

STEM CELLS AND REGENERATION

RESEARCH ARTICLE

Histone deacetylases 1 and 2 regulate the transcriptional programs of nephron progenitors and renal vesicles

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ABSTRACT

Nephron progenitor cells (NPCs) are Six2-positive metanephric mesenchyme cells, which undergo self-renewal and differentiation to give rise to nephrons until the end of nephrogenesis. Histone deacetylases (HDACs) are a group of epigenetic regulators that control cell fate, but their role in balancing NPC renewal and differentiation is unknown. Here, we report that NPC-specific deletion of *Hdac1* and *Hdac2* genes in mice results in early postnatal lethality owing to renal hypodysplasia and loss of NPCs. HDAC1/2 interact with the NPC renewal regulators Six2, Osr1 and Sall1, and are co-bound along with Six2 on the *Six2* enhancer. Although the mutant NPCs differentiate into renal vesicles (RVs), *Hdac1/2* mutant kidneys lack nascent nephrons or mature glomeruli, a phenocopy of *Lhx1* mutants. Transcriptional profiling and network analysis identified disrupted expression of *Lhx1* and its downstream genes, *Dll1* and *Hnf1a/4a*, as key mediators of the renal phenotype. Finally, although HDAC1/2-deficient NPCs and RVs overexpress hyperacetylated p53, *Tsp53* deletion failed to rescue the renal dysgenesis. We conclude that the epigenetic regulators HDAC1 and HDAC2 control nephrogenesis via interactions with the transcriptional programs of nephron progenitors and renal vesicles.

KEY WORDS: Epigenetics, Histone deacetylase, Kidney development, Nephron progenitors

INTRODUCTION

Kidney development requires precise integration of various progenitor cell populations. In ~1/500 births, some abnormality occurs in kidney development, leading to congenital anomalies of the kidney and urinary tract (CAKUT) (Schedl, 2007). CAKUT accounts for up to 30% of end-stage renal disease in children less than 4 years of age (North American Pediatric Renal Trials and Collaborative Studies 2008 Annual Report; <https://web.emmes.com/study/ped/annlrept/Annual%20Report%20-2008.pdf>). Moreover, CAKUT increases the risk of development of hypertension and other cardiovascular diseases in adulthood (Wuhl et al., 2013). The formation of a sufficient number of nephrons is crucial for final kidney function in the adult and requires a delicate balance between nephron progenitor cell (NPC) self-renewal and differentiation. Conversely, unrestrained NPC expansion and arrested differentiation lead to Wilms' tumor, an embryonic tumor of the kidney (Kreidberg and Hartwig, 2008).

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Six2, a homeodomain transcription factor, is a key factor within the kidney metanephric mesenchyme that maintains the NPC pool (Kobayashi et al., 2008; Self et al., 2006). In *Six2* null mice, ectopic renal vesicles (the earliest epithelialized forms of nascent nephrons) develop at the onset of nephrogenesis and the progenitor pool is rapidly lost (Self et al., 2006). Many transcriptional regulators – such as Osr1, WT1 and Sall1/Mi-2b (Chd4)/nucleosome remodeling and deacetylase (NuRD), which function to maintain the NPC pool – display genetic interactions with Six2 (Basta et al., 2014; Denner and Rauchman, 2013; Hartwig et al., 2010; Kanda et al., 2014; Xu et al., 2014). In addition, it has been shown that Six2 regulates self-renewal and commitment of NPCs through sharing gene regulatory networks with Wnt proteins (Park et al., 2012). However, the details of how these networks operate to maintain the multipotency of nephron progenitors are not well understood. This knowledge is necessary to understand mechanisms of nephrogenesis and for therapeutic intervention of kidney diseases.

Recent years have witnessed an expanded awareness of the crucial role of epigenetic mechanisms in health and disease (Egger et al., 2004). During development, epigenetic mechanisms – such as DNA methylation, histone modifications and miRNA biogenesis – program the genome in a particular cell by alteration of chromatin structure and DNA accessibility to the transcriptional machinery. Disruptions of these epigenetic mechanisms can lead to dysregulation of gene function, without altering the DNA sequence itself (Egger et al., 2004). As epigenetic abnormalities depend on the interplay between genes and the environment, they are often phenotypically variable, which fits well with the broad phenotypic spectrum of CAKUT. Therefore, understanding the epigenetic basis of kidney development might provide new insights into the pathological mechanisms of CAKUT and, hopefully, open new avenues to treatment or prevention of CAKUT, through pharmaceutical agents that target epigenetic modifiers. Histone deacetylases (HDACs) are an evolutionarily conserved group of enzymes that remove acetyl groups from histones as well as nonhistone proteins [e.g. p53 (tumor protein p53)]. HDACs regulate gene expression in a highly selective way, and exhibit both repressive and activating effects (Haberland et al., 2009). To date, 18 mammalian HDACs have been identified. HDAC1 and HDAC2 share high sequence identity of ~83% (de Ruijter et al., 2003) and regulate gene expression as the catalytic core of three major multiprotein co-repressor complexes: Sin3 (Sin3a), NuRD and co-repressor for element-1-silencing transcription factor (CoREST; Rcor2) (Kelly and Cowley, 2013). During embryogenesis, HDAC1 and HDAC2 play both redundant and distinct functions in a tissue-specific manner (Brunmeir et al., 2009; Jacob et al., 2011, 2014; LeBoeuf et al., 2010; Turgeon et al., 2013; Winter et al., 2013; Ye et al., 2009). Our previous studies showed that HDAC activity is required for key developmental pathways regulating overall renal growth and differentiation and ureteric bud (UB) branching (Chen

et al., 2011, 2015). In the present work, using conditional targeting in Six 2^+ NPCs, we unraveled novel roles of HDAC1/2 in the control of NPC maintenance. Moreover, our findings implicate HDAC1/2 in the regulation of the differentiation program of renal vesicles (RVs) into nascent nephrons. Thus, HDAC1/2 regulate nephron endowment through actions on multiple steps of nephrogenesis.

RESULTS

NPC-specific deletion of *Hdac1* and *Hdac2*

To gain insights into the role of HDAC1/2 in NPC maintenance and differentiation, we crossed *Six2eGFP*Cre (*Six2^{GC}*) mice (Kobayashi et al., 2008) with *Hdac1^{fl/fl};Hdac2^{fl/fl}* mice (Montgomery et al., 2007). To test the efficacy of Six2-driven Cre-mediated excision, we examined the expression of HDAC1 and HDAC2 proteins in wild-type (WT) and mutant kidneys. As previously reported by our group (Chen et al., 2011), HDAC1/2 are nuclear proteins abundantly expressed in the nephrogenic zone (Fig. 1A,C,E). In *Six2^{GC};Hdac1^{fl/fl};Hdac2^{fl/fl}* (herein referred to as HDAC1/2 mutant) mice, HDAC1/2 are not detected in the cap mesenchyme (CM) but are maintained in the surrounding UB branches and stromal cells (Fig. 1B,D,F). In accordance with the key functions of HDAC1/2 in deacetylation of histones and p53, the acetylation levels of H3K9,

H4 (K5, K8, K12 and K16), and p53 (K386) are substantially increased in the NPC and derivatives [pretubular aggregates (PTAs) and RVs] of HDAC1/2 mutant kidneys (Fig. 2A-F). Collectively, these results demonstrate the efficient deletion of *Hdac1* and *Hdac2* from the Six 2^+ nephron progenitor pool.

NPC-specific deletion of *Hdac1* and *Hdac2* causes renal hypodysplasia

Mice with NPC-specific double deletion of *Hdac1* and *Hdac2* (all four alleles) were born in normal Mendelian ratios; however, they died soon after birth. At birth, *Hdac1/2* mutant mice exhibited bilaterally small kidneys with full penetrance and there were some obvious petechial hemorrhagic spots on the surface of the mutant kidneys (Fig. 3A-C). Histological examination of mutant kidneys at postnatal day (P) 0 showed small kidney size, absence of the nephrogenic zone, lack of nascent nephrons and glomeruli, and formation of multiple cysts (Fig. 3D-I). *Lotus tetragonolobus* lectin (LTA) staining determined that the majority of cortical renal cysts originate from proximal tubules (LTA-positive tubules, Fig. 1B,D). In contrast, one allele of either *Hdac1* or *Hdac2* is sufficient to ensure nephrogenesis (Fig. 3B,E,H) and survival until adulthood, although these mice show subtle phenotypes including fewer nephrons with variable penetrance (data not shown).

NPC-specific deletion of *Hdac1/2* inhibits cell proliferation but not survival

The defects in nephrogenesis in HDAC1/2 mutant kidneys could have partly resulted from decreased cell proliferation and/or increased apoptosis. Proliferating cell nuclear antigen (PCNA) is a

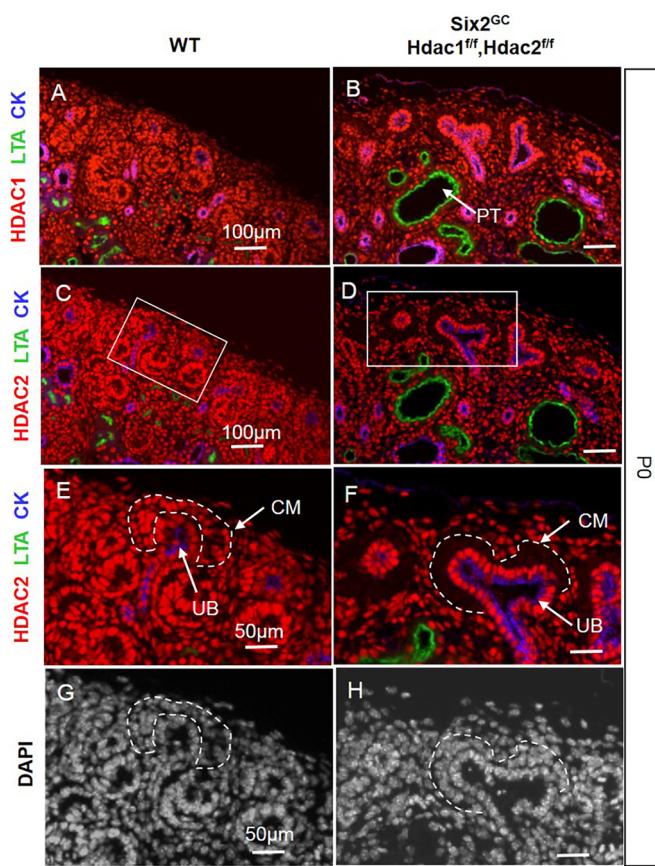


Fig. 1. Deletion of *Hdac1* and *Hdac2* genes in the CM.

(A,C,E,G) Consecutive section immunofluorescence (IF) at P0 showing the relatively abundant nuclear expression of HDAC1/2 proteins in the nephrogenic zone within the CM, UB and stroma. (B,D,F,H) Conditional Six2-Cre-mediated deletion of *Hdac1/2* genes results in efficient loss of HDAC1/2 proteins from the CM. Boxes in C and D are shown enlarged in E and F, respectively. The scale bar information is the same in the left-hand and right-hand panels. CK, pancytokeratin; CM, cap mesenchyme; LTA, *Lotus tetragonolobus* lectin; PT, proximal tubule; UB, ureteric bud branches.

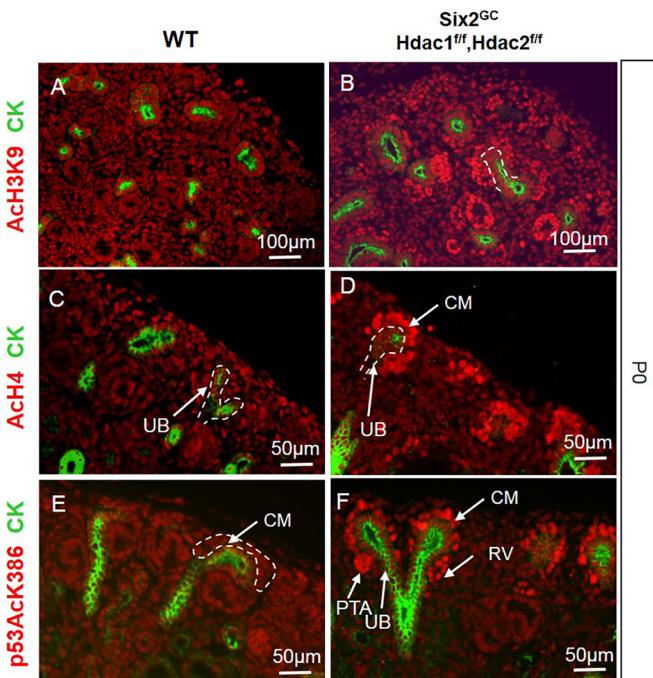


Fig. 2. NPC-specific deletion of *Hdac1* and *Hdac2* causes

hyperacetylation of histones H3 and H4 and p53. (A,C,E) AcH3K9, AcH4 and p53AcK386 are expressed at relatively low levels in all cell types of the developing kidney. (B,D,F) In HDAC1/2 mutant kidneys, there is upregulation of acetylated H3K9, H4 and p53 in NPCs and derived nascent tubules. AcH3K9, histone H3 (acetyl K9), AcH4, acetyl-histone H4; CK, pancytokeratin; CM, cap mesenchyme; p53AcK386, acetyl-Lys386 p53; PTA, pretubular aggregate; RV, renal vesicle; UB, ureteric bud branch.

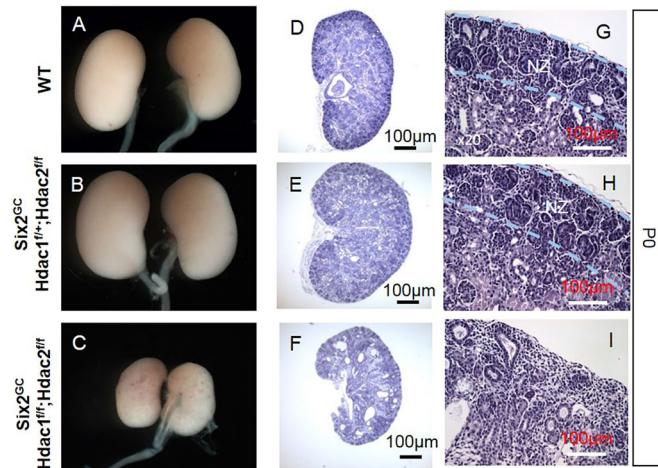


Fig. 3. NPC-specific deletion of *Hdac1* and *Hdac2* causes severe renal hypodysplasia. (A–I) Gross and histological morphology in wild-type (WT) (A,D,G), and conditional compound heterozygous (B,E,H) and homozygous null (C,F,I) HDAC1/2 mutant mice. Six2-Cre-mediated deletion of HDAC1/2 impairs renal growth and patterning owing to loss of the nephrogenic zone (NZ) and cystic tubular degeneration.

sliding clamp that serves as a loading platform for many proteins involved in DNA replication and DNA repair (Strzalka and Ziemienowicz, 2011). PCNA protein expression and synthesis is linked with cell proliferation, and PCNA associates with nuclear histone deacetylase activity (Milutinovic et al., 2002). Moreover, cell proliferation defects are commonly found in most HDAC1/2 knockout or knockdown models (Haberland et al., 2009; Kelly and Cowley, 2013). Immunostaining for PCNA at embryonic day (E) 16.5 and P0 revealed that HDAC1 and HDAC2 are essential for proliferation of NPCs and their derivatives in the nephrogenic zone (Fig. 4A–D). Quantitatively, *Hdac1/2* deletion resulted in a ~75% reduction in the number of proliferating cells per CM ($P<0.05$, $n=3$ per group) (Fig. 4E). We also observed that the remnant Six2 cells seem to form a single cell layer surrounding the UB tips in the mutant CM niches (Fig. 4B, Fig. S1). We do not have an explanation for this unusual observation and are not aware of other mutants exhibiting this abnormality in patterning of the CM around the UB tip. Whether this represents an intrinsic defect in the organization of HDAC1/2 mutant Six2⁺ cells, or results from abnormal organization of the UB tips, remains to be elucidated. We next investigated whether HDAC1/2-deficient NPCs exhibit increased levels of apoptosis. Co-immunostaining of active caspase 3 and Six2, as well as terminal deoxynucleotidyl transferase (TdT) mediated biotin-dUTP nick end-labeling (TUNEL) assay, at E14.5 (not shown) and P0 showed that deletion of *Hdac1/2* had no obvious effect on cell survival in the NPCs (Fig. S1). Taken together, these results indicate that HDAC1 and HDAC2 are essential for NPC growth, but not survival.

p53 hyperacetylation is not a mediator of renal dysgenesis in HDAC1/2 mutants

In addition to their chromatin modifying activities, HDAC1/2 deacetylate the transcription factor p53. p53 is induced by cell stress via post-translational modifications, including acetylation of its C-terminus by CBP (Crebbp)/p300 (Ep300). Hyperacetylated p53 has been linked to transcriptional activation, which in turn induces cell cycle arrest and/or apoptosis. We therefore tested whether the observed p53 hyperacetylation in NPCs and derivatives resulting

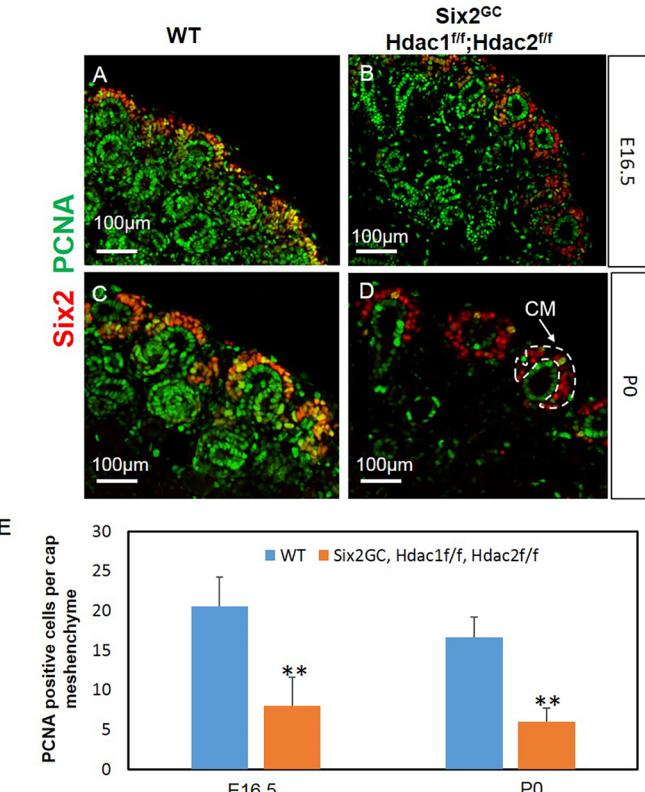


Fig. 4. NPC-specific deletion of *Hdac1* and *Hdac2* inhibits cellular proliferation in the CM and nephrogenic zone. Section IF for PCNA and the NPC-specific marker Six2 at E16.5 (A,B) or P0 (C,D). There is reduction/loss of proliferating cells in the CM and nephrogenic zone in HDAC1/2 mutants compared with controls. Original magnification $\times 20$. (E) Quantification of PCNA staining showed significantly decreased cell proliferation in E16.5 and P0 mutant CM. Data are mean \pm s.e.m. ** $P<0.05$; $n=3$ animals per group.

from HDAC1/2 deletion contributes to the renal dysgenesis. We generated triple mutant *Six2^{GC};Hdac1^{flox/flox};Hdac2^{flox/flox};p53^{+/-}* and *Six2^{GC};Hdac1^{flox/flox};Hdac2^{flox/flox};p53^{-/-}* mouse strains and examined the pups at P0. The results showed that triple mutant kidneys continue to exhibit depletion of NPCs and arrest of tubular differentiation (Fig. S2). In fact, loss of p53 exaggerated renal cystogenesis in this model (Fig. S2A–D). Thus, genetic p53 deletion fails to rescue the HDAC1/2 mutant renal phenotype.

NPC-specific deletion of *Hdac1/2* represses the NPC self-renewal genes

We next assessed the molecular phenotype resulting from deletion of *Hdac1/2* in the NPCs. Immunostaining of Six2, Pax2, Sall1 and WT1 and *in situ* hybridization (ISH) of *Osr1*, markers and key regulators of the CM, demonstrated that progenitor gene expression and the NPC pool are dramatically reduced or absent in E14.5, E16.5 and P0 HDAC1/2 mutant compared with WT kidneys (Fig. 5A–N, Fig. S3A,B).

HDAC1/2 interact with NPC regulators and are bound to the Six2 enhancer

We next investigated whether HDAC1/2 interact biochemically with the NPC regulators Six2, Osr1 and Sall1 in transfected human embryonic kidney (HEK) 293T cells. Immunoprecipitation of either Flag-HDAC1 or Flag-HDAC2 pulled down Myc-tagged Six2 (Fig. 6A). Conversely, immunoprecipitation of Myc-tagged Six2

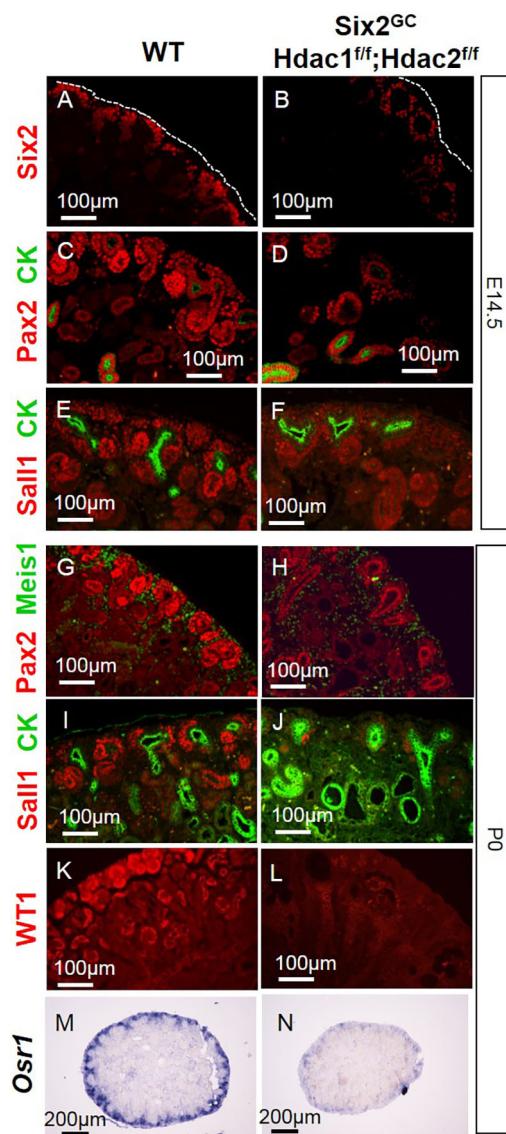


Fig. 5. NPC-specific deletion of *Hdac1* and *Hdac2* depletes nephron progenitors and results in loss of NPC markers. Section IF at E14.5 (A-F) or P0 (G-N) reveals decreased expression of Six2, Osr1, Pax2, Sall1 and WT1. Section ISH shows decreases expression of Osr1 at P0 (M,N) CK, cytokeratin.

pulled down Flag-HDAC1 and Flag-HDAC2 (Fig. 6A). Osr1 acts downstream of and interacts synergistically with Six2 to maintain NPCs (Xu et al., 2014). We tested whether co-expressed Myc-Osr1 is able to interact with transfected Flag-HDAC1 and Flag-HDAC2. Co-immunoprecipitation showed robust interactions of Osr1 with both HDAC1 and HDAC2 (Fig. 6B). Furthermore, immunoprecipitation of Flag-Sall1 pulled down endogenous HDAC1, HDAC2 and transfected Myc-Six2 (Fig. 6C). In addition, we also detected endogenous interaction between Six2 and HDAC1 and HDAC2 in mouse E16.5 kidneys (Fig. 6D), P0 kidneys and E16.5 NPCs (Fig. S4). Of note, immunoprecipitation of HDAC1 pulled down a small amount of endogenous HDAC1 and Six2, whereas HDAC2 immunoprecipitation pulled down HDAC1 and an obviously higher amount of Six2. Collectively, these data suggest that HDAC1 and HDAC2 interact with Six2, Sall1 and Osr1, which are essential players in the balance of NPC self-renewal and differentiation.

Chromatin immunoprecipitation (ChIP) followed by NextGen sequencing in embryonic kidneys revealed that Sall1 and Six2 co-occupy many loci containing genes essential for kidney development, as well as *Sall1* and *Six2* themselves (Kanda et al., 2014). Interestingly, in the *Six2* gene, Sall1 binding sites lie within 500 bp of the *Six2* binding site (Kanda et al., 2014). The *Six2/Sall1*-bound region corresponds to that reported by Park et al., and is located 60 kb upstream of the *Six2* transcription start site (Park et al., 2012). This region directs faithful spatial and temporal expression of a reporter in transgenic mice (Park et al., 2012). We tested whether HDAC1/2 and Six2 are bound to the *Six2* enhancer in NPCs. We isolated NPCs from E16.5 kidneys by magnetic-activated cell sorting (Brown et al., 2015) and performed ChIP-PCR using anti-HDAC1, anti-HDAC2 and anti-Six2 antibodies. The isolated NPCs are highly enriched with Six2 (90%), with minor contamination with stromal cells (Meis1) (Fig. S5). The results showed that HDAC1/2 and Six2 co-occupy the *Six2* enhancer (Fig. 6E). The specificity of the HDAC1 antibody was further validated by ChIP-PCR using positive and negative control primer sets (Fig. S6). Because HDAC1/2 and Six2 proteins interact (Fig. 6A), these findings suggest a model in which Six2 recruits HDAC1/2 to the *Six2* enhancer, and this interaction might be necessary for regulation of *Six2* expression.

HDAC1/2 are required for *Lhx1* gene expression and renal vesicle differentiation

In E14.5-E16.5 HDAC1/2 mutant kidneys, early nephron precursors such as pre-tubular aggregates and RVs form. However, only rare comma- and S-shaped nascent nephrons or proximal tubules were detected (Fig. 7A-F), suggesting that HDAC1/2 are required for the RVs to progress to comma- and S-shaped nephrons and eventually into segmented epithelial nephrons.

Genome-wide transcriptome analysis of whole kidney RNA (see below) revealed reduced expression of *Lhx1* in HDAC1/2 mutant kidneys. *Lhx1*, also known as LIM-class homeodomain transcription factor 1 (Lim-1), is expressed in the intermediate mesoderm, nephric duct, mesonephric tubules, ureteric bud, pretubular aggregates and RVs (Kobayashi et al., 2005; Pedersen et al., 2005). *Lhx1* function is required for patterning and RV maturation into comma- and S-shaped bodies because tubulogenesis is blocked at the RV stage in *Lhx1* null mice (Kobayashi et al., 2005; Pedersen et al., 2005). Accordingly, we examined *Lhx1* expression in HDAC1/2 mutant kidneys. In E16.5 WT kidneys, *Lhx1* protein is expressed in the RVs and nascent nephrons (Fig. 8A,C). In contrast, *Lhx1* expression is abrogated in the HDAC1/2-deficient RVs and nascent nephrons (Fig. 8B,D-F). Interestingly, the few remnant RVs and nascent nephrons observed in the HDAC1/2 mutant kidneys appear to have escaped Cre-mediated recombination (Fig. 8G,H).

