

SUPPLEMENTAL TABLE OF CONTENTS

This article contains the following supplemental materials:

Supplemental Table 1. Primers used for PCR, QPCR, cloning and vector construction were in list.

Supplemental Table 2. Fetal growth index of the affected fetal (II:4)

Supplemental Table 3. Quality data of WES for the investigated family.

Supplemental Table 4. The LOH regions shared by the two affected fetus.

Supplemental Table 5. The candidate homozygous variants identified in the family.

Supplemental Table 6. Data of 9 litters transmitted from F1 heterozygote ($Npnt^{K260*/WT}$) mice intercross.

Supplemental Table 7. Statistics in body weight and height between the $Npnt^{WT/WT}$ and $Npnt^{K260*/WT}$ mice.

Supplemental Table 8. Statistics in body weight and height between the $Npnt^{WT/WT}$ and $Npnt^{K260*/K260*}$ mice.

Supplemental Figure 1. Ultrasound images of affected fetal (II:2, II:3)

Supplemental Figure 2. Histological analysis of third affected fetus (II:4) at 17th week of gestation after anatomy.

Supplemental Figure 3. Histological analysis of homozygote mice at 0 dpp.

Supplemental Table 1: Primers used for PCR, QPCR, cloning and vector construction were in list.

Gene/Exon:	Forward (5'-3')	Reverse (5'-3')
Human NPNT-P	CCTAGAGCACTGAAAGGTCTCG	GCAAATTCTCAGGGAGGACTCA
NPNT-P1	GAGGATCCCCGGGTACCGGTGCCACCA TGGATTTTCTCCTGGCGCTGGTGC	-
NPNT-P2	-	CACACATTCCACAGGCTAGTTAGCGTTCT TCAGAGCAGTGGCC
NPNT-P3	AGTGCAAATGTAAAGAAGGATACCAG GGTGATGG	-
NPNT-P4	-	GTATCCTTCTTTAACATTGCACTTGTAG GACCCACG
WT-NPNT-P	CAATGACTTGCACTGGGAAC	-
K260ter-NPNT-P	CACCAGCTGCCAGTACACCTC	-
pEGFP-N-3	-	CGTCGCCGTCCAGCTCGACCAG
Plasmid-NPNT-P	TGACCTGCTCCATGGCAAAC	
Ubi-F-P	GGGTCAATATGTAATTTTCAGTG	
Mouse-NPNT-P	TACCTTAACCCACCAGTCATTCTG	AAGCAACCCCTAGACTTTACTCAG
Mouse-SRY-P	CATTTATGGTGTGGTCCCGTG	GTGTGCAGCTCTACTCCAG
Human NPNT- QPCR	GTGTTCAATCCACGGCAACC	CTGGGTCCCTGATTGGTTCC
Human Actb-QPCR	TGACGTGGACATCCGCAAAG	CTGGAAGGTGGACAGCGAGG

Supplemental Table 2: Fetal growth index of the affected fetal (II:4) at the first diagnosis of fetal renal abnormalities by Ultrasound in Maternal and Child Health Hospital of Ji'an City (2018.12.21). The affected fetus showed normal growth index and oligohydramnios. LMP (Last Menstrual Period), GA (Gestation Age callulated by LMP), BPD (BiParietal Diameter), HC (Head Circumference), FL (Femur Length), HL (Humerus Length), AC (Abdomen Circumference), DVP (The depth of the amniotic fluid).

	LMP	GA	BPD (mm)	HC (mm)	FL (mm)	HL (mm)	AC (mm)	DVP(mm)
II:4	2018.8.28	16W+3	32.4 (16W+1)	126.6 (16W+3)	22.2 (16W+5)	19.6 (15W+5)	-	24

Supplemental Table 3: Quality data of WES for the investigated family.

