Online Supplement

Detailed Methods

In Vivo Preclinical Studies

Animals were housed at the Baker IDI Heart and Diabetes Research Institute and studied according to National Health and Medical Research Council (NHMRC) guidelines in line with international standards. Animals had unrestricted access to water and feed, and were maintained on a 12 hour light/dark cycle on standard mouse chow (Barastoc; Ridley Agriproducts, St Arnaud, VIC, Australia). Six-week-old *ApoE*$^{-/-}$ male mice (C57BL/6 background) were rendered diabetic by 5 daily intraperitoneal (I.P.) injections of streptozotocin (Sigma-Aldrich, St Louis, MO) at a dose of 55 mg/kg. *ApoE*$^{-/-}$ mice were administered either ethanol (0.1%), LXA_4 (5 ug/kg; Merck, Calbiochem) or Benzo-LXA_4 (1.7 ug/kg; synthesized at University College Dublin, Ireland [1] twice weekly by I.P injection. For the prevention study design, mice were followed for 10 weeks (moderate disease) or 20 weeks (severe disease), and were administered ethanol, LXA_4, or Benzo-LXA_4 between weeks 1-10 or weeks 1-20, respectively. For the intervention study design, mice were followed for 16 weeks, and were administered ethanol, LXA_4, or Benzo-LXA_4 between weeks 10-16. Blood glucose levels were monitored weekly after STZ injections for the duration of the studies to confirm the diabetic status of these mice. Only animals with a blood glucose level >15 mmol/l 1 week after the induction of diabetes were included in the study. Ten weeks post induction of diabetes systolic blood pressure was assessed by non-invasive tail cuff system in conscious mice. Urine samples were collected in metabolic cage for 24 hours before the end of the experiment. Glycated haemoglobin (HbA1c) was measured using the Cobas Tina-quant® HbA1c Gen. 3 assay (Roche Diagnostics, VIC, Australia), and creatinine in blood and urine was analysed using the COBAS INTEGRA 400 PLUS (Roche Diagnostics, VIC, Australia), as per the manufacturers guidelines. Total glucose was measured in plasma with a standard commercial enzymatic assay (Beckman Coulter Diagnostics, Gladsville, NSW, Australia). Albumin in urine was measured using the Mouse Albumin ELISA Quantitation Set (Bethyl Laboratories Inc., Montgomery, TX). At study end-point, animals were anaesthetised by sodium pentobarbitone IP (100 mg/kg body weight; Euthatal, Sigma-Aldrich, Castle Hill, NSW, Australia) and organs were rapidly dissected.

In Vitro Studies

Immortalized human kidney epithelial cells (HK-2; ECACC, Porton Down, UK) were cultured at 37°C in a humidified atmosphere of 95% air/5% CO2 , and maintained in DMEM-F12 (Sigma-Aldrich, Steinheim, Germany) supplemented with 2 mM L-glutamine, 100 U/ml penicillin, 100 mg/ml streptomycin, 10 ng/ml endothelial growth factor, 36 ng/ml hydrocortisone, 3 pg/ml triiodothyronine, and 5 mg/ml insulin, 5 mg/ml transferrin, and 5 ng/ml selenium (ITS) solution (Sigma-Aldrich). After serum restriction for 24 hours, cells were stimulated with vehicle (0.1% ethanol), LXA_4 (0.1 nM; Merck, Calbiochem), or Benzo-LXA_4 (1nM) for 30 minutes and media was removed and replaced with media with or without TGF-β1 (10 ng/ml; PromoCell GmbH).

Gene expression Analyses by Reverse Transcriptase Quantitative PCR

RNA was extracted from mouse kidney tissue and HK-2 cells using TRIzol (Ambion). DNase treatment and cDNA synthesis were performed as previously described.[2] Gene expression was determined utilizing TaqMan reagents (Life Technologies) with fluorescence signals being normalized to 18s rRNA or Gapdh utilizing the ddCT method. Probes and primers were designed using a Primer Express program and were purchased from Applied Biosystems (ABI, Foster City, CA, USA). Where no probes were used, Fast SYBR® Green mastermix was employed with gene specific primers. Primer and Probe sequences are detailed in Supplemental Table 8.

Protein Extraction and Western Blot Analyses

Lysates were harvested in RIPA lysis buffer as previously described [3]. Total protein was estimated using the Bradford assay. For Western blot analysis, antibodies used included the following: Beta-actin (1:20,000; Sigma-Aldrich), CDH1 (1:1,000; BD Biosciences, Oxford, UK), JAG1 (1:2,000; Santa Cruz Biotechnology, Santa Cruz, CA), FN1 (1:2,000; BD Biosciences), CTGF (1:1,000; Santa Cruz Biotechnology, Santa Cruz, CA).

siRNA Transfections

siGENOME SMARTpool Egr1 siRNA and siGENOME RISC Free control siRNA were purchased from Dharmacon. siRNAs were transfected into HK-2 cells at 60% confluence using Lipofectamine 2000 (Invitrogen, Carlsbad, CA) at a final concentration of 20 nM for 24 hours. Cells were then stimulated with TNF-α or TGF-β as previously described.

Histological and Immunohistochemical Staining

Paraffin sections (4μm) of Kidney were used to stain for Masson's Trichrome as described previously.[4, 5] Briefly, 10 representative images per kidney section and single images of aortic arch, thoracic and abdominal aorta segments were quantitatively assessed in a blinded fashion. Quantification of all staining was determined using Image J software (http://imagej.net/Welcome).

Evaluation of Renal Pathologic Changes

Paraffin-embedded sections of mouse kidney with a thickness of 3 μm were stained by Periodic acid–Schiff method, and the morphologic changes reflecting the pathologic injuries in glomeruli were evaluated in a blinded fashion in a quantitative manner. Briefly, 20 representative glomerular images at 40x magnification were taken for each section using a light microscope (BX43, Olympus Corporation, Shinjuku, Tokyo) and proportional area of mesangial expansion from PAS stained sections were measured using Image-Pro Analyser 7.0 (Media cybernetics, Rockville, MD). Quantification was determined using Image J software (http://imagej.net/Welcome).

Renal RNA-Seq Profiling

RNA was isolated from kidney Trizol homogenates using the Direct-zol™ RNA MiniPrep Kit (Zymo Research; n=6 kidneys per treatment group). RNA quality was assessed by MultiNA Bioanalyzer (Shimadzu). Illumina HiSeq single end 100 cycle sequencing was performed at the Australian Genome Research Facility (AGRF, Melbourne). Reads were trimmed for quality using a minimum phred value of 20 and minimum length of 18 using Skewer.[6] Reads were mapped with STAR to the mouse genome downloaded from Ensembl (GRCm38).[7] Feature Counts was used to count reads mapped to gene bodies on the correct strand with a minimum mapping quality of 20 using Ensembl genome annotation (Mus musculus.GRCm38.86.gtf).[8] The resulting count matrix underwent differential analysis with the EdgeR package.[9] Transcripts with a false discovery rate (FDR) P-value <0.05 were deemed statistically significant. RNA-seq data is deposited in GEO (GSE107942), and normalized read counts for all transcripts in all samples are available in Supplemental Table 9. Upstream regulator analysis of differentially expressed gene sets was performed using Ingenuity Pathway Analysis Z-score algorithm (Ingenuity Systems, Qiagen). Detailed information on Ingenuity Pathway Analysis is available at www.qiagen.com. Briefly, this analysis examines how many known targets of each transcription regulator (transcription factor, cytokine, enzyme etc..) are present in the RNA-seq dataset, and also compares their direction of change. Relationships between molecules are supported by at least one reference from the literature, from a textbook, or from canonical information stored in the Ingenuity Knowledge Base. For each transcriptional regulator there are two statistical measures: an overlap p-value and an activation z-score. The overlap p-value measures whether there is a statistically significant overlap between the input dataset genes and the genes that are known to be regulated by a transcriptional regulator. It is calculated using a Fisher's Exact Test, and significance is attributed to p-values <0.01. The activation z-score infers the activation state of the transcriptional regulator. This score is assigned based on changes in expression of genes identified in our RNA-seq dataset that are associated with a literature-derived regulation direction (i.e. activating or inhibiting). The statistical approach here is to define a quantity (z-score) that determines whether an upstream transcription regulator has significantly more ‘activated’ predictions than ‘inhibited’ predictions. A cut-off Z-score of ≥ 2 or ≤ -2 was deemed significant. Analysis of promoters for enriched TFBSs was performed using Genomatix Matbase (Genomatix). Promoter regions were defined as -1000bp/+100bp from transcription start site. Overrepresentations of TFBSs in promoters of differentially expressed genes was determined against a background population of murine promoters, with a cut-off Z-score ≥ 2 or ≤ -2 considered statistically significant. NF-κB target genes were downloaded from the NF-κB Transcription Factors Database (https://www.bu.edu/nf-kb/gene-resources/target-genes/). Heatmaps of differentially expressed genes were generated using Morpheus (Broad Institute, USA). Publicly available human DKD datasets were downloaded from Nephroseq (https://nephroseq.org/resource/login.html).

Statistics

All statistical analyses were performed utilizing GraphPad Prism software. Experiments with only one treatment were assessed by Student’s t-test. Experiments with multiple treatment groups were analysed by one-way ANOVA with post-hoc comparisons of group means performed by Fisher’s least significant different method. A P-value ≤ 0.05 was considered statistically significant. Significance between groups is indicated for each figure. Unless otherwise specified, data are shown as mean ± S.E.M.

Supplemental Figures and Tables

Fig. S1. Masson’s Trichrome staining for ECM accumulation in kidneys.

Fig. S2. Smear plots for comparison of global gene expression in RNA-seq data from ApoE$^{-/-}$ mouse kidneys.

Fig. S3. Compartment-specific expression of gene set differentially expressed in diabetic versus non-diabetic ApoE$^{-/-}$ kidneys.

Fig. S4. Analysis of tubule compartment specific expression of gene set differentially expressed in diabetic versus non-diabetic ApoE$^{-/-}$ kidneys.

Fig. S5. Comparison of transcriptional responses between human DKD and diabetic ApoE$^{-/-}$ model.

Fig. S6. Expression of NF-κB target genes in ApoE$^{-/-}$ RNA-seq dataset.

Fig. S7. LXs regulate the EGR1 transcriptional network in DKD.

Fig. S8. Analysis of tubule compartment specific expression of genes identified as expressed in HK-2 renal tubule epithelial cells.

Table S1. Differentially expressed genes between control and diabetic ApoE$^{-/-}$ mice.

Table S2. Upstream regulator analysis: Control versus diabetic ApoE$^{-/-}$ mice.

Table S3. Upstream regulator analysis: Diabetic versus Diabetic + LXA$_4$ or Benzo-LXA$_4$ treated ApoE$^{-/-}$ mice.

Table S4. Differentially expressed genes: Diabetic versus Diabetic + LXA$_4$ treated ApoE$^{-/-}$ mice.

Table S5. Differentially expressed genes: Diabetic versus Diabetic + Benzo-LXA$_4$ treated ApoE$^{-/-}$ mice.

Table S6. TFBS promoter analysis of differentially expressed genes from ApoE$^{-/-}$ RNA seq experiment.

Table S7. RNA-seq read counts for HK-2 cells in comparison with micro-dissected renal tubule compartments.

Table S8. Details of primers and probes used for all quantitative PCR gene expression analysis.

Table S9. Normalized read counts for RNA-seq dataset.

Fig. S1. Masson's Trichrome staining for ECM accumulation in kidneys.

