2.59244488	1.374313319	up	yes
ENSMUSG00000029605	Oas1b	4.02299E-06	0.00151901	3.86326720	1.949821467	up	yes
ENSMUSG00000000049	ApoH	4.22957E-06	0.00156070	2173.23563	11.08562889	up	yes
ENSMUSG00000097654	Gm26714	8.41707E-06	0.00274617	2115.45333	11.04675115	up	yes
ENSMUSG00000058163	Gm5431	8.7812E-06	0.00281040	3.85275525	1.94589054	up	yes
ENSMUSG00000106247	Gm43720	1.45319E-05	0.00439950	6.39434779	2.676797215	up	yes
ENSMUSG00000018927	Ccl6	1.85443E-05	0.00533316	2.12489921	1.087394412	up	yes
ENSMUSG00000032596	Uba7	2.06787E-05	0.00574302	2.02363081	1.016946111	up	yes
ENSMUSG00000040170	Fmo2	2.47882E-05	0.00655912	2.08656164	1.061127541	up	yes
ENSMUSG00000116305	Lncppara	3.00349E-05	0.00770476	2.49026577	1.31629972	up	yes
ENSMUSG00000030165	Klrd1	4.87195E-05	0.01056269	1978.66639	10.95031268	up	yes
ENSMUSG00000035370	Gm49322	5.08822E-05	0.01068684	3.10085231	1.632664814	up	yes
ENSMUSG00000079017	Ifi2712a	5.84148E-05	0.011684689	6.14614003	2.619680637	up	yes
ENSMUSG00000028037	Ifi44	5.75204E-05	0.011684689	4.81192849	2.266615203	up	yes
ENSMUSG00000078922	Tgtp1	6.21152E-05	0.01215209	2.74632101	1.457500273	up	yes
ENSMUSG00000022014	Epsti1	6.36779E-05	0.01229824	2.35178571	1.233756613	up	yes
ENSMUSG00000063286	Gm8995	6.55223E-05	0.01254085	2.02845525	1.02038148	up	yes
ENSMUSG00000000386	Mx1	8.28173E-05	0.01530652	2.98400568	1.577250284	up	yes
ENSMUSG00000074151	Nlrc5	8.6358E-05	0.01585825	3.01071403	1.590105685	up	yes
ENSMUSG00000020641	Rsad2	0.00011988	0.01946252	2.21733930	1.148829554	up	yes
ENSMUSG00000038811	Gngt2	0.00014887	0.02253570	2.40504555	1.266064219	up	yes
ENSMUSG00000054072	Ilgp1	0.00015377	0.02286536	2.45923656	1.298210522	up	yes
ENSMUSG00000034947	Tmem106a	0.00015446	0.02286695	2.54046164	1.345090683	up	yes
ENSMUSG00000112248	Gm47910	0.00016762	0.02421614	702.413333	9.45617642	up	yes
ENSMUSG00000104713	Gbp6	0.00017103	0.02435464	2.21081022	1.144575188	up	yes
ENSMUSG00000103092	Pcdha5	0.00017533	0.02475626	2.27154966	1.183676847	up	yes
ENSMUSG00000072620	Slfn2	0.00018229	0.02563177	2.39828521	1.262003242	up	yes
ENSMUSG00000040613	Apobec1	0.00019298	0.02690996	2.10213621	1.071856158	up	yes
ENSMUSG00000070034	Sp110	0.00020558	0.02819809	2.19230947	1.132451468	up	yes
ENSMUSG00000054404	Slfn5	0.00020798	0.028411733	2.37852413	1.250066667	up	yes

ENSMUSG00000064147	Rab44	0.00027059	0.03301205	396.066362	8.62959837	up	yes
ENSMUSG00000059089	Fcgr4	0.00032158	0.03612883	3.00925440	1.589406078	up	yes
ENSMUSG00000067577	A430093F15Ri	0.00036109	0.03965536	678.136985	9.40543292	up	yes
ENSMUSG00000078153	Psme2b	0.00036660	0.03999923	2.01293434	1.009300119	up	yes
ENSMUSG00000024338	Psmb8	0.00037690	0.04072629	2.42629774	1.278756602	up	yes
ENSMUSG00000089929	Bcl2a1b	0.00041166	0.04363981	2.12978539	1.090708064	up	yes
ENSMUSG00000037580	Gch1	0.00043070	0.04508997	2.78647822	1.478442877	up	yes
ENSMUSG00000030577	Cd22	0.00046245	0.04733994	3.29593619	1.720688312	up	yes

Notes: DEGs: Differentially Expressed Genes; p: p value; q: q value; fc: fold change.