NPC-specific deletion of *Hdac1/2* downregulates *Pax8* and *Fgf8* in RVs

During nephrogenesis, *Lhx1* is downstream of *Fgf8*, *Pax8* and *Wnt4*, whereas *Wnt4* lies downstream of *Pax8/Fgf8* and upstream of *Lhx1* (Grieshammer et al., 2005; Kispert et al., 1998; Kobayashi et al., 2005; Narlis et al., 2007; Park et al., 2007; Pedersen et al., 2005; Perantoni et al., 2005; Stark et al., 1994). Section ISH in E16.5 and P0 mice demonstrated that both *Fgf8* and *Pax8* are markedly downregulated in the HDAC1/2 mutant versus control RVs (Fig. 9A-D,G,H). Also, we confirmed abrogated *Lhx1* expression in the mutant RVs (Fig. 9E,F,I,J). In contrast, *Wnt4*

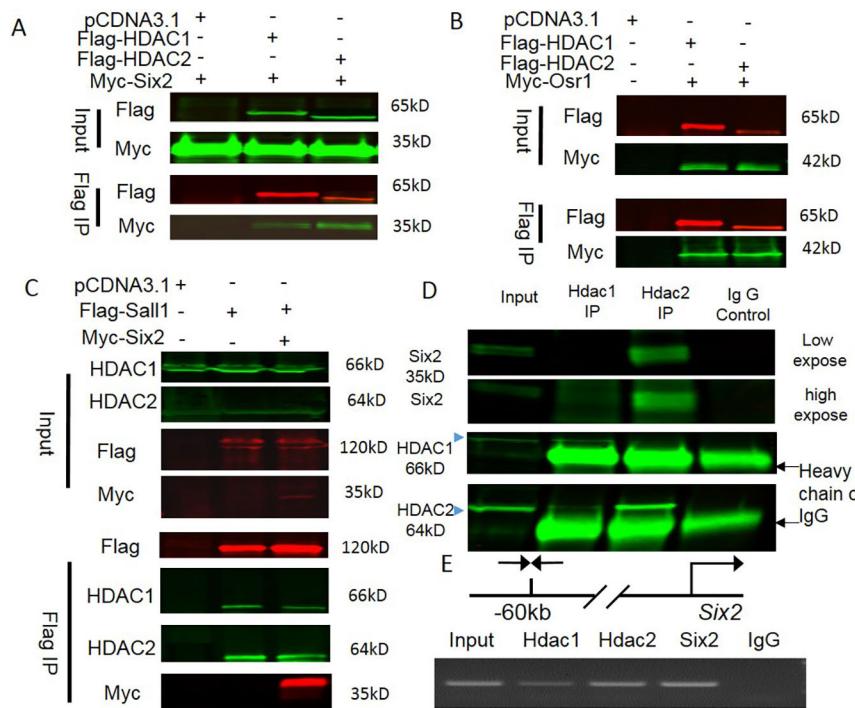


Fig. 6. HDAC1/2 interact with NPC transcriptional regulators and bind the *Six2* enhancer. (A-C) The designed plasmids (+) were transfected into HEK 293T cells and the cell lysates were subject to Flag-tag immunoprecipitation. Flag-HDAC1/2 co-immunoprecipitate with Myc-Six2 (A); Flag-HDAC1/2 co-immunoprecipitate with Myc-Osr1 (B); Flag-Sall1 and Myc-Six2 co-immunoprecipitate with endogenous HDAC1/2 (C). (D) Endogenous interaction between Six2 and HDAC1/2 was detected in E16.5 kidneys. (E) Chromatin immunoprecipitation-PCR showing HDAC1/2 and Six2 co-occupancy of the *Six2* enhancer.

mRNA expression [ISH and quantitative PCR (qPCR)] is maintained in the mutant RVs but not in NPCs (Fig. 10A-C). Thus, loss of *Lhx1* expression in HDAC1/2 mutant RVs is Wnt4 independent, but at least partly caused by decreased expression of *Pax8/Fgf8*.

Interestingly, we found enhanced expression of the canonical Wnt protein target, *Lef1*, in the stromal mesenchyme surrounding the UB branches as well as in the outer cortical stroma of HDAC1/2 mutant kidneys (Fig. 10D,E). This increase does not appear to be mediated by excess *Wnt9b* expression in the UB (Fig. S7).

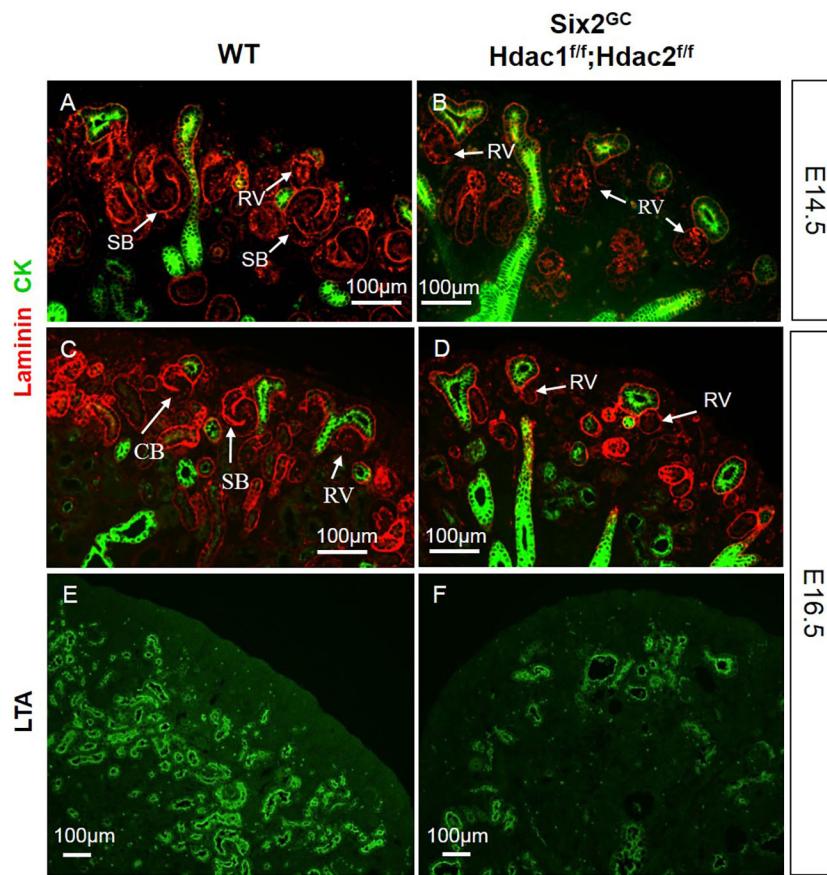


Fig. 7. NPC-specific deletion of *Hdac1* and *Hdac2* arrests nephrogenesis at the RV stage. (A-F) Section IF at E14.5 (A,B) and E16.5 (C-F). Laminin staining outlines the basement membrane of nascent nephrons showing that nephrogenesis is arrested at the RV stage in double HDAC1/2 mutant kidneys as early as E14.5. Few and scattered proximal tubules are formed in mutant kidneys. CK, pancytokeratin; LTA, *Lotus tetragonolobus* lectin; RV, renal vesicle; SB, S-shaped body.

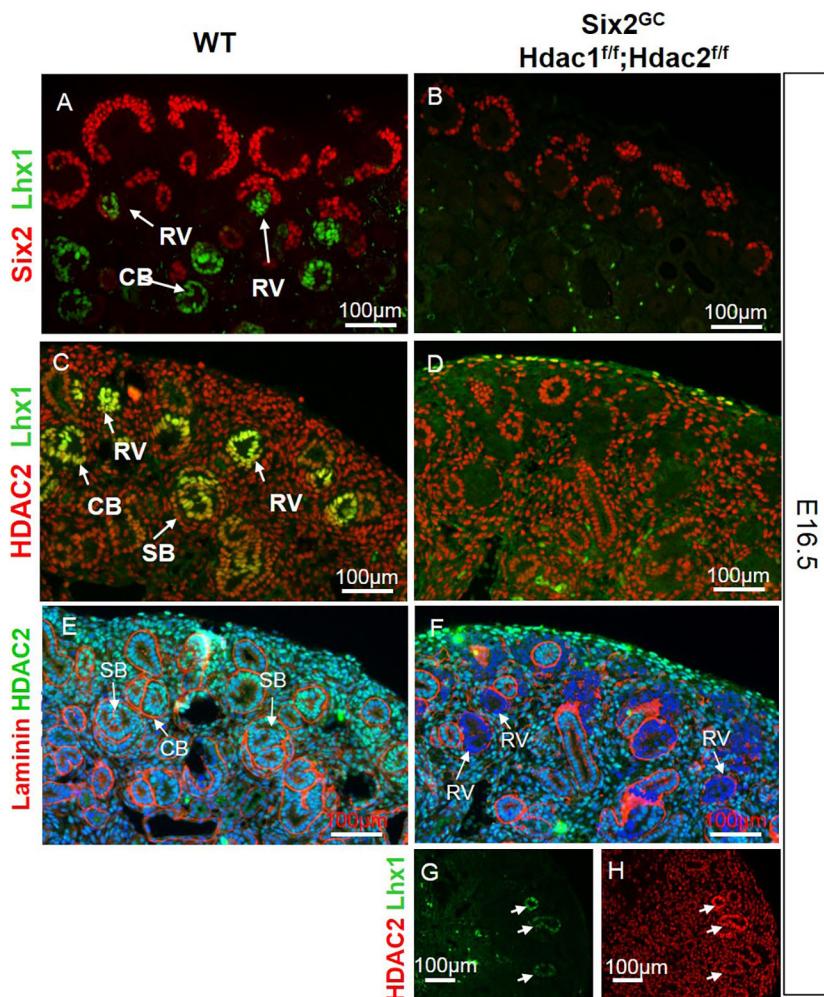


Fig. 8. RVs lacking HDAC1/2 fail to express the transcription factor Lhx1. (A-F) Section IF for Six2/Lhx1 (A,B), HDAC2/Lhx1 (C,D), and laminin/HDAC2 (E,F) showing abrogated Lhx1 protein expression in nascent nephrons of HDAC1/2-mutant kidneys, which correlates spatially with loss of HDAC1/2. (G,H) The few instances in which Lhx1 expression was preserved correlate with nascent nephrons that escaped Cre-mediated excision of HDAC1/2. Arrows indicate the different stages of nascent nephrons: renal vesicle (RV), comma-shaped body (CB) and S-shaped body (SB).

However, because it is difficult to clearly compare the *Lef1* levels between WT and mutant NPCs from *Lef1* immunostaining alone, we examined the effect of HDAC1 and HDAC2 deletion on *Lef1* gene expression in fluorescence-activated cell sorting (FACS)-isolated Six2-GFP⁺ NPCs from E16.5 WT and HDAC1/2 mutants. NPCs were cultured in differentiation (KO) medium (Brown et al., 2011, 2013) in the presence of 3.5 μM CHIR for 48 h. *Lef1* RNA copy number, quantitated by droplet digital PCR (ddPCR), was not different in CHIR-treated HDAC1/2 mutant and WT NPCs (Fig. 10F). In contrast, *Six2* RNA copy number was 50% lower in mutant CHIR-treated than in WT CHIR-treated NPCs. Collectively, these findings indicate that loss of HDAC1/2 in NPCs and derived cells activates stromal Wnt signaling, suggesting the presence of intercompartmental crosstalk. Of note, our transcriptome profiling identified multiple stromal genes (*Pbx1*, *Meis1*, *Foxd1*, *Fat4*) that are upregulated in the HDAC1/2 mutant kidneys. Our data also suggest that *Six2* expression is dependent on HDAC1/2 in the setting of activated Wnt signaling.

Transcriptome analysis of whole kidney RNA

To further understand the molecular pathogenesis of the renal phenotype and to elucidate the developmental pathways regulated by HDAC1 and HDAC2, we carried out a genome-wide microarray analysis of RNA samples extracted from E15.5 WT and *Hdac1/2* kidneys. The raw and analyzed data have been deposited in the NCBI Gene Expression Omnibus (GEO) under accession number GSE84305. The results revealed that 649 transcripts (1.17%) are

significantly altered in double-mutant kidneys (≥ 1.5 -fold, $P < 0.05$, $n=4$ independent experiments), of which 349 (69.24%) were upregulated (range +1.50- to +8.56-fold) and 155 transcripts (30.76%) were downregulated (range -1.50- to -12.40-fold) (Fig. S8A).

To analyze the pathways and biological processes that are sensitive to the loss of HDAC1/2, Ingenuity Pathway Analysis (IPA) was performed on the differentially expressed transcripts. This analysis indicated that the most significantly enriched pathways are concerned with cancer, embryonic development and organ development (Fig. S8B-D). A complete list of genes for each category and pathway is shown in Table S1. Further analysis using the Biological Networks Gene Ontology (BiNGO) tool revealed that many genes involved in kidney development processes are altered in HDAC1/2 mutant kidneys; for example, key factors involved in differentiation of the proximal and distal nephrons, such as *Lhx1* (-1.6-fold), *Hnf1a* (-1.90-fold), *Hnf4a* (-2.85-fold), *Irx1* (-2.346-fold), and the Notch signaling pathway [*Dll1* (-2.18-fold), *Hes5* (-2.24-fold), *Hey1* (-1.67-fold) and *Osr2* (-1.70-fold)] (Table S2). Network analysis placed *Lhx1* upstream of *Hnf1a* and *Hnf4a* as well as many components of the Notch pathway, such as *Hes5* and *Dll1* (Fig. 11A,B). Section ISH at E16.5 and P0 confirmed significant downregulation of *Hnf1a* and *Hnf4a* in HDAC1/2 mutant nascent tubules but preservation of *Hnf1b* (Fig. 11C). Similarly, the Notch ligands *Dll1* and *Jag1*, and several components of the Notch signaling pathway, including *Lfgn*, *Osr2*, *Hes1* and *Hes5* were repressed (Fig. 11D). Consistent with downregulation of

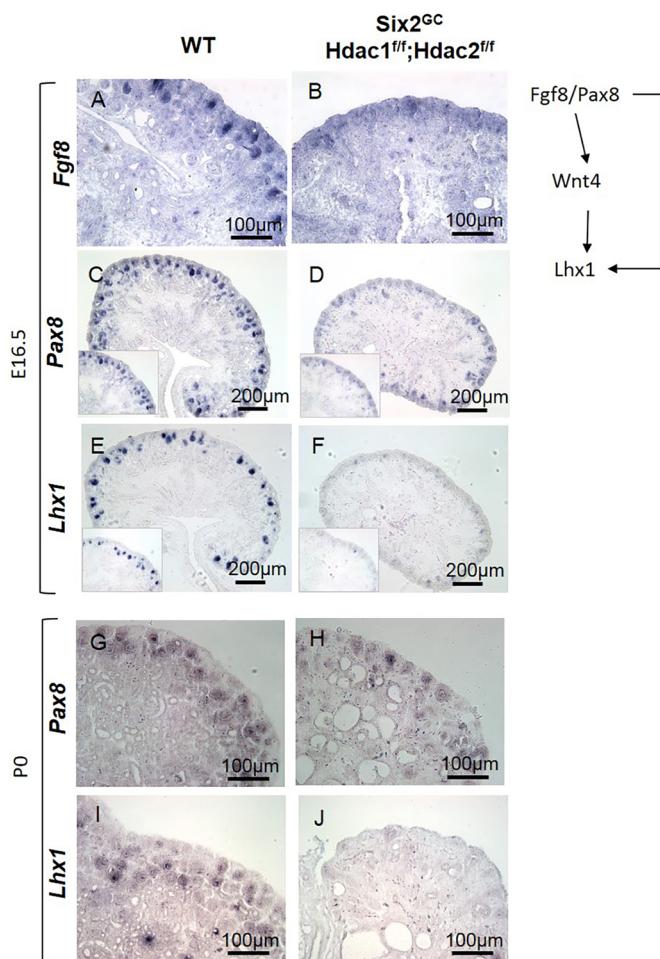


Fig. 9. HDAC1/2 deletion disrupts the RV regulatory network. (A–J) Section ISH at E16.5 (A–F) and P0 (G–J), showing early and persistent repression of *Pax8*, *Fgf8* and *Lhx1*, three major factors required for differentiation of RVs to nascent nephrons, in HDAC1/2 mutant kidneys.

the *Lhx1/Hnf1a/Hnf4a* network, there was a significant decrease in expression of the epithelial differentiation genes, such as *Nphs2*, *Slc34a1*, *Slc22a6*, *Slc37a4*, *CA4* (*Car4*) and *Cdh6*. In addition to the genes validated by section immunofluorescence (IF), ISH and reverse transcription (RT)-qPCR, NanoString gene expression

analysis confirmed nine out of 11 randomly selected genes (Table S2). Unlike the differences in differentiation gene expression, which were readily identified using microarray analysis of whole kidney RNA, only a few progenitor genes were detected [e.g. decreased expression of *Cited1* (−6.35-fold) and *c-Myc* (*Myc*) (−1.59-fold)]. Section ISH and section IF readily detected changes in expression of these genes (e.g. *Pax2*, *Six2*, *Sall1* and *Osr1*) (Figs 4 and 5).

DISCUSSION

The present study provides comprehensive insights into the role of HDAC1 and HDAC2 in nephrogenesis. NPC-specific deletion of *Hdac1/2* genes caused downregulation of key progenitor genes, including *Six2*, *Pax2*, *Sall1*, *Wt1*, *Osr1*, *c-Myc* and *Cited1*, and premature depletion of NPCs. Our biochemical and ChIP analyses revealed that HDAC1/2 interact with *Six2*, *Osr1* and *Sall1*, a network of transcriptional regulators that maintain the balance of NPC proliferation and differentiation, and that *Six2* is a potential *in vivo* target of HDAC1/2. Previous studies demonstrated that *Sall1* is upstream of *Six2*, and *Sall1* and *Six2* are required for gene expression and cell renewal in the CM (Basta et al., 2014; Kanda et al., 2014). *Six2* or *Sall1* deletion results in depletion of nephron progenitors (Basta et al., 2014; Kanda et al., 2014; Kobayashi et al., 2008). Also, conditional deletion of the NuRD-specific component *Mi2b* (*Chd4*) in NPCs led to depletion of the CM (Denner and Rauchman, 2013). *Sall1* and *Mi2b* exhibit a strong genetic interaction in the developing kidney, supporting a cooperative role for *Sall1* and NuRD in maintaining NPCs (Denner and Rauchman, 2013). Because HDAC1 and HDAC2 are key components of the NuRD complex, our data support a model in which the *Sall1/Six2/HDAC* complex is recruited to the *Six2* enhancer to maintain high *Six2* expression in the NPCs.

Osr1 acts downstream of and interacts synergistically with *Six2* and Groucho family transcriptional co-repressors to maintain the NPC pool via repression of *Wnt4*-directed nephrogenic differentiation (Xu et al., 2014). In *Osr1* mutant kidneys, *Wnt4* is ectopically activated throughout the CM, which undergoes premature mesenchyme-to-epithelium transition (Xu et al., 2014). Although our results showed protein-protein interactions between *Osr1* and HDAC1/2, and *Osr1* and HDAC1/2 target the *Wnt4* enhancer region, we did not observe ectopic *Wnt4* activation or RV formation in the CM. We surmise that *Osr1/Groucho* interactions compensate for the loss of HDAC1/2 in NPC, thus preventing ectopic *Wnt4* activation in the CM.

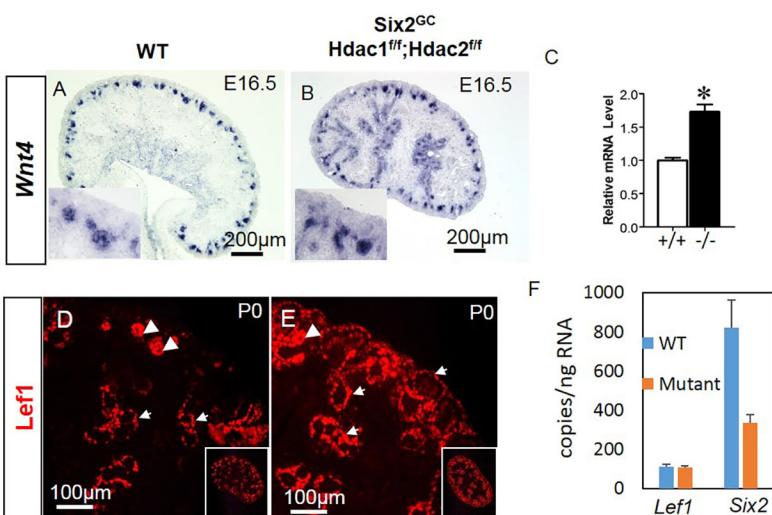


Fig. 10. Arrested RV differentiation in HDAC1/2 mutant kidneys is Wnt4 independent. (A–C) Section ISH shows maintained expression of *Wnt4* in the mutant RVs at E16.5 (A,B) and enhanced total kidney *Wnt4* by RT-qPCR (C). *P<0.05; n=4. (D,E) Section IF at P0 using antibodies against *Lef1*. In WT kidneys, *Lef1* is expressed in RVs (arrowheads) and in a thin layer of stromal cells surrounding the UB branches. In HDAC1/2 mutant kidneys, *Lef1* is ectopically expressed in the stroma (small arrows) and is upregulated in the peri-UB stroma. (F) FACS-isolated NPCs from WT (n=3) and HDAC1/2 mutant (n=2) were cultured in differentiation medium (with 3.5 μM CHIR) for 48 h. ddPCR showed that the *Lef1* RNA copy number of mutant NPCs is not significantly different from that of WT cells, whereas the *Six2* RNA copy number of mutant NPC is significantly lower than that of WT cells. Data are mean±s.e.m.

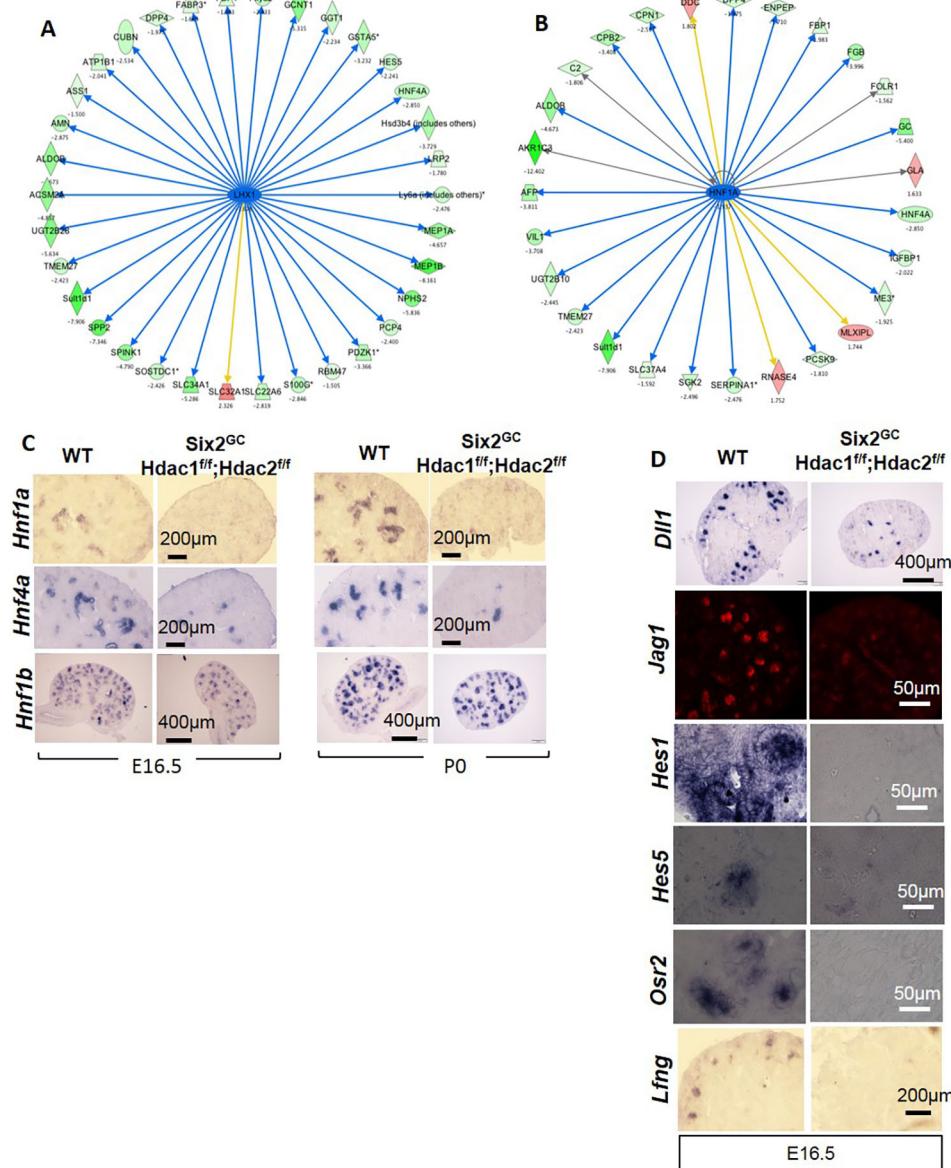


Fig. 11. Downregulation of the Notch/HNF network in *Six2^{GC}*, *Hdac^{flox/flox}*, *Hdhac1^{f/f};Hdhac2^{f/f}* kidneys. (A,B) Network analysis of differentially expressed genes shows altered (mostly decreased) genes that are downstream of *Lhx1* and *Hnf1a/4a*. Green, downregulated; red, upregulated. Numbers indicate fold change versus WT. (C,D) Section ISH showing downregulation of *Hhf1a/4a* (but not *Hnf1b*) and Notch genes in HDAC1/2 mutant kidneys. HNF1A/HNF4A control expression of a network of genes involved in metabolic and transport functions in the proximal tubules. Decreased HNF1A-mediated gene expression is likely secondary to downregulation of Notch signaling, which controls segmental tubular differentiation.

In line with NPC depletion of HDAC1/2 mutant kidneys and the known pro-proliferative functions of HDAC1/2, we found that HDAC1/2 are crucial for NPC growth. Surprisingly, HDAC1/2 are not required to protect against p53-mediated apoptosis in NPCs. These findings are in sharp contrast to the effects of *Hdac1/2* deletion in the UB epithelium, where p53 hyperacetylation was accompanied by increased UB cell apoptosis, and concomitant deletion of p53 partially rescued the defect in UB branching morphogenesis (Chen et al., 2015). Here, we show that accumulation of acetylated p53 in NPCs does not induce aberrant apoptosis and concomitant deletion of p53 fails to rescue the renal dysgenesis in HDAC1/2 mutants. Collectively, these findings point to the differential and context-dependent functions of HDAC1/2 in NPCs versus UB epithelium, which warrants further studies.

