

Table S1. Studies of bone and/or cardiovascular remodeling in rodent models of CKD-MBD

Reference	Model (relevant CKD stage)	Experimental exposure	Phosphate, PTH, FGF23	Bone turnover	Cardiac and vascular remodeling
Iwasaki-Ishizuka et al., 2005	1/2 Nx (S2) 3/4 Nx (S3) 5/6 Nx (S3-4)	Nx, TPTx, PTH infusion	Pi↔ PTH↔	Low (low bone formation rate (BFR), osteoclast (Oc) parameters)	NA
Mathew et al., 2007	LDLR-/- (S3)	Electrocoagulation, high fat diet	Pi↑ PTH↑	Low (low BFR, osteoblast (Ob) number)	NA
Moe et al., 2009	Cy/+ (S3-4)	Phosphate 0,2 or 0,7%	Pi↑ PTH↑ FGF23↑	High (in 0.7% Pi) (high Ob and Oc parameters, fibrosis)	NA
Nikolov et al., 2010	ApoE-/- (S3-4)	Genetic model	Pi↔ PTH↔	Higher bone mass, trabecular bone (TB) volume	NA
Sabbagh et al., 2012	Jck (S2-5)	Genetic model	Pi↑ PTH↑ FGF23↑	High (high BFR, TB, Ob number, mineralization)	NA
Stubbs et al., 2012	Col4a3+/+FGF23+/eGFP (S3)	Genetic model	Pi↑ PTH↑ FGF23↑	High (higher resorption parameters)	NA
Ferreira et al., 2013	5/6 Nx (S3-4)	TPTx and PTH infusion, phosphate 0,6 or 1,2%	Pi↑ PTH↓ FGF23↓	Low (low BFR, bone volume (BV), Ob and osteocyte (Ot) parameters, Ob and Oc apoptosis)	NA
Fang et al., 2014	LDLR-/- (S2-3)	Nx, high fat diet	Pi↑ PTH↔ FGF23↑	Low (low BFR, TB volume, TH thickness)	NA
Fang et al., 2014	LDLR-/- (S2-3)	Nx, high fat diet	Pi↑ PTH↔ FGF23↑	Low (low BFR, osteoid volume, Ob and Oc number)	NA
Frauscher et al., 2017	DBA/2 (S3-4)	High phosphate diet	Pi↑ PTH↑ FGF23↔	Low	NA
Liao et al., 2019	5/6 Nx (S3)	Nx	Pi↑ PTH↔ FGF23↑	High (high BFR, mineralization)	NA
Hsu et al., 2022	0.2% adenine C57BL/6 (S3)	Adenine	Pi↑ PTH↑ FGF23↑	Low (low TB volume and thickness)	NA
Mathew et al., 2007	LDLR-/- (S3)	High-cholesterol (0.15%) diet, electrocoagulation and left Nx	Pi↔	Low (low BFR, BV, osteoid volume, Ob surface) 10.1681/ASN.2006050490	Vascular Ca concentration ↑
Santhanam et al., 2021	C57BL/6J (S?)	Aged mice or western HFD (21.2% fat)	NA	Low (low BV) 10.1172/JCI147116	Aortic wall remodeling and calcification

Mace et al. 2021	Dark agouti (S?)	Transplanted aorta from 5/6 Nx rats (S3–4)	Pi↑ PTH↔ FGF23↔	Low (osteoid volume, tendency for lowering other bone formation indexes) 10.1002/jbmr.4203	Increase in Wnt inhibitors in aorta
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NA- not applicable; ↑ - increase, ↓ - decrease; ↔ - no differences