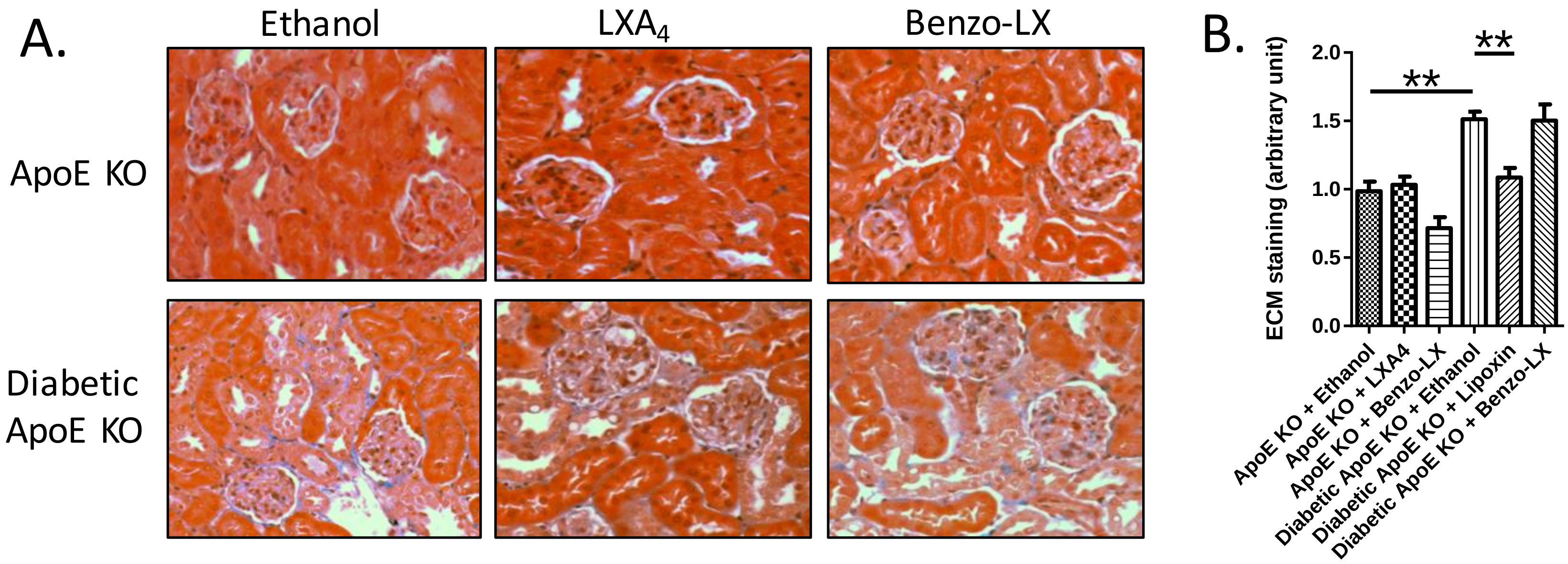
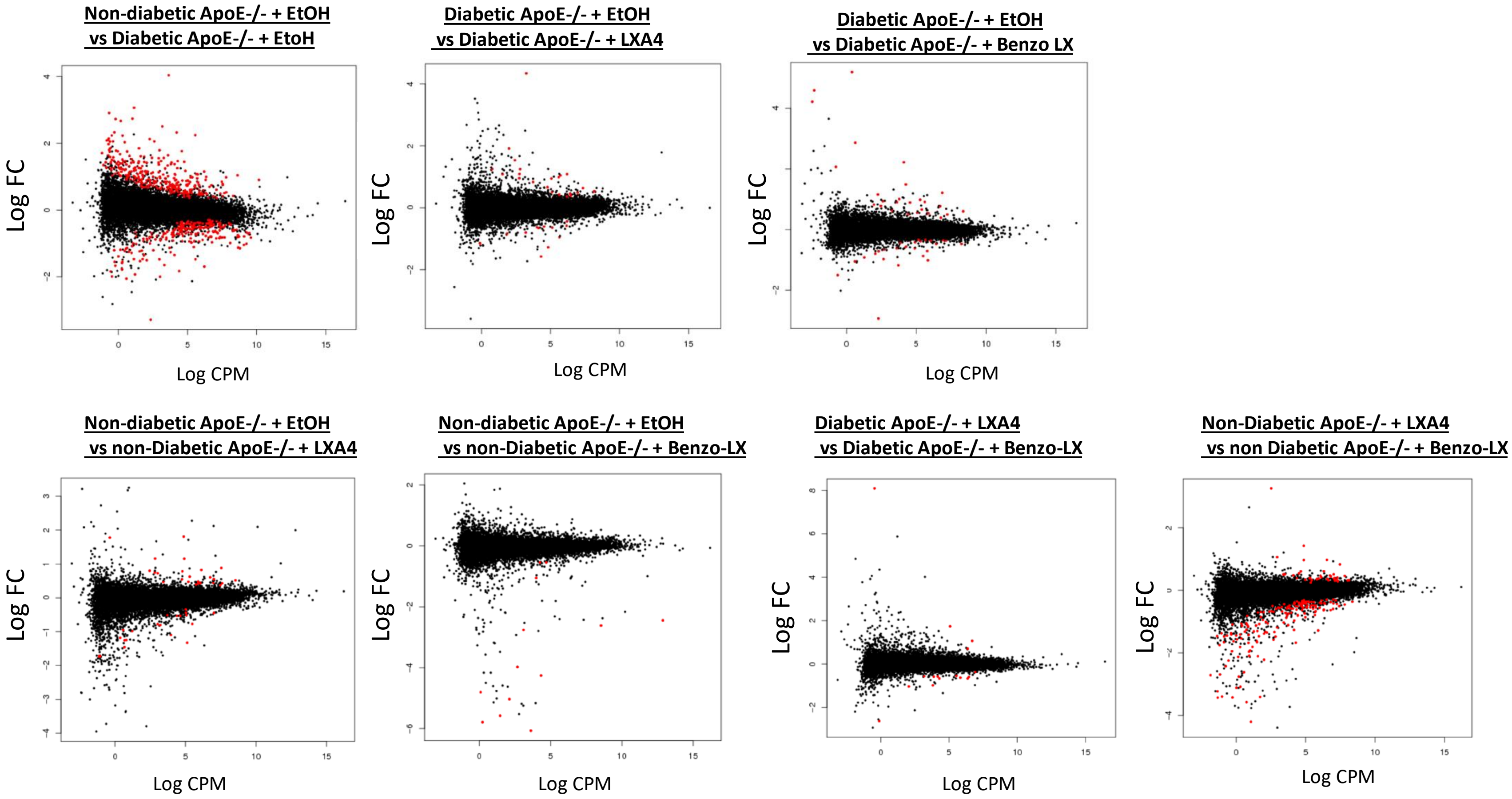


Fig. S1. (A) Masson's Trichrome staining for ECM accumulation in kidneys of 20-week diabetic and control ApoE$^{-/-}$ mice administered ethanol (0.1%), LXA_4 or Benzo-LXA_4 and **(B)** Quantification of the staining is shown in the bar graph as mean ± SEM (n=8–10/group; *P<0.05).

Fig. S2. Smear plots for comparison of global gene expression in RNA-seq data from ApoE$^{-/-}$ mouse kidneys.



*Each black point is a detected gene with non-significant changes in expression and red points are statistically significant (FDR<0.05). Log FC (Log2 fold-change); Log CPM (Log2 read-counts per million).

Fig. S3. Compartment-specific expression of gene set differentially expressed in diabetic versus non-diabetic ApoE$^{-/-}$ kidneys.

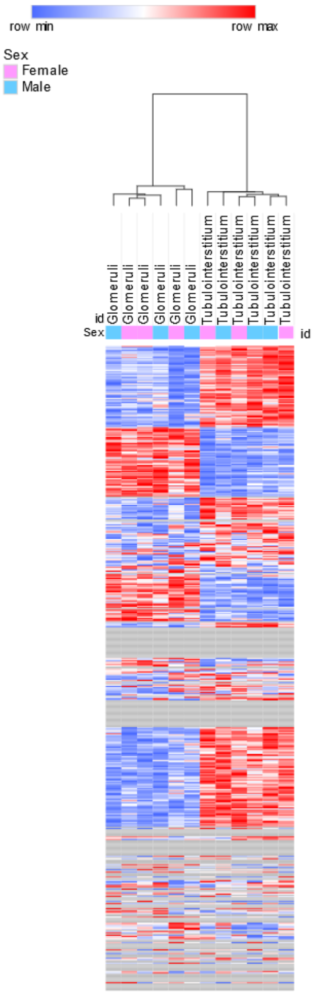


Fig. S3. Compartment-specific expression of gene set differentially expressed in diabetic versus non-diabetic ApoE$^{-/-}$ kidneys. Expression of 725 differentially expressed transcripts (identified in comparison of non-diabetic vs diabetic ApoE-/- mice) in micro-dissected healthy human kidneys (glomerular and tubule compartments). Human DKD microarray dataset was downloaded from Nephroseq (Lindenmeyer et al., PMID: 20634963). Red = higher expression; Blue = lower expression; Grey = no data available in human dataset for these genes.

Fig. S4. Analysis of tubule compartment specific expression of gene set differentially expressed in diabetic versus non-diabetic ApoE$^{-/-}$ kidneys.

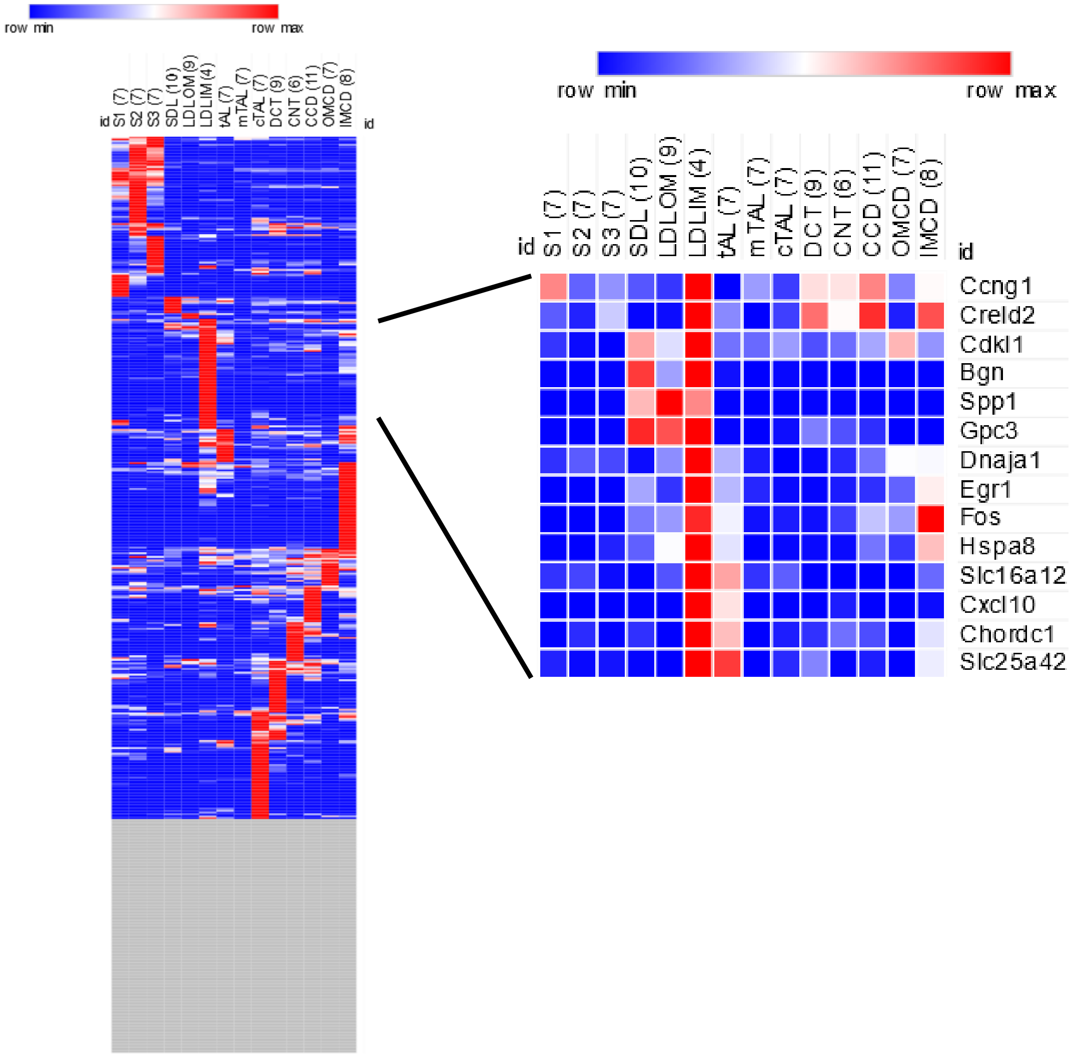


Fig. S4. Analysis of tubule compartment specific expression of gene set differentially expressed in diabetic versus non-diabetic ApoE$^{-/-}$ kidneys. Expression of 725 differentially expressed transcripts (identified in comparison of non-diabetic vs diabetic ApoE-/- mice) in 14 compartments of microsdissected rat renal tubule. Rat renal tubule data was downloaded from (https://hpcwebapps.cit.nih.gov/ESBL/Database/NephronRNAseq/index.html) Lee JW et al., JASN 2015. PMID: 25817355. Red = higher expression; Blue = lower expression; Grey = no data available in rat tubule dataset for these genes. Terminology for nephron segments: S1, first segment of the proximal tubule; S2, second segment of the proximal tubule; S3, third segment of the proximal tubule; SDL, short descending limb of the loop of Henle; LDLOM, long descending limb of the loop of Henle in the outer medulla; LDLIM, long descending limb of the loop of Henle in the inner medulla; tAL, thin ascending limb of the loop of Henle; mTAL, medullary thick ascending limb of the loop of Henle; cTAL, cortical thick ascending limb of the loop of Henle; DCT, distal convoluted tubule; CNT, connecting tubule; CCD, cortical collecting duct; OMCD, outer medullary collecting duct; IMCD, inner medullary collecting duct.

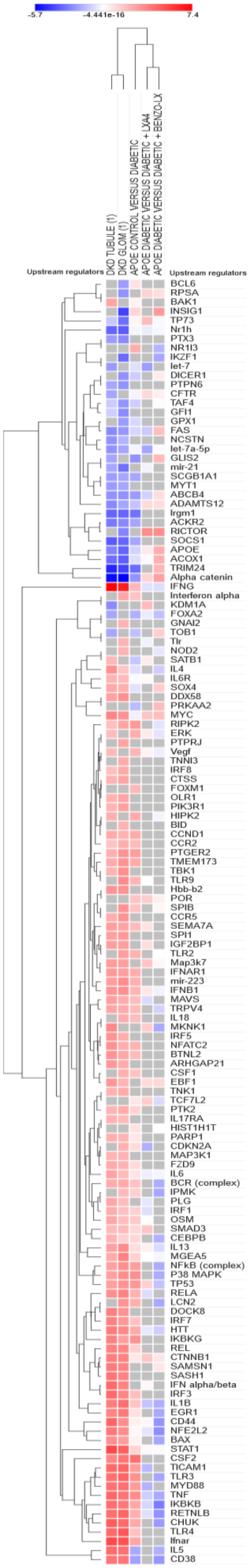


Fig. S5. Comparison of transcriptional responses between human DKD and diabetic ApoE$^{-/-}$ model. Human DKD microarray dataset was downloaded from Nephroseq (Ju et al., PMID: 26631632). Genes that were significantly differentially expressed (FDR $p<0.05$) in renal tissue between DKD patients and healthy controls were selected. Glomerular (n=979 genes at FDR $p<0.05$) and Tubule (n=1233 genes at FDR $p<0.05$) compartments were analysed separately. Analysis was performed on the human DKD gene sets, as well as the differential gene sets from the ApoE$^{-/-}$ model (control versus diabetic; diabetic versus diabetic + LXA_4, diabetic versus Benzo-LXA_4). Upstream regulator analysis was performed using Ingenuity Pathway Analysis software for interrogation of differentially expressed gene lists for putative upstream regulators that drive the differential expression. Z-score is the output. This is an activation score (red = activated; blue = repressed; grey = no evidence of this regulator being activated or repressed). A cut-off of >2 or <-2 was used to select the strongest regulators (as recommended by IPA) in human DKD datasets. These were then assessed in the ApoE model.