Sample	I:1	I:2	II:1	II:3	II:4
Raw bases(Mb)	15238.56	16610.03	22188.56	18936.36	14852.29
Clean bases(Mb)	14268.24	15311.74	21365.72	18512.95	13288.73
QCrate(%)	93.63	92.18	96.29	97.76	89.47
Average read length	140	138	146	147	129
Average base quality	36	36	36.3	35.8	36
Average insert size	223.4	212.2	196	227.5	199.9
Duplication rate(%)	19.45	20.49	17.85	15.12	22.15
Mapped reads(M)	82	88.57	145.9	107.14	82.57
Accurate mapped bases(Mb)	11385.55	12024.73	21182.17	15652.03	10146.47
Accurate mapping rate(%)	98.69	98.24	99.14	99.2	94.91
Target size	58231156	58231156	58231156	58231156	58231156
Target covered size	58175555	58077532	58077842	58181232	58052500
Coverage rate(%)	99.9	99.74	99.74	99.91	99.69
Target overlaped reads(M)	65.72	71.02	116.37	85.13	59.31
Reads capture rate(%)	80.14	80.18	79.76	79.46	71.83
Target effective bases(Mb)	7795.51	8354.66	16961.47	10366.62	6734.58
Bases capture rate(%)	68.47	69.48	80.07	66.23	66.37
Target mean depth	133.87	143.47	198.21	178.03	115.65
4X coverage rate(%)	99.76	99.58	99.62	99.82	99.42
10X coverage rate(%)	99.29	99.16	99.34	99.55	98.61
20X coverage rate(%)	98.01	98.07	98.56	98.87	96.44
20%X mean depth coverage rate(%)	96.88	96.72	95.57	97.13	95.55
50%X mean depth coverage rate(%)	80.87	80.83	74.68	80.62	78.54
Flank 10%X mean depth coverage rate(%)	13.99	13.8	10.98	13.74	13.03

Supplemental Table 4: The LOH regions (≥ 1 Mb) shared by the two affected fetus (II:3, II:4).

No.	Chr	Start	End	Length
1	1	74929075	76257074	1327999
2	1	241886754	243493907	1607153
3	3	66444615	69036707	2592092
4	3	153202348	154866522	1664174
5	4	106861755	113178966	6317211
6	5	147040822	149003627	1962805
7	9	35906347	37492721	1586374
8	9	92220499	94486331	2265832
9	10	86131659	88213508	2081849

10	11	86209110	88330321	2121211
11	11	99690461	100863319	1172858
12	11	122928952	123988331	1059379
13	12	94694743	96415888	1721145
14	12	117187950	118517275	1329325
15	12	123798133	125473454	1675321
16	14	53527816	55408294	1880478
17	14	60485026	63174891	2689865

Supplemental Table 5: The candidate homozygous variants identified in the family.

Chr	Position	Ref	Alt	Gene	Func.	Func.refGene	I:1	I:2	II:1	II:3	II:4
4	106861755	G	GT	NPNT	exonic	FRAME_SHIFT	Het	Het	Het	Hom	Hom
4	110834537	A	C	EGF	exonic	NON_SYNONYMOUS_CODING	Het	Het	Het	Hom	Hom

Supplemental Table 6. Data of 9 litters transmitted from F1 heterozygote *Npnt*^{K260^{+/}/WT} mice intercrosses. Total offspring=69, ♀=32, ♂=37; WT=17, Heterozygote=37, Homozygote=15

Litters	ID	Sex	Genotype	Weight (D0) (g)	Height (D0) (cm)
1	F1	♂	hom	1.20	2.5
	F2	♀	hom	1.14	2.5
	F3	♂	wt	1.22	2.7
	F4	♂	het	1.35	2.5
	F5	♀	hom	1.19	2.7
	F6	♀	wt	1.22	2.6
	F7	♂	het	1.24	2.7
	F8	♂	wt	1.19	2.7
2	F9	♀	het	1.39	2.7
	F10	♀	wt	1.50	2.8
	F11	♀	hom	1.55	2.8
	F12	♂	het	1.4	2.6
	F13	♂	het	1.5	2.8
	F14	♀	wt	1.49	2.8
3	F15	♀	wt	1.36	2.7
	F16	♀	wt	1.29	2.6
	F17	♂	het	1.58	2.8
	F18	♂	hom	1.36	2.6
	F19	♂	hom	1.24	2.5
	F20	♂	het	1.52	2.7
	F21	♀	het	1.36	2.5
	F22	♀	het	1.34	2.7
	F23	♂	wt	1.38	2.6

