

Legends for Supporting Figures

Figure S1. Effect of Adenoviral Vector Expressing *Gnb1* shRNA or Scrambled (Scr) shRNA on

Gβ1 Levels in Neuro 2A cells. Neuro 2A cells were transduced with adenovirus expressing

Gnb1 shRNA or scrambled shRNA (MOI 50), plated and incubated for the times indicated.

Cells were harvested and lysates subjected to immunoblotting using an antibody for Gβ1

(Protein Tech, 1:1000) followed by secondary antibody and visualization with ECL reagent (top

panel). Protein bands were quantified using BioRad Quantity One software, and values for Gβ1

were normalized for protein loading by calculating a ratio of Gβ1 to β-tubulin (bottom panel). U,

untransduced; S, Scr, transduced with adenoviral vector expressing scrambled shRNA and

harvested after 24 or 96 hr; G, *gnb1*, transduced with adenoviral vector expressing *Gnb1*

shRNA and harvested after 24 hr, 48 hr, 72 hr or 96 hr, as indicated.

Figure S2. Effect of Adenoviral Vector Expressing *Gnb1* shRNA on Gβ1 levels in Brains of

DBA/2 Mice. Mice were injected bilaterally into the nucleus accumbens with adenoviral vector

expressing *Gnb1* shRNA (n=3) or scrambled (Scr) shRNA (n=2) and Gβ1 and GFP were

visualized by immunohistochemistry, as described in the text. A. Brain sections from nucleus

accumbens (Bregma +0.98) of a mouse injected with adenovirus expressing *Gnb1* shRNA

(Gnb) and a mouse injected with adenovirus expressing scrambled shRNA (Scr) at 26 days

after injection. In both sections, representative GFP-expressing cells (green arrows; cells

infected by the adenovirus), Gβ1-expressing cells (red arrows) and cells coexpressing GFP and

Gβ1 (white arrows) are visible. B. Gβ1- and GFP-expressing cells in the nucleus accumbens

were counted across sections from Bregma +0.98 to Bregma +1.54 (2-4 sections per mouse),

as described in the text. Data represent mean ± SEM of cells from 5 (Scr shRNA) or 10 (*Gnb1*

shRNA) sections. *Student's t- test, $t(13)=4.25$, $P < 0.001$

Figure S3. Effectiveness of sampling scheme and batch effects adjustment. The 15,259 probe sets that survived filtering for masking for probe integrity and filtering for detection above background in the data set were included in the hierarchical clustering in A and B. Samples are labeled by line (HAP for high alcohol preference, LAP for low alcohol preference, or HS for heterogeneous stock), generation, sample number within that line/generation, and batch, with fields separated by periods. One minus the Pearson correlation coefficient was used as a distance measure. A) Expression values prior to batch effects adjustment clustered primarily on batch (first horizontal bar at bottom of graphic; ranging from dark purple for batch 1 to white for batch 6) with some effects of line (second horizontal bar; heterogeneous stock in green, HAP in red, and LAP in blue) and generation (third horizontal bar; ranging from white for generation 0, i.e., heterogeneous stock, to dark green for generation 13). B) Expression values after batch effects adjustment clustered primarily by line (second horizontal bar) with some secondary clustering by generation (third horizontal bar).

Figure S1

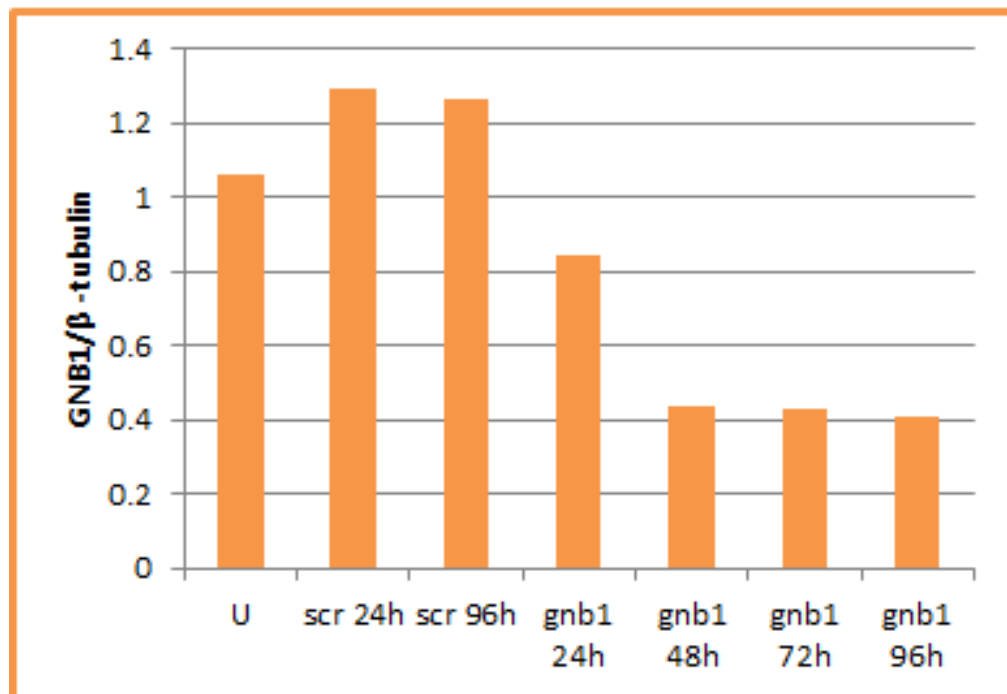
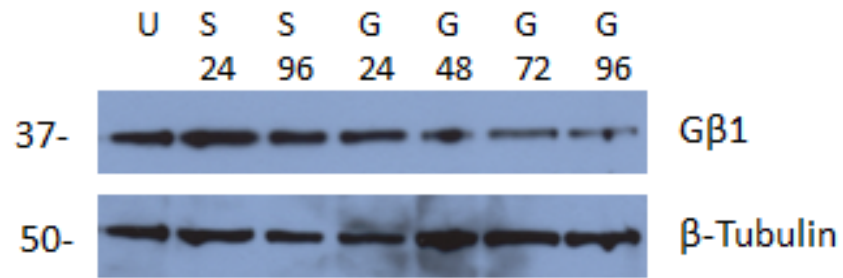