Fig. S6. Expression of NF-κB target genes in ApoE$^{-/-}$ RNA-seq dataset.

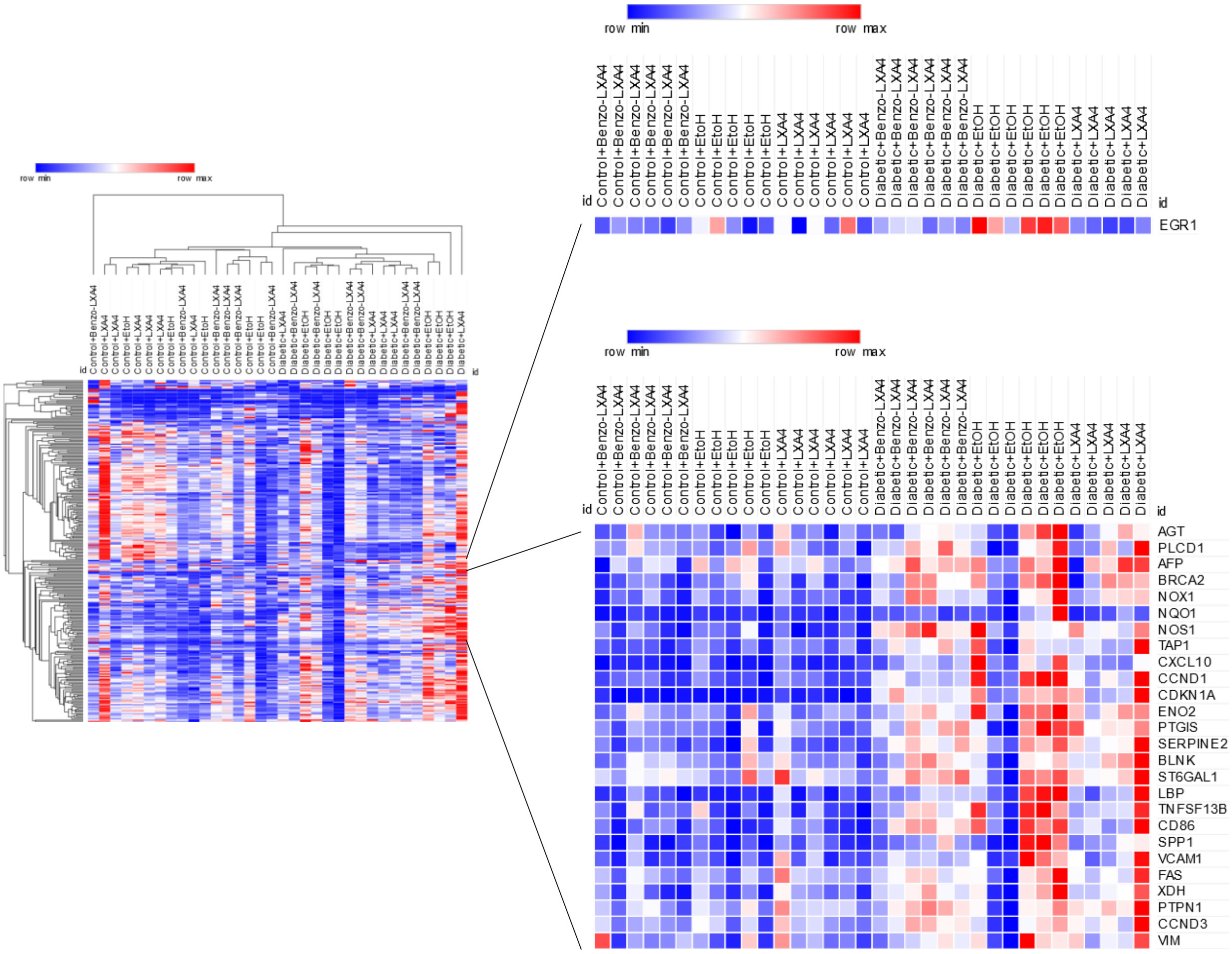


Fig. S6. Expression of NF-κB target genes in ApoE$^{-/-}$ RNA-seq dataset. NF-κB target gene database (https://www.bu.edu/nf-kb/gene-resources/target-genes/) was used for identification of target genes. The expression of 268 NF-κB targets expressed in ApoE$^{-/-}$ kidney RNA-seq data was then determined. Hierarchical clustering analysis indicates that there is clustering of non-diabetic and diabetic kidneys based on the expression of these genes. Red = higher expression; Blue = lower expression; Grey = no data available in ApoE$^{-/-}$ RNA-seq dataset for these genes.

Fig. S7. LXs regulate the EGR1 transcriptional network in DKD.

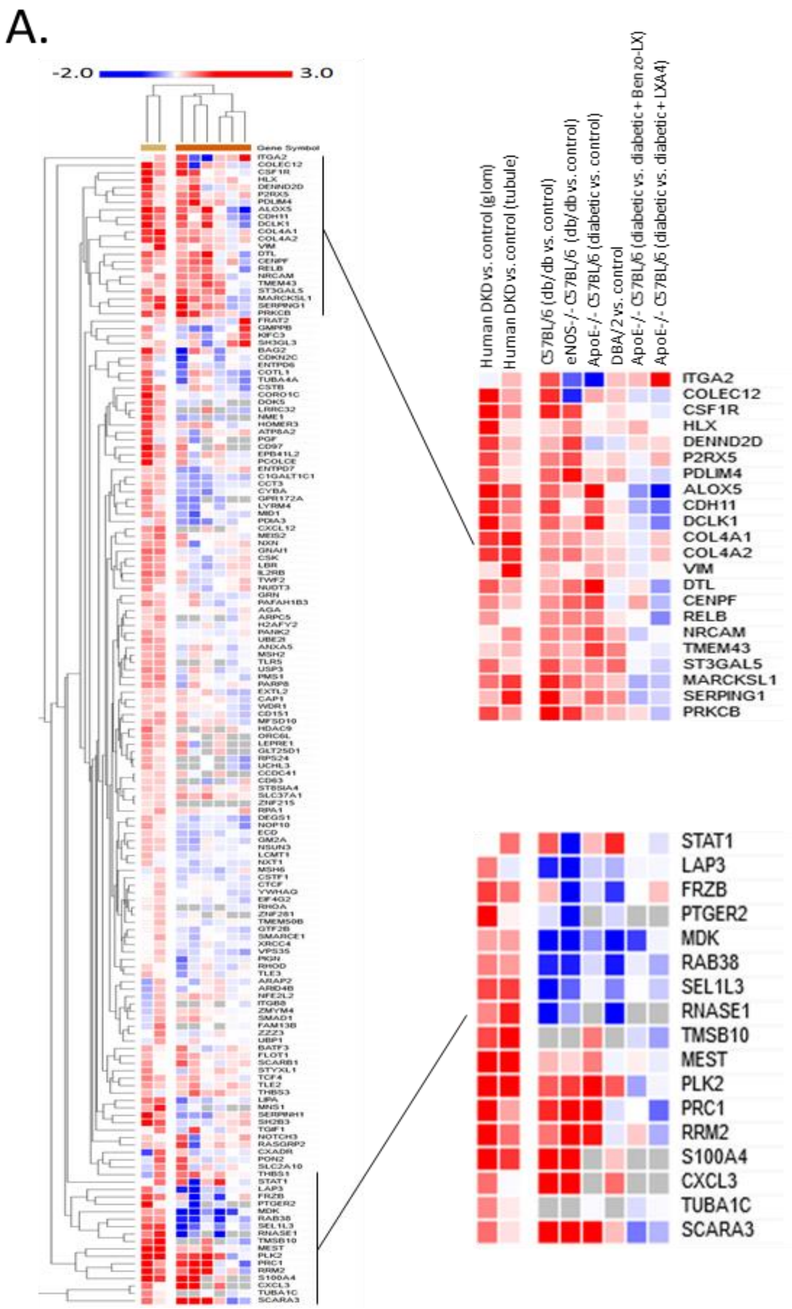


Fig. S7. Expression of EGR1 targets was determined in published transcriptomic data from patients with DKD versus healthy controls, and also in three diabetes mouse models. Transcriptomic datasets were downloaded from Nephroseq. [10, 11] Predicted Egr1 target genes that were significantly differentially expressed (FDR $p<0.05$) in renal tissue between DKD patients and healthy controls were selected ($n=155$; FDR $p<0.05$) Heatmaps were generated of gene expression indicating transcripts displaying significant differential expression (FDR P-value <0.05). Red = upregulated; blue = downregulated; grey = no evidence of expression.

Fig. S8. Analysis of tubule compartment specific expression of genes identified as expressed in HK-2 renal tubule epithelial cells.

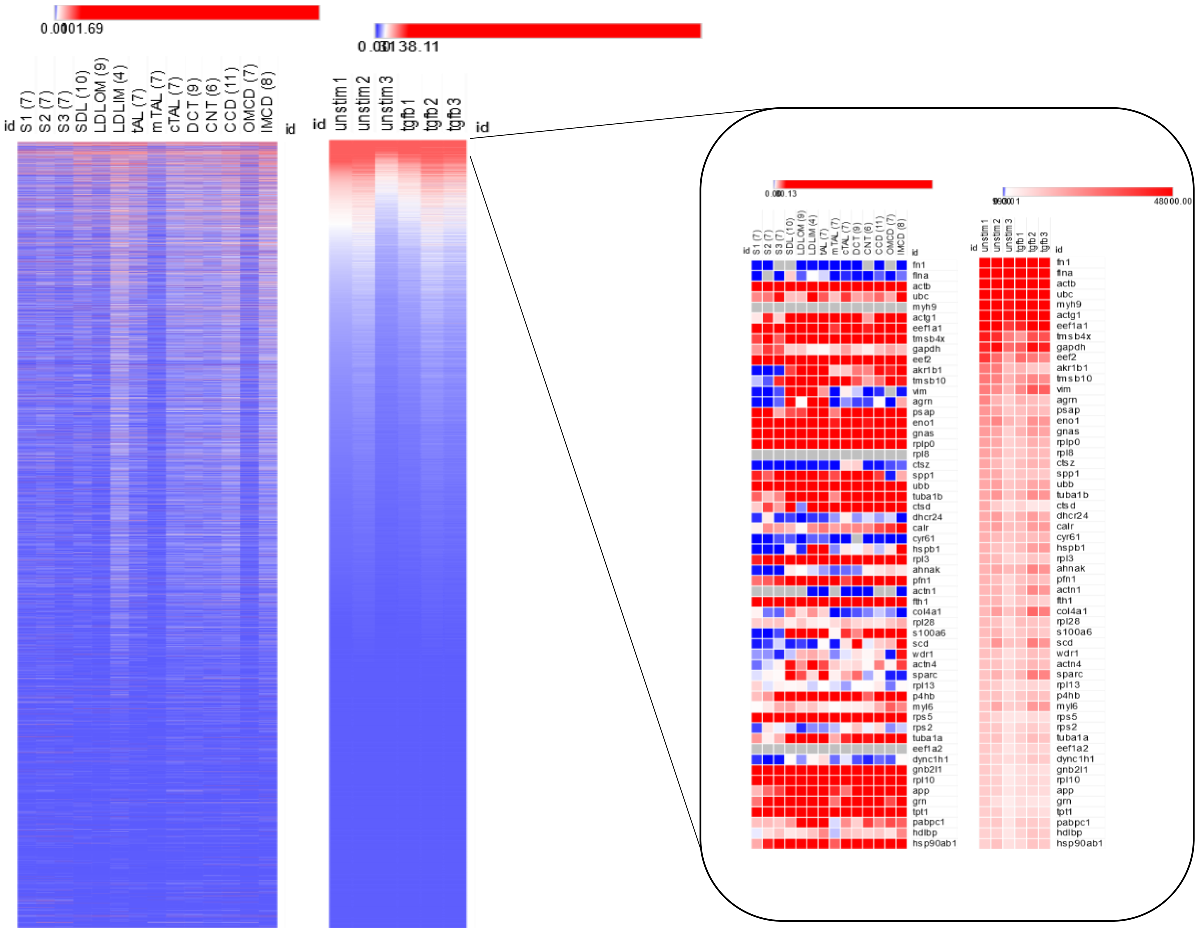


Fig. S8. Analysis of tubule compartment specific expression of genes identified as expressed in HK-2 renal tubule epithelial cells. We previously performed RNA-seq analysis of immortalized human proximal tubule epithelial cells (HK-2) (Brennan et al., PMID: 22266139). From these data, a total of 11,732 genes were robustly expressed in HK-2 cells. Here we investigated the tubule compartment-specific expression of these genes in 14 compartments of a micro-dissected rat renal tubule. Rat renal tubule data was downloaded from (https://hpcwebapps.cit.nih.gov/ESBL/Database/NephronRNAseq/index.html) Lee JW et al., JASN 2015. PMID: 25817355. Red = higher expression; Blue = lower expression. Terminology for nephron segments: S1, first segment of the proximal tubule; S2, second segment of the proximal tubule; S3, third segment of the proximal tubule; SDL, short descending limb of the loop of Henle; LDLOM, long descending limb of the loop of Henle in the outer medulla; LDLIM, long descending limb of the loop of Henle in the inner medulla; tAL, thin ascending limb of the loop of Henle; mTAL, medullary thick ascending limb of the loop of Henle; cTAL, cortical thick ascending limb of the loop of Henle; DCT, distal convoluted tubule; CNT, connecting tubule; CCD, cortical collecting duct; OMCD, outer medullary collecting duct; IMCD, inner medullary collecting duct.

