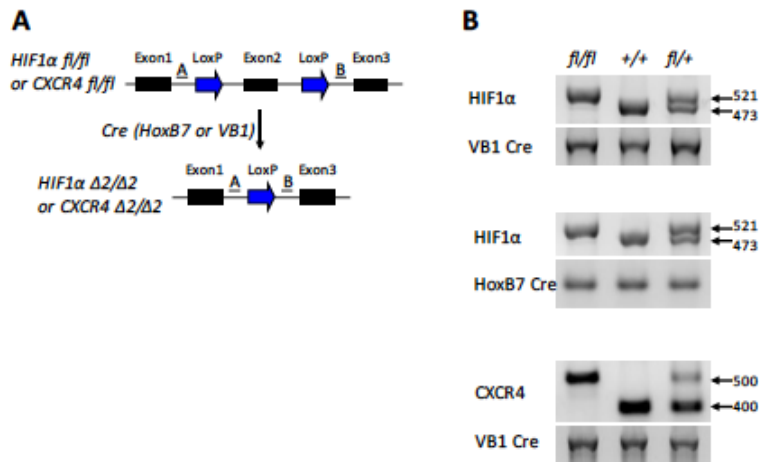
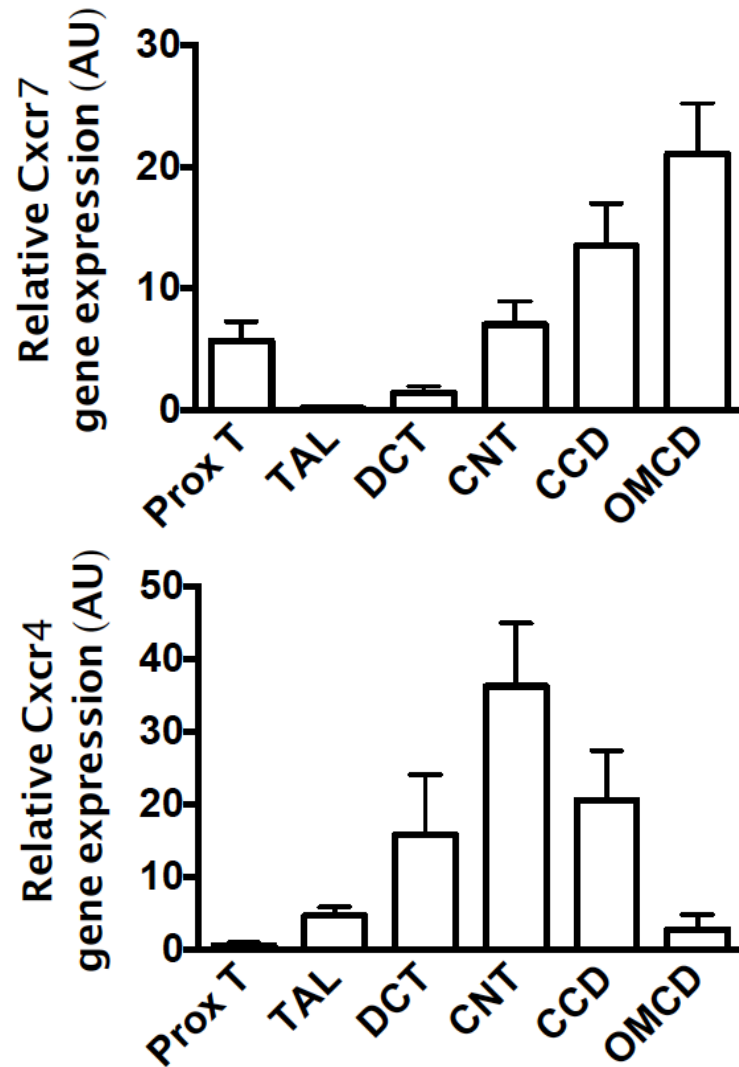