In addition to premature NPC depletion, deletion of *Hdac1/2* blocks nephrogenesis at RV stage. This effect appears to be mediated via downregulation of the *Lhx1*/HNF/Notch network. *Wnt4* and *Lhx1* are both expressed in the RV, and *Lhx1* is genetically downstream of *Wnt4* (Kispert et al., 1998; Kobayashi et al., 2005;

Stark et al., 1994). It is believed that the Wnt4-dependent transcriptional program leading to *Lhx1* activation serves to differentiate the pre-tubular aggregate into the epithelialized RVs (Halt and Vainio, 2014). Here, we show that deletion of *Hdac1/2* in NPCs abrogates *Lhx1* expression in RVs. Although downregulation of *Fgf8* and *Pax8* in HDAC1/2 mutant RVs can mediate *Lhx1* repression, it is conceivable that *Lhx1* is directly regulated by HDAC1/2 and is worthy of future study.

Aberrant Wnt4 expression in RVs in the face of downregulated expression of Pax8/Fgf8/Pax2/WT1 (upstream activators of Wnt4) was a surprising finding in this study. This suggests the presence of noncanonical upstream regulators of *Wnt4* gene expression within the RV that are unmasked by the loss of HDAC1/2. The nature of these factors remains to be determined. Our data also indicate that Wnt9b expression in the UB branches is not affected by the loss of HDAC1/2 in NPCs. Thus, the cause for maintained/enhanced Wnt4 expression in mutant HDAC1/2 RVs remains to be determined. Because our findings suggested that HDAC1/2 perform RV-specific functions, we attempted to delete *Hdac1/2* genes specifically from

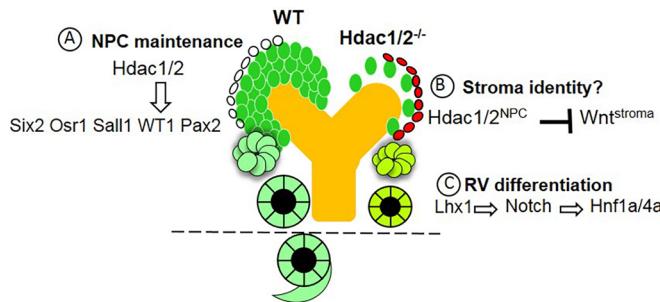


Fig. 12. Working model for the actions of HDAC1/2 in the regulation of nephrogenesis. HDAC1/2 perform sequential functions during NPC and epithelial differentiation. (A) In the NPCs, HDAC1/2 are recruited (possibly by Six2/Sall1) to Six2 enhancer where they serve a positive regulatory role. HDAC1/2 also interact with Osr1 in the maintenance of NPCs. (B) HDAC1/2 in the NPCs and/or nascent nephrons restrain Wnt protein activity in adjacent stroma via unknown mechanisms. (C) HDAC1/2 directly or indirectly regulate the RV transcriptional network (Pax8/Fgf8/Lhx1) upstream of the Notch/HNF1A/HNF4A pathway. The dotted line indicates that NPC-specific deletion of HDAC1/2 arrests nephrogenesis at the RV stage.

the RVs using Wnt4-Cre/GFP mice. Although GFP was expressed appropriately in the RVs, we were unable to eliminate HDAC1/2 proteins, presumably as a result of the long half of the proteins, as each generation of nascent RVs express abundant HDAC1/2 prior to the deletion occurring. Genome-wide analysis of HDAC1/2-bound genes in NPCs versus RVs will be necessary to illuminate the direct versus indirect pathways regulated by HDACs during nephrogenesis.

In addition to Lhx1, many components of the Notch signaling pathway are downregulated in HDAC1/2 mutant kidneys. Notch signaling plays a key role in segmentation of the nephron and in the progression of pretubular aggregates/RVs towards comma- and S-shaped bodies during nephrogenesis (Kopan et al., 2007). γ -Secretase releases the Notch intramembrane domain (NICD), which, along with RBPJ, mediates the transcriptional effects of Notch proteins. Knockout of PSEN proteins (essential component of γ -secretase) or treatment with γ -secretase inhibitors allows formation of pretubular aggregates/RVs but not comma- and S-shaped bodies (Cheng et al., 2003; Wang et al., 2003). In addition, Notch2-deficient RVs initiate the segmentation process but fail to establish the proximal fate (Cheng et al., 2007), and more recently, the distal fate as well (Chung et al., 2016). Inactivation of *Lhx1* causes loss of Dll1, and Dll1 hypomorphic mice have a severe reduction in nephron numbers and the loss of proximal segments (Kobayashi et al., 2005). Following loss of *Lhx1*, at least three other Notch signaling components, Jag1, Hes5 and musashi homolog2 (*Msi2*), are repressed (Kobayashi et al., 2005). Our immunostaining and ISH results revealed that the expression level of Notch ligands (Dll1 and Jag1) and many Notch protein targets (Hes1, Hes5 and Osr2) that are important for nephrogenesis are also dramatically downregulated. Based on these results, we conclude that impaired Notch signaling contributes significantly to the developmental arrest at the RV stage and tubulogenesis failure of HDAC1/2 mutant kidneys.

In summary, the present study demonstrates that HDAC1/2 perform redundant, sequential and essential roles in the balance of NPC self-renewal and differentiation as well as in progression of nephrogenesis (Fig. 12). In wild-type NPCs, HDAC1/2, working in concert with Six2, Sall1 and Osr1, maintain expression of progenitor genes cell autonomously favoring the expansion of the

multipotent nephron progenitor population. Additionally, HDAC1/2, presumably working together with other transcriptional regulators, are required to maintain the Pax8/Fgf8/Lhx1/HNF/Notch transcriptional regulatory network required for RV differentiation to nascent nephrons. It remains to be determined whether the effects of HDAC1/2 on NPC and RV transcriptional networks are mediated via locus-specific control/binding or more generalized effects on the epigenome. Future studies uncovering HDAC1/2 target genes in NPCs and RVs are clearly warranted to further understand the epigenetic regulation of nephrogenesis.

MATERIALS AND METHODS

Mice

Mice bearing conditional null alleles of *Hdac1*^{flox/flox} and *Hdac2*^{flox/flox} (Montgomery et al., 2007) were crossed to *Six2-CreEGFP* transgenic mice (*Six2-Cre^{g/+}*) (Kobayashi et al., 2008) to delete the *Hdac1* and *Hdac2* genes, singly or in combination, specifically in the NPCs. *Wnt4GFP* Cre BAC transgenic mice (Shan et al., 2010) were used to cross with *Hdac1*^{flox/flox}, *Hdac2*^{flox/flox} mice to inactivate *Hdac1/2* in the RVs. *Trp53*^{−/−} mice were obtained from the Jackson (JAX) Laboratory.

Histology and immunohistochemistry

Kidneys were fixed in 10% buffered formalin, embedded in paraffin and sectioned at 4 μ m. Histological analyses were performed by standard Hematoxylin and Eosin (H&E) staining. Section IF was performed as previously described (Chen et al., 2011, 2015). Antigen retrieval was accomplished by placing slides in 10 mM of boiling sodium citrate, pH 6.0, for 20 min. The following primary antibodies were used: anti-HDAC1 (1:100, 3601, BioVision), anti-HDAC2 (1:100, 3602, BioVision), anti-cytokeratin (1:200, C2562, Sigma-Aldrich), anti-Six2 (1:200, 11562-1-AP, Proteintechgroup), anti-Pax2 (1:200, 6160000, Invitrogen), anti-PCNA (clone PC10, 1:200; DAKO Corp.), anti-cleaved caspase 3 (1:100, 9661s, Cell Signaling Technology), anti-acH4 (1:100, 06-866, Millipore), anti-acH3K9 (1:100, ab4441, Abcam), anti-p53AcK386 (1:100, ab52172, Abcam), anti-Jag1 (H-114; 1:100, sc-8303, Santa Cruz Biotechnology), Lhx1 (1:100, 4F2-C, Developmental Studies Hybridoma Bank), anti-Lef1 (1:100, 2230s, Cell Signaling Technology), anti-GFP (1:100, ab13970, Abcam), anti-E-cadherin (1:100, 610181, BD Biosciences), anti-Sall1 (1:100, ab31526, Abcam), anti-WT1 (1:100, ab15247, Abcam) and anti-laminin (1:100, L9393, Sigma-Aldrich). In negative controls, the primary antibody was omitted or replaced by nonimmune serum. For IF, the secondary antibodies were Alexa Fluor 488-conjugated anti-rabbit and Alexa Fluor 594-conjugated anti-rabbit (1:2000, Invitrogen) and anti-mouse fluorescein isothiocyanate (FITC) (1:200, Sigma-Aldrich). In addition, FITC-conjugated *Lotus tetragonolobus* lectin agglutinin (1:100, Vector Laboratories) was used to label the apical brush border of proximal tubules. Nuclei were counterstained by 4',6-diamidino-2-phenylindole (DAPI) (1:500, D1306, Invitrogen). The immunofluorescent images were captured using a 3D or deconvolution microscope (Leica DMRXA2).

Section ISH

ISH was performed using digoxigenin-labeled antisense probes on kidney tissue fixed with 4% paraformaldehyde (PFA) as previously described (Chen et al., 2011). For section ISH, the kidney tissues were collected in DEPC-treated PBS, fixed in 4% PFA in diethyl pyrocarbonate (DEPC)-treated PBS overnight at 4°C, dehydrated in a series of alcohol, cleared in xylene and embedded in paraffin wax. Sections were cut to 10 μ m thickness. After rehydration in 0.1% Tween in PBS, the samples were digested with proteinase K, and then refixed in 4% PFA, followed by 0.2% glutaraldehyde, followed by three washes in PBS. After a 3-h incubation in hybridization solution, the explants were hybridized with the digoxigenin-labeled antisense probes (~1 μ g of probe/vial) overnight at 65°C. The next day, the samples were sequentially washed with hybridization solution, 2× saline sodium citrate (SSC), pH 4.5, 2× SSC, pH 7.0, 0.1% CHAPS, maleic acid buffer and PBS at room temperature. The slides were incubated with preblocked antibody (1:10,000, anti-Dig alkaline phosphatase, Roche Applied Science) at 4°C overnight. The following day,

after sequential washes of 0.1% bovine serum albumin in PBS, PBS and AP1 buffer at room temperature, the samples were stained by BM Purple (Roche Applied Science) at 4°C. When the desired level of staining was reached, the reaction was stopped by two washes of Stop Solution for 15 min each. The plasmids for *Dll1*, *Hes1*, *Hes5* probe preparation were gifts from Dr Ryoichiro Kageyama (Kita et al., 2007). The experimental and control samples were put in the same reaction vessel to allow for proper comparison. All the experiments, including ISH, immunostaining and TUNEL were repeated at least three times.

TUNEL assay

Apoptosis was assessed using TUNEL and was carried out using an *in situ* apoptosis detection kit (Trevigen) according to the manufacturer's guidelines. Four-micrometer paraffin sections were fixed in methanol-free PFA before and after proteinase K treatment at 20 µg/ml for 8–10 min at room temperature. The sections were incubated with the nucleotide mixture (which included fluorescein-tagged dUTP) and rTdT enzyme for 1 h at 37°C. The slides were mounted using Vectashield with DAPI (Vector Laboratories). The images were captured using a deconvolution fluorescent microscope.

Cell culture and transient transfection

HEK 293T cells were obtained from the laboratory of Dr Hua Lu (Tulane University, New Orleans, LA, USA, and Johns Hopkins University Cell Center, Baltimore, MD, USA). Cells were grown in high-glucose Dulbecco's modified Eagle medium (DMEM) with stable glutamine supplemented with 10% fetal bovine serum (FBS) and 10 mg/ml antibiotics (penicillin and streptomycin). All cells were maintained at 37°C in a 5% CO₂ humidified atmosphere. Cells seeded on the plate overnight were transfected with plasmids as indicated in figure legends using Lipofectamine LTX with Plus Reagent following the manufacturer's protocol (Thermo Fisher Scientific). Cells were harvested at 48–72 h post-transfection. The plasmid Flag-Sall1 was a gift from Dr Ryuichi Nishinakamura (Kanda et al., 2014), Flag-Six2 and Myc-Six2 were gifts from Dr Joo-Seop Park (Park et al., 2012), and Flag-Osr1 was a gift from Dr Rulan Jian (Xu et al., 2014).

Immunoprecipitation and western blotting

Immunoprecipitation (IP) was conducted using antibodies as indicated in the figure legends. Briefly, ~500–1000 µg of protein was incubated with the indicated antibody at 4°C for 4 h or overnight. Protein A or G beads (Santa Cruz Biotechnology) were then added, and the mixture was incubated at 4°C for an additional 1–2 h. Beads were washed at least three times with lysis buffer. Bound proteins, as well as the whole-cell extracted proteins, were detected by western blotting. The following primary antibodies were used: anti-HDAC1 (rabbit polyclonal, 1:1000, BioVision) and anti-HDAC2 (rabbit polyclonal, 1:1000, BioVision), anti-Flag (1:1000, Sigma-Aldrich), anti-Myc (1:1000, Sigma-Aldrich) and mouse anti-β-actin (1:5000, Sigma-Aldrich).

Isolation of NPCs

Six2⁺/Cited1⁺ NPCs were isolated from E16.5 kidneys by magnetic-activated cell sorting (Brown et al., 2015). Briefly, after dissecting kidneys and removing the capsule, the kidneys were digested in collagenase A/pancreatin enzyme digest solution at 37°C for 15 min. After digestion, FBS was added to the tube containing kidneys to stop the enzyme reaction. The cell suspension was transferred to new microfuge tubes and cells were collected by centrifugation at 300 g for 5 min. Subsequently, the cells were re-suspended and filtered through a 30-µm pre-separation filter. Magnetic depletion was carried out through the addition of anti-CD105-PE, anti-CD140-PE, anti-Ter119-PE and anti-CD326-PE. Finally, the NPCs (Cited1⁺ NPCs) were collected as the negative fractions.

RNA isolation and ddPCR

E16.5 NPCs were isolated, plated and expanded on Matrigel-coated plates in a monolayer in keratinocyte serum-free medium (Gibco) supplemented with 50 ng/ml FGF2 (R&D Systems) as described (Brown et al., 2011, 2013) for 48 h. Total RNA was isolated using an RNA isolation kit (Qiagen). RNA

concentration was quantified using Nanodrop 2000 (Thermo Fisher Scientific). ddPCR was performed on a Bio-Rad ddPCR system to determine *Lef1* and *Six2* gene expression. All reagents for the One-Step RT-ddPCR system were purchased from Bio-Rad to generate complementary DNA (cDNA) and quantify gene expression. Droplets were analyzed on the QX200 droplet reader and target cDNA concentration was determined using QuantaSoft analysis software (Bio-Rad).

ChIP

ChIP experiments were performed using an EZ ChIP chromatin immunoprecipitation kit (17-371, Millipore) according to the manufacturer's protocol. Immunoprecipitation was performed with ChIP-grade antibodies to HDAC1 (ab7028, Abcam), HDAC2 (ab7029, Abcam), Six2 (11562-1-AP, ProteinTech). Rabbit IgG (ab46540, Abcam) was used as a control antibody. The chromatin-antibody complexes were captured on protein G-coupled Dynabeads (Invitrogen). After washing and elution of the complexes from the beads, the DNA-protein cross-links were reversed at 65°C overnight. Next, the precipitated DNA was treated with RNase A and proteinase K and purified using spin columns. The purified DNA along with input genomic DNA (1:100) were analyzed by PCR. The primer sequences used for PCR were:

Six2Enh Forward: 5'-ACCGGATGGAAAGGCTTTAT-3'
Six2Enh Reverse: 5'-GGGCTGTTCCAGCTACAGAG-3'

Genome-wide microarray analysis

Microarray analysis was performed according to established protocols (Schanstra et al., 2007). Briefly, fluorescently labeled cRNA was generated from 0.5 µg total RNA in each reaction using a Fluorescent Direct Label Kit (Agilent) and 1.0 mM cyanine 3'- or 5'-labeled dCTP (PerkinElmer). Hybridization was performed using an Oligonucleotide Microarray Hybridization and *In Situ* Hybridization Plus Kit (Agilent). The labeled cRNA was hybridized to Agilent 44K whole mouse genome oligonucleotide microarray (containing ~41,000 probes) as previously described (Schanstra et al., 2007). The arrays were scanned using a dual-laser DNA microarray scanner (Agilent). The data were then extracted from images using Feature Extraction software 6.1 (Agilent). Microarray data are available at GEO under accession number GSE84305.

Data analysis

MultiExperiment Viewer v4.9 software was used to generate lists of genes differentially expressed between WT and HDAC1/2 mutant kidneys, using *P*<0.05 and a minimum 1.5-fold change in gene expression. Genes were classified according to their function using IPA software and BiNGO classification systems as previously described (Chen et al., 2011, 2015). Additional analysis of the microarray data was accomplished using IPA software.

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Competing interests

The authors declare no competing or financial interests.

Author contributions

Conceptualization: H.L., S.S.E.-D.; Methodology: S.C., Y.L., C.-H.C., J.L., Z.S.; Validation: Y.L.; Formal analysis: H.L.; Investigation: H.L., S.C., X.Y., C.-H.C., J.L., Z.S.; Resources: S.S.E.-D.; Data curation: H.L., S.C., X.Y.; Writing - original draft: H.L., S.S.E.-D.; Writing - review & editing: S.C., Z.S., S.S.E.-D.; Supervision: S.S.E.-D.; Project administration: H.L., S.S.E.-D.; Funding acquisition: H.L., S.S.E.-D.

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Data availability

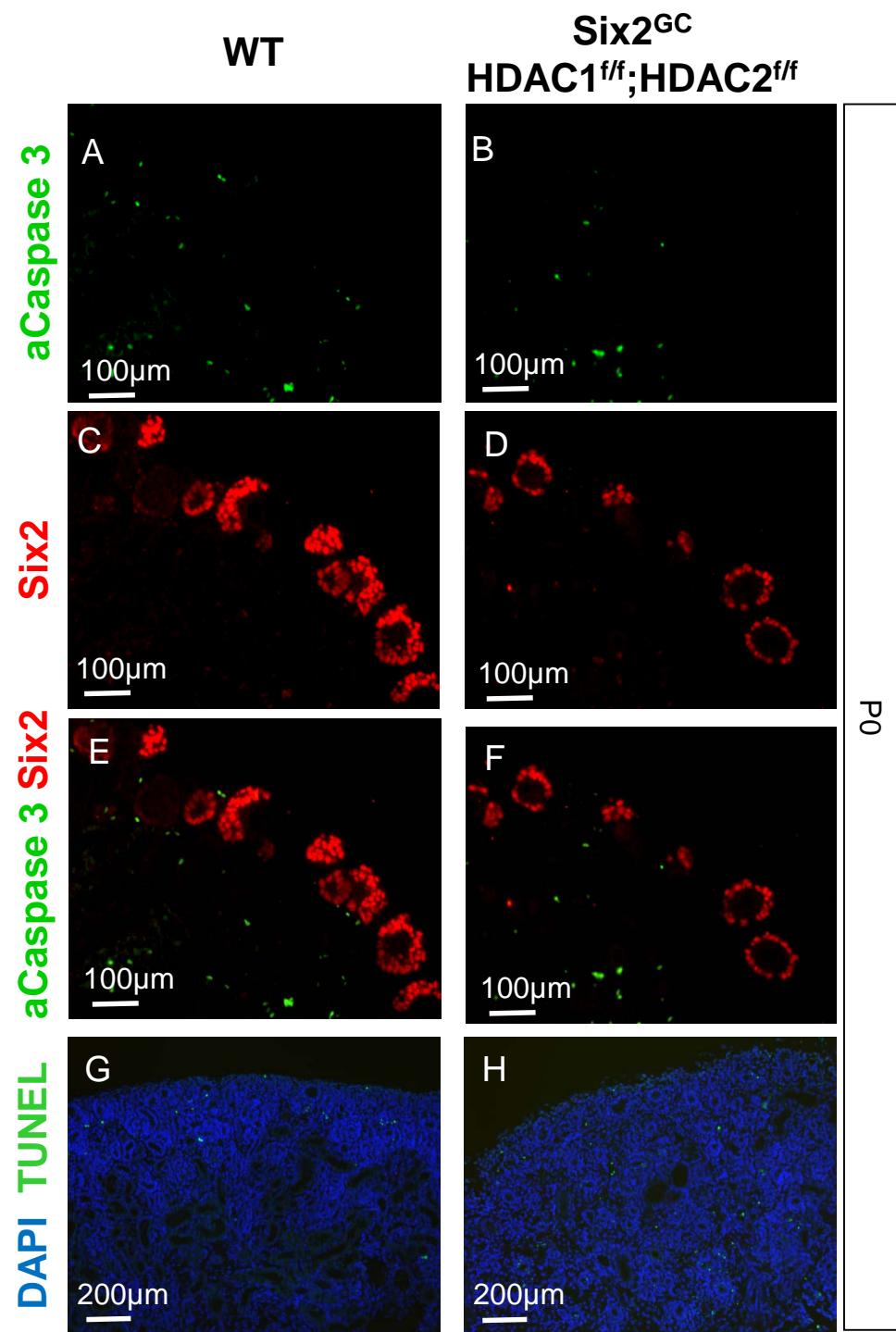
Microarray analysis data are available at GEO under accession number GSE84305.

Supplementary information

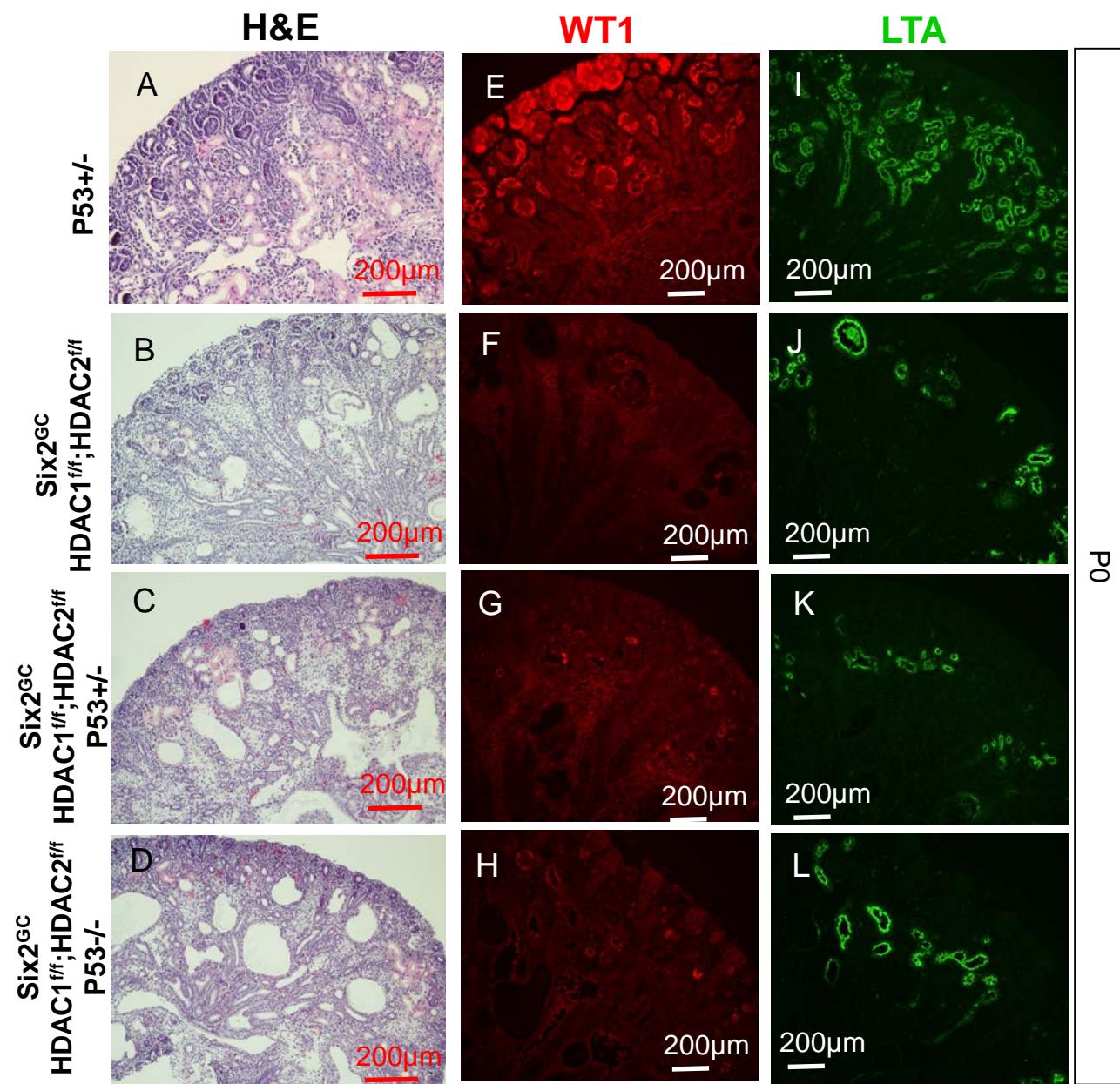
Supplementary information available online at
<http://dev.biologists.org/lookup/doi/10.1242/dev.153619.supplemental>

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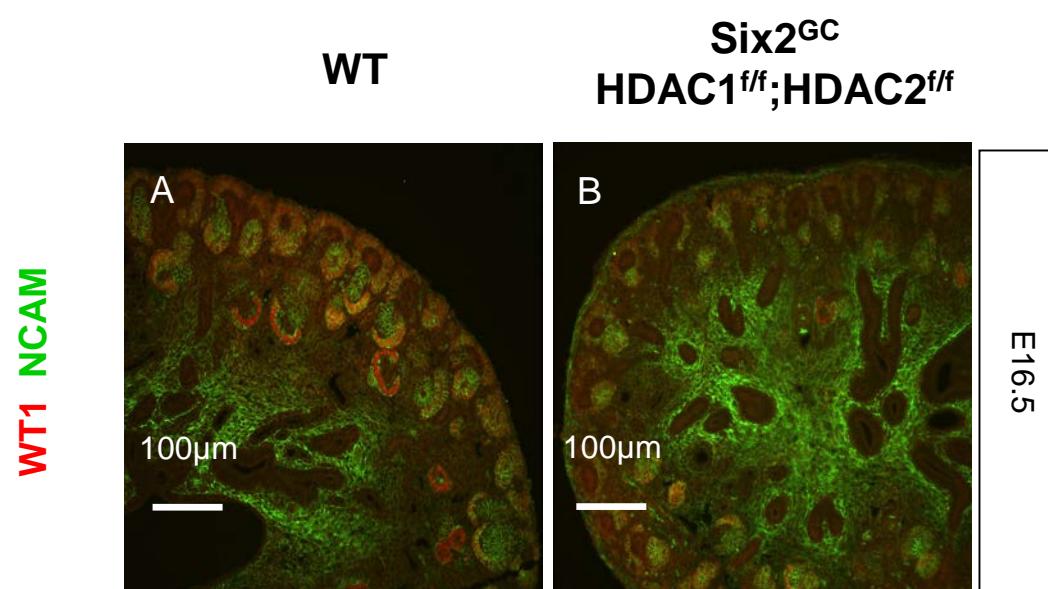
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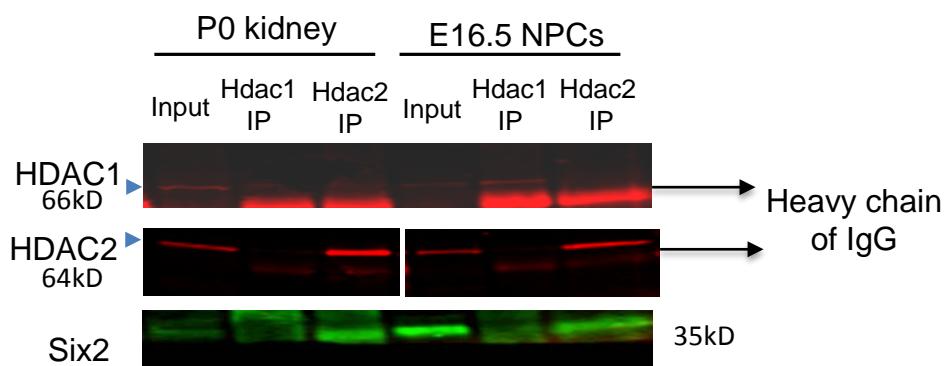
Supplementary Figure 1. NPC-specific deletion of HDAC1 and HDAC2 has no effect on cell apoptosis. Section immunofluorescence for active caspase 3 (A-F) or TUNEL assay (G, H). Although the NPC mass is reduced in size (C-F), there is no evidence of increased apoptosis in the Six2⁺ cap mesenchyme. Original Magnification X20 (A-F), X10 (G,H).