Table S1. Differentially expressed genes between control and diabetic ApoE$^{-/-}$ mice.

GENE ID	Log2 Fold-change	FDR (CORRECTED P-VALUE)	GENE ID	Log2 Fold-change	FDR (CORRECTED P-VALUE)
Eda2r	3.77	8.73E-65	**Kif23**	0.85	0.009579192
Cdkn1a	3.22	4.75E-54	**Adamts14**	0.82	0.009676948
Trp53cor1	3.25	1.63E-34	**Serpine2**	0.73	0.009843774
Gm45011	2.97	6.92E-30	**Espnl**	0.77	0.010012367
Psrc1	4.40	2.16E-26	**Nat8**	-0.71	0.010136542
Kcnip4	2.55	1.16E-25	**Lrrc32**	0.49	0.010142684
Dscaml1	2.96	1.16E-25	**Cd247**	0.84	0.010248419
Ano3	4.11	1.97E-22	**4933406I18Rik**	0.62	0.010332392
Mgmt	1.15	5.35E-17	**Hmgcr**	-0.92	0.01036763
Fam212b	2.75	2.16E-15	**Tnnc1**	-1.45	0.010553111
Zmat3	0.94	4.23E-14	**4933427D06Rik**	1.48	0.010554075
Trpm8	3.88	1.02E-13	**Kcnip2**	1.09	0.010564754
Sulf2	1.15	1.86E-13	**Rhoq**	0.39	0.01060559
Plcd4	1.46	5.28E-13	**Gm16432**	0.59	0.010622298
Dpp6	1.49	3.16E-12	**Ctsk**	0.75	0.010797885
Gtse1	2.11	1.70E-11	**Fmo5**	-0.66	0.010840349
Ugt1a10	4.26	1.74E-11	**Dtx4**	0.67	0.010987816
Trp53inp1	1.07	4.03E-11	**Cbr1**	1.20	0.011006467
Gm26542	1.18	4.89E-11	**Slc8a3**	1.26	0.011006467
Cldn1	1.12	1.58E-10	**Gm10830**	1.35	0.011066719
Plk2	1.04	1.58E-10	**Ttpa**	0.93	0.011309208
6030407O03Rik	1.69	2.81E-10	**Ube2e2**	0.42	0.011322178
4833428L15Rik	3.98	1.02E-09	**Blm**	0.73	0.011653609
Cyp2d12	-1.92	1.30E-09	**Ccl6**	1.06	0.011746526
Tnfaip8	-1.12	1.92E-09	**Psat1**	-0.72	0.01181329
Tll2	2.82	2.18E-09	**Xbp1**	-0.63	0.011909845
Alk	1.34	2.87E-09	**Polq**	0.84	0.012000339
D630023F18Rik	-1.74	3.37E-09	**Plk3**	1.15	0.012060378
Kynu	2.45	4.93E-09	**Acta2**	0.75	0.012162165
Gdf15	1.39	6.15E-09	**Tox**	0.72	0.012443309
Ddias	1.76	9.81E-09	**Chrna4**	-0.71	0.012443309
Gm13067	1.52	1.58E-08	**Vwc2**	2.24	0.012443309
Angptl7	-2.01	2.26E-08	**Gm19418**	1.08	0.012583916
Nudt19	-1.11	3.72E-08	**Nabp1**	0.48	0.012708693
Ccng1	0.85	3.72E-08	**Ces2b**	-1.33	0.012710387
Phlda3	1.84	4.41E-08	**RP23-403G9.6**	-0.58	0.012866647

Aldh1a7	1.27	5.82E-08	**Masp1**	1.42	0.012866647
Ppp1r1c	3.03	5.82E-08	**Iba57**	-0.61	0.012908268
Gm10787	-1.61	9.37E-08	**Egr1**	1.05	0.013002775
Gm10801	2.84	1.44E-07	**Pcdh9**	1.00	0.013088521
Ptprt	2.02	1.44E-07	**Art4**	0.72	0.013434097
Gpc3	0.94	2.07E-07	**Cyp2d9**	-0.58	0.013721646
Aen	0.82	3.29E-07	**Csrp1**	0.47	0.013779774
Ccnd1	1.05	3.30E-07	**Mmp14**	0.64	0.013882712
Ngef	-0.62	3.87E-07	**Dnajb1**	-0.46	0.013962789
Npr3	-0.96	3.97E-07	**Col24a1**	0.83	0.01405554
Gm6614	2.69	6.07E-07	**Hsp90aa1**	-0.75	0.014088302
Gjb1	-0.79	6.95E-07	**Isoc2b**	-0.59	0.014412196
Fn1	1.03	6.95E-07	**Tagln**	0.71	0.014448187
Sntg1	1.76	6.95E-07	**Ttk**	1.34	0.014691235
1700024P16Rik	1.77	7.69E-07	**Gpc5**	-1.10	0.015017502
Cpne4	-1.30	8.91E-07	**Mrvi1**	0.40	0.015095492
Ces1d	-0.90	1.81E-06	**Dclk3**	-0.50	0.015189655
Gm12153	1.29	1.86E-06	**Klhl9**	-0.42	0.015298851
Ltc4s	1.32	2.55E-06	**Hspe1**	-0.67	0.015298851
Nat8f6	-1.01	3.14E-06	**Ccnf**	0.99	0.015298851
Zak	0.87	3.22E-06	**Mctp2**	0.67	0.015576738
Mab21l3	1.21	3.22E-06	**Gm4593**	0.86	0.015589538
Diaph3	1.16	3.72E-06	**Svop**	1.51	0.016125581
Gm9732	2.66	4.61E-06	**Abhd3**	-0.55	0.016238576
Gm44202	1.65	4.61E-06	**Kif22**	1.28	0.016238576
Slc19a2	0.70	6.58E-06	**Gm13387**	0.83	0.016238576
Ppp2r2c	1.83	6.99E-06	**Rundc3a**	0.82	0.016238576
Tmem43	0.79	7.00E-06	**Chaf1b**	1.18	0.016304122
Aldh1a1	1.69	7.66E-06	**Gm12999**	-1.25	0.01662482
Tnfrsf10b	1.08	8.71E-06	**Spag6l**	0.72	0.016674081
Cdh2	-0.77	9.52E-06	**Mamld1**	0.80	0.0168547
A930001C03Rik	0.87	1.09E-05	**Atf3**	0.85	0.0168547
Gm37795	1.37	1.09E-05	**Rimkla**	0.88	0.0168547
Grem1	3.81	1.14E-05	**9130019P16Rik**	1.03	0.016879702
Gm29282	1.76	1.18E-05	**Tm4sf4**	-1.29	0.016892269
Mki67	1.30	1.19E-05	**Gckr**	1.20	0.016973187
Clca3a1	1.89	1.48E-05	**Gm11837**	-1.09	0.017027586
Olfr1442	2.54	1.65E-05	**Shh**	-1.26	0.017027586
Ckap2	1.84	1.67E-05	**Asic2**	1.29	0.017050281
Ephx1	1.20	1.70E-05	**Wisp1**	0.68	0.017050281
Hsph1	-0.96	1.91E-05	**Nepn**	-0.86	0.017064629

Hspa1a	-1.41	2.06E-05	**Gm15563**	-2.01	0.017167265
Anln	1.47	2.08E-05	**Gpr135**	1.00	0.017167265
Akr1c13	0.99	2.44E-05	**Gm44626**	-1.08	0.017167265
B3galt1	0.82	2.57E-05	**Tnfsf13b**	0.70	0.017272276
Zbtb40	-0.68	2.60E-05	**Birc5**	1.25	0.017289706
P2ry1	-0.87	3.56E-05	**Nlgn1**	0.89	0.017505002
G6pc	-1.13	4.31E-05	**Ankrd34b**	-1.49	0.017585986
Loxl4	1.32	4.44E-05	**Rell1**	0.45	0.017675365
Cxcl10	1.49	4.59E-05	**Ahcy**	-0.48	0.017675365
9230114K14Rik	0.57	4.80E-05	**Gabrb3**	-1.02	0.01771164
Cpe	-0.97	5.18E-05	**Entpd1**	0.72	0.017859166
Ces2e	0.80	5.32E-05	**Dpysl3**	0.59	0.017975549
Snhg11	-0.61	5.51E-05	**Gm16010**	1.26	0.017975549
Fbn1	0.67	5.51E-05	**Kcnmb2**	0.75	0.018197911
Esco2	1.93	5.51E-05	**G0s2**	-0.66	0.018346224
Cpb2	2.10	5.59E-05	**L3mbtl4**	1.04	0.018474941
Lbp	1.16	6.23E-05	**Dnaja1**	-0.56	0.018513498
Osr2	-1.20	6.58E-05	**Arhgef38**	0.52	0.018712977
Sh3rf3	1.45	7.56E-05	**Aspdh**	-0.87	0.01871427
Gm15441	-2.18	7.81E-05	**Ldhd**	-0.76	0.01871427
Mlip	1.77	7.83E-05	**Gm44829**	0.96	0.018722012
Vmn2r1	1.97	7.83E-05	**Gm15581**	0.84	0.018904148
Antxr1	0.88	7.83E-05	**Ces2c**	-0.75	0.018944215
Stc1	1.29	8.29E-05	**Ccdc6**	-0.48	0.019035014
Cyp2j8	1.14	8.42E-05	**Stra6l**	0.59	0.019125513
Synpo2	0.79	9.22E-05	**2310014F06Rik**	0.72	0.01915912
Gabra3	0.78	9.22E-05	**BC051142**	0.96	0.019163403
4833411C07Rik	-1.83	9.46E-05	**Rarres2**	1.05	0.019167588
Car3	-1.97	9.66E-05	**Adam22**	0.44	0.019549955
C3	1.44	9.74E-05	**Arhgef33**	0.81	0.019549955
Gucy1a3	0.67	0.000103542	**Hao2**	0.63	0.019564117
Slc39a5	-1.05	0.000103542	**2610027K06Rik**	-0.59	0.019564117
Kcnab1	1.40	0.000105161	**A830018L16Rik**	1.65	0.019564117
Arhgef4	0.97	0.000107839	**Fam195a**	-0.59	0.019564117
Col14a1	0.72	0.000109055	**Tmem50a**	-0.44	0.019564117
Kcnma1	0.82	0.000109088	**Slc6a15**	-0.53	0.019564117
1700027A15Rik	1.83	0.000123863	**Il20rb**	0.82	0.019564117
C630028M04Rik	2.33	0.00012486	**Gja5**	0.73	0.019564117

Tcf24	-0.84	0.000134654	**Gm906**	-1.49	0.020080732
Cemip	1.62	0.000156583	**Gm8439**	1.64	0.020102085
Aldh1b1	1.41	0.000174496	**Slc22a27**	1.19	0.020235153
Snap91	1.43	0.000174496	**Ms4a6c**	0.79	0.020622041
Zwilch	1.06	0.000178174	**Mfap2**	1.13	0.020776688
Hspa1b	-1.49	0.000180276	**Nsun7**	0.64	0.020926983
Brca1	1.09	0.000184119	**Cd84**	0.83	0.021183298
Iqgap3	1.39	0.000185756	**Kntc1**	0.98	0.021668322
Dlgap5	1.46	0.000185756	**Fat1**	0.42	0.02170867
Dll4	-0.91	0.000186624	**Ace**	-0.55	0.022130938
Adamts5	0.60	0.000200843	**Akr1d1**	0.51	0.022130938
Gm11100	2.07	0.000204423	**Rorc**	-0.49	0.022216895
1600010M07Rik	-1.08	0.000221037	**Vegfa**	-0.43	0.02245845
Asb11	1.49	0.000230907	**Gabrr2**	-0.92	0.02268808
Mis18bp1	1.40	0.000230907	**Angptl2**	0.43	0.022941247
Clspn	1.49	0.000251601	**Col12a1**	0.85	0.022941247
Tmem28	-1.06	0.000262189	**Tnip3**	1.02	0.023305612
Gm13412	-1.31	0.000262189	**Tmem205**	-0.51	0.023605316
Nusap1	1.02	0.000265928	**Sla**	0.73	0.023674524
Nefl	1.94	0.000276385	**Slc38a3**	0.88	0.023848864
Nkain1	-0.84	0.000284846	**Zfp958**	0.41	0.02387842
Depdc1b	-0.58	0.000304407	**Cyp51**	-0.50	0.02387842
Arhgap11a	1.12	0.000309154	**Cyp4b1**	-1.01	0.023911415
Ubiad1	-0.60	0.000311596	**Apol9b**	1.10	0.023911415
Svep1	0.51	0.000317005	**Epha7**	-0.85	0.02398354
Fam198b	0.78	0.000318875	**2810433D01Rik**	1.14	0.02398354
Cdk1	1.30	0.000335156	**Col8a1**	-0.94	0.02398354
Olfr1443	1.74	0.000344768	**Rad54b**	1.00	0.02398354
Car4	-0.80	0.000345106	**Nr4a1**	1.11	0.02398354
4732471J01Rik	-0.57	0.000348188	**Npl**	0.82	0.024041142
Ackr3	-0.77	0.000352541	**C030034L19Rik**	1.26	0.024041142
Samd5	1.30	0.00035903	**Shcbp1**	0.97	0.024041142
Nid1	0.52	0.00035903	**Crtam**	2.15	0.024041142
Fbln5	0.58	0.000398897	**Fcamr**	-1.14	0.024041142
Nat8f1	-0.93	0.000399305	**Acy3**	-0.94	0.024041142
Esm1	-1.21	0.000450988	**Dhrs4**	-0.59	0.024181005
Nebl	0.62	0.000464149	**Plekhb1**	-0.55	0.024653927
Gas2l3	1.01	0.000464149	**Cmya5**	0.61	0.024653927
Paqr7	-0.97	0.000470847	**C3ar1**	0.79	0.024698889
Pole	1.18	0.000475154	**D2hgdh**	-0.42	0.024698889