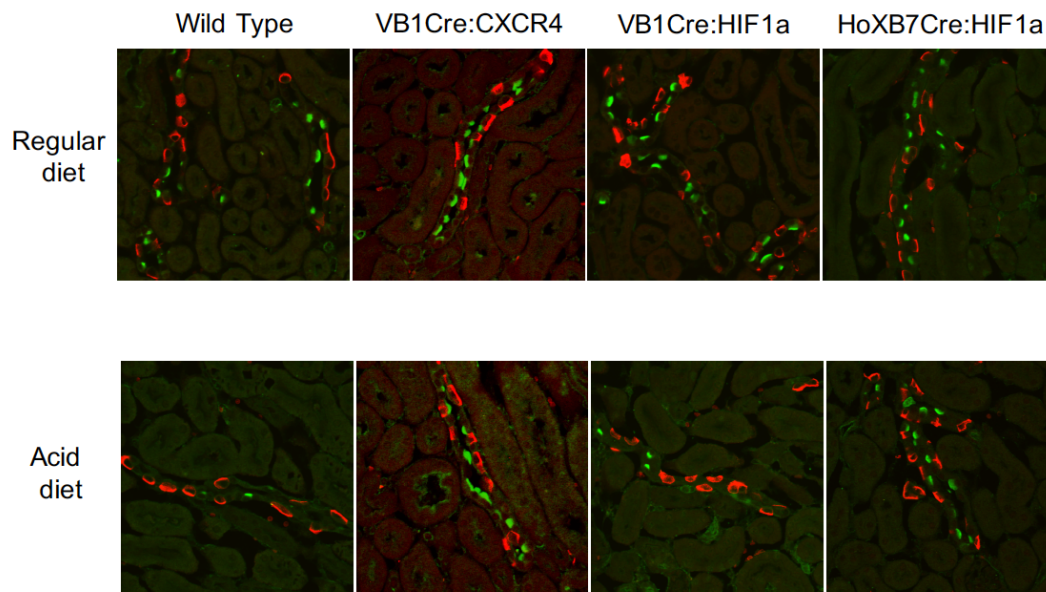


Supplementary Figure 1. HIF1 α and CXCR4 conditional knock-out mice (A) Schematic of the *HIF1 α fl/fl* or *CXCR4 fl/fl* allele showing the location of the LoxP sites flanking exon 2 and the primers (A,B) used for genotyping. (B) PCR of tail DNA using primers A and B reveals the expected band at 473 bp in wild-type mice, 521 bp in *HIF1 α fl/fl* mice, and both bands in heterozygotes; or 400 bp in wild-type mice, 500 bp in *CXCR4 fl/fl* mice, and both bands in heterozygotes. All three contain the Cre recombinase gene.



Supplementary Figure 2: Expression of CXCR4 and CXCR7 along the nephron. qPCR normalized to Rpl26, a housekeeping gene. Microdissected nephron segments from 5 mice were used for qPCR and the data displayed as mean $\pm$ SE.

ProxT, proximal tubule, TAL, thick ascending limb, DCT distal convoluted tubule, CNT, connecting tubule, CCD cortical collecting duct, OMCD, outer medullary collecting duct.



Supplementary Figure 3. Representative images of staining in kidney cortex of mutant mice and their littermates (termed wild type here) fed a normal diet or an acid diet. Sections were stained for **AE1 (red)** and **pendrin (green)**. The results of individual studies and averages are presented in [Supplementary Table 3](#) and [Figure 5](#) (in the main text). Magnification x400

Supplementary Table 1. Growth Factor Microarray. mRNA was isolated from kidney cortex of wild type mice given either an acid or a normal diet for 3 days. Results in bold where the expression was greater than two fold were later subjected to qPCR analysis of mRNA isolated from mice fed a normal and an acid diet.

