Supporting Information

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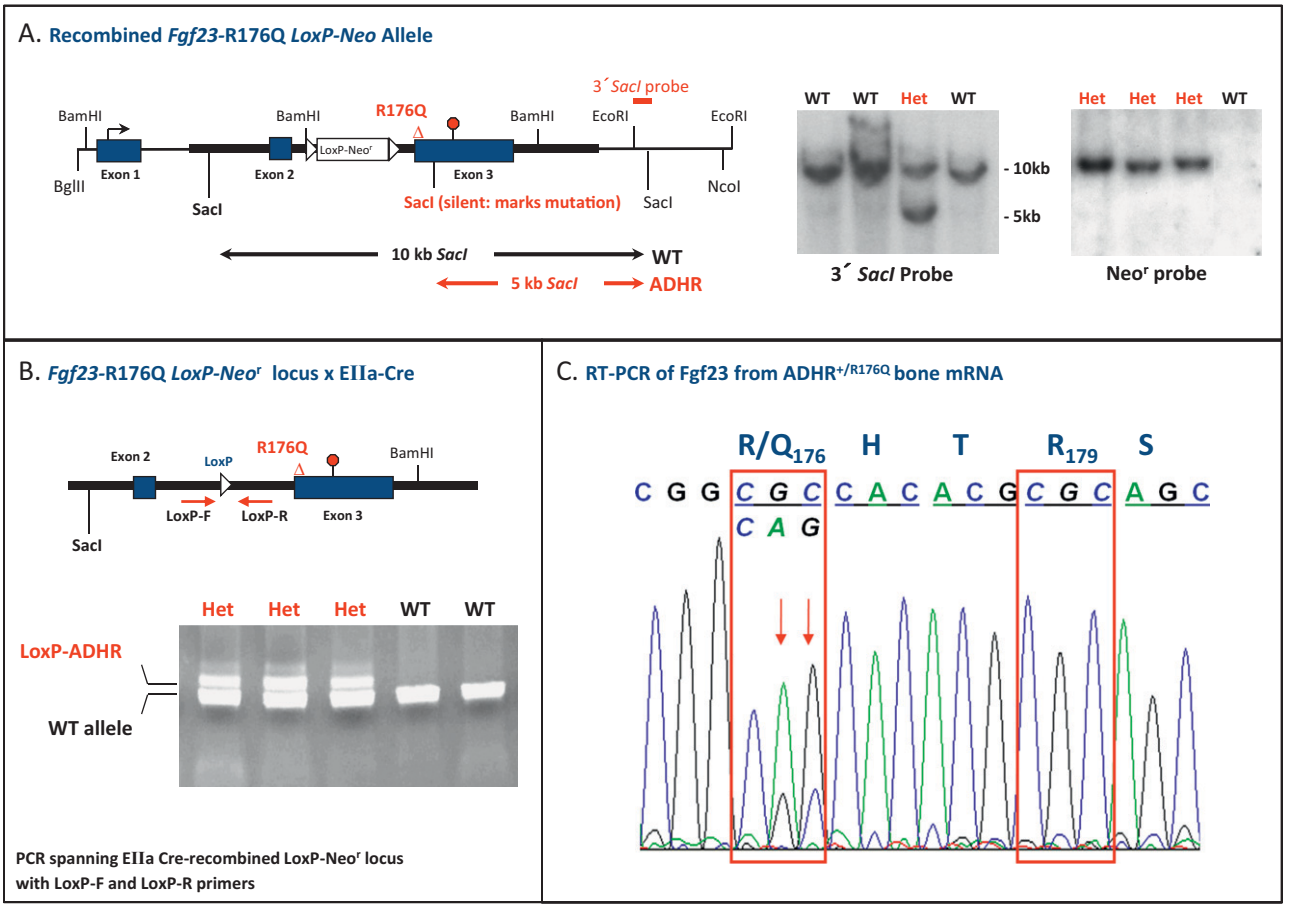