Tex15	1.33	0.000477106	**Trpv6**	0.91	0.024903267
Cfap44	1.16	0.000492976	**Tet2**	0.45	0.024903267
Apoh	-1.30	0.000492976	**Ccl5**	1.13	0.024903267
Gsta2	1.01	0.000492976	**Gmpr**	-0.41	0.024950708
E230016K23Rik	1.05	0.000527561	**Rad51b**	0.72	0.025158381
Sdk1	0.76	0.000543535	**Stra6**	1.25	0.02525358
Mmp2	1.29	0.000557573	**Gm3294**	1.29	0.02536072
Mgp	0.89	0.000572491	**Kcng3**	1.28	0.025624924
Tspan2	0.87	0.000572491	**Gm44127**	2.30	0.025750159
Mpped1	1.34	0.00058469	**Exoc4**	0.49	0.025968133
Coq10b	-0.54	0.000594251	**Gm15983**	0.76	0.026369828
Slc25a42	-0.66	0.000624609	**Cd4**	0.97	0.026395722
L3mbtl1	1.58	0.000643541	**Pappa**	0.71	0.026404126
Cox6a2	-2.00	0.000644584	**Aspg**	-0.78	0.026698243
Bgn	0.60	0.000699478	**Manf**	-0.75	0.027002345
Neat1	0.98	0.000701642	**Kif1a**	1.16	0.027160412
Neil3	1.56	0.000723987	**Calb1**	0.52	0.027160412
Stc2	1.01	0.000857293	**Hivep3**	0.46	0.027160412
Uhrf1	1.19	0.000858778	**Fkbp4**	-0.63	0.027160412
Pigz	1.43	0.000877231	**Lama2**	0.47	0.027160412
Mdm2	0.47	0.00099063	**Sobp**	0.71	0.02729716
Gm5717	1.02	0.00099063	**4930578G10Rik**	1.50	0.027913396
Poln	1.53	0.00099063	**Gm43016**	1.09	0.027913396
A930033H14Rik	-0.88	0.00099063	**Slc7a12**	1.85	0.02803113
Casc5	1.10	0.00099063	**Lgals3bp**	0.72	0.028090663
Akr1c20	1.91	0.000999734	**Gm13111**	-0.61	0.028090663
Gpnmb	2.50	0.00100703	**Kcnab2**	-0.64	0.028326102
F2r	0.74	0.001033634	**Slc16a14**	-0.92	0.028326102
Vcam1	0.79	0.001033634	**Parpbp**	0.88	0.028326102
Adamtsl3	1.01	0.001123391	**Kcnt2**	0.57	0.028568858
Gm3448	0.94	0.001123391	**Pir**	0.70	0.028790527
Tmtc4	-0.71	0.001147034	**Rab31**	0.54	0.028964715
Tmem132b	1.79	0.001147034	**Prima1**	-0.67	0.028969828
Sparcl1	0.87	0.001164123	**Gm16505**	-1.33	0.028969828
A330033J07Rik	1.41	0.001192759	**Smim22**	-1.00	0.029457905
Ms4a7	0.91	0.001214604	**Slc13a3**	-0.59	0.029805665
Slc16a10	-0.66	0.001361023	**Fcgr2b**	-0.54	0.029805665
Hmcn1	0.68	0.001393465	**Lonrf1**	-0.71	0.02990429
Trpm3	0.85	0.001393465	**Slc34a3**	-0.84	0.02990429
Melk	1.31	0.001393465	**Birc3**	0.48	0.03003825

Dgkb	-0.61	0.001393465	**Sap30**	-0.73	0.03003825
Exo1	1.69	0.001398249	**Hpgds**	0.80	0.03014368
Cp	1.09	0.001400168	**Fads2**	-0.42	0.030150818
Ftcd	0.74	0.001413579	**Nrap**	0.85	0.030151069
Pappa2	-1.96	0.001438359	**Gm38048**	1.02	0.030271805
Il33	0.83	0.001469406	**Card14**	0.65	0.030271805
Smad7	-0.64	0.001500351	**Plxna2**	0.39	0.030271805
Grm8	1.30	0.001509827	**Aldh3b3**	-0.95	0.030271805
Abca1	0.66	0.001561889	**Aadat**	-0.54	0.030311443
Prc1	1.03	0.001567868	**Lockd**	0.84	0.030311443
Slitrk4	2.61	0.001567868	**Slc17a1**	-0.52	0.030311443
Gm1604b	0.91	0.001620691	**Fos**	1.28	0.030311443
Ahsa2	-0.65	0.001635698	**Srgap1**	0.43	0.030486144
Gm34240	1.59	0.001635698	**Serping1**	0.63	0.030977724
Mt1	1.11	0.001644429	**Gm44174**	1.06	0.030990933
Ccdc18	1.16	0.00167064	**Ahsa1**	-0.52	0.030990933
Cacna1e	0.88	0.00169607	**RP24-420C18.2**	-1.50	0.030990933
Rasa3	0.55	0.001711702	**Ces1f**	-0.72	0.030990933
Spock1	1.96	0.00177848	**Gm10271**	-0.74	0.03159661
Stil	1.19	0.00177848	**Gda**	-0.45	0.03159661
Pcdh11x	-1.49	0.001804795	**Lyz2**	0.69	0.03159661
Rrm2	0.94	0.001823116	**Zfp385a**	0.59	0.03172998
Kif4	1.08	0.001837703	**Wdr27**	0.67	0.032079904
Zfp423	0.68	0.001842448	**Fbn2**	1.22	0.032205903
Acaa1b	-0.76	0.001848029	**Irf7**	0.70	0.032685999
Cd86	0.82	0.001899982	**Ggct**	-0.60	0.03292138
Lin7a	-0.67	0.002016067	**Plch1**	0.56	0.033011608
C1qtnf3	-0.88	0.002016067	**Tmem237**	-0.64	0.033022533
Ttr	-1.04	0.002023144	**Gm10388**	1.37	0.033022533
A2m	-2.15	0.002043764	**Cmtm6**	-0.65	0.033022533
Pate2	1.17	0.002051858	**Platr25**	0.80	0.033057218
Themis	1.04	0.002080101	**Stk35**	-0.41	0.033242429
2810407A14 Rik	1.12	0.002177895	**Slc16a12**	-0.44	0.033250425
St18	1.55	0.002210048	**Ncapg**	1.11	0.033553422
4932411K12 Rik	1.21	0.002374687	**Rasl10b**	1.15	0.033553422
Tpx2	0.99	0.002381173	**Hspa8**	-0.65	0.033553422
Hsd17b2	-0.64	0.002532463	**Amacr**	-0.84	0.033553422
Odc1	-1.17	0.002532463	**Fam129a**	0.55	0.033646919
Scg5	0.94	0.002599677	**8430419K02 Rik**	1.35	0.033646919
Bdkrb2	1.20	0.002599677	**Aspm**	0.77	0.033646919

Crb1	-1.32	0.002627013
Gm43948	1.79	0.002654872
Dtl	1.26	0.002654872
Xlr3a	-1.77	0.002654872
Pros1	0.58	0.00267056
Atp2b4	0.50	0.002729759
Myl9	0.58	0.002790733
Stip1	-0.62	0.002971899
Zdhhc19	1.75	0.002974115
Rbm11	1.23	0.003081189
Dcn	0.84	0.003081189
Dnaja4	-0.54	0.003092947
Agt	0.81	0.003096125
Miox	-0.83	0.003105081
C1s1	0.69	0.003114916
F5	-1.49	0.003123712
Gabbr2	1.04	0.003204399
Cyp1b1	0.74	0.00322941
Nqo1	1.12	0.003235666
Abca14	1.08	0.00325968
Dscam	1.76	0.003318636
Nrg1	0.61	0.00336306
Runx2	0.60	0.003416652
Rxrg	1.54	0.003452638
Cdh11	0.62	0.003481264
Ncapg2	0.75	0.003568569
Gm11766	-1.27	0.003568569
Ugt2b5	1.06	0.003568569
4930533I22Rik	-0.67	0.003573506
Ighg2b	1.78	0.00372872
Slc9a8	-0.61	0.003778066
Golm1	0.89	0.003792713
Pth2r	1.11	0.003820403
Polk	0.44	0.003860633
Arnt2	0.53	0.003879127
Ank1	1.00	0.00395734
Slc41a3	0.67	0.00395734
Gm45051	-1.40	0.004038009
Egfem1	0.83	0.004038009
Naip1	1.87	0.004043629
Nap1l5	-1.14	0.004043629
Acad10	-0.41	0.033646919
Mettl7b	-0.54	0.033646919
Echdc2	-0.55	0.033983605
Alox5	1.11	0.034123737
Ebp	-0.40	0.034251399
Rbm3	0.45	0.034558151
Amdhd1	1.05	0.034660217
Bard1	0.61	0.034781805
Gm28802	1.42	0.034781805
S100a10	0.43	0.034911821
Fasn	-0.48	0.034973702
Sdf2l1	-0.89	0.035105961
Kif11	0.83	0.035207811
Josd2	-0.81	0.03540355
A330093E20Rik	1.26	0.03540355
Haao	-0.56	0.035406525
Hspa4l	-0.41	0.035447112
Garnl3	0.83	0.035730371
Hells	0.62	0.036051544
Zfp706	-0.38	0.036147321
Pcyt2	-0.37	0.036323018
Kif18b	1.25	0.036324642
Mgat3	-0.44	0.036490376
Thsd1	0.56	0.036490376
Cpox	-0.51	0.036653391
Dnajb2	-0.42	0.036760048
Fanci	0.94	0.036847148
Gm14232	1.05	0.036847148
Cpt2	-0.41	0.036847148
Prune2	1.22	0.037013926
Ezh2	0.43	0.037180113
Wfdc15b	-0.77	0.037212028
Hist1h3c	1.08	0.037212028
Capsl	1.17	0.037212028
Cbr3	1.31	0.037212028
Grb7	-0.48	0.037401673
Zbed3	-0.43	0.037401673
Ctss	0.49	0.037401673
Galnt11	-0.47	0.037665631
Hhat	0.40	0.037741723
Pde10a	0.65	0.038099067

Palm3	0.71	0.004065742	**Gm14963**	-0.76	0.038138357
Col27a1	-0.94	0.004080484	**Iqcc**	-0.54	0.038138357
Fetub	1.11	0.004080484	**Gpr173**	0.85	0.038138357
Mcm5	0.82	0.004121968	**Cbs**	-0.40	0.038170561
Kif15	1.11	0.004173332	**Msh4**	0.91	0.038170561
Spp1	0.99	0.004231284	**Etv1**	-0.97	0.038189078
Ung	1.32	0.004237784	**Cpt1c**	0.83	0.038387017
Efcab11	0.86	0.004315425	**Kcnh7**	-1.91	0.03840228
Epha6	0.95	0.004394363	**St8sia6**	-0.37	0.038415909
Mttp	-0.61	0.004460026	**9130409J20 Rik**	-3.12	0.038456009
Gm26672	-1.23	0.004662414	**9930014A18 Rik**	0.67	0.038456009
Wdhd1	0.75	0.004765688	**Chaf1a**	0.64	0.038703022
Inmt	-1.19	0.004879528	**1500017E21 Rik**	1.29	0.038715575
Dpf3	-0.48	0.004906669	**Lif**	0.96	0.039174148
Gm7205	0.94	0.00515389	**Gm42636**	1.11	0.039396669
Extl1	1.27	0.00515389	**Tchhl1**	0.95	0.039560702
Rgs5	0.61	0.00515389	**Chrdl2**	1.73	0.039560702
Slitrk6	-0.97	0.00517332	**Creld2**	-0.76	0.039560702
Chordc1	-0.48	0.005227557	**Slc25a25**	-0.66	0.040067622
Efcab8	1.41	0.005244149	**Gm13660**	1.09	0.040067622
Ccdc148	0.49	0.005334889	**Zfp462**	0.35	0.040078084
Pde6h	0.80	0.005373115	**Cyp2j11**	-0.37	0.040078084
A430093F15 Rik	1.41	0.005591928	**C7**	1.07	0.040155285
Epha3	0.84	0.005637197	**Gbp8**	0.68	0.040222844
Akr1c12	0.87	0.005637329	**P2rx7**	0.66	0.041585874
Bhmt	1.11	0.005654491	**Pi15**	0.61	0.041868071
6030443J06 Rik	0.51	0.005659182	**Sparc**	0.45	0.04230449
Vegfd	0.65	0.005659182	**Hsp90ab1**	-0.62	0.042446532
RP24-335D17.3	-1.29	0.005673471	**Hfe**	0.47	0.042446532
Serpinf2	-0.82	0.005732809	**Cbfa2t3**	-0.45	0.043113383
Slc22a3	1.29	0.005732809	**Brca2**	0.55	0.043176121
Abcb1a	0.87	0.005732809	**Slc7a13**	-0.72	0.043479187
Ndnf	1.81	0.005736337	**Hmmr**	0.98	0.043547863
Cby3	1.81	0.005828929	**Zbtb7a**	-0.43	0.043547863
Lpo	1.89	0.005937133	**Zgrf1**	0.63	0.043547863
Aldh1a2	0.94	0.006062034	**Ddit4**	1.18	0.043547863
Mt2	1.24	0.006237894	**Pabpc1l**	1.69	0.043671738
Clic6	1.98	0.006250089	**Slc5a10**	0.42	0.043778655
Fancd2	1.00	0.00630813	**Lad1**	-0.33	0.043888974