Gene Symbol	Well	AVG ΔC_t (Ct(GOI) - Ave Ct (HKG))		$2^{-\Delta C_t}$		Fold Difference	
		Acid diet	Normal diet	Acid diet	Normal Diet	Acid diet/Normal Diet	
Amh	A01	12.96	12.98	1.3E-04	1.2E-04	1.01	
Artn	A02	9.66	9.28	1.2E-03	1.6E-03	0.77	
Bdnf	A03	6.16	7.68	1.4E-02	4.9E-03	2.87	
Bmp1	A04	5.36	5.18	2.4E-02	2.8E-02	0.88	
Bmp10	A05	12.96	12.98	1.3E-04	1.2E-04	1.01	
Bmp2	A06	8.66	9.28	2.5E-03	1.6E-03	1.54	
Bmp3	A07	8.36	8.28	3.0E-03	3.2E-03	0.95	
Bmp4	A08	2.56	2.68	1.7E-01	1.6E-01	1.09	
Bmp5	A09	8.76	8.68	2.3E-03	2.4E-03	0.95	
Bmp6	A10	2.76	2.48	1.5E-01	1.8E-01	0.82	
Bmp7	A11	3.96	4.08	6.4E-02	5.9E-02	1.09	
Bmp8a	A12	7.56	8.18	5.3E-03	3.4E-03	1.54	
Bmp8b	B01	12.96	12.98	1.3E-04	1.2E-04	1.01	
Csf1	B02	5.66	6.08	2.0E-02	1.5E-02	1.34	
Csf2	B03	12.96	12.98	1.3E-04	1.2E-04	1.01	
Csf3	B04	12.96	12.98	1.3E-04	1.2E-04	1.01	
Cxcl1	B05	10.86	11.58	5.4E-04	3.3E-04	1.65	
Cxcl12	B06	-0.14	0.88	1.1E+00	5.4E-01	2.03	
Egf	B07	-2.24	-2.42	4.7E+00	5.4E+00	0.88	
Ereg	B08	12.96	12.98	1.3E-04	1.2E-04	1.01	
Fgf1	B09	0.86	0.88	5.5E-01	5.4E-01	1.01	
Fgf10	B10	8.56	7.78	2.6E-03	4.5E-03	0.58	
Fgf11	B11	8.76	9.18	2.3E-03	1.7E-03	1.34	
Fgf13	B12	8.86	7.88	2.2E-03	4.2E-03	0.51	
Fgf14	C01	12.96	12.98	1.3E-04	1.2E-04	1.01	
Fgf15	C02	12.96	12.98	1.3E-04	1.2E-04	1.01	
Fgf17	C03	12.96	12.98	1.3E-04	1.2E-04	1.01	
Fgf18	C04	6.76	6.78	9.2E-03	9.1E-03	1.01	
Fgf2	C05	6.56	7.68	1.1E-02	4.9E-03	2.17	
Fgf22	C06	12.46	11.38	1.8E-04	3.8E-04	0.47	
Fgf3	C07	12.96	12.98	1.3E-04	1.2E-04	1.01	
Fgf4	C08	12.96	12.98	1.3E-04	1.2E-04	1.01	
Fgf5	C09	12.96	12.98	1.3E-04	1.2E-04	1.01	
Fgf6	C10	12.96	12.98	1.3E-04	1.2E-04	1.01	
Fgf7	C11	10.76	9.98	5.8E-04	9.9E-04	0.58	
Fgf8	C12	12.96	12.98	1.3E-04	1.2E-04	1.01	
Fgf9	D01	3.96	4.48	6.4E-02	4.5E-02	1.43	
Figf	D02	6.86	6.98	8.6E-03	7.9E-03	1.09	