Figure S2A

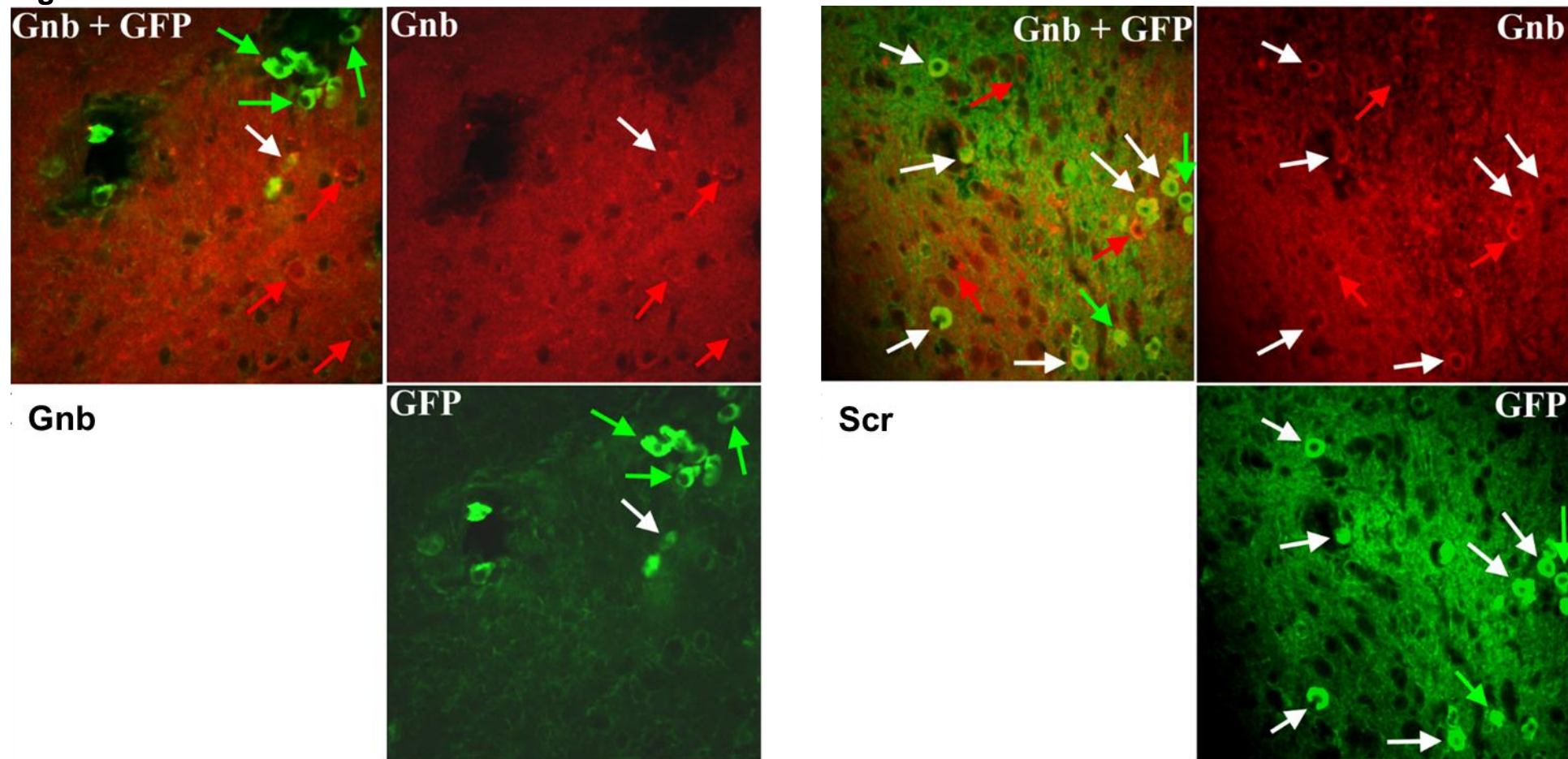


Figure S2B

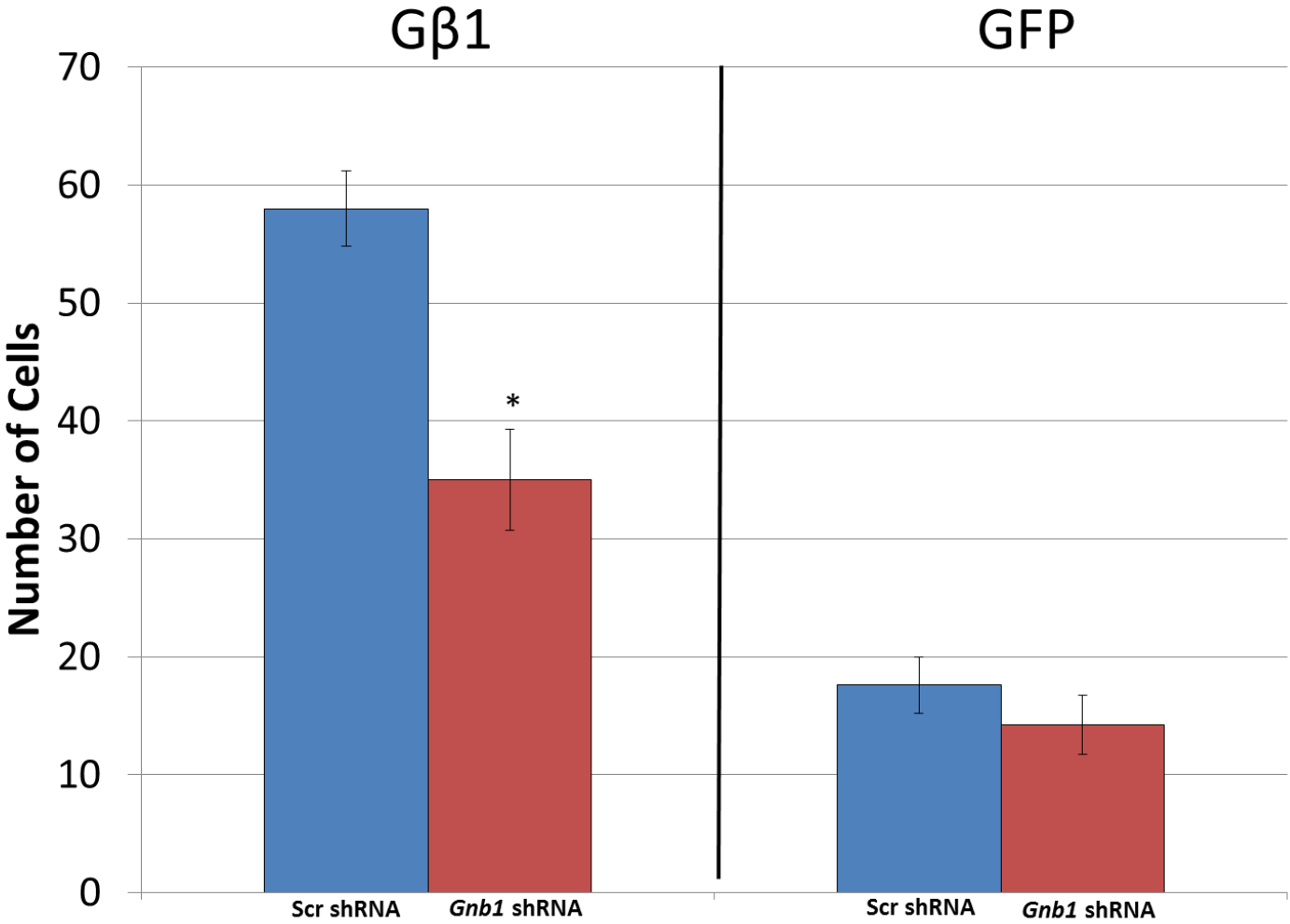


Figure S3

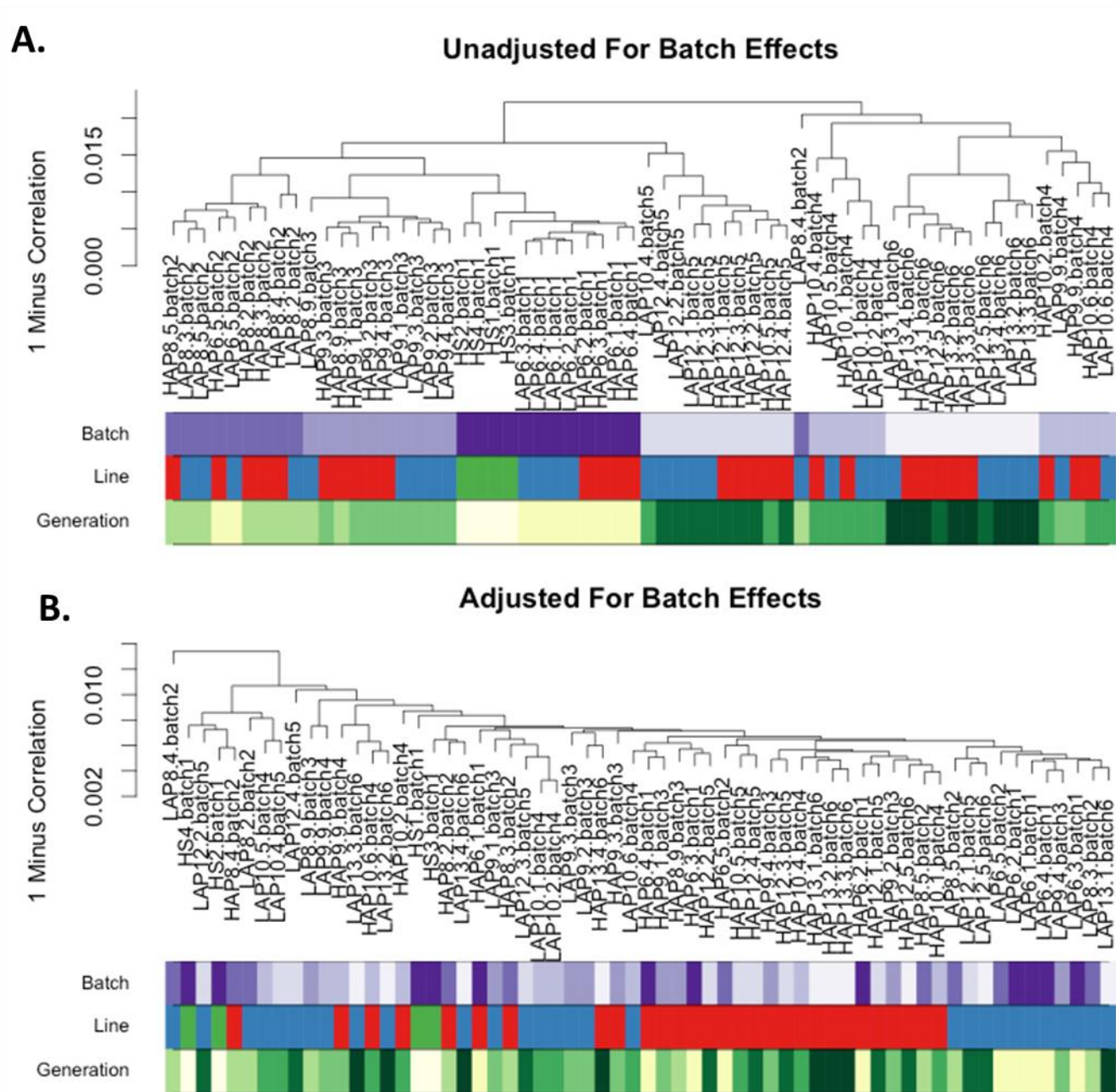


Table S1. Statistical Analysis of Differential Expression Scenarios.						
	Scenario 1	Scenario 2	Scenario 3	Scenario 4	Scenario 5	Scenario 6
	Differentially Expressed At Generation 6 and every subsequent generation	Differentially Expressed At Generation 8 and every subsequent generation	Differentially Expressed At Generation 9 and every subsequent generation	Differentially Expressed At Generation 10 and every subsequent generation	Differentially Expressed At Generation 12 and Generation 13	Differentially Expressed At Generation 13
Transcript 1	$p_6 < \text{threshold}_1$ and $p_8 < \text{threshold}_1$ and $p_9 < \text{threshold}_1$ and $p_{10} < \text{threshold}_1$ and $p_{12} < \text{threshold}_1$ and $p_{13} < \text{threshold}_1$	$p_8 < \text{threshold}_2$ and $p_9 < \text{threshold}_2$ and $p_{10} < \text{threshold}_2$ and $p_{12} < \text{threshold}_2$ and $p_{13} < \text{threshold}_2$	$p_9 < \text{threshold}_3$ and $p_{10} < \text{threshold}_3$ and $p_{12} < \text{threshold}_3$ and $p_{13} < \text{threshold}_3$	$p_{10} < \text{threshold}_4$ and $p_{12} < \text{threshold}_4$ and $p_{13} < \text{threshold}_4$	$p_{12} < \text{threshold}_5$ and $p_{13} < \text{threshold}_5$	$p_{13} < \text{threshold}_6$
Transcript 2	$p_6 < \text{threshold}_1$ and $p_8 < \text{threshold}_1$ and $p_9 < \text{threshold}_1$ and $p_{10} < \text{threshold}_1$ and $p_{12} < \text{threshold}_1$ and $p_{13} < \text{threshold}_1$	$p_8 < \text{threshold}_2$ and $p_9 < \text{threshold}_2$ and $p_{10} < \text{threshold}_2$ and $p_{12} < \text{threshold}_2$ and $p_{13} < \text{threshold}_2$	