Requirement of RIZ1 for cancer prevention by methyl-balanced diet

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Abstract

The typical Western diet is not balanced in methyl nutrients that regulate the level of the methyl donor S-adenosylmethionine (SAM) and its derivative metabolite S-adenosylhomocysteine (SAH), which in turn may control the activity of certain methyltransferases. Feeding rodents with amino acid defined and methyl-imbalanced diet decreases hepatic SAM and causes liver cancers. RIZ1 (PRDM2 or KMT8) is a tumor suppressor and functions in transcriptional repression by methylating histone H3 lysine 9. Here we show that a methyl-balanced diet conferred additional survival benefits compared to a tumor-inducing methyl-imbalanced diet only in mice with wild type RIZ1 but not in mice deficient in RIZ1. While absence of RIZ1 was tumorigenic in mice fed the balanced diet, its presence did not prevent tumor formation in mice fed the imbalanced diet. Unlike most of its related enzymes, RIZ1 was upregulated by methyl-balanced diet. Methyl-balanced diet did not fully repress oncogenes such as c-Jun in the absence of RIZ1. The data identify RIZ1 as a critical target of methyl-balanced diet in cancer prevention. The molecular understanding of dietary carcinogenesis may help people make informed choices on diet, which may greatly reduce the incidence of cancer.

Introduction:

The typical Western diet is linked to a third of all cancer deaths in the United States (1). The diet is rich in meat and low in vegetables and fruits. It is not balanced in methyl nutrients or low in folic acid. Dietary nutrients, and their metabolic intermediates and products, directly influence the activity of many cellular enzymes. One class of such enzymes is S-adenosylmethionine (SAM)-dependent methyltransferases, a broad group of enzymes that have one property in common, the use of SAM as methyl group donor. The cellular level of SAM depends on dietary intake of methyl group donors, such as methionine, folic acid, vitamin B6, B12, and choline. Some methylation reactions are inhibited by low level SAM or high level of the product inhibitor S-adenosylhomocysteine (SAH). Methyl imbalanced diet that is low in folic acid, methionine, or choline is known to lower SAM level and SAM/SAH ratio.

Feeding rodents with amino acid defined and methyl-imbalanced diet decreases hepatic SAM and causes liver cancers (2-4). The molecular mechanisms underlying the relationship between diet and cancer remain poorly understood. We have previously proposed that methyl-balanced diet prevents cancer by activating the histone lysine methyltransferase (KMT) class tumor suppressors such as RIZ1 (PRDM2 or KMT8) (5). The RIZ1 tumor suppressor functions in transcriptional repression by methylating histone H3 lysine 9 (6-8). Here, we determined whether RIZ1 may be a critical target of methyl balanced diet in cancer prevention.

Materials and Methods:

Animals, diets, and tissues. RIZ1 knockout mice in 129Sv/C57Bl6 background were crossed to 129Sv mice for 8 generations to produce RIZ1 knockout mice in 99.625%

129Sv background. These RIZ1-/- mice were then crossed with p53+/- 129Sv mice (from Jackson Laboratory) to generate RIZ1+/-p53+/- mouse in 129Sv background. Animals of the following genotypes were maintained for experimental use: RIZ1-/-p53+/- and RIZ1+/+p53+/-. The introduction of p53 heterozygous mutation was intended to shorten the latency of tumor development in the RIZ1 knockout mice (6). Male animals of each genotype were randomized into two groups of ~30 each. Starting at about 4 weeks of age, all animals were fed with a methyl-balanced and amino acid-defined diet or diet 1. After on this diet for one week, one group of animals continued to stay on diet 1 for the remaining period of the experiment. The other group were fed with methionine and choline deficient diet or diet 2. Diets were stored at 4 ^{0}C and given ad libitum with biweekly replacement. Animal growth was followed by monthly body weight measurement for upto 15 months. No significant difference in body weight was noted for different genotypes. Animals on diet 2 showed reduced (15% less at 15 months of age) body weight compared to animals on diet 1. This slight effect of diet 2 on body weight was similar to what others have found (2). Kaplan-Meyer survival curves were plotted using the Prism statistics program (GraphPad software). The liver tissues were fixed for histological analyses or snap frozen in liquid nitrogen and stored at -80 ^{0}C until used for biochemical analyses. Tissues fixed in 10% formalin were routinely processed for paraffin embedding, sectioned, and stained with hematoxylin and eosin.

Western blotting. Tissues were homoginized in RIPA buffer (150 mM NaCl, 1% Nonidet P-40, 0.25% Na-deoxycholate, 1mM EDTA, 50 mM Tris-HCl, pH 7.4, plus proteinase inhibitors). The whole lysates were then mixed with SDS gel loading buffer followed by SDS gel fractionation and western blotting. RIZ antibody was rabbit serum KG7.1S against RIZ1 aa 245-573 that reacts with both RIZ1 and RIZ2, as described previously (available from Abcam ab3790) (9). For western blot against RIZ1 but not

RIZ2, we used the abcam RIZ1 antibody ab9710. Antibodies for methylated histones were from Abcam and Upstate.

Quantitative RT-PCR. Total RNAs were extracted from tissues using the MagNa Lyser Green Beads (Roche) and the RNAmini kit (Qiagen). Quantitative RT-PCR analyses (SYBR green) were performed using the Mx3000P QPCR system of Stratagene. All gene specific primers were confirmed to give a single band of expected size. Cyclophilin A (PPIA) gene served as a control for RNA amount. This gene was not regulated by diet or RIZ1 knockout as indicated by microarray analysis.

DNA microarray analysis. cDNAs synthesized from total RNAs were hybridized with Sentrix Mouse-6 Expression BeadChip from Illumina containing 48,000 gene arrays. Data were obtained from replicate biological samples. Data normalization was performed using cubic spline normalization.

ChIP analysis. Rabbit antibody specific for RIZ1 but not RIZ2 from Abcam (ab9710) was used for ChIP analysis of RIZ1 binding to target genes. Antibodies for methylationed histones were from Abcam (ab9045 for H3K9me1, ab8898 for H3K9me3, ab9051 for H4K20me1) and Upstate (07-212 for H3K9me2). Liver tissues (~30 mg per antibody immunoprecipitation) were chopped to pieces using razor blades and cross linked in 1% formaldehyde at room temperature for 15 min. Chromatin was fragmented to an average size of 700 bp using a Misonix XL2020 sonicator. The ChIP assay kit from Upstate was used. For PCR, we used the following primer pairs: 5'-AAATCTCTGGTTTCCAGGTACAGC-3' (-801 to - 777) and 5'-GAGAAAGGGCTGAATGATCTGAGT-3' (-595 to -571) for c-Jun proximal promoter region, and 5'-GTGTGGGGGTAGAGGAGTGA-3' (-4337 to -4317) and 5'-

AGTGTCACTGGACCCTCACC -3’ (-4128 to -4108) for c-Jun distal region. For PCR of Elovl3 gene promoter, we used the primer pairs 5’-CCCCATTTTTCTCTCCAACA-3’ (-768 to -748) and 5’-CCAAGCTGGACCATAAGGAA-3’ (-578 to -558) for the Elovl3 promoter region, and 5’-CCAGGCTGTCCTGAAACTAATTCT-3’ (-8325 to -8301) and 5’-CTGTAGACCAGGTGACTGCAAACT-3’ (-8132 to -8108) for the Elovl3 distal region.

DNA methylation analysis. Genomic DNAs were extracted from tissues using standard procedures. Analysis of methylation in CpG rich regions by *Not1-Mse1* MS-AFLP method was as described previously (10). Genomic methyl-cytosine content was assayed by the methylation enzyme Sss1 method (11).

Results:

We compared RIZ1 mutant and wild type mice on a methyl-balanced diet (diet 1), versus an imbalanced diet lacking methionine and choline (diet 2). The methyl-imbalanced diet 2 (see Supplementary Table 1) is well known to lower hepatic SAM and cause liver cancers in rodents (2-4). Thus, this methyl-imbalanced diet caused liver tumors and decreased survival compared with the methyl-balanced diet (Figure 1A). In contrast, in the absence of wild type RIZ1, there was no difference in survival regardless of diet (Figure 1B). Therefore, while the balanced diet 1 conferred additional survival benefits compared to the imbalanced diet 2 in mice with wild type RIZ1, it failed to do so in mice deficient in RIZ1.

The data also shows that, consistent with previous work (6), RIZ1+/+ mice had lower mortality and tumor incidence than RIZ1-/- mice when fed methyl-balanced diet 1 (Figure 1C). However, when fed imbalanced diet 2, RIZ1+/+ mice showed similar mortality as RIZ1-/- mice (Figure 1D). Thus the tumor suppressor function of RIZ1 is dependent on a methyl-balanced diet. The similar survival rates of RIZ1-deficient and wild type animals on diet 2 (Figure 1D) also suggests that the capacity of diet 1 to confer additional survival benefits compared to diet 2 in RIZ1 wild type (Figure 1A) but not in RIZ1-deficient animals (Figure 1B) is not because of the trivial reason that the RIZ1-deficient animals may be too sick in general to respond to diet 1.

To determine the effects of diet on RIZ1, we examined RIZ1 gene expression in the liver target tissue using quantitative RT-PCR and Western blot analysis. RIZ1 mRNA level was downregulated 4.2 fold after treatment with diet 2 for 2 months (Supplementary Table 2). The downregulation was not evident at 1 month on diet 2 but became obvious at 2, 4, and 6 months (Supplementary Table 2). The downregulation of RIZ1 by the methyl-imbalanced diet was confirmed by western blot analysis (Figure 2). In contrast to RIZ1, the shorter RIZ2 protein that lacks the PR/SET domain (12) was not significantly affected by diet.

We also examined other methyltransferases and related enzymes by quantitative RT-PCR and DNA microarray analysis. A total of 25 histone methyltransferases were examined, including at least one enzyme specific for each of the amino acid residues that are known to be methylated. None of these enzymes, except RIZ1, was significantly downregulated (>2 fold) at 2 months of diet 2 treatment (Supplementary Table 2).

To further determine whether RIZ1 expression is sensitive to SAM levels, we used the MATA1 knockout mice model (13). These animals have lower (3 to 4 fold) hepatic SAM and also develop liver cancers. Quantitative RT-PCR analysis of animals at 4.5-5.5 months of age showed that RIZ1 expression in wild type livers (n =6) was 2.0 fold higher than in the MATA1 knockouts (n =5, P = 0.03, Student’s t test, 2 tailed), comparable to the fold reduction for the same aged wild type mice on diet 2 (Supplementary Table 2).

We next examined whether RIZ1 target genes were regulated by diet. DNA microarray analysis of livers of RIZ1 wild type animals at 2 months of diet treatment revealed a list of 1636 genes that were affected by diet by more than 2 fold (Supplementary Table 3). DNA microarray analysis of livers of RIZ1 knockout animals identified 97 putative RIZ1 target genes showing more than 2 fold difference between wild type and knockout (Supplementary Table 4). Of these, 29 were also present in the list of genes regulated by diet, indicating a significant enrichment of RIZ1 target genes in the list of diet-regulated genes (29/97 versus 1636/48000, $P < 0.0001$, Chi squared test, 2 tailed). The genes of interest that were upregulated by both RIZ1 knockout and methyl-imbalanced diet include c-Jun, c-Fos, and Ctgf. Some of these genes might play a direct role in liver cancers (i.e., c-Jun) (14). The effect of RIZ1 knockout or diet on the expression of these genes was confirmed by quantitative RT-PCR analysis (Table 1). The results suggest that downregulation of RIZ1 by diet 2 was associated with deregulation of RIZ1 target genes.

Since RIZ1 expression was not significantly altered by diet 2 at 1 month treatment (Supplementary Table 2), any expression changes of the target genes of RIZ1 at 1 month diet treatment may reflect changes in RIZ1 activity rather than in expression level. We selected seven RIZ1 target genes and determined their expression levels at either 1 month or 2 months diet treatment. As shown in Table 1, six of the seven genes were found upregulated by diet 2 at 1 month diet treatment. The data suggest that diet 2 caused deregulation of RIZ1 target genes before significantly decreasing RIZ1 expression levels.

We next used chromatin immunoprecipitation (ChIP) assay to examine changes in histone methylation on RIZ1 target genes as a result of decreased RIZ1 activity. We used a RIZ1-specific antibody ab9710 (Abcam) that does not react with RIZ2 (see Supplementary Figure 1 for a Western blot of RIZ1 by this antibody). As shown in

Figure 3A, the c-Jun proximal promoter was bound by RIZ1 and showed higher levels of H3 lysine 9 monomethylation in RIZ1 wild type versus knockout livers. RIZ1 did not bind to the distal region of the c-Jun promoter or the promoter of Elovl3 gene that was not repressed by RIZ1. At 1 month diet 2 treatment, H3K9me1 of c-Jun promoter was decreased even though RIZ1 binding was not changed, suggesting again that RIZ1 activity was decreased even when RIZ1 expression was at normal levels (Figure 3).

We also examined overall DNA methylation changes in response to methyl-imbalanced diet in DNA from livers of animals at 15 months of treatment (Supplementary Figures 2 and 3). While we found that diet 2 decreased overall DNA methylation, we did not find changes in DNA methylation (either hyper or hypo methylation) in individual random CpG rich regions using the technique of *Not1-Mse1* MS-AFLP (methylation sensitive amplified fragment length polymorphism) (10). By Western blot analysis, we did not find significant changes (>2 fold) in methylation of H3K9me1, H3K9me2, H3K9me3, H4K20me1, and H4K20me2 in the liver of animals that were on diet 2 for six months (data not shown).

Discussion:

Since only RIZ1 and 4 small molecule methyltransferases (GNMT, GAMT, NNMT, and TEMT) were found downregulated by diet 2 in a non-biased screening using both DNA microarray and RT-PCR methods (see Supplementary Table 2), we examined whether these 5 enzymes shared some common properties that could explain their sensitivity to diet. We found from the literature Km values for SAM for 3 of the 4 small molecule methyltransferases and all three turned out to have high Km value (> 49 μM) (see Supplementary Table 5). For the large number of methyltransferases that were not regulated by diet, we identified Km values for 7 of them and all 7 have Km values lower than 10 μM (see Supplementary Table 5). Thus, there is a significant association between high Km for SAM and downregulation by diet 2 (P = 0.0083, Fisher's exact test, 2 tailed).

Hepatic SAM concentration is ~60 μM and methyl-imbalanced diet typically causes a 1.5 to 3 fold drop in SAM levels (3, 15), which would be still high enough to allow near maximum activity for most methyltransferases with low Km for SAM but would significantly inhibit those enzymes with high Km values. The preferential downregulation by diet 2 of the methyltransferases with high Km for SAM may reflect a feedback inhibition on their own gene expression by unliganded or unused enzymes. The canonical SET domain shared by most KMTs has low Km for SAM (16). But RIZ1 may be an exception since its SET domain is different from others (17, 18).

Numerous effects of methyl-imbalanced diet, such as fat accumulation, protein kinase C activation, abnormal cell turnover, oxidative stress, low SAM/SAH ratio, DNA hypomethylation, and uracil incorporation into DNA or mutation, are prevented by a methyl-balanced diet. In addition, a methyl-imbalanced diet affects the expression of numerous genes as shown here. Our observation that deficiency of a single gene may neutralize the cancer preventive benefit of a methyl-balanced diet shows that at least one of the numerous effects of such diet may play a rate-limiting role in the cancer prevention process.

From all these observations it can be postulated that the molecular pathway of carcinogenesis by methyl-imbalanced diet may be the following: a methyl-imbalanced diet — chronic low SAM/SAH ratio in most cells of a diet-responsive target tissue — inhibition and downregulation of RIZ1 in most cells of the target tissue — upregulation of prosurvival and progrowth oncogenes such as c-Jun in most cells of the target tissue — stochastic accumulative genetic and epigenetic changes in a single cell — clonal proliferation of the single cell — cancer. In this model, inactivation of RIZ1 and upregulation of some oncogenes such as c-Jun in most cells of a diet-responsive tissue may not be sufficient to cause clonal proliferation but may allow a large pool of less than fully normal cells to be more prone to clonal proliferation in response to stochastic strong oncogenic mutations in a single cell. In contrast, fully normal cells may undergo senescence or cell death in response to oncogenic mutations (19).

The key to cancer prevention has been commonly thought to be the prevention of mutations. But the results here show for the first time that cancer prevention by at least some environmental factors is achieved by preventing the deregulation of epigenetic enzymes.

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References:

1. Doll R, Peto R. The causes of cancer: quantitative estimates of avoidable risks of cancer in the United States today. J Natl Cancer Inst 1981;66(6):1191-308.
2. Mikol YB, Hoover KL, Creasia D, Poirier LA. Hepatocarcinogenesis in rats fed methyl-deficient, amino acid-defined diets. Carcinogenesis 1983;4(12):1619-29.
3. Shivapurkar N, Poirier LA. Tissue levels of S-adenosylmethionine and S-adenosylhomocysteine in rats fed methyl-deficient, amino acid-defined diets for one to five weeks. Carcinogenesis 1983;4(8):1051-7.
4. Shivapurkar N, Wilson MJ, Hoover KL, Mikol YB, Creasia D, Poirier LA. Hepatic DNA methylation and liver tumor formation in male C3H mice fed methionine- and choline-deficient diets. J Natl Cancer Inst 1986;77(1):213-7.
5. Huang S. Histone methyltransferases, diet nutrients, and tumor suppressors. Nat Rev Cancer 2002;2:469-76.
6. Steele-Perkins G, Fang W, Yang XH, et al. Tumor formation and inactivation of RIZ1, an Rb-binding member of a nuclear protein-methyltransferase superfamily. Genes Dev 2001;15:2250-62.
7. Kim K-C, Geng L, Huang S. Inactivation of a histone methyltransferase by mutations in human cancers. Cancer Res 2003;63:7619-23.
8. Garcia-Bassets I, Kwon YS, Telese F, et al. Histone methylation-dependent mechanisms impose ligand dependency for gene activation by nuclear receptors. Cell 2007;128(3):505-18.

9. Buyse IM, Shao G, Huang S. The retinoblastoma protein binds to RIZ, a zinc finger protein that shares an epitope with the adenovirus E1A protein. Proc Natl Acad Sci USA 1995;92:4467-71.

10. Yamamoto F, Yamamoto M, Soto JL, et al. NotI-MseI methylation-sensitive amplified fragment length polymorphism for DNA methylation analysis of human cancers. Electrophoresis 2001;22(10):1946-56.

11. De Smet C, De Backer O, Faraoni I, Lurquin C, Brasseur F, Boon T. The activation of human gene MAGE-1 in tumor cells is correlated with genome-wide demethylation. Proc Natl Acad Sci U S A 1996;93(14):7149-53.

12. Liu L, Shao G, Steele-Perkins G, Huang S. The retinoblastoma interacting zinc finger gene RIZ produces a PR domain lacking product through an internal promoter. J Biol Chem 1997;272:2984-91.

13. Lu SC, Alvarez L, Huang ZZ, et al. Methionine adenosyltransferase 1A knockout mice are predisposed to liver injury and exhibit increased expression of genes involved in proliferation. Proc Natl Acad Sci U S A 2001;98(10):5560-5.

14. Eferl R, Ricci R, Kenner L, et al. Liver tumor development. c-Jun antagonizes the proapoptotic activity of p53. Cell 2003;112(2):181-92.

15. Wilson MJ, Shivapurkar N, Poirier LA. Hypomethylation of hepatic nuclear DNA in rats fed with a carcinogenic methyl-deficient diet. Biochem J 1984;218(3):987-90.