### Supplementary table 6 The enriched pathways of DEGs

Pathway ID	Pathway Name	Rich Factor	Q value	Significant (Q)
mmu04621	NOD-like receptor signaling pathway	0.0663	4.60667E-13	****
mmu05169	Epstein-Barr virus infection	0.0448	2.93449E-09	****
mmu05160	Hepatitis C	0.0467	2.04419E-07	****
mmu05164	Influenza A	0.0458	2.04419E-07	****
mmu05162	Measles	0.0451	2.28596E-06	****
mmu05168	Herpes simplex virus 1 infection	0.0198	7.13429E-06	****
mmu04622	RIG-I-like receptor signaling pathway	0.0678	5.14075E-05	****
mmu04623	Cytosolic DNA-sensing pathway	0.0577	0.001414805	**
mmu04080	Neuroactive ligand-receptor interaction	0.0156	0.00263165	**
mmu04612	Antigen processing and presentation	0.0411	0.003108272	**
mmu04974	Protein digestion and absorption	0.0361	0.004125995	**
mmu04060	Cytokine-cytokine receptor interaction	0.015	0.010433031	*
mmu04650	Natural killer cell mediated cytotoxicity	0.0242	0.01123492	*
mmu04010	MAPK signaling pathway	0.0137	0.012449166	*
mmu04514	Cell adhesion molecules	0.0196	0.017511021	*
mmu05165	Human papillomavirus infection	0.0119	0.017511021	*
mmu04151	PI3K-Akt signaling pathway	0.0118	0.017511021	*
mmu00600	Sphingolipid metabolism	0.0435	0.017511021	*
mmu05202	Transcriptional misregulation in cancer	0.0175	0.017511021	*
mmu05332	Graft-versus-host disease	0.0417	0.017511021	*
mmu03050	Proteasome	0.0435	0.017511021	*
mmu04062	Chemokine signaling pathway	0.016	0.020719371	*
mmu05167	Kaposi sarcoma-associated herpesvirus infection	0.016	0.020719371	*
mmu05203	Viral carcinogenesis	0.0142	0.026643334	*
mmu05140	Leishmaniasis	0.0308	0.026643334	*
mmu04662	B cell receptor signaling pathway	0.0286	0.029589025	*
mmu00983	Drug metabolism - other enzymes	0.026	0.034269672	*
mmu00232	Caffeine metabolism	0.2	0.037834625	*
mmu04658	Th1 and Th2 cell differentiation	0.0233	0.03948157	*
mmu04640	Hematopoietic cell lineage	0.0225	0.040762671	*
mmu05032	Morphine addiction	0.022	0.041164655	*
mmu04713	Circadian entrainment	0.0208	0.044174913	*

mmu04925	Aldosterone synthesis and secretion	0.0198	0.047191979	*
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Notes: DEGs: Differentially Expressed Genes; \*: p<0.05; \*\*: p<0.01; \*\*\*: p<0.001; \*\*\*\*: p<0.0001.

Supplementary table 7 DEMs of MOTS-c VS TBI groups

HMDB	Metabolite name	VIP	P value	regulation	significant
HMDB0032231	Dimethylethanolamine	2.821352005	0.000283694	down	yes
		2.73740952	0.000753404	down	yes
		2.597937554	0.000856888	down	yes
		2.888207443	0.001395312	down	yes
HMDB0000123	Glycine	2.503363959	0.001879567	down	yes
		2.704342838	0.001930188	down	yes
		2.215092496	0.002124729	down	yes
		2.022490755	0.002209568	down	yes
		2.70203825	0.002288819	down	yes
		2.30219169	0.002550056	down	yes
		2.595185923	0.002561096	down	yes
		2.329819681	0.002573347	down	yes
		1.86713322	0.002898452	down	yes
		2.503555273	0.003111726	down	yes
		2.126184412	0.003163752	down	yes
		2.33457664	0.003469313	down	yes
		2.621949794	0.003526997	down	yes
		2.432743372	0.003817645	down	yes
		2.621159097	0.003915146	down	yes
		2.794214805	0.00397131	down	yes
		2.576602029	0.004076242	down	yes
		2.350146755	0.004135985	down	yes
		2.195032099	0.004320259	down	yes
		2.579451778	0.004416405	down	yes
		2.475324201	0.004530228	down	yes
		2.496764805	0.004549787	down	yes
		2.270184187	0.004690052	down	yes
2.192751126	0.004931676	down	yes		
2.227365479	0.005053274	down	yes		
2.388289702	0.005098676	down	yes		
2.379576395	0.005169646	down	yes		
2.249765866	0.005431724	down	yes		
HMDB0031004	Diatretin 2	2.383770699	0.005535939	down	yes
		2.170147634	0.005703581	down	yes
		2.143876126	0.005835642	down	yes
		2.373664376	0.006021024	down	yes
		1.85824927	0.006023892	down	yes
		2.228662973	0.006215177	down	yes
		2.33680669	0.006312163	down	yes
		2.502613677	0.006542304	down	yes
		2.310193058	0.006573191	down	yes
		2.307345127	0.006879567	down	yes
		2.11845396	0.007013191	down	yes
		2.081068777	0.007422792	down	yes
		1.911174016	0.007680523	down	yes
		2.205889612	0.007860007	down	yes
		2.310377801	0.007901345	down	yes
		2.379429646	0.007925159	down	yes
		2.207979167	0.007944493	down	yes
2.283283038	0.008077797	down	yes		
2.547869859	0.008323066	down	yes		