Mpeg1	0.62	0.006459064	**Gm17597**	-1.04	0.043955773
Veph1	-0.50	0.006755023	**Nxpe4**	0.63	0.04410416
Papln	0.77	0.006840456	**Gucy1a2**	0.39	0.04410416
Prdm1	-0.82	0.006840456	**Acss2**	-0.44	0.04411085
Egflam	0.50	0.006853085	**Eps8l1**	-0.58	0.044230408
Scara3	1.84	0.006994451	**Pard3bos3**	-1.26	0.044248429
Btnl9	-0.78	0.007005095	**Spp2**	-0.64	0.04457674
Lsmem1	1.03	0.00707001	**Scrn2**	-0.67	0.045363229
Ddo	-0.40	0.007081921	**Vwa2**	-0.46	0.045760312
Slc17a4	-1.12	0.007081921	**Txlng**	-0.33	0.045806295
Atp8b5	0.89	0.007081921	**Celsr2**	-0.36	0.045837082
Neurog2	-1.15	0.007176829	**Mgst1**	0.49	0.045912116
Ptprq	1.47	0.007231643	**Syt2**	1.05	0.045915511
Mybl1	0.83	0.007268832	**Mpzl2**	0.62	0.045965473
Snhg15	0.93	0.007297226	**Pdzk1**	-0.55	0.045965473
Oasl1	0.92	0.007297226	**Cdkl1**	-0.48	0.046124427
Fam149a	-0.59	0.007328242	**Myrfl**	0.88	0.046390059
Nectin1	0.53	0.007364756	**Irak3**	0.73	0.046390059
Acad12	-0.42	0.007390619	**D630003M21Rik**	-0.72	0.046390059
A330015K06Rik	1.20	0.007390619	**Ccdc180**	-1.11	0.046390059
1810064F22Rik	1.25	0.00742241	**Chst7**	-0.78	0.046398145
Gm1604a	1.08	0.007542888	**Fcgbp**	-2.12	0.046398145
Cys1	-0.59	0.007574571	**Procr**	1.02	0.046662811
Dnajc12	-0.70	0.007701768	**Rnf145**	-0.35	0.046700417
Gria3	0.60	0.007764025	**Gm43568**	-0.68	0.046972621
Glyctk	-0.62	0.007764025	**Spats2l**	-0.64	0.047350128
Ak4	-0.67	0.007844291	**Gm6999**	0.57	0.047350128
Clec12a	0.87	0.00788046	**Acat1**	-0.48	0.047350128
2010300C02Rik	-0.82	0.00788046	**Gm15264**	0.56	0.047418026
Nrep	-0.82	0.007899711	**Myof**	0.75	0.047418026
Aldh1a3	-3.40	0.008037724	**Akr1b7**	0.92	0.047566544
Wnt11	-2.65	0.008046393	**Impg2**	0.52	0.047747713
Slc15a1	1.02	0.00817401	**Tgfbi**	0.51	0.047756606
Arhgap27	-0.42	0.008283679	**Klf6**	0.37	0.047888831
Gm45083	0.63	0.008453823	**Tmem150a**	-0.55	0.047888831
Xkr4	0.88	0.00849699	**P4ha1**	-0.40	0.047976242
Tcf23	2.03	0.008745751	**Ccnb1**	1.03	0.048066198
Trim9	2.05	0.008782161	**Msi1**	0.95	0.048066198
Ltbp2	1.87	0.008873874	**Gcnt3**	-2.96	0.048066198
Vwa3a	0.88	0.008873874	**Nek6**	0.37	0.048066198

Igfbp4	-0.80	0.008874681	**Knstrn**	0.71	0.048614289
Gm20755	1.10	0.009074906	**Tubb6**	0.80	0.048614289
Adh6b	2.64	0.009100906	**Fam169b**	-0.36	0.048853805
Acsbg1	1.22	0.009104592	**Cfh**	0.49	0.048971437
Slc16a13	-0.74	0.009104592	**Tlr13**	0.85	0.0490811
Ogn	0.71	0.009161829	**Srpx**	0.84	0.049755752
C330027C09Rik	0.77	0.009381493	**Rnf183**	-0.63	0.04998003
Unc13c	-1.09	0.009392039			

Table S2. Upstream regulator analysis: Control versus diabetic ApoE$^{-/-}$ mice.

Upstream Regulator	Predicted Activation State	Activation z-score	p-value of overlap
TRIM24	Inhibited	-3.317	0.00000441
NEUROG1	Inhibited	-3.162	0.00000861
SPARC	Inhibited	-3.162	0.000752
Irgm1	Inhibited	-3.148	0.000000342
IRF4	Inhibited	-2.946	0.00054
ATP7B	Inhibited	-2.828	0.00000143
KDM5B	Inhibited	-2.651	0.00203
HSF1	Inhibited	-2.46	4.95E-11
GLIS2	Inhibited	-2.449	0.00000381
miR-34a-5p	Inhibited	-2.443	0.000564
Alpha catenin	Inhibited	-2.388	0.000165
AURK	Inhibited	-2.345	0.00000895
ANLN	Inhibited	-2.333	0.00000895
CBX5	Inhibited	-2.333	0.00156
TAB1	Inhibited	-2.236	0.000367
BNIP3L	Inhibited	-2.219	0.0191
ABCB4	Inhibited	-2.216	0.00119
ZFP36	Inhibited	-2.213	0.000564
SCAP	Inhibited	-2.183	0.0151
RB1	Inhibited	-2.138	0.272
CD38	Inhibited	-2.111	0.00383
PPARG	Inhibited	-2.044	0.000000506
SAV1	Inhibited	-2	0.0000237
MST1	Inhibited	-2	0.0000813
STAR	Inhibited	-2	0.000298
STK3	Inhibited	-2	0.00042
TSC2	Inhibited	-2	0.0117
LRP1	Inhibited	-2	0.0122
ACKR2	Inhibited	-2	0.0223
PRNP	Inhibited	-2	0.0513
MAPK14	Activated	2.04	0.00215
IL17A	Activated	2.06	0.0673
ERBB2	Activated	2.064	4.91E-14
FGFR1	Activated	2.091	0.0514
FOXM1	Activated	2.094	0.0000772
IFNG	Activated	2.097	0.000033
PRKCD	Activated	2.131	0.00000726
Vegf	Activated	2.138	0.000596
TLR9	Activated	2.141	0.00778

TAL1	Activated	2.145	0.00278
IFNB1	Activated	2.151	0.000157
SRF	Activated	2.158	0.00111
VEGFA	Activated	2.162	0.000205
F2	Activated	2.177	0.000565
HRAS	Activated	2.19	0.000124
FOXO3	Activated	2.195	0.000051
TREM1	Activated	2.197	0.000579
KITLG	Activated	2.197	0.0151
E2f	Activated	2.2	0.0016
MAP2K4	Activated	2.213	0.0014
TLR2	Activated	2.23	0.309
NFATC2	Activated	2.236	0.0126
IL12B	Activated	2.236	0.0164
RELA	Activated	2.248	0.0000999
EZH2	Activated	2.263	0.0000672
mir-223	Activated	2.331	0.000129
RETNLB	Activated	2.345	0.000301
LCN2	Activated	2.353	0.00264
NR1I3	Activated	2.371	0.0000567
CREB1	Activated	2.375	0.00000291
AKT1	Activated	2.376	0.0000568
IFNAR1	Activated	2.378	0.00501
CYP1A1	Activated	2.4	0.00591
ERK	Activated	2.412	0.000472
Akt	Activated	2.415	0.000326
ELAVL1	Activated	2.433	0.0108
TNFRSF1A	Activated	2.439	0.0000321
HTT	Activated	2.449	1.04E-08
NQO1	Activated	2.449	0.000482
TMEM173	Activated	2.449	0.00131
HIPK2	Activated	2.449	0.00741
CCND1	Activated	2.466	4.23E-11
CHUK	Activated	2.535	0.0000024
IKBKB	Activated	2.548	1.1E-09
Ifnar	Activated	2.592	0.0122
CREBBP	Activated	2.599	0.0292
Jnk	Activated	2.613	0.00000119
SMARCA4	Activated	2.64	0.000997
NEDD9	Activated	2.646	0.0000707
ERK1/2	Activated	2.765	0.0000672

PDGF BB	Activated	2.777	0.000151
Cg	Activated	2.823	1E-12
PTGER2	Activated	2.84	1.31E-08
NFkB (complex)	Activated	2.843	0.000311
TICAM1	Activated	2.883	0.0107
RIPK2	Activated	2.918	0.000139
MYD88	Activated	2.938	0.0000623
TGFB1	Activated	2.957	2.53E-11
TP53	Activated	3.005	1.6E-21
FOXO1	Activated	3.102	0.000000193
IKBKG	Activated	3.182	0.0000102
TLR3	Activated	3.201	0.00235
P38 MAPK	Activated	3.283	0.00000115
RABL6	Activated	3.317	0.00000262
TNF	Activated	3.377	2.47E-09
CSF2	Activated	4.176	1.29E-11

Table S3. Upstream regulator analysis: Diabetic versus Diabetic + LXA$_4$ or Benzo-LXA$_4$ treated ApoE$^{-/-}$ mice.

Upstream Regulator	Molecule Type	Predicted Activation State	Activation z-score	p-value of overlap
PDGF BB	complex	Inhibited	-3.213	0.00000641
SREBF1	transcription regulator	Inhibited	-2.795	0.00199
RABL6	other	Inhibited	-2.449	0.0409
PTPN1	phosphatase	Inhibited	-2.425	0.00692
C3	peptidase	Inhibited	-2.4	0.00429
Growth hormone	group	Inhibited	-2.345	0.00025
NCOA1	transcription regulator	Inhibited	-2.236	0.144
PI3K (family)	group	Inhibited	-2.225	0.00584
NR1I2	ligand-dependent nuclear receptor	Inhibited	-2.224	0.398
PLIN5	other	Inhibited	-2.219	0.00417
let-7	microrna	Inhibited	-2.2	0.0356
AR	ligand-dependent nuclear receptor	Inhibited	-2.171	0.207
PGR	ligand-dependent nuclear receptor	Inhibited	-2.13	0.000223
GMNN	transcription regulator	Inhibited	-2.121	0.0127
PTEN	phosphatase	Inhibited	-2.09	0.242
TNF	cytokine	Inhibited	-2.09	0.0000856
IL27	cytokine	Inhibited	-2.082	0.0034
TREM1	transmembrane receptor	Inhibited	-2.07	0.135
AHR	ligand-dependent nuclear receptor	Inhibited	-2.044	0.000000756
HAND1	transcription regulator	Inhibited	-2	0.000851
ATP7B	transporter	Inhibited	-2	0.0172
miR-182-5p	mature microrna	Inhibited	-2	0.0314
TNFRSF1B	transmembrane receptor	Inhibited	-2	0.0977
APC	enzyme	Inhibited	-2	0.145
UPF2	other	Inhibited	-2	0.0395
BMP15	growth factor	Activated	2	0.000888
KDM1A	enzyme	Activated	2	0.0754
HDAC1	transcription regulator	Activated	2.121	0.0152
FADD	other	Activated	2.219	0.15
BACH2	transcription regulator	Activated	2.236	0.0253
H2AFY	other	Activated	2.236	0.00645
KLF4	transcription regulator	Activated	2.299	0.0468
FIGLA	transcription regulator	Activated	2.387	0.0233
NR3C1	ligand-dependent nuclear receptor	Activated	2.401	0.0809

PPARA	ligand-dependent nuclear receptor	Activated	2.581	0.000000039
RICTOR	other	Activated	3.308	0.00678

Table S4. Differentially expressed genes: Diabetic versus Diabetic + LXA_4 treated $ApoE^{-/-}$ mice.

Gene ID	logFC	FDR (CORRECTED P-VALUE)
Egr1	-1.43	2.06E-07
1600010M07Rik	1.24	0.004551304
Rorc	1.04	0.005418383
Jchain	-1.48	0.005443802
Gm15441	1.47	0.005443802
Lamb3	0.93	0.006032177
Fcnaos	1.11	0.006357033
Gm45064	-1.47	0.007896206
Msmo1	-0.75	0.008307286
Cyp2c69	-1.61	0.00904752
Iglc1	-2.51	0.010555067
Insig1	-0.79	0.015245182
Igfbp1	-1.19	0.015245182
Lrat	-1.24	0.020743571
Ngef	0.57	0.020743571
Tfrc	-0.73	0.027328174
Aldh1a3	4.27	0.035119141
Adamtsl3	1.10	0.040081492
Per2	1.11	0.040081492
Lonrf3	0.94	0.049713619

Table S5. Differentially expressed genes: Diabetic versus Diabetic + Benzo-LXA$_4$ treated ApoE$^{-/-}$ mice.