$p_9 < \text{threshold}_3$ and $p_{10} < \text{threshold}_3$ and $p_{12} < \text{threshold}_3$ and $p_{13} < \text{threshold}_3$	$p_{10} < \text{threshold}_4$ and $p_{12} < \text{threshold}_4$ and $p_{13} < \text{threshold}_4$	$p_{12} < \text{threshold}_5$ and $p_{13} < \text{threshold}_5$	$p_{13} < \text{threshold}_6$
Transcript 15,259	$p_6 < \text{threshold}_1$ and $p_8 < \text{threshold}_1$ and $p_9 < \text{threshold}_1$ and $p_{10} < \text{threshold}_1$ and $p_{12} < \text{threshold}_1$ and $p_{13} < \text{threshold}_1$	$p_8 < \text{threshold}_2$ and $p_9 < \text{threshold}_2$ and $p_{10} < \text{threshold}_2$ and $p_{12} < \text{threshold}_2$ and $p_{13} < \text{threshold}_2$	$p_9 < \text{threshold}_3$ and $p_{10} < \text{threshold}_3$ and $p_{12} < \text{threshold}_3$ and $p_{13} < \text{threshold}_3$	$p_{10} < \text{threshold}_4$ and $p_{12} < \text{threshold}_4$ and $p_{13} < \text{threshold}_4$	$p_{12} < \text{threshold}_5$ and $p_{13} < \text{threshold}_5$	$p_{13} < \text{threshold}_6$

p_i = p-value at generation i

$$\text{Threshold}_j = (0.05 / 15,259)^{1/(6-j+1)}$$

Table S2. QTL for Alcohol Preference/Consumption in the 2-Bottle Choice Paradigm			
Chr	Mb Range (NCBIM37)		Source
1	1.80	13.57	Bice et al 2011
1	95.13	108.62	Bice et al 2011
1	128.78	134.67	Bice et al 2011
2	3.45	146.16	Belknap and Atkins 2001; Rodriguez et al 1995: 65.9-91.9
3	0.00	224.84	Belknap and Atkins 2001; Bice et al 2011: 128.52-129.96, 137.82-138.00, 145.36-145.46
4	52.01	202.78	Belknap and Atkins 2001
7	114.40	136.30	Rodriguez et al 1995
9	0.00	113.49	Belknap and Atkins 2001; Bice et al 2011: 60.60-62.71, 68.52-70.67, 102.48-103.09, 106.47-110.94
11	91.50	111.50	Rodriguez et al 1995
12	80.10	100.10	Rodriguez et al 1995

