

E-cigarette and DNA methylation

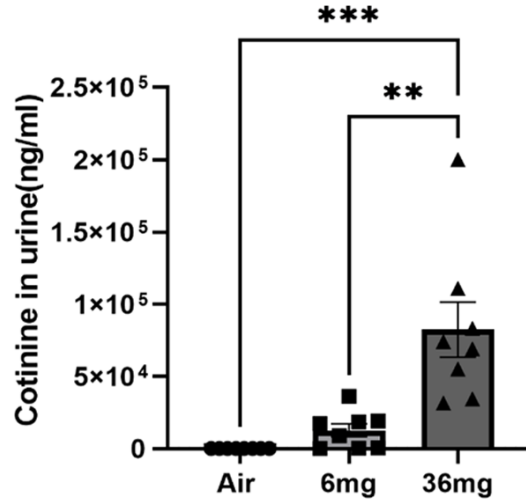


Figure S1. Measurement of urine cotinine level after 14 weeks E-cigarette exposure. Cotinine level change column after E-cigarette exposure. For each group, N=8. Data points and error bars are means and SEMs, respectively, analyzed by Dunnett's multiple comparisons tests; **P<0.01; ***P<0.005, respectively.

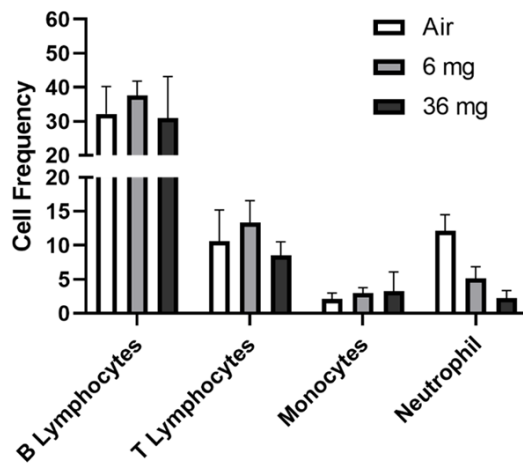


Figure S2. Flow cytometry analysis of white blood cell composition after 14 weeks of E-cigarette exposure. Column of the cell frequency for each cell type, N=3 for each group, no significant cell type change after E-cigarette exposure.

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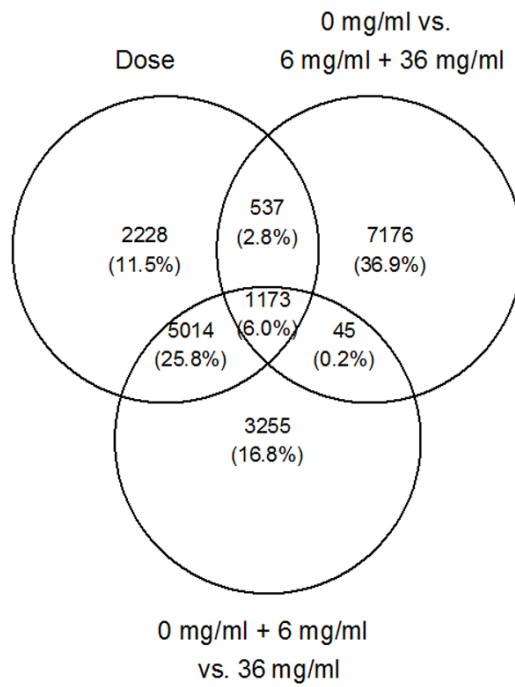


Figure S3. Venn graph to show the overlaps of significant CpG sites from dose analysis, comparing 0 mg/ml group to 6 mg/ml + 36 mg/ml groups, and comparing 0 mg/ml + 6 mg/ml groups to 36 mg/ml group.

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Table S4. Significant KEGG pathways when using genes that are associated with any significant CpG sites for the enrichment analysis