		2.062242244	0.008506621	down	yes
		2.23955332	0.008559824	down	yes
		1.980525037	0.008592402	down	yes
		2.06834008	0.008656086	down	yes
		2.170478361	0.008794611	down	yes
		2.389950741	0.008995538	down	yes
HMDB0125371	2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy-3,4-	1.760038424	0.00901561	down	yes
		2.221267267	0.009158855	down	yes
		2.233054853	0.009286621	down	yes
		1.928664682	0.009302548	down	yes
		2.390497658	0.00938244	down	yes
		2.389093874	0.009436041	down	yes
		1.636718912	0.009493245	down	yes
		2.141388988	0.009780805	down	yes
		2.238176868	0.009830311	down	yes
		2.075675262	0.009991662	down	yes
		2.278322166	0.010106944	down	yes
		1.737152667	0.010186458	down	yes
		2.433747537	0.010290299	down	yes
		2.453138049	0.01048556	down	yes
		2.385103691	0.010649727	down	yes
		1.920196511	0.010739228	down	yes
		2.048333795	0.01074575	down	yes
		2.021497478	0.010879772	down	yes
		2.29277936	0.010923438	down	yes
		1.98952551	0.011240411	down	yes
		2.549842671	0.011420969	down	yes
		2.03022719	0.011576267	down	yes
		2.173878789	0.012163172	down	yes
		2.102831844	0.012168746	down	yes
		2.146643072	0.012434448	down	yes
		1.936297897	0.012480244	down	yes
		2.041291395	0.012752377	down	yes
		2.251956362	0.013175464	down	yes
		1.903038719	0.013298289	down	yes
		2.176256711	0.013452572	down	yes
		2.012136948	0.013518814	down	yes
		2.332748524	0.013521273	down	yes
		2.280293837	0.013786872	down	yes
		2.286746326	0.01381145	down	yes
		2.062855991	0.014024388	down	yes
		2.318723654	0.014133378	down	yes
		2.512472497	0.014179229	down	yes
		1.816564203	0.014635704	down	yes
	Nimustine (hydrochloride)	2.495412264	0.014755785	down	yes
		1.936731274	0.01479426	down	yes
		1.870600087	0.014858807	down	yes
		1.391371309	0.014975375	down	yes
		1.906827485	0.015099946	down	yes
		1.733329051	0.015268998	down	yes
		1.945248615	0.015286423	down	yes
	2-Propylpiperidine	2.237349926	0.015315643	down	yes
		2.156484823	0.015387848	down	yes
		1.944716062	0.015461136	down	yes
		2.340214002	0.015540448	down	yes
		2.201413597	0.015666661	down	yes
		2.172182847	0.015776552	down	yes
		2.219749799	0.015876396	down	yes
		2.360746388	0.016052512	down	yes
		2.468868383	0.016072552	down	yes
		1.639919526	0.016082031	down	yes