Table S3. Transcripts with maintained differential expression across generations

Probe Set ID	Gene Symbol	Physical Location of Probe Set (chromosome: Mb)	Generation Where Significant Differential Expression Began	Generation Where Significant Differential Variation Began (Line of DV)	deQTL Associated With Transcription Levels of Gene - Univariate (chromosome: Mb range)	deQTL Associated with Transcription Levels of Gene-Multivariate Model (Chromosome: Mb range)	proportion of variance in the gene's expression explained by multivariate model	Location of Major eQTL [chromosome: Mb (p-value)]	Difference in Expression at Generation 13 [log 2 difference (p-value)]	Difference in Expression Between HAP1 and LAP1 [log 2 difference (p-value)]	Difference in Expression Between HAP2 and LAP2 [log 2 difference (p-value)]	Difference in Expression Between C57BL/6J and DBA/2J [log 2 difference (p-value)]
1419469_at	Gnb4	3:32.48 Mb	9					3:32.48 Mb (0.0080)	-0.40 (0.0244)	0.08 (0.2346)	0.24 (0.0247)	-0.46 (<0.0001)
1421139_a_at	Zfp386	12:117.3 Mb	9					12:114.5 Mb (0.3770)	-0.75 (<0.0001)	0.37 (0.0015)	-0.76 (<0.0001)	-0.27 (0.0003)
1421907_at	Med1	11:98.02 Mb	10					11:98.78 Mb (0.0700)	-0.48 (0.0117)	0.11 (0.0651)	0.31 (0.0161)	0.54 (<0.0001)
1424737_at	Thrsp	7:104.56 Mb	10					7:103.13 Mb (0.0020)	0.72 (<0.0001)	0.80 (<0.0001)	-0.07 (0.4164)	0.75 (<0.0001)
1426288_at	Lrp4	2:91.35 Mb	6					2:88.19 Mb (0.8180)	0.23 (0.0765)	0.80 (<0.0001)	0.20 (0.3985)	0.53 (<0.0001)
1428692_at	Hddc3	7:87.49 Mb	6					7:81.49 Mb (<0.0001)	0.84 (0.0029)	-0.27 (0.1068)	0.64 (0.0127)	-1.31 (<0.0001)
1428889_at	Alkbh3	2:93.82 Mb	6					5:84.27 Mb (0.6130)	-0.48 (0.0001)	-0.63 (0.0001)	0.16 (0.3836)	0.09 (0.1647)
1429215_at		12:117.62 Mb	9					12:115.17 Mb (0.0105)	-0.67 (0.0002)	0.09 (0.3458)	-0.60 (0.0007)	0.61 (<0.0001)
1429410_at	Eny2	15:44.27 Mb	10					3:23.72 Mb (0.0730)	-0.32 (0.0004)	0.01 (0.8867)	0.56 (0.0086)	-0.42 (0.0008)
1429441_at	Fbxo30	10:11.02 Mb	6					8:120.9 Mb (0.6580)	-0.14 (0.0713)	-0.04 (0.5829)	0.06 (0.4337)	-0.06 (0.1773)
1429902_at	Tcf12	9:71.76 Mb	6					1:73.26 Mb (0.4610)	0.24 (0.0253)	0.23 (0.0106)	0.71 (0.0021)	1.30 (<0.0001)
1430368_s_at	1700019D03Rik	1:52.98 Mb	8					5:33.93 Mb (0.4270)	0.23 (0.0153)	0.15 (0.0354)	0.01 (0.9311)	-0.08 (0.1502)
1431266_at	Gpatch2	1:189.06 Mb	8	6 (HAP)				1:187 Mb (<0.0001)	0.40 (0.0013)	-0.07 (0.2809)	-0.01 (0.7851)	0.35 (<0.0001)
1434339_at	Fnbp11	3:122.24 Mb	9					3:89.35 Mb (0.2260)	-0.24 (0.0104)	-0.06 (0.2856)	0.16 (0.0485)	0.18 (0.0067)
1435606_at	Gal3st4	5:138.71 Mb	8					3:74.54 Mb (0.8470)	-0.18 (0.0449)	0.00 (0.9430)	-0.16 (0.0281)	0.05 (0.3074)
1436145_at	2410003K15Rik	6:49.03 Mb	10					3:36.74 Mb (0.8230)	-0.36 (0.0023)	0.02 (0.7030)	-0.24 (0.0741)	0.46 (0.0014)
1438249_at	Usp7	16:8.7 Mb	9					1:73.26 Mb (0.5250)	-0.29 (0.0226)	-0.03 (0.7616)	0.47 (0.0009)	-0.21 (0.0013)
1439138_at	2310035C23Rik	1:107.59 Mb	6					14:8.85 Mb (0.7210)	-0.98 (0.0003)	0.03 (0.6960)	0.06 (0.5473)	-0.74 (<0.0001)
1440091_at	Meis2	2:115.82 Mb	10					1:126.52 Mb (0.9020)	-0.45 (0.0027)	0.23 (0.0048)	0.78 (<0.0001)	-0.30 (0.1542)

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1440153_at		16:84.95 Mb	6					19:21.21 Mb (0.2360)	0.28 (0.0146)	-0.14 (0.1679)	0.00 (0.9567)	0.20 (0.0121)
1441238_at	Pds5a	5:66.05 Mb	8					5:65.14 Mb (<0.0001)	-0.52 (0.0100)	0.30 (0.0001)	0.04 (0.7817)	0.93 (<0.0001)
1443745_s_at	Dmp1	5:104.64 Mb	8					5:13.82 Mb (0.3490)	0.87 (0.0015)	0.08 (0.5280)	0.29 (0.0982)	0.39 (0.0033)
1444620_at	Tcf12	9:71.9 Mb	8					9:71.41 Mb (0.0022)	0.27 (0.0706)	0.22 (0.0019)	0.19 (0.0082)	0.56 (0.0001)
1448096_at	Ogfod1	8:96.56 Mb	9					19:59.53 Mb (0.3370)	-0.27 (0.0064)	0.12 (0.0485)	0.28 (0.0054)	0.04 (0.4166)
1448793_a_at	Sdc4	2:164.25 Mb	6	6 (HAP)				12:101.87 Mb (0.4380)	1.51 (0.0008)	0.73 (<0.0001)	1.25 (0.0060)	0.39 (0.0001)
1449018_at		:NA Mb	6					11:62.07 Mb (0.0030)	-0.40 (0.0421)	-0.53 (<0.0001)	0.14 (0.4229)	-0.47 (<0.0001)
1451146_at	Zfp386	12:117.3 Mb	9					5:3.14 Mb (0.6380)	-0.81 (<0.0001)	0.42 (0.0009)	-0.84 (<0.0001)	-0.26 (0.0013)
1451506_at	Mef2c	13:83.8 Mb	9					1:43.8 Mb (0.4070)	-0.23 (0.0334)	-0.11 (0.1054)	0.23 (0.0726)	0.13 (0.1945)
1452379_at	Auts2	5:131.92 Mb	10					2:9.75 Mb (0.0080)	-0.36 (0.0004)	0.29 (0.0001)	0.26 (0.0279)	0.03 (0.5370)
1456387_at	Nol4	18:22.85 Mb	9					18:16.57 Mb (0.0040)	-0.30 (0.0048)	0.26 (0.0012)	-0.01 (0.9269)	-0.78 (<0.0001)
1458129_at	Rora	9:69.23 Mb	6					3:23.72 Mb (0.1160)	1.07 (<0.0001)	0.27 (0.0021)	0.66 (0.0003)	-0.28 (0.0103)
1459307_at	Sec24b	3:129.73 Mb	6	6 (LAP)				2:16.23 Mb (0.5850)	-0.19 (0.0369)	-0.10 (0.1868)	0.55 (0.0044)	-0.17 (0.0076)
1417355_at	Peg3	7:6.66 Mb	8	6 (HAP)		rs3669485 (1:13.98 - 20.77)	0.14	3:23.72 Mb (0.0920)	1.33 (0.0009)	-1.22 (<0.0001)	0.11 (0.7723)	-0.09 (0.1830)
1437901_a_at	Vps41	13:18.92 Mb	6		rs6241342 (7:126.33 - 126.33)	rs6241342 (7:126.33 - 126.33)	0.15	12:82.69 Mb (0.6730)	-0.35 (0.0001)	0.36 (0.0002)	0.00 (0.9705)	-0.03 (0.6501)
1456293_s_at	Ccnh	13:85.35 Mb	6		rs6241342 (7:126.33 - 126.33)	rs6241342 (7:126.33 - 126.33)	0.15	8:14.76 Mb (0.2070)	0.13 (0.0749)	0.25 (0.0005)	0.06 (0.4168)	-0.09 (0.2205)
1443037_at	Nptn	9:58.47 Mb	9			rs13478906 (6:92.57 - 98.03)	0.16	10:64.17 Mb (0.2800)	-0.28 (0.0026)	0.07 (0.3292)	0.36 (0.0006)	0.01 (0.8302)
1423179_at	Kcnb1	2:166.93 Mb	10			CEL-	0.17	2:165.61 Mb	-0.36	-0.08	-0.03	-0.02