Table S2. Primer and probe sequences for RT-PCR

Gene	Primer sequence (5'→3')	Probe R-sequence-Q (5'→3')
Phosphate and pyrophosphate transporters		
Slc20a1	F: CTCATCCTGGGCTTCATCAT	FAM-CATTTGTCTTGGCATTCTCCGTGGG-BHQ1
	R: CCGGATGGTTTCACTCACTT	
Slc20a2	F: GCTCTACCATTTGGCTTCTCG	R6G-ATCGTTGCCTCCTGGTTCATATCCC-BHQ1
	R: ACAGAGGAAGTGCCTGGAGA	
Xpr1	F: AAGACGTGATTCTGCGCTTT	ROX-TGCTACAACTTTTAAGCCTCATGTTGGG-BHQ2
	R: CACGGAATTCACCACAGTTG	
Ankh	F: CAAGAGAGACAGGGCCAAAG	FAM-CAGTCTTCCACACCCTGATAGCCTBHQ1
	R: AAGGCAGCGAGATACAGGAA	
MAPK signaling		
Mapk3	F: TCCAAGGGCTACACCAAATC	FAM-CTACCTGGACCAGCTCAACCACA-BHQ1
	R: AGGTAGTTTCGGGCCTTCAT	
Mapk1	F: TTGCTGAAGCACCATTCAAG	R6G-CAGGACAAGGGCTCAGAGGACTG-BHQ1
	R: ACGGCTCAAAGGAGTCAAGA	
Klotho/FGF23 regulatory axis		
Kl	F: AGCTGCTTGTGTTGTGATGC	FAM-ATGGTGGCGGTTTTAAACAGGCA-BHQ1
	R: TACGGGGGTGCTGTAGAAAC	
Fgfr2	F: ACTGGACCAACACCGAAAAG	FAM-ACGAAACCAGCACTGGAGCCTTATT-BHQ1
	R: CTCCACCAGGCAGGTGTAAT	
Fgf23	F: TGGGCACTGCTAGAGCCTAT	ROX-CAAGGTGTACAGTGACCCCCAGC-BHQ2
	R: GCGGAGATCCATACAAAGGA	
Canonical Wnt signaling and its inhibitors		
Ctnnb1	F: GCCAGTGGATTCCGTACTGT	Cy5-CACCACGCTGCATAATCTCCTGCT-BHQ2
	R: GAGCTTGCTTTCCTGATTGC	
Wnt10b	F: GCACTGTCTAGGGGCAAGAG	Cy5-CCAGCCCTATTCTGGCTCTGTC-BHQ2
	R: CACTTCCGCTTCAGGTTTTT	
Fzd2	F: GAACTCCTGCGCTACTCACC	ROX-CCTCAAGGTGCCGTCCTATCTCA-BHQ2
	R: TCCTCCTGCGAGAAGAACAT	
Dkk1	F: TTA CTGTGGGGAAGGTCTGG	Cy5-CCAACAGCCTAAATGCGATGGACTC-BHQ2
	R: ACATCCTTGGGATTGAGCTG	
Sost	F: CAGCTCTCACTAGCCCCTTG	ROX-CTGCTTGTACATGCAGCCTTCGT-BHQ2
	R: CGGTTTCATGGTCTGTTGTT	
Sfrp2	F: TGTCCGATAGGGACCTGAAG	R6G-TGGGACAGAAACAGGGTGGAGAG-BHQ1
	R: CGAGAAGCCACTCCACTAGG	
VDR/OPG/RANKL regulatory axis		
Vdr	F: AACTCCTCCTCCTCCAGCTC	ROX-CCTGTCTCCTCTCTCCATGCTGCBHQ2
	R: CTGGTCATCGGAGGTGAGAT	
Cyp27b1	F: GGTGAGAGGCTTGGCTAGTG	Cy5-ATGGGGACAGTTGAAACTGCACCTT-BHQ2
	R: TCTGGAGTTCAGGAGCCAGT	
Tnfrsf11B	F: GAATGGTCACTGGGCTGTTT	Cy5-TGGGAATGAAGATCCTCCAGCCC-BHQ2
	R: CCTCTTTCTCAGGGTGCTTG	
Tnfrsf11	F: CATCGGGTTC CCATAAAGTCAGT	FAM-TCAGGCATCATGAAACCTCAGGGAG-BHQ1
	R: GAACTTGGGATTTTGATGCTGGT	
Lgr4	F: GGGAAGAGCAGTCACCTCAG	R6G-CCCTCTTAGCTTTGCTGGGTGC-BHQ1
	R: TAACGATGGGGTTTCTCCTG	