16. Patnaik D, Chin HG, Esteve PO, Benner J, Jacobsen SE, Pradhan S. Substrate specificity and kinetic mechanism of mammalian G9a histone H3 methyltransferase. J Biol Chem 2004;279(51):53248-58.

17. Huang S, Shao G, Liu L. The PR domain of the Rb-binding zinc finger protein RIZ1 is a protein binding interface and is related to the SET domain functioning in chromatin-mediated gene expression. J Biol Chem 1998;273.:15933-40.

18. Briknarova K, Zhou X, Satterthwait A, Hoyt DW, Ely KR, Huang S. Structural studies of the SET domain from RIZ1 tumor suppressor. Biochem Biophys Res Commun 2008;366(3):807-13.

19. Braig M, Lee S, Loddenkemper C, et al. Oncogene-induced senescence as an initial barrier in lymphoma development. Nature 2005;436(7051):660-5.

Table 1. Quantitative RT-PCR analysis of genes that were upregulated by RIZ1 deficiency or by diet 2 treatment. Fold changes in liver RNA expression of 7 putative RIZ1 target genes in RIZ1 knockout versus wild type animals were shown. Also shown are fold changes in liver RNA expression of 7 putative RIZ1-target genes in RIZ1 wild type animals on diet 2 versus diet 1 after either 1 month or 2 months of diet treatment. Data represent means of at least 3 animals per subgroup. $P < 0.05$ (Student's t-test, 2 tailed) for all data set except Alas1 at 1 month diet treatment.

	KO *vs.* WT	Diet 2 *vs.* Diet 1	
		2 month	1 month
Abcc4	2.1	13.1	10.2
Alas1	4.0	2.3	1.3
Ctgf	2.2	2.4	2.3
Fos	2.4	5.0	4.7
Gdf15	2.3	2.7	3.7
Jun	2.0	8.0	2.6
Mthfd1l	1.6	5.1	3.0

Figure Legends:

Figure 1. Survival of RIZ1 wild type and mutant animals on diet 1 versus diet 2. A. The viability of RIZ1 wild type animals on diet 1 versus diet 2. **B.** The viability of RIZ1 mutant animals on diet 1 versus diet 2. **C.** The viability of RIZ1 wild type and mutant animals on diet 1. **D.** The viability of RIZ1 wild type and mutant animals on diet 2. Most of the dead or moribund animals that were suitable for autopsy analysis were found to have tumors. The graph was drawn with the Prism statistics software program (GraphPad Software) based on the Kaplan-Meyer theory. *P* values were calculated by Fisher's exact test (2 tailed) using the survival rate at ages 20 to 22 months.

Figure 2. Regulation of RIZ1 protein expression by diet. A. Whole cell extracts of liver from animals on diet 1 and diet 2 for two months were analyzed by Western blot analysis using an antibody that reacts with both RIZ1 and RIZ2 proteins. Western blot using beta-actin antibody served as loading control. **B.** Quantification of protein levels by densitometry analysis. Data are the means $\pm$ SD of 4 animals per subgroup. **P* = 0.012 (Student's t-test, 2 tailed).

Figure 3. Regulation of histone methylation on RIZ1 target genes. A. Soluble chromatin was prepared from livers of RIZ1 wild type and knockout animals. Immunoprecipitation was performed using the indicated antibodies. DNA was amplified using primer sets that cover the proximal or the distal promoter regions of c-Jun and Elovl3 gene. **B.** Soluble chromatin was prepared from livers of wild type animals on either diet 1 or diet 2 for 1 month. Immunoprecipitation was performed using the indicated antibodies. DNA was amplified using primer sets that cover the proximal or the

distal promoter regions of c-Jun and Elovl3 gene. One representative data set is shown out of four experiments performed.

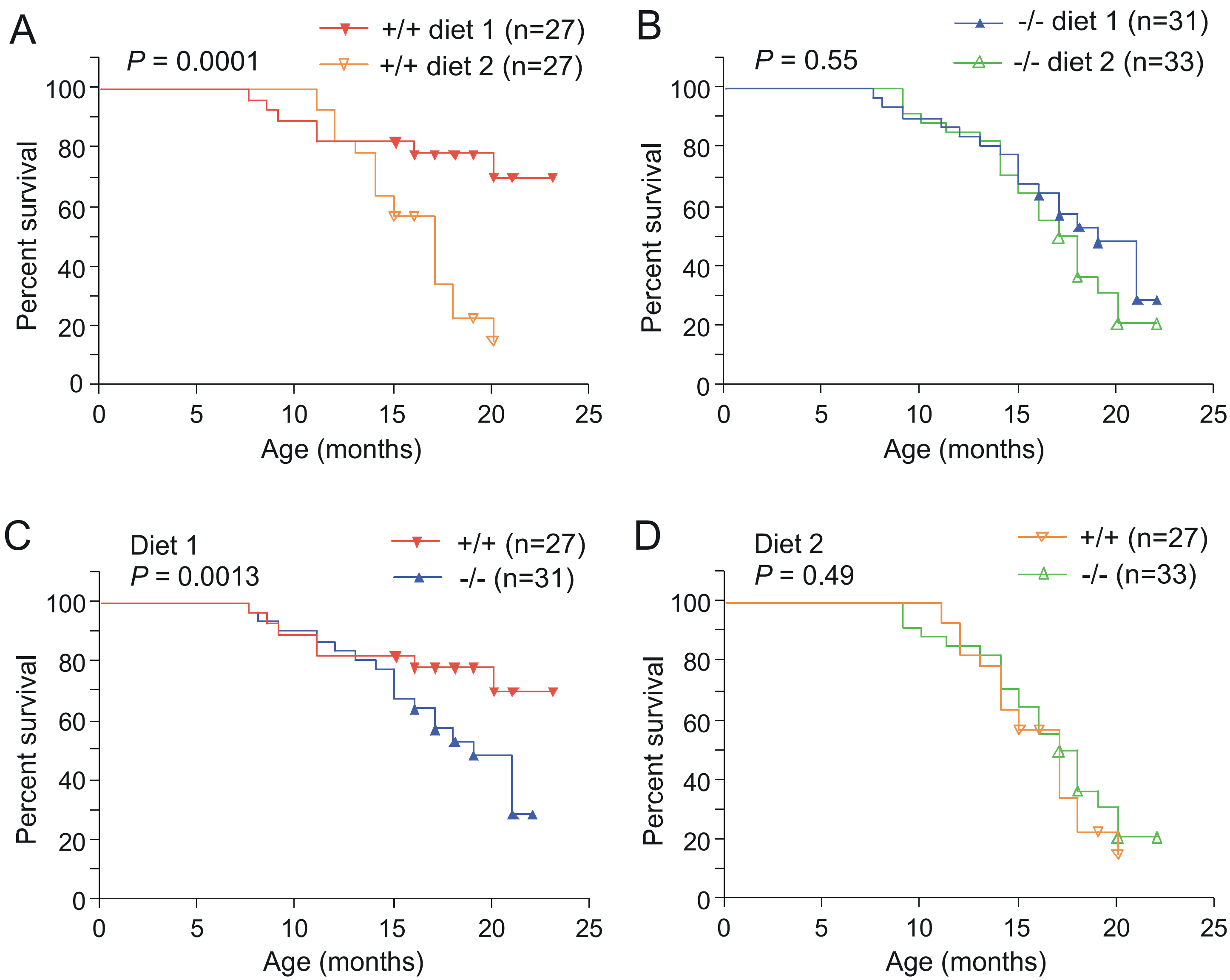

A
P = 0.0001
+/+ diet 1 (n=27)
+/+ diet 2 (n=27)
Percent survival
Age (months)
B
P = 0.55
-/- diet 1 (n=31)
-/- diet 2 (n=33)
Percent survival
Age (months)
C
Diet 1
P = 0.0013
+/+ (n=27)
-/- (n=31)
Percent survival
Age (months)
D
Diet 2
P = 0.49
+/+ (n=27)
-/- (n=33)
Percent survival
Age (months)

Figure 1

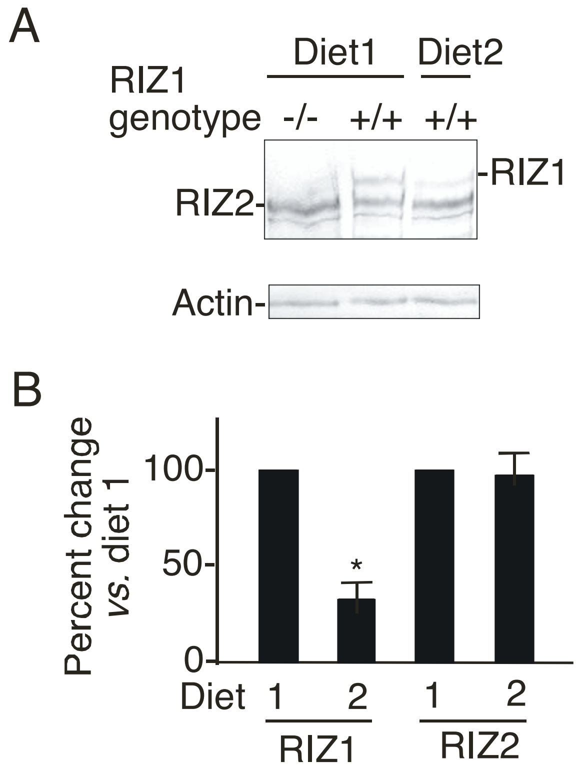

A
Diet1
Diet2
RIZ1 genotype
-/-
+/+
+/+
RIZ1
RIZ2
Actin
B
Percent change vs. diet 1
100
50
0
*
Diet
1
2
1
2
RIZ1
RIZ2

Figure 2

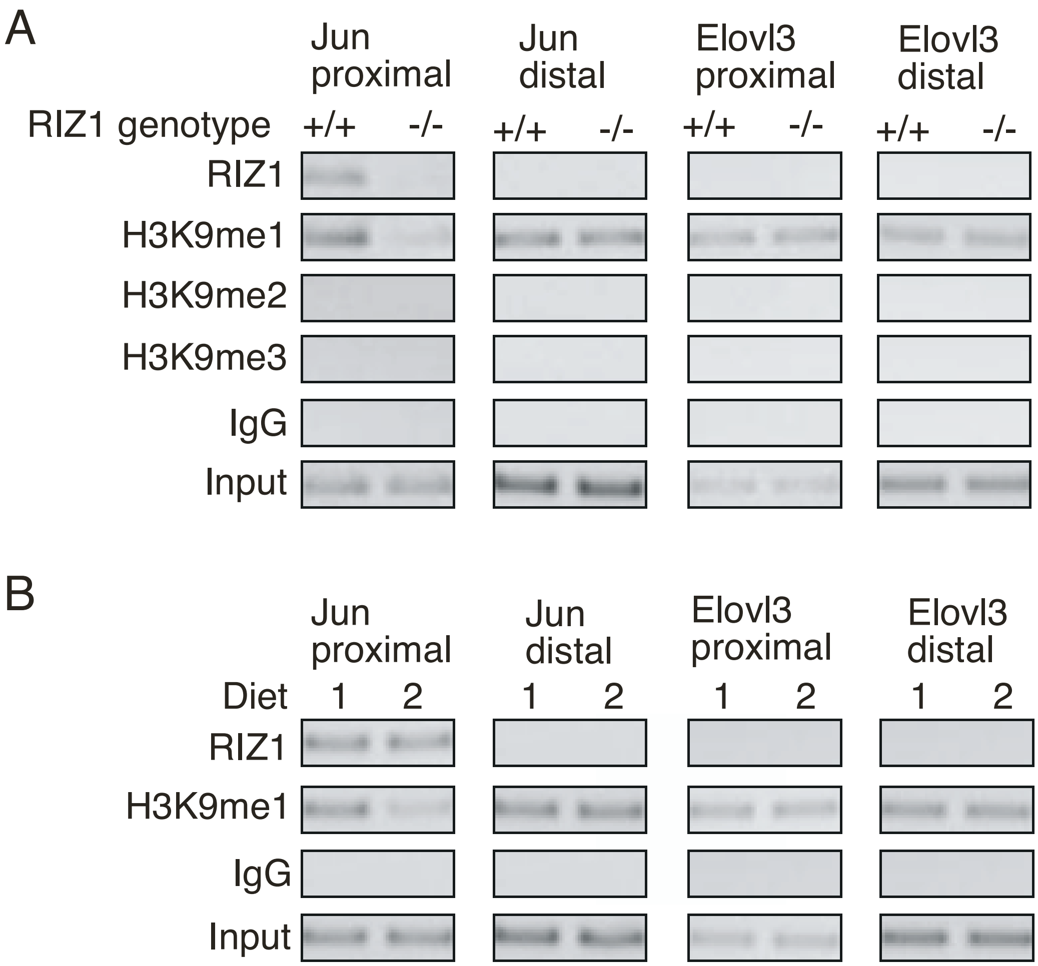

A
Jun proximal
Jun distal
Elovl3 proximal
Elovl3 distal
RIZ1 genotype
+/+
-/-
RIZ1
H3K9me1
H3K9me2
H3K9me3
IgG
Input
B
Jun proximal
Jun distal
Elovl3 proximal
Elovl3 distal
Diet
1
2
RIZ1
H3K9me1
IgG
Input

Figure 3

Supplementary Data Table of contents:

Supplementary data:

Supplementary Table 1. Composition of the amino acid-defined and methyl-balanced basal diet (Teklad Product No. TD 99366). This is referred as Diet 1.

	g/Kg
L-Alanine	3.5
L-Arginine HCl	12.1
L-Asparag	6.0
L-Aspartic Acid	3.5
L-Cystine	3.5
L-Glutamic Acid	40.0
Glycine	23. 3
L-Histidine HCl-H2O	4.5
L-Isoleucine	8.2
L-Leucine	11.1
L-Lysine HCl	18.0
L-Methionine	8.2
L-Phenylalanine	7.5
L-Proline	3.5
L-Serine	3.5
L-Threonine	8.2
L-Tryptophan	1.8
L-Tyrosine	5.0
L-Valine	8.2
Sucrose	351.68
Corn Starch	150.0
Maltodextrin	150.0
Soybean Oil	80.0
Cellulose (fiber)	30.0
Mineral Mix, AIN-93M-MX (TD 94049)	35.0
Calcium Phosphate, monobasic	8.2
Vitamin Mix, AIN-93-VX (TD 94047)	13.0
Choline Bitartrate	2.5
TBHQ (antioxidant)	0.02

The methyl-imbalanced diet or diet 2 formulation ((Teklad Product No. TD 01513) is the same as diet 1 except that it contains 9.0 g/Kg DL-Homocystine and lacks methionine and choline bitartrate.

Supplementary Table 2. Quantitative RT-PCR and microarray analysis of some histone methyltransferases and related enzymes. Wild type male animals were treated with diet 1 or diet 2 (starting from 3-4 weeks of age) for 1, 2, 4, and 6 months before RNA extraction from livers. Levels of 25 histone methyltransferases and 8 other related enzymes were determined by either quantitative RT-PCR or microarray or both, and the ratio (fold change) Diet 1 versus Diet 2 calculated. Data from quantitative RT-PCR represent means of at least 3 animals per subgroup. *$P < 0.05$ Diet 1 *vs.* Diet 2 (Student's t-test, 2 tailed). Histone methyltransferases that are not listed here did not show significant expression in the liver as revealed by DNA microarray analysis. Data from microarray analysis represent means of 2 animals per subgroup. DNA microarray analysis revealed downregulation by diet 2 of four small molecule methyltransferases, GNMT, GAMT, NNMT, and TEMT, which were subsequently confirmed by quantitative RT-PCR.

Supplementary Table 2.

	Diet 1 *vs.* Diet 2			
Months on diet	**1m**	**2m**	**4m**	**6m**
Histone methyltransferases				
RIZ1	1.1	4.2*	2.3*	3.1*
Prdm3		1.0		
Prdm9		1.6	1.1	
Carm1		1.5	0.9	
Dot1		1.5	1.0	
Ehmt		1.5	1.2	
Eset		1.4	1.1	
Smyd2		1.2	1.1	
Suv39H1		1.4	0.9	1.1
PR-SET7		1.1	0.8	0.7
Prdm1-alpha	0.4*	0.2*	0.2*	
Ezh1		0.8	0.3*	
Ezh2		0.6	0.6	
Eed (array)		1.0		
Suv4-20H2 (array)		1.3	1.0	
Mll1 (array)		0.8		
Ash1l (array)		1.0		
Smyd1 (array)		0.9		
SET7/9 (array)		0.6		
PRDM4(array)		1.1		
G9a (array)		1.0		
G9a		0.9		
Prmt1 (array)		1.0		
Prmt1		0.9		
Prmt3 (array)		0.7		
Prmt5 (array)		0.7		
Prmt7 (array)		0.9		
Histone demethylases				
Jmjd2a		1.1		
Lsd1		1.3		
DNA methyltransferases				
DNMT1		1.2		
DNMT3A		0.9		
Small molecule methyltransferases				
GNMT(array)		3.0		
GNMT	2.0	4.6*		
TEMT(array)		3.0		
TEMT	5.0*	8.2*		
GAMT(array)		1.5		
GAMT		2.3*		
NNMT (array)		9.5		
NNMT		4.1*		

Supplementary Table 3. Genes regulated by diet as revealed by DNA microarray analysis. Wild type mice were fed with either diet 1 or diet 2 for two months before their livers were collected for RNA extraction. Data represent means of 2 animals per subgroup. Only genes showing more than 2 fold changes are listed.