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						9_29909656 (9:29.75 - 40.27)		(0.2280)	(0.0013)	(0.4057)	(0.8444)	(0.7767)
1440915_at	Mphosph9	5:124.7 Mb	8			rs3669485 (1:13.98 - 20.77)	0.17	5:123.74 Mb (0.0025)	-0.50 (<0.0001)	-0.14 (0.0438)	0.08 (0.3059)	-0.34 (<0.0001)
1442358_at	Rnf169	7:107.11 Mb	10	6 (HAP)		CEL-9_29909656 (9:29.75 - 40.27)	0.18	9:56.7 Mb (0.7350)	-0.39 (0.0001)	-0.08 (0.2175)	0.50 (0.0006)	-0.39 (0.0001)
1434374_at	Fam168a	7:107.99 Mb	8			rs3669485 (1:13.98 - 20.77)	0.19	7:103.13 Mb (0.0930)	0.88 (<0.0001)	0.13 (0.0476)	0.00 (0.9709)	0.10 (0.1418)
1458010_at		4:77.46 Mb	9	6 (LAP)		rs13478906 (6:92.57 - 98.03)	0.19	7:103.13 Mb (0.3590)	-0.66 (0.0005)	0.24 (0.2790)	-0.34 (0.2084)	-0.38 (0.0005)
1455993_at	Odz4	7:104.06 Mb	13		rs3659787 (11:4.41 - 16.85) rs13479416 (7:95.16 - 121.84)	rs13479416 (7:95.16 - 121.84)	0.20	7:117.12 Mb (0.3440)	-0.92 (<0.0001)	0.41 (0.0045)	0.50 (0.0002)	-0.83 (<0.0001)
1434375_at	Fam168a	7:107.99 Mb	8	8 (HAP)		rs3669485 (1:13.98 - 20.77)	0.20	7:103.13 Mb (<0.0001)	1.20 (<0.0001)	-0.02 (0.7331)	0.07 (0.4214)	1.28 (<0.0001)
1447864_s_at	Pogk	1:168.33 Mb	6		gnf18.021.931 (18:24.6 - 24.6)	gnf18.021.931 (18:24.6 - 24.6)	0.21	1:147.39 Mb (0.0003)	0.21 (0.0423)	-0.14 (0.0514)	0.19 (0.1154)	-0.37 (<0.0001)
1459464_at	Macf1	4:123.32 Mb	9			rs13478906 (6:92.57 - 98.03)	0.22	14:8.85 Mb (0.5390)	-0.22 (0.0110)	0.78 (<0.0001)	-0.01 (0.9764)	0.39 (0.0014)
1431053_at	Mphosph9	5:124.7 Mb	6		gnf18.021.931 (18:24.6 - 24.6) rs13477323 (3:109.4 - 141.7)	rs13477323 (3:109.4 - 141.7)	0.25	5:119.76 Mb (0.0370)	-1.13 (<0.0001)	-0.01 (0.9403)	-0.09 (0.5472)	-1.13 (<0.0001)
1455441_at	Map3k7	4:32.11 Mb	6		rs3701432 (4:29.19 - 34.04)	rs3701432 (4:29.19 - 34.04)	0.28	4:31.65 Mb (0.1480)	-0.24 (0.0042)	0.15 (0.0154)	0.02 (0.7304)	0.18 (0.0007)

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1443621_at	Xaf1	11:72.13 Mb	6		rs13478067 (4:154.37 - 155.38)	rs13478067 (4:154.37 - 155.38) rs6241342 (7:126.33 - 126.33)	0.28	11:69.42 Mb (<0.0001)	-0.42 (0.0002)	-0.93 (<0.0001)	-0.14 (0.7667)	-0.72 (<0.0001)
1456257_at	Fam126b	1:58.58 Mb	9			rs13478906 (6:92.57 - 98.03)	0.29	1:57.88 Mb (0.0001)	-0.88 (0.0284)	0.40 (0.0092)	-0.48 (0.0121)	1.34 (<0.0001)
1451457_at	Sc5d	9:42.06 Mb	10	9 (LAP)		CEL-9_29909656 (9:29.75 - 40.27)	0.30	9:41.47 Mb (0.0001)	0.71 (0.0090)	0.05 (0.7470)	0.34 (0.1235)	2.29 (<0.0001)
1425795_a_at	Map3k7	4:32.11 Mb	6		rs3701432 (4:29.19 - 34.04) rs13478067 (4:154.37 - 155.38)	rs3701432 (4:29.19 - 34.04) rs13478067 (4:154.37 - 155.38)	0.50	4:31.65 Mb (0.0260)	-0.39 (0.0004)	0.42 (0.0002)	0.08 (0.4502)	0.23 (0.0032)
1419988_at	Map3k7	4:32.11 Mb	6		rs3701432 (4:29.19 - 34.04)	rs3701432 (4:29.19 - 34.04)	0.62	4:31.65 Mb (<0.0001)	-0.33 (0.0005)	0.29 (0.0006)	0.06 (0.5031)	0.30 (0.0006)
1444507_at	Usp53	3:122.69 Mb	6	6 (LAP)	gnf18.021.931 (18:24.6 - 24.6) rs13477323 (3:109.4 - 141.7) rs13478067 (4:154.37 - 155.38)	rs13477323 (3:109.4 - 141.7) rs13478067 (4:154.37 - 155.38)	0.73	3:118.29 Mb (<0.0001)	-0.47 (<0.0001)	-0.17 (0.0736)	0.57 (<0.0001)	0.46 (<0.0001)
1454696_at	Gnb1	4:154.93 Mb	6	6 (LAP)	rs13478067 (4:154.37 - 155.38)	rs13478067 (4:154.37 - 155.38)	0.74	4:155.24 Mb (<0.0001)	-1.98 (<0.0001)	-1.61 (<0.0001)	-1.09 (<0.0001)	-1.36 (<0.0001)
1417432_a_at	Gnb1	4:154.93 Mb	6		rs13478067 (4:154.37 - 155.38)	rs13478067 (4:154.37 - 155.38)	0.85	4:154.88 Mb (<0.0001)	-1.16 (<0.0001)	-1.12 (<0.0001)	-1.36 (<0.0001)	-1.67 (<0.0001)
1438435_at	Acer3	7:105.36 Mb	13	8 (HAP)	rs3659787 (11:4.41 - 16.85) rs13479416	rs13479416 (7:95.16 - 121.84)	0.98	7:103.13 Mb (<0.0001)	1.46 (<0.0001)	1.82 (<0.0001)	-0.22 (0.1782)	1.67 (<0.0001)

Table S3. Transcripts with maintained differential expression across generations

Probe Set ID	Gene Symbol	Physical Location of Probe Set (chromosome: Mb)	Generation Where Significant Differential Expression Began	Generation Where Significant Differential Variation Began (Line of DV)	deQTL Associated With Transcription Levels of Gene - Univariate (chromosome: Mb range)	deQTL Associated with Transcription Levels of Gene-Multivariate Model (Chromosome: Mb range)	proportion of variance in the gene's expression explained by multivariate model	Location of Major eQTL [chromosome: Mb (p-value)]	Difference in Expression at Generation 13 [log 2 difference (p-value)]	Difference in Expression Between HAP1 and LAP1 [log 2 difference (p-value)]	Difference in Expression Between HAP2 and LAP2 [log 2 difference (p-value)]	Difference in Expression Between C57BL/6J and DBA/2J [log 2 difference (p-value)]
					(7:95.16 - 121.84)							
1424410_at	Ttc8	12:100.22 Mb	12					19:4.85 Mb (0.7270)	-0.38 (0.0005)	0.15 (0.0394)	0.15 (0.1132)	-0.08 (0.2075)
1426766_at	6330403K07Rik	11:70.85 Mb	12					11:116.91 Mb (0.6690)	-0.32 (0.0007)	0.06 (0.2548)	0.03 (0.6437)	-0.37 (0.0007)
1430183_at	Pbx1	1:170.35 Mb	12					2:16.23 Mb (0.0014)	-0.40 (0.0012)	0.28 (0.0074)	0.70 (0.0009)	-0.35 (0.0194)
1434909_at	Rragd	4:33.11 Mb	12					4:29.19 Mb (0.0008)	-0.37 (0.0012)	0.10 (0.0743)	0.26 (0.0065)	0.16 (0.0621)
1436325_at	Rora	9:69.23 Mb	12					15:63.15 Mb (0.5980)	0.57 (<0.0001)	0.31 (0.0001)	0.26 (0.0460)	-0.15 (0.0326)
1442489_at	Agfg1	1:82.88 Mb	12					3:23.72 Mb (0.2070)	-0.42 (0.0015)	-0.39 (0.0004)	0.46 (0.0192)	0.10 (0.4658)
1450843_at	Serpinh1	7:106.49 Mb	12					7:103.13 Mb (0.0100)	0.56 (0.0001)	0.28 (0.0018)	-0.07 (0.4130)	0.45 (<0.0001)
1451458_at	Tmem2	19:21.93 Mb	12					12:37.6 Mb (0.2200)	-0.29 (0.0015)	0.07 (0.3567)	0.17 (0.0733)	0.01 (0.9054)
1452330_at	Mxra8	4:155.22 Mb	12	6 (LAP)				4:155.24 Mb (<0.0001)	-0.34 (0.0003)	-0.29 (0.0001)	-0.40 (0.0002)	-0.22 (0.0002)
1454639_at	Rpl41	10:127.99 Mb	12					2:50.5 Mb (0.0270)	-0.45 (<0.0001)	0.31 (0.0008)	0.12 (0.1332)	-0.20 (0.0029)
1454902_at	Prkcz	4:154.63 Mb	12					4:150.31 Mb (0.2840)	0.56 (0.0009)	0.27 (0.0004)	0.25 (0.0002)	0.06 (0.2434)
1456216_at	Csnk1a1	18:61.72 Mb	12					1:45.57 Mb (0.8720)	-0.29 (0.0008)	0.00 (0.9844)	0.11 (0.2381)	0.05 (0.4074)
1456735_at	Acpl2	9:96.72 Mb	12					2:128.2 Mb (0.6660)	-0.49 (0.0001)	-0.49 (0.0001)	-0.24 (0.2580)	-0.21 (0.0055)
1459844_at	Tnip2	5:34.84 Mb	12					5:84.27 Mb (0.9790)	-0.59 (0.0002)	-0.02 (0.7094)	0.13 (0.3988)	-0.12 (0.3530)