ID	Description	GeneRatio	BgRatio	P value	FDR	geneID	Count
mmu04261	Adrenergic signaling in cardiomyocytes	79/2380	239/11633	2.87E-06	0.00049138	Q5SW28/P97718/Q8BUE5/Q9Z1L5/Q01815/Q0PCR6/P09542/P23299/Q545H6/P97490/Q923T9/Q8VHW3/Q9R0K7/Q3UHH0/Q8BH52/Q9Z125/A0A0R4J082/P10417/P20444/Q4VA93/Q9JJV4/Q9WUI1/P11798/Q9DBL0/Q9ERT9/PODP27/PODP28/Q8CC27/P97414/Q60996/S4R2P9/Q99246/Q6PHS9/Q6PHZ2/B2RXC8/P50752/Q6P3Z7/Q54AB6/P27699/Q8VCC8/P84309/A3K-GF7/P68181/Q02789/Q76MZ3/P08752/Q64518/Q8R0X5/Q91Z83/Q6Q477/P58774/Q9Z1B7/P51667/P61014/P63094/P58771/Q545Y3/Q5RJF7/F8VPL1/Q9EQZ6/P62715/Q01341/F8VQ52/Q9WUA6/O88602/Q3ZB20/Q7TNP2/O08532/Q14BH8/Q7M729/Q8K596/Q8R3Z5/A2A545/P48787/Q497F1/Q6PD03/B1AYL1/Q9JJV9/K3W4N7	79
mmu04010	MAPK signaling pathway	138/2380	474/11633	3.01E-06	0.00049138	P48455/Q3UFB7/Q9Z1L5/Q0VG15/Q01815/Q0PCR6/Q8CE90/O35608/Q1HKZ5/Q03145/P25118/Q3U479/P97820/A0A0A6YWR8/P20826/Q62312/Q61696/P16627/Q9J11/P70424/Q8VHW3/E9Q7P2/P14404/P15209/Q9ESL4/Q9WTK5/P18653/Q8BYC6/P20444/Q4VA93/Q9JJV4/Q62132/Q9WUI1/Q9D7X3/Q925I7/P31938/Q3TMJ8/Q8BWG8/P01132/P52801/Q04690/P41158/Q8CC27/P27090/Q99246/P61148/Q6ZWS1/Q9WVS7/O55017/P21237/Q541P3/Q6PHS9/P09535/Q99K90/P32883/Q5J7N1/P28028/Q04863/A0A0A0M087/F8VQL0/P68181/P17156/Q8BTM9/P30306/Q3U535/Q9DBN8/Q02789/P31240/A0A0R4IZW4/Q62073/P60764/Q14A12/Q9WUL6/O09112/O08989/Q3TPX5/Q80X90/O35099/Q9Z1B7/Q91Y86/P22339/Q61526/P54830/O08605/A2A8W8/A0A087WS83/Q549C9/P27671/Q9ESN9/P36993/Q5RJF7/F8VPL1/P47809/Q543X6/Q9WUT3/Q9WVI9/Q02858/P97953/P15655/Q541T2/Q9WUA6/P26618/O88602/Q3ZB20/Q3UMW7/P49138/Q3U2P8/O08532/Q14BH8/Q64729/P01139/A0A0A0M082/Q9ESS0/Q91Z46/P63318/Q3UN66/P21803/E9QK53/P62071/P13504/Q32MH0/P10637/O35613/Q3UKR0/P10749/Q9QUG9/Q8R3Z5/A2A545/Q50L42/P63001/P17879/O08543/Q61161/Q8CFN5/Q7TTSI8/P97445/P35639/Q9Z1S3	138
mmu04520	Adherens junction	46/2380	121/11633	6.15E-06	0.00067065	Q8BUN5/Q62417/Q924A0/E9Q091/Q9QUI0/Q65CL1/Q9JLB9/Q62312/P70424/Q9JKF1/Q99NH2/A0A0R4J1Y4/Q64727/B2RU80/Q9Z1J1/A1A550/A2A8L5/P39688/Q7TPR4/Q02248/Q9JKF6/F8VQL0/Q64455/E9Q4S7/P28828/Q68FM4/Q62073/P60764/Q14A12/P30999/P39447/F8VPR5/Q8BH43/P70451/Q3TZJ5/E9QNA7/Q64729/Q04736/Q3TJ17/Q9D358/Q561M1/Q61301/P63001/P27782/Q3TYB0/Q8BGZ9	46
mmu05414	Dilated cardiomyopathy	54/2380	153/11633	1.31E-05	0.00107134	Q9Z1L5/Q01815/Q0PCR6/A2A864/P09542/P97490/Q8VHW3/Q9JJV4/Q62470/Q8CC27/Q3TZS3/S4R2P9/P27090/Q99246/Q6PHS9/P50752/Q6P3Z7/Q54AB6/P84309/P68181/Q02789/Q64518/Q8R0X5/Q91Z83/P58774/P51667/E9PXZ3/P61014/A0A0B4J1F0/P63094/Q62165/P58771/Q545Y3/Q5RJF7/F8VPL1/Q01341/F8VQ52/O88602/Q3ZB20/O08532/Q14BH8/P82347/P19137/B8JK39/P11688/Q0VBD0/O70309/Q6PE70/Q8K596/Q8R3Z5/A2A545/Q60675/P48787/Q497F1	54
mmu04360	Axon guidance	82/2380	261/11633	1.65E-05	0.00107822	Q80TR4/P22726/P48455/Q69ZX8/Q812A2/F8VPQ4/Q9J133/Q8BL65/Q62178/Q03145/Q9WVB4/Q76179/O08644/Q9QUI0/Q8K120/Q923T9/P70206/Q8K1S3/Q62181/Q99NH2/A0A0R4J1Y4/Q8R4F1/P20444/Q4VA93/P11798/Q9DC04/Q8CBF3/Q8CA63/P52801/P43029/P39688/Q8C031/Q99PH1/Q6PHZ2/Q6PCX7/O55222/P23359/Q60591/P97333/Q80UG2/P32883/Q5J7N1/Q76KF0/Q8K330/P45591/Q3UHW9/F8VQL0/Q62226/Q60519/Q5SW75/P52800/Q4FJM3/G1K381/P08752/P60764/Q14A12/O88632/Q60629/P00520/P54763/B2RXS4/O09118/P54754/O09126/Q03137/Q91Z69/Q9QUQ5/Q9JK84/Q8CIH5/D3Z4M6/Q9QUR8/Q8CHT1/E9QK62/O08747/Q8K4G5/E9QK41/M9MMKO/O54785/O35904/P63001/O08543/P35235	82
mmu05410	Hypertrophic cardiomyopathy	53/2380	152/11633	2.32E-05	0.00126214	Q9Z1L5/Q01815/Q0PCR6/A2A864/P09542/Q91WG5/O54950/Q3TWR3/Q8VHW3/Q9JJV4/Q6PAM0/Q62470/Q8CC27/Q3TZS3/S4R2P9/P27090/Q99246/Q6PHS9/P50752/Q6P3Z7/Q54AB6/Q02789/Q64518/Q8R0X5/Q91Z83/P58774/P51667/E9PXZ3/A0A0B4J1F0/Q62165/P58771/Q545Y3/Q5RJF7/F8VPL1/O88602/Q3ZB20/O08532/Q14BH8/P82347/P19137/B8JK39/P09470/Q3TU20/P11688/Q0VBD0/O70309/Q6PE70/Q8K596/Q8R3Z5/A2A545/Q60675/P48787/Q497F1	53

