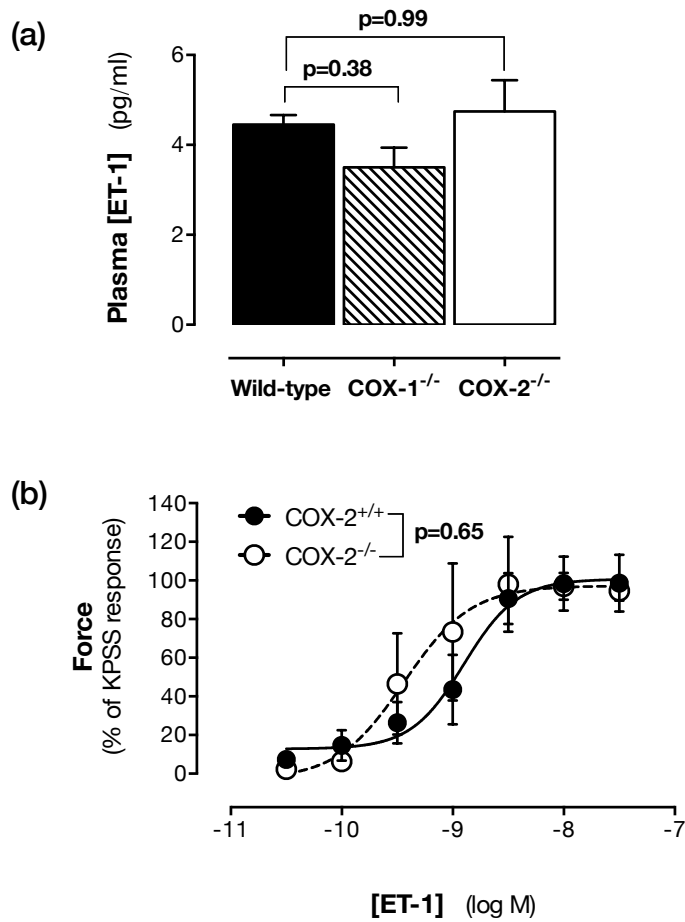
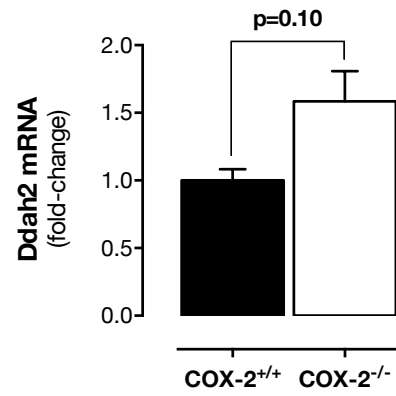