GeneID	logFC	FDR (CORRECTED P-VALUE)
Capn11	2.86	5.79E-08
Socs2	0.90	5.79E-08
Egr1	0.93	1.20E-05
Hbb-bs	1.21	0.000125237
Hba-a2	0.98	0.000237253
Glt1d1	-0.71	0.000260207
Ngef	-0.47	0.000260207
Prr5	0.54	0.000299969
8430408G22Rik	-1.18	0.000340402
Pak7	2.07	0.000373996
Hba-a1	0.91	0.001281152
Dscaml1	-1.01	0.001550101
Cfd	5.19	0.001877703
Atp2b2	-0.57	0.002746252
Plau	0.60	0.003776998
Kcnma1	0.77	0.008654365
Gm4450	0.52	0.00994191
Gm16010	1.49	0.011420084
Nat8f6	-0.87	0.012461811
Angptl7	-1.05	0.01523872
Slc7a12	2.22	0.01523872
Igfals	0.78	0.01523872
G6pc	-0.47	0.01523872
Erdr1	-2.94	0.01526526
Lamb3	-0.62	0.020141288
Gm13052	-0.66	0.020141288
Zbtb40	-0.39	0.020798055
Insrr	-0.62	0.021177013
Csgalnact1	0.39	0.021332777
D630039A03Rik	0.63	0.022088759
Ucp1	4.59	0.022088759
Tfr2	-1.51	0.023870615
Halr1	0.82	0.025706594
Nr4a1	1.16	0.025706594
Cish	1.00	0.027261422
Alk	0.66	0.031167045
Gm10787	-0.92	0.032380875

Retn	4.21	0.032789954
Gm17189	-0.72	0.033243619
Tmem37	0.89	0.034670499
Pitpnm2	-0.35	0.035585409
Gpc3	0.55	0.035585409
Adamtsl3	-0.98	0.036717043
Kyat1	-0.34	0.036955478
Ybx2	-0.43	0.039671637
Ncor2	-0.36	0.039671637
Aim1	-0.32	0.039671637
Slc7a7	0.50	0.039671637
Hspa1a	-0.80	0.039767456
Slc15a4	-0.32	0.045446994
Tspan18	-0.42	0.049402702

Table S6. TFBS promoter analysis of differentially expressed genes from ApoE-/- RNA seq experiment

Control versus diabetic ApoE-/- mice.		diabetic ApoE-/- VS diabetic ApoE-/- + LXA4		diabetic ApoE-/- VS diabetic ApoE-/- + Benzo-LXA4	
TF Families	**Z-Score (promoters)**	**TF Families**	**Z-Score (promoters)**	**TF Families**	**Z-Score (promoters)**
V$ZF5F	18.42	V$ZF5F	14.35	V$ZF02	21.04
V$E2FF	16.33	V$E2FF	8.11	V$EGRF	19.43
V$ZF02	13.38	V$NRF1	7.83	V$BEDF	16.07
V$NRF1	13.16	V$ZF02	7.63	V$PLAG	15.96
V$EGRF	12.74	V$EGRF	6.84	V$SP1F	14.91
V$GABF	11.71	V$HNFP	5.88	V$KLFS	14.91
V$BEDF	11.71	V$BEDF	5.76	V$ZTRE	13.92
V$SP1F	11.07	V$GCF2	5.43	V$GCF2	13.43
V$ZTRE	10.76	V$SP1F	5.19	V$MAZF	12.81
V$CTCF	10.31	V$CDEF	5.04	V$CTCF	12.19
V$MAZF	9.85	V$PLAG	4.72	O$XCPE	12.11
V$KLFS	9.16	V$EBOX	4.72	V$GLIF	11.68
V$PLAG	8.87	V$MAZF	4.52	V$E2FF	10.34
O$XCPE	8.45	V$NDPK	4.31	V$AP2F	10.08
O$MTEN	8.43	V$OAZF	4.3	V$ZF5F	10.05
V$CDEF	8.3	V$HESF	4.27	V$NDPK	9.98
V$NDPK	7.84	V$AP2F	4.21	V$NOLF	7.19
V$HDBP	7.8	V$GLIF	4.21	V$NFKB	7.11
V$GCF2	7.03	V$AHRR	4.1	V$STAF	6.99
V$HNFP	6.72	V$CTCF	3.91	V$ZF07	6.75
V$OAZF	6.26	V$ZTRE	3.87	V$RXRF	6.66
O$TF2B	6.24	V$BNCF	3.67	O$MTEN	6.63
V$GLIF	6.22	V$ZFXY	3.64	V$MZF1	6.63
V$ZF15	5.87	O$MTEN	3.59	V$RREB	6.47
V$AHRR	5.66	V$KLFS	3.53	V$HDBP	6.23
V$EBOX	5.33	V$ZF07	3.46	V$HESF	6.15
V$NFKB	5.06	V$CHRE	3.37	V$GCMF	5.98
V$HESF	5	V$NF1F	3.23	V$INSM	5.95
V$MZF1	4.94	V$NRSF	3.21	V$NRF1	5.86
V$ZF57	4.68	O$XCPE	3.16	V$SPZ1	5.83
V$ZF07	4.52	V$ZF57	3.13	V$SAL2	5.77
V$PAX9	4.47	V$SMAD	3.01	V$NRSF	5.2
V$NOLF	4.33	V$HAND	2.97	V$SMAD	4.95
V$MTF1	4.32	V$GABF	2.8	V$PEG3	4.88
V$SAL2	4.23	V$MOKF	2.76	V$PURA	4.54
V$AP2F	4.14	V$ZF11	2.72	V$ZF57	4.49
V$NRSF	4.05	V$NOLF	2.71	V$BNCF	4.32
V$WHNF	4.02	V$NFKB	2.68	V$EBOX	4.26

V$PRDM	3.77	V$MTF1	2.38	V$PAX5	4.15
V$ZICF	3.51	V$SPZ1	2.34	V$NF1F	4.04
V$HIFF	3.44	V$IKRS	2.26	V$CHRE	3.97
V$CHRE	3.32	V$ZICF	2.25	V$ZF11	3.84
V$MIZ1	3.04	V$THAP	2.19	V$ZFXY	3.66
V$PERO	2.94	V$ZF15	2.18	V$NR2F	3.57
V$NF1F	2.94	V$MIZ1	2.08	V$AHRR	3.53
V$GCMF	2.93	V$RXRF	2.08	V$OAZF	3.47
V$PURA	2.82	V$MYOD	2.03	V$PRDM	3.46
V$HEAT	2.8	V$LTFM	1.99	V$ZICF	3.44
V$PAX5	2.75	V$HDBP	1.97	V$ESRR	3.41
V$STAF	2.62	V$CREB	1.97	V$CDEF	3.3
V$CARE	2.59	V$AP4R	1.88	O$TF2B	3
V$INSM	2.46	V$PAX9	1.75	V$MIZ1	3
V$GTBX	2.44	V$DICE	1.74	V$HNFP	2.83
V$AP4R	2.39	V$HIFF	1.71	V$MYOD	2.6
V$ZBED	2.21	V$ZF04	1.69	V$PAX9	2.59
V$ZFHX	2.13	V$RREB	1.68	V$DMTF	2.47
V$DEAF	2.11	V$STAF	1.57	V$EREF	2.45
V$ETSF	2.04	O$TF2B	1.56	V$SRFF	2.43
V$MYBL	2	V$CSEN	1.5	V$ZF35	2.42
V$ZF35	2	V$SAL2	1.47	V$SF1F	2.36
V$SREB	2	V$INSM	1.46	V$ZF04	2.27
V$MYOD	1.93	V$TEAF	1.46	V$YBXF	2.27
V$HZIP	1.87	V$ZF01	1.38	V$HICF	2.26
V$HASF	1.86	V$CARE	1.18	V$RBPF	2.26
V$FXRE	1.71	V$RBPF	1.09	V$PERO	2.24
V$PRDF	1.7	V$GRHL	1.01	V$HIFF	2.19
V$NGRE	1.69	V$MEF3	0.99	V$NACA	2.16
V$DMTF	1.63	V$EREF	0.97	V$TAIP	1.95
V$RREB	1.62	V$PRDM	0.96	V$HASF	1.88
V$PROX	1.4	V$MZF1	0.93	V$MOKF	1.88
V$SNAI	1.39	V$NEUR	0.9	V$PTF1	1.86
V$XBBF	1.35	V$CP2F	0.87	V$RORA	1.84
V$ESRR	1.32	V$PROX	0.79	V$HAND	1.74
V$AP1R	1.31	V$SNAI	0.75	V$LTFM	1.68
V$CP2F	1.19	V$NGRE	0.69	V$DEAF	1.63
V$RBPF	1.18	V$PAX5	0.69	V$WHNF	1.61
V$P53F	1.17	V$TALE	0.69	V$CARE	1.59
V$BARB	1.15	V$DMTF	0.6	V$GTBX	1.58
V$SMAD	1.13	V$SRFF	0.57	V$NGRE	1.49
V$DICE	1.09	V$GCMF	0.56	V$SREB	1.45
V$ZF11	1.04	V$E4FF	0.56	V$ZF10	1.43

V$NACA	0.99	V$NACA	0.52	V$CP2F	1.4
O$INRE	0.98	V$MYRF	0.5	V$RBP2	1.36
V$NR2F	0.91	V$RBP2	0.49	V$P53F	1.35
V$YBXF	0.91	V$ZF35	0.46	V$CSEN	1.29
O$TF2D	0.91	V$ZF06	0.42	V$AP1R	1.27
V$SPZ1	0.89	V$NFAT	0.4	V$NEUR	1.18
V$CHOP	0.89	V$ESRR	0.33	V$SNAI	1.17
V$RXRF	0.89	V$HICF	0.29	V$XBBF	1.16
V$RBP2	0.83	V$SF1F	0.28	V$ZF01	1.15
V$IRFF	0.83	V$NKX1	0.27	V$IKRS	1.13
V$TALE	0.75	V$ZBED	0.23	V$MYRF	1.08
V$MOKF	0.72	V$YBXF	0.21	V$CAAT	1.05
V$PAX1	0.71	V$SREB	0.19	V$DICE	1.02
V$PAX3	0.62	V$ZFHX	0.19	O$TELO	1.01
V$NBRE	0.61	V$BRAC	0.18	V$NBRE	1
V$PAX6	0.58	V$P53F	0.17	V$GREF	0.97
V$GRHL	0.57	V$PPAR	0.13	V$AP4R	0.92
V$AP1F	0.54	O$TF2D	0.11	V$MTF1	0.84
V$NFAT	0.49	V$PURA	0.06	V$PAX3	0.76
V$GCNR	0.47	V$AP1R	0.01	V$PAX6	0.64
V$SF1F	0.45	V$ZF03	0	V$BRAC	0.55
V$GMEB	0.44	V$HASF	-0.01	V$HAML	0.54
V$GZF1	0.42	V$WHNF	-0.02	V$CIZF	0.53
V$ZF01	0.34	V$GTBX	-0.03	V$TALE	0.52
O$TELO	0.27	V$GFI1	-0.04	V$ZF08	0.5
V$IKZF	0.24	V$PERO	-0.05	V$YY1F	0.48
V$BCL6	0.17	O$TELO	-0.06	V$GCNR	0.45
V$MYT1	0.12	V$PTF1	-0.06	V$BTBF	0.45
V$PCBE	0.02	V$DEAF	-0.08	V$ZF06	0.37
V$IKRS	-0.03	V$HZIP	-0.15	V$ZFHX	0.36
V$OSRF	-0.05	V$PAX1	-0.19	V$FXRE	0.31
O$TF3A	-0.05	V$GMEB	-0.28	V$GRHL	0.28
V$ZF08	-0.05	V$PCBE	-0.37	V$PBXC	0.28
V$GFI1	-0.07	O$TF3C	-0.38	V$GMEB	0.23
V$TCFF	-0.12	V$ZF09	-0.39	V$THAP	0.2
V$PEG3	-0.14	V$CAAT	-0.41	V$IKZF	0.16
V$CEBP	-0.15	V$DUXF	-0.44	V$ETSF	0.13
V$CSEN	-0.22	V$RORA	-0.45	V$HEAT	-0.01
V$ZFXY	-0.22	V$HOXH	-0.45	V$MEF3	-0.03
V$TEAF	-0.24	V$PAXH	-0.46	V$ZF15	-0.05
V$CAAT	-0.32	V$BCL6	-0.47	V$HUB1	-0.05
V$GUCE	-0.38	V$TAIP	-0.5	V$GUCE	-0.26
V$HUB1	-0.41	V$OVOL	-0.54	V$CHOP	-0.34