Supplementary Table 3

Symbol	Accession	Diet 2	Diet 1	Diet 2/Diet 1
Nupr1	NM_019738.1	442.3	1.3	340.231
Mmp13	NM_008607.1	433.2	1.3	333.231
Ly6d	NM_010742.1	2525.7	12.3	205.341
D17H6S56E-5	NM_033075.2	809.5	4	202.375
Cdc20	NM_023223.1	291	1.5	194.000
9530018I07Rik		56.8	0.3	189.333
Clecsf12	NM_020008.1	178.2	1.1	162.000
Gsta1	NM_008181.1	5210.9	38.1	136.769
Ccl4	NM_013652	308.8	2.3	134.261
Cdc2a	NM_007659.2	80.3	0.6	133.833
Ccnb1	NM_172301.2	133.3	1.5	88.867
Ubd	NM_023137.2	967.2	11	87.927
Fcgr1	NM_010186.2	58.7	0.7	83.857
Ddit4l	NM_030143.2	53.5	0.7	76.429
Myo1f	NM_053214.1	349.4	4.6	75.957
Csprs	NM_033616.2	99.6	1.5	66.400
Cidec	NM_178373.2	423.8	6.8	62.324
Asns	NM_012055.1	1098.3	18.2	60.346
Cd14	NM_009841.2	507.6	8.5	59.718
Guca2a	NM_008190.1	85.6	1.5	57.067
Bcl2a1a	NM_009742.2	461.1	8.1	56.926
Bcl2a1d	NM_007536	809.6	15.1	53.616
Cib3	XM_356089.1	4150.4	78.6	52.804
Gpr65	NM_008152.1	105.4	2	52.700
Mrc2	NM_008626	68.2	1.3	52.462
D17H6S56E-5	NM_033075.2	2376.7	45.9	51.780
LOC327957	XM_282993.1	96.8	1.9	50.947
Gpnmb	NM_053110	280.6	6	46.767
Areg	NM_009704.2	114.9	2.5	45.960
Osbpl3	NM_027881.1	878.8	19.9	44.161
Plcg2	NM_172285.1	132.4	3.3	40.121
Cd68	NM_009853.1	376.4	10.8	34.852
BC064033	NM_173375	93	2.8	33.214
Blnk	NM_008528.3	377.1	11.4	33.079
BC024955	NM_201352.1	52.9	1.6	33.063
Uap1l1	XM_130172.4	1653.6	53.4	30.966
Lcn2	NM_008491.1	9281.5	302.5	30.683
DXImx50e	NM_207202.1	314.7	10.3	30.553
Prc1	NM_145150.1	416.3	13.7	30.387
Cdkn1a	NM_007669.2	550.6	19	28.979
Slpi	NM_011414.1	249	8.6	28.953
Gng2	NM_010315.2	110.2	3.9	28.256
Cd83	NM_009856.1	122.7	4.4	27.886
Cx3cr1	NM_009987.2	104.8	3.9	26.872
Lilrb4	NM_013532.1	168	6.4	26.250
Cdkn3	XM_354809.1	436.5	16.7	26.138
Ncf4	NM_008677.1	236.9	9.1	26.033
Cxcl14	NM_019568.1	211.4	8.4	25.167
C2ta	NM_007575.1	147.2	6	24.533

Rmcs1	NM_207105.1	4121.9	170.7	24.147
Serpine2	AK045954	73.8	3.3	22.364
Cln6	XM_134858.5	158.3	7.1	22.296
Bcl2a1b	NM_007534	993.2	44.6	22.269
Samsn1	NM_023380.1	72.3	3.3	21.909
Gstm3	NM_010359.1	3888.1	180.3	21.565
Mmp24	NM_010808	84	3.9	21.538
Calml4	NM_138304.1	704	32.9	21.398
Gstm3	NM_010359.1	15712.1	736	21.348
Cbr3	NM_173047.2	109.8	5.2	21.115
H2-Eb1	NM_010382.1	3120.6	148.3	21.042
LOC386456	XM_359279.1	83	4	20.750
Gp49a	AK089366	303.7	14.7	20.660
Gus-s	AK002832	64.5	3.2	20.156
Stmn1	NM_019641	269.6	13.5	19.970
		237.4	11.9	19.950
Fgf21	NM_020013.2	1827.8	92.5	19.760
Lgals3	NM_010705.1	4054.1	205.4	19.738
Pparg	NM_011146.1	89.7	4.6	19.500
B930041F14Rik	NM_178699	618	31.8	19.434
H2-Aa	NM_010378.2	5406.6	283.3	19.084
S3-12	NM_020568.1	800.8	42.2	18.976
Sprr1a	NM_009264.1	140.9	7.5	18.787
Plp2	NM_019755.2	87.9	4.7	18.702
Cxcl13	NM_018866.1	111.4	6	18.567
4930539E08Rik	NM_172450.1	75.9	4.1	18.512
Ear2	NM_007895	437.9	24.2	18.095
Rmcs1	NM_207105.1	6603.2	369.4	17.875
9930027N05Rik	NM_198405.1	142.5	8	17.813
Cd207	NM_144943.2	147.4	8.4	17.548
Igfbp1	NM_008341.2	326.2	19	17.168
Pik3cg	NM_020272	73.7	4.3	17.140
9630054F20Rik	NM_173784.3	53	3.1	17.097
Ii	BC003476	389	22.8	17.061
Abcc4	XM_139262.2	237.3	14.2	16.711
Lyzs	NM_017372.2	2359.3	142.1	16.603
Cyp4f16	NM_024442.1	59	3.6	16.389
BC051083	NM_181409.2	460.9	28.7	16.059
Capg	NM_007599	330.7	21	15.748
Jun	NM_010591.1	396.1	25.5	15.533
Thy1	NM_009382.2	52.2	3.4	15.353
Hist1h3i	NM_178207	55.2	3.6	15.333
Golph2	NM_027307.1	562	36.9	15.230
Ms4a6d	NM_026835.1	336	22.2	15.135
Tbxas1	NM_011539	87.6	5.9	14.847
E030040G24Rik	AK087259	174	11.8	14.746
Ear1	NM_007894	1546.6	105.5	14.660
9130019I15Rik	XM_356104	68	4.7	14.468
Cxcl4	NM_019932.1	186.9	13	14.377
Copeb	NM_011803	131.8	9.2	14.326
Cd44	AK045226	409	28.6	14.301
H2-DMb1	NM_010387.2	400.3	28.1	14.246
BC032204	NM_153795.1	65.9	4.7	14.021

LOC218617	XM_122636.2	261.5	18.7	13.984
Cdca2	NM_175384.3	70.1	5.2	13.481
BC018222	NM_144936.1	221.6	16.5	13.430
Cdkn1a	NM_007669.2	825.2	61.6	13.396
Ear2	NM_007895.2	2407.2	180.3	13.351
H2-Ab1	NM_010379.2	2769.4	208.7	13.270
Glipr2	NM_027450	77.8	5.9	13.186
Matn2	AK035102	53.6	4.1	13.073
S100a11	NM_016740	187.4	14.4	13.014
Hspb1	NM_013560.1	442.1	34	13.003
Slc15a3	NM_023044.1	75.3	5.8	12.983
Gsta2	NM_008182	8615.2	666.2	12.932
Ear10	NM_053112.1	1171.1	91	12.869
Ly86	NM_010745.1	281.9	22.2	12.698
Gsta2	NM_008182.1	12192.9	976.1	12.491
Arhgef16	XM_149562.4	57.1	4.6	12.413
Cxcl14	NM_019568	87.2	7.1	12.282
Pparg	NM_011146.1	650.5	53.4	12.182
Fpr-rs2	NM_008039.1	1027.6	85.1	12.075
Tes	NM_011570	299	25.4	11.772
H2-DMa	NM_010386	268.9	22.9	11.742
2310061N23Rik	NM_029803.1	2132.6	183.1	11.647
Anxa2	NM_007585.2	10072.4	872.1	11.550
Dusp8	NM_008748.1	103.4	9.1	11.363
Unc119	NM_011676.2	62.3	5.5	11.327
Lgals1	NM_008495.1	1183.5	105.1	11.261
2700004G04Rik		87.6	7.8	11.231
Stk6	NM_011497.2	67.9	6.1	11.131
Oas1g	NM_011852.2	246.3	22.2	11.095
Dpep2	NM_176913.3	75	6.8	11.029
Saa3	NM_011315	1013.5	92.9	10.910
Cd72	NM_007654.1	443.1	41.1	10.781
Mad2l1	NM_019499	101.1	9.4	10.755
Gsta2	NM_008182.1	7785.1	728.7	10.684
Gsta1	NM_008181.1	4099.2	390.4	10.500
Klra22	NM_053152.1	75.6	7.2	10.500
Sla	NM_009192	241.5	23.1	10.455
Ii	NM_010545.2	4085.8	395.3	10.336
Pilrb	NM_133209.1	92.7	9	10.300
Cd68	NM_009853	2007.4	197.6	10.159
Ncf2	NM_010877	866.1	86.9	9.967
Mt2	NM_008630.1	671.8	67.9	9.894
Tagln2	NM_178598.1	979.1	99.4	9.850
Il10ra	NM_008348.1	83.5	8.5	9.824
Niban	NM_022018	54	5.5	9.818
Il1b	NM_008361	183.1	19	9.637
Mas1	NM_008552.2	127.4	13.3	9.579
Pscdbp	NM_139200.2	295.5	30.9	9.563
E430004N04Rik	NM_178666.3	88.6	9.3	9.527
Ier3	NM_133662.1	160.6	17.1	9.392
Kif23	NM_024245	155.9	16.7	9.335
Fthfsdc1	NM_172308.2	238	25.6	9.297
Fos	NM_010234.2	134.8	14.5	9.297

Xcl1	NM_008510.1	76.1	8.2	9.280
Spink3	NM_009258.2	325.7	35.1	9.279
Lsp1	NM_019391.1	202.2	22.1	9.149
Mapre2	NM_153058.2	56.3	6.2	9.081
LOC226691	XM_129595.2	469.8	52.3	8.983
Oxct1	NM_024188.3	200.1	22.4	8.933
BC042423		74.1	8.3	8.928
Oas1g	NM_011852.2	814.7	92.5	8.808
Hist1h4a	NM_178192.1	103	11.7	8.803
Bex2	NM_009749	105.7	12.1	8.736
LOC240672	XM_140740.3	277.1	31.8	8.714
Rac2	NM_009008.2	194.4	22.6	8.602
LOC381276	XM_355218.1	75.5	9	8.389
Rgs10	NM_026418.1	207.3	25	8.292
Tlr2	NM_011905.2	759.3	92	8.253
Csf1r	NM_007779.1	113.4	13.9	8.158
		87.1	10.7	8.140
Psat1	XM_129211.2	79.7	9.8	8.133
Cklfsf7	NM_133978.1	84.4	10.4	8.115
Btk	NM_013482.1	102.8	12.7	8.094
Plekhh1	XM_126961.4	83	10.3	8.058
Ccl6	NM_009139.1	127.9	15.9	8.044
2210010C17Rik	XM_133228.2	122.9	15.4	7.981
AY078069	NM_172142.1	70.6	9	7.844
Fer1l3	XM_283556	484	62.1	7.794
Evl	NM_007965.2	160.2	20.6	7.777
S100a8	NM_013650.1	229.4	29.5	7.776
Gabrb3	NM_008071	127.2	16.4	7.756
Treh	NM_021481.1	783.1	101	7.753
Birc5	NM_009689.1	188.8	24.5	7.706
Abhd2	NM_018811.4	98.1	12.9	7.605
Cdca5	NM_026410.1	60.7	8	7.588
Npn3	NM_029688.2	727.5	97.1	7.492
Epb4.1l1	XM_487678	107.7	14.4	7.479
Ptpn9	NM_019651	142.2	19.1	7.445
Mogat1	NM_026713.1	313.4	42.1	7.444
Pla2g7	NM_013737.2	158.8	21.4	7.421
Nme5	NM_080637	54.8	7.5	7.307
Pdgfb	NM_011057.2	103.6	14.2	7.296
Coro1a	NM_009898.2	1051.4	144.5	7.276
Prom1	NM_008935.1	68.7	9.5	7.232
BC051083	NM_181409.2	121.3	16.8	7.220
Tgfb1	NM_011577.1	96.6	13.5	7.156
AI449441	NM_172453.1	128.4	18	7.133
2410004L22Rik	NM_029621.1	162.5	22.8	7.127
Cklfsf7	NM_133978.1	165.2	23.4	7.060
Ly6c	NM_010741	137.2	19.5	7.036
9230112O05Rik	NM_173347.2	82.3	11.7	7.034
Tlr13	NM_205820.1	139.6	19.9	7.015
Nusap1	NM_133851.1	124	17.7	7.006
Was	NM_009515.1	170.2	24.3	7.004
Ccnd1	NM_007631.1	1278.1	182.7	6.996
Icsbp1	NM_008320.2	287.3	41.1	6.990

Anxa5	NM_009673.1	6866.4	982.4	6.989
Fcrl3	NM_144559.1	1394	200.8	6.942
Cdca3	NM_013538.3	685.3	99.4	6.894
7330423F06Rik		90.5	13.2	6.856
Pscd4	NM_028195	2034	297.1	6.846
Hemp1	NM_153505.2	566.2	82.8	6.838
2610318C08Rik	XM_149213.1	150.6	22.1	6.814
F830002E14Rik	AK089567	7836.1	1151.5	6.805
C1qb	NM_009777.1	2234.4	331.5	6.740
Coro1a	NM_009898.2	116.9	17.4	6.718
LOC381484	XM_355437.1	171.5	25.6	6.699
AI840980	NM_153119.2	210.7	31.6	6.668
2810052M02Rik	NM_023320.1	56	8.4	6.667
2900076A13Rik		943.1	141.5	6.665
Lpl	NM_008509.1	3825.3	575.1	6.652
Cd84	NM_013489.1	159.5	24	6.646
Selpl	NM_009151.2	701.8	105.9	6.627
Nav1	NM_173437	72.1	10.9	6.615
2010003K11Rik	XM_129092.1	1263.8	191.9	6.586
Aif1	NM_019467.2	307.6	46.8	6.573
2310057H16Rik	NM_026473.2	1280.6	196.4	6.520
Itga6	NM_008397	114.1	17.5	6.520
Evi2a	NM_010161.1	201.8	31.1	6.489
H2-DMb2	NM_010388	472.7	73.1	6.466
Tnfaip3	NM_009397.2	106.4	16.5	6.448
Npn3	NM_029688.2	1072.3	166.4	6.444
Ccnd1	NM_007631.1	1328.9	207.4	6.407
		293.3	46	6.376
Cd53	NM_007651.2	485.6	76.5	6.348
Tyrobp	NM_011662.2	769.9	121.7	6.326
Ccnd1	NM_007631.1	7205.7	1153.4	6.247
6330414G02Rik		94.8	15.2	6.237
Kcnab2	NM_010598.2	119.1	19.1	6.236
Ltbp2	NM_013589.1	175.5	28.2	6.223
Cd63	NM_007653.1	884	142.5	6.204
Fcgr3	NM_010188.2	686.7	110.8	6.198
	BC038148.1	69.9	11.3	6.186
1110017L21Rik	AK003755	135.9	22	6.177
Xlkd1	NM_053247.3	98.2	15.9	6.176
Fxyd5	NM_008761.2	141.4	22.9	6.175
Csf2ra	NM_009970.1	658.3	106.8	6.164
Rragd	NM_027491	58.5	9.5	6.158
Adrb1	NM_007419	54.7	8.9	6.146
Slc39a4	NM_028064.2	111.8	18.3	6.109
Lbcl1	AK035683	230	37.7	6.101
Villp	NM_011700	67.6	11.1	6.090
S100a9	NM_009114.1	162.2	26.8	6.052
4833427B12Rik	AK014776	100.7	16.7	6.030
6720469N11Rik	NM_177138.2	65.6	10.9	6.018
Arhgef2	NM_008487	107	17.8	6.011
Srd5a2l	NM_020611.3	66.1	11	6.009
Mt1	NM_013602.2	20945.9	3490.9	6.000
Tnfrsf22	NM_023680.2	129.1	21.6	5.977

Amn	NM_033603.2	107.4	18	5.967
5730410E15Rik	NM_178765.2	86.4	14.5	5.959
Tceal5	NM_177919	204.8	34.4	5.953
A930008A22Rik	NM_172768	56.4	9.5	5.937
St14	NM_011176.3	92	15.5	5.935
Ptpns1	XM_149178.1	6575.9	1116.6	5.889
Hist1h3b	NM_178203	159.1	27.1	5.871
Basp1	NM_027395	940.7	161.3	5.832
Fbn1	NM_007993	79.3	13.6	5.831
Arhgap4	NM_138630.1	112.5	19.3	5.829
P2ry6	NM_183168.1	458.4	78.8	5.817
5830467P10Rik	NM_198029.1	120.9	20.8	5.813
Pilra	NM_153510.1	126.4	21.8	5.798
Slc8a1	NM_011406.1	79.2	13.7	5.781
Sn	NM_011426.1	133.6	23.2	5.759
Col3a1	NM_009930.1	310	53.9	5.751
Tbxas1	NM_011539.2	329.3	57.4	5.737
C330027I04Rik	NM_026561.2	58.5	10.2	5.735
Ccdc3	XM_129987.2	458.5	80.2	5.717
AA545217	NM_013726.1	116.9	20.5	5.702
BC049975	XM_138237.2	218.2	38.3	5.697
Tsrc1	NM_144899.2	99.1	17.4	5.695
1110036D12Rik		74	13	5.692
Emp3	NM_010129.1	259.8	45.9	5.660
Abhd2	NM_018811.4	202.4	36	5.622
	AK081844.1	94.4	16.8	5.619
7420404O03Rik	AK078662	125.4	22.4	5.598
Col1a1	NM_007742.2	60.9	10.9	5.587
Hcst	NM_011827	79.7	14.3	5.573
C230090D14	NM_173019.2	178.6	32.1	5.564
5530400B01Rik		123.9	22.3	5.556
Cybb	NM_007807	363.5	65.6	5.541
Ctss	NM_021281.1	566	102.2	5.538
Oas1g	NM_011852	131.2	23.8	5.513
Enc1	NM_007930.3	271.5	49.3	5.507
Kctd12	NM_177715	305.7	55.6	5.498
Rapgef5	NM_175930.2	53.1	9.7	5.474
		299.1	54.7	5.468
4432409M07Rik	NM_153551.1	55.2	10.2	5.412
Timp1	NM_011593	155	28.7	5.401
A430104N18Rik		142.9	26.5	5.392
Rtn4	NM_024226	74.3	13.8	5.384
Dm15	NM_032418	1905.5	354	5.383
Hcls1	NM_008225.1	137.5	25.6	5.371
Gdf15	NM_011819.1	633.5	118.1	5.364
Dhrs9	NM_175512	199.8	37.4	5.342
Cyp2a5	NM_007812.1	16417.1	3077.7	5.334
AI132321	NM_178911.2	531.7	100	5.317
Dock2	NM_033374.1	72	13.6	5.294
Ly78	AK089613	59.7	11.3	5.283
Cyln2	NM_009990	105.1	19.9	5.281
0610041G09Rik	NM_183274	622.3	118.5	5.251
Slc37a1	AK028984	74.5	14.2	5.246

Dock2	NM_033374	118.7	22.7	5.229
Adcy7	AK012436	100.1	19.2	5.214
Cyp2a5	NM_007812.1	15146.2	2911.2	5.203
Hist1h2ah	NM_175659.1	1002.6	194.3	5.160
Cxcl9	NM_008599	161.2	31.3	5.150
Treml4	NM_172623.1	81.6	15.9	5.132
Cyba	NM_007806.1	1552	303.2	5.119
Clecsf12	NM_020008.1	206.4	40.4	5.109
Il28ra	NM_174851.2	64.8	12.7	5.102
Mmp24	NM_010808	555	108.8	5.101
Spon2	NM_133903.2	2656.1	521.5	5.093
Coro1a	NM_009898.2	142.6	28	5.093
LOC381150	XM_358516.1	248	48.8	5.082
Tgfbr2	NM_009371.2	1496	295	5.071
C1qg	NM_007574.1	1647.3	326.4	5.047
Pira1	NM_011087.1	61.2	12.2	5.016
Gngt2	NM_023121.1	169.5	34	4.985
Cyp2a5	NM_007812.1	12148.1	2444.7	4.969
Icam1	NM_010493.2	1171.7	236.2	4.961
Camk1	NM_133926.1	65.9	13.3	4.955
Map3k14	NM_016896.2	144.6	29.2	4.952
Cdc42ep3	NM_026514	52.9	10.7	4.944
Gbp1	NM_010259.1	398.5	80.8	4.932
Pitpnm1	NM_008851.1	453.4	92.1	4.923
1810054O13Rik	NM_026436.1	835.9	170.3	4.908
2610001E17Rik	NM_026439.1	376.1	76.8	4.897
2210013M04Rik	NM_178595.2	73.5	15.1	4.868
Cxcl9	NM_008599.1	685.2	141	4.860
Gpc1	NM_016696.1	570.5	117.4	4.859
Tnfrsf12a	NM_013749.1	923.1	190.8	4.838
4631422O05Rik	XM_156304.1	79.1	16.4	4.823
Hist4h4	NM_175652.1	65.1	13.5	4.822
Hist1h2ag	NM_178186.1	4083.7	848	4.816
Slc11a1	NM_013612.1	121.1	25.2	4.806
Hist1h2ai	NM_178182.1	3477.3	724.7	4.798
Loxl1	NM_010729.2	147.3	30.7	4.798
Alox5ap	NM_009663	372.8	77.7	4.798
Gal3st1	NM_016922.2	162.9	34.1	4.777
E430014K09Rik	AK088390	117.7	24.7	4.765
Hivep3	NM_010657	71.9	15.1	4.762
Scamp5	NM_020270.2	55.7	11.7	4.761
1200002N14Rik	NM_027878.1	116.4	24.5	4.751
D14Ertd171e	NM_177814.3	60.2	12.7	4.740
C030002B11Rik		223.2	47.1	4.739
Sh3kbp1	NM_021389.3	121.1	25.6	4.730
A230102O09Rik		267	56.5	4.726
Gpx7	NM_024198.1	167.4	35.5	4.715
Lst1	XM_359281.1	518.8	110.1	4.712
Phlda2	NM_009434	79.5	16.9	4.704
Hist1h2ae	NM_178187.2	53.1	11.3	4.699
1200013B08Rik	NM_028773.2	210.8	45.2	4.664
Hist1h2ah	NM_175659.1	694.7	149	4.662
Csf1r	NM_007779.1	601.6	129.5	4.646