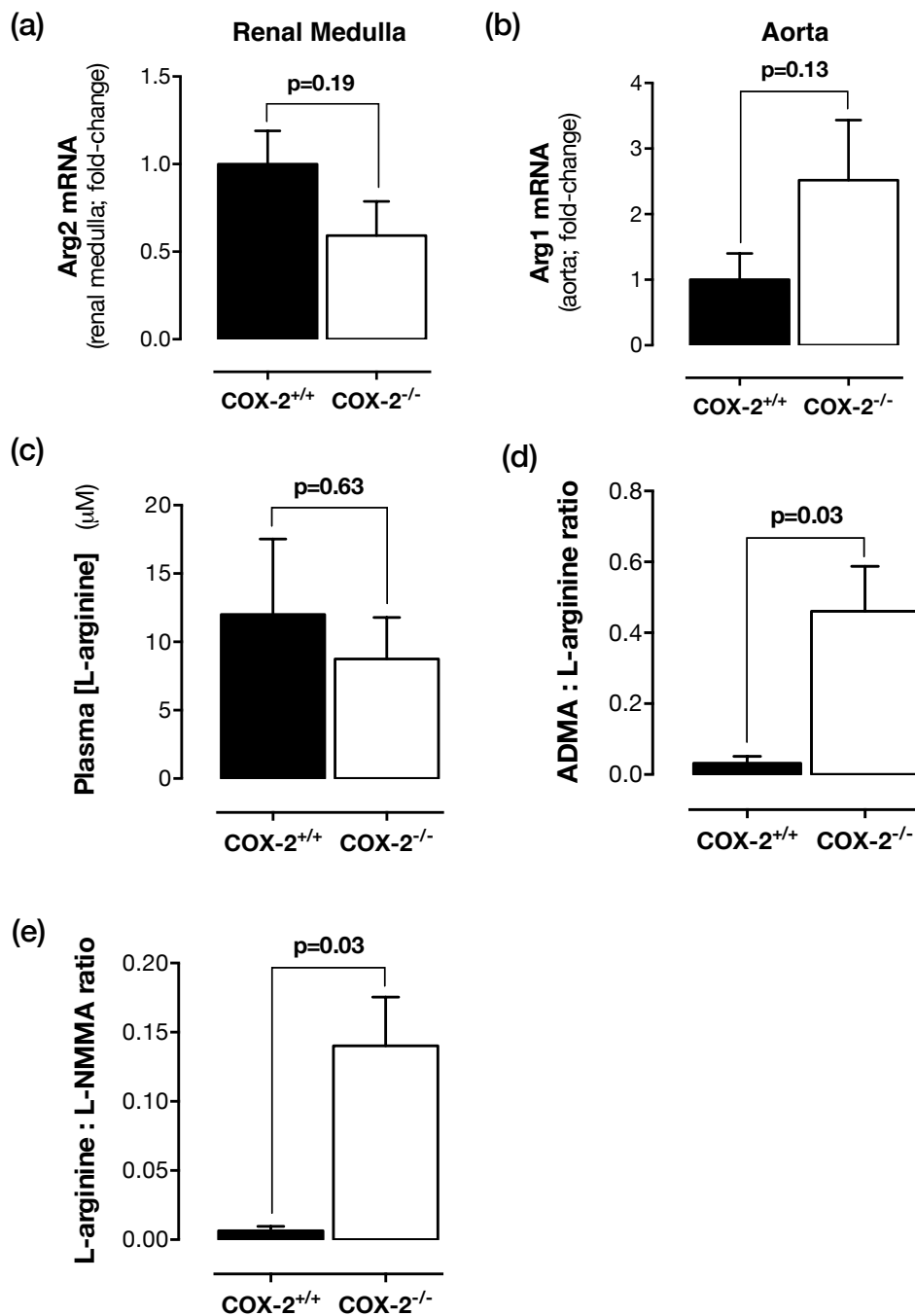
## **SUPPLEMENTARY MATERIAL**



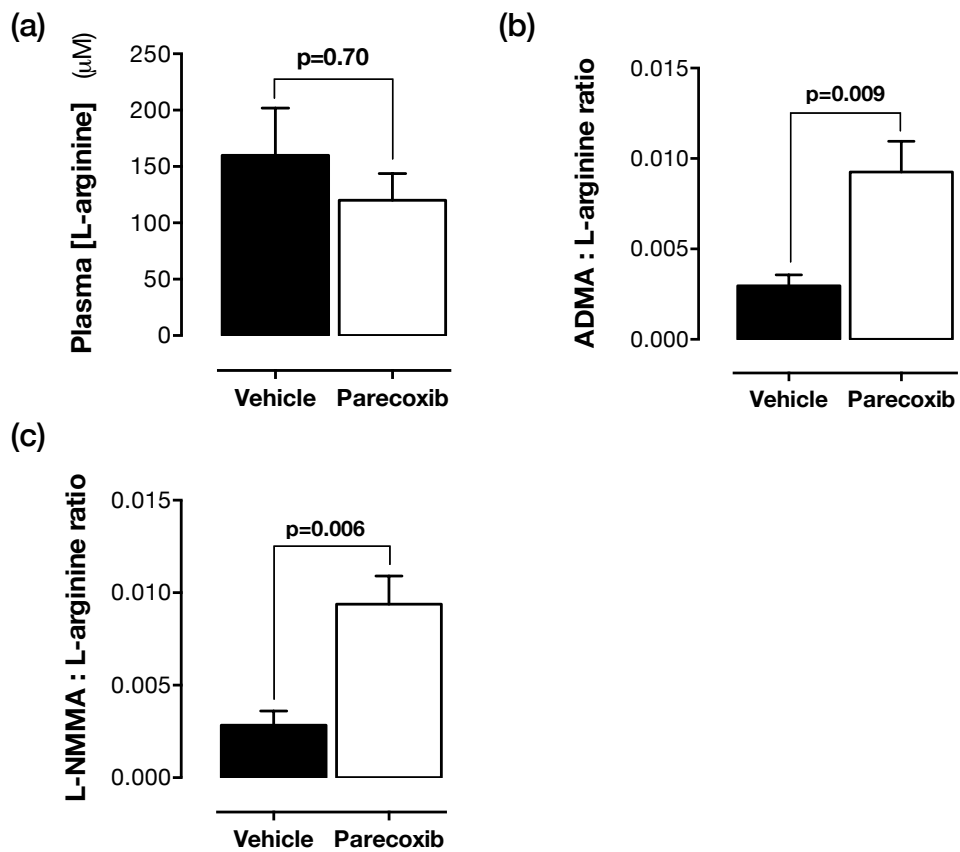
**Supplementary Fig. 1:** Effect of COX-1 and COX-2 gene deletion on (a) circulating endothelin-1 (ET-1) and (b) contractile effect of ET-1 on aorta. Aorta were incubated in Krebs' buffer containing 100  $\mu$ M L-N<sup>G</sup>monomethyl-L-arginine to inhibit eNOS activity. Data is the mean  $\pm$  S.E.M for (a) n=8-9 mice and (b) n=4 vessels from 2 mice. Data was analysed using (a) Kruskal-Wallis with Dunn's post-hoc test and (b) by Quades two-way ANOVA.



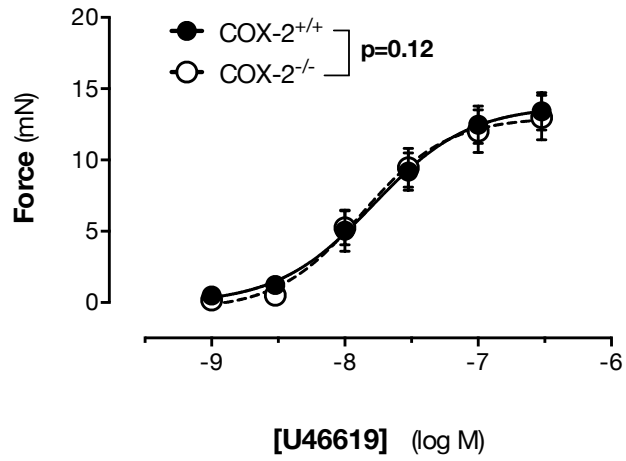
**Supplementary Fig 2:** Effect of COX-2 gene deletion on Ddah2 expression in the renal medulla. The data is the mean mean  $\pm$  S.E.M for n=7. Data was analysed using a Mann-Whitney U-test.



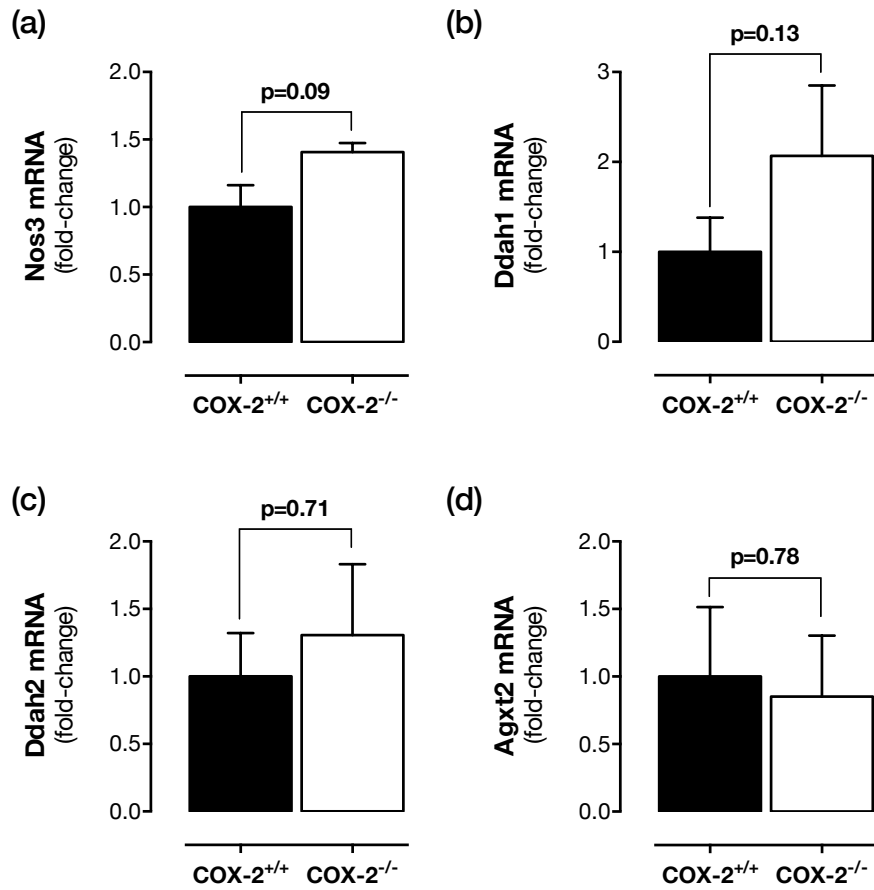
**Supplementary Fig. 3:** Effect of COX-2 gene deletion on the expression of (a) Arg2 in the renal medulla, (b) Arg1 in the aorta and plasma levels of (c) L-arginine, (d) ratio of ADMA: L-arginine and (e) L-NMMA:L-arginine in the plasma. The data is the mean  $\pm$  S.E.M for (a) and (b)  $n=7-8$ , (c-e)  $n=4$ . Data was analysed Mann-Whitney U-test.