Table S4. Transcripts with maintained reduced variation across generations (compared to starting heterogeneous stock)

Probe Set ID	Gene Symbol	Physical Location of Probe Set (chromosome: Mb)	Generation Where Significant Differential Expression Began	Generation Where Significant Variation Began (Line of DV)	Location of Major eQTL [chromosome:Mb (p-value)]	Difference in Expression at Generation 13 [log 2 difference (p-value)]
1430136_at	Grm3	5:9.49 Mb		6 (HAP) 6 (LAP)	2:13.36 Mb (0.0840)	0.04 (0.6565)
1451728_at	Wdr13	X:7.7 Mb		6 (HAP) 6 (LAP)	8:129.11 Mb (0.0700)	-0.04 (0.5260)
1417211_a_at	1110032A03Rik	9:50.57 Mb		6 (HAP)	9:46.34 Mb (0.0005)	0.05 (0.6421)
1417355_at	Peg3	7:6.66 Mb	8	6 (HAP)	3:23.72 Mb (0.0920)	1.33 (0.0009)
1420537_at	Gtf2f2	14:76.36 Mb		6 (HAP)	18:73.59 Mb (0.6750)	-0.05 (0.5262)
1420994_at	B3gnt5	16:19.77 Mb		6 (HAP)	19:21.21 Mb (0.5990)	-0.26 (0.0253)
1422165_at		X:108.01 Mb		6 (HAP)	18:49.45 Mb (0.1420)	0.01 (0.9015)
1422773_at	Myt1	2:181.56 Mb		6 (HAP)	8:98.23 Mb (0.7800)	-0.23 (0.0088)
1423894_a_at	Dalrd3	9:108.47 Mb		6 (HAP)	19:38.91 Mb (0.1400)	-0.03 (0.7345)
1424223_at	1700020C11Rik	11:3.99 Mb		6 (HAP)	11:47.59 Mb (0.6900)	-0.12 (0.1630)
1424483_at		6:83.29 Mb		6 (HAP)	15:73.96 Mb (0.5090)	-0.16 (0.0342)
1426409_at	Lzts2	19:45.1 Mb		6 (HAP)	14:63.11 Mb (0.0004)	-0.11 (0.1504)
1426890_a_at	Rpap1	2:119.59 Mb		6 (HAP)	2:117.12 Mb (0.0110)	0.05 (0.6217)
1428101_at	Rnf38	4:44.14 Mb		6 (HAP)	4:40.97 Mb (0.0016)	0.20 (0.0278)
1428351_at	Ppm1m	9:106.1 Mb		6 (HAP)	9:105.82 Mb (0.0670)	-0.13 (0.0922)
1428636_at	Steap2	5:5.67 Mb		6 (HAP)	12:97.34 Mb (0.0670)	-0.13 (0.1388)
1431266_at	Gpatch2	1:189.06 Mb	8	6 (HAP)	1:187 Mb (<0.0001)	0.40 (0.0013)
1433571_at	Serinc5	13:93.48 Mb		6 (HAP)	11:116.91 Mb (0.0500)	-0.15 (0.2009)
1434210_s_at	Lrig1	6:94.55 Mb		6 (HAP)	8:89.79 Mb (0.4970)	-0.13 (0.0888)
1434416_a_at		17:26.1 Mb		6 (HAP)	7:103.13 Mb (0.0660)	-0.18 (0.0218)
1434612_s_at	Sbno1	5:124.82 Mb		6 (HAP)	5:40.03 Mb (0.1770)	0.07 (0.3309)
1434648_a_at	Ccm2	11:6.5 Mb		6 (HAP)	5:3.14 Mb (0.3930)	0.01 (0.9211)
1435148_at	Atp1b2	11:69.41 Mb		6 (HAP)	1:186.15 Mb (0.6320)	-0.13 (0.0748)
1436183_at		6:38.26 Mb		6 (HAP)	1:183.94 Mb (0.8190)	-0.15 (0.0838)
1436388_a_at	3830406C13Rik	14:13.13 Mb		6 (HAP)	14:10.59 Mb (0.0020)	0.05 (0.6503)
1437045_at	Mapk8	14:34.2 Mb		6 (HAP)	1:45.57 Mb (0.3660)	-0.20 (0.0134)
1437759_at	Pfkip	13:6.59 Mb		6 (HAP)	2:13.36 Mb (0.1340)	-0.06 (0.6175)
1439805_at	Nfat5	8:109.85 Mb		6 (HAP)	1:21.63 Mb (0.2820)	-0.21 (0.0147)
1439998_at	Jmjd1c	10:66.65 Mb		6 (HAP)	10:64.17 Mb (0.3470)	0.05 (0.5203)

Table S4. Transcripts with maintained reduced variation across generations (compared to starting heterogeneous stock)