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mmu04070	Phosphatidylinositol signaling system	44/2380	121/11633	3.52E-05	0.00164624	Q7TT16/E9QAN8/Q8CDA1/P20444/Q4VA93/Q8K3R3/Q9EPW0/F6V2U0/Q3UEQ1/PODP27/PODP28/Q6ZQB6/Q7TNC9/P98191/Q9R1C6/Q6P549/Q7TS72/E9Q7S0/Q8BYN3/Q6PD10/A3KGF7/O88673/D3YXJ0/Q8BKC8/D3YWQ0/E9PUQ8/P70227/Q8R3B1/B2RXC2/O70167/Q8OXI4/Q8CIH5/O70161/Q9D2G5/Q9ES52/Q8CBQ5/Q6NS52/A2ARP1/P63318/Q3UN66/Q99L43/Q35904/Q91WG7/P11881	44
mmu04020	Calcium signaling pathway	105/2380	360/11633	4.18E-05	0.00170898	P97718/Q8BUE5/P48455/Q3UFB7/O08786/Q0VG15/Q01815/Q0PCR6/Q01098/Q60613/Q9Z0J4/P97490/Q923T9/P35438/P70424/Q9R0K7/Q3UHH0/E9Q7P2/P15209/Q9QVP9/Q3UDE9/Q03391/Q62463/Q3UMR5/Q02152/P20444/Q4VA93/Q8BWG9/P11798/Q9DBL0/Q925I7/Q8K3R3/P30678/P01132/Q9ERZ4/PODP27/PODP28/S4R2P9/Q99246/P61148/Q6ZWS1/O55017/Q7TS72/Q6PHZ2/P26928/A3KGF7/F8VQLO/P68181/P29477/Q3UIZ8/Q02789/P35546/O54803/P31240/A0A0R4IZW4/Q64518/Q8R0X5/Q62035/Q6Q477/P30549/Q3KP20/P70227/B1B1A8/Q61616/Q61526/P61014/Q60930/A0A087WS83/Q9Z1M0/C8YIX4/Q8R3B1/P63094/Q8BSY0/P35375/B2RXC2/O09161/Q8CIH5/P97953/P15655/Q541T2/P21278/Q3UPA1/P26618/O09165/Q61125/P47937/P97772/P30677/P01139/P30558/Q3UR32/P63318/Q3UN66/P21803/E9QK53/Q91VB2/E9PZQ0/Q8K596/Q8VCR8/P35436/P11881/P32304/Q7TSI8/Q99J21/P97445	105
mmu05412	Arrhythmogenic right ventricular cardiomyopathy	46/2380	130/11633	5.19E-05	0.00188415	Q9Z1L5/Q01815/Q0PCR6/A2A864/Q924A0/E9Q091/Q65CL1/Q8VHW3/Q9JJV4/Q62470/Q9Z1J1/A1A550/Q8CC27/Q02248/Q3TZS3/S4R2P9/Q99246/Q6PHS9/E9Q557/Q02789/Q64518/Q8R0X5/E9PXZ3/A0A0B4J1F0/Q62165/Q5RJF7/F8VPL1/O88602/Q3ZB20/O08532/Q14BH8/P82347/P19137/B8JK39/P11688/Q0VBD0/O70309/Q6PE70/Q8K596/Q61301/Q8R3Z5/A2A545/Q60675/P27782/Q3TYB0/Q8BGZ9	46
mmu00533	Glycosaminoglycan biosynthesis - keratan sulfate	13/2380	22/11633	8.16E-05	0.00266843	Q9EQC0/Q11204/Q9R111/A0A0R4J1C9/P54751/Q544T4/P15535/Q3U478/P97325/Q9CZ48/Q80WV3/Q9Z2Y2/Q9JJ04	13
mmu04072	Phospholipase D signaling pathway	72/2380	233/11633	9.52E-05	0.0028289	Q5SW28/Q35083/A0A0R4J263/P39053/Q9QUI0/P97490/P20826/Q9D517/Q9QX11/Q9QVP9/Q3UDE9/Q62463/P20444/Q4VA93/Q8BMC3/Q925I7/P31938/Q3TMJ8/P01132/P39688/Q9JIW9/Q9R1C6/P32883/Q5J7N1/Q8VCC8/P84309/Q61469/A0A0A0M0Q87/A3KGF7/P62331/Q3U0D7/Q9QYY0/O88673/D3YXJ0/Q8BZ98/P31240/A0A0R4IZW4/Q03385/D3YWQ0/P39054/E9PUQ8/Q5NCH9/Q68ED2/O08989/Q3TPX5/P47743/Q9JLN9/Q99JY8/Q68EF4/A0A140T8R6/P63094/Q9EQZ6/Q8CIH5/O70161/P63034/Q01341/F8VQ52/Q9WUA6/P27601/Q9D034/P26618/P97772/Q6NS52/P30558/Q61120/Q8K4X7/P62071/Q7TT21/O35904/Q91WG7/Q50L42/P35235	72
mmu04310	Wnt signaling pathway	76/2380	251/11633	0.00012846	0.00350054	P22726/P48455/Q9WVB2/Q3UN01/Q8BUN5/P56546/Q3UGL5/Q99MH6/Q924A0/E9QQ91/Q8C4U3/Q9QUI0/Q8K120/Q9Z1N6/Q923T9/Q8OZ96/Q08122/P20444/Q4VA93/P11798/Q9Z1J1/A1A550/Q8BHJ5/O88572/A0A0R4J0A9/Q9WU66/A0A0R4J001/Q02248/P17553/Q6PHZ2/P97298/Q60591/Q80Y24/A7YQ68/A3KGF7/Q64527/P68181/O35468/Q2TBA6/Q62073/P60764/Q14A12/P30282/Q3TSW4/Q9WTX6/Q91Y86/Q8BQD1/P27467/Q549C9/Q9Z139/D3Z6Q6/P48755/Q3UMK5/Q3UVD5/Q91VNO/A2ARI4/O88712/F8VPR5/O35927/E9QKH8/Q61473/Q3ULA2/P63318/Q3UN66/O54908/Q9Z132/B1ASC1/Q3UN27/P97299/Q3UI35/O88566/Q8VE28/P63001/P27782/Q3TYB0/Q8BGZ9	76
mmu01521	EGFR tyrosine kinase inhibitor resistance	41/2380	119/11633	0.00025053	0.00630179	Q62120/P70424/P10417/P20444/Q4VA93/Q8BMC3/Q925I7/P31938/Q3TMJ8/P01132/Q04690/D3YZR2/P32883/Q5J7N1/P28028/Q8BSK8/A0A0A0M0Q87/F8VQLO/Q9QYY0/P31240/A0A0R4IZW4/Q9WVH4/Q61526/Q9JLN9/Q61337/O54918/Q542N5/Q8CIH5/P15655/Q541T2/Q61592/Q9WUA6/P26618/Q3UTA9/Q61120/P63318/Q3UN66/P21803/E9QK53/O35904/Q7TSI8	41
mmu04725	Cholinergic synapse	53/2380	167/11633	0.00037097	0.00808725	Q9JMF3/Q5SW28/P32211/Q62120/Q01815/Q0PCR6/P97490/Q923T9/Q9JK97/P21836/Q543Z1/Q8BH52/Q9Z125/A0A0R4J082/Q61011/P10417/P20444/Q4VA93/P11798/P31938/Q3TMJ8/Q9ERZ4/P63250/P39688/P97414/Q99246/O55017/Q6PHZ2/Q8R4G9/P32883/Q5J7N1/P84309/A3KGF7/P68181/Q02789/P52187/P08752/Q61017/P70227/P48542/Q0VB45/P18872/Q01341/F8VQ52/Q9WUA6/P21278/Q3UPA1/P29387/P63318/Q3UN66/O35904/P11881/P97445	53