Serpinb6a	NM_009254.2	1467.8	316.4	4.639
Saa2	NM_011314.1	488.7	105.6	4.628
Emp3	NM_010129	979.1	211.8	4.623
Npn3	NM_029688.2	2103.4	456.4	4.609
LOC381687	XM_355664.1	158.3	34.4	4.602
Anxa1	NM_010730.1	78.8	17.2	4.581
Jak3	NM_010589	60.2	13.2	4.561
Iqgap1	AK029434	52.1	11.5	4.530
Slc16a5	XM_126601	1405	310.2	4.529
	AY267348.1	73.8	16.3	4.528
Ust	NM_177387	85.3	18.9	4.513
Mthfd2	NM_008638	118	26.2	4.504
Mbp	AK039047	76.7	17.1	4.485
Tm7sf1	NM_031999	124.1	27.7	4.480
Scara3	NM_172604.1	262.9	58.7	4.479
Cxcl16	NM_023158.3	301.8	67.4	4.478
Acas2l	NM_080575.1	65.7	14.7	4.469
Map4k4	NM_008696.1	60.3	13.5	4.467
Pkm2	NM_011099.2	252.2	56.5	4.464
Axl	NM_009465.2	2277.4	513.5	4.435
Hist1h2ak	NM_178183.1	1096.6	247.8	0.000
P2rx4	NM_011026.1	66.3	15	4.420
CSF-1	X05010	86.1	19.5	4.415
0610010O12Rik	XM_488847	1691	383.1	4.414
Stk10	NM_009288.1	264.3	60.1	4.398
Nid1	NM_010917.1	631.4	144.2	4.379
Vav1	NM_011691.2	266.4	60.9	4.374
Mcm5	NM_008566.1	319.7	73.1	4.373
Iqgap1	NM_016721.1	694.3	158.8	4.372
Mustn1	NM_181390.1	236.9	54.2	4.371
8430426K15Rik		168.4	38.6	4.363
Slc1a1	NM_009199.1	63.2	14.6	4.329
Anxa3	NM_013470.1	612	141.7	4.319
Iqgap1	NM_016721	488.2	113.1	4.317
Cd97	NM_011925.1	316.4	73.5	4.305
Oxct	AK010029	372	86.9	4.281
4921501M20Rik	NM_028728.1	61.5	14.4	4.271
Ccnd1	NM_007631.1	451.7	106.3	4.249
Olig1	NM_016968.2	588.8	138.6	4.248
Glipr1	NM_028608.1	265.9	62.6	4.248
Tinag	NM_012033.2	202.9	47.8	4.245
Ptpn18	NM_011206.1	385.3	90.8	4.243
Hapln4	NM_177900.3	119.3	28.2	4.230
E430002G05Rik	NM_173749	133.7	31.7	4.218
Slfn2	NM_011408.1	129.2	30.7	4.208
AW112037		2433	579.1	4.201
Hist1h2an	NM_178184.1	1927	459.5	4.194
Rbl1	NM_011249.1	54.4	13	4.185
Serpina3g	XM_354694.1	628.1	150.4	4.176
2900008M13Rik	XM_110121	320.3	76.7	4.176
Nfkb2	NM_019408.1	130.2	31.2	4.173
Cxcl1	NM_008176.1	2179.6	522.7	4.170
Uhrf1	NM_010931.2	241.7	58.1	4.160

S100a6	NM_011313.1	1118.1	268.9	4.158
Rtn4	NM_194054.1	145.1	34.9	4.158
Nqo1	NM_008706.1	209.2	50.5	4.143
Clec2	NM_019985.1	235.9	57	4.139
Slc7a7	NM_011405.1	185.4	44.8	4.138
C730033N22Rik	AK050284	62.2	15.1	4.119
Hrmt1l1	NM_133182	126.6	30.8	4.110
Akr1b3	NM_009658.2	863.2	210.2	4.107
Gmfg	NM_022024.1	65.7	16	4.106
Stx11	XM_203312.2	119.9	29.2	4.106
Abcg1	NM_009593.1	926.8	225.8	4.105
Kctd12	NM_177715.2	159.5	39	4.090
C1qa	NM_007572	1129.5	276.4	4.086
Satb1	NM_009122.1	104.6	25.6	4.086
Slco3a1	NM_023908.1	63.3	15.6	4.058
H2-T22	NM_010397	116.6	28.8	4.049
Prg	NM_011157.1	144.2	35.7	4.039
Smoc2	NM_022315.1	586.2	145.2	4.037
Synpo		1079.1	267.9	4.028
5330417C22Rik	XM_203978.3	60.4	15	4.027
Pdk4	NM_013743.1	517.4	128.6	4.023
Csrp1	NM_007791.2	757.3	188.3	4.022
	AK081365.1	64.1	16	4.006
Olfml3	NM_133859.1	152.6	38.1	4.005
Lig1	NM_010715.1	198.4	49.6	4.000
6230400I06Rik		316.2	79.1	3.997
Hk2	NM_013820.1	196.4	49.4	3.976
Lgmn	NM_011175.1	2617.3	658.4	3.975
Ostb	NM_178933.2	121.6	30.6	3.974
5730528L13Rik	NM_028137.1	72.2	18.2	3.967
Hist1h4m	NM_175657	239.1	60.4	3.959
Fmo3	NM_008030.1	341.2	86.8	3.931
1810011H11Rik	XM_358452	108.7	27.7	3.924
Cenpe	NM_173762	161.6	41.2	3.922
Aldh3b1	NM_026316.2	176.6	45.2	3.907
Ifi205	NM_172648.2	74.6	19.1	3.906
Laptm5	NM_010686.2	4328.5	1108.3	3.906
BC013712	XM_131779.2	94.6	24.3	3.893
Mglap	NM_008597.2	120.2	30.9	3.890
Abr	NM_198894.1	283	73.1	3.871
Copeb	NM_011803.1	1145.7	296	3.871
Ly6e	NM_008529	9384.9	2444.2	3.840
Emr1	NM_010130.1	1529.7	398.4	3.840
Ppap2c	NM_015817	4800.3	1250.8	3.838
Sh3bgrl3	NM_080559.1	472.8	123.3	3.835
2900075A18Rik		408.4	107.2	3.810
Trpv2	NM_011706.1	113.9	30	3.797
Apobec1	NM_031159.2	730.9	192.8	3.791
Gdf3	NM_008108.1	96.5	25.5	3.784
Xlr3a	NM_011726.1	312.1	82.5	3.783
H2-M3	NM_013819.1	108.1	28.6	3.780
Hist1h2ao	NM_178185.1	3930	1040.9	3.776
Dock10	XM_129913.4	204.5	54.4	3.759

Lpxn	NM_134152.1	281	75	3.747
2610041P08Rik	NM_198008.1	186.4	49.8	3.743
Ltbp3	NM_008520	135.8	36.3	3.741
Smox	NM_145533.1	110.3	29.6	3.726
Adamts2	NM_175643.1	132.5	35.6	3.722
Pilra	NM_153510	306.3	82.4	3.717
2900042O04Rik		62.3	16.8	3.708
Trrp7	AK036731	127.8	34.5	3.704
Fgd2	NM_013710.1	315.9	85.7	3.686
4631422C13Rik	XM_128857.3	95.7	26	3.681
9530034E10Rik		65.1	17.8	3.657
Adrb2	NM_007420.2	72	19.7	3.655
C130081G24		72.9	20	3.645
Chk	AK053818	299.7	82.3	3.642
Tpx2	NM_028109.2	143.8	39.6	3.631
Cyp2a5	NM_007812	27029.5	7452	3.627
Spp1	NM_009263.1	2464.2	679.8	3.625
Il10rb	NM_008349.1	378.5	104.5	3.622
AI854251	XM_128597.4	931.1	257.3	3.619
Pygb	NM_153781.1	86.8	24	3.617
Aif1	NM_019467.2	165.8	45.9	3.612
Snn	NM_009223	113.1	31.4	3.602
Pdlim4	NM_019417.1	160.2	44.5	3.600
Gltp	NM_019821.2	996.4	278	3.584
2310005E10Rik	NM_172398.2	200.6	56.2	3.569
Abcg1	NM_009593	70.8	19.9	3.558
Hist1h2af	NM_175661.1	2622.6	737.3	3.557
Anln	NM_028390.1	192.5	54.2	3.552
Mvp	NM_080638.1	2837.4	800.1	3.546
Inpp5d	NM_010566.1	122.5	34.6	3.540
Pkib	AK005281	99.4	28.1	3.537
2310014H01Rik	XM_355011.1	770.8	218	3.536
Prg	NM_011157.1	405.7	114.9	3.531
P2ry14	NM_133200.2	416.6	118.1	3.528
Slc7a8	NM_016972.2	224.5	63.8	3.519
Tnfrsf11b	NM_008764.2	130.3	37.1	3.512
Man1c1	NM_207237	81	23.1	3.506
Lcp2	NM_010696.2	178.6	51.1	3.495
Col6a1	NM_009933.1	210.9	60.7	3.474
Cdc20	NM_023223.1	53.5	15.4	3.474
Elf3	NM_007921.1	60.1	17.3	3.474
AI481214	NM_054098.2	113.1	32.6	3.469
Mki67	XM_133912.3	133.5	38.5	3.468
	BC064076.1	109	31.5	3.460
Hist1h4m	NM_175657.1	801.5	232.2	3.452
Slc6a8	NM_133987.1	407.8	118.3	3.447
Hist1h2ai	NM_178182	3523.1	1022.4	3.446
1110008L20Rik	NM_028643.1	296.6	86.5	3.429
Fgl2	NM_008013.2	79.8	23.3	3.425
Mfge8	NM_008594	631	184.3	3.424
C130033B18Rik	AK048072	95.4	27.9	3.419
Ehd4	NM_133838.2	617	180.5	3.418
LOC381171	XM_358520.1	67.8	19.9	3.407

Myh10	NM_175260.1	164.2	48.4	3.393
AA175286	NM_010156.2	1248.4	369.3	3.380
Wbscr5	NM_022964.2	70.8	21	3.371
Gcnt1	NM_173442.1	104.5	31	3.371
Bcl2	NM_009741.2	56.9	16.9	3.367
4930553C05Rik	AK016099	98.6	29.3	3.365
Asns	NM_012055.1	95.9	28.6	3.353
Mpeg1	XM_129176	2817.6	843.1	3.342
Cdc42ep5	NM_021454.3	100.9	30.2	3.341
Lor	NM_008508.1	57.4	17.2	3.337
1200009F10Rik	NM_026166.1	60.4	18.1	3.337
Prkcb	NM_008855.1	238.5	71.5	3.336
2600017H08Rik	NM_025565.1	107.9	32.5	3.320
Sftpd	NM_009160.1	56.7	17.1	3.316
Cyp2c39	NM_010003.1	12121	3660.6	3.311
1200015A22Rik	NM_028766.1	755	228.8	3.300
Ptpn8	NM_008979.1	64.6	19.6	3.296
Sox9	NM_011448	553.6	169	3.276
Sult1e1	NM_023135.1	279.3	85.4	3.270
Entpd2	NM_009849.1	246.7	75.5	3.268
Pttg1	NM_013917.1	390.1	119.5	3.264
2310067E08Rik	NM_028013.1	321.2	98.4	3.264
Krt2-8	NM_031170.1	12621.1	3868.9	3.262
6330439P19Rik	AK031886	87.1	26.7	3.262
Btc	NM_007568.2	268.8	82.4	3.262
Unc5b	NM_029770	356.2	109.5	3.253
Rab8b	NM_173413.2	647.7	199.4	3.248
1300018P11Rik	NM_025829.2	438.7	135.1	3.247
Prkcd	NM_011103.1	428.9	132.6	3.235
1810046I24Rik	NM_027218.1	82.7	25.6	3.230
LOC231663	XM_124621.2	9903.5	3074.8	3.221
A630077B13Rik	NM_175449.3	131.9	41	3.217
Gus	NM_010368.1	66.9	20.8	3.216
Pdcd1lg1	NM_021893.2	276.1	85.9	3.214
Slc11a1	NM_013612.1	96.3	30	3.210
Arl10b	NM_026823.1	2720.4	851.4	3.195
BC036718	NM_153136.1	4027.3	1261.1	3.193
Plac8	NM_139198.1	739.2	231.5	3.193
Hist1h3e	NM_178205	227.4	71.3	3.189
Klk8	NM_008457.1	59.3	18.6	3.188
2310061F22Rik	XM_134537.3	157.4	49.4	3.186
Rasgrp1	NM_011246.2	318.9	100.1	3.186
Gstm2	NM_008183.2	1930.2	606	3.185
Ear3	NM_017388.1	177.4	55.7	3.185
Cd9	NM_007657.2	1217.2	382.9	3.179
Nrm	NM_134122.1	296.6	93.5	3.172
0610007N19Rik	AK007719	84	26.5	3.170
Ly6a	NM_010738.2	856.4	271.2	3.158
A130001G05Rik		54.6	17.3	3.156
Hn1	NM_008258.1	1141.8	362.1	3.153
Ms4a6c	NM_028595	100.8	32	3.150
Fstl1	NM_008047.2	164.7	52.3	3.149
Cd151	NM_009842.1	68.9	21.9	3.146

Fxyd5	NM_008761.2	246.7	78.5	3.143
Gadd45g	NM_011817.1	145.9	46.5	3.138
Lrp11	NM_172784.1	75.9	24.2	3.136
Ckb	NM_021273.2	1653	527.8	3.132
Tcirg1	NM_016921.2	72.8	23.3	3.124
Fyb	NM_011815.1	135.5	43.4	3.122
Pira3	NM_011090.1	77.3	24.8	3.117
Cpeb1	NM_007755.1	252.8	81.2	3.113
Abi3	NM_025659.1	494.6	159.3	3.105
Col12a1	AK076278	188.2	60.8	3.095
Renbp	NM_023132.1	242	78.3	3.091
Cstb	NM_007793.2	12408.8	4023.3	3.084
Folr2	NM_008035	392.2	127.2	3.083
Rod1	NM_144904.1	85.7	27.8	3.083
Osmr	NM_011019.1	81.6	26.5	3.079
Tfpi	NM_011576.1	52.3	17	3.076
Ctgf	NM_010217	143.6	46.7	3.075
Cdc20	NM_023223.1	59.2	19.3	3.067
1700093E07Rik	NM_133685.1	457.2	149.1	3.066
Rpl27a	NM_011975.2	57.3	18.7	3.064
Ppl	NM_008909	747.4	244	3.063
Fchsd1	NM_175684.3	224	73.3	3.056
Col16a1	NM_028266.3	300.3	98.3	3.055
Rab8b	NM_173413.2	666.9	218.9	3.047
4833424O12Rik		63.3	20.8	3.043
Nt5c2	NM_029810.2	57.8	19	3.042
Cerk	NM_145475	547.1	180.2	3.036
Gpr124	NM_054044.1	94.1	31	3.035
Myh10	NM_175260	375	123.6	3.034
Arpc1b	NM_023142.1	928.1	307.7	3.016
Ctsk	NM_007802.2	65.1	21.6	3.014
Cotl1	XM_150115.1	352.5	117.4	3.003
Tcrb-V13		296.4	98.8	3.000
Ptk9l	NM_011876.2	127.1	42.4	2.998
Dscr1l2	NM_022980.2	330.1	110.2	2.995
Dpt	NM_019759.1	64.7	21.6	2.995
Fkhl18	NM_010226.1	112.8	37.7	2.992
Myo1g	NM_178440.2	225.4	75.4	2.989
Rhod	NM_007485.2	1403	469.4	2.989
Emilin1	NM_133918.1	137.2	46	2.983
3010003L21Rik	NM_175404.2	58.7	19.7	2.980
1110004P15Rik		876.4	294.4	2.977
Vsig4	NM_177789.2	2282.6	767.3	2.975
H2-T10	NM_010395.2	2304.8	775.2	2.973
Oasl1	NM_145209.2	120.8	40.7	2.968
Hrb	NM_010472.1	91.4	30.9	2.958
Cygb	NM_030206.1	1233	417	2.957
Msn	AK031171	111.9	37.9	2.953
H2-D4	NM_008200.1	242	82	2.951
Hist1h4f	NM_175655.1	545.6	185.3	2.944
Col6a3	NM_009935.1	347.4	118	2.944
Vcam1	NM_011693.2	1099.7	374.4	2.937
Arpc1b	NM_023142.1	757.5	258.3	2.933

Ssbp4	XM_356132.1	543.1	185.2	2.933
Trim47	NM_172570.2	150.4	51.3	2.932
Rad51l1	AK077994	508.9	173.6	2.931
	AK050360.1	87.2	29.8	2.926
Icmt	XM_131821.3	57.3	19.6	2.923
Rbp1	NM_011254.2	2340.9	801.3	2.921
Tmc7	NM_172476.2	75	25.7	2.918
LOC245069	XM_159529.3	91.2	31.3	2.914
Dscr1	NM_019466.2	117	40.2	2.910
Gmip	NM_198101.1	89.2	30.7	2.906
T2bp	NM_145133.2	164.7	56.7	2.905
Pawr	XM_125814.2	226.3	78.1	2.898
Tpm1	NM_024427	733.9	253.3	2.897
Htatip2	NM_016865.2	6106.6	2108.1	2.897
4930533K18Rik		107.4	37.1	2.895
Hao3	NM_019545.2	62.2	21.5	2.893
5830417C01Rik	NM_024282.2	97.2	33.6	2.893
Ptp4a3	NM_008975.2	82.4	28.5	2.891
Plscr1	NM_011636.1	1086	375.9	2.889
Clecsf10	NM_020001.1	191	66.4	2.877
Gstm6	NM_008184.1	24125.5	8390.1	2.875
Serpina7	NM_177920	1138.9	396.4	2.873
Fath	XM_134149.5	136	47.4	2.869
Nedd9	NM_017464.2	182.7	63.8	2.864
H2-L		8187.7	2861.1	2.862
Emp1	NM_010128.3	573.2	200.5	2.859
Dock11	XM_486647	73.7	25.8	2.857
9430080K19Rik		557.4	195.4	2.853
Hist1h4f	NM_175655.1	72.4	25.4	2.850
P2ry13	NM_028808.1	226.3	79.6	2.843
Gstm2	NM_008183.2	3985.2	1404.4	2.838
Hip1	NM_146001	367.1	129.4	2.837
C1qr1	NM_010740.1	241.5	85.3	2.831
Hist1h1c	NM_015786	7319.6	2594.6	2.821
Myef2	NM_010852.1	69.8	24.8	2.815
Tm4sf4	NM_145539.1	3370.3	1198.4	2.812
Hist2h2be	NM_178214.1	133.6	47.6	2.807
4832420L08Rik	AK029315	63.7	22.7	2.806
Rad51l1	NM_009014.2	362.2	129.2	2.803
Mcm2	NM_008564.1	136.9	48.9	2.800
Tnip1	NM_021327.1	654.8	234.1	2.797
2810048G17Rik	NM_133746.2	121.9	43.6	2.796
Arhgap9	NM_146011.1	101.6	36.4	2.791
E430025L02Rik	NM_146069	354.2	126.9	2.791
BC016495	NM_145497.1	136.2	48.9	2.785
Mgst3	NM_025569.1	1171.2	420.6	2.785
LOC270157	XM_196479.2	56.2	20.2	2.782
Ifi30	NM_023065.2	498.4	179.5	2.777
Gpx3	NM_008161.1	175.9	63.4	2.774
D630011N09Rik	AK085324	108.5	39.2	2.768
Scamp5	NM_020270.2	1434.9	519.5	2.762
Arl2bp	NM_024191.1	65.7	23.8	2.761
2310016E02Rik	AK003569	308	111.7	2.757