Gdf10	D03	5.16	5.68	2.8E-02	2.0E-02	1.43
Gdf11	D04	5.16	5.48	2.8E-02	2.2E-02	1.25
Gdf5	D05	11.76	10.88	2.9E-04	5.3E-04	0.54
Mstn	D06	12.96	12.98	1.3E-04	1.2E-04	1.01
Gdnf	D07	9.16	10.68	1.7E-03	6.1E-04	2.87
Hgf	D08	6.16	6.68	1.4E-02	9.8E-03	1.43
Igf1	D09	6.46	5.88	1.1E-02	1.7E-02	0.67
Igf2	D10	1.76	2.38	3.0E-01	1.9E-01	1.54
II11	D11	11.66	12.18	3.1E-04	2.2E-04	1.43
II12a	D12	12.96	12.98	1.3E-04	1.2E-04	1.01
II18	E01	6.86	6.58	8.6E-03	1.0E-02	0.82
II1a	E02	9.06	9.98	1.9E-03	9.9E-04	1.89
II1b	E03	7.76	8.58	4.6E-03	2.6E-03	1.77
II2	E04	12.96	12.68	1.3E-04	1.5E-04	0.82
II3	E05	12.96	12.98	1.3E-04	1.2E-04	1.01
II4	E06	11.26	10.68	4.1E-04	6.1E-04	0.67
II6	E07	12.96	12.98	1.3E-04	1.2E-04	1.01
II7	E08	10.86	11.68	5.4E-04	3.0E-04	1.77
Inha	E09	8.56	8.18	2.6E-03	3.4E-03	0.77
Inhba	E10	11.16	12.18	4.4E-04	2.2E-04	2.03
Inhbb	E11	9.96	8.68	1.0E-03	2.4E-03	0.41
Kitl	E12	2.76	3.28	1.5E-01	1.0E-01	1.43
Lefty1	F01	8.26	8.78	3.3E-03	2.3E-03	1.43
Lefty2	F02	8.16	9.58	3.5E-03	1.3E-03	2.68
Lep	F03	11.96	8.38	2.5E-04	3.0E-03	0.08
Lif	F04	11.76	12.98	2.9E-04	1.2E-04	2.33
Mdk	F05	2.66	0.78	1.6E-01	5.8E-01	0.27
Ngf	F06	5.56	6.28	2.1E-02	1.3E-02	1.65
Nodal	F07	12.96	12.98	1.3E-04	1.2E-04	1.01
Ntf3	F08	5.36	6.08	2.4E-02	1.5E-02	1.65
Ntf5	F09	11.46	11.28	3.5E-04	4.0E-04	0.88
Pdgfa	F10	5.86	6.48	1.7E-02	1.1E-02	1.54
Pgf	F11	6.96	7.48	8.0E-03	5.6E-03	1.43
Rabep1	F12	3.76	4.68	7.4E-02	3.9E-02	1.89
S100a6	G01	3.86	3.48	6.9E-02	9.0E-02	0.77
Spp1	G02	-1.94	-2.42	3.8E+00	5.4E+00	0.72
Tdgf1	G03	12.96	12.98	1.3E-04	1.2E-04	1.01
Tff1	G04	4.96	4.68	3.2E-02	3.9E-02	0.82
Tgfa	G05	8.16	8.48	3.5E-03	2.8E-03	1.25
Tgfb1	G06	5.46	5.78	2.3E-02	1.8E-02	1.25
Tgfb2	G07	6.66	6.78	9.9E-03	9.1E-03	1.09
Tgfb3	G08	9.16	9.38	1.7E-03	1.5E-03	1.16
Vegfa	G09	1.66	1.98	3.2E-01	2.5E-01	1.25
Vegfb	G10	4.16	4.08	5.6E-02	5.9E-02	0.95
Vegfc	G11	6.56	6.78	1.1E-02	9.1E-03	1.16
Zfp91	G12	5.56	5.88	2.1E-02	1.7E-02	1.25
Gusb	H01	4.76	4.18	3.7E-02	5.5E-02	0.67
Hprt1	H02	0.46	0.78	7.3E-01	5.8E-01	1.25

Hsp90ab1	H03	-1.44	-1.42	2.7E+00	2.7E+00	1.01
Gapdh	H04	-1.94	-1.92	3.8E+00	3.8E+00	1.01
Actb	H05	-1.84	-1.62	3.6E+00	3.1E+00	1.16

Supplementary Table 2.