Probe Set ID	Gene Symbol	Physical Location of Probe Set (chromosome: Mb)	Generation Where Significant Differential Expression Began	Generation Where Significant Variation Began (Line of DV)	Location of Major eQTL [chromosome:Mb (p-value)]	Difference in Expression at Generation 13 [log 2 difference (p-value)]
1440651_at	Dusp16	6:134.69 Mb		6 (HAP)	6:133.92 Mb (<0.0001)	-0.23 (0.0193)
1440830_at	Gpr116	17:43.59 Mb		6 (HAP)	11:33.54 Mb (0.2790)	-0.17 (0.0224)
1441266_at	Strn3	12:52.74 Mb		6 (HAP)	10:108.82 Mb (0.9810)	-0.33 (0.0002)
1442207_at		7:108.43 Mb		6 (HAP)	7:103.13 Mb (<0.0001)	-0.37 (0.0004)
1442358_at	Rnf169	7:107.11 Mb	10	6 (HAP)	9:56.7 Mb (0.7350)	-0.39 (0.0001)
1442760_x_at	Rtn4	11:29.62 Mb		6 (HAP)	11:21.12 Mb (0.4380)	-0.32 (0.0052)
1443366_at	Napg	18:63.14 Mb		6 (HAP)	2:11.71 Mb (0.0200)	-0.23 (0.0442)
1445867_at	Rsf1	7:104.75 Mb		6 (HAP)	1:165.32 Mb (0.2820)	-0.23 (0.0042)
1447679_s_at	Bms1	6:118.33 Mb		6 (HAP)	1:183.94 Mb (0.4480)	-0.17 (0.0209)
1448529_at	Thbd	2:148.23 Mb		6 (HAP)	10:27.85 Mb (0.0390)	0.04 (0.5586)
1448793_a_at	Sdc4	2:164.25 Mb	6	6 (HAP)	12:101.87 Mb (0.4380)	1.51 (0.0008)
1449770_x_at	Tmem191c	16:17.28 Mb		6 (HAP)	1:181.8 Mb (0.5450)	-0.19 (0.0291)
1450985_a_at	Tjp2	19:24.17 Mb		6 (HAP)	5:72.42 Mb (0.1880)	0.03 (0.6517)
1451047_at	Itn2a	X:104.59 Mb		6 (HAP)	12:82.69 Mb (0.6100)	-0.02 (0.8035)
1453109_at	Arsk	13:76.2 Mb		6 (HAP)	13:75.9 Mb (0.0017)	-0.03 (0.6853)
1455078_at		11:77.27 Mb		6 (HAP)	19:56.68 Mb (0.4110)	-0.11 (0.1015)
1458700_at	Lrrc8c	5:106.02 Mb		6 (HAP)	3:7.68 Mb (0.5590)	-0.16 (0.0853)
1434375_at	Fam168a	7:107.99 Mb	8	8 (HAP)	7:103.13 Mb (<0.0001)	1.20 (<0.0001)
1438435_at	Acer3	7:105.36 Mb	13	8 (HAP)	7:103.13 Mb (<0.0001)	1.46 (<0.0001)
1441577_at	Efna5	17:63.21 Mb		8 (HAP)	11:47.59 Mb (0.2160)	-0.07 (0.3752)
1417121_at	Gabra6	11:42.12 Mb		9 (HAP)	8:93.35 Mb (0.8220)	-0.06 (0.7041)
1418868_at	En2	5:28.5 Mb		9 (HAP)	19:25.74 Mb (0.4090)	-0.42 (0.0002)
1419271_at	Pax6	2:105.54 Mb		9 (HAP)	8:129.11 Mb (0.1700)	-0.23 (0.0177)
1423286_at	Cbln1	8:89.99 Mb		9 (HAP)	8:93.35 Mb (0.0280)	-0.27 (0.0415)
1423287_at	Cbln1	8:89.99 Mb		9 (HAP)	8:93.35 Mb (0.1200)	-0.25 (0.0977)
1423477_at	Zic1	9:91.26 Mb		9 (HAP)	9:86.2 Mb (0.0016)	-0.26 (0.0031)
1426412_at	Neurod1	2:79.29 Mb		9 (HAP)	19:32.96 Mb (0.4920)	0.12 (0.2296)
1426413_at	Neurod1	2:79.29 Mb		9 (HAP)	1:72.74 Mb (0.9110)	0.00 (0.9972)
1427482_a_at	Car8	4:8.07 Mb		9 (HAP)	4:6.82 Mb (0.0016)	-0.10 (0.4997)
1428370_at	1500011B03Rik	5:115.26 Mb		9 (HAP)	5:115.6 Mb (<0.0001)	0.20 (0.1396)
1437205_at	Tcf25	8:125.93 Mb		9 (HAP)	2:16.23 Mb (0.2700)	-0.24 (0.0064)

Table S4. Transcripts with maintained reduced variation across generations (compared to starting heterogeneous stock)

Probe Set ID	Gene Symbol	Physical Location of Probe Set (chromosome: Mb)	Generation Where Significant Differential Expression Began	Generation Where Significant Differential Variation Began (Line of DV)	Location of Major eQTL [chromosome:Mb (p-value)]	Difference in Expression at Generation 13 [log 2 difference (p-value)]
1449240_at	Gsbs	6:55.98 Mb		9 (HAP)	19:32.96 Mb (0.3710)	-0.31 (0.0770)
1421360_at	Inpp4a	:NA Mb		6 (LAP)	1:36.05 Mb (0.0001)	0.28 (0.0669)
1421814_at	Msn	X:93.36 Mb		6 (LAP)	13:111.23 Mb (0.7490)	0.12 (0.0867)
1422943_a_at		13:45.17 Mb		6 (LAP)	2:179.01 Mb (0.3030)	0.31 (0.0012)
1436790_a_at	Sox11	12:28.02 Mb		6 (LAP)	1:60.7 Mb (0.6010)	0.38 (0.0037)
1437567_at	Zfp772	7:7.15 Mb		6 (LAP)	1:173.16 Mb (0.2940)	0.26 (0.0415)
1439166_at	Nol11	11:107.05 Mb		6 (LAP)	7:144.22 Mb (0.9250)	-0.32 (0.0011)
1440579_at	Mib1	18:10.77 Mb		6 (LAP)	17:69.15 Mb (0.5320)	-0.19 (0.0205)
1444507_at	Usp53	3:122.69 Mb	6	6 (LAP)	3:118.29 Mb (<0.0001)	-0.47 (<0.0001)
1445410_at	Naa35	13:59.73 Mb		6 (LAP)	2:13.36 Mb (0.7400)	-0.21 (0.0073)
1446150_at	Tmem47	X:78.33 Mb		6 (LAP)	X:99.32 Mb (0.5310)	-0.29 (0.0019)
1446550_at	Gspt1	16:11.25 Mb		6 (LAP)	5:123.74 Mb (0.3250)	-0.17 (0.0870)
1452330_a_at	Mxra8	4:155.22 Mb	12	6 (LAP)	4:155.24 Mb (<0.0001)	-0.34 (0.0003)
1454696_at	Gnb1	4:154.93 Mb	6	6 (LAP)	4:155.24 Mb (<0.0001)	-1.98 (<0.0001)
1456886_at		12:112.11 Mb		6 (LAP)	12:110.14 Mb (0.0950)	-0.31 (0.0007)
1457480_at	Pcgf3	5:108.9 Mb		6 (LAP)	12:104.27 Mb (0.1300)	-0.29 (0.0040)
1458010_at		4:77.46 Mb	9	6 (LAP)	7:103.13 Mb (0.3590)	-0.66 (0.0005)
1458947_at	2010111I01Rik	13:63.35 Mb		6 (LAP)	13:63.06 Mb (0.0001)	-0.30 (0.0148)
1459307_at	Sec24b	3:129.73 Mb	6	6 (LAP)	2:16.23 Mb (0.5850)	-0.19 (0.0369)
1460189_at	Dcaf11	14:56.19 Mb		6 (LAP)	8:129.11 Mb (0.6300)	-0.09 (0.3087)
1451457_at	Sc5d	9:42.06 Mb	10	9 (LAP)	9:41.47 Mb (0.0001)	0.71 (0.0090)

Table S5. Differential expression and differential variance eQTL for HAP3/LAP3 mice.