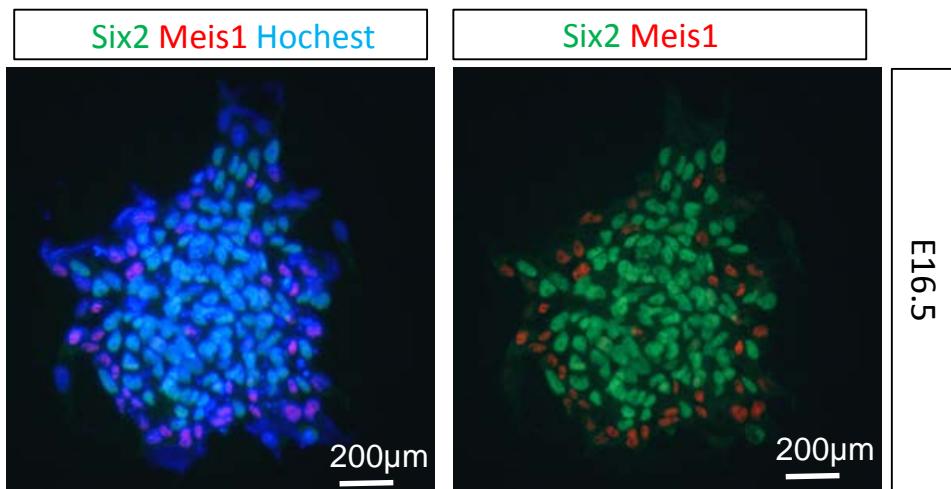
Supplementary Figure 2. p53 gene deletion fails to rescue the renal dysgenesis in mice with NPC-specific deletion of HDAC1/2. H&E staining (A-D) and immunofluorescence for WT1 (marker of CM and glomeruli, and LTA, a marker of differentiating proximal tubules. (B, F, J) NPC-specific deletion of HDAC1/2 causes loss of WT1 and proximal tubules. (C, D, G, H, K, L) Deletion of one or two p53 alleles fails to rescue nephrogenesis or cyst formation. Original Magnification X10



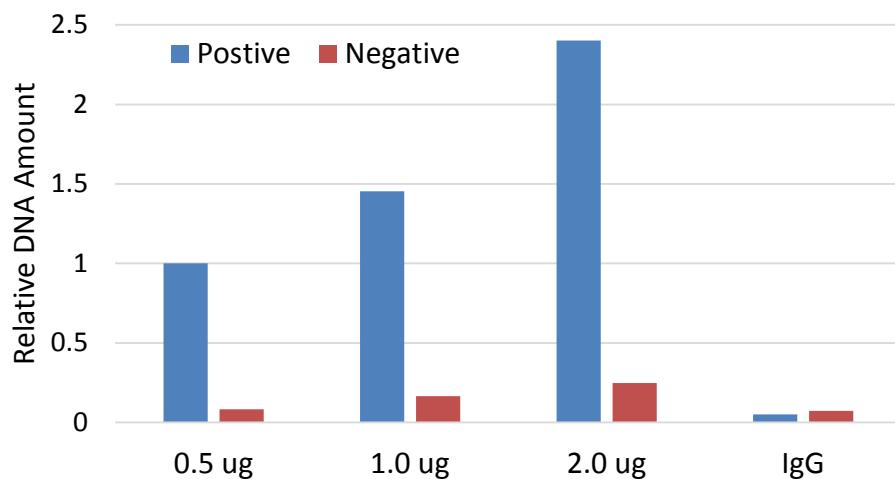
Supplementary Figure 3. NPC-specific deletion of HDAC1 and HDAC2 reduces the expression of WT1 in the cap mesenchyme. NCAM: neural cell adhesion molecule.



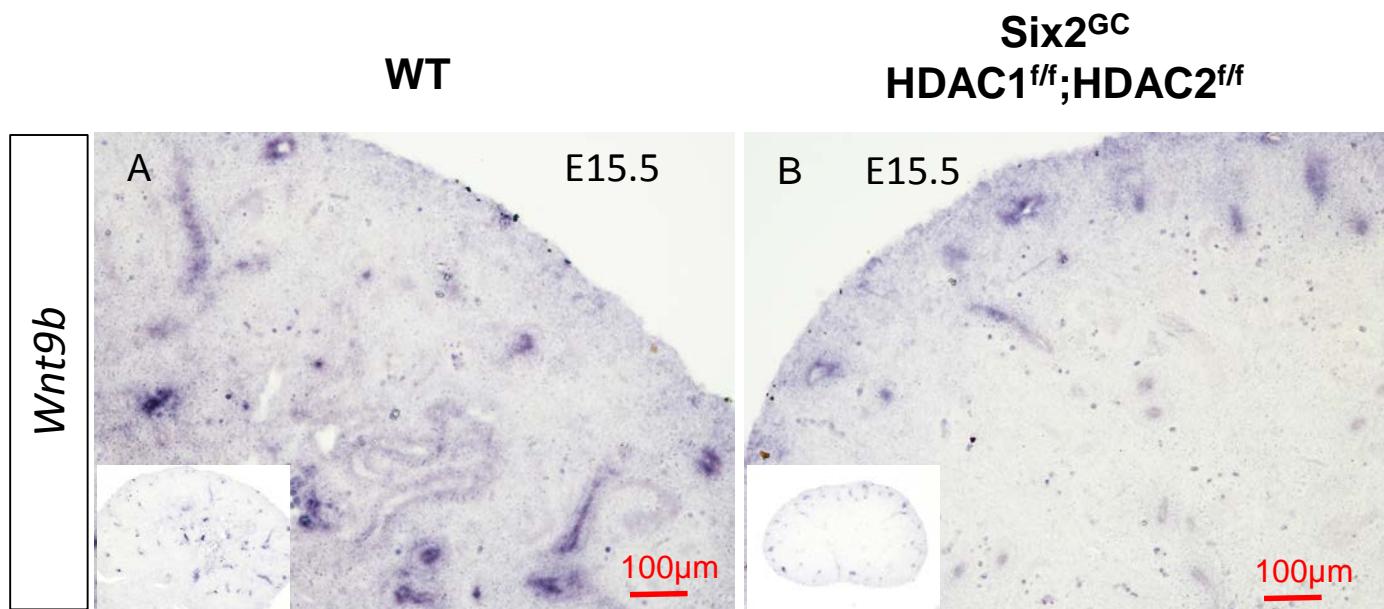
Supplementary Fig 4. Endogenous interaction between Six2 with HDAC1 and HDAC2 was detected in P0 kidneys and E16.5 NPCs



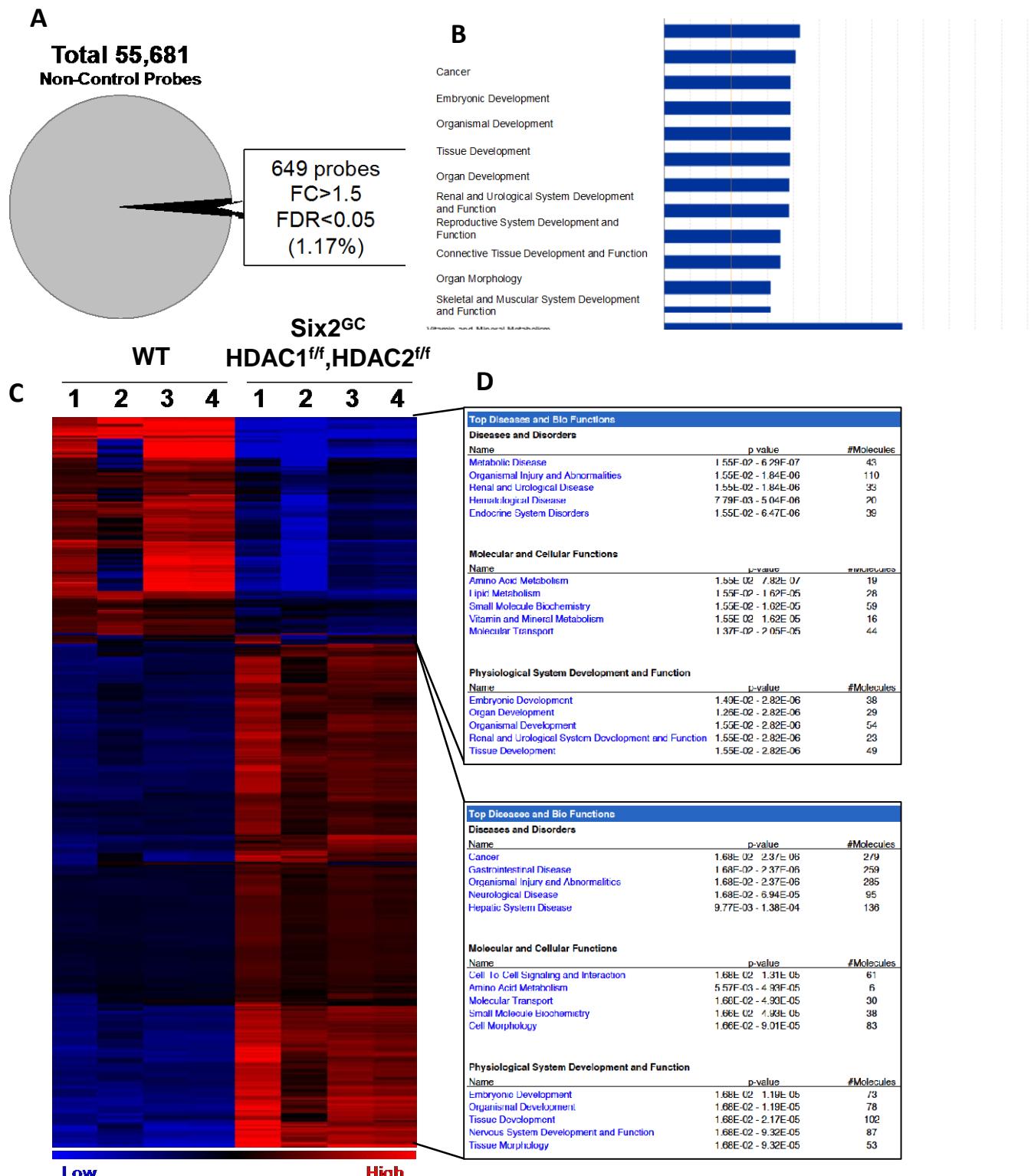
Supplementary Fig 5 Isolated Six2+/Cited1+ NPCs from E16.5 kidneys by magnetic activated cell sorting. The isolated NPCs are highly enriched with Six2 (90%) with minor contamination with stromal cells (Meis1).



Supplementary Fig 6 Validation of HDAC1 ChIP by qPCR. ChIP assays were performed on 3.75 millions cells per IP (immunoprecipitation) using different amount of Hdac1 antibody (0.5 µg, 1.0 µg, and 2.0 µg). An IP with a control isotype (IgG) was also performed in parallel (1 µg/IP). After the IP, the ChIP DNA was analyzed by qPCR to evaluate the specificity of the reaction. Mouse Positive Control Primer Set Actb-2 (Active Motif 71017) was used to amplify HDAC1-bound DNA as positive control and mouse Negative control Primer Set 1 (Active Motif 71011) was used as a negative control region.



Supplementary Figure 7. Ureteric bud *Wnt9b* expression is not affected by NPC-specific deletion of HDAC1/2. Section *in situ* hybridization at P0. In wild-type kidneys (A), *Wnt9b* expression is observed in the UB trunks. This spatial pattern and the intensity of staining are unaltered by loss of HDAC1/2 in NPC (B). Original magnification X10.



Supplementary Figure 8. Transcriptome profiling of total kidney RNA from E15.5 wild-type and Six2^{GC};HDAC1^{f/f},HDAC2^{f/f} kidneys. (A) About 1% of the total transcriptome is altered in the NPC-specific HDAC1/2 mutant kidneys. (B) Top 10 biological processes affected as identified by Ingenuity Pathway Analysis. (C) Heatmap analysis of the differentially expressed. (D) Top diseases, molecular and cellular functions and physiological functions either up-regulated (red) and down-regulated (blue) in wild-type vs. HDAC1/2 mutant kidneys (N=4 separate experiments per group).

Table S1. A complete list of genes for each category and pathway

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Symbol	Fold Change	Synonym(s)
1700047I17Rik2/Far	1.663	1700047I17Rik, 1700047I17Rik1, 1700047I17Rik2, C14orf24, D730001C10Rik, Fam177a, Faf
1700110I01Rik	1.693	1700016F01Rik, Gm2938, RIKEN cDNA 1700110I01 gene, RP23-388I12.4
2310002F09Rik	1.640	RIKEN cDNA 2310002F09 gene
2310015B20Rik	-2.642	RIKEN cDNA 2310015B20 gene
3830612M24	2.094	uncharacterized protein 3830612M24
4732423E21Rik	1.632	AL024288, RIKEN cDNA 4732423E21 gene
4930412O13Rik	1.594	ENSMUSG0000075535, Gm10853, RIKEN cDNA 4930412O13 gene
4930432E11Rik/493.	-2.136	4930432E11Rik, 4932431P20Rik, LOC100504864, RIKEN cDNA 4930432E11 gene, RIKEN c
4933427D06Rik	1.631	proline rich 20E, Prr20e, RIKEN cDNA 4933427D06 gene
6720422M22Rik	1.550	BB143565, RIKEN cDNA 6720422M22 gene
8030425K09Rik	2.257	RIKEN cDNA 8030425K09 gene
9030419F21Rik	1.666	RIKEN cDNA 9030419F21 gene
9030619P08Rik	-2.707	lymphocyte antigen 6 complex pseudogene
9130020K20Rik	1.657	RIKEN cDNA 9130020K20 gene
9530083O12Rik	1.799	RIKEN cDNA 9530083O12 gene
9630010G10Rik	1.907	RIKEN cDNA 9630010G10 gene
A230065H16Rik	-1.651	Gm898, Lbh2, RGD1560608, RIKEN cDNA A230065H16 gene, similar to novel protein
A530006G24Rik	1.652	Gm1003, RIKEN cDNA A530006G24 gene, RP23-18D24.3
ACOT11	1.874	1110020M10Rik, 201309H15Rik, acyl-CoA thioesterase 11, AW060409, BFIT, BFIT1, mKIAA
ACOX3	1.562	acyl-CoA oxidase 3, pristanoyl, acyl-Coenzyme A oxidase 3, pristanoyl, BI685180, EST-s59, F
ACSM2A	-4.857	A-923A4.1, ACSM2, acyl-CoA synthetase medium-chain family member 2, acyl-CoA synthetase
ACSS2	1.517	1110017C11Rik, ACAS, Acas1, ACAS2, ACECS, AceCS1, Acetyl-coa synthetase 1, amp form
ADAMTS17	1.597	a disintegrin-like and metalloproteinase (reprolysin type) with thrombospondin type 1 motif, 17,
ADAMTS7	1.570	a disintegrin-like and metalloproteinase (reprolysin type) with thrombospondin type 1 motif, 7, /
AFP	-3.811	AFPD, Alpha fetoprotein, FETA, Fetoprotein a, HPAFP, a foetoprotein, α-fetoprotein, α-fetoprotein
AKR1C3	-12.402	17-beta HSD5, 17-β HSD5, 20-alpha-hydroxysteroid dehydrogenase, 20-α-hydroxysteroid dehydrogenase
ALDH1A2	1.505	aldehyde dehydrogenase 1 family, member A2, aldehyde dehydrogenase family 1, subfamily 1, member 2
ALDH1A3	1.885	aldehyde dehydrogenase 1 family, member A3, aldehyde dehydrogenase family 1, subfamily 1, member 3
ALDOB	-4.673	ALDB, ALDO2, aldolase B, fructose-bisphosphate, BC016435, Fructose Bisphosphatase Aldc
AMN	-2.875	5033428N14Rik, amnion associated transmembrane protein, amnionless, AV002116, PRO10
ANKH	-1.682	ANK, ANKH inorganic pyrophosphate transport regulator, CCAL2, CMDJ, CPPDD, D15Ert2d2
ANXA13	-4.114	1810034H17Rik, annexin A13, ANX13, AV055219, ISA
APL1	1.583	amyloid beta (A4) precursor-like protein 1, amyloid β (A4) precursor-like protein 1, APLP, Appl
ARHGAP26	1.591	1810044B20Rik, 2610010G17Rik, 4933432P15Rik, A1853435, GRAF, GRAF1, GTPASE RE
ARHGEF15	1.679	ARGE15, D130071N09, D530030K12Rik, E5, Ephexin5, Rho guanine nucleotide exchange
ARL6IP6	1.709	2310057C01Rik, 2610529A11Rik, ADP-ribosylation factor-like 6 interacting protein 6, AIP-6, N
ARRB1	1.542	1200006I17Rik, ARB1, ARR1, Arr2, ARRBeta1, Arrestin 2, Arrestin β 1, arrestin, beta 1, arrestin 2
ART4	-1.632	4432404K01Rik, ADP-ribosyltransferase 4, ADP-ribosyltransferase 4 (Dombrock blood group)
ASB9	-3.489	1700011M07Rik, ankyrin repeat and SOCS box containing 9, LOC100364446, LOC684606, F
ASIC4	2.312	ACCN4, acid-sensing (proton-gated) ion channel family member 4, BNAC4, Spasic
ASPG	1.769	A530050D06Rik, AI429460, asparaginase, asparaginase homolog (S. cerevisiae), C14orf76,
ASS1	-1.500	AA408052, ARGININOSUCCINATE SYNTHASE, argininosuccinate synthase 1, argininosuccinate synthetase 1
ATP1B1	-2.041	ATP1B, Atpb, ATPase, Na+/K+ transporting, beta 1 polypeptide, ATPase, Na+/K+ transporter
ATP6V0E2	-1.561	0610006O14Rik, ATP6V0E2L, ATPase, H+ transporting V0 subunit e2, ATPase, H+ transporter
ATXN7	1.714	A430107N12Rik, ADCALL, A1627028, ATAXIN-7, OPCA3, RGD1562692, SCA7
AW011956	1.544	expressed sequence AW011956, W51672
AW549542	1.773	expressed sequence AW549542
BACH2	1.610	BTB and CNC homology 1, basic leucine zipper transcription factor 2, BTB and CNC homolog 2
BDH1	1.583	2310032J20Rik, 3-HYDROXYBUTYRATE DEHYDROGENASE, 3-hydroxybutyrate dehydrogenase
BEND4	1.677	BEN domain containing 4, CCDC4, D330027G24Rik, EG666938, LOC100365335, LOC68724
BPIFC	1.726	4732454E24, BPI fold containing family C, BPIL2, RP1-149A16.10-011
BRINP1	1.523	bone morphogenetic protein/retinoic acid inducible neural-specific 1, bone morphogenic protein 1
BSND	-3.010	BART, Barter syndrome, infantile, with sensorineural deafness (Barttin), BARTTIN, barttin CL
BTN1A1	1.702	BOS 21855, BT, BTN, BTN1, Butyrophilin, subfamily 1, member a1, RP23-16H24.3
C10orf35	-1.535	2010107G23Rik, AA545165, chromosome 10 open reading frame 35, hypothetical protein LO
C12orf73	-1.687	1190007I07Rik, chromosome 12 open reading frame 73, hypothetical protein LOC691921, LC
C1orf54	1.584	BC028528, cDNA sequence BC028528, chromosome 1 open reading frame 54, L259, RP4-7
C2	-1.806	ARMID14, C3/c5 convertase, CFB isoform 1, CO2, complement component 2, complement component 2
C230096K16Rik	1.547	RIKEN cDNA C230096K16 gene
C5AR2	1.987	C5L2, complement component 5a receptor 2, E030029A11Rik, GPF77, GPR77
C9orf16	1.690	1110008P14Rik, C79326, chromosome 9 open reading frame 16, EST00098, LOC100365430
CA4	-2.337	AW456718, CAIV, CAR4, carbonic anhydrase 4, Carbonic anhydrase IV, RP17, RP23-167D6
CALB1	1.662	Brain-2, Cabp-d28k, Cabp28K, Cad28k, CALB, calbindin 1, calbindin 1, 28kDa, CALBINDIN 1
CALML4	-1.519	2010002G05Rik, Calmodulin related, Calmodulin-like 4, LOC686783, MGC4809, NY-BR-20
CALN1	1.558	9630012C17Rik, CABP8, calneuron 1, MNCB-0849
CAMKK1	1.503	4732414G09Rik, AI846603, calcium/calmodulin-dependent protein kinase kinase 1, alpha, calcium/calmodulin-dependent protein kinase kinase 1, alpha
CAPN6	-1.888	calpain 6, CalpM, CANPX, CAPNX, DJ914P14.1, RP23-462G16.1
CCDC138	1.690	6230424H07Rik, BC042726, coiled-coil domain containing 138, FLJ32745, RGD1566050
CDC42EP5	1.506	1700027J19Rik, 2010007O02Rik, Borg3, C85526, CDC42 effector protein (Rho GTPase bind
CDH6	-1.772	CAD6, cadherin 6, type 2, K-cadherin, cadherin 6, type 2, K-cadherin (fetal kidney), cadherin 6