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mmu04928	Parathyroid hormone synthesis, secretion and action	53/2380	167/11633	0.00037097	0.00808725	P28700/O09102/A0A0R4J021/E9Q394/Q9QUI0/P97490/Q8BH52/Q9Z125/A0A0R4J082/Q06219/Q3TYI4/P10417/P20444/Q4VA93/Q3UEI1/P31938/Q3TMJ8/Q8BWG8/O88572/A0A0R-4J0A9/O35235/Q9R0S3/Q08775/P28028/P84309/Q01063/P48281/A3KGF7/Q68FM7/P68181/Q9DBF0/P08752/P70227/Q60929/Q61210/P63094/Q9D2V6/Q91VN0/Q01341/F8VQ52/P21278/Q3UPA1/Q9QY96/P27601/Q9D034/P70670/Q06186/Q5FW64/P63318/Q3UN66/Q64441/P11881/Q8CFN5	53
mmu04371	Apelin signaling pathway	61/2380	199/11633	0.00039893	0.00815304	Q9JMF3/Q5SW28/P12242/Q8BUN5/P09542/O70343/Q91WG5/Q9Z0J4/Q61982/P97490/O54950/Q3TWR3/Q8CGN5/PODMC4/P16054/Q61011/Q6PAMO/P31938/Q3TMJ8/PODP27/PODP28/Q3UJF1/S4R2P9/Q60843/P32883/Q5J7N1/P84309/Q8BSK8/A3KGF7/P68181/P29477/Q3UIZ8/P11214/P08752/Q61017/P70227/Q60929/O08989/Q3TPX5/B1B1A8/P51667/Q9JLN9/P54310/Q01341/F8VQ52/Q9WUA6/P27601/Q9D034/Q9WU00/Q8COT9/Q64729/P29387/Q9CQV6/P62071/E9PZQ0/Q8K596/Q8VCR8/P11881/Q61409/E9QLQ3/Q8CFN5	61
mmu05223	Non-small cell lung cancer	41/2380	122/11633	0.00045299	0.00871336	P28700/O08734/P42230/Q9JIA0/Q9J11/P70424/P42232/P20444/Q4VA93/Q64261/P31938/Q3TMJ8/PO1132/Q5EBH1/P51480/P22605/Q6DFX0/P32883/Q5J7N1/P28028/A0A0A0MQ87/F8VQLO/P35546/Q9WVH4/Q62137/A0A0R4J0R7/P22339/Q549C9/Q61337/P97793/Q8CIH5/O89106/Q9WUA6/Q61768/P28738/Q3UMY5/A0A3Q4EHV9/A7ISP9/P63318/Q3UN66/O35904	41
mmu04724	Glutamatergic synapse	53/2380	169/11633	0.0005111	0.00928489	Q9JMF3/P48455/Q8BMF5/Q01815/Q0PCR6/Q01098/Q3TXX4/P97490/P35438/Q03391/Q8BLE7/A0A0R4J0A6/P43006/Q3UYK6/Q9D415/Q61011/P20444/Q4VA93/Q9DCP2/P63250/P23818/Q7TNB5/Q99246/D3Z7P3/P84309/B1AS29/A3KGF7/P68181/P08752/D3YZU1/Q61017/P70227/Q5NCH9/Q68ED2/P47743/Q62108/P18872/Q68EF4/A0A140T8R6/P63094/Q80Z38/Q99MK8/Q01341/F8VQ52/P97772/P29387/P63318/Q3UN66/P35436/P11881/Q99JP6/Q50L42/P97445	53