4732465J09Rik	XM_356161	157.4	57.1	2.757
Hist1h4d	NM_175654.1	67.4	24.5	2.751
Cyp2c55	NM_028089.1	303.2	110.7	2.739
Acate2	NM_019736.2	53.3	19.5	2.733
H2-T22	NM_010397.2	392.6	143.8	2.730
Dfna5h	XM_147318.1	71.7	26.3	2.726
Ywhah	NM_011738	89.9	33	2.724
Eml1	XM_127139.5	88.5	32.6	2.715
D330008I21Rik	AK052205	146.2	53.9	2.712
F830005D05Rik		56.3	20.8	2.707
Lgals3bp	NM_011150.1	1969.2	727.7	2.706
A630001G21Rik	NM_177055.2	83	30.7	2.704
Copg2as2	AK018238	62.3	23.1	2.697
Ifit2	NM_008332.2	142.9	53	2.696
Ets2	NM_011809.2	2159.1	802.5	2.690
Smpd3	NM_021491.2	402.4	150.2	2.679
Pip5k2a	NM_008845.2	631.2	235.7	2.678
Elmo1	NM_198093.2	188.7	70.5	2.677
Tbc1d1	NM_019636	130.5	48.8	2.674
AI606181	NM_183215	59	22.1	2.670
Tpm4	XM_134274.3	1163.7	436.6	2.665
Mmp23	NM_011985.1	76.2	28.6	2.664
Apoa4	NM_007468.1	17283.6	6493.2	2.662
AU020206		181.8	68.3	2.662
Nedd9	NM_017464.2	293.7	110.4	2.660
6030404G09Rik	AK077882	258.5	97.2	2.659
2810027O19Rik	NM_026613.2	92	34.6	2.659
Sfxn3	NM_053197.2	196.8	74.1	2.656
D2Bwg0891e	NM_026797.1	2589.8	975.2	2.656
Serpina7	NM_177920.4	1180.5	444.6	2.655
Galnt10	NM_134189.2	331.3	124.9	2.653
B4galt5	NM_019835	54.6	20.6	2.650
5330401P04Rik	NM_172654	56.9	21.5	2.647
Rhbdf1	NM_010117.1	987.4	373.1	2.646
4.93E+26	NM_177858.2	138.9	52.6	2.641
Gsta4	NM_010357.1	4976	1884.7	2.640
Gcap27		78.2	29.7	2.633
Tmc6	NM_145439.1	113.4	43.1	2.631
Epb4.1l2	NM_013511.1	88.6	33.7	2.629
Frzb	NM_011356.2	77.8	29.6	2.628
Rab3d	NM_031874.3	384.4	146.3	2.627
D12Ertd553e	NM_029758.3	619.4	236.1	2.623
2900060B22Rik		90.9	34.7	2.620
3321401G04Rik	XM_133096.5	55	21	2.619
AA960558	NM_133942.1	2087.9	797.8	2.617
Cblb	XM_358863.1	71.7	27.4	2.617
Unc93b	NM_019449.1	270.7	103.7	2.610
LOC223672	XM_128064.4	2677	1025.8	2.610
Nagk	NM_019542.1	393.3	150.9	2.606
Dyrk3	NM_145508.1	147.5	56.6	2.606
Cp	NM_007752	268.4	103.1	2.603
Nfkbie	NM_008690.2	73.4	28.2	2.603
Mat2a	NM_145569	535.5	206	2.600

Rab11fip5	XM_358365.1	93.5	36	2.597
Cdc42ep3	NM_026514.1	63.5	24.5	2.592
Hlx1	NM_008250.1	104.4	40.3	2.591
A130092J06Rik	NM_175511.2	144.8	55.9	2.590
Tmprss2	NM_015775.2	253.3	98	2.585
Fkbp1a	NM_008019	1468.5	569.2	2.580
Cklfsf3	NM_024217.2	402.4	156	2.579
App	NM_007471.1	1073.4	417	2.574
Tuba1	NM_011653	55.5	21.6	2.569
Ppp1r9b	NM_172261.1	223.4	87	2.568
AI605517		57.5	22.4	2.567
Fbln2	NM_007992.1	144.3	56.3	2.563
Mylc2b	NM_023402.1	1361.9	531.4	2.563
Casp1	NM_009807.1	452.5	176.6	2.562
Tcrb-V8.2		72.5	28.3	2.562
4733401I05Rik		96	37.5	2.560
0610006O14Rik	NM_133764.1	96.6	37.9	2.549
Cxcl16	NM_023158	90.9	35.7	2.546
Hist1h3d	NM_178204.1	201.7	79.3	2.544
Lum	NM_008524	487.2	191.8	2.540
Kcnk13	NM_146037.1	89.9	35.4	2.540
E030030K01Rik	AK087162	107	42.2	2.536
Hspa1b		53.7	21.2	2.533
Msn	NM_010833	937.9	370.3	2.533
Zfp90	NM_011764.2	143.2	56.7	2.526
		59.3	23.5	2.523
B230385N19Rik	AK046447	152.8	60.6	2.521
Alas1	NM_020559.1	10581.2	4200	2.519
Mbd1	AK007371	79.3	31.5	2.517
4930438D12Rik	AK015335	95.9	38.1	2.517
Pfc	XM_135820.3	2412.6	960.7	2.511
9030405D14Rik	NM_027819.1	56.4	22.5	2.507
LOC381259	XM_355201.1	408.6	163.7	2.496
Napsa	NM_008437.1	57.4	23	2.496
D430039N05Rik	NM_175514.1	86.3	34.6	2.494
Tyki	NM_020557.3	164.6	66	2.494
Hexb	NM_010422.1	87.7	35.2	2.491
Pkig	NM_011106.1	104.6	42	2.490
Csf3r	NM_007782.1	56.2	22.6	2.487
Krt1-18	NM_010664.1	5721.9	2303.4	2.484
Krt1-23	NM_033373.1	488.6	196.7	2.484
Camk1	NM_133926.1	140.7	56.7	2.481
Cd86	NM_019388.2	176.6	71.2	2.480
Hmox1	NM_010442.1	321	129.5	2.479
Dcn	NM_007833.1	1731	701	2.469
Il4i1	NM_010215.1	60.7	24.6	2.467
4831437C03Rik	AK029240	52.8	21.4	2.467
Rassf1	NM_019713	56	22.7	2.467
Adam15	NM_009614.1	67.1	27.2	2.467
Gstm2	NM_008183.2	14992.7	6078.5	2.467
Cyp2a4	NM_009997	14109.4	5721.5	2.466
Col6a1	NM_009933.1	318.5	129.2	2.465
D330037A14Rik	NM_153537.3	82.7	33.6	2.461

Spag5	NM_017407.1	59.3	24.1	2.461
Calr3	NM_029782.2	133.6	54.3	2.460
Rad51l1	NM_009014.2	2272.6	924.9	2.457
2610300B10Rik	XM_283661	237.1	96.5	2.457
Apoa4	NM_007468	50073.9	20384.6	2.456
Saa1	NM_009117.1	2125.1	865.2	2.456
C230050J15Rik	AK048763	192.9	78.6	2.454
Atp9a	NM_015731.2	165.4	67.4	2.454
Usp18	NM_011909.1	383.5	156.5	2.450
Ppl	XM_148334.1	339.1	138.4	2.450
9530090G24Rik	NM_145537.1	216	88.2	2.449
Zfhx1b	AK012377	67.8	27.7	2.448
Mat2a	NM_145569	193.3	79	2.447
Gstm1	NM_010358.2	39224.6	16055.1	2.443
2510048K03Rik	NM_028243.1	628.5	257.4	2.442
1810009M01Rik	NM_023056.2	6302.4	2582.1	2.441
Ifngr1	NM_010511.1	455.3	186.7	2.439
4833422F24Rik	NM_029021.1	119.4	49	2.437
Thbs2	NM_011581.1	58.7	24.1	2.436
2310015A16Rik		446.7	183.7	2.432
Adamts2	NM_175643.1	201.9	83.1	2.430
Mknk2	NM_021462	232.1	95.6	2.428
Serpinh1	NM_009825	556.6	229.3	2.427
Mlp	NM_010807.2	368.5	151.9	2.426
4632417K18Rik	NM_026640.1	289.7	119.5	2.424
Itm2c	NM_022417.1	2225.4	918.5	2.423
H2-L		20302.1	8386.9	2.421
Pdgfa	NM_008808	1364.6	564.7	2.417
7-Sep	NM_009859.2	54.6	22.6	2.416
H2-D1	NM_010380.2	15327.6	6353.8	2.412
Col14a1	AK052963	356.8	148.1	2.409
		54.8	22.8	2.404
Dkk3	NM_015814.2	150.4	62.6	2.403
Guca1a	NM_008189.2	334.1	139.1	2.402
Agtrap	NM_009642.3	83.3	34.7	2.401
Zfp28	NM_009552.1	69.5	29	2.397
Tor2a	AK019246	101.7	42.5	2.393
AU040829	NM_175003.2	197.4	82.5	2.393
Mgst3	NM_025569.1	2302.7	963.1	2.391
4930577N17Rik		55.7	23.3	2.391
Eln	NM_007925.2	63.3	26.5	2.389
1700012B18Rik	NM_027950.1	4867.2	2040.3	2.386
Col4a1	NM_009931.1	709.4	298.1	2.380
Csf1	NM_007778.1	59	24.8	2.379
Slc2a3	NM_011401.2	52.3	22	2.377
BC022145	NM_144830.1	223.7	94.1	2.377
4833427B12Rik	XM_195728.3	83.6	35.2	2.375
Hp	NM_017370.1	19534.5	8246.3	2.369
H2-T9	NM_010399	4186.5	1767.4	2.369
9530083O12Rik		119.3	50.5	2.362
1810048P08Rik	NM_133717.1	66.1	28	2.361
Traf1	AK089281	60.9	25.8	2.360
Dcn	NM_007833.1	4326.7	1833.3	2.360

Ucp2	NM_011671.2	556.7	235.9	2.360
Gas6	NM_019521.1	1005.8	426.8	2.357
Gss	NM_008180.1	383.5	162.8	2.356
Tpm4	XM_134274.3	134.8	57.3	2.353
Limk1	NM_010717.1	156.1	66.4	2.351
BC003236	NM_030249.2	115.6	49.2	2.350
Arl6ip5	NM_022992.1	591.2	252.3	2.343
Slc9a6	NM_172780.1	62.3	26.6	2.342
Dusp3	NM_028207.1	75.6	32.3	2.341
8430408G22Rik	NM_145980.1	4199.3	1794.8	2.340
2310015N21Rik	NM_181397.1	64.1	27.4	2.339
Hist1h4i	NM_175656	769.2	330.2	2.329
Rttn	NM_175542.3	73.1	31.4	2.328
C330027I04Rik	NM_026561.2	223	95.8	2.328
Cyp3a41	NM_017396.1	276.5	118.8	2.327
Mef2c	NM_025282.1	139.7	60.1	2.324
BC011209	NM_145447.1	461.1	198.5	2.323
Marcks	NM_008538	662.1	285.4	2.320
Hspbap1	NM_175111.2	196	84.5	2.320
Ifi205	NM_172648	599	258.3	2.319
Slc25a30	NM_026232	757.8	327.7	2.312
LOC329190	XM_283627.2	79	34.2	2.310
Incenp	NM_016692.1	89.2	38.7	2.305
Col4a2	NM_009932.2	1439.5	625.6	2.301
Car2	NM_009801.3	130.9	57	2.296
H2-T17	NM_010396	5468.3	2383	2.295
B230312L03Rik	AK045826	236.4	103.1	2.293
		56.9	24.9	2.285
9130020G22Rik	XM_131773.3	332.6	145.7	2.283
Lrmp	NM_008511	163.1	71.5	2.281
1700012F10Rik	XM_181295.3	69.1	30.3	2.281
Col5a1	NM_015734.1	417.5	183.3	2.278
Slc13a3	NM_054055.1	467	205.1	2.277
D930046M07Rik	AK053082	71.3	31.4	2.271
Bicc1	NM_031397.1	284	125.1	2.270
Ppp2r5c	AK012612	74.9	33	2.270
9530090G24Rik	NM_145537.1	215.7	95.1	2.268
LOC234486	XM_134462.2	79	34.9	2.264
Flna	XM_289920.2	326.8	144.4	2.263
Tgif	NM_009372.2	831.2	367.5	2.262
Zfp532	NM_207255.1	72.8	32.2	2.261
BC025206	NM_146184.2	52.9	23.4	2.261
9030625A04Rik	NM_172488.1	1262.2	558.9	2.258
Sdf2l1	XM_147210.1	308.8	136.8	2.257
Tmc6	NM_145439.1	278.4	123.4	2.256
Plk3	NM_013807.1	1408.9	624.8	2.255
1110008L20Rik	NM_028643.1	1937.6	859.5	2.254
9330129D05Rik	NM_178799.2	437.1	193.9	2.254
Cttn	NM_007803.1	79.7	35.4	2.251
Pfkfb3	NM_172976.1	466.2	207.1	2.251
Crip1	NM_007763	255.7	113.6	2.251
Tnxb	NM_031176.1	65.7	29.2	2.250
E130203B14Rik	NM_178791.2	86.7	38.6	2.246

Rps19	NM_023133.1	60.8	27.1	2.244
9530006C21Rik		533.7	238.1	2.241
Edg5	NM_010333	823.8	368.3	2.237
D130016B08Rik		86.6	38.8	2.232
Evc2	NM_145920	67.6	30.3	2.231
Tnfaip8	NM_134131.1	126.7	56.9	2.227
LOC381201	XM_355134.1	185.2	83.2	2.226
2200002D01Rik		1250.9	563	2.222
LOC114601	NM_053252.1	78.4	35.3	2.221
Tnfrsf8	NM_009401.1	92.4	41.7	2.216
A830007P12Rik	NM_146115.2	151.1	68.2	2.216
Stk17b	NM_133810.2	111.6	50.4	2.214
Lmna	NM_019390.1	999.4	451.8	2.212
9130017C17Rik	NM_027840.1	71	32.1	2.212
Slc25a30	NM_026232.1	365.8	165.5	2.210
Sqstm1	NM_011018.1	7912.6	3583.7	2.208
Myo9b	NM_015742.1	1098.8	498.7	2.203
Hist2h3c2	NM_054045.2	247.5	112.5	2.200
9530081N05Rik	AK035655	125.6	57.1	2.200
Rdh9	NM_153133.1	4671.1	2125.1	2.198
D930007N19Rik		71.4	32.5	2.197
	AK081027.1	159.4	72.7	2.193
2310058A03Rik	AK009971	67.3	30.8	2.185
0610011I04Rik	NM_025326.2	1781	815.1	2.185
Irf7	NM_016850.1	315	144.2	2.184
Hist1h4k	NM_178211.1	179.5	82.2	2.184
Hk1	NM_010438	254.5	116.6	2.183
4732486I23Rik	XM_130565.3	63.5	29.1	2.182
B130017P16Rik	NM_178638.2	75.2	34.5	2.180
Igfbp3	NM_008343.1	301.2	138.2	2.179
Lass5	NM_028015.2	75.4	34.6	2.179
5830484A20Rik	XM_284155.2	65.3	30	2.177
Atp2a3	NM_016745.2	126	57.9	2.176
1200015A19Rik	NM_026388.1	182.7	84	2.175
Pgm3	NM_028352.2	133.1	61.2	2.175
Gja1	NM_010288.2	521.7	239.9	2.175
Grn	NM_008175.2	4824.6	2219.9	2.173
Cyp2a4	NM_009997.1	6051.7	2785.8	2.172
Ifngr2	NM_008338.2	1968.5	906.2	2.172
1700022C02Rik	NM_025495.1	150.9	69.5	2.171
D12Ertd647e	NM_026790.1	5182.3	2387.5	2.171
5830417C01Rik	NM_024282.2	490.9	226.5	2.167
Minpp1	NM_010799.1	79.5	36.7	2.166
1110060M21Rik	NM_025424.1	1725.7	797.2	2.165
Clecsf13	NM_016751.2	1451.3	672.7	2.157
Csad	NM_144942	2067.8	958.6	2.157
Sdcbp	NM_016807	692.6	321.2	2.156
LOC384710	XM_357808.1	411.4	190.8	2.156
Thbd	NM_009378.1	66.6	30.9	2.155
AI481214	NM_054098.2	144.8	67.2	2.155
	BC068122.1	106.2	49.3	2.154
Armcx1	NM_030066.2	65.7	30.5	2.154
A830007P12Rik	NM_146115.2	304.9	141.6	2.153