		2.05704561	0.016148166	down	yes
		2.308764674	0.016161417	down	yes
		1.848933921	0.016669246	down	yes
		1.673420584	0.016871327	down	yes
		1.679750032	0.017085673	down	yes
		2.02690743	0.017305772	down	yes
		1.582422563	0.017390266	down	yes
		2.350726987	0.017566331	down	yes
		2.161115267	0.017569748	down	yes
		1.980537111	0.017643998	down	yes
		2.140626547	0.018243544	down	yes
		1.971385599	0.018503125	down	yes
		2.10349421	0.018566217	down	yes
		1.877167567	0.018790812	down	yes
		1.996693257	0.01887683	down	yes
		1.75973598	0.019297302	down	yes
		2.44655547	0.01940395	down	yes
		1.779656249	0.019405253	down	yes
		2.249458564	0.019565149	down	yes
		2.331474013	0.01965807	down	yes
HMDB0240280	Mesylate	2.540062889	0.019747326	down	yes
		2.019423205	0.01977392	down	yes
		1.737173782	0.019801291	down	yes
		2.163258241	0.020185262	down	yes
		2.051347652	0.020731608	down	yes
		2.045201511	0.020991542	down	yes
		2.16803033	0.021141624	down	yes
		2.142791266	0.021249638	down	yes
		2.412448517	0.021339444	down	yes
		2.326226682	0.021423963	down	yes
		2.27457312	0.021442991	down	yes
		2.122012315	0.021557087	down	yes
		1.799350641	0.021714076	down	yes
		2.127835596	0.021721607	down	yes
		1.852337554	0.021727281	down	yes
		2.275664941	0.02227766	down	yes
		1.620727627	0.022284199	down	yes
		1.821357985	0.022328942	down	yes
		2.221873521	0.022482354	down	yes
		2.222572059	0.022546614	down	yes
		2.069887302	0.0226785	down	yes
		1.664054455	0.022717772	down	yes
		1.871525112	0.022930327	down	yes
		2.252569966	0.022946018	down	yes
		1.904112723	0.023083441	down	yes
		1.977030903	0.023161436	down	yes
		1.830269925	0.023580105	down	yes
		2.008449701	0.023673465	down	yes
		1.985081449	0.023802538	down	yes
		1.860630992	0.023922391	down	yes
		1.801861743	0.023999442	down	yes
		2.020245153	0.02408834	down	yes
		1.632336919	0.02442585	down	yes
		2.128547976	0.024925085	down	yes
		1.406284098	0.025041788	down	yes
HMDB0000202	Methylmalonic acid	1.698986726	0.025162608	down	yes
		1.883155672	0.025170318	down	yes
		2.30035463	0.025461841	down	yes
		2.139616177	0.025480084	down	yes
		1.448590946	0.025588668	down	yes
		1.70567357	0.025636372	down	yes

		1.716240356	0.025672497	down	yes
		1.988821459	0.025740387	down	yes
		2.359122937	0.025802971	down	yes
		2.143495061	0.026126908	down	yes
		2.043001717	0.026289042	down	yes
HMDB0008064	PC(18:1(11Z)/14:0)	1.988850139	0.026305933	down	yes
HMDB0001062	N-Acetyl-D-Glucosamine 6-Phosphate	1.840892391	0.026336294	down	yes
		1.737307682	0.026341157	down	yes
		2.016641103	0.026400275	down	yes
		2.034232412	0.026555261	down	yes
		1.916357189	0.02682194	down	yes
HMDB0010169	SM(d18:1/16:0)	2.116963599	0.026902083	down	yes
		2.12090048	0.027038037	down	yes
		2.206491475	0.027039923	down	yes
		1.887917286	0.027071895	down	yes
		2.194142523	0.02719234	down	yes
		1.706768208	0.027703742	down	yes
		1.909993024	0.028097158	down	yes
HMDB0034777	Epidermin	2.141012542	0.028097262	down	yes
		1.921499619	0.029133081	down	yes
		2.10972483	0.029185492	down	yes
		2.142627024	0.029367531	down	yes
		2.14219938	0.029444701	down	yes
		1.963407776	0.029488725	down	yes
		2.284788884	0.029810891	down	yes
HMDB0010396	LysoPC(20:4(8Z,11Z,14Z,17Z))	1.920072469	0.030511193	down	yes
		1.692574279	0.030518672	down	yes
		2.041386009	0.030618489	down	yes
		1.952844746	0.030859317	down	yes
		1.95199571	0.031411647	down	yes
		1.71399004	0.031507978	down	yes
		1.959639337	0.031553563	down	yes
		1.882611776	0.031582421	down	yes
		1.848355051	0.03158842	down	yes
		1.943206277	0.031789799	down	yes
		1.746427899	0.031862698	down	yes
		1.703648891	0.031897502	down	yes
	3-Aminobenzamide	1.624750489	0.032162635	down	yes
		2.043070779	0.032450843	down	yes
		1.70934942	0.03246392	down	yes
		2.056656962	0.032627449	down	yes
		1.532585978	0.033733596	down	yes
		2.100923775	0.033914412	down	yes
		1.916652231	0.034127096	down	yes
		1.78167661	0.0341712	down	yes
		1.730646011	0.034185373	down	yes
		2.192734877	0.034290954	down	yes
		2.287199147	0.034606691	down	yes
		1.585183634	0.034743014	down	yes
		1.692314594	0.034786618	down	yes
		2.062122531	0.03508695	down	yes
		1.990901065	0.03533604	down	yes
		2.017316894	0.035447218	down	yes
		2.071909141	0.035580718	down	yes
		1.878957767	0.035725768	down	yes
		1.532145033	0.035755688	down	yes
		1.858176827	0.03578536	down	yes
		1.734242427	0.035939706	down	yes
		2.138915973	0.036370738	down	yes
		1.560748233	0.036651609	down	yes
		2.056356013	0.036667378	down	yes