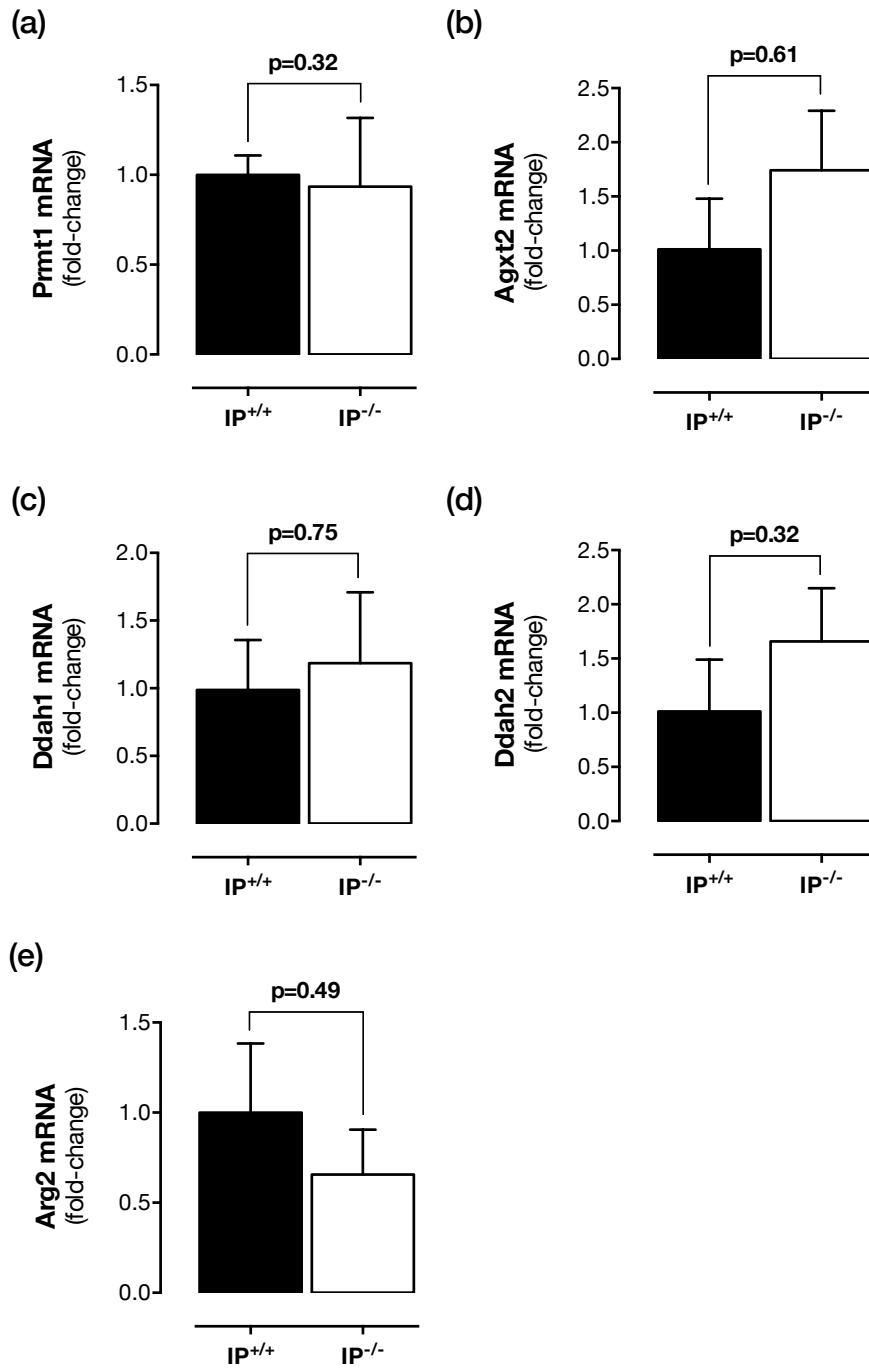
**Supplementary Fig. 4:** Effect of parecoxib (100 mg/kg/day) compared to vehicle (water) on plasma levels of (a) L-arginine and (b) ADMA:L-arginine and (c) L-NMMA:L-arginine ratios in plasma of wild type mice. The data is the mean  $\pm$  S.E.M n=3-7. Data was analysed using a Mann-Whitney U-test.



**Supplementary Fig. 5:** Effect of COX-2 gene deletion on the contractile responses of U46619 in aorta. The data the mean  $\pm$  S.E.M for n=6-10. Data was analysed using a Quades two-way ANOVA.

