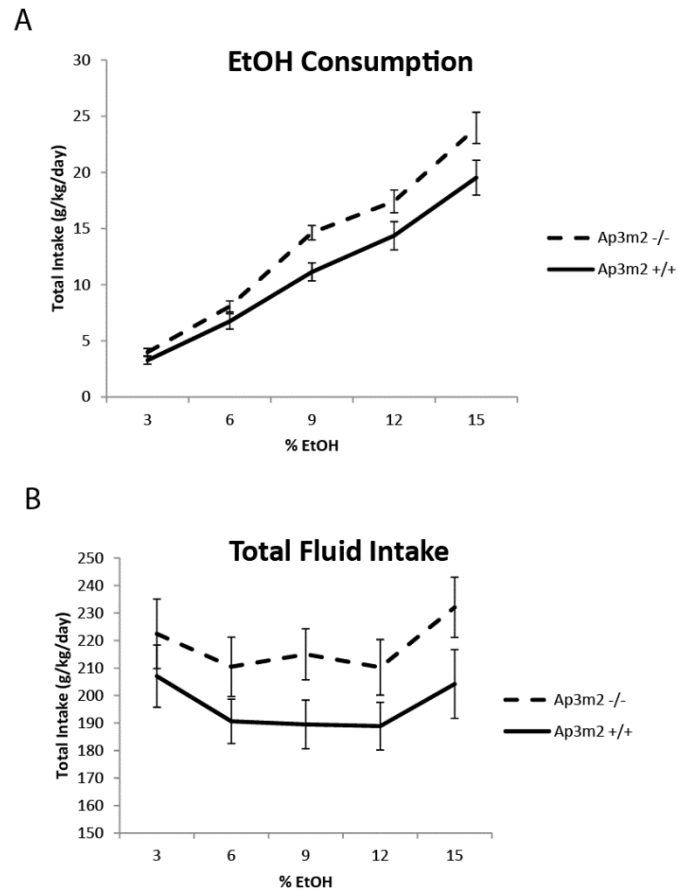
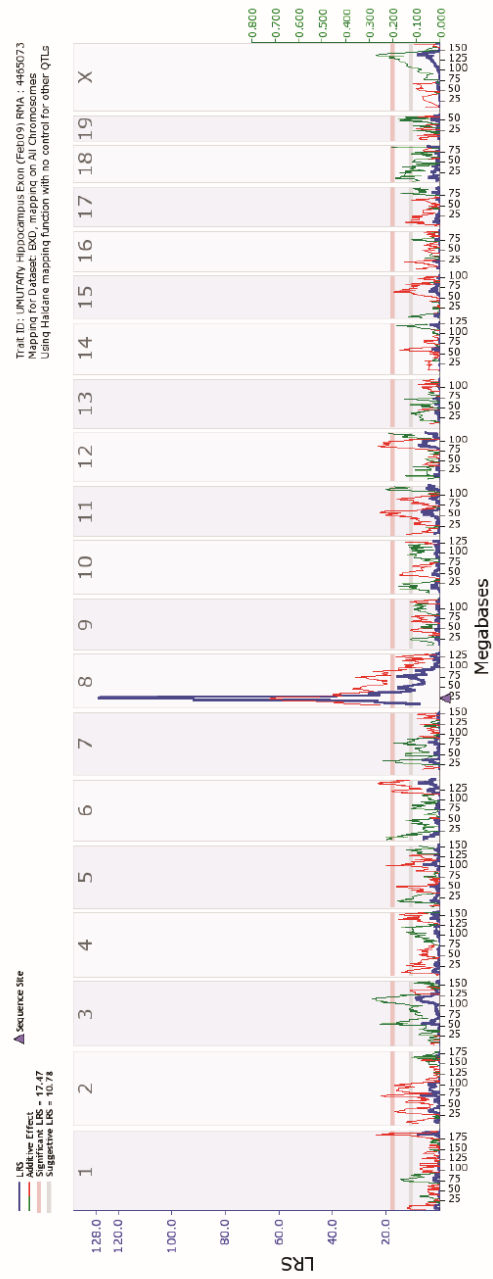