Type of QTL Derived from HAP3/LAP3	Generation DE/DV established	Chromosome	Locus with minimum p-value in region	Mb location of minimum p-value	Minimum Mb of significant SNPs in area (FDR<0.05)	Maximum Mb of significant SNPs in area (FDR<0.05)	Number of significant loci in area	minimum unadjusted p-value in area	minimum FDR in area	Overlap with deeQTL	Overlap with HAP3 _{rv} eQTL	Overlap with LAP3 _{rv} eQTL	Overlap with bQTL
deeQTL	6	3	rs13477323	109.396	99.396	151.705	9	<0.0001	<0.0001		3:118 - 138 (generation 9)	3:135.1 - 155.1 (generation 6)	3:0 - 224.84 (Belknap and Atkins 2001) 3:128.52 - 129.96 (Bice et al 2011) 3:137.82 - 138 (Bice et al 2011) 3:145.36 - 145.56 (Bice et al 2011)
deeQTL	6	4	rs3701432	29.190	19.190	44.041	3	<0.0001	<0.0001				
deeQTL	6	4	rs13478067	154.365	144.365	165.385	4	<0.0001	<0.0001		4:139.68 - 159.68 (generation 8)	4:134.56 - 165.38 (generation 6)	4:52.01 - 202.78 (Belknap and Atkins 2001)
deeQTL	6	7	rs6241342	126.326	116.326	136.326	1	0.0005	0.0306		7:71.49 - 155.33 (generation 8)		7:114.4 - 136.3 (Rodriguez et al 1995)
deeQTL	6	18	gnf18.021.931	24.601	14.601	34.601	1	0.0003	0.0196				
deeQTL	8	1	rs3669485	13.975	3.975	30.774	4	0.0001	0.0327		1:3.37 - 35.63 (generation 8)		1:1.8 - 13.57 (Bice et al 2011)
deeQTL	9	6	rs13478906	95.024	82.570	108.028	3	<0.0001	<0.0001		6:67.07 - 87.07 (generation 8)		
deeQTL	10	9	CEL-9_29909656	29.749	19.749	50.268	4	<0.0001	<0.0001				9:0 - 113.49 (Belknap and Atkins 2001)
deeQTL	13	7	rs13479416	103.132	85.155	131.843	6	<0.0001	<0.0001		7:71.49 - 155.33 (generation 8)		7:114.4 - 136.3 (Rodriguez et al 1995)
deeQTL	13	11	rs3659787	4.409	0.000	26.853	2	0.0004	0.0490		11:0 - 57.93 (generation 8)		
hap _{rv} eQTL	6	10	rs3712998	9.329	0.000	19.329	1	<0.0001	<0.0001			10:0 - 29.8 (generation 6)	
hap _{rv} eQTL	8	1	rs6404446	20.774	3.373	35.632	8	<0.0001	<0.0001	1:3.98 - 30.77 (generation 8)		1:33.8 - 53.8 (generation 6)	1:1.8 - 13.57 (Bice et al 2011)
hap _{rv} eQTL	8	1	rs13475984	94.608	84.608	104.608	1	0.0006	0.0159				1:95.13 - 108.62 (Bice et al 2011)
hap _{rv} eQTL	8	2	gnf02.006.767	9.751	0.000	27.962	5	<0.0001	<0.0001				2:3.45 - 146.16 (Belknap and Atkins 2001)

Table S5. Differential expression and differential variance eQTL for HAP3/LAP3 mice.

Type of QTL Derived from HAP3/LAP3	Generation DE/DV established	Chromosome	Locus with minimum p-value in region	Mb location of minimum p-value	Minimum Mb of significant SNPs in area (FDR<0.05)	Maximum Mb of significant SNPs in area (FDR<0.05)	Number of significant loci in area	minimum unadjusted p-value in area	minimum FDR in area	Overlap with deQTL	Overlap with HAP3 _{ve} QTL	Overlap with LAP3 _{ve} QTL	Overlap with bQTL
hap. _{ve} QTL	8	4	rs13478048	149.684	139.684	159.684	1	0.0023	0.0417	4:144.37 - 165.38 (generation 6)		4:134.56 - 165.38 (generation 6)	4:52.01 - 202.78 (Belknap and Atkins 2001)
hap. _{ve} QTL	8	6	rs6199416	77.070	67.070	87.070	1	0.0005	0.0148	6:82.57 - 108.03 (generation 9)			
hap. _{ve} QTL	8	7	rs13479374	91.031	71.492	155.329	17	<0.0001	<0.0001	7:116.33 - 136.33 (generation 6) 7:85.16 - 131.84 (generation 13)			7:114.4 - 136.3 (Rodriguez et al 1995)
hap. _{ve} QTL	8	9	rs3654196	79.991	67.217	89.991	2	0.0003	0.0109				9:0 - 113.49 (Belknap and Atkins 2001) 9:68.52 - 70.67 (Bice et al 2011)
hap. _{ve} QTL	8	11	rs3659787	4.409	0.000	57.931	13	<0.0001	<0.0001	11:0 - 26.85 (generation 13)			
hap. _{ve} QTL	8	14	rs13482388	116.961	104.013	126.961	2	0.0011	0.0251				
hap. _{ve} QTL	8	17	rs3657117	69.399	59.149	79.399	2	0.0003	0.0109				
hap. _{ve} QTL	8	19	rs13483549	18.231	5.844	48.910	4	0.0013	0.0283				
hap. _{ve} QTL	9	2	rs6411422	128.199	118.199	138.199	1	0.0012	0.0392				2:3.45 - 146.16 (Belknap and Atkins 2001)
hap. _{ve} QTL	9	2	rs3143843	169.778	159.778	179.778	1	0.0001	0.0065				
hap. _{ve} QTL	9	3	rs13477011	21.266	11.266	31.266	1	0.0009	0.0315				3:0 - 224.84 (Belknap and Atkins 2001)
hap. _{ve} QTL	9	3	rs3674810	67.947	51.270	99.347	7	<0.0001	<0.0001				3:0 - 224.84 (Belknap and Atkins 2001)
hap. _{ve} QTL	9	3	rs3670168	127.995	117.995	137.995	1	0.0016	0.0490	3:99.4 - 151.7 (generation 6)		3:135.1 - 155.1 (generation 6)	3:0 - 224.84 (Belknap and Atkins 2001) 3:128.52 - 129.96 (Bice et al 2011) 3:137.82 - 138 (Bice et al 2011)
hap. _{ve} QTL	9	4	CEL-4_8632642	87.698	77.698	118.880	5	<0.0001	<0.0001				4:52.01 - 202.78 (Belknap and Atkins 2001)

Table S5. Differential expression and differential variance eQTL for HAP3/LAP3 mice.

Type of QTL Derived from HAP3/LAP3	Generation DE/DV established	Chromosome	Locus with minimum p-value in region	Mb location of minimum p-value	Minimum Mb of significant SNPs in area (FDR<0.05)	Maximum Mb of significant SNPs in area (FDR<0.05)	Number of significant loci in area	minimum unadjusted p-value in area	minimum FDR in area	Overlap with deQTL	Overlap with HAP3 <i>rv</i> eQTL	Overlap with LAP3 <i>rv</i> eQTL	Overlap with bQTL
			8										2001)
hap. <i>rv</i> eQTL	9	5	rs3716195	42.448	32.448	68.079	3	0.0003	0.0140				
hap. <i>rv</i> eQTL	9	6	rs6215575	38.079	28.079	48.079	1	0.0009	0.0315				
hap. <i>rv</i> eQTL	9	8	rs13479914	93.350	83.172	115.278	4	<0.0001	<0.0001				
hap. <i>rv</i> eQTL	9	14	rs6265743	120.111	110.111	134.508	3	<0.0001	<0.0001				
hap. <i>rv</i> eQTL	9	16	rs4221305	96.944	86.944	106.944	1	0.0005	0.0196				
hap. <i>rv</i> eQTL	9	17	rs13482947	31.770	21.770	41.770	1	0.0003	0.0140				
hap. <i>rv</i> eQTL	9	19	rs13483589	30.056	20.056	42.962	3	<0.0001	<0.0001				
lap. <i>rv</i> eQTL	6	1	rs13459182	43.799	33.799	53.799	1	0.0009	0.0441		1:3.37 - 35.63 (generation 8)		
lap. <i>rv</i> eQTL	6	3	rs3688244	145.095	135.095	155.095	1	<0.0001	<0.0001	3:99.4 - 151.7 (generation 6)	3:118 - 138 (generation 9)		3:0 - 224.84 (Belknap and Atkins 2001) 3:137.82 - 138 (Bice et al 2011) 3:145.36 - 145.56 (Bice et al 2011)
lap. <i>rv</i> eQTL	6	4	rs4224919	144.563	134.563	165.385	10	<0.0001	<0.0001	4:144.37 - 165.38 (generation 6)	4:139.68 - 159.68 (generation 8)		4:52.01 - 202.78 (Belknap and Atkins 2001)
lap. <i>rv</i> eQTL	6	10	CEL-10_14430696	14.293	0.000	29.804	5	<0.0001	<0.0001		10:0 - 19.33 (generation 6)		
lap. <i>rv</i> eQTL	6	10	rs13480625	64.173	54.173	74.173	1	0.0002	0.0109				
lap. <i>rv</i> eQTL	6	X	rs13484030	135.887	123.125	145.887	2	0.0001	0.0070				