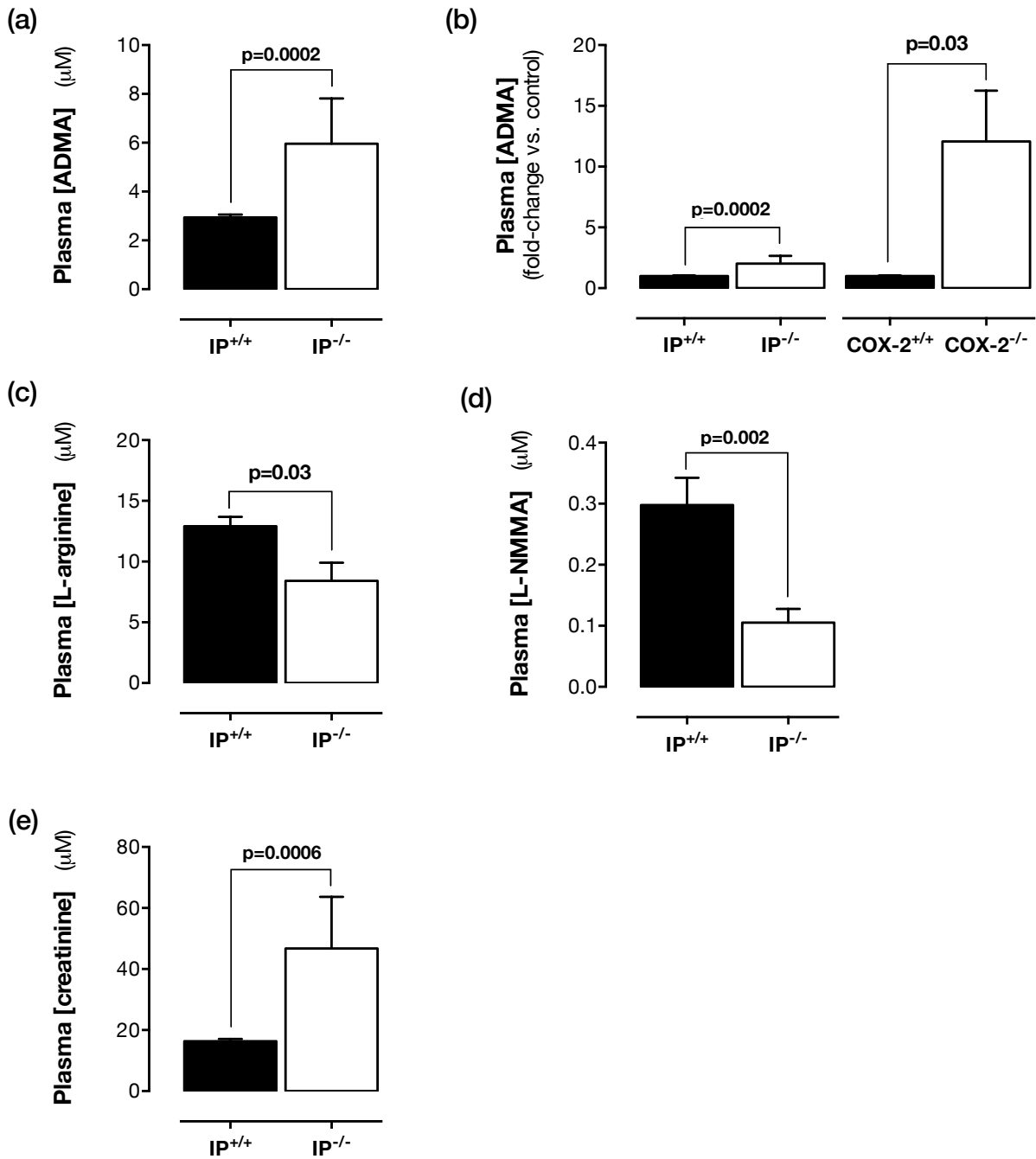


**Supplementary Fig. 6:** Effect of COX-2 gene deletion on aortic expression of (a) Nos3, (b) Ddah1, (c) Ddah2 and (d) Agxt2. The data is the mean  $\pm$  S.E.M for n=5-7 mice. Data was analysed using a Mann-Whitney U-test



**Supplementary Fig. 7:** Effect of IP gene deletion on the expression of (a) Prmt1, (b) Agxt2, (c) Ddah1, (d) Ddah2 and (e) Arg2 in the renal medulla. The data is the mean  $\pm$  S.E.M n=8. Data was analysed using a Mann-Whitney U-test.





**Supplementary Fig. 8:** (a) Effect of IP gene deletion on plasma levels of ADMA. (b) Comparison of the effect of IP gene deletion versus COX-2 gene deletion on relative (fold) change in ADMA. (c) Effect of IP gene deletion on plasma levels of (c) L-arginine, (d) L-NMMA and (e) creatinine. The data is the mean  $\pm$  S.E.M for  $n=8$ . Data was analysed using Mann-Whitney U-test

Gene Symbol	Fold-Change	Gene Symbol	Fold-Change	Gene Symbol	Fold-Change
Igfbp2	3.2	Nupr1	1.8	Spon2	1.7
Upk2	2.8	Arhgef4	1.8	Spnb3	1.7
Psca	2.5	Stab1	1.8	Sppl3	1.7
Nrip3	2.5	Ccdc3	1.8	Sepw1	1.7
Neurl	2.4	Lgals3	1.8	Pea15	1.7
Rgs4	2.4	Gpr123	1.8	Kdelr3	1.7
Egr1	2.4	Jun	1.8	Susd4	1.7
Lypd2	2.4	Col6a1	1.8	Ctsk	1.7
Npy	2.3	Spon1	1.8	Ptprb	1.7
Lyz	2.2	Slc24a3	1.8	Rasl11b	1.7
Spnb1	2.2	Ophn1	1.8	Ssbp4	1.7
Cacna2d1	2.1	Gprc5a	1.8	Samd14	1.7
Nbl1	2.1	Elf3	1.8	Abi3	1.7
Loc100047934	2.1	F13a1	1.8	Fst	1.7
Aoc3	2.1	Serpinf1	1.8	Tnrc6c	1.7
Fbn1	2.1	Asah3l	1.8	Itgb4	1.7
Lynx1	2.1	Cntn1	1.8	Cfp	1.7
Ndn	2.1	Tmem118	1.8	D12ertd553e	1.7
Aatk	2.1	Megf9	1.8	S100a13	1.7
Purb	2.0	Ptprs	1.8	Txnip	1.7
Zeb2	2.0	Scara3	1.8	Mmp17	1.7
Upk1b	2.0	Serpina3n	1.8	Anxa2	1.7
Lcn2	2.0	D0h4s114	1.8	Bok	1.7
Sprr1a	2.0	Cyp1b1	1.8	Serinc2	1.7
Klf5	2.0	Gja1	1.8	Aqp2	1.7
Satb1	2.0	Rhoj	1.8	Loc100045019	1.7
Ankrd1	1.9	Vwf	1.8	Cdkn1c	1.7
Bc025575	1.9	Loc100046044	1.8	Stat3	1.7
Cldn5	1.9	Loc100043671	1.8	Axin2	1.7
Lyzs	1.9	Wnt7b	1.8	Pof1b	1.7
Chst1	1.9	Slc44a2	1.8	Laptm5	1.7
Flrt3	1.9	P2ry6	1.8	F2r	1.7
Loc100047200	1.9	Bcl9l	1.8	Endod1	1.7
Krt18	1.9	Klf6	1.8	Atf5	1.7
Fxyd6	1.9	Fscn1	1.8	C030011o14rik	1.7
Rab15	1.9	Cldn4	1.8	D16ertd472e	1.7
Grit	1.9	E430002d04rik	1.8	Hist1h2af	1.7
Tmem119	1.9	Dusp7	1.7	Stxbp1	1.7
Col16a1	1.9	Upk3a	1.7	Ckb	1.7
Krt14	1.9	Cygb	1.7	2310022b05rik	1.7
Nav1	1.9	Il18r1	1.7	Tmem110	1.7
Loc100048721	1.9	Hist1h2an	1.7	Ap3m2	1.7
Mmp14	1.9	Gnaz	1.7	Gjb6	1.7
Scarf2	1.9	Rgs5	1.7	Ankrd47	1.7
9130213b05rik	1.9	Pip4k2a	1.7	Col1a2	1.7
Ccdc80	1.9	Ppp1r9b	1.7	Des	1.7
Ddit4	1.8	Zfp52	1.7	H2-aa	1.7