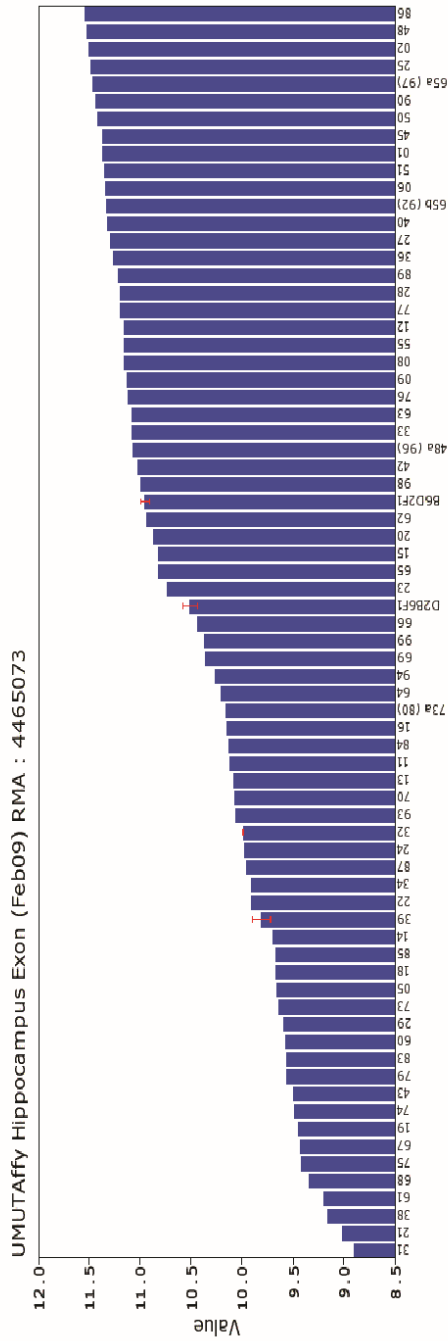