	F24	♀	wt	1.29	2.6
	F25	♀	wt	1.38	2.7
4	F26	♀	het	1.34	2.7
	F27	♀	het	1.43	2.7
	F28	♂	hom	1.29	2.8
	F29	♀	het	1.39	2.7
	F30	♀	hom	1.22	2.6
	F31	♀	hom	1.15	2.6
	F32	♂	het	1.36	2.7
	F33	♂	het	1.31	2.7
	F34	♂	het	1.19	2.6
	F35	♀	het	1.21	2.7
5	F36	♀	het	1.35	2.7
	F37	♀	hom	1.58	2.8
	F38	♀	wt	1.51	2.8
6	F39	♂	het	1.25	2.7
	F40	♂	het	1.25	2.7
	F41	♂	wt	1.36	2.7
	F42	♀	wt	1.21	2.8
	F43	♂	het	1.40	2.8
	F44	♂	het	1.36	2.6
	F45	♂	wt	1.24	2.5
	F46	♂	wt	1.25	2.8
	F47	♂	hom	1.32	2.8
	F48	♀	het	1.39	3.0
7	F49	♀	hom	1.41	2.9
	F50	♂	het	1.45	3.0
	F51	♂	het	1.44	2.8
	F52	♂	wt	1.44	2.7
	F53	♀	het	1.50	2.8
	F54	♂	het	1.39	2.9
8	F55	♂	hom	1.39	2.7
	F56	♂	wt	1.49	2.8
	F57	♂	het	1.42	2.7
	F58	♀	het	1.39	2.8
	F59	♂	het	1.24	2.6
	F60	♀	het	1.36	2.8
	F61	♀	het	1.52	3.0
	F62	♂	het	1.41	2.8
9	F63	♀	hom	1.32	2.6
	F64	♂	hom	1.42	2.8

	F65	♂	het	1.26	2.7
	F66	♂	het	1.36	2.8
	F67	♀	het	1.36	2.8
	F68	♀	het	1.42	2.9
	F69	♂	het	1.38	2.8

Supplemental Table 7. Statistics in body weight and height between the *Npnt*^{WT/WT} and *Npnt*^{K260*/WT} mice.

Groups	weight	height
Het (n=37)	1.3732±0.08935	2.7432±0.11912
WT (n=17)	1.3424±0.11311	2.7000±0.09354
t	1.084	1.319
p	0.283	0.193

Supplemental Table 8: Statistics in body weight and height between the *Npnt*^{WT/WT} and *Npnt*^{K260*/K260*} mice.

Groups	weight	height
Hom (n=15)	1.3187±0.13495	2.6800±0.13202
WT (n=17)	1.3424±0.11311	2.7000±0.09654
t	0.691	-0.488
p	0.593	0.630

Figure S1. Ultrasound images of affected fetal (II:2, II:3) detected by Dongguan Maria Maternity Hosiptal in 2016.8 and Maternal and Child Health Hospital of Ji'an County in 2017.5 respectively. (A) The yellow asterisks showed no kidneys, the arraws showed the "lying-down" adrenal glands, LAD and RAD repersented the left adrenal gland and right adrenal gland respectively. (B) The arraws showed no kidneys, LK and RK repersented the left kidney region and right kidney region respectively.