Gene Symbol	Fold-Change	Gene Symbol	Fold-Change	Gene Symbol	Fold-Change
Gp38	1.7	Fxyd4	1.6	Myst4	1.6
Ppp1r3c	1.7	D6wsu176e	1.6	Gata2	1.6
Emid2	1.7	Slc1a3	1.6	Scx	1.6
Crip2	1.6	Kpnb1	1.6	Sidt1	1.6
Notch1	1.6	Ahi1	1.6	A230050p20rik	1.6
Ier3	1.6	Edg2	1.6	Npnt	1.6
Fcho1	1.6	4930572j05rik	1.6	Traf7	1.6
Slco4a1	1.6	Cugbp2	1.6	Spire2	1.6
Lrrc26	1.6	Loc100045343	1.6	Esam1	1.6
Nnmt	1.6	Tcof1	1.6	Magee1	1.6
Tiam1	1.6	Loc676420	1.6	Pkm2	1.6
Actb	1.6	Phc2	1.6	Xlr4a	1.6
Prkcbp1	1.6	Ccdc85b	1.6	Loc100042777	1.6
Dkk3	1.6	Adora1	1.6	Ppap2b	1.6
Myo9b	1.6	Grasp	1.6	Tspan17	1.6
Dusp26	1.6	Pdlim1	1.6	Itga3	1.6
Slc2a6	1.6	Gja5	1.6	Serf2	1.6
Pitpnm2	1.6	Sh3pxd2b	1.6	Csf1	1.6
2310010m24rik	1.6	Rcan2	1.6	Sh3bgrl3	1.6
Adamts2	1.6	Sepn1	1.6	Pip4k2b	1.6
Pitx2	1.6	Prep	1.6	Psmb10	1.6
Pfkl	1.6	Dusp3	1.6	Hn1	1.6
Bace1	1.6	Capn13	1.6	Bc021381	1.5
Csnk1e	1.6	Mmp2	1.6	Col18a1	1.5
Ccnd2	1.6	Irf2bp1	1.6	Btg1	1.5
Chrnbl	1.6	Sema3f	1.6	Notch4	1.5
Gstm2	1.6	Hcn2	1.6	Ragefl1	1.5
Efemp2	1.6	Rgs10	1.6	Fmn13	1.5
Dag1	1.6	9130404d14rik	1.6	Cldn23	1.5
Cav1	1.6	Csrp1	1.6	Upk1a	1.5
Myd116	1.6	Pik3r1	1.6	Dusp8	1.5
Pdgfra	1.6	Pls3	1.6	Phactr1	1.5
Scnn1b	1.6	Mbc2	1.6	Mospd3	1.5
Slc38a2	1.6	Dab2ip	1.6	Foxj2	1.5
Rbms3	1.6	Meis1	1.6	Smarcd2	1.5
Zfp46	1.6	Axl	1.6	Arrdc2	1.5
Pdlim7	1.6	Edn1	1.6	Rem1	1.5
Cxcl4	1.6	Mef2c	1.6	Slc9a1	1.5
Kctd10	1.6	Pold1	1.6	Pdpx	1.5
Wfdc2	1.6	Ehd4	1.6	Pacs1	1.5
St6gal1	1.6	Tmem23	1.6	Mmd	1.5
Cbr2	1.6	Mmrn2	1.6	Olfml3	1.5
Bat2	1.6	Bc063749	1.6	Akap8l	1.5
Timp2	1.6	Mcl1	1.6	Hoxd4	1.5
Sort1	1.6	Bc057552	1.6	Pygo2	1.5
Ccnd1	1.6	Large	1.6	Mfap2	1.5
Smpd13b	1.6	Rassf5	1.6	8430408g22rik	1.5

Gene Symbol	Fold-Change	Gene Symbol	Fold-Change	Gene Symbol	Fold-Change
Vamp2	1.5	Slco2a1	-1.5	Fads2	-1.5
Cox4i2	1.5	Gpr177	-1.5	Aadacl1	-1.5
Ahdc1	1.5	Syap1	-1.5	Strap	-1.5
Ptk7	1.5	Dock1	-1.5	Gm2a	-1.5
Arid2	1.5	Mto1	-1.5	Rheb	-1.5
Ptplad2	1.5	Tmem174	-1.5	1810049h13rik	-1.5
Tubb2b	1.5	Commd1	-1.5	Loc100047261	-1.5
Fpr2	1.5	1110031b06rik	-1.5	Tnfrsf21	-1.5
Socs3	1.5	Ppp1ca	-1.5	Surf1	-1.5
Hmha1	1.5	Ppapdc1	-1.5	Ppm1g	-1.5
Zfhx3	1.5	Tpk1	-1.5	Eg434858	-1.5
Cdc42ep5	1.5	Acox2	-1.5	Glb1l2	-1.5
Tcf4	1.5	Spg21	-1.5	Hspe1	-1.5
Atox1	1.5	Cul3	-1.5	4930403o06rik	-1.5
Vat1	1.5	Pycrl	-1.5	Mgst1	-1.5
Cpne2	1.5	Atpif1	-1.5	Dnajb9	-1.5
Mmp23	1.5	Nrbf2	-1.5	Snx6	-1.5
Dpt	1.5	Pdss1	-1.5	Ttc8	-1.5
Tkt	1.5	Mcat	-1.5	Pdcl	-1.5
Fxyd5	1.5	2410022l05rik	-1.5	Med21	-1.5
Scamp5	1.5	Fcgr2b	-1.5	Rpl31	-1.5
Atp6v0a1	1.5	Creld2	-1.5	Slc6a20b	-1.5
Ednrb	1.5	Eif4g2	-1.5	Fgf9	-1.5
S100a6	1.5	Hax1	-1.5	Adfp	-1.5
Hexa	1.5	Rps27a	-1.5	Slc41a2	-1.5
2300002d11rik	1.5	D10bwg1364e	-1.5	Fga	-1.5
Zfp259	1.5	Acad10	-1.5	Slc9a8	-1.5
Smtn	1.5	1500032l24rik	-1.5	Gng10	-1.5
Aip	1.5	Sdf2	-1.5	5730469m10rik	-1.5
Stx12	1.5	Loc100048331	-1.5	Loc677528	-1.5
Spink8	1.5	Ctsf	-1.5	Tmem159	-1.5
Loc100047619	1.5	Xdh	-1.5	Dcun1d4	-1.5
Tubb6	1.5	2810439f02rik	-1.5	Mboat5	-1.5
Bmpr1b	1.5	Letm1	-1.5	Dnajb12	-1.5
Nfatc4	1.5	Slc5a9	-1.5	Rab38	-1.5
Loc641240	1.5	Ak2	-1.5	Rpl36al	-1.5
Brd2	1.5	Zc3h14	-1.5	Cyp27a1	-1.5
Slc4a2	1.5	E030010a14rik	-1.5	lyd	-1.5
Capn5	1.5	Caml	-1.5	Tm2d3	-1.5
Rab31	1.5	Hpn	-1.5	Atp5s	-1.5
Rgma	1.5	Cd55	-1.5	Sat2	-1.5
Atpbd1b	1.5	Zfp207	-1.5	Uqcrc2	-1.6
Gfod2	1.5	Ccnc	-1.5	Mrpl30	-1.6
Efna5	1.5	Sod1	-1.5	Nsdhl	-1.6
Krt7	1.5	Errfi1	-1.5	Nqo1	-1.6
Flywch2	1.5	Aqp7	-1.5	Med10	-1.6
Cdh1	1.5	Akr1c14	-1.5	Epdr1	-1.6