mmu04722	Neurotrophin signaling pathway	56/2380	182/11633	0.00060978	0.01038057	Q3UFB7/Q8CE90/E9Q9B7/Q9QUI0/Q923T9/Q6PHU5/P15209/P18653/P10417/Q9WU11/P11798/Q8BMC3/P31938/Q3TMJ8/Q9Z1E3/PODP27/PODP28/Q9WVS7/P21237/Q541P3/Q6PHZ2/P41242/P32883/Q5J7N1/P28028/A0A0A0MQ87/Q8K4B2/Q3UHC1/Q3UGX8/Q9QYYO/Q61144/Q3U4P5/O09039/P00520/Q9WVH4/O35099/Q9Z1B7/Q60778/Q91Y86/Q549C9/Q61337/Z4YK94/Q9JJP2/Q99PT1/Q9WUT3/Q8CIH5/Q9WUA6/P49138/Q3U2P8/PO1139/Q61120/P28867/Q53YN4/O35904/P63001/P35235	56
mmu04024	cAMP signaling pathway	94/2380	338/11633	0.0006349	0.01038057	E1AZ71/Q91WA8/Q7TN16/Q01815/Q0PCR6/Q01098/P30873/Q543T0/Q60613/P22389/Q9QUI0/P97490/Q9EPL9/Q923T9/P35438/Q9R0K7/Q3UHHO/Q9Z239/Q03391/Q8BH52/Q9Z125/A0A0R4J082/Q8BWG9/P11798/Q3UEI1/P31938/Q3TMJ8/Q60992/Q7TSI6/Q9Z1E3/Q9ERZ4/PODP27/PODP28/Q61224/P23818/Q7TNB5/Q9EQX0/Q99246/P21237/Q541P3/Q6PHZ2/P57774/Q60829/P28028/Q8VCC8/P84309/Q01063/P68181/P70205/Q6NXJ9/Q02789/Q60612/P08752/P60764/Q14A12/Q64518/Q8R0X5/E9Q236/Q3UW12/Q6Q477/Q91Y86/Q61616/Q8CA95/P61014/Q61337/P63094/P54310/Q80T41/Q9EQZ6/Q0P543/P23204/Q542P9/F8VPR5/Q6P1D6/Q01341/F8VQ52/Q9WUA6/Q8COT9/P30558/Q60748/Q3UQP0/Q61602/Q9R0C8/P62071/O35904/Q9JJZ8/P35436/P48787/Q497F1/P63001/Q61409/E9QLQ3/O35659/Q9EP66	94
mmu04720	Long-term potentiation	34/2380	99/11633	0.00086934	0.01327786	P48455/Q01815/Q0PCR6/Q01098/P97490/Q923T9/P35438/Q03391/P18653/P20444/Q4VA93/P11798/P31938/Q3TMJ8/Q9ERT9/PODP27/PODP28/P23818/Q7TNB5/Q6PHZ2/P32883/Q5J7N1/P28028/Q8VCC8/A3KGF7/P68181/P70227/Q9WUT3/F8VPR5/P97772/P63318/Q3UN66/P35436/P11881	34
mmu00562	Inositol phosphate metabolism	31/2380	88/11633	0.00089331	0.01327786	Q7TT16/E9QAN8/Q8CDA1/P17751/Q8K3R3/Q9EPW0/F6V2U0/Q3UEQ1/Q7TNC9/Q6P549/Q7TS72/E9Q7S0/Q8BYN3/A2AP18/A3KGF7/Q8BK8/P59644/Q91WF7/Q8R3B1/Q6U7H8/B2RXC2/O70167/Q80XI4/Q8CIH5/O70161/Q9D2G5/Q9ES52/Q8CBQ5/Q9Z2L6/Q9JHU9/O35904	31
mmu04713	Circadian entrainment	47/2380	150/11633	0.00105152	0.0143293	Q9JMF3/Q01815/Q0PCR6/Q01098/Q9Z0J4/P97490/Q923T9/P35438/E9Q7P2/Q03391/Q61011/P20444/Q4VA93/P11798/O70361/P63250/PODP27/PODP28/P23818/Q7TNB5/Q99246/Q6PHZ2/P84309/A3KGF7/P68181/P70205/Q6NXJ9/POC605/Q8BND1/P08752/Q61017/P70227/P48542/Q0VB45/P18872/P63094/O54943/A0A0R4J0U3/Q01341/F8VQ52/Q8COT9/P29387/P63318/Q3UN66/E9PZQ0/P35436/P11881	47