Mylc2b	NM_023402.1	7481.4	3476.1	2.152
3110050N22Rik	NM_173181.1	156.8	72.9	2.151
1700012F10Rik	AK005902	543.3	252.7	2.150
Ica1	NM_010492.2	66.4	30.9	2.149
Arl6ip5	NM_022992.1	408.3	190.3	2.146
Pld3	NM_011116.1	368.3	171.7	2.145
Chka	NM_013490.1	624.2	291.2	2.144
Gnb1	NM_008142.2	1090	509.1	2.141
Dnmt1	NM_010066.2	108.1	50.5	2.141
Hexa	NM_010421	1687.1	789.8	2.136
Aldh3a2	NM_007437	11620.4	5440	2.136
Cyp3a11	NM_007818.2	24484.1	11472	2.134
2810417M05Rik	NM_026516.1	64.4	30.2	2.132
Gpx4	NM_008162	19811.7	9318.6	2.126
Cklfsf4	NM_153582.3	381.4	179.4	2.126
Ostf1	NM_017375.1	1478.3	695.5	2.126
Cyr61	NM_010516.1	75.2	35.4	2.124
Ggta1	NM_010283.1	102.6	48.3	2.124
Ampd3	NM_009667	68.4	32.2	2.124
Dmn	NM_207663.2	94	44.3	2.122
Unc5b	NM_029770.1	141.7	66.8	2.121
Lmna	NM_019390.1	2122.7	1001.6	2.119
Gas2l1	NM_144560.1	262.1	123.7	2.119
0610007L01Rik	AK002297	1969.7	931.4	2.115
Gdf10	NM_145741.2	170.8	80.8	2.114
Mylc2b	NM_023402	1912.3	905.5	2.112
Pofut2	NM_030262.2	71.8	34	2.112
Rtn4	NM_194054.1	3965.8	1878.1	2.112
Flot1	NM_008027.1	1597	756.6	2.111
Rassf4	NM_178045.3	436.5	207	2.109
Hist1h4i	NM_175656.1	385.5	183	2.107
Bat1a	NM_019693.2	90.7	43.1	2.104
Sat1	NM_009121.3	3263.5	1551.2	2.104
Scd2	NM_009128.1	700.6	333.1	2.103
Arntl	NM_007489.1	279.6	133	2.102
Igfbp7	NM_008048.1	10855.5	5166.6	2.101
Cp	AK033842	173.5	82.6	2.100
Adfp	NM_007408.2	6582.7	3139.4	2.097
Gus	NM_010368.1	239.4	114.2	2.096
Msn	NM_010833.1	89.6	42.8	2.093
2210415K03Rik		53.8	25.7	2.093
4930463P07Rik		191.7	91.6	2.093
Tnxb	NM_031176	117.6	56.2	2.093
LOC223653	XM_147965.2	459.7	220	2.090
3110068G20Rik		64.9	31.1	2.087
LOC381358	XM_355324.1	55.7	26.7	2.086
Tgm2	NM_009373.2	4339.7	2081.1	2.085
4.93E+26	NM_177858.2	147.6	70.8	2.085
Cyp7a1	NM_007824.2	4176.5	2003.4	2.085
Rps24	NM_011297.2	131.1	62.9	2.084
	AK011353.1	286.5	137.5	2.084
Sepn1	NM_029100.1	337.6	162.1	2.083
Grb10	NM_010345	181.4	87.1	2.083

Crym	NM_016669.1	68.9	33.1	2.082
Slc39a4	NM_028064.2	4563.7	2192.6	2.081
Tens1	XM_109868	278.8	134	2.081
Arhgef5	XM_133067.3	832.5	400.4	2.079
A930001D11Rik	AK044207	102.5	49.3	2.079
Sdc3	NM_011520.2	1106.2	532.3	2.078
Psmb8	NM_010724	2239.6	1078.2	2.077
Nagk	NM_019542.1	638.1	307.2	2.077
Gstm4	NM_026764.2	1290.7	621.6	2.076
Chk	AK014174	414.5	199.8	2.075
0610012H03Rik	NM_028747.1	177.9	85.9	2.071
Crim1	XM_128751.4	227.7	110	2.070
LOC98434		251.9	121.7	2.070
2610002J02Rik	XM_131827.3	429.9	207.8	2.069
Ctse	NM_007799	1315.2	636.1	2.068
Pvrl1	XM_147334.1	61.4	29.7	2.067
Grwd1	NM_153419.1	65.2	31.6	2.063
	AF390178.1	55.5	26.9	2.063
Mmp9	NM_013599.2	79	38.3	2.063
Upp1	NM_009477.1	79	38.3	2.063
Ifi30	NM_023065.2	265.9	129.1	2.060
D630004K10Rik		1041.7	505.8	2.060
1700023M03Rik	NM_027078.1	221.9	107.8	2.058
6720458D17Rik		785.6	381.7	2.058
Sh3glb1	NM_019464.1	53.7	26.1	2.057
BC032967		82.9	40.3	2.057
Itgal	NM_008400.1	101.8	49.5	2.057
Ube1l	NM_023738.2	725.2	352.8	2.056
Rcn3	NM_026555.1	83.4	40.6	2.054
LOC382162	XM_356262.1	52.1	25.4	2.051
2600003E23Rik	NM_027373	137	66.8	2.051
Ccrl2	NM_017466.3	75.6	36.9	2.049
Mat2a	NM_145569	1342	655.4	2.048
Rassf4	NM_178045.3	276	134.8	2.047
Nudt13	NM_026341.1	89.2	43.6	2.046
Nap1l1	NM_015781.2	1002.3	490	2.046
2810489O06Rik	NM_175386.3	417.8	204.4	2.044
A930001C03Rik		160	78.3	2.043
4921528G01Rik	NM_023884.2	381.8	187.1	2.041
Robo1	NM_019413.1	56.3	27.6	2.040
Myo9b	NM_015742.1	468.2	230	2.036
Rasa2	NM_053268.1	87.7	43.1	2.035
4631426J05Rik	NM_029935	79.4	39.1	2.031
1200016E24Rik	XM_489305	5071.2	2500.5	2.028
Emp2	NM_007929.1	471.9	232.7	2.028
Rp2h	NM_133669	174.7	86.2	2.027
Psmb8	NM_010724	920.6	454.3	2.026
2510015F01Rik	XM_354801.1	217.8	107.5	2.026
AA407930	NM_133349.2	494.7	244.3	2.025
Ifitm1	NM_026820.2	711.4	351.6	2.023
9230112O05Rik	NM_173347.2	147.6	73	2.022
Rassf1	NM_019713.2	450.2	222.7	2.022
Pltp	NM_011125.1	535.8	265.1	2.021

Pecam1	NM_008816	508	251.4	2.021
Nt5e	NM_011851.2	227.3	112.5	2.020
Ifi47	NM_008330.1	751.1	372	2.019
2510009E07Rik	NM_001001881	750.6	372.2	2.017
AI642036	XM_109767.2	109.5	54.3	2.017
Set7	NM_080793	231.9	115	2.017
Tpm3	NM_022314	1040.5	516	2.016
4930579E17Rik	NM_178629	107.2	53.2	2.015
	AK087461.1	67.5	33.5	2.015
Zfyve16	NM_173392.1	57.8	28.7	2.014
6230425C21Rik	AK012678	455.2	226.6	2.009
Gas2l3	XM_137276	122.3	60.9	2.008
Samhd1	NM_018851.2	322	160.6	2.005
Cri1	NM_025613.1	54.5	27.2	2.004
Psap	NM_011179	7878	3932.7	2.003
Il1a	NM_010554	63.5	31.7	2.003
G630055P03Rik	NM_177150.1	168.6	84.3	2.000
Dhrs6	NM_027208.1	719	1440.1	0.499
1110007M04Rik	NM_026742.1	619.2	1240.4	0.499
Ddx6	NM_007841.2	552.3	1106.6	0.499
2310067G05Rik	XM_147277.1	253.6	508.9	0.498
Slc1a2	NM_011393	580.6	1165.9	0.498
4833416J08Rik		55.6	111.8	0.497
E130319B15Rik	NM_178663	44.2	88.9	0.497
5830406C17Rik	XM_488874	79.3	159.5	0.497
5730466C23Rik	NM_027469.1	48.1	96.9	0.496
Csnk2a1	NM_007788.2	36.5	73.6	0.496
2010005J08Rik	NM_178623.2	77	155.3	0.496
0710001D07Rik		118.1	238.2	0.496
Slc29a1	NM_022880.1	529.2	1067.4	0.496
Pard6a	NM_019695	52.2	105.3	0.496
6030411K04Rik	XM_486150	37.7	76.1	0.495
2610302F08Rik	AK011964	30.9	62.4	0.495
9030612M13Rik	NM_172458.2	215.5	435.2	0.495
LOC386068	XM_359052.1	130.4	263.4	0.495
2810455D13Rik		47.4	95.8	0.495
Pdk2	NM_133667.1	255.6	516.7	0.495
Saa4	NM_011316.2	1637.4	3312.1	0.494
Abca6	NM_147218.1	56	113.3	0.494
Tef	NM_017376.2	2107.6	4267.6	0.494
C430014D17Rik	NM_139304.1	57.9	117.3	0.494
LOC243823	XM_145307.2	133.9	271.3	0.494
Kifc2	NM_010630.1	36.1	73.2	0.493
Dlgh3	NM_016747.1	258.8	524.9	0.493
Knsl5	AK076271	137.5	278.9	0.493
6430590A07Rik	AK078307	49.2	99.8	0.493
4930527B16Rik	XM_147531.1	38.5	78.1	0.493
F11	NM_028066.1	98.9	200.7	0.493
1700008N02Rik		87	176.6	0.493
Eef2k	NM_007908	38.3	77.8	0.492
Krt1-10	NM_010660.1	63.8	129.6	0.492
A630034E16Rik	AK041749	31.6	64.2	0.492
1600021C16Rik	NM_028059.1	37.6	76.4	0.492

Ttc7b	XM_127105.4	296.3	602.2	0.492
4732496O19Rik	NM_133853.1	32.5	66.1	0.492
C730043O17		415.6	845.3	0.492
D5Bwg0860e	NM_027530.2	57	116	0.491
BC027174	NM_172260.1	36.2	73.7	0.491
Cklfsf8	NM_027294.1	935	1903.8	0.491
		35.1	71.5	0.491
4732466D17Rik	XM_129420.4	679.9	1385.3	0.491
Cbx2	NM_007623.2	51.7	105.4	0.491
Dgka	NM_016811.2	53.4	109	0.490
2510022D24Rik		97.4	199	0.489
Csnk2a1-rs3	AK031617	156.7	320.2	0.489
9030617O03Rik	NM_145448	40.6	83	0.489
C130071E11Rik	AK081716	32.1	65.7	0.489
Klf15	NM_023184.2	390.6	799.5	0.489
Adcy9	NM_009624.1	263.7	540.3	0.488
Car14	NM_011797.1	366.2	750.9	0.488
Pcsk4	NM_008793.1	138.5	284.4	0.487
Rdh11	NM_021557	2046.1	4201.8	0.487
Pfdn2	NM_011070.2	862	1770.4	0.487
Slc37a4	NM_008063.1	762.3	1565.7	0.487
Bcl2l12	NM_029410.1	32.1	66	0.486
Fgfrl1	NM_054071.1	193.8	398.5	0.486
Hpd	NM_008277.1	7967.3	16409.2	0.486
Pte2a	NM_134246.2	88.5	182.3	0.485
Hagh	NM_024284.1	2540.5	5234.5	0.485
1810020D17Rik	NM_183251.2	760.8	1567.6	0.485
Tle2	NM_019725.1	77.4	159.5	0.485
1500041I23Rik	XM_356257.1	75.3	155.2	0.485
E130013N09Rik	XM_488964	115.9	239	0.485
LOC235860	XM_142431.1	122.7	253.3	0.484
2810021G02Rik		144.1	297.6	0.484
C730014E05Rik	NM_177051.2	29.7	61.4	0.484
B130033B12Rik		29.7	61.4	0.484
Adh5	NM_007410.2	49.5	102.4	0.483
Amhr2	NM_144547.1	34.7	71.8	0.483
1300015B04Rik	XM_129157.2	140.5	290.8	0.483
Bai2	NM_173071.1	80.7	167.2	0.483
Msh3	NM_010829.1	27.8	57.6	0.483
4921531D08Rik	AK076602	54.3	112.6	0.482
Nr5a2	NM_030676.1	942.8	1958.4	0.481
Haao	BC012872	2595.9	5393.7	0.481
Bach2	NM_007521.2	81.3	169.1	0.481
1110020G09Rik	XM_127934.4	50.1	104.3	0.480
Olfr1380	NM_207573.1	31.7	66	0.480
LOC380712	XM_354627.1	382.2	796.7	0.480
4933439F18Rik	AK017120	30.1	62.8	0.479
Lin7a	XM_193582.3	44.1	92.1	0.479
9130422G05Rik	NM_025782	152	317.6	0.479
Rdh7	NM_017473.1	4436.1	9272.1	0.478
Gls2	XM_125928	3005.2	6288.8	0.478
Cpsf6		45.3	94.9	0.477
Zfml	BC076615	31.6	66.2	0.477

2900026A02Rik	NM_172884.1	34.6	72.5	0.477
Fzd8	NM_008058.1	61.7	129.4	0.477
Ga-pending	XM_125928.4	276.7	581	0.476
LOC381527	XM_355488.1	68.7	144.3	0.476
2400009B11Rik	NM_025886	132.3	278.1	0.476
Ppp2r5e	NM_012024.1	92.1	193.6	0.476
BC048082	NM_177922.2	33.1	69.6	0.476
Fxyd1	NM_052992.1	57.2	120.3	0.475
D030006P03Rik	AK083427	28	58.9	0.475
4833426J09Rik		555.3	1168.2	0.475
Cntf	NM_053007.1	142.7	300.4	0.475
Fxr2h	NM_011814.1	33.1	69.7	0.475
Rbks	NM_153196.1	208	438.3	0.475
Eva1	NM_007962.2	644.2	1357.5	0.475
Asb2	NM_023049.1	68.8	145	0.474
Zfp276	NM_020497.1	140.7	296.9	0.474
Np15	NM_019435.2	52.6	111.3	0.473
Ankhd1		76.8	162.6	0.472
Fbxo30	XM_125493	77.7	164.7	0.472
2400009B11Rik	NM_025886.2	66.6	141.2	0.472
Mospd3	NM_030037.1	192.7	408.8	0.471
BC023823	NM_153566.1	108.7	230.6	0.471
Slc25a22	NM_026646.1	1225.5	2600.1	0.471
5033421J10Rik		37.3	79.2	0.471
Tuba4	NM_009447.2	38.9	82.7	0.470
Peo1	NM_153796	37.1	78.9	0.470
Pxmp2	NM_008993	2025.3	4307.3	0.470
Slc29a1	BC004828	113.3	241	0.470
Mast3	NM_199308.1	682.6	1452.7	0.470
E430023L22Rik	AK088688	33.2	70.7	0.470
Dnajb9	NM_013760	330.2	703.8	0.469
1500031N24Rik	XM_128010.4	476.9	1016.8	0.469
Hgd	AK050193	362.5	772.9	0.469
Alas2	NM_009653.1	1589.7	3392.4	0.469
2810408E11Rik	NM_029582	40.3	86	0.469
Ttc14	NM_025978.2	133.6	285.6	0.468
Gorasp1	NM_028976.1	64.8	138.6	0.468
Crygn	NM_153076	28	59.9	0.467
4833424P18Rik	NM_029017	325.7	697.5	0.467
3021401C12Rik		148.8	319	0.466
AI854408	NM_172538.2	30	64.4	0.466
Ak4	NM_009647.1	268.4	576.3	0.466
Zfp523	NM_172617.1	38	81.6	0.466
Cyp2j9	NM_028979.1	117.9	253.2	0.466
1810009N02Rik	NM_026939.1	243.9	524	0.465
B930008K04Rik	NM_175446.2	150.6	323.7	0.465
Pcsk4	NM_008793.1	57.6	123.9	0.465
Etnk2	NM_175443	30.4	65.4	0.465
5730478M09Rik	XM_358792.1	123.8	266.4	0.465
AI849156	NM_183142.1	50	107.6	0.465
Tob2	NM_020507.2	265.1	570.8	0.464
Upk3b	NM_175309.3	28.6	61.6	0.464
C430014B12Rik		37.6	81	0.464

D030010H02Rik	AK083433	51	110	0.464
Pdk1	NM_172665.1	712.8	1538.3	0.463
A230075M04Rik		74.7	161.3	0.463
BC024868	NM_199149	59	127.5	0.463
Lss	NM_146006	491.2	1061.9	0.463
Fahd1	NM_023480.1	1083.3	2342	0.463
Cstf3	NM_145529.1	290.6	629.7	0.461
A930037O16Rik		157.7	341.8	0.461
Car1	NM_009799.1	105.4	228.5	0.461
Acy1	NM_025371.1	48.2	104.5	0.461
Foxb1	NM_022378	28.6	62.1	0.461
2900064A13Rik	NM_133749	97.5	212	0.460
Dexi	NM_021428.3	149.3	324.7	0.460
2700038N03Rik	NM_027356.1	52.5	114.2	0.460
C86987	XM_127523.2	32.5	70.7	0.460
Adck5	NM_172960.1	151.3	329.2	0.460
Prkaa2	XM_131633	36	78.5	0.459
4632428M11Rik	NM_028730.2	129.7	282.9	0.458
Hes6	NM_019479.2	3727.9	8132.1	0.458
0610007P08Rik	XM_484269	58.9	128.6	0.458
AW491445	NM_134154.1	1188.4	2597.7	0.457
Slc38a3	NM_023805.2	3025.6	6616.5	0.457
D0H4S114	NM_053078.3	309	675.8	0.457
4631409F12Rik	AK028452	39.7	86.9	0.457
Akap9	NM_194462.1	37.3	81.7	0.457
Acy1	NM_025371.1	219.5	481	0.456
BC026432	NM_146202.1	100.6	220.5	0.456
Extl1	NM_019578	214.9	471.1	0.456
E130302P19Rik	AK087474	103.4	226.9	0.456
Krt2-6b	NM_010669.1	27.4	60.2	0.455
LOC381534	XM_355502.1	29.2	64.2	0.455
D7Ertd743e	NM_153525.2	82.5	181.4	0.455
Edg8	NM_053190.1	27.9	61.4	0.454
6820449I09Rik	NM_177128.2	132.5	291.6	0.454
Sca1	NM_009124.2	280.5	617.4	0.454
9030625G08Rik	NM_025780	82	180.5	0.454
Rad51l3	NM_011235.2	51.4	113.2	0.454
Cc1	XM_123485.1	40.1	88.5	0.453
2310002J21Rik		211.4	467.6	0.452
Otub2	NM_026580.1	31.1	68.8	0.452
BB114266	NM_172763.1	49.8	110.2	0.452
6430543K15Rik		35.2	77.9	0.452
1810014B01Rik		36.9	81.7	0.452
C330020G15Rik		36.7	81.3	0.451
Tmem25	NM_027865.1	360.9	800.4	0.451
C920004H05Rik	AK083320	32	71	0.451
D130043K22Rik	XM_111397.3	140.3	311.3	0.451
Fasn	NM_007988.1	5468.5	12136.6	0.451
Phf7	NM_027949.1	63.8	141.6	0.451
E2f2	NM_177733.2	72.4	160.7	0.451
Fgf1	NM_010197.2	263.3	584.9	0.450
Zfp354a	NM_009329.2	57.5	128	0.449
5730577G12Rik	AK030766	126.8	282.3	0.449