Gene Symbol	Fold-Change	Gene Symbol	Fold-Change	Gene Symbol	Fold-Change
Ubr1	-1.6	Exoc4	-1.6	Dusp28	-1.6
Chchd4	-1.6	Cpn1	-1.6	Loc668492	-1.6
Ndufa9	-1.6	Tmem5	-1.6	1110038d17rik	-1.6
Ogfrl1	-1.6	Susd3	-1.6	Metap1	-1.6
Eno1	-1.6	Msrb2	-1.6	Mettl9	-1.6
Rnaset2b	-1.6	Psm12	-1.6	Tmem9b	-1.6
Arf5	-1.6	Insig2	-1.6	Ubl5	-1.6
Suclg1	-1.6	Gstt2	-1.6	Stx18	-1.6
Wdr55	-1.6	Dnajc15	-1.6	Rcan1	-1.6
Loc667370	-1.6	Nsbp1	-1.6	Arl3	-1.6
Sri	-1.6	Cobll1	-1.6	Capns1	-1.6
Tceal8	-1.6	Prosc	-1.6	Mrps16	-1.6
4933434e20rik	-1.6	Rala	-1.6	Akr1c12	-1.6
Fundc1	-1.6	Bxdc2	-1.6	Tmem77	-1.6
Cldn1	-1.6	Eif2b1	-1.6	Ranbp9	-1.6
Pfkip	-1.6	P2rx4	-1.6	Zfyve20	-1.6
Net1	-1.6	Htatip2	-1.6	Ddx1	-1.6
L7rn6	-1.6	Maea	-1.6	Agps	-1.6
Decr2	-1.6	Kctd12	-1.6	Calm2	-1.6
Arpc1a	-1.6	Iars2	-1.6	Anpep	-1.6
Tmem85	-1.6	Sypl2	-1.6	Serpina1f	-1.6
Pdzd11	-1.6	Vps29	-1.6	Gchfr	-1.6
Ostf1	-1.6	Snrpd1	-1.6	Ccdc47	-1.6
Fmo4	-1.6	Bc048355	-1.6	Ostm1	-1.6
Pcmt1	-1.6	Napsa	-1.6	2010316f05rik	-1.7
Hist1h4h	-1.6	Htra1	-1.6	Thoc4	-1.7
Dynll2	-1.6	Rab1b	-1.6	Ndufa4	-1.7
Dpy30	-1.6	2810008m24rik	-1.6	Nxt2	-1.7
5033414d02rik	-1.6	Atp5d	-1.6	Nbr1	-1.7
Dab2	-1.6	Nsmaf	-1.6	1300018j18rik	-1.7
Als2cr2	-1.6	Hagh	-1.6	Top1	-1.7
Rps12	-1.6	Cyp4f14	-1.6	Agpat2	-1.7
Steap2	-1.6	Pitpnc1	-1.6	Rnf11	-1.7
Slc25a33	-1.6	Efr3a	-1.6	Echs1	-1.7
Slc35a1	-1.6	1700034h14rik	-1.6	Tspo	-1.7
Tmem131	-1.6	Tbca	-1.6	Entpd5	-1.7
Hpd	-1.6	Gtpbp4	-1.6	Arl6ip5	-1.7
Papss2	-1.6	Ppp2cb	-1.6	Afmid	-1.7
Tomm7	-1.6	Acn9	-1.6	Loc100046457	-1.7
Yif1a	-1.6	4931417g12rik	-1.6	Rabggtb	-1.7
Cyb5r4	-1.6	Gjb2	-1.6	Atp5j	-1.7
Mrps31	-1.6	Fbxo9	-1.6	Nat2	-1.7
Actn4	-1.6	Slc34a3	-1.6	Hsd17b2	-1.7
Rab17	-1.6	Bc026682	-1.6	Hdhd2	-1.7
Sypl	-1.6	Hmox2	-1.6	Pcbd1	-1.7
Atp6v0e	-1.6	A030007117rik	-1.6	2510010f15rik	-1.7
Mrpl40	-1.6	Loc100047012	-1.6	Fkbp2	-1.7

Gene Symbol	Fold-Change	Gene Symbol	Fold-Change	Gene Symbol	Fold-Change
Sec61b	-1.7	Qdpr	-1.7	0610012d14rik	-1.8
Tmem106a	-1.7	Lpar3	-1.7	Rps16	-1.8
Car3	-1.7	Car12	-1.7	Eg632778	-1.8
1810022c23rik	-1.7	Ncoa4	-1.7	Tfam	-1.8
Galnt1	-1.7	Gnas	-1.7	Sqstm1	-1.8
Synj2bp	-1.7	Trappc4	-1.7	Proc	-1.8
Bc040758	-1.7	Ufsp2	-1.7	Bud31	-1.8
Lrrc8	-1.7	1500031102rik	-1.7	Socs2	-1.8
Col4a5	-1.7	Cideb	-1.7	Echdc2	-1.8
Rpl27	-1.7	Gm1821	-1.7	Eg622339	-1.8
Dtymk	-1.7	Tmem166	-1.7	Ndufa12	-1.8
1110019n10rik	-1.7	Ppp1cb	-1.7	Kl	-1.8
Ndufc1	-1.7	Mcts1	-1.7	Plscr1	-1.8
Mlstd2	-1.7	Mpst	-1.7	Pgam1	-1.8
Psen1	-1.7	Clptm1	-1.7	Fh1	-1.8
Ly6c1	-1.7	Gcdh	-1.7	Rnf4	-1.8
2410129h14rik	-1.7	Tmem116	-1.7	Loc100048480	-1.8
2310045a20rik	-1.7	Mdh1	-1.7	Atp6v1g1	-1.8
Hmgn2	-1.7	Klk1b5	-1.7	Ddx52	-1.8
Fbxo3	-1.7	Rbbp7	-1.7	Coasy	-1.8
Mrpl22	-1.7	Slc22a18	-1.7	Cox15	-1.8
Zfp313	-1.7	Crym	-1.7	Jtb	-1.8
Cnih	-1.7	Ppp2r1a	-1.8	Tmem9	-1.8
Dcxr	-1.7	Mrpl4	-1.8	Rab18	-1.8
Klhl9	-1.7	Asl	-1.8	Usp16	-1.8
Acss2	-1.7	Suclg2	-1.8	Capn7	-1.8
Leprel1	-1.7	Xylb	-1.8	Ntan1	-1.8
4631427c17rik	-1.7	Nhsl1	-1.8	Rps27l	-1.8
Pcx	-1.7	Hnrpf	-1.8	Mertk	-1.8
Fads3	-1.7	Sdhb	-1.8	Ube2k	-1.8
Mrpl9	-1.7	Loc654426	-1.8	Rps13	-1.8
Ndrl	-1.7	Cyba	-1.8	Gde1	-1.8
Hpgd	-1.7	Zfp810	-1.8	Nfs1	-1.8
Dnajc6	-1.7	Hnrph1	-1.8	Rpl9	-1.8
Gstp1	-1.7	Tmed10	-1.8	Thnsl2	-1.8
Ubb	-1.7	Pcdh24	-1.8	Ufc1	-1.8
Btf3	-1.7	G6pc	-1.8	2310005n03rik	-1.8
Jak2	-1.7	Tmem41a	-1.8	Ap2a2	-1.8
Ube2e3	-1.7	Mrps22	-1.8	Bc051227	-1.8
Pvalb	-1.7	Plscr2	-1.8	Ccdc91	-1.8
Tfg	-1.7	Ces3	-1.8	2610204l23rik	-1.8
Pcca	-1.7	Sumo2	-1.8	Nap1l1	-1.8
Mpv17l	-1.7	Gss	-1.8	Acad8	-1.8
Uchl3	-1.7	D10ertd322e	-1.8	Bc038156	-1.9
Acsm5	-1.7	Pdia3	-1.8	Agt	-1.9
Tnfaip8	-1.7	Eef1e1	-1.8	Efhd1	-1.9
Serpina1d	-1.7	Rars2	-1.8	Paqr9	-1.9