**Figure S1** Blood ethanol concentrations at 72 hours post vapor exposure were not significantly different in *Ap3m2* (-/-) mice compared to wild-type littermates (+/+).



**Figure S2** (A) Ethanol intake in g/kg/day for 3, 6, 9, 12 and 15% EtOH concentrations. Ethanol intake in g/kg/day for 3, 6, 9, 12 and 15% EtOH concentrations.  $F_{\text{time} \times \text{genotype}(4,33)}=2.8294$ ,  $p=0.0402$ . (B) No differences in total intake over time by genotype  $F_{(4,33)}=0.01526$ ,  $p=0.9605$  but an overall genotype effect  $F_{(1,36)}=5.7433$ ,  $p=0.0219$ .



**Figure S3** (A) Log<sub>2</sub> expression levels for *Ap3m2* in hippocampus of BXD RI strains and (B) corresponding cis eQTL signal. Chromosome numbers are at the top of the plot. The blue line represents the likelihood ratio statistic (LRS) across the genome. Two horizontal lines mark the genome-wide significance levels at  $p < 0.05$  (red line) and  $p < 0.63$  (gray line).

**Table S1 Table of oligonucleotide primer pairs used for the sequencing of *Ap3m2* and genotyping of *Ap3m2KO* mice.**

Primer Sequence 5' to 3'	Primer Name
ATG CTG GAC AAT GGG TTC CCC	Ap3m2WTFwd
AAT TGT AGG GTT CTC ATC GGG	Ap3m2WTRev
CAC CGG CCT CTC CAC CAT G	Egfp_fwd
GTG TTC TGC TGG TAG TGG TCG	Egfp_REV
AGC CCA CCA AAG GTT TGG T	Ap3m2Fwdcds
GAC AGT GTC GTG TTG GCA GTA TC	Ap3m2Revcds-r
GTA CTT CTC CCC GTA CAT ATC CAG A	Ap3m23'Fwd
GAA CCT CTT AAT GGG CCC TAA AG	Ap3m23'Rev-r
GGA GAC ACC CTA GTT TGT CTA CAG TG	Ap3m25utr fwd
GTG CAA GGA GCA CTG CG	Ap3m25utrRev-r
GAA ACC ACA GAG AAA CTC TAC TCG G	Ap3m2Proxfwd
CAG GAC TGA GAG GCT GGT GTG	Ap3m2proxrev-r
GAG ACT CAT CTA GAT TGG CAC GAC	Ap3m2p1r
ACT GTG CAC CTG CGT TGC	Ap3m2p1
CGG TAA GAT GAA GTG TGA AGG G	Ap3m2p2
AAC AGT GTG CAG AGA AAA ATA GGC	Ap3m2p2r
GAC CGT GAC CAC TCC CTC C	Ap3m2p3
CCA GGG ACC AAC TTT CAC AAG	Ap3m2p3r
CAA ACA GAA TCA GTT TGC CGG	Ap3m2p4
CCA CCC AAC CTC AAG ATC TCT C	Ap3m2p4r
GGG ACC CTC CCT AAA TTA ACC A	Ap3m2p5
ACT GTC AGT CTG GAT AAC ACA CTG C	Ap3m2p5r
GGA AAT TGT TGT GTT CAC CTC TAC A	Ap3m2p6
CCA AGA GCT GAT CTT GAG GTT C	Ap3m2p6r
GCC ACC AGG CTC TCC AAC	Ap3m2p7
CAT TTT CTT CTG TTA TAA TGG ACC ATT CT	Ap3m2p7r
CAC AGC TCT GTG AGA GAT TTG AAA C	Ap3m2p8
GTT TGC TCA GGT CTC CTG TGC	Ap3m2p8r
GAG TAG ATC TCT CGT GTG GGA AAA C	Ap3m2p9
CTG CGC TGA GCT GTT GAA C	Ap3m2p9r
CTG CTC CCC ACA ATT GAC TC	Ap3m2p10
AGT GTG ATG GTA AAT ACT GAT TTT CAA CT	Ap3m2p10r

**Table S2 Hardy-Weinberg Equilibrium analysis of the region of *Ap3m2* at the time of the F2 mapping.**

	AA	AB	BB	observed		expected		$P(X)^2$	$X^2$
				$p$	$q$	$p$	$q$		
D8Mit4	24	46	17	47	40	43.5	43.5	0.452966	86.88635
D8Mit25	27	44	17	49	39	44	44	0.286422	93.95222
D8Mit312	22	48	20	46	44	45	45	0.833029	76.11416
D8Mit113	30	37	17	48.5	35.5	42	42	0.156069	95.98514
D8Mit320	23	45	19	45.5	41.5	43.5	43.5	0.668036	79.78677

**Table S3** (A) SNPs which exist in the region of *Ap3m2* fit the distribution pattern of C57BL/6J=I/LnJ=iWSP-2 and AKR=129=DBA2=iWSR-1 and are the likely underlying causative nucleotides involved in the altered regulation of *Ap3m2* and the phenotypic differences mapped in the two QTL studies due to their identification as being within a regulatory feature. (B) Summary of the reported experimental evidence for each of the Ensembl regulatory features identified in A.