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mmu05034	Alcoholism	62/2380	210/11633	0.00105169	0.0143293	Q9JMF3/Q01098/Q60613/Q64478/P84228/Q64525/P35438/Q8VBY2/P15209/Q03391/Q8BH52/P62806/P24529/COHKE9/P10853/Q9Z125/A0A0R4J082/Q61011/Q8BMC3/P31938/Q3TMJ8/Q64524/Q64522/PODP27/PODP28/Q3UJF1/P84244/P21237/Q541P3/P57774/Q60829/Q64523/P32883/Q5J7N1/P28028/P84309/A0A0A0MQ87/P68181/P08752/POC0S6/Q61017/Q61616/COHKE8/Q91WA3/P18872/P63094/Q6GSS7/Q99N13/A0A0R4J1F3/Q35852/P13346/Q8CGP5/P68433/Q9JIM1/P29387/Q8CGP7/Q61120/Q8CCK0/Q6ZWY9/P35436/Q8CGP2/COHKE7	62
mmu04510	Focal adhesion	84/2380	304/11633	0.00147578	0.01891567	P11087/008863/A2CGA5/Q61711/A2A864/Q9EPC1/Q8BUR4/Q9QUI0/Q9ES46/P70424/E9Q2T3/Q64727/Q62523/P10417/P20444/Q4VA93/E9PYT0/Q8BMC3/Q62470/Q925I7/P31938/Q3TMJ8/Q71LX4/E9PUM4/Q8CDM9/Q61140/P01132/Q60992/Q7TSI6/P39688/Q7TPR4/Q02248/Q3TZS3/Q60841/P02463/O55222/P28028/A0A0A0MQ87/F8VQLO/Q3UHC1/Q3UGX8/Q3UIZ8/Q05895/A6H644/P31240/A0A0R4IZW4/P60764/Q14A12/P30282/Q3TSW4/Q8OX90/B1B1A8/Q91Y86/P51667/Q91YM2/Q61292/E9PXZ3/Q62082/A0A0B4J1F0/Q61337/P27671/O70161/Q9QZR9/P97953/Q9WUA6/P26618/Q3UMT1/P19137/B8JK39/Q9ROC8/Q61120/P63318/Q3UN66/P11688/Q0VBD0/O08529/O70309/Q6PE70/Q8VCR8/O35904/Q60675/P63001/Q8BYI9/Q80YQ1	84
mmu04015	Rap1 signaling pathway	92/2380	338/11633	0.001504	0.01891567	Q0VG15/A2ALS5/Q35608/Q6RHR9/Q03145/Q60613/Q9QUI0/P97490/G3X9J0/Q80TE4/P20826/Q9JJV2/P35438/E9Q0Y4/Q99NH2/A0A0R4J1Y4/P20444/Q4VA93/Q9WU11/Q9WVQ1/Q925I7/P31938/Q3TMJ8/Q71LX4/E9PUM4/Q8CDM9/Q61140/P01132/Q60992/Q7TSI6/P52801/PODP27/PODP28/Q9JIW9/Q02248/Q5EBH1/P61148/Q6ZWS1/P32883/Q5J7N1/P28028/Q8VCC8/P84309/A3KGF7/F8VQLO/Q3UHC1/Q3UGX8/Q3UV74/Q8COT5/P3127/A0A0R4IZW4/Q03385/P08752/P60764/Q14A12/P30999/O08989/Q3TPX5/Q921B7/Q8BZ03/P18872/P63094/Q8C0Q9/Q9DAD6/Q9JK84/G5E8F1/Q9EQZ6/Q02858/P97953/P15655/Q541T2/Q6P1D6/Q01341/F8VQ52/Q9WUA6/P26618/P01139/P30558/Q8K1Y2/Q9ROC8/P63318/Q3UN66/P21803/E9QK53/O35904/P35436/Q9QUG9/P70429/P63001/O08543/Q7TSI8/Q80YQ1	92
mmu04270	Vascular smooth muscle contraction	61/2380	209/11633	0.00156268	0.01892578	P97718/Q8BUE5/E9QA16/Q01815/Q0PCR6/Q6URW6/Q08460/A0A286YD35/Q60613/P22389/Q9QUI0/P97490/Q62463/P16054/P20444/Q4VA93/Q9DBL0/P31938/Q3TMJ8/PODP27/PODP28/Q99246/P28028/P84309/A3KGF7/Q68FM7/P68181/Q3UIZ8/A6H644/Q02789/POC605/Q8BND1/Q9WUP1/Q3UR44/G5E8V5/P70227/B1B1A8/Q61210/P63094/P63268/Q3UJ36/Q8VC81/P97391/Q6GTW1/Q01341/F8VQ52/P21278/Q3UPA1/P27601/Q9D034/Q9EPR2/Q3UMT1/P63318/Q3UN66/P28867/Q53YN4/Q61879/Q3UH59/Q8VCR8/P11881/Q50L42	61
mmu04921	Oxytocin signaling pathway	66/2380	230/11633	0.00165647	0.01934523	Q5SW28/P48455/Q05769/Q9Z1L5/Q01815/Q0PCR6/Q9QUI0/Q8K120/Q91WG5/P97490/Q54950/Q3TWR3/Q923T9/Q8VHW3/P20444/Q4VA93/Q9JJV4/Q6PAM0/P11798/P31938/Q3TMJ8/P63250/PODP27/PODP28/Q8CC27/Q99246/Q9WVS7/Q6PHS9/Q6PHZ2/Q60591/P32883/Q5J7N1/P84309/A3KGF7/P68181/Q3UIZ8/A6H644/Q02789/P52187/P08752/P70227/B1B1A8/P48542/Q0VB45/P18872/P63094/Q5RJF7/F8VPL1/Q01341/F8VQ52/O88602/Q3ZB20/O08532/Q14BH8/Q9JHG6/Q3UMT1/P63318/Q3UN66/Q91VB2/E9PZQ0/Q8VCR8/Q8R3Z5/A2A545/P11881/Q50L42/Q8CFN5	66
mmu04810	Regulation of actin cytoskeleton	88/2380	323/11633	0.00182587	0.02058824	Q3UQ44/Q5DU57/E0CYU0/P32211/Q0VG15/Q6URW6/A2A864/Q76I79/Q8BUR4/Q9QUI0/Q9JJV2/Q5SQX6/Q9JKF1/Q64727/Q9WTL4/Q62470/Q925I7/P31938/Q3TMJ8/Q61140/Q8K1X4/P01132/Q60992/Q7TSI6/Q9ERZ4/Q7TPR4/Q3TZS3/P61148/Q6ZWS1/P26043/P32883/Q5J7N1/P28028/Q8K330/P45591/Q3UHW9/A0A0A0MQ87/Q3UIZ8/P26040/Q4KML7/A6H644/Q3UV74/Q5SW75/P31240/A0A0R4IZW4/P60764/Q14A12/O08989/Q3TPX5/B1B1A8/P51667/Q91YM2/E9PXZ3/Q62082/A0A0B4J1F0/Q61210/Q9DAD6/G5E8F1/Q8OXI4/O70161/P15655/Q541T2/Q6P1D6/Q8BH43/P27601/Q9D034/P26618/Q61125/P30558/Q3UMT1/B8JK39/Q9ROC8/P11688/P21803/E9QK53/Q0VBD0/Q61879/Q3UH59/O70309/Q6PE70/P62071/O54785/P13020/Q8VCR8/O35904/P63001/Q91VR8/Q7TSI8	88