Gene Symbol	Fold-Change	Gene Symbol	Fold-Change	Gene Symbol	Fold-Change
Acsl1	-1.9	Dpep1	-1.9	Sumo3	-2.0
Cndp1	-1.9	Slc22a2	-1.9	Hsd17b11	-2.0
Il13ra1	-1.9	Hist1h2bm	-1.9	Slc2a2	-2.0
Sqle	-1.9	Cox7a2l	-1.9	Akr1a4	-2.0
Sod3	-1.9	Loc100043257	-1.9	Cbs	-2.0
Wwp1	-1.9	Myo5a	-1.9	Loc100046650	-2.0
Scoc	-1.9	Msn	-1.9	Abcc2	-2.0
Sult1d1	-1.9	Rps4x	-1.9	Tcp1	-2.0
Adss	-1.9	Car4	-1.9	Dio1	-2.1
Slc39a11	-1.9	Nus1	-1.9	Slc26a4	-2.1
Cmb1	-1.9	Pepd	-1.9	Syng2	-2.1
Acaa2	-1.9	Arl5a	-1.9	Slc25a5	-2.1
Hspd1	-1.9	Gpr137b	-1.9	Tfrc	-2.1
Mrpl18	-1.9	Slc6a13	-1.9	Hip2	-2.1
Tmco3	-1.9	Pdzd3	-2.0	Ctsh	-2.1
Atp5l	-1.9	Ndufb6	-2.0	Tsc22d1	-2.1
Nudt19	-1.9	Hnrnpa2b1	-2.0	Gatad1	-2.1
Galm	-1.9	Timm8b	-2.0	Rab5a	-2.1
Eif5a	-1.9	Ccbl2	-2.0	Cth	-2.1
Gna11	-1.9	Tmem126a	-2.0	Rps2	-2.1
Slc13a3	-1.9	Car14	-2.0	Aldh11l	-2.1
Tst	-1.9	Pbld	-2.0	Bpnt1	-2.1
Gsto1	-1.9	2810410p22rik	-2.0	Slc46a3	-2.1
Scl0003251.1_2	-1.9	Eif3eip	-2.0	Zfp330	-2.1
1	-1.9	Zmynd10	-2.0	Mme	-2.1
Znrf2	-1.9	Rdh14	-2.0	Jam4	-2.1
Grpel1	-1.9	Bola3	-2.0	L2hgdh	-2.1
Slc35a3	-1.9	Mapk14	-2.0	Tmem59	-2.1
Il1rl1l	-1.9	Aqp11	-2.0	Frrs1	-2.1
Pex7	-1.9	Lonp2	-2.0	5730437n04rik	-2.1
Ppt1	-1.9	A530050d06rik	-2.0	Slc7a9	-2.1
Mrpl3	-1.9	Gfm1	-2.0	1810063b05rik	-2.1
As3mt	-1.9	Ndufa6	-2.0	Vil1	-2.1
Pdia4	-1.9	0610010d20rik	-2.0	Ebp	-2.1
Nit2	-1.9	Rpl24	-2.0	Agxt2	-2.1
Nudt4	-1.9	4833421e05rik	-2.0	Dgat2	-2.1
Morf4l1	-1.9	Arsb	-2.0	Apom	-2.1
Eif3s8	-1.9	Adh5	-2.0	Sar1b	-2.1
9630015d15rik	-1.9	Dhrs1	-2.0	Loc667609	-2.1
Ceacam2	-1.9	Capn2	-2.0	Sult1c2	-2.1
Nox4	-1.9	Acadm	-2.0	Cyp2j11	-2.1
Sap30	-1.9	Slc13a2	-2.0	Gsta2	-2.1
Cml1	-1.9	Snx7	-2.0	Kdelr2	-2.1
Atp5o	-1.9	Loc100047353	-2.0	Higd1c	-2.1
Adhfe1	-1.9	Tmem139	-2.0	Hist1h2bj	-2.1
Commd3	-1.9	H47	-2.0	Bc026585	-2.1
Psmb7	-1.9	Cyc1	-2.0	Cyp2d26	-2.1