(A)

RefSnplD	Build 37 SNP location	Build 38 SNP location	SNP Genotypes		Ensembl Regulatory Feature ID	Transfac regulatory features (BIOBASE ID)
			C57BL/6J; I/LnJ (+)	129P3/J;AKR/J; DBA/2J (-)		
rs33255299	23605138	22494666	C	T		Pax-3 (M00327)
rs45867690	23604110	22493638	C	T		POU1F1 (M00744)
rs33346701	23601865	22491393	A	T		VDR, CAR, PXR (M00096)
rs51987012	23597278	22486806	A	G	ENSMUSR00000225022	VDR, CAR, PXR (M00096)
rs45944337	23597260	22486788	A	T	ENSMUSR00000225022	C - GR (M00205)
rs49759176	23594851	22484379	T	C		SMAD3 (M00701)
rs32743569	23589809	22479337	C	T		myogenin / NF-1 (M00056)
rs32650954	23589790	22479318	T	C		myogenin / NF-1 (M00056)
<b>rs32926479</b>	23587531	<b>22477059</b>	<b>C</b>	<b>T</b>	<b>ENSMUSR00000299557</b>	
<b>rs25959964</b>	23587232	<b>22476760</b>	<b>C</b>	<b>G</b>	<b>ENSMUSR00000299557</b>	<b>GABP (M00341)</b>
<b>rs52251207</b>	23587140	<b>22476668</b>	<b>T</b>	<b>C</b>	<b>ENSMUSR00000299557</b>	<b>ETF (M00695)</b>
<b>rs32882991</b>	23587093	<b>22476621</b>	<b>T</b>	<b>C</b>	<b>ENSMUSR00000299557</b>	
rs33346694	23583851	22473379	C	A		Kid3 (M01160);myogenin / NF-1 (M0056)
rs33468918	23259740	22149268	G	A		CdxA (M00101)
rs32693908	23259552	22149080	A	T		myogenin / NF-1 (M00056)
rs33391608	23259407	22148935	C	T		myogenin / NF-1 (M00056)
rs48407506	23257246	22146774	A	G		FAC1 (M00456)
rs49292343	23257245	22146773	T	A		FAC1 (M00456)
rs51735649	23257094	22146622	C	T		Muscle initiator sequences-19 (M00323)
rs33612810	23256679	22146207	A	G	ENSMUSR00000397963	
rs33559386	23256427	22145955	G	C	ENSMUSR00000397963	
rs33189424	23256368	22145896	A	G	ENSMUSR00000397963	
rs49087640	23256134	22145662	C	T		Tst-1 (M00133)

rs33450716	23242568	22132096	C	T	PPARGgamma:RXRalpha (M00512), LEF1, TCF1 (M00978), PPAR, HNF-4, COUP, RAR (M00762), HNF-4 (M01031), PPAR direct repeat 1 (M00763), HNF4alpha (M00638), COUP direct repeat 1 (M00765)
rs49767895	23242250	22131778	G	T	Oct-1 (M00136)
rs13474140	23238914	22128442	T	C	Ets-1 p54 (M01078), v-Myb (M00227), BRCA1:USF2 (M01082) FOXJ2 (M00423), PLZF (M01075), C/EBP/gamma (M00622)
rs32641536	23236602	22126130	A	G	
rs51839162	23235528	22125056	G	A	ENSMUSR00000397962
rs48010023	23235514	22125042	C	T	ENSMUSR00000397962
rs33210112	23228975	22118503	C	T	Tst-1 (M00133)
rs45645647	23154126	22043654	G	A	STAT (M00777)
rs33155370	23085975	21975503	C	T	VDR, CAR, PXR (M00966)
rs50493771	23057769	21947297	T	G	HNF3alpha (M00724)

(B)

Ensembl Regulatory Feature ID	Sensitivity to		Transcription Factor Binding							Histone Methylation				Histone Acetylation		Polymerase Binding
	DNase1		CTCF	Esrrb	C/Nmyc	E2F1	Esrrb	Max	NELFe	Zfx	H3K36me3	H3K4me1	H3K4me3	H3K4me2	H3K9ac	PoII
ENSMUSR00000225022	3	3	1								3	1				
<b>ENSMUSR00000299557</b>	5				7	1	2	4	1	3	1		10	1	2	4
ENSMUSR00000397963	1															
ENSMUSR00000397962	2	1											1	1		

Cell values indicate the number of experimental sources providing evidence for each transcription regulatory relation to a given feature.