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mmu04728	Dopaminergic synapse	58/2380	200/11633	0.00235795	0.0257016	Q9JMF3/P48455/Q01815/Q0PCR6/Q923T9/Q8BH52/P24529/Q9Z125/A0A0R4J082/Q61011/P20444/Q4VA93/Q9WUI1/P11798/Q8BWG8/Q9WTL8/P63250/PODP27/PODP28/P23818/Q7TNB5/Q60996/Q2NL51/Q99246/O55017/Q6PHZ2/B2RXC8/Q60829/P84309/A3KGF7/P68181/A1Y919/O08785/Q76MZ3/P08752/Q61017/P70227/Q9Z1B7/Q91Y86/Q61616/P48542/Q0VB45/P18872/P63094/P62715/Q9WUA6/Q7TNP2/Q61768/P28738/P30728/P29387/A2APX8/P63318/Q3UN66/P35436/P11881/Q6PD03/P97445	58
mmu05206	MicroRNAs in cancer	73/2380	263/11633	0.00256124	0.02701696	Q9R0G7/Q05769/Q35516/O08734/Q9D3F7/Q9QUI0/Q61982/P31695/P70424/Q61823/P21447/E9Q2T3/P16054/O88898/P10417/P20444/Q4VA93/P58462/Q64261/P13864/P31938/Q3TMJ8/P61979/Q5FWJ5/Q9QXV8/P52801/Q61188/Q6AXH7/Q3UJF1/P51480/P27090/P17553/P26043/D3Z7P3/P32883/Q5J7N1/A0A0A0M0Q87/F8VQL0/P26040/Q4KML7/P30306/Q3U535/Q9DBN8/P31240/A0A0R4IZW4/P00520/Q61526/P48754/Q9JLN9/Q09143/Q3UGD6/P27467/Q549C9/P58771/Q545Y3/O54918/Q542N5/Q8CIH5/F8VPR5/P26618/P06869/Q0V-BAB/P63318/Q3UN66/P11688/Q64441/P46414/O35904/Q1PSW8/O08543/Q8BYI9/Q7TSI8/Q80YQ1	73
mmu04911	Insulin secretion	41/2380	134/11633	0.00344146	0.03516747	O08786/Q01815/Q0PCR6/Q08460/A0A286YD35/O35526/Q497P1/P97490/Q923T9/Q8BH52/Q9Z125/A0A0R4J082/P20444/Q4VA93/P11798/Q99246/Q6PHZ2/P63011/Q0PD63/Q9EQZ7/P84309/Q7TN37/A3KGF7/P68181/P70205/Q6NXJ9/Q61743/Q02789/P70227/P63094/P09240/Q9EQZ6/P58391/Q9QYX7/Q01341/F8VQ52/P21278/Q3UPA1/P63318/Q3UN66/O35659	41
mmu04730	Long-term depression	31/2380	96/11633	0.00424655	0.04207943	Q9Z0J4/P20444/Q4VA93/P31938/Q3TMJ8/P23818/Q7TNB5/P32883/Q5J7N1/P28028/A3KGF7/POC605/Q8BND1/Q76MZ3/P08752/P70227/P18872/P63094/P62715/P21278/Q3UPA1/P27601/Q9D034/Q7TNP2/P97772/P63318/Q3UN66/E9PZQ0/P11881/Q50L42/P97445	31
mmu05210	Colorectal cancer	43/2380	144/11633	0.00456737	0.04392732	Q8BUN5/Q9JK91/O08734/Q924A0/E9QQ91/O70201/Q549P2/Q9QUI0/Q62312/P10417/P31938/Q3TMJ8/Q9Z1J1/A1A550/P01132/Q9JIW9/Q02248/P27090/Q8K3H0/P32883/Q5J7N1/P28028/Q8BSK8/A0A0A0M0Q87/Q03385/P60764/Q14A12/Q91Y86/P22339/Q9JLN9/Q549C9/Q61337/O54918/Q542N5/Q56A15/Q9WUA6/Q64729/O35904/O88566/P63001/P27782/Q3TYB0/Q8BGZ9	43
mmu04912	GnRH signaling pathway	42/2380	141/11633	0.00526992	0.04923616	Q01815/Q0PCR6/Q8CE90/P97490/Q923T9/Q9QVP9/Q3UDE9/P20444/Q4VA93/Q9WUI1/P11798/P31938/Q3TMJ8/PODP27/PODP28/Q99246/Q6PHZ2/P32883/Q5J7N1/P84309/A0A0A0M0Q87/A3KGF7/P68181/Q02789/P70227/Q9Z1B7/Q91Y86/P63094/P47809/Q543X6/Q01341/F8VQ52/P21278/Q3UPA1/Q06186/Q5FW64/P33434/Q3UG07/P28867/Q53YN4/P11881/Q50L42	42