Gene Symbol	Fold-Change	Gene Symbol	Fold-Change	Gene Symbol	Fold-Change
2310008m10rik	-2.1	Gnmt	-2.3	Ndufs2	-2.6
Nola3	-2.1	D630023f18rik	-2.3	Pxmp2	-2.6
Dpp4	-2.2	Loc100045617	-2.3	Slc19a1	-2.6
Mtap7	-2.2	Ldhd	-2.3	Ai747699	-2.6
Ahcy1	-2.2	Pdk3	-2.3	Gstm5	-2.6
Nt5e	-2.2	Tinag	-2.3	Ppcs	-2.6
Spcs1	-2.2	Eef2	-2.3	Folr1	-2.6
Etfa	-2.2	Defb29	-2.3	Clrn3	-2.6
Loc100045567	-2.2	Vdac3	-2.4	Hist1h2bf	-2.6
Sepp1	-2.2	Abhd3	-2.4	Bc026439	-2.6
Bc055107	-2.2	Acot3	-2.4	Cldn2	-2.6
Bc016495	-2.2	Loc381629	-2.4	Lrrk2	-2.6
Acad9	-2.2	Upb1	-2.4	Loc100047046	-2.7
1110008f13rik	-2.2	Cryz	-2.4	D630042f21rik	-2.7
Slc25a15	-2.2	Loc268782	-2.4	Csad	-2.7
Pcbp2	-2.2	Tspan3	-2.4	Etfhdh	-2.7
Nudt12	-2.2	Bc006662	-2.4	Mrpl53	-2.7
Ubie	-2.2	Bhmt2	-2.4	Nme2	-2.7
Ottmusg000000		Tmem33	-2.4	Chuk	-2.7
05148	-2.2	Galnt11	-2.4	Fgf1	-2.7
Slc5a2	-2.2	Ppa2	-2.4	Hint1	-2.7
Slc25a30	-2.2	Calr	-2.4	Dhrs4	-2.7
Sfrs5	-2.2	Hist1h2bn	-2.5	Col4a3	-2.8
Adi1	-2.2	Hao3	-2.5	Loc100047937	-2.8
Loc677144	-2.2	Loc100044204	-2.5	Mpp1	-2.8
Ela1	-2.2	Calml4	-2.5	Sephs2	-2.8
B230339h12rik	-2.2	H3f3a	-2.5	Coq9	-2.8
Sigirr	-2.2	C1qbp	-2.5	Ugt3a2	-2.8
Supt4h2	-2.2	Qprt	-2.5	Rps6	-2.9
Slc12a3	-2.2	Mtch2	-2.5	Kng2	-2.9
Khk	-2.2	Arl6	-2.5	Loc333331	-2.9
2010311d03rik	-2.2	Ai317395	-2.5	Gm853	-2.9
Dars	-2.3	Slc7a7	-2.5	Prdx3	-2.9
Bc021608	-2.3	Dnajc12	-2.5	Fmo1	-2.9
Smpdl3a	-2.3	2610528j11rik	-2.5	Nckap1	-2.9
Bc021785	-2.3	Sucnr1	-2.5	Ostb	-2.9
H2afz	-2.3	Cct6a	-2.5	Glud1	-2.9
Agtr1a	-2.3	Igfbp3	-2.5	Oxct1	-3.0
Ak3l1	-2.3	Pah	-2.5	Pcbp1	-3.0
Pdhb	-2.3	Loc100048413	-2.5	Mep1b	-3.1
Ndfip1	-2.3	Frap1	-2.5	Cat	-3.1
Slc25a36	-2.3	Ddc	-2.5	Rbpms2	-3.2
Ndufc2	-2.3	Klk1b4	-2.5	Slc27a2	-3.2
Nola2	-2.3	Hist1h2bh	-2.6	Plekhb2	-3.2
F13b	-2.3	Vps35	-2.6	Slc6a19	-3.2
Rpl7a	-2.3	Eps8	-2.6	Rgl1	-3.2
lah1	-2.3	Loc433479	-2.6	Slc22a9	-3.2



Gene Symbol	Fold-Change
Ivns1abp	-3.2
Slc47a1	-3.3
5033411d12rik	-3.3
Ugt3a1	-3.3
2500002l14rik	-3.3
Rps7	-3.4
Klk1b27	-3.4
Lgmn	-3.5
Slc17a3	-3.6
Cyp4a31	-3.6
Gpx1	-3.6
Rnaset2	-3.7
Tcn2	-3.8
Cml3	-3.9
Ehhadh	-3.9
Slc16a4	-4.0
Idh1	-4.0
Fbp1	-4.2
Scp2	-4.2
Spp2	-4.3
Slc22a13	-4.3
Hrsp12	-4.5
Atp5f1	-5.0
Miox	-5.0
Eg433923	-5.1
Chpt1	-5.3
Loc100046918	-5.4
Tmem27	-5.6
Cyp51	-5.9
Cyp4b1	-6.4
Ugt1a10	-6.5
Hspa8	-7.6
Dnase1	-8.7

**Supplementary Table 1:** Genes altered by >1.5-fold in kidney (renal medulla) from COX-2<sup>-/-</sup> mice. Heat map scale: +3-fold (green) to red -3-fold (red). Data are from n=8 mice. Statistical significance (q<0.05) determined using linear models for microarray data modified t-test and false discovery rate corrected.

	<b>ADMA (µM)</b>	<b>L-NMMA (µM)</b>	<b>SDMA (µM)</b>	<b>Creatinine (fold change)</b>
<b>Wild-type</b>	0.28 ± 0.02	0.070 ± 0.01	0.24 ± 0.02	1.00 ± 0.04
<b>COX-1<sup>-/-</sup></b>	0.86 ± 0.26 (p=0.16)	0.085 ± 0.01 (p=0.99)	0.63 ± 0.14 (p=0.09)	0.89 ± 0.05 (p=0.46)
<b>COX-2<sup>-/-</sup></b>	3.36 ± 1.16* (p=0.007)	0.38 ± 0.11* (p=0.02)	1.25 ± 0.90 (p>0.99)	1.53 ± 0.18* (p=0.01)
<b>Wild type normal salt; vehicle</b>				
	0.41 ± 0.044	0.27 ± 0.079	N/A	N/A
<b>Wild type normal salt; parecoxib</b>				
	0.86 ± 0.13* (p=0.005)	1.19 ± 0.26* (p=0.02)	N/A	N/A
<b>Wild type high salt; vehicle</b>				
	0.73 ± 0.14	0.78 ± 0.17	N/A	N/A
<b>Wild type high salt; parecoxib</b>				
	1.12 ± 0.10 (p=0.18)	0.75 ± 0.07 (p=1.00)	N/A	N/A
<b>IP<sup>+/+</sup></b>				
	2.93 ± 0.12	0.30 ± 0.04	1.74 ± 0.18	1.0 ± 0.04
<b>IP<sup>-/-</sup></b>				
	4.11 ± 0.11* (p=0.0002)	0.11 ± 0.02* (p=0.002)	1.88 ± 0.31 (p=0.44)	1.85 ± 0.29* (p=0.0006)

**Supplementary Table 2:** Effect of gene deletion of COX inhibition on plasma methylarginines. Methylarginines (ADMA, L-NMMA and SDMA) and creatinine in the plasma of wild-type, COX-1<sup>-/-</sup>, COX-2<sup>-/-</sup> (p-values by Kruskal-Wallis with Dunn's post-hoc test) and IP<sup>-/-</sup> mice and wild type mice treated with vehicle or parecoxib fed a normal or a high salt diet (p-values by Mann-Whitney U-test).