Fig. S1. Gene targeting for development of an autosomal dominant hypophosphatemic rickets (ADHR) mouse carrying the R176Q-fibroblast growth factor 23 (Fgf23) allele. *(A)* (*Left*) Targeting strategy for the mouse R176Q-*Fgf23* ADHR allele. The R176Q ADHR mutation was introduced (triangle) into exon 3 of the mouse *Fgf23* gene. A floxed-neomycin resistance gene (Neo^r) cassette was placed into intron 2, and a silent SacI site was introduced into exon three, 3′ to the R176Q mutation. (*Right*) Southern analyses with SacI digests on DNA lysates from ES cells and a 3′ external probe detected the R176Q-ADHR allele as a 5-kb band, in contrast to the 10-kb WT band. Het, ADHR heterozygous R176Q cells; WT, homozygous wild-type cells. Offspring from founder mice were positive for the floxed-Neo^r cassette. (*B*) The LoxP-Neo^r cassette in the R176Q-ADHR allele was removed by breeding to an EIIa-Cre transgenic mouse as shown by PCR analyses within intron 2. A slightly larger PCR product in the Het mice contained the LoxP site that remained following Cre-mediated recombination. (*C*) Sequence analysis of Fgf23 RT-PCR products from heterozygous ADHR mouse bone mRNA demonstrated properly spliced ADHR-mutant and WT Fgf23 mRNAs (WT codon: cgc; ADHR codon: cag, arrows). The R(Q)$_{176}$HTR$_{179}$/S$_{180}$ protein sequence comprising the Fgf23 SPC site is shown above the sequence traces for orientation.

Table S1. Complete blood cell counts in WT and ADHR mice

Genotype and diet	Mean corpuscular volume (fL)	Mean corpuscular hemoglobin (pg)	Hemoglobin (g/dL)	Hematocrit (%)	Red blood cell distribution width (%)	Red blood cells (M/μL)
WT control diet	46.1 ± 0.68	14.4 ± 0.17	10.2 ± 1.0	32.9 ± 3.19	18.3 ± 0.87	7.1 ± 0.65
WT low-iron diet	38.4 ± 1.20*	10.1 ± 0.16*	7.1 ± 0.68†	27.2 ± 2.87	28.7 ± 1.86†	6.99 ± 0.65
ADHR control diet	45.7 ± 0.56	14.7 ± 0.38	9.5 ± 0.96	29.4 ± 2.81	16.84 ± 0.36	6.44 ± 0.63
ADHR low-iron diet	35.8 ± 1.07*	11.3 ± 0.37*	6.9 ± 0.97‡	21.8 ± 2.99	22.2 ± 1.35‡	6.04 ± 0.78

n = 9–11 mice per cohort.
*$P < 0.001$.
†$P < 0.05$.
‡$P < 0.08$.

Table S2. Biochemistries for heterozygous ADHR mice

Biochemistry	Control diet 8 wk	Low-iron diet 8 wk	Control diet 12 wk	Low-iron diet 12 wk
Intact Fgf23 (pg/mL)	135.4 ± 9.1	86.9 ± 8.3*	123.3 ± 14.0	71.8 ± 15.0*
C-terminal Fgf23 (pg/mL)	356.0 ± 19.5	1297.1 ± 264.2†	327.8 ± 28.0	1687.6 ± 286.0†
Serum phosphorus (mg/dL)	10.3 ± 0.27	8.75 ± 0.38*	10.19 ± 0.37	8.49 ± 0.25*
Serum calcium (mg/dL)	10.1 ± 0.10	10.25 ± 0.10	10.3 ± 0.18	10.3 ± 0.12
Alkaline phosphatase (U/L)	116.1 ± 6.1	136.5 ± 9.1*	100.9 ± 8.6	108.1 ± 5.2
Serum creatinine (mg/dL)	0.34 ± 0.03	0.34 ± 0.04	0.36 ± 0.04	0.37 ± 0.04

n = 11–23 mice per cohort.
*$P < 0.01$.
†$P < 0.0001$.