HIF1 α loxP

NORMAL DIET					ACID DIET				
Total	AE1+	% α	Pds+	% β	VB1+	AE1+	% α	Pds+	% β
1451	821	56.6	630	43.4	1451	1127	77.7	324	22.3
1233	708	57.4	525	42.6	1674	1309	78.2	365	21.8
2011	1120	55.7	891	44.3	1796	1410	78.5	386	21.5
1801	1007	55.9	794	44.1	1833	1448	78.1	401	21.9
AVG		56.4		43.6			78.1		22.9
SD		0.77		0.67			0.29		0.33

VB1Cre:HIF1 α loxP

NORMAL DIET					ACID DIET				
Total	AE1+	% α	Pds+	% β	VB1+	AE1+	% α	Pds+	% β
1809	1009	55.8	800	44.2	1795	1411	78.6	384	21.4
1514	851	56.2	663	43.8	1824	1448	79.4	376	20.6
1765	985	55.8	780	44.2	1534	1207	78.7	327	21.3
1654	926	56	728	44	1423	1131	79.5	292	20.5
AVG		55.9		44.1			79.05		20.95
SD		0.19		0.19			0.46		0.46

HIF1 α loxP

NORMAL DIET					ACID DIET				
Total	AE1+	% α	Pds+	% β	VB1+	AE1+	% α	Pds+	% β
2051	1151	56.1	900	43.9	2258	1757	77.8	501	22.2
1555	866	55.7	689	44.3	1559	1222	78.4	337	21.6
1387	785	56.6	891	43.4	1311	1028	78.4	283	21.6
1836	1036	56.4	794	43.6	2232	1741	78.0	491	22
AVG		56.2		43.8			78.1		21.9
SD		0.39		0.39			0.3		0.3

HoxB7Cre:HIF1 α loxP

NORMAL DIET					ACID DIET				
Total	AE1+	% α	Pds+	% β	VB1+	AE1+	% α	Pds+	% β
1874	1012	54	862	46	2407	1346	55.9	1061	44.1
1927	1056	54.8	871	45.2	2003	1104	55.1	899	44.9
1906	1060	55.6	846	44.4	1888	1054	55.8	834	44.2
1643	904	55	739	45	2346	1323	56.4	1023	43.6
AVG		54.8		45.2			55.8		44.2
SD		0.66		0.66			0.54		0.54

CXCR4:loxP

NORMAL DIET					ACID DIET				
Total	AE1+	% α	Pds+	% β	Total	AE1+	% α	Pds+	% β
2011	1120	55.7	891	44.3	1796	1410	78.5	386	21.5
1801	1007	55.9	794	44.1	1833	1432	78.1	401	21.9
1609	903	56.1	706	43.9	2099	1646	78.4	453	21.6
1514	861	56.9	653	43.1	2103	1661	79.0	442	21.0
AVG		56.2		43.8			78.5		21.5
SD		0.85		0.85			0.37		0.37

VB1Cre:CXCR4 loxP

NORMAL DIET					ACID DIET				
Total	AE1+	% α	Pds+	% β	Total	AE1+	% α	Pds+	% β
1814	713	39.3	110	60.7	2171	938	43.2	1233	56.8
1522	607	39.9	915	60.1	1764	776	44.0	988	56
1366	520	38.1	846	61.9	2216	971	43.8	1245	56.2
1758	677	38.5	1081	61.5	2712	1204	44.4	1508	55.6
AVG		38.9		61.1			43.8		56.2
SD		0.81		0.81			0.5		0.5

Supplementary Table 3. The effect of various gene mutations on the number and proportion of α -IC and β -IC in kidney cortex of mice fed a normal and others fed an acid diet. As can be seen, 4 mice were analyzed in each group. α -IC were defined as those that stain for AE1 and β -IC were those that stained for pendrin. Wild type were littermates of the mutants examined rather than actual wild type mice. See supplementary Figure 3 for an illustrative example.