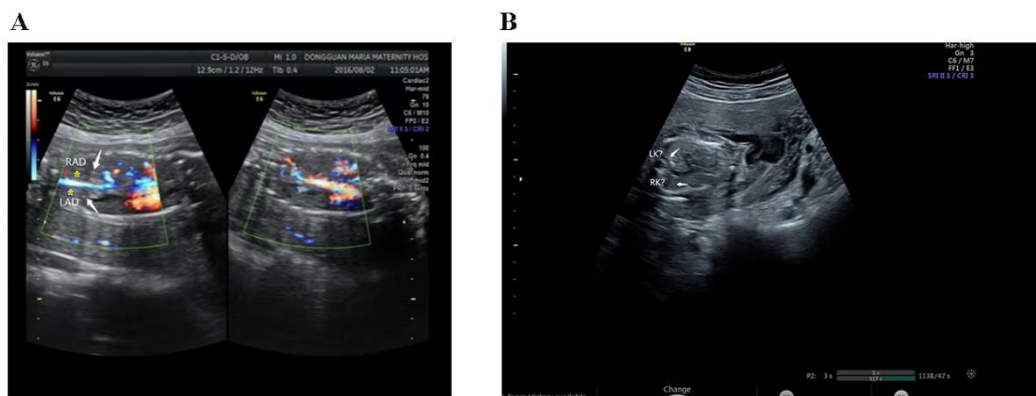


Figure S2: Histological analysis of third affected fetus (II:4) at 17th week of gestation after anatomy. A, B, C, D, E, F, G, H, I, J, K, L are showed as thyroid gland, thymus gland, pancreas, spleen, adrenal gland, lung, heart, vermiform appendix, small intestine, large intestine, pituitary gland and brain, respectively. Because liquefactive necrosis was occurred in liver tissue due to the long-term preservation of the induced labor fetus at

-20°C for 3 month before dissection, the image of fetal liver was not shown in the figure. Scale bars: 100 μ m.

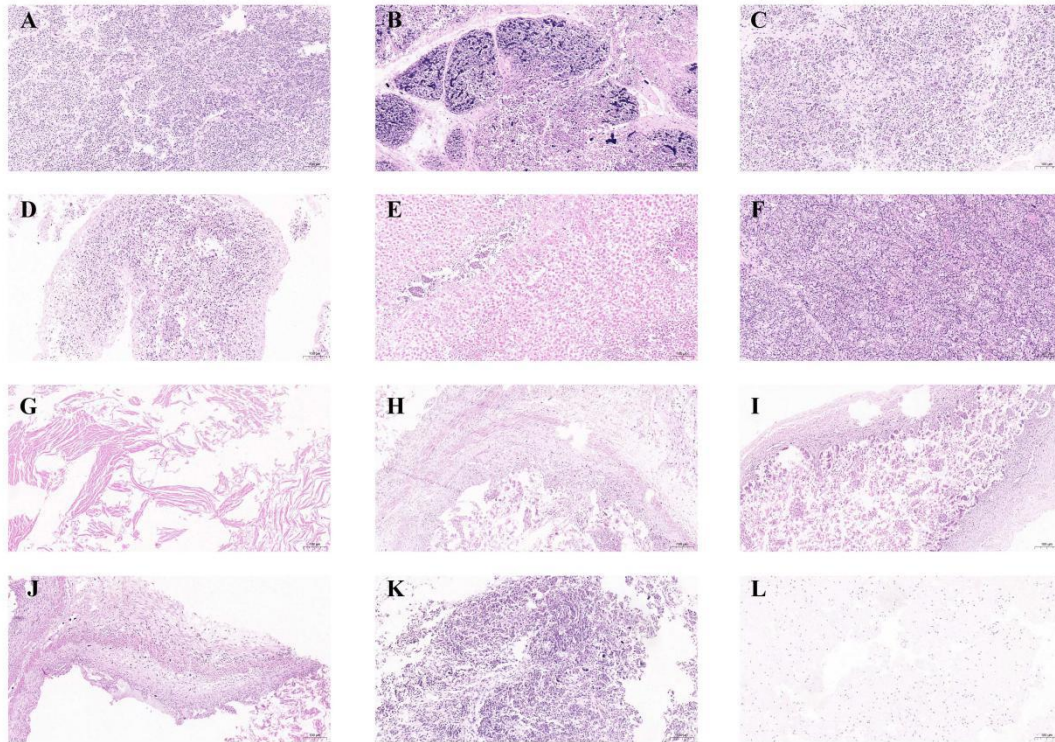


Figure S3: Histological analysis of homozygote mice at 0 day post-partum (dpp). A, B, C, D, E, F, G, H, I and J are showed as brain, heart, liver, spleen, lung, pancreas, stomach, large intestine, small intestine and eye respectively. Scale bars: 100 μ m.