		2.270876648	0.036774863	down	yes
		1.621748665	0.03679006	down	yes
	Kifunensine	2.33046411	0.037249019	down	yes
		2.115881206	0.037268462	down	yes
		1.883672598	0.037953179	down	yes
HMDB0009454	PE(20:5(5Z,8Z,11Z,14Z,17Z)/18:1(11Z))	1.97700702	0.038143954	down	yes
		1.838733393	0.038154143	down	yes
HMDB0059611	Thiomorpholine 3-carboxylate	2.15809825	0.038363135	down	yes
		1.700786378	0.038402232	down	yes
		1.546609222	0.038482176	down	yes
		1.889841671	0.038601037	down	yes
		1.84391127	0.038807551	down	yes
		1.757236094	0.039012776	down	yes
		2.090184109	0.039049283	down	yes
		1.78537979	0.039501131	down	yes
		2.242819026	0.039723319	down	yes
		1.828368387	0.039860455	down	yes
		1.756822014	0.040274222	down	yes
		1.526157159	0.040348596	down	yes
		1.533855207	0.040564088	down	yes
		1.718215258	0.040668604	down	yes
		1.997577954	0.041120108	down	yes
		1.821334628	0.041144832	down	yes
		1.869597624	0.041253139	down	yes
		1.734296087	0.041408405	down	yes
		2.228397012	0.041488208	down	yes
		1.654520903	0.041840714	down	yes
HMDB0003411	D-Proline	1.806841637	0.041870291	down	yes
		1.68243216	0.042000185	down	yes
		2.112404286	0.042091715	down	yes
		1.977674057	0.04212705	down	yes
		1.608289166	0.04216883	down	yes
		1.297676733	0.042401434	down	yes
		1.749026251	0.042410728	down	yes
		1.944535425	0.042860591	down	yes
		1.973757032	0.042979373	down	yes
		2.005341265	0.043269281	down	yes
		1.498840302	0.043495907	down	yes
		2.189009303	0.043579334	down	yes
		2.083156228	0.043777645	down	yes
		2.061660224	0.044125209	down	yes
		1.962418261	0.04419214	down	yes
		1.909402989	0.044337168	down	yes
		2.028960875	0.045069912	down	yes
		2.114123006	0.045475201	down	yes
	S-1-Propenyl-L-cysteine	2.127759222	0.045826135	down	yes
		1.824859231	0.045964589	down	yes
		1.786755652	0.04639608	down	yes
		1.830846281	0.046469965	down	yes
		1.473154001	0.046514293	down	yes
HMDB0000904	Citrulline	1.941879457	0.046572475	down	yes
		1.595959244	0.046578	down	yes
		1.890293816	0.046678699	down	yes
		2.018838023	0.046803303	down	yes
		1.758633089	0.046863764	down	yes
		1.926355146	0.047256387	down	yes
		1.681227126	0.047557489	down	yes
HMDB0000300	Uracil	1.958704593	0.047670873	down	yes
HMDB0061695	1-Palmitoylglycerophosphoinositol	1.877576166	0.048010551	down	yes
		2.040886582	0.048369912	down	yes
		1.831332438	0.048389747	down	yes