CDK5R1	1.515 CDK5P35, CDK5R, CDK5R1 p35, CDK5R1/p35, cyclin-dependent kinase 5, regulatory subunit
CDKL1	-1.771 4933411O17Rik, cyclin-dependent kinase-like 1 (CDC2-related kinase), KKIALRE, P42
CELF4	1.950 A230070D14Rik, Brul4, BRUNOL-4, C130060B05Rik, CUGBP, Elav-like family member 4, L1f
CEP170B	1.735 AI466840, AW555464, centrosomal protein 170B, CEP170R, FAM68C, KIAA0284, mKIAA028
CGREF1	-1.509 1110004G24Rik, AW045201, cell growth regulator with EF-hand domain 1, CGR11
CHMP4B	1.536 2010012F05Rik, C20orf178, C76846, charged multivesicular body protein 4B, CHMP4A, Chr
CHPF2	1.728 2010209012Rik, AW060945, chondroitin polymerizing factor 2, CHONDROITIN SULFATE GL
CHST8	-1.514 1500011J21Rik, AI426009, carbohydrate (N-acetylgalactosamine 4-O) sulfotransferase 8, Gal
CIDEA	-10.261 AW212747, cell death-inducing DFFA-like effector a, cell death-inducing DNA fragmentation f, CIDEA
CIDEB	-1.978 1110030C18Rik, AI790179, cell death-inducing DFFA-like effector b, cell death-inducing DNA
CITED1	-6.359 AI316840, AU019144, Cbp/p300-interacting transactivator with Glu/Asp-rich carboxy-terminal
CLCNKA	-3.543 C75963, chloride channel Kb, chloride channel, voltage-sensitive Ka, chloride channel, voltage
CLEC18B	-1.842 C-type lectin domain family 18, member A, C-type lectin domain family 18, member B, Clec18
CLIC6	-1.718 5730466J16Rik, AL022908, AW045520, chloride intracellular channel 6, CLIC1L, CLIC6B
COL1A1	1.551 alpha 1 (I) PROCOLLAGEN, alpha 1(I) COLLAGEN, Alpha1 type i collagen, Alpha1 Type I Pro
COL26A1	1.567 9430032K24Rik, BC002218, Col26a, Collagen Type26, collagen, type XXVI, alpha 1, collagen
COL2A1	2.047 ANFH, AOM, CG2A1A, COL11A3, COL2, Col2a, Collagen type II, Collagen type ii α, Collager
COL4A6	1.890 BB116301, collagen, type IV, alpha 6, collagen, type IV, α 6, CXDELq22.3, DELXq22.3, DFN4
COL5A1	1.504 AI413331, Collagen type v alpha1, collagen, type V, alpha 1, collagen, type V, α 1, RP11-263F
COL7A1	1.593 AW209154, Collagen type 7 alpha chain, Collagen type 7 α chain, collagen, type VII, alpha 1,
COLQ	2.184 A130034K24Rik, collagen-like tail subunit (single strand of homotrimer) of asymmetric acetyl
COX6B2	1.633 1700067P11Rik, BC048670, COXIVB2, CT59, cytochrome c oxidase subunit VIb polypeptide
CPA1	2.073 0910001L12Rik, Carboxypeptidase A, Carboxypeptidase a1, carboxypeptidase A1 (pancreatic)
CPA2	1.593 carboxypeptidase A2 (pancreatic), carboxypeptidase A2, pancreatic
CPB2	-3.408 1110032P04Rik, 4930405E17Rik, AI255929, C5A-INACTIVATING FACTOR, carboxypeptidas
CPN1	-2.597 0610011F20Rik, CARBOXYYPEPTIDASE N, carboxypeptidase N, polypeptide 1, CPN, LOC11
CRABP2	1.898 AI893628, cellular retinoic acid binding protein 2, cellular retinoic acid binding protein II, CRAF
CRB2	-1.919 5930402A21, BC043114, crumbs family member 2, crumbs homolog 2 (Drosophila), RGD130
CREB5	1.712 cAMP responsive element binding protein 5, CRE-BPA, D430026C09Rik, LOC100910345, RC
CRMP1	1.567 collapsin response mediator protein 1, DPYSL1, DRP-1, Tuc-1a, ULIP-3
CSPG5	1.530 Caleb, chondroitin sulfate proteoglycan 5, chondroitin sulfate proteoglycan 5 (neuroglycan C),
CUBN	-2.534 AA408369, AL022750, cubilin (intrinsic factor-cobalamin receptor), CUBULIN, D2Wsu88e, GF
CYB561	1.548 CYB561A1, Cytochrome b-561, FRRS2, RP23-186E14.2
CYB5R4	-1.530 2810034J18Rik, B5+B5R, b5/b5r, b5b5r, C79736, cb5/cb5R, Cb5cb5r, cytochrome b5 reduct
CYP26B1	2.050 CP26, CYP26A2, cytochrome P450, family 26, subfamily B, polypeptide 1, P450 26A2, P450f
Cyp2d26	-4.223 1300006E06Rik, Cyp2d2, cytochrome P450, family 2, subfamily d, polypeptide 2, cytochrome
CYP2U1	1.707 8430436A10Rik, cytochrome P450, family 2, subfamily U, polypeptide 1, P450TEC, SPG49, :
CYP4A11	-2.563 AI647584, CP4Y, Cyp4a, Cyp4a1, Cyp4a10, CYP4A2, Cyp4a22, Cyp4a31, Cyp4a32, CYP4A
D230019N24Rik	1.563 RIKEN cDNA D230019N24 gene
D230040J21Rik	1.727 RIKEN cDNA D230040J21 gene
D430019H16Rik	1.527 AI852661, LOC100909954, RIKEN cDNA D430019H16 gene, uncharacterized LOC10090995
D8Ert158e	1.960 DNA segment, Chr 8, ERATO Doi 158, expressed
DAO	-2.668 AI987963, D-Amino Acid Oxidase, DAO, DAMOX, DAO1, DEAMINOACID OXIDASE, OXDA
DAPL1	-2.311 2310032F03Rik, death associated protein-like 1, EEDA, RGD1309610, RP23-151F21.4
DCAF12L2	1.652 A130007F10Rik, DDB1 and CUL4 associated factor 12-like 2, RGD1560768, RP11-13E5.1, F
DCX	-1.584 DBCN, Dbct, DC, doublecortin, Lissencephalin-X, LISX, rCG 23159, RP23-462G16.2, RP5-9-
DCXR	1.601 0610038K04Rik, 1810027P18Rik, DCR, dicarbonyl L-xylulose reductase, dicarbonyl/L-xylulos
DDC	1.802 AAAD, AACD, ADC, aromatic L-amino acid decarboxylase, Dihydroxyphenylalanine decarbox
DENND4A	1.696 AI115600, AI851943, DENN/MADD domain containing 4A, F730015K02Rik, IRLB, mCG 1454
DERA	1.847 2-deoxyribose-5-phosphate aldolase homolog (C. elegans), 2010002D22Rik, 2500002K03Ri
DKK3	1.649 AW061014, C87148, DICKKOPF HOMOLOG 3, dickkopf homolog 3 (Xenopus laevis), dickko
DLGAP3	1.687 BC058433, DAP-3, discs, large (Drosophila) homolog-associated protein 3, PRPL8, RP23-81
DLK1	1.607 AW742678, delta, Delta-like 1 homolog, delta-like 1 homolog (Drosophila), Delta1, DLK, DLK1,
DLL1	-2.180 Delta, delta-like 1 (Drosophila), DELTA1, DL-1, UNQ146/PRO172
DMTN	1.632 AI325486, DEMATIN, dematin actin binding protein, DMT, EPB4.9, Epb4.9 predicted, EPB49,
DNAJA4	1.749 1110021L12Rik, AV358213, Dj4, Dnaj (Hsp40) homolog, subfamily A, member 4, Hsj4, mmDj
DNAJC19	1.570 1810055D05Rik, AA959924, Dnaj (Hsp40) homolog, subfamily C, member 19, Dnaj (Hsp40)
DNAJC22	-2.144 2810451A06Rik, AI506245, Dnaj (Hsp40) homolog, subfamily C, member 22, RGD1311098,
DOCK5	-1.635 1110060D06Rik, AI666732, AI956923, BC016533, dedicator of cytokinesis 5, E130320D18, L
DPF1	1.524 BAF45b, D4, zinc and double PHD fingers family 1, NEUD4, neuro-d4
DPP4	-1.975 ADABP, ADCP2, Adenosine Deaminase Binding Protein, CD26, DDP4, Dipeptidyl Peptidase I
DPYSL5	1.677 CRAM, CRMP-5, dihydropyrimidinase-like 5, dihydropyrimidinase-related protein 5-like, DRP-
Duxbl1 (includes oth	1.807 1110051B16Rik, doubl homeobox B-like 2, double homeobox B-like 1, double homeobox B-like
DYNC1I1	-2.302 DH IC-1, DIC, DNCI1, DNCI1C1, dynein cytoplasmic 1 intermediate chain 1, dynein, cytoplasm
Eda	1.554 ectodysplasin-A, Ed1, EDA1, HED, RGD1563178, RP23-281K21.1, Ta, tabby, XLHED
EGFR	1.658 9030024J15Rik, AI552599, C-ERBB, EGF receptor, EGF-TK, EGFR VIII, EGFR1, epidermal
EHMT1	1.560 9230102N17Rik, ba188C12.1, D330003E03, euchromatin histone methyltransferase 1, euch
Eif2s3y	1.647 Eif-2gy, eukaryotic translation initiation factor 2, subunit 3, structural gene Y-linked, Spy, Tf
Eif5	1.513 E74-like factor 5, ESE-2, ESE-5, ESE-5., RP23-445A5.2
EMILIN2	1.645 elastin microfibril interfacer 2, FOAP-10
ENDOV	1.570 A730011L01Rik, endonuclease V, FLJ35220, RP23-25M3.5
ENO2	1.673 AI837106, D6Ert375e, enolase 2 (gamma, neuronal), enolase 2 (γ, neuronal), enolase 2, ga

ENPEP	-1.710 6030431M22Rik, AMINOPEPTIDASE A, APA, Bp-1/6C3, CD249, Gamma-Glutamyl Peptidase
EPB41L4B	1.890 6430543G08Rik, AA589614, AU021054, BB007528, CG1, D4Ert346e, EHM2, Epb4.11b, e1
EPHA5	1.670 AI854630, AW125296, bsk, CEK7, EHK-1, EK7, ELS1, Els1., EPH receptor A5, HEK7, Rek7,
EPHB3	1.665 AW456895, Cek10, Efnb3r, EPH receptor B3, ETK2, HEK2, MDK5, Sek4, TYRO6
EPHX1	1.900 AI195553, Ehm, Eph-1, EPHX, EPOX, Epoxide Hydrolase, epoxide hydrolase 1, microsomal,
EPS8	-2.023 AW261790, DFNB102, epidermal growth factor receptor pathway substrate 8
ESPN	-1.651 DFNB36, Espin, ESPN1, Je, LP2654, RP23-284C20.3
ESRRG	-1.897 Err γ , ERR3, Errg, ERRG2, ERRgamma, estrogen-related receptor gamma, estrogen-related
EXOC6	-1.592 4833405E05Rik, AW143330, C430002C19, EXOC6A, exocyst complex component 6, hbd, m
EXOSC9	1.665 exosome component 9, p5, p6, PM/SCL-75, PMSCL1, Polymyositis/scleroderma autoantigen
EYA1	1.709 BOP, BOR, BOS1, EYA transcriptional coactivator and phosphatase 1, eyes absent 1 homolog
FABP3	-1.665 BOS 2157, FABP, FABP11, Fabph-1, Fabph-4, fatty acid binding protein 3, muscle and heart,
FAM160B2	1.637 family with sequence similarity 160, member B2, FLJ11125, FP13191, G430067P06Rik, RA11
FAM219A	1.606 2310028H24Rik, ba573M23.5, C9orf25, family with sequence similarity 219, member A, LOC
FBN1	1.854 ACMICD, AI536462, B430209H23, BOS 10884, ECTOL1, FBN, Fib-1, Fibrillin-1, fibrillin 1, FN
FBP1	-1.983 F1.6 biphasphatase, FBP, Fbp-2, FBP3, FBPAse, Fdp, Fructose biphasphatase, fructose bisph
FBXL16	1.812 BC042620, C16ORF22, c380A1.1, F-box and leucine-rich repeat protein 16, Fbl16, MGC339;
FBXL7	1.600 AL023057, D230018M15RIK, F-box and leucine-rich repeat protein 7, FBL6, FBL7
FCHO1	1.552 3322402E17RIK, FCH domain only 1, N28152
FCHSD1	1.671 A030002D08Rik, FCH and double SH3 domains 1, NWK2, UNQ737/PRO1431
FGB	-3.996 2510049G14Rik, Ab1-181, Ab1-216, Ac1-581, Beta fibrinogen, Fg beta chain, Fg β chain, Fib
FGF1	-2.318 ACIDIC FGF, AFGF, BOS 8269, Dffrx, ECGF, ECGF-beta, ECGF- β , ECGFA, ECGFB, Fam, F
FIG4	1.507 A53008917Rik, AI326867, ALS11, BTOP, CMT4J, dj24914.1, FIG4 homolog (S. cerevisiae), I
FLRT1	2.664 AW742165, D630040I23RIK, fibronectin leucine rich transmembrane protein 1, RGD1565152
FLRT3	1.516 5530600M07RIK, C43004710RIK, fibronectin leucine rich transmembrane protein 3, HH21, n
FN1	1.632 BOS 2065, cFn, CIG, E330027I09, ED-B, FIBNEC, FIBRONECTIN 1, Fibronectin i, Fibronect
FNBP1	1.582 1110057E06Rik, B221001H06RIK, FBP1, FBP17, Formin binding, formin binding protein 1, R
FOLR1	-1.562 FBP, FBP1, FOLATE binding, folate receptor 1 (adult), FOLATE receptor alpha, FOLATE rece
FOXD1	1.540 AI385632, BF-2, FKH8, Forkhead box d1, FREAC-4, Hfh10, Hfhbf2, LOC684320
FOXI1	-1.949 5830401E05Rik, FKH10, FKH10, forkhead box I1, FREAC-6, HFH-3, RP23-32J15.1
FOXO6	1.615 forkhead box O6, LOC100131908, RP23-421C7.1
FOXP4	1.546 1200010K03Rik, 2310007G05Rik, FKHLA, forkhead box P4, hFKHLA, mFKHLA, RP11-328M
FREM1	1.777 BC037594, BNAR, C9orf143, C9orf145, C9orf154, crf11, D430009N09, D630008K06, eye\timesmembrane
FRMPD2	1.712 ENSMUSG00000071536, FERM and PDZ domain containing 2, Gm1582, Gm626, PDZD5C,
FRZB	1.889 BOS 1606, FRE, frezzled, FRITZ, frizzled-related protein, Frp, FRP-3, FRZB-1, FRZB-PEN, F
FST	2.337 AL033346, D2Mgi51, FOL1, follistatin, Follistatin 288, FS, fs315, Fst-288, RATFOL1
Fxyd2	-2.433 Atp1g1, FXYD domain-containing ion transport regulator 2, Na ⁺ K ⁺ Atpase γ Subunit
FZD10	1.721 CD350, frizzled class receptor 10, frizzled homolog 10 (Drosophila), FZ-10, Fzd10-ps1, FzE7,
GABRA3	1.514 GABA A receptor alpha-3, Gaba A receptor subunit α 3, GABA A receptor α -3, gamma-aminot
GAL	1.786 GAL-GMAP, galanin, galanin/GMAP prepropeptide, GALN, GLNN, GMAP
GARNL3	1.552 AW120551, bA356B19.1, GTPase activating RANGAP domain-like 3, GTPase activating Rap
GATSL2	1.626 7530428J21Rik, AW742413, Gats, GATS protein-like 2, GATSL1
GC	-5.400 DBP, DBP/GC, DBP02, GRD3, Group-specific Component, group-specific component (vitamin
GCNT1	-5.315 5630400D21Rik, B130048E03, beta-1,6-N-ACETYLGLUCOSAMINYLTRANSFERASE, C2 G
GFRA2	1.525 GDNF family receptor alpha 2, GDNF family receptor alpha 2, GDNF receptor alpha2, GDNFALPI
GFRA3	1.569 GDNF family receptor alpha 3, GDNF family receptor alpha 3, GDNFR3, GFRalpha3, glial cell line
GGT1	-2.234 Alpha1-GGT, CD224, D22S672, D22S732, dwg, Gamma-glutamyl transpeptidase, gamma-gli
GIPC2	-1.692 2200002N01Rik, AU021850, GIPC PDZ domain containing family, member 2, SEMCAP-2
GLA	1.633 agalsidase alfa, agalsidase beta, agalsidase β , Ags, alpha D-GALACTOSIDASE A, Alpha Gal
Gm10576	1.666 ENSMUSG00000073788, predicted gene 10576
Gm12258	1.551 LOC100502966, OTTMUSG00000005767, predicted gene 12258, RP23-419P16.7
Gm21596/Hmgb1	-2.005 amphoterin, DEF, Gm21596, high mobility group box 1, high-mobility group (nonhistone chrom
Gm266	-2.035 DIRAS family, GTP-binding RAS-like 3, Diras3, predicted gene 266, RGD1565168
Gm5097/Gm8978	1.641 EG329055, EG668106, Gm5097, Gm8978, predicted gene 5097, predicted gene 8978, RGD-
Gm5176	-2.006 EG382421, high mobility group box 2 pseudogene
Gm6115	-2.040 EG619937, predicted gene 6115, RGD1563668, similar to High mobility group protein 1 (HMC
Gm6213	1.653 EG621335, predicted gene 6213
Gm6994	1.659 EG629678, predicted gene 6994
Gm9780 (includes o)	1.857 ENSMUSG00000043248, ENSMUSG00000072674, Gm10393, MGC41689, Plac9, Plac9a, F
Gm9900	1.722 ENSMUSG00000053218, predicted gene 9900
CNB5	1.638 ftr, G protein beta 5, G protein β 5, GB5, Gbeta5, GBS, Guan nuc b5, guanine nucleotide bind
GNG7	1.551 AI840417, FLJ00058, G protein binding protein, gamma7, G protein gamma 7, G protein γ 7,
GPD1	-1.991 AI747587, Gdc-1, Glycerol-3-phosphate dehydrogenase, glycerol-3-phosphate dehydrogenase
GPRASP1	1.522 2210415K24Rik, 3110031014Rik, C87852, G protein-coupled receptor associated sorting pro
GRIA4	1.780 GluA4, GLUR4, GLUR4C, Gluralpha4, GLURD, glutamate receptor, ionotropic, AMPA 4, gluta
GSTA5	-3.232 ENSMUSG00000074179, glutathione S-transferase alpha 5, glutathione S-transferase α 5, gl
GSTM5	1.703 glutathione S-transferase mu 1, glutathione S-transferase mu 5, glutathione S-transferase, mu
Gstm6	1.707 glutathione S-transferase, mu 6, RGD1563391
GULP1	1.702 3110030A04Rik, 5730529O06Rik, CED-6, GULP, GULP, engulfment adaptor PTB domain cor
GXYLT2	1.505 GLT8D4, glucoside xylosyltransferase 2, Gm152, LOC100365223, LOC686935
H2-K2/H2-Q9	1.895 EG630499, Gm7035, H-2K1, H-2K1K, H2-K2, H2-Q9, histocompatibility 2, K region locus 2, h
H2-Q5	1.589 histocompatibility 2, Q region locus 5, LOC100044874, Qa, Qa-5, Qat-5

HAGH	1.605 BC019817, GLO2, Glutathione Hydrolase, GLX2, GLXII, Glyoxalase II, HAGH1, Hydroxyacyl
HAP1	1.621 HAP2, hHLP1, HIP5, HLP, huntingtin-associated protein 1, neuroan 1, RP23-392I3.11-001
HAS2	-1.645 hyaluronan synthase 2, Hyaluronan synthase homolog
HDC	-3.550 AW108189, Hdc-a, Hdc-c, Hdc-e, Hdc-s, histidine decarboxylase, RP23-251E2.2
HDDC3	-1.956 (ppGpp)ase, 1110033O09Rik, C86475, HD domain containing 3, MESH1, RGD1311839
HECW1	1.656 9330116H24Rik, AV273951, BUL1, E130207I19Rik, HECT, C2 and WW domain containing E:
HEMGN	1.697 4921524M03Rik, Al317176, CT155, EDAG, EDAG-1, EDAG2, haemogen, hemogen, Hgn, ml
HES5	-2.241 bHLHb38, hairy and enhancer of split 5 (<i>Drosophila</i>), hes family bHLH transcription factor 5, F
HEY1	-1.678 Al316788, Al414254, BHLHb31, CHF2, hairy/enhancer-of-split related with YRPW motif 1, HE
HHIP	1.764 Hedgehog-interacting protein, Hhip, HIP, HIP1, LOC100366089, RGD1564108, UNQ5825/P
HLA-A	1.923 0610037M15Rik, A-28, Aw-24, Aw-33, Aw-34, Aw-66, Aw-68, Aw-69, Aw-74, Aw-80, BE13676:
HLA-E	1.599 37b, 37c, BM1, C920025E04Rik, DAMA-277I14.1, EA1.2, EA2.1, H2-Qa1, H2-T11, H2-T23; t
HMP19	1.631 HMP19 protein, neuron specific gene family member 2, Neurospecific gene family membrane
HNF1A	-1.937 Al323641, HNF1, HNF1 homeobox A, HNF1-alpha, HNF1- α , HNF1alpha (MODY3), HNF1 α (f
HNF4A	-2.850 FLJ39654, FRTS4, hepatic nuclear factor 4, alpha, hepatic nuclear factor 4, α , hepatocyte nu
HOXC4	2.168 cp19, homeo box C4, Hox-3.5, HOX3, HOXE, Hox3 β , Hs.567289
HOXD12	1.819 homeo box D12, Hox-4.7, Hox-5.6, HOX4H, RP23-313J15.7
HOXD4	1.939 6030436D05RIK, HHO.C13, homeo box D4, Hox-4.2, HOX-5.1, HOX4, HOX4B
HSD17B14	-1.658 0610039E24RIK, DHRS10, hydroxysteroid (17-beta) dehydrogenase 14, hydroxysteroid (17- β
Hsd3b4 (includes ot)	-3.729 3 beta Hsd, 3 Beta hydroxysteroid dehydrogenase, 3 beta-hydroxysteroid dehydrogenase typ
I730030J21Rik	1.736 RIKEN cDNA I730030J21 gene
Ifitm7	1.722 4933438K12Rik, interferon induced transmembrane protein 7, Mil4
IGDCC3	2.005 2810401C09RIK, Al851425, HsT18880, immunoglobulin superfamily, DCC subclass, member
IGDCC4	1.920 9330155G14RIK, DDM36, immunoglobulin superfamily, DCC subclass, member 4, NOPE, W
IGFBP1	-2.022 AFBP, BOS 4373, hIGFBP-1, IBP1, IGF-BP25, IGFB, IGFBP-RP1, insulin-like growth factor
IL15RA	1.676 AA690181, CD215, IL-15 Receptor Alpha, IL-15 Receptor α , IL-15R, IL-15Ralpha, IL15R α , in
IL33	1.893 9230117N10Rik, C9orf26, DVS27, IL1F11, interleukin 33, NF-HEV, NFEHEV, RGD1311155, F
IPO9	1.762 0710008K06Rik, Al845704, C78347, Imp9, importin 9, KIAA1192, mKIAA1192, Ranbp9, RP1-
IRX1	-2.346 iroquois homeobox 1, Iroquois related homeobox 1 (<i>Drosophila</i>), IRX-5, IRXA1, LOC501463
ITIH5	2.274 4631408O11RIK, 5430408M01Rik, Al317339, E130106B02, FLJ14641, inter-alpha (globulin)
ITPKA	1.928 inositol 1,4,5-trisphosphate 3-kinase A, inositol-trisphosphate 3-kinase A, IP3-3KA, IP3KA, RF
ITSN1	1.714 AA517634, AA545208, Al316805, Al839402, Al848451, Ehsh1, Ese1, INTERSECTIN, Interse
JADE2	1.536 1200017K05Rik, Al480685, jade family PHD finger 2, KIAA0239, mKIAA0239, PHF15, RP23-
KANK2	1.567 Al504612, ANKRD25, BC010245, DKFZp43N161, KN motif and ankyrin repeat domains 2, N
KAZALD1	-3.362 Al842353, BONO1, FKSG28, FKSG40, IGFBP-rP10, Kazal-type serine peptidase inhibitor do
KCNA4	1.704 HBK4, HK1, HPCN2, HUKII, K+ CHANNEL A, KCCHAN, KCNA4L, KCNA8, KV1.4, Kv1.4 α , Kv
KCND2	1.898 Al839615, AW555701, KV4.2, mKIAA1044, MNCb-7013, potassium voltage-gated channel, S
KCNJ1	-7.396 Kcnj, KIR1.1, potassium inwardly-rectifying channel, subfamily J, member 1, ROMK, ROMK1,
KCP	1.703 AW060220, CRIM-2, Gm793, KCP-1, kielin/chordin-like protein, NET67, RGD1561119
KIAA1467	1.650 8430419L09Rik, mKIAA1467, RGD1306151, RIKEN cDNA 8430419L09 gene, similar to hypc
KIF1A	1.705 ATSV, C2orf20, C630002N23Rik, Gm1626, HSN2C, Kin1a, kinesin family member 1A, Kinesi
KIF21B	1.729 2610511N21Rik, KIAA0449, kinesin family member 21B, mKIAA0449
KIF5C	1.518 CDCBM2, Khc, KIAA0531, Kif5c (predicted), kinesin family member 5C, KINN, NKHC, NKHC
KIFC2	1.755 kinesin family member C2
KLC2	1.546 8030455F02RIK, AW212649, kinesin light chain 2, Klc2 predicted
KRT36	-2.646 HA6, hHa6, HRa-1, K36, Ka31, keratin 36, Keratin complex 1, acidic, gene 5, Krt1-22, Krt1-5,
LARGE	1.547 BPFD#36, CTA-282F2.1, ENR, fg, froggy, Gylt1a, like-glycosyltransferase, Mbp-1, MDC1D, N
LDB2	1.686 Al035351, AW146358, CLIM1, CLP-36, LDB1, Ldb3, LIM domain binding 2
LDLRAD3	1.708 6430500P08, Al194318, LOC100909436, low density lipoprotein receptor class A domain con
LHX1	-1.676 LIM homeobox 1, LIM homeobox protein 1, LIM-1, RP23-381C21.1
LIMK1	1.528 LIM domain kinase 1, LIM-domain containing, protein kinase, LIMK
LOC102635467	1.548 uncharacterized LOC102635467
LOC102638978	1.684 uncharacterized LOC102638978
LOC102641046	1.596 h-2 class I histocompatibility antigen, D-37 alpha chain-like, h-2 class I histocompatibility antic
LOC102641638	-1.907 high mobility group protein B1-like
LPIN2	-1.524 2610511G02Rik, Al481352, AW742896, Lipin 2
LRP11	1.711 1700034J19RIK, 6330533B21, 9830160H19RIK, bA350J20.3, low density lipoprotein recepto
LRP2	-1.780 Al315343, AWS536255, b2b1625.2Clo, D230004K18Rik, DBS, GP330, HEYMANN NEPHRITI:
Lrrc31	1.579 E230002P03Rik, leucine rich repeat containing 31
LRRC4B	1.812 A830007M12, HSM, leucine rich repeat containing 4B, LRIG4, NGL-3
LUC7L2	1.822 4930471C18Rik, AA522013, AU015269, CGI-59, CGI-74, LOC100504012, LUC7-like 2 (S. ce
Ly6a (includes other:	-2.476 AA682074, AA959465, Al789751, Gr-1, I830127L07Rik, LOC100911104, LOC300024, Ly-6.2
LY86	-1.687 dj80N2.1, lymphocyte antigen 86, MD-1, MMD-1, RP1-80N2.1
LZTS1	1.605 F37, FEZ1, leucine zipper, putative tumor suppressor 1, leucine zipper, putative tumour suppr
MADD	1.721 9630059K23Rik, IG20, KIAA0358, MAP-kinase activating death domain, RAB3GEP, RP23-20
MAFB	-1.984 b-maf, Basic domain/leucine zipper transcription factor, kr, Kreisler, KRML, Krml1, Maf1, MCT
MALAT1	1.596 2210401K01RIK, 9430072K23RIK, Al647968, HCN, LINC00047, masCRNA, metastasis asso
MARK4	1.518 2410090P21Rik, C79806, LOC686800, MAP/microtubule affinity-regulating kinase 4, MARK4
MB21D1	1.749 C6orf150, cGAS, E330016A19Rik, h-cGAS, Mab-21 domain containing 1, RP11-398K22.2
MBD1	1.650 CXGC3, methyl-CpG binding domain protein 1, PCM1, RFT
MCAM	1.634 1-gicerin, AV025631, CD146, CD149, melanoma cell adhesion molecule, MELCAM, MUC18,
MCTP2	1.804 Gm489, multiple C2 domains, transmembrane 2, RGD1562967, RP11-4F5.2