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Table S5. Significant gene sets in GO when using genes that are associated with any significant CpG sites in promoter region for the enrichment analysis

Ontology	ID	Description	GeneRatio	BgRatio	P value	FDR	geneID	Count
BP	GO:0032543	mitochondrial translation	21/2100	93/30636	9.95E-07	0.00255328	Mrps11/Yars2/Mrpl43/Alkbh1/Mrps14/Mrps14/Ndufa7/Gatb/Uqcc2/Mrpl57/Mrps21/Mrps21/Shmt2/Trmt10c/Tsfm/Mief1/Lars2/Mrps34/Mtg2/Mrpl2/Mrpl23	21
BP	GO:0050796	regulation of insulin secretion	48/2100	335/30636	1.04E-06	0.00255328	Rptor/Nnat/Nnat/Nnat/Nnat/Jak2/Mpc2/Gpr39/Uqcc2/Pde4c/Uts2/Sirt4/Ghrl/Stx4a/Kcnj11/Vsn1/Epha5/Epha5/Nos1/Tardbp/Tardbp/Tardbp/Foxa2/Ano1/Ano1/Ano1/Phpt1/Bad/Bad/Per2/Per2/Adra2a/Tfap2b/Kcnq1/Kcnb1/Tcf712/Tcf712/Tcf712/Nr1d1/Srebf1/Alox5/Il1b/Pfkfb2/Pfkfb2/Pfkfb2/Pfkfb2/Pde3b/Pde3b	48
BP	GO:0140053	mitochondrial gene expression	27/2100	142/30636	1.18E-06	0.00255328	Mrps11/Yars2/Twnk/Mrpl43/Trmt5/Alkbh1/Mrps14/Mrps14/Mterf1a/Ndufa7/Chchd10/Gatb/Uqcc2/Mrpl57/Mrps21/Mrps21/Shmt2/Trmt10c/Tsfm/Mief1/Lars2/Foxo3/Mrps34/Mtg2/Mrpl2/Mettl4/Mrpl23	27
BP	GO:0071696	ectodermal placode development	12/2100	41/30636	1.27E-05	0.02048432	Pou2f1/Pou2f1/Pou2f1/Lrp6/Lrp6/Nrp1/Gnas/Gnas/Gnas/Ctnnb1/Gnas/Pou2f1	12
BP	GO:0071875	adrenergic receptor signaling pathway	14/2100	60/30636	4.19E-05	0.03670044	Adra1a/Adra1a/Akap13/Akap13/Adra1b/Gsk3a/Arrdc3/Nos1/Gnas/Gnas/Gnas/Adra2a/Kcnq1/Gnas	14
BP	GO:0060788	ectodermal placode formation	11/2100	40/30636	5.52E-05	0.03670044	Pou2f1/Pou2f1/Pou2f1/Lrp6/Lrp6/Gnas/Gnas/Gnas/Ctnnb1/Gnas/Pou2f1	11
BP	GO:0071697	ectodermal placode morphogenesis	11/2100	40/30636	5.52E-05	0.03670044	Pou2f1/Pou2f1/Pou2f1/Lrp6/Lrp6/Gnas/Gnas/Gnas/Ctnnb1/Gnas/Pou2f1	11
BP	GO:0014003	oligodendrocyte development	17/2100	85/30636	5.54E-05	0.03670044	Prdm8/Prdm8/Shh/Ulk4/Ulk4/Hdac11/Tenm4/Abca2/Tcf712/Tcf712/Tcf712/Eif2b5/Zfp488/Fgfr3/Fgfr3/Fgfr3/Fgfr3	17
BP	GO:0009743	response to carbohydrate	45/2100	358/30636	6.38E-05	0.03670044	Nnat/Nnat/Nnat/Nnat/Ccdc186/Mpc2/Gpr39/Pde4c/Sin3a/Ghrl/Rmi1/Pck2/Stx4a/Aqp4/Aqp4/Vsn1/Epha5/Epha5/Mapk13/Foxa2/Ano1/Ano1/Ano1/Phpt1/Bad/Bad/Adra2a/Grk2/Grk2/Kcnb1/Tcf712/Tcf712/Tcf712/Nr1d1/Srebf1/Eif2b5/P2rx3/Il1b/Pfkfb2/Pfkfb2/Pfkfb2/Pfkfb2/Pde3b/Pde3b/Thbs1	45
BP	GO:0002089	lens morphogenesis in camera-type eye	13/2100	55/30636	6.78E-05	0.03670044	Hipk1/Pou2f1/Pou2f1/Pou2f1/Cryaa/Cryaa/Cryaa/Ctnnb1/Pou2f1/Fgfr3/Fgfr3/Fgfr3	13
BP	GO:0030073	insulin secretion	50/2100	415/30636	7.73E-05	0.03670044	Rptor/Nnat/Nnat/Nnat/Nnat/Jak2/Cckar/Ccdc186/Mpc2/Gpr39/Uqcc2/Pde4c/Uts2/Sirt4/Ghrl/Stx4a/Kcnj11/Vsn1/Epha5/Epha5/Nos1/Tardbp/Tardbp/Tardbp/Foxa2/Ano1/Ano1/Ano1/Phpt1/Bad/Bad/Per2/Per2/Adra2a/Tfap2b/Kcnq1/Kcnb1/Tcf712/Tcf712/Tcf712/Nr1d1/Srebf1/Alox5/Il1b/Pfkfb2/Pfkfb2/Pfkfb2/Pfkfb2/Pde3b/Pde3b	50
BP	GO:0090276	regulation of peptide hormone secretion	51/2100	426/30636	7.76E-05	0.03670044	Rptor/Nnat/Nnat/Nnat/Nnat/Jak2/Cckar/Mpc2/Gpr39/Uqcc2/Pde4c/Uts2/Rasl10b/Sirt4/Ghrl/Stx4a/Aimp1/Kcnj11/Vsn1/Epha5/Epha5/Nos1/Tardbp/Tardbp/Tardbp/Foxa2/Ano1/Ano1/Ano1/Phpt1/Bad/Bad/Per2/Per2/Adra2a/Tfap2b/Kcnq1/Kcnb1/Tcf712/Tcf712/Tcf712/Nr1d1/Srebf1/Alox5/Il1b/Pfkfb2/Pfkfb2/Pfkfb2/Pfkfb2/Pde3b/Pde3b	51
BP	GO:0032024	positive regulation of insulin secretion	26/2100	168/30636	8.05E-05	0.03670044	Nnat/Nnat/Nnat/Nnat/Jak2/Mpc2/Gpr39/Ghrl/Stx4a/Vsn1/Tardbp/Tardbp/Tardbp/Ano1/Ano1/Ano1/Phpt1/Bad/Bad/Tcf712/Tcf712/Tcf712/Pfkfb2/Pfkfb2/Pfkfb2/Pfkfb2	26
BP	GO:0009749	response to glucose	42/2100	330/30636	8.30E-05	0.03670044	Nnat/Nnat/Nnat/Nnat/Ccdc186/Mpc2/Gpr39/Pde4c/Sin3a/Ghrl/Rmi1/Pck2/Stx4a/Aqp4/Aqp4/Vsn1/Epha5/Epha5/Foxa2/Ano1/Ano1/Ano1/Phpt1/Bad/Bad/Adra2a/Grk2/Grk2/Kcnb1/Tcf712/Tcf712/Tcf712/Nr1d1/Srebf1/Eif2b5/Pfkfb2/Pfkfb2/Pfkfb2/Pfkfb2/Pde3b/Pde3b/Thbs1	42
BP	GO:0071880	adenylate cyclase-activating adrenergic receptor signaling pathway	12/2100	49/30636	8.86E-05	0.03670044	Adra1a/Adra1a/Akap13/Akap13/Adra1b/Arrdc3/Nos1/Gnas/Gnas/Gnas/Adra2a/Gnas	12