		1.927048379	0.048646383	down	yes
		1.602634357	0.048719988	down	yes
		1.931266592	0.048939743	down	yes
		1.964705361	0.049119053	down	yes
		2.035001916	0.049249818	down	yes
		1.708504983	0.04928279	down	yes
		1.657343064	0.04928653	down	yes
		2.054589945	0.049387963	down	yes
HMDB0032255	N-[(Ethoxycarbonyl)methyl]-p-menthane-3-	1.822868759	0.049681661	down	yes
		2.408879463	0.000409922	up	yes
		2.803558811	0.000491415	up	yes
		2.811715157	0.000538638	up	yes
		2.806633966	0.000561405	up	yes
		2.789318032	0.000660928	up	yes
		2.607224912	0.000661617	up	yes
		2.661600977	0.000731593	up	yes
		2.759600729	0.000811529	up	yes
		2.735914063	0.00083193	up	yes
		2.703301661	0.001471705	up	yes
		2.462334782	0.001484956	up	yes
HMDB0000101	Deoxyadenosine	2.593163018	0.001687792	up	yes
		2.505664403	0.001693801	up	yes
HMDB0000050	Adenosine	2.665599684	0.001866762	up	yes
HMDB0032593	4-(Hydroxymethyl)benzenediazonium(1+)	2.668893672	0.0018891	up	yes
		2.39956734	0.002547344	up	yes
		2.381362148	0.002802227	up	yes
		2.574314275	0.002907817	up	yes
		2.264900099	0.003207329	up	yes
		2.368352563	0.003468416	up	yes
		2.537488499	0.003629429	up	yes
		1.860758712	0.003696873	up	yes
		2.65044491	0.004107578	up	yes
		2.638517646	0.00433689	up	yes
		2.424377531	0.004476935	up	yes
		2.192980765	0.004897572	up	yes
		2.458945684	0.005025504	up	yes
		2.465755864	0.005742115	up	yes
		2.119788374	0.006872236	up	yes
		1.854536546	0.0076583	up	yes
		2.495930238	0.007932851	up	yes
		2.425125224	0.007979132	up	yes
		2.316135126	0.008438243	up	yes
		2.276366014	0.008630997	up	yes
		2.335241957	0.00866854	up	yes
		2.285326806	0.008737097	up	yes
		1.935716039	0.008863252	up	yes
		2.485714192	0.00901468	up	yes
		1.887730772	0.009119628	up	yes
		2.434759966	0.009479247	up	yes
		2.152859705	0.009780439	up	yes
		2.496899377	0.010074526	up	yes
		2.419423807	0.010086146	up	yes
		2.101422407	0.010355632	up	yes
		2.249111755	0.010453692	up	yes
		2.228379227	0.010485877	up	yes
		2.181801744	0.010862066	up	yes
		2.01186061	0.010970616	up	yes
		2.387706763	0.011573418	up	yes
		2.184556219	0.011618804	up	yes
		2.272349988	0.01171744	up	yes
HMDB0000247	Sorbitol	2.022951537	0.011929195	up	yes

	2.1398392	0.012240911	up	yes
	2.157414192	0.0123401	up	yes
	2.194799749	0.012627798	up	yes
	2.373157868	0.012918115	up	yes
	2.286896358	0.013634378	up	yes
	2.307520892	0.013880281	up	yes
	1.385275706	0.014014261	up	yes
	2.296233458	0.01434704	up	yes
	2.50655685	0.014544756	up	yes
	1.948295161	0.014678	up	yes
	2.313181736	0.014778351	up	yes
	2.154804836	0.01477856	up	yes
	2.321929063	0.014848547	up	yes
	1.893151314	0.014993655	up	yes
	2.379929907	0.015217763	up	yes
	2.231105614	0.01606771	up	yes
	2.293804523	0.016529598	up	yes
	2.017160151	0.016794377	up	yes
	1.963155222	0.017059106	up	yes
3-Hydroxy-3-methylglutaric acid	2.175414136	0.017260586	up	yes
	1.732784498	0.018449686	up	yes
	2.003671847	0.01867844	up	yes
	2.228546013	0.018741903	up	yes
	1.893932728	0.01915022	up	yes
	2.308932915	0.019488521	up	yes
	1.924457429	0.020663182	up	yes
	2.27177848	0.020836563	up	yes
	1.828202469	0.020904389	up	yes
	2.036817283	0.021298945	up	yes
	2.320753308	0.021478255	up	yes
	2.136863076	0.022184431	up	yes
	1.845340018	0.022918368	up	yes
	1.73321476	0.023173132	up	yes
	1.862895656	0.023378018	up	yes
	2.271849409	0.023577029	up	yes
	1.621468366	0.023983545	up	yes
	1.953897094	0.024120252	up	yes
	1.940607364	0.024405063	up	yes
	2.288761228	0.024661283	up	yes
	2.02335716	0.025078911	up	yes
	2.138361385	0.025732118	up	yes
	2.280708858	0.025746226	up	yes
	2.16929691	0.025754954	up	yes
	1.52121349	0.025969912	up	yes
	1.675608009	0.0260818	up	yes
	1.865936273	0.026327288	up	yes
D-(+)-Mannose	1.875075204	0.026510011	up	yes
	1.557832053	0.026645982	up	yes
	2.264755074	0.026704563	up	yes
	1.728009406	0.026824424	up	yes
	2.188882737	0.026897984	up	yes
	1.798187622	0.02753598	up	yes
	1.688626789	0.028054124	up	yes
	2.137248161	0.028376226	up	yes
	2.158011469	0.029008124	up	yes
	1.787418364	0.029018043	up	yes
	1.845728132	0.029068449	up	yes
	1.988540785	0.029279004	up	yes
	2.017051328	0.029348311	up	yes
	1.696971355	0.029516171	up	yes
	2.099387695	0.029533509	up	yes