Osteogenesis genes		
Sp7	F: CACTGGCTCCTGGTTCTCTC	R6G-AGCTCACTATGGCTCCAGTCCC-BHQ1
	R: GGGGCTGAAAGGTCAGTGTA	
Bmp4	F: TAGGAGCCATTCCGTAGTGC	ROX- TCTCTGAGCCTTTCAGCAAGTTGT-BHQ2
	R: CTTCCCGGTCTCAGGTATCA	
Bmp2	F: AGAGCTTTGATGTCACCCCG	Cy5-CAGCACAGGGACACACCAACCAT-BHQ2
	R: AAGGACATTCCCCATGGCAG	
Dmp1	F: CGGCTGGTGGTCTCTCTAAG	R6G-CAGTCCAGTGAAGACAGCACGTCT-BHQ1
	R: CATCACTGTGGTGGTCCTTG	
Notch signaling		
Notch1	F: TGAGTGTGTGAAAAGCCCGT	FAM-CGCCAGCAATCCATGCCAAAATG-BHQ1
	R: ACAGGAGCTCTCGGTACAGT	
Jag1	F: GCGCACTGTGAGAACAACA	FAM-CTAGAAACAGTAGCTGCCTGCCGA-BHQ1
	R: AGTCTCCATTGACCACGCAG	
Hes1	F: GGCTCCTGACGGCCAATTT	R6G-CGGTCTACACCAGCAACAGCG-BHQ1
	R: AAGGCGACACTGCGTTAGG	
Numb	F: TAGTGCTACCACCAGTCCCT	R6G-CAATGGTGTAGACAATAGCGGGCTAG-BHQ1
	R: GTGCAGGTCTGTTTCCTGAGA	
Hedgehog signaling		
Ptch1	F: CAGTACATCAGCCTGCGTCA	FAM-CATTGGGATCAAGCTGAGTGCTGTG-BHQ1
	R: CCTGTGGTTCTTGTCCCCAA	
Calcineurin signaling		
Ppp3ca	F: ACGCCTGTATGGATGCCTTC	Cy5-CAACACAGTCAGGGGTTGTTCTGTAC-BHQ2
	R: GCAGCGACCAGGTGAAAAC	
Tgfβ-signaling		
Tgfβ1	F: CGTCAGACATTCCGGGAAGCA	ROX-CAGTGGCTGAACCAAGGAGACG-BHQ2
	R: TCGACGTTTGGGACTGATCC	
Reference gene		
Gapdh	F: AGACAGCCGCATCTTCTTGT	R6G-TGCCAGCCTCGTCTCATAGACAAG-BHQ1
	R: CTTGCCGTGGGTAGAGTCAT	

Slc20a1 – solute carrier family 20 member 1 (Pit-1), *Slc20a2* – solute carrier family 20 member 2 (Pit2), *Xpr1* – xenotropic and polytropic retrovirus receptor 1, *Ankh* – ANKH PPI transport regulator, *Mapk3* – mitogen activated protein kinase 3 (Erk1), *Mapk1* – mitogen activated protein kinase 1 (Erk2), *KL* – Klotho, *Fgf23* – fibroblast growth factor 23, *Fgfr2* – fibroblast growth factor receptor 2, *Ctnnb1* – catenin beta 1, *Sfrp2* – secreted frizzled-related protein 2, *Fzd2* – frizzled class receptor 2, *Wnt10b* – Wnt family member 10B, *Sost* – sclerostin, *Dkk1* – dickkopf 1, *Vdr* – vitamin D receptor, *Cyp27b1* – cytochrome P450, family 27, subfamily b, polypeptide 1 (1-alpha-(OH)ase), *Tnfrsf11B* – TNF receptor superfamily member 11 B (OPG), *Tnfrsf11* – TNF superfamily member 11 (RANKL), *Lgr4* – leucine-rich repeat-containing G protein-coupled receptor 4, *Sp7* – Sp7 transcription factor (osterix), *Bmp4* – bone morphogenetic protein 4, *Dmp1* – dentin matrix acidic phosphoprotein 1, *Gapdh* – glyceraldehyde-3-phosphate dehydrogenase;

Notch1 – notch receptor 1, *Jag1* – jagged canonical Notch ligand 1, *Hes1* – hes family bHLH transcription factor 1, *Numb* – NUMB endocytic adaptor protein, *Ptch1* – patched 1, *Ppp3ca* – calcineurin A, *Tgf-beta 1* – transforming growth factor beta 1.