MDFI	1.697 I-MF, I-mfa, MyoD family inhibitor, RGD1560271, RP4-696P19.1
ME3	-1.925 1700020C08Rik, B230207H15RIK, malic enzyme 3, NADP(+)-dependent, mitochondrial, NAE
MEDAG	1.574 6330406115Rik, AVWMS3, C13orf33, hAWMS3, mAWMS3, MEDA-4, mesenteric estrogen-dep
MEF2A	1.675 A430079H05Rik, ADCAD1, M-S EF2A, mef2, myocyte enhancer factor 2A, RSRFC4, RSRFC
Meg3	1.643 2900016C05Rik, 3110050O07Rik, 6330408G06Rik, AI425946, AW108224, D12Bwg1266e, G
MEOX2	-3.693 AI528662, GAX, mesenchyme homeobox 2, MOX2, Mox2a
MEP1A	-4.657 AI098089, AW107200, LOC688307, Mep-1, meprin 1 alpha, meprin a subunit alp1
MEP1B	-8.161 Endopeptidase-2, meprin 1 beta, meprin 1 β, Meprin a subunit beta, Meprin a subunit β, mepr
MGEA5	1.604 2810009A20Rik, 4833427O07Rik, 5830447M11Rik, AA408215, Hy5, MEA5, meningioma exp
MIB2	1.550 221000811Rik, FLJ20648, LOC100128968, mindbomb E3 ubiquitin protein ligase 2, mindbor
Mir1	1.551 Allergin-1, Gm885, mast cell immunoglobulin-like receptor 1, Mca32
MLF1	1.673 HSL7, myeloid leukaemia factor 1, myeloid leukemia factor 1
MLXIPL	1.744 bHLHd14, CHREBP, MIO, MLX interacting protein-like, MONDOB, WBSCR14, WS-bHLH
MMS22L	1.674 C6orf167, dj39B17.2, F730047E07Rik, Gm134, MMS22-like, DNA repair protein, RGD13046
MN1	1.575 AA003644, AA009236, CTA-437G10_B.1, dj353E16.2, meningioma (disrupted in balanced tr
Ms4a4b (includes oth)	1.713 2210417J23Rik, 5830413L19Rik, AI449185, A1463180, Chandra, Ly116, membrane-spanning
MTFR2	1.715 2610016C23Rik, 4933412C16Rik, DUFD1, FAM54A, LOC100911069, mitochondrial fission re
MYC	-1.593 AU016757, bHLHe39, BOS 13758, C-MYC-P64, CMYC, mMyC, MRTL, Myc2, MYCC, myeloc
MYH7	1.854 B-MHC, beta cardiac myosin heavy chain, beta MYHC, beta myosin, Beta Myosin Heavy Cha
NAV1	1.556 9530089B19, 9930003A20Rik, BC028801, C230080M11Rik, LOC685707, mKIAA1151, neur
NCL	-1.545 B530004O11Rik, C23, D0Nds28, D1Nds28, LOC100289394, NUCL, nucleolin
NDR1	1.546 4930447P04Rik, ba350014.9, LOC648245, NADPH dependent diflavin oxidoreductase 1, Nc
NDRG4	1.556 AF045564, BDM1, D8Bwg1337e, N-myc downstream regulated gene 4, Ndr1-rs, NDR4, NDR
NELFCD	1.560 2410003I03Rik, C77797, HSPC130, negative elongation factor complex member C/D, negati
NELL1	1.566 B230343H07Rik, IDH3GL, I7R6, NEL-like 1, NEL-like 1 (chicken), NRP1
NEURL1B	1.719 C230078M08Rik, DKFZp761M1511, EG240055, hNeur2, neur2, neuralized E3 ubiquitin prote
NFIB	1.562 6720429L07Rik, CTF, E030026I10Rik, NF-I/B, Nf1-b1, NFI-RED, NFIB2, NFIB3, Nuc
NME5	1.577 1700019D05Rik, NM23-H5, NM23-H5, NME/NM23 family member 5, RSPH23
NPB	-1.696 LOC653419, neuropeptide B, PPL7, PPNPB, RP23-84C12.7
Npcd	1.668 Cbx6-Nptxr, neuronal pentraxin chromo domain
NPHS2	-5.836 AI790225, nephrosis 2, idiopathic, steroid-resistant, nephrosis 2, idiopathic, steroid-resistant (
NRSN1	3.977 Neurensin-1, Neuro-p24, p24, RP11-176J5.1, RP23-19G4.1, VMP
NT5DC3	1.564 5'-nucleotidase domain containing 3, AU040402, AW540062, C630002B14Rik, LOC687698, t
NTSR1	1.735 Neurotensin Receptor, neurotensin receptor 1, neurotensin receptor 1 (high affinity), NT-1R, N
NXPH3	1.566 neurexophilin 3, NPH3, RP23-67E18.5, UNQ667/PRO1327
OCM	1.650 hCG 18255, LOC730297, OCM1, Ocm2, OM, ONCM, oncomodulin, Oncomodulin, oncomoduli
OGFOD1	1.698 2-oxoglutarate and iron-dependent oxygenase domain containing 1, 4930415J21Rik, AA3871
OSR2	-1.704 5430409I15Rik, odd-skipped related 2, odd-skipped related transcription factor 2, Osr2A, Osr
PAK4	1.678 5730488L07Rik, AW555722, mKIAA1142, p21 protein (Cdc42/Rac)-activated kinase 4
PAPD5	1.543 5730445M16Rik, 5830428A09, PAP associated domain containing 5, TRF4-2
PAQR5	-1.778 0610010I15Rik, AV002411, BB115488, MPRG, Pmrgamma, progestin and adipoQ receptor ft
PAQR6	1.507 1500001B10Rik, LOC686392, progestin and adipoQ receptor family member VI, RP11-54H1!
PARD3	-2.410 AA960621, AI256638, ASIP, atypical pkc-specific binding, Baz, D8Ert580e, MPAR3, PAR-3,
PARK2	1.511 AR-JP, KB-152G3.1, LPR52, Park, Parkin, parkin RBR E3 ubiquitin protein ligase, Parkinson
PBLD	1.613 0610038K03Rik, MAWBP, MAWDBP, Pbld1, Pbld2, phenazine biosynthesis-like protein doma
PBX1	1.544 2310056B04Rik, D230003C07Rik, PBX, pre-B-cell leukaemia homeobox 1, pre-B-cell leuke
PCDH17	1.549 C030033F14Rik, Gm78, LOC144997, PCDH68, PCH68, protocadherin 17
PCDH19	1.565 B530002L05Rik, EFMR, EIEE9, Gm717, LOC279653, mKIAA1313, protocadherin 19, RGD15
PCDH8	2.496 1700080P15Rik, ARCADLIN, PAPC, protocadherin 8
PCLO	1.788 ACZ, aczonin, KIAA0559, Piccolo, piccolo (presynaptic cytomatrix protein), piccolo presynapti
PCP4	-2.400 P16Rimb19, PEP-19, PEPZ19, Purkinje cell protein 4
PCSK2	-2.336 6330411F23Rik, AI837907, NEC-2, PC2, Phpp-2, proprotein convertase subtilisin/kexin type 2
PCSK9	-1.810 AI415265, AI747682, FH3, HCHOLA3, LDLCQ1, NARC-1, PC9, proprotein convertase subtilis
PDHB	1.914 2610103L06Rik, AL024199, C81408, Odpb, PDHBD, PDHE1-B, PHE1B, Pyruvate dehydroge
PDP1	1.634 Gm1024, PDP, PDP, Pdp1c, PDPC, PYRUVATE DEHYDROGENASE, Pyruvate Dehydrogenase Enzyme
PDZK1	-3.366 1700023D20Rik, 2610507N21Rik, 4921513F16Rik, AI267131, AI314638, AL022680, CAP70,
PEAK1	1.618 1110049L02Rik, 9530046P14, AA690169, BE132841, C230081A13Rik, KIAA2002, mKIAA20
PERP	-1.597 1110017A08Rik, d4J96H19.1, ineligibleperp, KCP1, KRTCAP1, p53 apoptosis-associated tar
PGM2L1	2.022 4931406N15Rik, AI553438, BM32A, FLJ32029, LOC683619, phosphoglucomutase 2-like 1
PIGT	1.540 2510012P17Rik, 4930534E15Rik, CGI-06, GPI AMIDASE, MCAHS3, NDAP, Ndap7, phosphatidylglycerol acyltransferase
PIPOX	-2.896 LPIPOX, Peroxisomal sarcosine oxidase, piepecolic acid oxidase, Pso, SOX
PLEKHG3	1.576 ARHGEF43, BC030417, KIAA0599, pleckstrin homology domain containing, family G (with R)
PNMA2	3.747 A830049P17Rik, MA2, mKIAA0883, MM2, paraneoplastic antigen MA2, paraneoplastic Ma antigen
POT1	1.615 1500031H18Rik, AI851169, CMM10, HPOT1, Pot1a, protection of telomeres 1, protection of telomeres 1, Pot1a
Pou3f1	1.635 Oct-6, Otf-6, POU domain, class 3, transcription factor 1, RP23-230F2.2, Scip, Test1, Tst-1
Ppfia4	1.563 1110008G13Rik, AI448359, AI852265, C81506, protein tyrosine phosphatase, receptor type, 1
PPM1K	1.568 2900063A19Rik, A930026L03Rik, BDP, MSUDMV, PP2Ckappa, PP2Cm, protein phosphatases 1, 2A, 2B
PPP1R13B	1.505 AI449786, ASPP1, AW545810, p53BP2-like, p85, protein phosphatase 1, regulatory (inhibitor)
PPP1R3B	1.764 6430576E21, AW821953, GL, LOC192280, LOC286044, PPP1R4, protein phosphatase 1, regulatory (inhibitor)
PRKCA	1.517 AAG6, AI875142, BOS 19579, LOC146784, PKC-alpha, PKC-α, PKCA, PRKACA, PRKACB, PRKACB
PRKCB	1.696 A130082F03Rik, BOS 22739, PKC Type II, PKC Type III, PKC β 1, PKC-Beta, PKC-β, PKCB, PRKCB
Psg18 (includes oth)	-1.599 1600019C01Rik, 1600025N01Rik, 1600026N13Rik, 1620401C02Rik, AA408604, Cea-2, Cea

PSME3	1.724 AA410043, Ab2-371, AU020960, HEL-S-283, Ki, Ki Nuclear Autoantigen, PA28-gamma, PA28
PTPN5	4.853 FLJ1442, protein tyrosine phosphatase, non-receptor type 5, protein tyrosine phosphatase, non-receptor type 5
PTPRO	-3.608 D28, GLEPP, GLEPP1, NPHS6, protein tyrosine phosphatase, receptor type, O, PTP PHI, PT
PTPRS	1.571 AC073761.1, AL022616, Lar-ptp2, protein tyrosine phosphatase, receptor type, S, PTP, PTP-I
QPRT	-1.812 2410027J01RIK, AI647766, HEL-S-90n, LOC100912382, Qaprt, QPRTase, QUINOLINATE P
R3HDM1	-12.051 dJ881L22.3, LOC100046603, OTTMUSG00000001070, R3H domain containing-like, RP23-3
RAB3B	1.605 2610528C18Rik, RAB3B, member RAS oncogene family, RP23-31C9.4
RAB43	1.577 1810048P08Rik, 250004H21Rik, AW490415, RAB11B, RAB41, RAB43, member RAS oncogene family
RAD51C	1.597 BROVCA3, FANCO, R51H3, RAD51 homolog C, RAD51 paralog C, RAD51L2, RGD1563765
RALGPS1	1.588 5830418G11Rik, AI853783, AI854138, mKIAA0351, Ral GEF with PH domain and SH3 bindir
RBFOX1	1.550 2BP1, A2bp, A2BP1, FOX-1, HRNBP1, LOC100287538, MNcb-3035, RNA binding protein, fc
RBM47	-1.505 9530077J19Rik, FLJ20273, NET18, RGD1359713, RNA binding motif protein 47
RET	1.722 C-RET, CDHF12, CDHR16, HSCR1, MEN2A, MEN2B, MTC1, PTC, RET PROTO-ONCOGENE
RGS10	1.691 2310010N19Rik, regulator of G-protein signaling 10, Regulator of G-protein signalling 10
RIMKLA	-1.652 Ak047164, B930030J24, FAM80A, NAAGS, NAAGS-II, ribosomal modification protein rimk-lil
RIMS3	1.874 A730060M23Rik, KIAA0237, mKIAA0237, Nim2, NIM3, regulating synaptic membrane exocyt
RIN2	1.517 2010003K16Rik, 4632403N06Rik, AW821980, MACS, RAB5 interacting protein 2, Ras and R
RIPK3	1.560 2610528K09Rik, AW107945, HCYP2, receptor-interacting serine-threonine kinase 3, RIP3
RIPPLY2	-5.658 C030002E08Rik, C6orf159, dj23715.1, Gm1122, RGD1308746, ripply transcriptional repres
RNASE4	1.752 C730049F20Rik, RAB1, RIBONUCLEASE 4, ribonuclease, RNase A family 4, ribonuclease, I
RNF213	1.636 6030403J01, ALO17, C17ORF27, D11Erdt759e, FRAG-6, hCG 1812857, KIAA1554, KIAA16
ROBO2	-1.657 2600013A04Rik, 9430089E08Rik, BB097918, D230004I22Rik, mKIAA1568, roundabout hom
ROR2	1.603 BDB, BDB1, mRor2, NTRKR2, receptor tyrosine kinase-like orphan receptor 2, RP11-818.2
RPH3AL	-1.538 6530413F01RIK, AI551877, Gm1753, NOC2, rabphilin 3A-like (without C2 domains), RP23-7.
RSPH1	1.703 CT79, MCA, radial spoke head 1 homolog (Chlamydomonas), RSP44, RSPH10A, TSA2, TSC
RTP4	1.594 5830458K16Rik, IFRG28, receptor (chemosensory) transporter protein 4, receptor transpor
RUNX1T1	1.608 AML1T1, CBFA2T1, Cbfa2t1h, CDR, ETO, MTG8, RP23-134H12.1, Run1tl, runt-related trans
S100G	-2.846 AU042539, CAPB, CaBP-D9K, CABP1, CABP9K, Cad9k, CALB3, Calbindin D-9K, Cbp1, Rnc
SAP25	1.513 LOC100289367, RGD1562406, sin3 associated polypeptide, Sin3A-associated protein 25, Sii
SCN8A	1.674 AI853486, C630029C19Rik, CERIII, CIAT, drmu, E1EE13, FLJ33996, MED, mnd-2, NaCh6, Ne
Sct	1.524 Secr, Secretin
SCUBE1	1.791 7330410C13Rik, A630023E24Rik, AL583887.1, signal peptide, CUB domain, EGF-like 1
SCX	-1.765 BB114693, bHLHa41, bHLHa48, LOC684826, Scl, scleraxis, scleraxis basic helix-loop-helix tr
SEMA4C	1.639 AI426163, M-SEMA-F, mKIAA1739, RGD1562837, sema domain, immunoglobulin domain (Ig)
SEMA4G	1.506 AI507908, AW554132, RP11-108L7.1, sema domain, immunoglobulin domain (Ig), transmembr
SEMA6C	1.597 m-SemaY, m-SemaY2, mKIAA1869, RP11-6818.3, sema domain, transmembrane domain (T
SEMA6D	1.669 1110067B02Rik, AA409156, D330011G23, mKIAA1479, RP23-455E2.1, sema domain, trans
SEPT3	1.730 3110018K01RIK, AV154067, B530002E20Rik, bK250D10.3, CTA-250D10.3, SEP3, septin 3
SERPINA1	-2.476 A1-PI, A1A, A1AT, AAT, AAT2, AI118301, alpha 1 antiprotease, Alpha 1 Protease Inhibitor, alpi
SERPINB8	1.717 CAP-2, NK10, ovalbumin, Pl8, PROTEINASE INHIBITOR 8, serine (or cysteine) peptidase inl
SERPINF2	-2.879 A2AP, AAP, AI747498, alpha 2 PLASMIN INHIBITOR, ALPHA-2-PI, alpha2 ANTIPLASMIN, AI
SGK2	-2.496 AI098171, AW146006, dj138B7.2, H-SGK2, RP1-138B7.2, RP23-335N12.5, Serum/glucocor
SGSH	1.714 4632406A19Rik, HSS, MPS3A, N-sulfoglucosamine sulfohydrolase, N-sulfoglucosamine sulf
SHISA2	-1.908 9430059P22Rik, bA398O19.2, C13orf13, hShisa, LOC387914, MAD2, Mem46, mShisa, PRO
SKAP1	2.127 1700091G21Rik, HEL-S-81p, RP23-196B19.1, SCAP1, SKAP55, src family associated phosp
Skint7/Skint8	1.717 C130057D23Rik, LOC684023, OTTMUSG00000009475, RP23-269E13.1, selection and upke
SLC14A2	1.584 hUT-A6, HUT2, Rut, Slc14a2 v4, Slc14a2T, solute carrier family 14 (urea transporter), membe
SLC1A4	1.741 ASCT-1, AW045657, Neutral amino acid transporter, Neutral amino acid transporter a, RP23-
SLC22A6	-2.819 HOAT1, mOat1, NKT, OAT1, Orct1, PAHT, ROAT1, solute carrier family 22 (organic anion tra
SLC23A3	-3.201 E2BP3, hCG 1811885, solute carrier family 23 (nucleobase transporters), member 3, solute c
SLC26A11	1.549 F630021I08RIK, LOC688294, MG46523, RP23-25M3.3, solute carrier family 26 (anion exch
SLC29A4	2.504 ENT4, mPMAT, PMAT, PSEC0113, solute carrier family 29 (equilibrative nucleoside transport
Slc2a4rg-ps	1.552 C430010C01, Gm14462, OTTMUSG00000016710, Slc2a4 regulator, pseudogene
SLC32A1	2.326 hVIAT, LOC100364703, R75019, RP23-392P11.5, solute carrier family 32 (GABA vesicular t
SLC34A1	-5.286 FRTS2, NaPi/Cotransporter Type 2a, Napi iia, NaPi-2, NAPI-3, NaPi2A, NPHLOP1, NPT2, N
SLC35G1	1.616 AA590464, C10orf60, D330039I19Rik, solute carrier family 35, member G1, TMEM20
SLC37A4	-1.592 G6PT, G6PT1, G6PT2, G6PT3, Glycogen Storage Disease Type Ib, GSD-1b, GSD1c, GSD1c
SLC38A5	2.078 AF276870, C81234, E330031E14, JM24, PP7194, RP23-224M4.2, SN2, SNAT5, solute carri
SLC4A11	2.255 AI503023, BTR1, CDPD1, CHE2, dj79416.2, NABC1, RP4-794I6.3, Slc4a11 predicted, solu
SLC6A13	-1.552 Gabt3, GAT-2, GAT3, solute carrier family 6 (neurotransmitter transporter), member 13, solute
SLC8A2	1.504 NCX2, SLC8A, solute carrier family 8 (sodium/calcium exchanger), member 2
SLIT1	1.544 MEGF4, mKIAA0813, RP11-175O19.2, SLIL1, slit homolog 1 (Drosophila), SLIT3
SLN	8.563 2310045A07Rik, sarcolipin
SMARCA2	1.594 2610209L14RIK, BAF190, brahma, BRM, BRM1, hBRM, hSNF2a, NCBRS, SNF2, SNF2alph
SMIM24	-1.566 2210404O07Rik, C19orf77, HSPC323, small integral membrane protein 24
SNED1	1.633 6720455I24Rik, AI197264, AI642697, D430044C15RIK, DKFZp586B2420, FLJ00133, IRE-BF
SOD3	-1.747 AI314465, EC-SOD, ECSODPT, superoxide dismutase 3, extracellular
SOSTDC1	-2.426 0610006G05Rik, CDA019, ECTODIN, sclerostin domain containing 1, Sostl, USAG-1, Wise
SP110	1.732 5031415C07RIK, 5830484A20RIK, ENSMUSG00000075603, Gm15753, IFI41, IFI75, IPR1, I
SP5	2.185 Sp5 transcription factor, trans-acting transcription factor 5
SPAG7	1.762 5730443G10, ACRP, DN-183N8.18-002, FSA-1, Fsa1, sperm associated antigen 7
SPINK1	-4.790 LOC266602, p12, PCTT, PST1, Pst1-1, Pst1-ii, serine peptidase inhibitor, Kazal type 1, serine p

SPOCK2	-1.776 AA407235, GCAP26, KIAA0275, mKIAA0275, sparc/osteonectin, cwcv and kazal-like domain
SPP2	-7.346 0610038O04Rik, LOC94168, pp-24, secreted phosphoprotein 2, secreted phosphoprotein 2,
SREK1	1.648 8430401B01, AI450757, AI462342, SFRS12, splicing regulatory glutamine/lysine-rich protein
ST3GAL6	-1.780 1700023B24Rik, AI930218, alpha-2,3-sialyltransferase VI, AW552396, RP24-293N14.3, Sialy
STAB2	1.786 FEEL-2, FELE-2, FELL, FELL2, FEX2, HARE, MFEEL-2, STABILIN-2
STEAP1	-1.742 2410007B19Rik, PRSS24, six transmembrane epithelial antigen of the prostate 1, STEAP, tca
STEAP2	-1.672 4921538B17Rik, AI930049, AW045895, ENSMUSG00000073232, IPCA-1, PCANAP1, PUMI
STIM1	1.703 D11S4896E, GOK, IMD10, SIM, STRMK, stromal interaction molecule 1, TAM, TAM1
STMN2	2.199 AI159727, SCG10, SCGN10, stathmin 2, stathmin-like 2, Stmb2
STXBP1	1.516 AI317162, AI326233, ANC18HA, MMS10-G, Ms10g, Munc-18a, MUNC18-1, NSEC1, NSEC1.
Sult1d1	-7.906 5033411P13Rik, AI987815, Amino n-sulfotransferase, ST1D1, sulfotransferase family 1D, me
SUV39H2	1.600 4930507K23Rik, AA536750, D030054H19Rik, D2Ertd544e, KMT1B, RP11-2K17.2, RP23-16
SVOPL	-1.573 9430071P14Rik, RGD1566053, similar to RIKEN cDNA 9430071P14 gene, SV2 related prote
SYNJ1	1.760 A930006D20Rik, AA675315, INPP5G, mKIAA0910, PARK20, synaptotanin 1
SYNPO2L	1.643 1110054M18Rik, Chap, FLJ12921, RGD1565434, synaptopodin 2-like
TBX3	1.547 D5Ertd189e, LOC100047200, T-box 3, TBX3-ISO, UMS, XHL
TCEAL5	1.507 6430401A05Rik, LLOXNC01-177E8.1, LOC678833, RP23-132M9.2, transcription elongation 1
TCF24	3.384 bHLHa25, ENSMUSG00000073738, Gm10567, Gm2330, LOC100045893, transcription factc
TCP11L2	1.701 E430026E19Rik, RGD1307494, t-complex 11 (mouse) like 2, t-complex 11, testis-specific-like
TENM4	1.612 Doc4, ELM2, I(7)-3Rn, ITn3, mKIAA1302, ODZ4, R75022, Ten-4, teneurin transmembrane p
TFEB	1.726 ALPHATFEB, BHLHE35, RP4-696P19.3, TCFEB, transcription factor EB
TGM5	1.534 2310007C07Rik, LOC688031, LOC691932, RP23-263D22.4, similar to transglutaminase 7, T
THNSL2	-1.565 BC051244, FLJ10916, RGD1309144, threonine synthase-like 2 (bacterial), threonine synthas
THY1	1.528 CD7, CD90, LOC94105, T25, Thy-1 cell surface antigen, Thy1.1, Thymus cell antigen 1, theta
TIAM2	1.626 3000002F19Rik, LOC100362710, mKIAA2016, RP3-414L4.2, STEF, T-cell lymphoma invasic
TINAG	-2.733 AI452335, RP11-12414.1, tubulointerstitial nephritis antigen
TMEM174	-2.675 0610009B10Rik, AA986094, transmembrane protein 174
TMEM213	-1.977 D630002J15Rik, LOC684143, transmembrane protein 213
TMEM239	1.689 4933425O20Rik, LOC100048703, LOC100291033, LOC100291571, RP23-29K12.6, transme
TMEM25	-1.833 0610039J01Rik, AI429491, LOC683488, transmembrane protein 25, UNQ2531/PRO6030
Tmem254a (includes:	1.580 0610008K04Rik, 0610010A22Rik, AA960404, D14Ertd449e, ENSMUSG00000021867, ENSM
TMEM27	-2.423 0610008J07Rik, collectrin, NX-17, RP23-59N7.2, transmembrane protein 27, UNQ679/PRO1
TMEM59L	1.560 5330410G16Rik, BSMAP, C19orf4, RGD1305557, transmembrane protein 59-like
TMEM8B	1.583 493050005Rik, C9orf127, NAG-5, NGX6, RGD130012, RP11-112J3.10, RP23-191F22.12-
TMPRSS3	1.742 DFNB10, DFNB8, ECHOS1, TAGD12, transmembrane protease, serine 3, UNQ323/PRO382
TNFRSF10A	1.589 APO2, CD261, Death receptor 4, DR, DR4, DR5, KILLER, Ly98, MK, Tnfrsf10b, TR1, TRAIL r
TNFRSF9	1.663 4-1BB, A93004011Rik, AA408498, AI325004, CD137, CDw137, ILA, Ly63, RP23-272N19.6,
TNNI1	-1.662 2700018B22Rik, AI747285, Slow tri, SSTNI, TNN1, Troponin I slow, troponin I type 1 (skeleta
TPBG	2.099 5T4, 5T4AG, AW495680, M6P1, trophoblast glycoprotein, WAIF1
TRAF1	-3.625 4732496E14Rik, EBI6, ineligibletraf1, MGC:10353, RP23-9N11.6, TNF receptor-associated fa
TRH	-4.460 Pro-TRH, THR, thyrotropin-releasing hormone, TRF, TRH01
TRIB3	1.744 C20orf97, HTRB-3, Ifld2, LOC246273, NIPK, RP23-396N8.1, RP5-1103G7.7, SINK, SKIP3, T
TRIM25	1.688 AA960166, AL022677, EFP, estrogen-responsive finger, RNF147, RP23-176J13.7, TRIM25 a
TSPAN17	1.738 2210021G21Rik, AI047581, FBX23, FBXO23, GHB-R, MGC14859, tetraspanin 17, TM4SF11
TTYH2	1.573 1110001A03Rik, C17orf29, LOC100505117, RGD1562969, RP23-273C14.1, tweety family m
TUBB2B	1.612 2410129E14Rik, bA506K6.1, Beta-tubulin T beta15, Beta1 Tubulin, brdp, MGC8685, PMGYS
TWIST2	1.503 bHLHa39, DERMO1, FFDD3, SETLSS, twist basic helix-loop-helix transcription factor 2, twist
UBE2I	1.674 5830467E05Rik, C358B7.1, F830028017Rik, LA16c-358B7.1, P18, SUMO E2, UBC9, UbcE
UBTF	1.705 A930005G04Rik, LOC679205, NOR-90, RP23-461C4.7, TCFUBF, UBF, UBF1, upstream bin
UGT1A6	-1.775 A9, GNT1, HLUGP, HLUGP1, UDP glucuronosyltransferase 1, UDP glucuronosyltransferase
UGT2B10	-2.445 A1788959, UDP glucuronosyltransferase 2 family, polypeptide B10, UDP glucuronosyltransfer
UGT2B28	-5.634 0610033E06Rik, 9430041C03Rik, AA986709, AI118071, Androsterone UDP-glucuronosyltran
UNCX	-1.701 Chx4, LOC100510018, PHD1, tcag7.1272, UNC homeobox, UNCX4.1
UNG	1.722 DGU, HIGM4, HIGM5, UDG, UNG1, UNG15, UNG2, Uracil hydrolase, uracil-DNA glycosylase
USP51	1.837 AV136873, RGD1562211, RP23-415B4.1, ubiquitin specific peptidase 51, ubiquitin specific pr
VAT1L	-1.586 9430073I07, AI427515, KIAA1576, mKIAA1576, vesicle amine transport 1-like, vesicle amine
VEGFC	1.600 AW228853, Flt4 ligand, Flt4-L, LMPH1D, vascular endothelial growth factor C, VRP
VIL1	-3.708 D2S1471, VIL, Villin, villin 1
WDFY1	1.653 1700013B03Rik, 1700120F24Rik, FENS-1, Jr1, mKIAA1435, SR1, WD repeat and FYVE do
WDFY4	1.666 C10orf64, Gm18810, hCG 1745555, RGD1564142, WD repeat and FYVE domain containing
WDR89	1.646 2600001A11Rik, C14orf150, MSTP050, RGD1307393, WD repeat domain 89
WSCD2	2.008 4933413A10, 4933413A10Rik, C530024P05Rik, Gm450, WSC domain containing 2, Wscd2-1
XPNPEP2	-2.162 9030008G12Rik, AEACE1, APP2, mAmP, mAPP, Membrane-bound aminopeptidase p, Membr
YBX2	1.657 CONTRIN, CSDA3, DBPC, MSY2, RGD1305068, Y box binding protein 2, Y box protein 2
ZCCHC9	1.701 1810019C21Rik, PPP1R41, zinc finger, CCHC domain containing 9
Zfp133-ps	1.679 OTTMUSG00000003825, Zfp133, zinc finger protein 133, pseudogene
Zfp941	1.640 zinc finger protein 941
ZFPM1	1.703 FOG, FOG1, LOC100365064, ZC2HC11A, zinc finger protein, FOG family member 1, zinc fin
ZFPM2	1.536 B330005D23Rik, DIH3, FOG-2, hFOG-2, ZC2HC11B, zinc finger protein, FOG family membe
ZMAT4	2.200 9630048M01Rik, LOC684906, MATRIN-4, zinc finger, matrin-type 4
ZNF512B	1.513 GM632, RP23-138J20.2, Urk1, Zfp512b, zinc finger protein 512B
ZNF536	1.513 9630010P11Rik, KIAA0390, mKIAA0390, RGD1563363, Zfp536, zinc finger protein 536