Anks1	NM_181413.2	73.2	163	0.449
Ppp1r15b	NM_133819	87.9	195.8	0.449
Igfals	NM_008340.2	1799.4	4018.4	0.448
Es22	NM_133660.1	1126.8	2522.2	0.447
5730460G06Rik		30.4	68.1	0.446
LOC380997	XM_354908.1	57.5	129	0.446
Slc4a1	NM_011403.1	56.1	125.9	0.446
9530082I15Rik	AK035657	31.6	71	0.445
Leng1	NM_027203.2	49.2	110.7	0.444
Hsd17b7	AK077914	33.5	75.4	0.444
Tpd52l1	NM_009413.1	58.2	131.1	0.444
Il1rap	NM_008364.1	1594.2	3601.1	0.443
6330400D04		91	205.6	0.443
Shmt1	NM_009171	1139.1	2575	0.442
Ceacam1	NM_011926.1	206	468.3	0.440
B130016H12Rik		102.8	233.7	0.440
BC024659	XM_488673	73.5	167.2	0.440
Sbk	NM_145587.1	485.5	1106.5	0.439
Rab22a	NM_024436.1	63.2	144.2	0.438
3222402P14Rik	XM_135153.4	30.5	69.7	0.438
Zfp128	NM_153802	29.4	67.2	0.438
D430045C01Rik	AK085153	35.3	80.7	0.437
7420701I03Rik		56.8	130.2	0.436
Acy1	NM_025371.1	255.3	585.8	0.436
A530050D06Rik	XM_203596	886.9	2035.2	0.436
Cat	NM_009804	124.5	286.2	0.435
1810005K13Rik		147.5	339.4	0.435
BC023892	XM_135029.3	70	161.3	0.434
BC031575	XM_484525	39.6	91.6	0.432
Tardbp	NM_145556.2	62.8	145.3	0.432
1700080G11Rik		195.9	453.7	0.432
Stard4	NM_133774.2	1472.7	3412.6	0.432
Fbxo3	NM_020593.2	36.1	83.7	0.431
2210420L05Rik		413.6	959.2	0.431
Lce-pending	AK087440	138.8	321.9	0.431
Ptk6	NM_009184.1	33.5	77.7	0.431
Stau2	NM_025303	57.9	134.3	0.431
Paqr9	NM_198414.1	1062.4	2465.2	0.431
4632419F02Rik	AK028526	46.8	108.6	0.431
Sms	NM_009214.2	34.1	79.2	0.431
E430033B07Rik	AK088947	199.2	462.8	0.430
Map17	NM_026018.1	43.7	101.6	0.430
D930048J18Rik	AK086738	25.5	59.3	0.430
B230342M21Rik	NM_133898.1	579.3	1347.9	0.430
Gbe1	AK050423	32.6	75.9	0.430
D830044I01Rik	AK052922	34.1	79.4	0.429
Abca8a	NM_153145.1	843.3	1964.2	0.429
Hmg20a	AK039222	30.9	72	0.429
2810439F02Rik	AK080904	54	125.9	0.429
BC024386		1476.8	3452.8	0.428
Car11	NM_009800.2	38.7	90.6	0.427
D630035N04Rik	AK085505	948.3	2220.2	0.427
9230112E08Rik	NM_177264	45.4	106.3	0.427

LOC381277	XM_355219.1	35	82	0.427
A730016A17		32.7	76.7	0.426
Ulk1	NM_009469.3	379.7	891	0.426
1700020C11Rik	NM_026443.2	92.2	216.4	0.426
A630084C02Rik	AK042344	25	58.7	0.426
E130106K10	XM_136506.3	113.6	267.1	0.425
2010001J22Rik	XM_128172.4	191.4	450.1	0.425
9430088D19Rik		135.6	319.5	0.424
3110057O12Rik	NM_026622.1	71.1	167.8	0.424
Il1rap	NM_134103.1	613.2	1447.5	0.424
Prodh	NM_011172.1	756.7	1787.3	0.423
Paox	NM_153783.2	327.4	773.4	0.423
Ppargc1b	NM_133249	233.4	551.6	0.423
	AK002608.1	1896.2	4489.7	0.422
Ng23	XM_358322.1	24.6	58.3	0.422
BC037135	NM_173763.2	140.6	334	0.421
AV071179	NM_031180.1	282.5	671.5	0.421
Dbp	NM_016974.1	1682.3	4001.8	0.420
Mup3	NM_010845	15483.3	36837.9	0.420
Cyp4a12	NM_172306.1	830.6	1976.7	0.420
Bat9	NM_198886.2	92.5	220.3	0.420
Zap70	NM_009539.2	290.9	693.9	0.419
2610009I02Rik	NM_028115	43	103.6	0.415
Ccbl1	NM_172404.2	835.2	2013.1	0.415
Smarca2	NM_011416	48.7	117.4	0.415
Sult5a1	NM_020564.1	26.4	63.7	0.414
Per3	NM_011067	180.3	435.3	0.414
2210039O17Rik	AK019056	106.2	256.5	0.414
Harp	NM_028085.1	83.4	202	0.413
0610031G08Rik		221.9	537.5	0.413
Pank1	NM_023792.1	337.3	817.5	0.413
3110045D15Rik	AK014178	43.2	104.8	0.412
AU018778	NM_144930.1	1190.6	2899.1	0.411
Sntg2	NM_172951.1	207.1	505.8	0.409
Onecut1	NM_008262	44.9	109.7	0.409
Mpst	NM_138670.1	48.2	117.8	0.409
B430005K18Rik	AK046551	169.6	415.3	0.408
	AK012972.1	31.5	77.3	0.408
BC016198	NM_203507.1	63.8	156.6	0.407
Pqlc2	NM_145384	30.3	74.4	0.407
A930034L06Rik	NM_175692.2	28.3	69.6	0.407
9430098F02Rik		29.7	73.1	0.406
LOC383125	XM_356890.1	135.9	334.6	0.406
Accn5	NM_021370.1	399.2	983.8	0.406
Dpm1	NM_010072.2	230	567.1	0.406
MGC25972	NM_177406.2	6156.3	15191.8	0.405
Elovl6	NM_130450.1	680	1681.3	0.404
Sned1	NM_172463.3	339.1	839.5	0.404
C730048C13Rik	NM_177002.2	454.9	1126.9	0.404
Slc43a1	XM_130259.4	32.4	80.5	0.402
Timm10	NM_013896	37.2	92.6	0.402
B230105J10	XM_484075	33.3	83	0.401
Zfp445	NM_173364.3	39.7	99	0.401

BC039632	XM_284356.2	89.6	223.7	0.401
9430088B20Rik		82.5	206.1	0.400
A930014K01Rik	NM_175537.2	24	60	0.400
C230004L04		24	60	0.400
C730048C13Rik	NM_177002.2	50.7	126.9	0.400
Caln1	NM_021371.1	59	147.7	0.399
2610301B20Rik	NM_026005.2	29.4	73.8	0.398
Hyal1	NM_008317.2	225.4	568.4	0.397
Grem2	NM_011825.1	60.4	152.5	0.396
2210401K01Rik		129.5	327	0.396
2610009I02Rik	NM_028115.2	108.2	273.4	0.396
Enpep	NM_007934.1	57.9	146.4	0.395
C730018L13Rik	AK050126	1206.1	3055.6	0.395
1300010A20Rik	NM_146173.1	48.3	122.4	0.395
BC066107	NM_207245.1	23.7	60.1	0.394
Lrpprc	NM_028233.1	84.1	213.3	0.394
Wbscr14	NM_021455.2	607.8	1543.7	0.394
2310035P21Rik		124.2	315.8	0.393
Prkcdbp	NM_028444.1	105	267.4	0.393
Abcb10	NM_019552.1	114.1	290.7	0.393
0610012D14Rik	NM_026690.1	147.2	375.6	0.392
Hook3	XM_134108.3	164.7	420.6	0.392
Got1	NM_010324.1	594.5	1519.4	0.391
Kcnk5	NM_021542.2	77.3	198.4	0.390
Ppargc1a	NM_008904.1	79.2	203.6	0.389
Ppm1l	NM_178726.1	78.5	202.2	0.388
Afmid	NM_027827.2	1081.7	2788.5	0.388
Terf2	AK048767	71.8	185.4	0.387
Npr2	NM_173788.2	205.5	531.8	0.386
Srd5a1	NM_175283.2	173.7	450.4	0.386
D130067I07Rik	AK051715	28.8	75.2	0.383
Thea	NM_025590.3	187.2	489.1	0.383
E130106K10Rik	XM_136506	143.1	374.9	0.382
A930029B02Rik	NM_178779.2	415.1	1087.7	0.382
A330081F11Rik	AK039667	120.4	315.5	0.382
LOC386288	XM_359160.1	28.3	74.2	0.381
Hes6	NM_019479.2	142.9	375	0.381
Sucnr1	NM_032400.1	375.3	985.8	0.381
Onecut1	NM_008262.2	24.1	63.4	0.380
1300007L22Rik	NM_027917.1	466.8	1228.7	0.380
4930528F23Rik	XM_128478.2	214.5	565.8	0.379
B930075F07		191.9	507	0.379
Car14	AK009805	42.5	112.3	0.378
D1Bwg0212e	NM_028043.2	56.6	150	0.377
2010305C02Rik	NM_027249	463.1	1228.3	0.377
C530044G15Rik	AK083075	75	199	0.377
Acly	NM_134037.2	3891.1	10354	0.376
E430016L07Rik		35.5	94.5	0.376
5730414N17Rik		95.6	254.9	0.375
Cyp4f14	NM_022434.1	3116.9	8325.3	0.374
BC005682	NM_033562.2	39.5	105.6	0.374
Homer2	XM_133550.4	407.6	1089.9	0.374
A930018M24Rik	NM_199318	61	163.2	0.374

4933437K13Rik	AK086865	48.4	129.8	0.373
6230415M23Rik		96.6	260	0.372
BC020535	NM_145536.1	94.7	256	0.370
Timm17b	NM_011591	68	183.9	0.370
2310001H17Rik	XM_489155	314.2	851.4	0.369
1810046K07Rik	XM_134800.2	57.7	156.5	0.369
AA407809	NM_030724.1	50.8	137.8	0.369
0610031O16Rik		62.4	169.3	0.369
Smo	NM_176996.3	30.8	83.7	0.368
A530030B07Rik	AK040847	26.1	71.1	0.367
Prok1	XM_487748	158.2	431.9	0.366
CRAD-L	NM_145424	1167.6	3193.7	0.366
Zfp297b	NM_027947.1	83.6	229.1	0.365
F7	NM_010172.1	336.1	922.1	0.364
2900060F21Rik	AK013732	50.9	139.7	0.364
Reck	NM_016678	32.2	88.6	0.363
Srprb	NM_009275.2	30.3	83.4	0.363
Cyp17a1	NM_007809.2	380	1048.4	0.362
2610009I02Rik	NM_028115.2	89	246.1	0.362
Ccrn4l	NM_009834.1	114	315.5	0.361
Adpn	NM_054088	142.8	395.6	0.361
Ppm1l	NM_178726	131.6	364.7	0.361
Afmid	NM_027827.2	180.1	502	0.359
2310007J06Rik		28.1	78.5	0.358
4931413A09Rik	XM_147407.2	43.5	122.1	0.356
LOC383215	XM_356927.1	328.3	922	0.356
Fthfd	AK007822	86.2	242.3	0.356
Ppm1l	NM_178726.1	42.8	120.9	0.354
LOC385673	XM_358902.1	21.3	60.2	0.354
Cmah	NM_007717.1	80.9	228.8	0.354
	XM_129087.4	578.5	1637.2	0.353
D11Ertd636e	NM_029794.1	234.3	665.3	0.352
Slc25a10	NM_013770	67.4	191.4	0.352
Afmid	NM_027827.2	357.4	1016.3	0.352
Avpr1a	NM_016847.2	66.7	190.5	0.350
9030616G12Rik		54.8	157.8	0.347
Narfl	NM_026238.2	21.4	61.7	0.347
9030622O22Rik		34.4	99.2	0.347
Pxmp2	NM_008993.1	944.2	2728.8	0.346
2010001J22Rik	XM_128172.4	58.8	170.2	0.345
Sds	NM_145565.1	1239.6	3588.9	0.345
Abcc6	NM_018795.1	61.5	178.4	0.345
1110006G14Rik	XM_355930.1	53.9	156.9	0.344
Ell3	NM_145973.2	97.3	284.1	0.342
Arl8	NM_029466.2	31.8	93.2	0.341
Ccrn4l	NM_009834.1	108.4	318.4	0.340
9530025L08Rik		66.4	195.2	0.340
Afmid	NM_027827.2	183.6	540.6	0.340
Mid1ip1	NM_026524.2	746.1	2198	0.339
LOC218276	XM_122579.3	454.3	1348.5	0.337
Gnpda1	XM_124695.2	47.3	140.5	0.337
Mcm10	NM_027290.1	184	547.1	0.336
2610110G12Rik	NM_028476.2	19.9	59.2	0.336

C730048C13Rik	NM_177002.2	178.6	533	0.335
9130221J18Rik		264.1	791.9	0.334
Pklr	NM_013631.1	317.2	951.3	0.333
Clcn2	XM_147240.1	116.7	350	0.333
9030618K22Rik		382	1145.7	0.333
Cmah	NM_007717.1	43.8	131.4	0.333
9530091C08Rik	NM_177159	20.7	62.1	0.333
LOC245892	XM_147335.2	77.2	231.9	0.333
6330514A18Rik	NM_183152.1	30.3	91.4	0.332
Mpv17l	NM_033564.1	26.4	79.8	0.331
BC056929	NM_172928.1	163.9	497.9	0.329
Sc5d	NM_172769	494.1	1501.7	0.329
Pipox	NM_008952.1	478.8	1457.1	0.329
Rad23b	AK084917	20.8	63.4	0.328
Temt	NM_009349	9959.6	30411	0.327
A230013K13Rik	AK038454	30.7	93.8	0.327
Per2	NM_011066.1	248.4	759.4	0.327
Acacb	NM_133904	449.6	1376.7	0.327
Nudt7	NM_024437	1636.2	5014.2	0.326
LOC383576	XM_357131.1	44.8	137.4	0.326
A530020H22Rik	AK079944	236.6	730.9	0.324
Egfr	NM_207655.1	54.6	168.7	0.324
AI317395	NM_144821.2	226.8	705	0.322
C730029A08Rik		409.3	1276.3	0.321
LOC384348	XM_357593.1	119.9	375.7	0.319
B130034H21Rik	AK045115	29	91.1	0.318
E130014J05Rik	NM_145989.1	21.4	67.4	0.318
Slc2a9	NM_145559.1	87.8	279	0.315
Gnmt	AK082459	673.1	2142.4	0.314
Zfp50	XM_127016.2	291.3	927.6	0.314
Kif13b	XM_283218.2	25.6	81.6	0.314
Fn3k	NM_022014.1	110	351.1	0.313
4933432P15Rik	NM_175164.2	28.7	91.7	0.313
Agxt2l1	NM_027907.1	525.9	1685.1	0.312
Zfp395	NM_199029.1	42.1	134.9	0.312
A930023F12Rik	AK044567	26.6	85.3	0.312
Nox4	NM_015760.2	295.1	948.9	0.311
Lin7a	XM_193582	275.2	885.7	0.311
Sdro	NM_027301.3	91.1	293.5	0.310
5730594E01Rik	AK077748	37.8	122.2	0.309
Sds	NM_145565.1	759.8	2458.1	0.309
Coxvib2	NM_183405.1	39.6	128.4	0.308
Afmid	NM_027827.2	370.6	1206.4	0.307
Polr3g	XM_283153	36.3	118.3	0.307
9130422G05Rik	NM_025782.2	145.8	477.2	0.306
Nfe2	NM_008685.2	29.3	95.9	0.306
LOC385792	XM_358947.1	22.3	73	0.305
D830041I17Rik	AK052921	44.5	145.9	0.305
LOC385389	XM_358219.1	19.6	64.8	0.302
Slc11a2	NM_008732.1	50.5	167.2	0.302
1810033M07Rik	NM_026983.1	49.3	163.7	0.301
AI481316	XM_148986.1	165.4	550.3	0.301
Ddx6	NM_007841.2	17.9	60	0.298

Slc25a25	NM_146118.2	281.3	943.1	0.298
Scd1	NM_009127.2	9931.2	33740.7	0.294
Fndc4	NM_022424.2	46.1	156.9	0.294
Ar	NM_013476.2	57.9	199.3	0.291
Slc22a7	NM_144856.1	139.1	481.1	0.289
2810439F02Rik	NM_028341.1	635.7	2204.1	0.288
Ppp1r3b	NM_177741	716.1	2513.9	0.285
9530075P13Rik	AK035604	22	77.7	0.283
Mpv17l	NM_033564.1	92.2	325.8	0.283
Acas2	NM_019811.2	1972.3	7032.2	0.280
9030617O03Rik	NM_145448.2	16.4	58.9	0.278
Egfr	NM_007912.3	714	2564.6	0.278
Spag4	NM_139151	71.1	255.7	0.278
Pde6h	NM_023898	32.4	116.9	0.277
Aacs	NM_030210.1	1213.5	4381.7	0.277
LOC381806	XM_355806.1	477.3	1735.1	0.275
C330008L01Rik	NM_175351	19	69.2	0.275
Ppp1r3b	NM_177741.2	185.1	678.6	0.273
9630019E01Rik		26.5	98.9	0.268
Afmid	NM_027827.2	120.5	449.9	0.268
D930010J01Rik	NM_134147.2	306.2	1156.3	0.265
	AK052902.1	19.2	73.9	0.260
1700051I12Rik	XM_181390.2	83.9	323.7	0.259
Mpp4	NM_145143.1	19.7	76.5	0.258
4833439F03Rik		30.8	120.6	0.255
Spry4	NM_011898.2	46.9	184.9	0.254
G430046L24Rik	AK089991	15.1	59.6	0.253
Plg	AK040840	28.1	111.1	0.253
Upp2	NM_029692.1	332.3	1319.6	0.252
4833413G10Rik	XM_149575.1	22.5	89.4	0.252
Mvd	NM_138656.1	103.9	420.8	0.247
Egfr	NM_207655.1	870.5	3525.7	0.247
Upp2	NM_029692.1	316.4	1292.4	0.245
2810439F02Rik	NM_028341.1	674.1	2753.9	0.245
BC024139	NM_198172	59.2	243.7	0.243
G6pc	NM_008061.2	1405.4	5823	0.241
LOC386294	XM_359162.1	72.6	303.5	0.239
Cmah	NM_007717.1	37.2	156.3	0.238
Ela1	NM_033612.1	274.4	1157.9	0.237
Upp2	NM_029692.1	257.7	1114.6	0.231
9030024J15Rik		848.9	3688	0.230
LOC381770	XM_355767.1	55.9	246.7	0.227
A330072B11Rik	AK039609	68.4	305.5	0.224
A930036K24Rik		110.6	500.8	0.221
Hsd3b2	NM_153193.2	14.9	69	0.216
Gnat1	NM_008140.2	61.1	284.5	0.215
1700001C19Rik	XM_128669	53.2	249.1	0.214
LOC13909	NM_144511.1	163.8	768.3	0.213
Lin7a	XM_193582.3	63.2	300.8	0.210
BC024137		94.2	453.5	0.208
Sdro	NM_027301.3	56	272.3	0.206
A930016D02Rik	NM_176920.2	40.3	204.9	0.197
Slc10a1	NM_011387.1	69.2	352.4	0.196

A930016D02Rik	NM_176920.2	85.4	441	0.194
2900016G23Rik	XM_147738.1	12.3	64.3	0.191
Tmie	NM_146260.1	121.3	635.6	0.191
1700012D01Rik		28.2	159	0.177
Scnn1a	NM_011324.1	49.6	299.5	0.166
Thrsp	AK050300	48.9	299.3	0.163
Mmd2	NM_175217.3	180.4	1112.1	0.162
5730512J02Rik	AK017766	28.5	175.9	0.162
A630078J04Rik	AK042286	11	68.1	0.162
B230342N21Rik	AK046118	16.1	101	0.159
Col27a1	NM_025685	31.4	198.4	0.158
B430114K07Rik	AK046591	18.1	116.5	0.155
4930481A15Rik	XM_148889.4	11.8	76.6	0.154
Chrna4	NM_015730.4	60.1	392.5	0.153
1700018L02Rik		8.7	57.1	0.152
		10	66.6	0.150
Cyp7b1	NM_007825.1	729.3	5051.1	0.144
1810059H22Rik		16.6	117.1	0.142
1700001C19Rik	XM_128669.1	19	145.4	0.131
4930513E20Rik	XM_149158.1	7.9	65.4	0.121
Camk4	NM_009793	8.1	68	0.119
Got2	NM_010325	23.7	204.5	0.116
2810007J24Rik	NM_175250.3	913.6	7932.3	0.115
Hsd3b2	NM_153193.2	134.2	1190.9	0.113
LOC239727	XM_156408.2	88.7	803.9	0.110
Nnmt	NM_010924.1	38.6	368.2	0.105
Thrsp	NM_009381.2	573.7	5521	0.104
Col27a1	NM_025685.2	14.3	142.9	0.100
LOC241041	XM_136557.2	96.2	962.9	0.100
Hsd3b2	NM_153193.2	20.7	211.6	0.098
Mup2	NM_008647	1730.7	17843.1	0.097
Gna14	NM_008137.2	29.2	311	0.094
LOC384022	XM_357375.1	530	6096.4	0.087
1810073K19Rik	NM_183257.1	2334.8	27788.4	0.084
Sp4	NM_009239.1	4.9	59.2	0.083
AW320017		6.9	84.1	0.082
LOC236060	XM_135472.3	998.7	12951.5	0.077
Serpina4-ps1	XM_127122.2	18	317.9	0.057
LOC383483	XM_357088.1	21.4	417.8	0.051
0610008F07Rik	NM_197983.1	24.9	488.2	0.051
Mup4	NM_008648.1	161.8	3675	0.044
E430021N18Rik	NM_144796	67.8	1990.5	0.034
1810029C22Rik	XM_284386.2	5.7	168.8	0.034
Elovl3	NM_007703.1	6	282.8	0.021
LOC194586	XM_112088.2	30.7	3401.8	0.009
Slc38a5	NM_172479.1	0.8	90.4	0.009
Slco1a1	NM_013797	5.4	2162	0.002
Hsd3b5	NM_008295.1	2.6	6810.8	0.000

Supplementary Table 4. Genes regulated by RIZ1 knockout as revealed by DNA microarray analysis. The RNAs used for analysis were from wild type and knockout mice of four months of age on balanced diet. Data represent means of 2 animals per subgroup. Genes in bold were also regulated by diet. Only genes showing more than 2 fold changes are listed.