		2.318217563	0.029585885	up	yes
		1.823075695	0.029737556	up	yes
		1.832087866	0.029812435	up	yes
		1.849657969	0.030176693	up	yes
		1.884173192	0.030329081	up	yes
		1.850793826	0.031563809	up	yes
		2.150992905	0.031822277	up	yes
		2.135323257	0.032005234	up	yes
		1.46264195	0.032171874	up	yes
		2.07801907	0.032645531	up	yes
		2.181570519	0.032900025	up	yes
		2.143702102	0.032941215	up	yes
		1.747449853	0.03358861	up	yes
		2.289757379	0.03365383	up	yes
		1.934406347	0.033830084	up	yes
HMDB0000114	Glycerolphosphorylethanolamine	2.106169743	0.034110186	up	yes
		1.695595402	0.034116398	up	yes
		1.981270258	0.034730251	up	yes
		1.893245812	0.035068943	up	yes
		2.088124468	0.035409006	up	yes
		2.073665638	0.03596806	up	yes
		1.748138704	0.036214435	up	yes
		1.87809325	0.036568767	up	yes
HMDB0000086	Glycerophosphocholine	2.061136288	0.037038603	up	yes
		1.6508035	0.037048389	up	yes
		2.207011059	0.03726192	up	yes
		1.755610491	0.037601167	up	yes
		1.939729566	0.037688921	up	yes
		1.697006093	0.037806431	up	yes
		2.134333839	0.037825581	up	yes
		2.038297247	0.038682597	up	yes
		1.959417444	0.039350745	up	yes
		2.079120521	0.039356881	up	yes
HMDB0000190	L-Lactic acid	1.603348544	0.039419229	up	yes
		1.681470072	0.039637663	up	yes
		1.859143987	0.039745298	up	yes
		1.662990829	0.039987092	up	yes
		1.964764321	0.0403896	up	yes
		2.102287169	0.041397108	up	yes
		2.114910349	0.041907669	up	yes
		2.120175882	0.042346021	up	yes
		1.517269004	0.042576278	up	yes
		1.911740257	0.042633001	up	yes
		2.216143856	0.043227612	up	yes
		1.84286065	0.043457279	up	yes
		1.753224234	0.043860743	up	yes
		2.068932433	0.043944742	up	yes
		2.062638142	0.044125733	up	yes
		2.10944788	0.044471319	up	yes
		1.740576334	0.044573028	up	yes
		2.102622705	0.044853569	up	yes
		1.56798123	0.045991903	up	yes
		1.891241189	0.046022318	up	yes
		1.619464937	0.046116562	up	yes
		1.791809574	0.046321111	up	yes
		1.622834782	0.046696293	up	yes
		1.739141768	0.046795362	up	yes
		2.032610761	0.046867402	up	yes
		2.097332426	0.047172227	up	yes
		1.564536972	0.047499963	up	yes
		1.728744819	0.047645031	up	yes

2.091749623	0.047653954	up	yes
1.668813207	0.047837122	up	yes
1.406619022	0.048108991	up	yes
1.722783376	0.0481971	up	yes
1.61342549	0.048430399	up	yes
1.765466911	0.048641227	up	yes
1.505124775	0.048813888	up	yes
2.010127635	0.048853631	up	yes
1.503694132	0.049015523	up	yes
2.041542214	0.049156749	up	yes
1.870413918	0.049167061	up	yes
1.715239175	0.049522492	up	yes
1.792269175	0.04960253	up	yes

Notes: DEMs: Differentially Expressed Metabolites; VIP: variable importance in projection values.

### Supplementary table 8 The enriched pathways of DEMs

Pathway2	-lg2(p)	Impact
Glycerophospholipid metabolism	3.5319	0.0463
Cyanoamino acid metabolism	2.9208	0
Arginine and proline metabolism	2.8274	0.03042
Methane metabolism	2.528	0
Nitrogen metabolism	2.528	0
Purine metabolism	2.0721	0.00581
Pantothenate and CoA biosynthesis	2.0424	0
beta-Alanine metabolism	1.9256	0
Fructose and mannose metabolism	1.731	0.03142
Pyruvate metabolism	1.6483	0
Glycolysis or Gluconeogenesis	1.5382	0
Galactose metabolism	1.5382	0
Glutathione metabolism	1.5382	0.00573
Porphyrin and chlorophyll metabolism	1.5046	0
Glycine, serine and threonine metabolism	1.383	0.26884
Amino sugar and nucleotide sugar metabolism	1.2307	0.04649
Valine, leucine and isoleucine degradation	1.2081	0
Pyrimidine metabolism	1.1444	0.04182
Primary bile acid biosynthesis	1.0496	0.02976
Aminoacyl-tRNA biosynthesis	0.73628	0

Notes: DEMs: Differentially Expressed Metabolites.