ZNF703
ZSWIM8

1.687 1110032O19RIK, AI430822, AL022941, Csmn1, End2, FLJ14299, LOC684528, ZEPPO1, Zfp
1.506 2310021P13Rik, 4832404P21Rik, KIAA0913, LOC196752, mKIAA0913, RGD1309414, zinc f

Entrez Gene Name	Agilent	Location	Family	Drugs
family with sequence similarity 177, member A	A_55_P2114269	Other	other	
RIKEN cDNA 1700110I01 gene	A_55_P2067463	Other	other	
RIKEN cDNA 2310002F09 gene	A_55_P2292737	Other	other	
RIKEN cDNA 2310015B20 gene	A_51_P199352	Other	other	
uncharacterized protein 3830612M24	A_55_P2345853	Other	other	
RIKEN cDNA 4732423E21 gene	A_55_P2210213	Other	other	
RIKEN cDNA 4930412O13 gene	A_55_P2064776	Other	other	
RIKEN cDNA 4932431P20 gene	A_55_P1976682	Other	other	
RIKEN cDNA 4933427D06 gene	A_55_P2038484	Other	other	
RIKEN cDNA 6720422M22 gene	A_55_P2244677	Other	other	
RIKEN cDNA 8030425K09 gene	A_55_P2258216	Other	other	
RIKEN cDNA 9030419F21 gene	A_55_P2279035	Other	other	
lymphocyte antigen 6 complex pseudogene	A_66_P122086	Other	other	
RIKEN cDNA 9130020K20 gene	A_55_P2402134	Other	other	
RIKEN cDNA 9530083O12 gene	A_55_P2209308	Other	other	
RIKEN cDNA 9630010G10 gene	A_55_P2296118	Other	other	
RIKEN cDNA A230065H16 gene	A_55_P2076916	Other	other	
RIKEN cDNA A530006G24 gene	A_55_P2131820	Other	other	
acyl-CoA thioesterase 11	A_55_P2096043	Cytoplasm	enzyme	
acyl-CoA oxidase 3, pristanoyl	A_55_P1971579	Cytoplasm	enzyme	
acyl-CoA synthetase medium-chain family member 2A	A_55_P2325038	Cytoplasm	enzyme	
acyl-CoA synthetase short-chain family member 2	A_55_P1988789	Cytoplasm	enzyme	
ADAM metallopeptidase with thrombospondin type 1 motif, 17	A_55_P2038422	Extracellular Space	other	
ADAM metallopeptidase with thrombospondin type 1 motif, 7	A_55_P1961451	Extracellular Space	peptidase	
alpha-fetoprotein	A_51_P510891	Extracellular Space	transporter	
aldo-keto reductase family 1, member C3	A_55_P2163098	Cytoplasm	enzyme	
aldehyde dehydrogenase 1 family, member A2	A_52_P58145	Cytoplasm	enzyme	
aldehyde dehydrogenase 1 family, member A3	A_52_P87843	Cytoplasm	enzyme	
aldolase B, fructose-bisphosphate	A_51_P337269	Cytoplasm	enzyme	
amnion associated transmembrane protein	A_51_P343350	Plasma Membrane	other	
ANKH inorganic pyrophosphate transport regulator	A_51_P155152	Plasma Membrane	transporter	
annexin A13	A_52_P662711	Plasma Membrane	other	
amyloid beta (A4) precursor-like protein 1	A_55_P1991605	Extracellular Space	other	
Rho GTPase activating protein 26	A_55_P2080562	Cytoplasm	other	
Rho guanine nucleotide exchange factor (GEF) 15	A_55_P2035087	Cytoplasm	other	
ADP-ribosylation factor-like 6 interacting protein 6	A_55_P2042993	Other	other	
arrestin, beta 1	A_51_P436727	Cytoplasm	other	
ADP-ribosyltransferase 4 (Dombrock blood group)	A_55_P2108248	Nucleus	enzyme	
ankyrin repeat and SOCS box containing 9	A_51_P247963	Nucleus	transcription regulator	
acid-sensing (proton-gated) ion channel family member 4	A_55_P2162747	Plasma Membrane	ion channel	amiloride, amiloride
asparaginase	A_52_P338956	Other	enzyme	
argininosuccinate synthase 1	A_55_P2143070	Cytoplasm	enzyme	
ATPase, Na ⁺ /K ⁺ transporting, beta 1 polypeptide	A_51_P151484	Plasma Membrane	transporter	
ATPase, H ⁺ transporting V0 subunit e2	A_51_P212038	Cytoplasm	enzyme	
ataxin 7	A_55_P2099890	Nucleus	other	
expressed sequence AW011956	A_55_P2319035	Other	other	
expressed sequence AW549542	A_55_P2274378	Other	other	
BTB and CNC homology 1, basic leucine zipper transcription factor 2	A_66_P114768	Nucleus	transcription regulator	
3-hydroxybutyrate dehydrogenase, type 1	A_51_P163106	Cytoplasm	enzyme	
BEN domain containing 4	A_55_P2199118	Other	other	
BPI fold containing family C	A_55_P1966583	Extracellular Space	transporter	
bone morphogenetic protein/retinoic acid inducible neural-specific 1	A_55_P2124941	Nucleus	peptidase	
barttin CLCNK-type chloride channel accessory beta subunit	A_55_P2056704	Plasma Membrane	other	
butyrophilin, subfamily 1, member A1	A_55_P2029235	Plasma Membrane	other	
chromosome 10 open reading frame 35	A_51_P308029	Other	other	
chromosome 12 open reading frame 73	A_52_P598634	Other	other	
chromosome 1 open reading frame 54	A_55_P1985519	Other	other	
complement component 2	A_51_P497985	Extracellular Space	peptidase	
RIKEN cDNA C230096K16 gene	A_55_P2270412	Other	other	
complement component 5a receptor 2	A_55_P2106106	Plasma Membrane	G-protein coupled receptor	
chromosome 9 open reading frame 16	A_51_P207153	Other	other	
carbonic anhydrase IV	A_55_P2087182	Plasma Membrane	enzyme	ethoxzolamide, di-
calbindin 1, 28kDa	A_66_P102374	Cytoplasm	other	
calmodulin-like 4	A_52_P367760	Other	other	
calneuron 1	A_55_P2113439	Cytoplasm	other	
calcium/calmodulin-dependent protein kinase kinase 1, alpha	A_55_P2113165	Cytoplasm	kinase	
calpain 6	A_52_P474089	Cytoplasm	peptidase	
coiled-coil domain containing 138	A_55_P2043117	Other	other	
CDC42 effector protein (Rho GTPase binding) 5	A_55_P2057686	Cytoplasm	other	
cadherin 6, type 2, K-cadherin (fetal kidney)	A_55_P2414619	Plasma Membrane	other	

cyclin-dependent kinase 5, regulatory subunit 1 (p35)	A_55_P2173183	Nucleus	kinase
cyclin-dependent kinase-like 1 (CDC2-related kinase)	A_51_P234140	Nucleus	kinase
CUGBP, Elav-like family member 4	A_55_P1992572	Nucleus	translation regulator
centrosomal protein 170B	A_55_P2050488	Other	other
cell growth regulator with EF-hand domain 1	A_51_P372550	Extracellular Space	other
charged multivesicular body protein 4B	A_55_P2008538	Cytoplasm	other
chondroitin polymerizing factor 2	A_55_P1987904	Cytoplasm	enzyme
carbohydrate (N-acetyl)galactosamine 4-0) sulfotransferase 8	A_51_P277006	Cytoplasm	enzyme
cell death-inducing DFFA-like effector a	A_51_P199168	Cytoplasm	other
cell death-inducing DFFA-like effector b	A_66_P108685	Cytoplasm	other
Cbp/p300-interacting transactivator, with Glu/Asp-rich carboxy-terminal domain, 1	A_55_P1979833	Nucleus	transcription regulator
chloride channel, voltage-sensitive Ka	A_55_P2080880	Plasma Membrane	ion channel
C-type lectin domain family 18, member B	A_55_P2063980	Other	other
chloride intracellular channel 6	A_52_P447284	Plasma Membrane	ion channel
collagen, type I, alpha 1	A_55_P2118520	Extracellular Space	other
collagen, type XXVI, alpha 1	A_55_P1954271	Extracellular Space	other
collagen, type II, alpha 1	A_55_P2004179	Extracellular Space	other
collagen, type IV, alpha 6	A_52_P516409	Extracellular Space	other
collagen, type V, alpha 1	A_51_P414637	Extracellular Space	other
collagen, type VII, alpha 1	A_55_P2064292	Extracellular Space	other
collagen-like tail subunit (single strand of homotrimer) of asymmetric acetylcholinesterase	A_55_P2043337	Extracellular Space	other
cytochrome c oxidase subunit VIB polypeptide 2 (testis)	A_51_P300506	Cytoplasm	enzyme
carboxypeptidase A1 (pancreatic)	A_52_P161237	Extracellular Space	peptidase
carboxypeptidase A2 (pancreatic)	A_52_P320261	Extracellular Space	peptidase
carboxypeptidase B2 (plasma)	A_51_P262701	Extracellular Space	peptidase
carboxypeptidase N, polypeptide 1	A_52_P308669	Extracellular Space	peptidase
cellular retinoic acid binding protein 2	A_55_P2059432	Cytoplasm	transporter
crumbs family member 2	A_51_P300618	Extracellular Space	other
cAMP responsive element binding protein 5	A_55_P2097474	Nucleus	transcription regulator
collapsin response mediator protein 1	A_55_P2017600	Cytoplasm	enzyme
chondroitin sulfate proteoglycan 5 (neuroglycan C)	A_55_P2046744	Extracellular Space	growth factor
cubilin (intrinsic factor-cobalamin receptor)	A_55_P2047639	Plasma Membrane	transmembrane receptor
cytochrome b561	A_55_P1954718	Cytoplasm	enzyme
cytochrome b5 reductase 4	A_52_P505827	Cytoplasm	enzyme
cytochrome P450, family 26, subfamily B, polypeptide 1	A_51_P501844	Cytoplasm	enzyme
cytochrome P450, family 2, subfamily d, polypeptide 26	A_51_P120295	Cytoplasm	enzyme
cytochrome P450, family 2, subfamily U, polypeptide 1	A_55_P1966734	Cytoplasm	enzyme
cytochrome P450, family 4, subfamily A, polypeptide 11	A_55_P2050628	Cytoplasm	enzyme
RIKEN cDNA D230019N24 gene	A_55_P2208260	Other	other
RIKEN cDNA D230040J21 gene	A_55_P2261882	Other	other
RIKEN cDNA D430019H16 gene	A_52_P97699	Other	other
DNA segment, Chr 8, ERATO Doi 158, expressed	A_55_P2236382	Other	other
D-amino-acid oxidase	A_55_P2108933	Cytoplasm	enzyme
death associated protein-like 1	A_51_P391955	Other	other
DDB1 and CUL4 associated factor 12-like 2	A_55_P2084980	Other	other
doublecortin	A_52_P244349	Cytoplasm	other
dicarbonyl/L-xylulose reductase	A_55_P2077628	Cytoplasm	enzyme
dopa decarboxylase (aromatic L-amino acid decarboxylase)	A_55_P2110497	Cytoplasm	enzyme
DENN/MADD domain containing 4A	A_55_P2048650	Nucleus	other
deoxyribose-phosphate aldolase (putative)	A_51_P512820	Cytoplasm	enzyme
dickkopf WNT signaling pathway inhibitor 3	A_55_P2083609	Extracellular Space	cytokine
discs, large (Drosophila) homolog-associated protein 3	A_52_P138806	Cytoplasm	other
delta-like 1 homolog (Drosophila)	A_66_P117477	Extracellular Space	other
delta-like 1 (Drosophila)	A_51_P306017	Plasma Membrane	enzyme
dematin actin binding protein	A_55_P1956482	Plasma Membrane	other
DnaJ (Hsp40) homolog, subfamily A, member 4	A_55_P2085546	Nucleus	other
DnaJ (Hsp40) homolog, subfamily C, member 19	A_55_P2028243	Cytoplasm	other
DnaJ (Hsp40) homolog, subfamily C, member 22	A_51_P257743	Other	other
dedicator of cytokinesis 5	A_52_P88983	Cytoplasm	other
D4, zinc and double PHD fingers family 1	A_51_P131442	Nucleus	other
dipeptidyl-peptidase 4	A_51_P467110	Plasma Membrane	peptidase
dihydropyrimidinase-like 5	A_55_P2052555	Cytoplasm	enzyme
double homeobox B-like 1	A_66_P125035	Nucleus	other
dynein, cytoplasmic 1, intermediate chain 1	A_55_P2090429	Cytoplasm	other
ectodysplasin-A	A_55_P2030662	Other	other
epidermal growth factor receptor	A_52_P106259	Plasma Membrane	kinase
euchromatic histone-lysine N-methyltransferase 1	A_55_P2045163	Nucleus	transcription regulator
eukaryotic translation initiation factor 2, subunit 3, structural gene Y-linked	A_55_P2011877	Other	other
E74-like factor 5	A_51_P455866	Other	other
elastin microfibril interfacer 2	A_52_P527800	Extracellular Space	other
endonuclease V	A_55_P1954925	Other	enzyme
enolase 2 (gamma, neuronal)	A_55_P2019457	Cytoplasm	enzyme

glutamyl aminopeptidase (aminopeptidase A)	A_51_P161830	Plasma Membrane peptidase
erythrocyte membrane protein band 4.1 like 4B	A_52_P286098	Other transporter
EPH receptor A5	A_55_P2062911	Plasma Membrane kinase
EPH receptor B3	A_55_P2054332	Plasma Membrane kinase
epoxide hydrolase 1, microsomal (xenobiotic)	A_55_P2002578	Cytoplasm peptidase
epidermal growth factor receptor pathway substrate 8	A_55_P1982454	Plasma Membrane peptidase
espin	A_66_P108003	Cytoplasm other
estrogen-related receptor gamma	A_65_P19089	Nucleus ligand-dependent n diethylstilbestrol
exocyst complex component 6	A_52_P631499	Plasma Membrane transporter
exosome component 9	A_55_P2043187	Nucleus enzyme
EYA transcriptional coactivator and phosphatase 1	A_55_P2423586	Nucleus phosphatase
fatty acid binding protein 3, muscle and heart (mammary-derived growth inhibitor)	A_55_P2033780	Cytoplasm transporter
family with sequence similarity 160, member B2	A_55_P2088296	Other other
family with sequence similarity 219, member A	A_55_P1991778	Other other
fibrillin 1	A_51_P467224	Extracellular Space other
fructose-1,6-bisphosphatase 1	A_51_P474701	Cytoplasm phosphatase
F-box and leucine-rich repeat protein 16	A_52_P49457	Cytoplasm other
F-box and leucine-rich repeat protein 7	A_52_P423364	Cytoplasm enzyme
FCH domain only 1	A_55_P2047461	Plasma Membrane other
FCH and double SH3 domains 1	A_52_P456158	Other other
fibrinogen beta chain	A_51_P428483	Extracellular Space other
fibroblast growth factor 1 (acidic)	A_55_P2047188	Extracellular Space growth factor pentosan polysulfat
FIG4 phosphoinositide 5-phosphatase	A_51_P405985	Cytoplasm enzyme
fibronectin leucine rich transmembrane protein 1	A_55_P2110915	Plasma Membrane other
fibronectin leucine rich transmembrane protein 3	A_55_P2110925	Plasma Membrane other
fibronectin 1	A_55_P2130178	Extracellular Space enzyme ocriplasmin
formin binding protein 1	A_55_P2030775	Nucleus enzyme
folate receptor 1 (adult)	A_55_P1977792	Plasma Membrane transporter
forkhead box D1	A_52_P128134	Nucleus transcription regulator
forkhead box I1	A_55_P2166513	Nucleus transcription regulator
forkhead box O6	A_52_P589568	Nucleus transcription regulator
forkhead box P4	A_55_P2149983	Nucleus transcription regulator
FRAS1 related extracellular matrix 1	A_55_P1999641	Extracellular Space other
FERM and PDZ domain containing 2	A_55_P2173664	Plasma Membrane other
frizzled-related protein	A_51_P286748	Extracellular Space other
follistatin	A_55_P2394308	Extracellular Space other
FXYD domain-containing ion transport regulator 2	A_55_P2137941	Plasma Membrane other
frizzled class receptor 10	A_52_P203560	Plasma Membrane G-protein coupled receptor
gamma-aminobutyric acid (GABA) A receptor, alpha 3	A_55_P1963463	Plasma Membrane ion channel methohexitol, primi
galanin/GMAP prepropeptide	A_51_P258281	Extracellular Space other
GTPase activating Rap/RanGAP domain-like 3	A_55_P2114133	Other other
GATS protein-like 2	A_55_P2014987	Other other
group-specific component (vitamin D binding protein)	A_55_P2022158	Extracellular Space transporter
glucosaminyl (N-acetyl) transferase 1, core 2	A_52_P21550	Cytoplasm enzyme
GDNF family receptor alpha 2	A_55_P1968703	Plasma Membrane transmembrane receptor
GDNF family receptor alpha 3	A_55_P1984103	Plasma Membrane transmembrane receptor
gamma-glutamyltransferase 1	A_51_P468073	Plasma Membrane enzyme
GIPC PDZ domain containing family, member 2	A_51_P446131	Cytoplasm other
galactosidase, alpha	A_55_P2146136	Cytoplasm enzyme
predicted gene 10576	A_55_P2090782	Other other
predicted gene 12258	A_55_P2115260	Other other
high mobility group box 1	A_55_P2025153	Nucleus transcription regulator
predicted gene 266	A_55_P2073694	Other other
predicted gene 5097	A_55_P2067952	Other other
high mobility group box 2 pseudogene	A_52_P30877	Other other
predicted gene 6115	A_55_P2176917	Other other
predicted gene 6213	A_52_P900300	Other other
predicted gene 6994	A_55_P1993640	Other other
predicted gene 9780	A_55_P1986332	Other other
predicted gene 9900	A_55_P2005315	Other other
guanine nucleotide binding protein (G protein), beta 5	A_55_P2000643	Plasma Membrane enzyme
guanine nucleotide binding protein (G protein), gamma 7	A_55_P1988018	Plasma Membrane enzyme
glycerol-3-phosphate dehydrogenase 1 (soluble)	A_52_P16419	Cytoplasm enzyme
G protein-coupled receptor associated sorting protein 1	A_55_P2132902	Cytoplasm transporter
glutamate receptor, ionotropic, AMPA 4	A_55_P1987725	Plasma Membrane ion channel talampanel, faramp
glutathione S-transferase alpha 5	A_55_P2170454	Cytoplasm enzyme
glutathione S-transferase mu 5	A_55_P2062190	Cytoplasm enzyme
glutathione S-transferase, mu 6	A_55_P2031692	Cytoplasm enzyme
GULP, engulfment adaptor PTB domain containing 1	A_51_P381218	Cytoplasm other
glucoside xylosyltransferase 2	A_55_P1974542	Other other
histocompatibility 2, K region locus 2	A_51_P502456	Plasma Membrane other
histocompatibility 2, Q region locus 5	A_51_P400752	Other other

hydroxyacylglutathione hydrolase	A_55_P2154536	Cytoplasm	enzyme
huntingtin-associated protein 1	A_51_P516728	Cytoplasm	other
hyaluronan synthase 2	A_51_P213359	Plasma Membrane	enzyme
histidine decarboxylase	A_51_P254656	Cytoplasm	enzyme
HD domain containing 3	A_52_P521882	Other	other
HECT, C2 and WW domain containing E3 ubiquitin protein ligase 1	A_55_P2424767	Cytoplasm	enzyme
hemogen	A_55_P1975660	Nucleus	other
hes family bHLH transcription factor 5	A_52_P622850	Nucleus	other
hes-related family bHLH transcription factor with YRPW motif 1	A_51_P258409	Nucleus	transcription regulator
hedgehog interacting protein	A_55_P1969276	Plasma Membrane	other
major histocompatibility complex, class I, A	A_51_P198434	Plasma Membrane	other
major histocompatibility complex, class I, E	A_51_P237754	Plasma Membrane	transmembrane receptor
HMP19 protein	A_51_P163953	Cytoplasm	other
HNF1 homeobox A	A_55_P1970929	Nucleus	transcription regulator
hepatocyte nuclear factor 4, alpha	A_55_P1959633	Nucleus	transcription regulator
homeobox C4	A_55_P2074688	Nucleus	transcription regulator
homeobox D12	A_55_P2160638	Nucleus	transcription regulator
homeobox D4	A_51_P260265	Nucleus	transcription regulator
hydroxysteroid (17-beta) dehydrogenase 14	A_55_P2056774	Cytoplasm	enzyme
hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-isomerase 4	A_55_P1969665	Cytoplasm	enzyme
RIKEN cDNA I730030J21 gene	A_55_P1973399	Other	other
interferon induced transmembrane protein 7	A_55_P2097161	Other	other
immunoglobulin superfamily, DCC subclass, member 3	A_51_P179921	Other	other
immunoglobulin superfamily, DCC subclass, member 4	A_55_P2001553	Plasma Membrane	other
insulin-like growth factor binding protein 1	A_51_P447545	Extracellular Space	other
interleukin 15 receptor, alpha	A_55_P2060707	Plasma Membrane	transmembrane receptor
interleukin 33	A_55_P1964960	Extracellular Space	cytokine
importin 9	A_65_P15675	Nucleus	transporter
iroquois homeobox 1	A_52_P1092823	Nucleus	transcription regulator
inter-alpha-trypsin inhibitor heavy chain family, member 5	A_55_P2077048	Other	other
inositol-trisphosphate 3-kinase A	A_51_P273609	Cytoplasm	kinase
intersectin 1 (SH3 domain protein)	A_55_P1994603	Cytoplasm	other
jade family PHD finger 2	A_55_P2139753	Nucleus	other
KN motif and ankyrin repeat domains 2	A_55_P2167112	Nucleus	transcription regulator
Kazal-type serine peptidase inhibitor domain 1	A_55_P2015032	Extracellular Space	other
potassium voltage-gated channel, shaker-related subfamily, member 4	A_55_P2084251	Plasma Membrane	ion channel
potassium voltage-gated channel, Shal-related subfamily, member 2	A_52_P124472	Plasma Membrane	ion channel
potassium inwardly-rectifying channel, subfamily J, member 1	A_52_P499907	Plasma Membrane	ion channel
kielin/chordin-like protein	A_55_P2074499	Extracellular Space	other
KIAA1467	A_55_P1975947	Other	other
kinesin family member 1A	A_52_P49378	Cytoplasm	other
kinesin family member 21B	A_52_P282500	Cytoplasm	other
kinesin family member 5C	A_55_P2048937	Cytoplasm	other
kinesin family member C2	A_55_P2149500	Cytoplasm	other
kinesin light chain 2	A_55_P2002918	Cytoplasm	other
keratin 36	A_55_P2140036	Cytoplasm	other
like-glycosyltransferase	A_55_P2069979	Cytoplasm	enzyme
LIM domain binding 2	A_55_P2013601	Nucleus	transcription regulator
low density lipoprotein receptor class A domain containing 3	A_55_P2054728	Plasma Membrane	other
LIM homeobox 1	A_52_P652336	Nucleus	transcription regulator
LIM domain kinase 1	A_55_P1966987	Cytoplasm	kinase
uncharacterized LOC102635467	A_55_P2068496	Other	dabrafenib, dabrafene
uncharacterized LOC102638978	A_55_P1972915	Other	other
h-2 class I histocompatibility antigen, D-37 alpha chain-like	A_55_P1972481	Other	other
high mobility group protein B1-like	A_55_P1991911	Other	other
lipin 2	A_66_P138976	Nucleus	phosphatase
low density lipoprotein receptor-related protein 11	A_51_P295237	Other	other
low density lipoprotein receptor-related protein 2	A_52_P285470	Plasma Membrane	transporter
leucine rich repeat containing 31	A_55_P2078994	Other	other
leucine rich repeat containing 4B	A_55_P1953503	Plasma Membrane	other
LUC7-like 2 (<i>S. cerevisiae</i>)	A_55_P1953361	Other	other
lymphocyte antigen 6 complex, locus A	A_51_P265495	Plasma Membrane	other
lymphocyte antigen 86	A_51_P465350	Plasma Membrane	other
leucine zipper, putative tumor suppressor 1	A_55_P2261772	Nucleus	transcription regulator
MAP-kinase activating death domain	A_55_P2112424	Cytoplasm	other
v-maf avian musculoaponeurotic fibrosarcoma oncogene homolog B	A_52_P495869	Nucleus	other
metastasis associated lung adenocarcinoma transcript 1 (non-protein coding)	A_55_P2021187	Nucleus	other
MAP/microtubule affinity-regulating kinase 4	A_55_P2142580	Cytoplasm	kinase
Mab-21 domain containing 1	A_66_P137605	Cytoplasm	other
methyl-CpG binding domain protein 1	A_55_P2105843	Nucleus	transcription regulator
melanoma cell adhesion molecule	A_55_P1986552	Plasma Membrane	other
multiple C2 domains, transmembrane 2	A_55_P1965313	Other	other