Supplementary Table 4

Symbol	Accesion	Wt	Ko	Wt/Ko
Dmbt1	NM_007769.1	201.9	17	11.876
BC003277	NM_145402.2	2641.9	558.2	4.733
LOC381534	XM_355502.1	69.2	17.1	4.047
Socs3	NM_007707.2	332.5	86.5	3.844
Nrp	AK030358	561.7	146.9	3.824
Gadd45g	NM_011817.1	938.2	264.6	3.546
Serpina9	NM_027997	76.6	22.3	3.435
Socs2	NM_007706.1	524	154.2	3.398
Chk	AK014174	64.1	19.1	3.356
2700060E02Rik	NM_026528.1	59.2	18.1	3.271
2900064B18Rik		253	80.4	3.147
2310035P21Rik		132.4	44.8	2.955
LOC383125	XM_356890.1	117.8	40.1	2.938
Idb2	AK013239	1688.5	619.7	2.725
Nxf1	AK086527	56.9	20.9	2.722
Hnrpk	NM_025279.1	109.6	40.7	2.693
9530029F08Rik		61.5	23	2.674
D830014E11Rik	NM_177251.2	67.3	25.7	2.619
Elovl3	NM_007703.1	418.8	160.5	2.609
Rutbc2	NM_172718.1	94	37.4	2.513
2810405K07Rik	NM_028141	127.4	52	2.450
B230314M03Rik	NM_001033800.1	71.6	29.6	2.419
4930588K23Rik	NM_001033809.1	65.4	27.3	2.396
Cited2	NM_010828.1	76.4	31.9	2.395
LOC239727	XM_156408.2	929.1	390.8	2.377
Insig2	NM_178082.2	213	89.6	2.377
Sox9	NM_011448	232.5	99.9	2.327
Fmn2	NM_019445.1	76.7	33	2.324
1110067D22Rik	NM_173752.1	73.6	31.9	2.307
Tgfb1i4	NM_009366.1	170.5	74.5	2.289
LOC383483	XM_357088.1	257.8	112.9	2.283
	AK041123.1	65.2	29.1	2.241
Acaca	NM_133360.1	60.5	27.1	2.232
Ugt1a6	NM_145079	287.4	128.9	2.230
Rnf125	NM_026301.1	466.1	214.2	2.176
Ugt1a6	NM_145079	66.7	30.7	2.173
B930007L02Rik	NM_001015507.1	64	30.5	2.098
2810411C16Rik	AK013079	134.3	64.2	2.092
Gjb2	NM_008125.2	61.5	29.4	2.092
Bcl6	NM_009744.2	806.9	386	2.090
Slc25a30	NM_026232.1	60.1	29.3	2.051
5033430I15Rik	XM_127301.2	95.4	46.6	2.047
Hrg	NM_053176.1	290.4	142.3	2.041
Rasl11b	XM_355606	156.3	77.4	2.019
Insig2	NM_133748.1	885.5	441.4	2.006
9530025L08Rik		68.1	136.3	0.500
LOC329554	XM_287194.1	34.3	69.3	0.495

1500041J02Rik	NM_026424.2	279.2	568.8	0.491
Pte2a	NM_134246.2	258.7	534.5	0.484
2310067E08Rik	NM_028013.1	39.5	81.9	0.482
LOC333621	XM_289715.2	28	58.7	0.477
Upp2	NM_029692.1	1065.5	2251	0.473
8430436L14Rik	XM_355454	37.5	79.4	0.472
8430403J19Rik	AK033358	155.4	331.7	0.468
Fthfsdc1	NM_172308.2	28.6	61.1	0.468
G0s2	NM_008059.1	980.7	2115.3	0.464
Kcnk5	NM_021542.2	171.2	372.3	0.460
Upp2	NM_029692.1	931.6	2031.9	0.458
Ren1	NM_031192	209.2	480.6	0.435
1810011O10Rik	NM_026931.1	34.8	80.1	0.434
LOC380906	XM_354819.1	30.6	71	0.431
1700018O18Rik	XM_131683.2	2779.9	6491.1	0.428
Bhlhb9	NM_198161.1	39.8	93	0.428
Per1	NM_011065.2	89.3	208.7	0.428
BC016495	NM_145497.1	45.3	108.3	0.418
Sirt1	NM_019812.1	23.2	55.8	0.416
Hrasls3	NM_139269.1	24	58.9	0.407
6430406H24Rik	AK032164	26.7	65.8	0.406
4833416J08Rik		24.7	61.7	0.400
Abcc4	XM_139262.2	35.6	89.1	0.400
LOC194586	XM_112088.2	426.6	1077.6	0.396
2310011C19Rik		29.7	75.3	0.394
Alas1	NM_020559.1	8787.3	22428.4	0.392
Nrg4	NM_032002.1	41.4	105.7	0.392
Igsf10		30.3	78.2	0.387
LOC241901	XM_143135.3	100.5	263	0.382
Cyp4a14	NM_007822.1	3523.7	9313.8	0.378
Gdf15	NM_011819.1	77.6	212.9	0.364
Thrsp	NM_009381.2	3997	11092.6	0.360
Igl-V1	XM_148393.1	47.9	133.3	0.359
Ibrdc3	XM_204030	22.7	64	0.355
Pfkfb3	NM_133232.1	75.2	213.4	0.352
Lpin1	NM_015763	251.3	727.1	0.346
9530051K01Rik	XM_485965	172.8	503.2	0.343
1110028A07Rik	NM_026808.1	21.9	63.9	0.343
Cd79b	NM_008339.1	19.6	57.7	0.340
Nrg4	NM_032002	68.7	212.9	0.323
Tmc7	NM_172476.2	24.1	78.3	0.308
Usp2	NM_198091.1	188.5	655.8	0.287
LOC229599	XM_131070.3	19.3	74.5	0.259
Usp2	NM_198091.1	26	102.1	0.255
Cyp7a1	NM_007824.2	1659.4	6611.9	0.251
Ctgf	NM_010217	12.3	56.4	0.218
Ccrn4l	NM_009834.1	130.6	664.3	0.197
Ccrn4l	NM_009834.1	26.1	159.4	0.164
Jun	NM_010591.1	53.4	333.1	0.160
1600032L17Rik	XM_127272	25.1	218.5	0.115
1110005F07Rik	NM_025383	46.8	449.2	0.104
Egr1	NM_007913.2	216.4	2368.3	0.091
Fos	NM_010234.2	1.1	95	0.012

Supplementary Table 5. Methyltransferases with high Km value for SAM were downregulated by methyl-imbalanced diet. The Km value for SAM and Ki value for SAH are shown for various methyltransferases. The ratio (fold changes) Diet 1 *vs*. Diet 2 in expression levels of the methyltransferases was calculated from quantitative RT-PCR. Data represent means of at least 3 animals per subgroup at 2 months of diet treatment. **P* < 0.05 Diet 1 *vs.* Diet 2 (Student's t-test, 2 tailed).

	SAM km/SAH ki (μM)	Diet 1 *vs*. Diet 2
GNMT	100/35	4.6*
GAMT	49/16	2.3*
TEMT/INMT	54/8.6	8.2*
COMT	3.1/1	1.1
TPMT	3/5.8	1.0
PCMT	2/0.08	1.0
ICMT	2.1/9.2	0.8
DNMT1	1.4/1.4	1.2
PRMT1	8/2.3	0.9
G9a	1.8/2.3	0.9

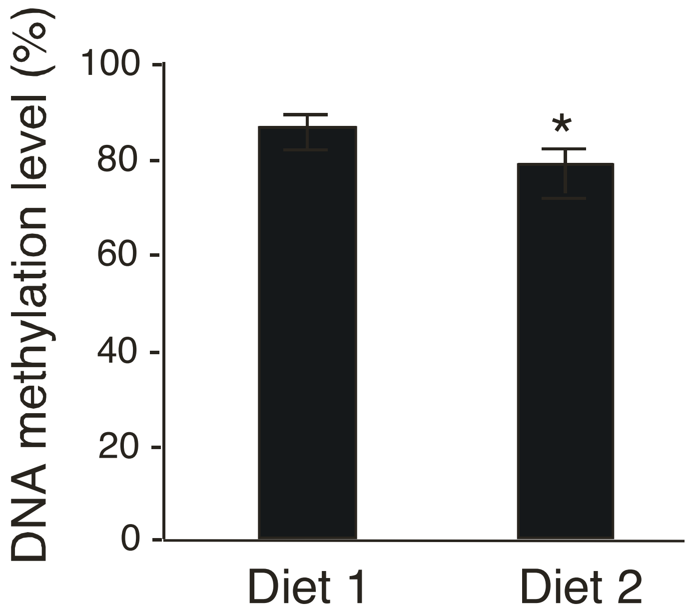
Supplementary Figure Legends:

Supplementary Figure 1. Western blot analysis confirming recognition of RIZ1 but not RIZ2 by the Abcam RIZ1-specific antibody ab9710. Total protein extracts of livers from either RIZ1 wild type or knockout animals were resolved by SDS gel followed by western blot using RIZ1 antibody ab9710. Equal loading was confirmed by western blot using beta-actin antibody.

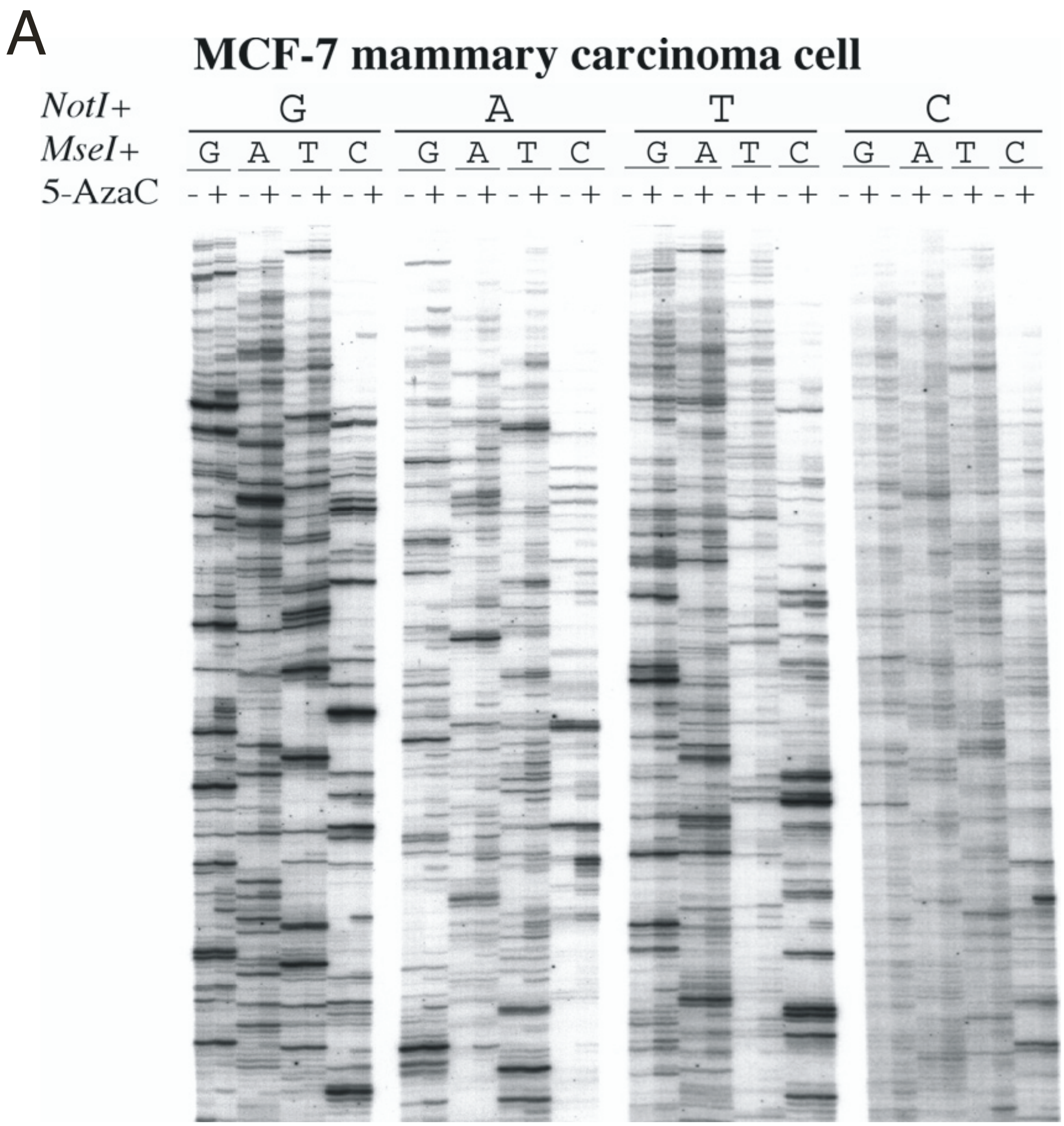
Supplementary Figure 2. DNA hypomethylation in mice fed with diet 2. Total genomic DNAs were isolated from livers of mice on either diet 1 or diet 2 for 15 months. The methylation levels of these DNAs were determined by the Sss1 enzyme assay. Data are the means $\pm$ SD of 3 animals per subgroup. *$P = 0.03$ (Student's t-test, 2 tailed).

Supplementary Figure 3. Analysis of methylation changes in CpG rich regions of the genome by MS-AFLP. A. Genomic DNA isolated from MCF7 cells that were either treated or not treated with the demethylating agent Aza-C were used as a positive control for the MS-AFLP method. **B.** The genomic DNAs used for analysis were from brain (B) and liver (L) tissues of mice on either diet 1 or diet 2 for 15 months.

Supplementary Figure 1

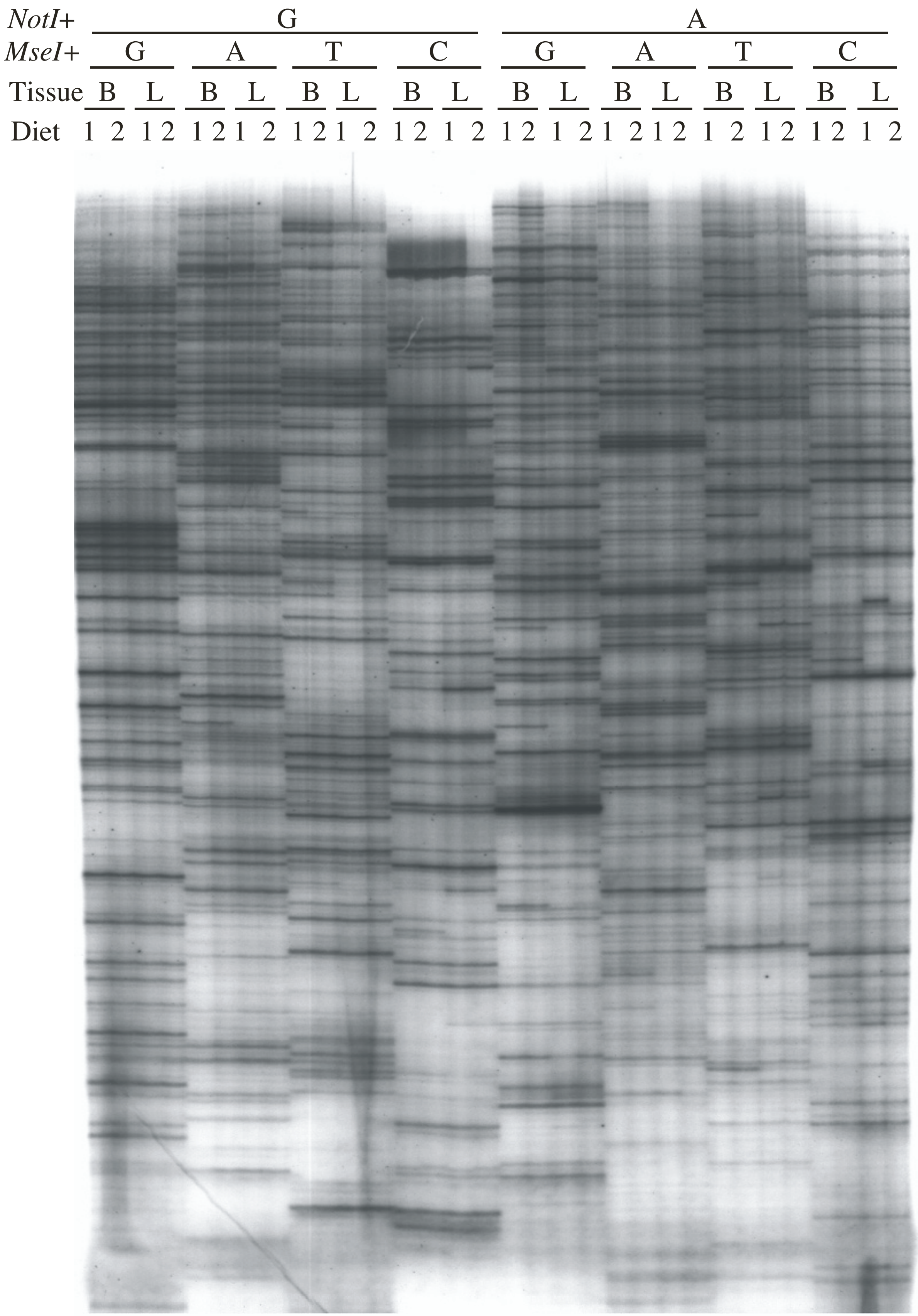


Supplementary Figure 2



Supplementary Figure 3A

B


NotI+ G A
MseI+ G A T C G A T C
Tissue B L B L B L B L B L B L B L B L
Diet 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2