### Supplementary table 9 KEGG pathways involving both DEGs and DEMs

ID	Description	DEGs and DEMs	Count
mmu01100	Metabolic pathways	cpd: C00106 Uracil; cpd:C00794 D-Sorbitol; cpd:C00550 Sphingomyelin; cpd:C00350 Phosphatidylethanolamine; cpd:C00157 Phosphatidylcholine; cpd:C00357 N-Acetyl-D-glucosamine 6-phosphate; cpd:C02170 Methylmalonate; cpd:C00186 (S)-Lactate; cpd:C00037 Glycine; cpd:C01233 sn-	19

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		Glycero-3-phosphoethanolamine; cpd:C00763 D-Proline; cpd:C04308 Phosphatidyl-N-dimethylethanolamine; cpd:C00559 Deoxyadenosine; cpd:C00327 L-Citrulline cpd:C00212 Adenosine; mmu:17319 Mif: macrophage migration inhibitory factor (glycosylation-inhibiting factor); mmu:75406 Ndufs7: NADH:ubiquinone oxidoreductase core subunit S7; mmu:103149 Upb1: ureidopropionase, beta; mmu:12346 Car1: carbonic anhydrase 1	
mmu00564	Glycerophospholipid metabolism	cpd: C00350 Phosphatidylethanolamine; cpd:C00157 Phosphatidylcholine; cpd:C04230 1-Acyl-sn-glycero-3-phosphocholine; cpd:C01233 sn-Glycero-3-phosphoethanolamine; cpd:C00670 sn-Glycero-3-phosphocholine; cpd:C04308 Phosphatidyl-N-dimethylethanolamine; mmu:12647 Chat: choline acetyltransferase	7
mmu04080	Neuroactive ligand-receptor interaction	cpd: C00037 Glycine; cpd:C00212 Adenosine; mmu:21333 Tac1: tachykinin 1; mmu:13490 Drd3: dopamine receptor D3; mmu:11552 Adra2b: adrenergic receptor, alpha 2b; mmu:13488 Drd1: dopamine receptor D1	6
mmu05231	Choline metabolism in cancer	cpd: C00157 Phosphatidylcholine; cpd:C04230 1-Acyl-sn-glycero-3-phosphocholine; cpd:C00670 sn-Glycero-3-phosphocholine; mmu:63993 Slc5a7: solute carrier family 5 (choline transporter), member 7	4
mmu00240	Pyrimidine metabolism	cpd: C00106 Uracil; cpd:C02170 Methylmalonate; mmu:103149 Upb1: ureidopropionase, beta	3
mmu04723	Retrograde endocannabinoid signaling	cpd: C00350 Phosphatidylethanolamine; cpd:C00157 Phosphatidylcholine;mmu:75406 Ndufs7: NADH:ubiquinone oxidoreductase core subunit S7	3
mmu04024	cAMP signaling pathway	cpd: C00186 (S)-Lactate; cpd:C00212 Adenosine; mmu:13488 Drd1: dopamine receptor D1	3
mmu05012	Parkinson disease	cpd: C00212 Adenosine; mmu:75406 Ndufs7: NADH:ubiquinone oxidoreductase core subunit S7; mmu:13488 Drd1: dopamine receptor D1	3
mmu00770	Pantothenate and CoA biosynthesis	cpd: C00106 Uracil; mmu:103149 Upb1: ureidopropionase, beta	2
mmu00410	beta-Alanine metabolism	cpd: C00106 Uracil; mmu:103149 Upb1: ureidopropionase, beta	2
mmu05415	Diabetic cardiomyopathy	cpd: C00794 D-Sorbitol; mmu:75406 Ndufs7: NADH:ubiquinone oxidoreductase core subunit S7	2
mmu04022	cGMP-PKG signaling pathway	cpd: C00212 Adenosine; mmu:11552 Adra2b: adrenergic receptor, alpha 2b	2
mmu05034	Alcoholism	cpd: C00212 Adenosine; mmu:13488 Drd1: dopamine receptor D1	2
mmu05032	Morphine addiction	cpd: C00212 Adenosine; mmu:13488 Drd1: dopamine receptor	2

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Notes: DEMs: Differentially Expressed Metabolites; DEGs: Differentially Expressed Genes; KEGG: Kyoto Encyclopedia of Genes and Genomes.