Table S3. Description of experimental groups

Group	WKY2 (1)	SO2 (2)	SO6 (3)	Nx2 (4)	Nx6 (5)
Strain	Wistar Kyoto rats		Spontaneously hypertensive rats		
Model	normotensive control	control	mild CKD models		
Surgery		sham	3/4 nephrectomy		
Duration of the experiment, mo	2	2	6	2	6
Rats number, n	8	8	8	8	8
Initial body weight, g	228 (224;230)	220 (215;226)	215 (207;228)	224 (217;228)	222 (212;229)
Final body weight, g	345 (336;361)	317 (311;337)	317 (306;336)	320 (300;370)	331 (309;365)
Systolic blood pressure, mmHg	135 (130;142) ^{2-5#}	170 (160;182) ^{3,4*5#}	195 (183;200)	195 (180;205)	208 (195;223)
Myocardial mass index, mg/g	2.5 (2.1;2.8) ^{3,4*5‡}	2.8 (2.8;3.1) ^{5*}	3.0 (2.9;3.4)	3.3 (2.8;3.5)	3.4 (3.2;3.6)
Myocardial wall thickness, mm	2.1 (2.0;2.2) ^{3‡4*5#}	2.3 (2.2;2.5) ^{5‡}	2.5 (2.4;2.7) ^{5*}	2.4 (2.2;2.5) ^{5‡}	2.9 (2.8;2.9)
IA diameter, mcm	99 (77-108) ^{3,5#}	90 (82-94) ^{3,5‡}	126 (111-145)	80 (69-98)	176 (148-214)
Left kidney mass, g	1.2 (1.1;1.2) ^{3-5‡}	1.1 (1.1;1.2) ^{4*5‡}	1.2 (1.1;1.3) ^{5‡}	1.3 (1.2;1.4) ^{5‡}	2.0 (1.8;2.0)
Kidney phosphorus, mg/kg	818 (770;877)	872 (606;1241)	822 (637;1024)	699 (668;825)	734 (671;862)
Bone phosphorus, g/kg	59 (33;63)	63 (58;64)	63 (61;64)	63 (55;65)	60 (59;64)
Myocardial phosphorus, mg/kg	506 (374;839)	629 (593;726) ^{4*}	578 (546;607) ^{5*}	859 (683;920)	675 (588;837)
Estimated serum phosphorus per rat, mg	0.9 (0.8;1.0) ^{5#}	1.1 (1.0;1.2) ^{5‡}	1.1 (1.0;1.2) ^{5#}	1.0 (1.0;1.0) ^{5#}	1.4 (1.3;1.5) ^{5#}
Serum inorganic phosphate, mmol/L	1.5 (1.2;1.60) ^{3-5#}	1.9 (1.7;1.9) ^{5*}	1.9 (1.8;2.0) ^{5‡}	1.6 (1.5;1.8) ^{5*}	2.2 (2.1;2.3)
Fractional phosphate excretion, %	29 (23;33) ^{4,5‡}	32 (27;42) ^{4,5‡}	38 (32;44) ^{4,5‡}	63 (47;65)	56 (45;59)
Urinary phosphate/creatinine, mg/mg	5.6 (4.5;6.5) ^{2-5*}	8.9 (6.9;10.1)	8.6 (7.9;9.8)	10.1 (7.6;12.7)	9.3 (8.9;11.2)
Intact parathyroid hormone, pg/mL	55.1(12.7;112.9)	76.6 (18.4;111.0)	45.5 (12.6;67.1)	45.9 (21.2;76.6)	33.5 (9.6;84.9)
Intact fibroblast growth factor 23, pg/mL	351 (290;836)	361 (330;1530)	468 (326;694)	676 (330;793)	630 (330;953)
Serum Klotho, pg/mL	2698 (2413;2831)	2916 (2520;5374) ^{3-5*}	2043 (1676;2663)	2304 (2074;2524)	2259 (1428;2696)

Superscripts correspond to *p*-values of inter-group differences (each group is indicated by a group number); * *p* < 0.05, ‡ *p* < 0.005, # *p* < 0.001.