V$BTBF	-0.45	V$AP1F	-0.54	V$MITF	-0.39
V$BZIP	-0.49	V$NBRE	-0.55	V$CREB	-0.57
V$PBXC	-0.51	V$SIXF	-0.58	V$ZF09	-0.58
V$STAT	-0.56	V$ZF05	-0.58	V$ZBED	-0.61
V$MEF3	-0.56	V$CHOP	-0.61	V$OSRF	-0.64
V$EREF	-0.59	V$NR2F	-0.66	V$PAX1	-0.66
V$LTFM	-0.66	V$CHRF	-0.69	V$PPAR	-0.72
V$LTSM	-0.73	V$PBXC	-0.72	V$TEAF	-0.82
V$ZF12	-0.73	V$FXRE	-0.78	O$TF3C	-1.02
V$HICF	-0.73	V$SAL1	-0.83	V$BARB	-1.07
V$BRAC	-0.74	V$GZF1	-0.86	V$LTSM	-1.07
V$CIZF	-0.92	V$ZF08	-0.93	V$PROX	-1.11
V$OVOL	-0.93	V$BHLH	-0.93	V$RP58	-1.13
V$ZF04	-1	V$GUCE	-0.94	V$HZIP	-1.14
V$HMTB	-1.04	V$MYBL	-0.95	V$AP1F	-1.23
V$NEUR	-1.09	V$STAT	-0.96	V$ZF13	-1.29
V$BNCF	-1.1	V$TCFF	-1.05	O$TF2D	-1.37
V$SAL1	-1.11	V$PEG3	-1.09	V$PCBE	-1.44
V$THAP	-1.11	V$GCNR	-1.09	V$E4FF	-1.47
V$ZF10	-1.17	V$CEBP	-1.11	V$NFAT	-1.51
V$AARF	-1.23	V$PAX3	-1.12	V$GABF	-1.65
V$ZF13	-1.25	V$PAX6	-1.12	V$SIX3	-1.75
V$MYRF	-1.37	V$SIX3	-1.14	V$RU49	-1.8
O$TF3C	-1.39	V$HMTB	-1.16	V$CHRF	-1.81
V$PTF1	-1.44	V$CIZF	-1.18	V$ZF14	-1.82
V$HOXH	-1.45	V$ZF10	-1.19	V$AARF	-1.95
V$SRFF	-1.5	V$PAX7	-1.2	V$ZF05	-1.96
V$RORA	-1.51	V$PRDF	-1.22	V$GFI1	-1.97
V$TAIP	-1.54	V$PARF	-1.26	V$OVOL	-2.01
V$ZF14	-1.68	V$ZF14	-1.27	V$BCL6	-2.21
V$SNAP	-1.72	V$SATB	-1.28	V$PRDF	-2.32
V$CREB	-1.75	V$XBBF	-1.29	V$ZF12	-2.43
V$ZF06	-1.81	V$IKZF	-1.31	V$SIXF	-2.56
V$RU49	-1.96	V$YY1F	-1.34	V$HOXH	-2.56
V$RP58	-2.01	V$PDX1	-1.34	V$CABL	-2.63
V$E4FF	-2.04	V$ATBF	-1.35	V$ZF03	-2.69
V$CHRF	-2.15	V$OSRF	-1.38	V$TCFF	-2.7
V$ZF03	-2.21	V$DLXF	-1.38	V$CEBP	-2.78
V$STEM	-2.29	V$GATA	-1.52	V$GZF1	-2.85
V$HAML	-2.3	V$ETSF	-1.67	V$STAT	-2.93
V$SATB	-2.35	V$BARB	-1.73	V$MYBL	-2.94
V$LEFF	-2.42	V$SNAP	-1.73	V$AIRE	-3.08
V$HAND	-2.46	V$BTBF	-1.76	O$INRE	-3.37

V$BPTF	-2.49	V$ZF13	-1.77	V$BZIP	-3.43
V$PAX2	-2.72	V$HUB1	-1.81	V$HMTB	-3.58
V$GREF	-2.78	V$PIT1	-1.82	V$SNAP	-3.67
V$CLOX	-2.86	V$HOMF	-1.84	V$IRFF	-3.74
V$PPAR	-2.9	V$HEAT	-1.85	V$SAL1	-3.79
V$PAX7	-3.06	V$AIRE	-1.88	V$BHLH	-3.83
V$ZF09	-3.08	V$HAML	-1.91	V$HOXC	-4.04
V$SIXF	-3.25	V$MITF	-1.97	V$DUXF	-4.12
V$SIX3	-3.3	V$BCDF	-2.01	V$BPTF	-4.22
V$HNF6	-3.34	V$GREF	-2.03	V$PAX7	-4.3
V$AIRE	-3.47	O$INRE	-2.07	V$RUSH	-4.33
V$EVI1	-3.53	V$BPTF	-2.17	V$EVI1	-4.41
V$DUXF	-3.57	V$RP58	-2.19	V$FAST	-4.62
V$RUSH	-3.58	V$NKX6	-2.25	V$LEFF	-4.71
V$ATBF	-3.65	V$RU49	-2.26	V$PAX2	-4.76
O$VTBP	-3.7	V$DMRT	-2.27	V$ATBF	-5.07
V$YY1F	-3.75	V$MYT1	-2.28	V$IRXF	-5.11
V$ZF05	-3.89	V$PLZF	-2.3	V$SATB	-5.21
V$PAXH	-3.94	V$FAST	-2.31	V$PLZF	-5.25
V$GATA	-3.98	V$HNF6	-2.64	V$PAXH	-5.26
V$HNF1	-4.04	V$BZIP	-2.68	V$CLOX	-5.26
V$MITF	-4.04	V$BRN5	-2.69	V$BCDF	-5.35
V$FAST	-4.07	V$ZF12	-2.74	V$NKX1	-5.43
V$CABL	-4.27	V$LTSM	-2.81	V$MYT1	-5.64
V$NKX1	-4.34	V$CART	-2.96	V$PIT1	-6.14
V$PLZF	-4.37	V$CABL	-3	V$STEM	-6.18
V$HOXC	-4.55	V$RUSH	-3	V$GATA	-6.24
O$PTBP	-4.59	V$LEFF	-3.03	V$PDX1	-6.33
V$NKXH	-4.63	V$IRFF	-3.21	V$HNF6	-6.76
V$DLXF	-4.63	V$MEF2	-3.24	V$NKXH	-6.81
V$PDX1	-4.66	V$EVI1	-3.35	V$NKX6	-7.63
V$PIT1	-4.75	V$LHXF	-3.35	V$MEF2	-7.7
V$BHLH	-4.78	V$ARID	-3.48	V$PARF	-7.84
V$CDXF	-4.88	V$HOXC	-3.63	V$DLXF	-7.95
V$PARF	-4.91	V$HNF1	-3.78	V$DMRT	-8.4
V$NKX6	-4.92	V$NKXH	-3.83	V$CDXF	-8.42
V$BCDF	-4.99	V$HBOX	-3.83	V$ARID	-9.36
V$MEF2	-5.13	O$VTBP	-3.86	V$HOXF	-9.6
V$ABDB	-5.41	V$STEM	-3.97	V$HNF1	-9.82
V$HOMF	-5.69	V$PAX2	-4.03	O$PTBP	-10.06
O$YTBP	-5.73	V$HOXF	-4.04	O$YTBP	-10.22
V$IRXF	-6.08	V$CDXF	-4.16	V$BRN5	-10.22
V$HBOX	-6.55	O$PTBP	-4.16	V$HBOX	-10.24

V$DMRT	-7.02	V$ABDB	-4.33	V$LHXF	-10.25
V$LHXF	-7.85	V$IRXF	-4.34	V$HOMF	-10.39
V$OCT1	-8.07	V$FKHD	-4.36	V$ABDB	-10.41
V$BRN5	-8.08	O$YTBP	-4.39	O$VTBP	-10.74
V$ARID	-8.15	V$CLOX	-4.4	V$CART	-11.93
V$HOXF	-8.42	V$OCT1	-4.91	V$FKHD	-12.17
V$BRNF	-8.69	V$BRNF	-5.39	V$BRNF	-13
V$CART	-8.91	V$SORY	-8.43	V$OCT1	-13.44
V$SORY	-9.6			V$SORY	-17.17
V$FKHD	-10.08				

Table S7 – PROVIDED AS SEPARATE .XLS FILE

Table S8. Details of primers and probes used for all quantitative PCR gene expression analysis.

NAME	DESCRIPTION	ACCESSION	PROBE SEQUENCE 5' - 3'	FORWARD PRIMER 5' - 3'	REVERSE PRIMER 5' - 3'
ARG1	Arginase 1	NM_007482	SYBER	GAAAGTTCCCAGATGTACCAGGAT	CGATGTCTTTGGCAGATATGCA
CD64	Fc recepter, igG, high affinity I	NM_007482	SYBER	GAAAGTTCCCAGATGTACCAGGAT	CGATGTCTTTGGCAGATATGCA
CD204	Macrophage scavenger receptor 1	NM_031195	SYBER	GGAGGAGAGAATCGAAAGCATTT	TCTGGAAGCGTTCCGTGTCT
COLLAGEN 1	Procollagen type 1	NM_007742	6- FAM ATCGACCCTAACCAAG	GACTGGAAGAGCGGAGAGTACTG	CCTTGATGGCGTCCAGGTT
COLLAGEN 3	Procollagen type 3	BC58724	6- FAM AATATCAAACACGCAAGGC	GGGAATGGAGCAAGACAGTCTT	TGCGATATCTATGATGGGTAGTCTCA
COLLAGEN 4	Procollagen type 4	J04694	6- FAM CAGTGCCCTAACGGT	GGCGGTACACAGTCAGACCAT	GGAATAGCCGATCCACAGTGA
COLLAGEN 4A3	Collagen 4 alpha 3	NM_007734	6-FAM CCCTGAAGGAACACAGC	ACCACGGCCATTCCTTCAT	CAAAAAGAAGAGAAAACCCACTATAGAGT
CTGF	Connective tissue growth factor	BC006783	6- FAM ACTGCCTGGTCCAGAC	GCTGCCTACCGACTGGAAGA	CTTAGAACAGGCGCTCCACTCT
F4/80	F4/80	X93328	SYBR	GGTACAGTCATCTCCCTGGTATGTCT	GGTTCTGAACAGCACGACACA
FPR2	Formyl peptide receptor 2	NM_008039	6-FAM TGTGTTCTGCATCCAGTC	GCCTTGGACCGCTGCAT	TCACAGTGCGGTGGTTCTGA
FPR2	Formyl peptide receptor 2	M88107	6-FAM CGCACAGTCACCACCAT	TGGCTGGATTCCGGATGA	AGGGCCAGGTTCAGGTAACA
ICAM1	Intercellular adhesion molecule 1	NM_010493	6-FAM CCCTGGAACTGCACG	GGAGGTGGCGGGAAAGTT	TCCAGCCGAGGACCATACAG
IL-1 beta	Interleukin 1 beta	M15131	6- FAM CTGAAAGCTCTCCACCTC	TCGTGCTGTCGGACCCATA	TTGTTGGTTGATATTCTGTCCATTG
IL-6	Interleukin 6	NM_031168	6- FAM ATTGCCATTGCACAACT	GGGAAATCGTGGAAATGAGAAA	AAGTGCATCATCGTTGTTCATACA
1L-10	Interleukin 10	NM_010548	6-FAM CATGGCCCAGAAAT	GATGCCCCAGGCAGAGAA	CACCCAGGGAATTCAAATGC
MCP-1	Monocyte chemoattractant protein-1	NM_011333	6- FAM AATGGGTCCAGACATAC	GTCTGTGCTGACCCCAAGAAG	TGGTTCCGATCCAGGTTTTTA
p21	Cyclin-dependent kinase inhibitor 1A (p21)	NM_007669	6-FAM AGAGCCACAGGCACC	TCCACAGCGATATCCAGACATT	CGGACATCACCAGGATTGG
NFKappaB p65 (RelA)	Transcription factor p65, also known as RelA	M61909	6-FAM AGCTCAAGATCTGCCG	TCTCACATCCGATTTTTGATAACC	CGAGGCAGCTCCCAGAGTT
p53	Nuclear oncoprotein p53	AF151353	6-FAM TTTGTATCCCGAGTATCTG	CGTATCCGGGTGGAAGGAA	GGCGAAAAGTCTGCCTGTCT
PCNA	Proliferating cell nuclear antigen	X53068	6- FAM CACAGCTGTACTCCTGTTC	TCAAGAGAAAGTTTCAGACTATGAAATGA	AAATTCACCAGATGGCATCTTTATT
PDGF	Platelet derived growth factor	NM_011057	6- FAM TCGCGGAACCTC	TGTAATCGCCGAGTGCAAGA	CATTGCACATTGCGGTTATTG
PDGF REC B	Platelet derived growth factor receptor beta	NM_008809	6- FAM CCACCATGAAAGTGG	TCACGGTCTGAGCCATTCG	TCTGGCTGTCGATTTCAGCAT

RAGE	Advanced glycosylation end product specific receptor	NM_007425	6- FAM CACAGCCCGGATTG	GCTGTAGCTGGTGGTCAGAACA	CCCCTTACAGCTTAGCACAAGTG
SMA-alpha	Smooth muscle actin - alpha	NM_007392	6- FAM TGCCAGATCTTTTCC	GACGCTGAAGTATCCGATAGAACA	GGCCACACGAAGCTCGTTAT
TGF-beta	Transforming growth factor - beta	NM_011577	6- FAM AAAGCCCTGTATTCCGT	GCAGTGGCTGAACCAAGGA	GCAGTGAGCGCTGAATCGA
TGF-beta TYPE 1 REC	Transforming growth factor - beta type 1 receptor	D25540	6-FAM CATCACTAGATCGCCC	CGTGTGCCAAATGAAGAGGAT	AAGGTGGTGCCCTCTGAAATG
TNF-alpha	Tumor necrosis factor - alpha	NM_013693	6- FAM TCACCCACACCGTCAG	GGCTGCCCCGACTACGT	TTTCTCCTGGTATGAGATAGCAAATC
TNFRSF11b	Tumour Necrosis Factor Receptor member 11b	NM_008764	6-FAM CGAACCTCACCACAGAG	GCGTGCAGCGGCATCT	TCAATCTCTTCTGGGCTGATCTT
VCAM	vascular cell adhesion molecule-1	L22354	6-FAM CCAAAATCCTGTGGAGCAG	CTGCTCAAGTGATGGGATACCA	ATCGTCCCTTTTTGTAGACATGAAG
VEGF	Vascular endothelial growth factor	M95200	6- FAM CTGTACCTCCACCATGC	GCACTGGACCCTGGCTTTACT	ATGGGACTTCTGCTCTCCTTCTG

TABLE S9. PROVIDED AS SEPARATE .XLS FILE

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