MyoD family inhibitor	A_55_P2076777	Cytoplasm	other
malic enzyme 3, NADP(+)-dependent, mitochondrial	A_55_P1953919	Cytoplasm	enzyme
mesenteric estrogen-dependent adipogenesis	A_55_P2065731	Cytoplasm	other
myocyte enhancer factor 2A	A_55_P1985159	Nucleus	transcription regulator
maternally expressed 3	A_55_P2033407	Other	other
mesenchyme homeobox 2	A_51_P383001	Nucleus	transcription regulator
meprin A, alpha (PABA peptide hydrolase)	A_55_P2067707	Plasma Membrane	peptidase
meprin A, beta	A_55_P2220748	Plasma Membrane	peptidase
meningioma expressed antigen 5 (hyaluronidase)	A_55_P2333126	Cytoplasm	enzyme
mindbomb E3 ubiquitin protein ligase 2	A_55_P1963900	Nucleus	transcription regulator
mast cell immunoglobulin like receptor 1	A_55_P2109485	Plasma Membrane	other
myeloid leukemia factor 1	A_51_P205106	Nucleus	other
MLX interacting protein-like	A_55_P2119957	Nucleus	transcription regulator
MMS22-like, DNA repair protein	A_55_P2044364	Nucleus	other
meningioma (disrupted in balanced translocation) 1	A_55_P2174935	Nucleus	other
membrane-spanning 4-domains, subfamily A, member 4B	A_55_P2135980	Plasma Membrane	other
mitochondrial fission regulator 2	A_55_P1997300	Cytoplasm	other
v-myc avian myelocytomatosis viral oncogene homolog	A_52_P108346	Nucleus	transcription regulator
myosin, heavy chain 7, cardiac muscle, beta	A_55_P2093232	Cytoplasm	enzyme
neuron navigator 1	A_52_P201551	Other	enzyme
nucleolin	A_52_P620748	Nucleus	other
NADPH dependent diflavin oxidoreductase 1	A_55_P2082604	Cytoplasm	enzyme
NDRG family member 4	A_55_P2019483	Other	other
negative elongation factor complex member C/D	A_55_P1982156	Nucleus	other
NEL-like 1 (chicken)	A_55_P1967500	Extracellular Space	growth factor
neutralized E3 ubiquitin protein ligase 1B	A_55_P2011727	Other	other
nuclear factor I/B	A_55_P2086682	Nucleus	transcription regulator
NME/NM23 family member 5	A_55_P1966102	Other	kinase
neuropeptide B	A_55_P1952076	Extracellular Space	other
neuronal pentraxin chromo domain	A_55_P2147846	Plasma Membrane	other
nephrosis 2, idiopathic, steroid-resistant (podocin)	A_55_P1996484	Plasma Membrane	other
neurensin 1	A_51_P448784	Plasma Membrane	other
5'-nucleotidase domain containing 3	A_51_P507023	Other	other
neurotensin receptor 1 (high affinity)	A_55_P2005655	Plasma Membrane	G-protein coupled r contulakin-G
neurexophilin 3	A_51_P254262	Extracellular Space	other
oncomodulin	A_55_P2073825	Cytoplasm	other
2-oxoglutarate and iron-dependent oxygenase domain containing 1	A_55_P2063166	Other	other
odd-skipped related transcription factor 2	A_51_P499599	Nucleus	transcription regulator
p21 protein (Cdc42/Rac)-activated kinase 4	A_55_P2117731	Cytoplasm	kinase
PAP associated domain containing 5	A_55_P1996988	Nucleus	enzyme
progesterin and adipoQ receptor family member V	A_52_P421344	Other	other
progesterin and adipoQ receptor family member VI	A_55_P1971025	Plasma Membrane	other
par-3 family cell polarity regulator	A_55_P1985015	Plasma Membrane	other
parkin RBR E3 ubiquitin protein ligase	A_55_P1978226	Cytoplasm	enzyme
phenazine biosynthesis-like protein domain containing	A_55_P1956063	Cytoplasm	enzyme
pre-B-cell leukemia homeobox 1	A_55_P1953998	Nucleus	transcription regulator
protocadherin 17	A_52_P111031	Other	other
protocadherin 19	A_52_P432969	Extracellular Space	other
protocadherin 8	A_51_P274488	Plasma Membrane	other
piccolo presynaptic cytomatrix protein	A_55_P2014755	Cytoplasm	transporter
Purkinje cell protein 4	A_51_P253984	Cytoplasm	other
proprotein convertase subtilisin/kexin type 2	A_51_P229613	Extracellular Space	peptidase
proprotein convertase subtilisin/kexin type 9	A_51_P397673	Extracellular Space	peptidase
pyruvate dehydrogenase (lipoamide) beta	A_55_P1953972	Cytoplasm	enzyme
pyruvate dehydrogenase phosphatase catalytic subunit 1	A_55_P2033055	Cytoplasm	phosphatase
PDZ domain containing 1	A_65_P16483	Plasma Membrane	transporter
pseudopodium-enriched atypical kinase 1	A_55_P2154307	Plasma Membrane	kinase
PERP, TP53 apoptosis effector	A_51_P317941	Plasma Membrane	other
phosphoglucomutase 2-like 1	A_55_P2150108	Cytoplasm	enzyme
phosphatidylinositol glycan anchor biosynthesis, class T	A_55_P1987439	Cytoplasm	enzyme
pipecolic acid oxidase	A_51_P337195	Cytoplasm	enzyme
pleckstrin homology domain containing, family G (with RhoGef domain) member 3	A_55_P1974961	Other	other
paraneoplastic Ma antigen 2	A_52_P596595	Nucleus	transporter
protection of telomeres 1	A_55_P2115458	Nucleus	other
POU domain, class 3, transcription factor 1	A_55_P1961152	Nucleus	transcription regulator
protein tyrosine phosphatase, receptor type, f polypeptide (PTPRF), interacting protein (liprin), alpha 4	A_55_P1963002	Plasma Membrane	other
protein phosphatase, Mg ²⁺ /Mn ²⁺ dependent, 1K	A_55_P1968606	Cytoplasm	phosphatase
protein phosphatase 1, regulatory subunit 13B	A_55_P1973965	Cytoplasm	phosphatase
protein phosphatase 1, regulatory subunit 3B	A_55_P1967133	Cytoplasm	other
protein kinase C, alpha	A_66_P105791	Cytoplasm	kinase
protein kinase C, beta	A_65_P20249	Cytoplasm	kinase
pregnancy specific glycoprotein 18	A_55_P2067741	Extracellular Space	other

proteasome (prosome, macropain) activator subunit 3 (PA28 gamma; Ki)	A_55_P2020572	Cytoplasm	peptidase	
protein tyrosine phosphatase, non-receptor type 5 (striatum-enriched)	A_55_P1955726	Plasma Membrane	phosphatase	
protein tyrosine phosphatase, receptor type, O	A_55_P2227355	Plasma Membrane	phosphatase	
protein tyrosine phosphatase, receptor type, S	A_55_P1991985	Plasma Membrane	phosphatase	
quinolinolate phosphoribosyltransferase	A_51_P394014	Cytoplasm	enzyme	atorvastatin/niacin,
R3H domain containing-like	A_55_P2096545	Other	other	
RAB3B, member RAS oncogene family	A_55_P2125311	Cytoplasm	enzyme	
RAB43, member RAS oncogene family	A_65_P09032	Cytoplasm	enzyme	
RAD51 paralog C	A_55_P1955891	Nucleus	enzyme	
Ral GEF with PH domain and SH3 binding motif 1	A_55_P2094626	Cytoplasm	other	
RNA binding protein, fox-1 homolog (<i>C. elegans</i>) 1	A_55_P1953400	Cytoplasm	other	
RNA binding motif protein 47	A_55_P1959305	Other	other	
ret proto-oncogene	A_55_P2160676	Plasma Membrane	kinase	sunitinib, motesanib
regulator of G-protein signaling 10	A_51_P218774	Cytoplasm	other	
ribosomal modification protein rimK-like family member A	A_52_P69194	Cytoplasm	other	
regulating synaptic membrane exocytosis 3	A_55_P2143251	Plasma Membrane	other	
Ras and Rab interactor 2	A_55_P2013996	Cytoplasm	other	
receptor-interacting serine-threonine kinase 3	A_51_P491987	Plasma Membrane	kinase	
ripply transcriptional repressor 2	A_66_P125741	Nucleus	other	
ribonuclease, RNase A family, 4	A_51_P237383	Extracellular Space	enzyme	
ring finger protein 213	A_51_P159503	Cytoplasm	enzyme	
roundabout, axon guidance receptor, homolog 2 (<i>Drosophila</i>)	A_55_P2083929	Plasma Membrane	transmembrane receptor	
receptor tyrosine kinase-like orphan receptor 2	A_66_P131398	Plasma Membrane	kinase	
rabphilin 3A-like (without C2 domains)	A_55_P2027157	Plasma Membrane	other	
radial spoke head 1 homolog (<i>Chlamydomonas</i>)	A_55_P2044684	Nucleus	other	
receptor (chemosensory) transporter protein 4	A_51_P304170	Plasma Membrane	other	
runt-related transcription factor 1; translocated to, 1 (cyclin D-related)	A_52_P612137	Nucleus	transcription regulator	
S100 calcium binding protein G	A_55_P2013236	Cytoplasm	other	
Sin3A-associated protein, 25kDa	A_52_P38964	Other	other	
sodium channel, voltage gated, type VIII, alpha subunit	A_55_P2057132	Plasma Membrane	ion channel	riluzole
secretin	A_51_P234359	Extracellular Space	other	
signal peptide, CUB domain, EGF-like 1	A_55_P2299524	Plasma Membrane	transmembrane receptor	
scleraxis basic helix-loop-helix transcription factor	A_51_P380432	Nucleus	other	
sema domain, immunoglobulin domain (Ig), transmembrane domain (TM) and short cytoplasmic domain (Ig), transmembrane domain (TM) and short cytoplasmic domain (Ig)	A_55_P1953866	Plasma Membrane	other	
sema domain, immunoglobulin domain (Ig), transmembrane domain (TM) and short cytoplasmic domain (Ig), transmembrane domain (TM) and short cytoplasmic domain (Ig)	A_51_P331003	Plasma Membrane	other	
sema domain, transmembrane domain (TM), and cytoplasmic domain, (semaphorin) 6C	A_55_P2156126	Plasma Membrane	other	
sema domain, transmembrane domain (TM), and cytoplasmic domain, (semaphorin) 6D	A_55_P2125351	Plasma Membrane	other	
septin 3	A_55_P2072110	Cytoplasm	enzyme	
serpin peptidase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 1	A_55_P2165414	Extracellular Space	other	
serpin peptidase inhibitor, clade B (ovalbumin), member 8	A_55_P2027012	Cytoplasm	other	
serpin peptidase inhibitor, clade F (alpha-2 antiplasmin, pigment epithelium derived factor), member 2	A_55_P1956497	Extracellular Space	other	
serum/glucocorticoid regulated kinase 2	A_55_P2042923	Cytoplasm	kinase	
N-sulfoglucosamine sulfohydrolase	A_55_P2028571	Cytoplasm	enzyme	
shisa family member 2	A_51_P408649	Other	other	
src kinase associated phosphoprotein 1	A_55_P2059110	Cytoplasm	kinase	
selection and upkeep of intraepithelial T cells 8	A_55_P2120388	Other	other	
solute carrier family 14 (urea transporter), member 2	A_55_P1964028	Plasma Membrane	transporter	
solute carrier family 1 (glutamate/neutral amino acid transporter), member 4	A_55_P2109589	Plasma Membrane	transporter	riluzole
solute carrier family 22 (organic anion transporter), member 6	A_51_P360655	Plasma Membrane	transporter	colchicine/probenecid
solute carrier family 23, member 3	A_55_P1964752	Other	transporter	
solute carrier family 26 (anion exchanger), member 11	A_51_P113403	Cytoplasm	transporter	
solute carrier family 29 (equilibrative nucleoside transporter), member 4	A_55_P2048119	Plasma Membrane	transporter	
Slc2a4 regulator, pseudogene	A_55_P2293351	Other	other	
solute carrier family 32 (GABA vesicular transporter), member 1	A_52_P138926	Plasma Membrane	transporter	tiagabine
solute carrier family 34 (type II sodium/phosphate contranporter), member 1	A_51_P498442	Plasma Membrane	transporter	
solute carrier family 35, member G1	A_55_P1959828	Plasma Membrane	other	
solute carrier family 37 (glucose-6-phosphate transporter), member 4	A_51_P385598	Cytoplasm	transporter	
solute carrier family 38, member 5	A_55_P2010641	Plasma Membrane	transporter	
solute carrier family 4, sodium borate transporter, member 11	A_66_P121976	Plasma Membrane	transporter	
solute carrier family 6 (neurotransmitter transporter), member 13	A_51_P438083	Plasma Membrane	transporter	tiagabine
solute carrier family 8 (sodium/calcium exchanger), member 2	A_55_P2095563	Cytoplasm	transporter	
slit homolog 1 (<i>Drosophila</i>)	A_55_P1958379	Extracellular Space	other	
sarcolipin	A_52_P413395	Cytoplasm	other	
SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 2	A_55_P2007802	Nucleus	transcription regulator	
small integral membrane protein 24	A_55_P2031403	Cytoplasm	other	
sushi, nidogen and EGF-like domains 1	A_52_P550147	Plasma Membrane	other	
superoxide dismutase 3, extracellular	A_55_P2077558	Extracellular Space	enzyme	
sclerostin domain containing 1	A_55_P2158121	Extracellular Space	other	
SP110 nuclear body protein	A_55_P2066792	Nucleus	other	
Sp5 transcription factor	A_51_P404193	Nucleus	other	
sperm associated antigen 7	A_55_P2102365	Nucleus	other	
serine peptidase inhibitor, Kazal type 1	A_51_P365516	Extracellular Space	other	

sparc/osteonectin, cwcv and kazal-like domains proteoglycan (testican) 2	A_52_P221756	Extracellular Space other
secreted phosphoprotein 2, 24kDa	A_55_P2179676	Extracellular Space other
splicing regulatory glutamine/lysine-rich protein 1	A_55_P1966372	Nucleus other
ST3 beta-galactoside alpha-2,3-sialyltransferase 6	A_51_P281333	Cytoplasm enzyme
stabinil 2	A_55_P1974028	Plasma Membrane transmembrane receptor
six transmembrane epithelial antigen of the prostate 1	A_51_P484158	Plasma Membrane transporter
STEAP family member 2, metalloreductase	A_55_P2133315	Plasma Membrane transporter
stromal interaction molecule 1	A_55_P2005982	Plasma Membrane ion channel
stathmin 2	A_55_P2068673	Plasma Membrane other
syntaxis binding protein 1	A_55_P2077188	Cytoplasm transporter
sulfotransferase family 1D, member 1	A_55_P2181542	Cytoplasm enzyme
suppressor of variegation 3-9 homolog 2 (Drosophila)	A_55_P2072403	Nucleus transcription regulator
SVOP-like	A_51_P316902	Other other
synaptojanin 1	A_55_P1955517	Cytoplasm phosphatase
synaptopodin 2-like	A_55_P1968863	Cytoplasm other
T-box 3	A_55_P1969002	Nucleus transcription regulator
transcription elongation factor A (SII)-like 5	A_66_P104980	Other other
transcription factor 24	A_55_P2106608	Other other
t-complex 11, testis-specific-like 2	A_51_P497317	Other other
teneurin transmembrane protein 4	A_55_P2141088	Plasma Membrane other
transcription factor EB	A_55_P1997898	Nucleus transcription regulator
transglutaminase 5	A_55_P1958487	Cytoplasm enzyme
threonine synthase-like 2 (S. cerevisiae)	A_52_P487599	Other other
Thy-1 cell surface antigen	A_55_P2072035	Plasma Membrane other
T-cell lymphoma invasion and metastasis 2	A_51_P256066	Cytoplasm enzyme
tubulointerstitial nephritis antigen	A_51_P283004	Extracellular Space peptidase
transmembrane protein 174	A_51_P492346	Other other
transmembrane protein 213	A_51_P401501	Other other
transmembrane protein 239	A_55_P2046253	Other other
transmembrane protein 25	A_55_P2126572	Extracellular Space other
transmembrane protein 254c	A_55_P1967553	Other other
transmembrane protein 27	A_55_P2042753	Plasma Membrane other
transmembrane protein 59-like	A_51_P215038	Cytoplasm other
transmembrane protein 8B	A_55_P2043932	Plasma Membrane other
transmembrane protease, serine 3	A_55_P2011151	Plasma Membrane peptidase
tumor necrosis factor receptor superfamily, member 10a	A_55_P2027836	Plasma Membrane transmembrane rec trm-1
tumor necrosis factor receptor superfamily, member 9	A_55_P2029061	Plasma Membrane transmembrane rec urelumab
troponin I type 1 (skeletal, slow)	A_52_P657360	Cytoplasm other
trophoblast glycoprotein	A_55_P2098200	Plasma Membrane other
TNF receptor-associated factor 1	A_51_P343833	Cytoplasm other
thyrotropin-releasing hormone	A_55_P2071349	Extracellular Space other
tribbles pseudokinase 3	A_55_P2009988	Nucleus kinase
tripartite motif containing 25	A_55_P2098076	Cytoplasm transcription regulator
tetraspanin 17	A_55_P2067453	Other enzyme
weety family member 2	A_55_P1985768	Other ion channel
tubulin, beta 2B class IIb	A_55_P2034864	Cytoplasm other brentuximab vedotin
twist family bHLH transcription factor 2	A_51_P165504	Nucleus transcription regulator
ubiquitin-conjugating enzyme E2I	A_55_P2326517	Nucleus enzyme
upstream binding transcription factor, RNA polymerase I	A_55_P1992680	Nucleus transcription regulator
UDP glucuronosyltransferase 1 family, polypeptide A6	A_55_P1962404	Cytoplasm enzyme
UDP glucuronosyltransferase 2 family, polypeptide B10	A_55_P1977418	Cytoplasm enzyme
UDP glucuronosyltransferase 2 family, polypeptide B28	A_66_P131389	Cytoplasm enzyme
UNC homeobox	A_55_P2022241	Other transcription regulator
uracil-DNA glycosylase	A_55_P2040878	Nucleus enzyme
ubiquitin specific peptidase 51	A_55_P2176953	Other peptidase
vesicle amine transport 1-like	A_52_P577533	Other enzyme
vascular endothelial growth factor C	A_51_P433870	Extracellular Space growth factor
villin 1	A_52_P260555	Cytoplasm other
WD repeat and FYVE domain containing 1	A_55_P2092730	Cytoplasm other
WDFY family member 4	A_52_P199614	Other other
WD repeat domain 89	A_55_P2056280	Other other
WSC domain containing 2	A_52_P173442	Other other
X-prolyl aminopeptidase (aminopeptidase P) 2, membrane-bound	A_55_P1985950	Plasma Membrane peptidase
Y box binding protein 2	A_55_P1973447	Cytoplasm translation regulator
zinc finger, CCHC domain containing 9	A_55_P2146708	Other other
zinc finger protein 133, pseudogene	A_55_P2161675	Other other
zinc finger protein 941	A_55_P2109479	Other other
zinc finger protein, FOG family member 1	A_55_P2048518	Nucleus transcription regulator
zinc finger protein, FOG family member 2	A_51_P336509	Nucleus transcription regulator
zinc finger, matrin-type 4	A_51_P422685	Nucleus other
zinc finger protein 512B	A_55_P2044252	Nucleus other
zinc finger protein 536	A_51_P218953	Other other

zinc finger protein 703
zinc finger, SWIM-type containing 8

A_66_P126332 Nucleus other
A_55_P2039180 Extracellular Space other

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654231	18261	25503
55239	270086	307657
116039	107587	315039
10298	70584	292756
64282	214627	307745
54852	74090	315741
79957	68957	681021
56288	93742	81918
5071	50873	56816
64081	68371	171564 100360692
5087	18514	304947
27253	219228	306055
57526	279653	317183
5100	18530	64865
27445	26875	56768
5121	18546	25510
5126	18549	25121
255738	100102	298296
5162	68263	289950
54704	381511	54705
5174	59020	65144
79834	244895	315686
64065	64058	292949
283209	70974	685076
51604	78928	296360
51268	19193	303272
26030	263406	314249
10687	239157	305977
25913	101185	500054
	18991	
	68507	140592
152926	243382	312381
23368	21981	314465
79660	244416	192280
5578	18750	24680
5579	18751	25023
	56868 243862 26438 72242 26437 434540 114871 114868 574429 26439 545925	

10197	19192	287716
84867	19259	29644
5800	19277	50677
5802	19280	25529
23475	67375	293504
140902	100043899	366245
5865	69908	81755
339122	69834	500249
5889	114714	497976
9649	241308	100361774
54715	268859	302920
54502	245945	305340
5979	19713	24716
6001	67865	54290
284716	194237	
9783	242662	65025
54453	74030	311494
11035	56532	246240
134701	382089	363111
6038	58809	56759
57674	672511	303735
6092	268902	84409
4920	26564	306782
9501	380714	171123
89765	22092	361818
64108	67775	360733
862	12395	362489
795	12309	24249
100316904	751865	288559
6334	20273	29710
	20287	24769
80274	64706	315174
642658	20289	680712
54910	20353	301346
57715	26456	361764
10500	20360	29744
80031	214968	311384
55964	24050	56003
5265	20703 20704 20704 24648	
5271	20725	288937
5345	18816	287527
10110	27219	171497
6448	27029	
387914	219134	498528
8631	78473	286975
	639774 328505	689792
8170	27411	54302
6509	55963	305540
9356	18399	29509
151295	22626	367298
284129	268512	360670
222962	243328	288499
	329584	
140679	22348	83612
6569	20505	25548
159371	240660	294072
2542	14385	29573
92745	209837	192208
83959	269356	311423
6540	14412	171163
6543	110891	140447
6585	20562	65047
6588	66402	
6595	67155	361745
284422	72273	100366121
25992	208777	316638
6649	20657	25352
25928	66042	266803
3431	109032 546061 62 301570	
389058	64406	296510
9552	216873	303260
6690	20730	

9806	94214	361840
6694	75396	94168
140890	218543	56763
10402	54613	304023
55576	192188	282580
26872	70358	297738
261729	74051	312052
6786	20866	361618
11075	20257	84510
6812	20910	25558
	53315	60393
79723	64707	364785
136306	320590	500085
8867	104015	85238
79933	68760	305675
6926	21386	353305
340543	331532	680282
100129654	100039596	680678
255394	216198	314683
26011	23966	308831
7942	21425	316214
9333	74176	691932
55258	232078	297332
7070	21838	24832
26230	24001	100362710
27283	26944	300846
134288	68344	499516
155006	77522	689748
100288797	66766	688109
84866	71687	689172
	100039257 66039 100039192	
57393	57394	57395
25789	67937	306349
51754	242409	313490
64699	140765	309665
8797	21933	364420
3604	21942	500590
7135	21952	29388
7162	21983	83684
7185	22029	687813
7200	22044	25569
57761	228775	246273
7706	217069	494338
26262	74257	306771
94015	117160	287803
347733	73710	291081
117581	13345	59327
7329	22196	25573
7343	21429	25574
54578	94284 394435	113992
7365	100727	305264
54490	22238 100559 1124	24862
340260	22255	29375
7374	22256	304577
158880	635253	317398
57687	270097	361414
7424	22341	114111
7429	22349	316521
57590	69368	
57705	545030	498582
112840	72338	314243
9671	320916	360824
7512	170745	117522
51087	53422	303250
84240	69085	309986
	668917	
	407812	
161882	22761	691504
23414	22762	314930
79698	320158	684961
57473	269401	311721
9745	243937	292820

80139	353310	680717
23053	268721	361004

Table S2. Microarray and nanostring data

Gene Symbol	Microarray Expression FC	Nanostring Expression FC	qRT-PCR Expression FC	IF	ISH
	p<0.05 highlighted in Red font				
Cited1	-6.016	-8.828			
Cox6b2	1.653	1.854			
Pdgfra	1.417	2.352			
Col1a1	1.53	1.612			
Slc16a2	1.452	1.867			
Col6a1	1.418	1.783			
Col6a2	1.408	1.768			
Odc1	1.352	-1.150			
Col1a2	1.376	1.483			
Pck1	-6.002	1.333			
Tbp	1.192	1.356			
Idh1	#N/A	-1.318			
Col6a3	#N/A	1.924			
Meox1	#N/A	-1.907			
Cyp2s1	#N/A	1.418			
Igfbp6	#N/A	1.559			
Pgm1	#N/A	1.466			
Cyp4a10	#N/A	-1.943			
Rras	#N/A	1.540			
Cyp2d26	#N/A	-1.379			
Aldob	#N/A	-1.554			
B2m	#N/A	1.376			
Osr1	#N/A	1.727			
Fbp1	#N/A	-1.879			
Alas1	#N/A	1.170			
Arhgap5	#N/A	1.270			
Tbx2	#N/A	1.357			
Gpd2	#N/A	-1.236			
Pck2	#N/A	1.263			
Ctgf	#N/A	-1.411			
Gpd1	#N/A	-1.395			
Ppp1r14a	#N/A	1.948			
Elf4	#N/A	1.578			
Mef2c	#N/A	1.277			
Ogdh	#N/A	1.128			
Fgfr4	#N/A	-1.280			
Fgf1	#N/A	-1.825			
Ntrk1	#N/A	1.954			

Eno1	#N/A	1.075			
Pdgfrb	#N/A	1.264			
Aldoa	#N/A	1.118			
Socs2	#N/A	1.542			
Trp53	#N/A	1.143			
Bmp2	#N/A	1.262			
Ldha	#N/A	1.100			
Six2	#N/A	1.064			
Mapkapk3	#N/A	1.307			
Atp5j2	#N/A	1.057			
Igfbp3	#N/A	-1.165			
H6pd	#N/A	1.091			
Acta2	#N/A	1.168			
Cdkn1a	#N/A	1.326			
Chrd	#N/A	1.577			
Pax2	#N/A	1.108			
Tpi1	#N/A	1.271			
Cldn5	#N/A	1.072			
Gm5506	#N/A	1.361			
Hprt	#N/A	1.077			
Ndufs5	#N/A	1.061			
Igfbp7	#N/A	-1.030			
Pklr	#N/A	-1.133			
Aldoc	#N/A	1.109			
Rps6ka3	#N/A	1.025			
Pfkl	#N/A	1.065			
Sgk1	#N/A	1.030			
Cldn6	#N/A	1.013			
Atp5j	#N/A	-1.006			
Pgk1	#N/A	1.010			
Gapdh	#N/A	-1.000			