Supplemental Table 1. Thirty genes, known to cause monogenic forms of NL/NC that were included in the study

	Gene Symbol	Gene Name	Accession #	Disease entity	MIM-Phenotype #	Mode	Coding Exons	Ref.
1	***ADCY10/SAC***	adenylate cyclase 10 (soluble)	NM_018417.4	Hypercalciuria, Calcium oxalate nephrolithiasis	143870	AD	32	1
2	***AGXT***	alanine-glyoxylate aminotransferase	NM_000030.2	Primary hyperoxaluria, type 1	259900	AR	11	2
3	***APRT***	adenine phosphoribosyltransferase	NM_000485.2	Adenine phosphoribosyltransferase deficiency, Urolithiasis (DHA stones), renal failure	614723	AR	5	3
4	***ATP6V0A4***	ATPase, H+ transporting, lysosomal V0 subunit a4	NM_020632.2	dRTA	602722	AR	20	4
5	***ATP6V1B1***	ATPase, H+ transporting, lysosomal 56/58kDa, V1 subunit B1	NM_001692.3	Distal renal tubular acidosis (dRTA) with deafness	267300	AR	14	5
6	***CA2***	carbonic anhydrase II	NM_000067.2	Osteopetrosis + d/pRTA	259730	AR	7	6
7	***CASR***	calcium-sensing receptor	NM_001178065.1	Hypocalcemia with Bartter syndrome / hypocalcemia, autosomal dominant	601198	AD	6	7
8	***CLCN5***	chloride channel, voltage-sensitive 5	NM_001127898.3	Dent disease / Nephrolithiasis, type 1	300009 / 310468	XR	14	8
9	***CLCNKB***	chloride channel, voltage-sensitive Kb	NM_000085.4	Bartter syndrome, type 3	607364	AR	19	9
10	***CLDN16***	claudin 16	NM_006580.3	Familial hypomagnesemia with hypercalciuria & nephrocalcinosis, FHHNC	248250	AR	5	10
11	***CLDN19***	claudin 19	NM_001123395.1	Familial hypomagnesemia with hypercalciuria & nephrocalcinosis with ocular abnormalities	248190	AR	4	11
12	***CYP24A1***	cytochrome P450, family 24, subfamily A, polypeptide 1	NM_000782.4	1,25-(OH) D-24 hydroxylase deficiency , infantile Hypercalcemia	143880	AR	11	12
13	***FAM20A***	family with sequence similarity 20, member A	NM_017565.3	Enamel-Renal syndrome, amelogenesis imperfecta and nephrocalcinosis	204690	AR	12	13
14	***GRHPR***	glyoxylate reductase/hydroxypyruvate reductase	NM_012203.1	Primary hyperoxaluria, type 2	260000	AR	9	14
15	***HNF4A***	hepatocyte nuclear factor 4, alpha	NM_000457.4	MODY + Fanconi syndrome + Nephrocalcinosis	125850	AD	1	15
16	***HOGA1***	4-hydroxy-2-oxoglutarate aldolase 1	NM_138413.3	Primary hyperoxaluria, type 3	613616	AR	7	16
17	***HPRT1***	hypoxanthine phosphoribosyltransferase 1	NM_000194.2	Kelley-Seegmiller syndrome, partial HPRT deficiency, HPRT-related gout	300323	XR	9	17
18	***KCNJ1***	potassium inwardly-rectifying channel, subfamily J, member 1	NM_000220.4	Bartter syndrome, type 2	241200	AR	2	18
19	***OCRL***	oculocerebrorenal syndrome of Lowe	NM_000276.3	Lowe syndrome / Dent disease 2	309000 / 300555	XR	24	19
20	***SLC12A1***	solute carrier family 12, member 1	NM_000338.2	Bartter syndrome, type 1	601678	AR	27	20
21	***SLC22A12***	solute carrier family 22 (organic anion/urate transporter), member 12	NM_144585.3	Renal hypouricemia, RHUC1	220150	AD/AR	10	21
22	***SLC2A9***	solute carrier family 2 (facilitated glucose transporter), member 9	NM_001001290.1	Renal hypouricemia, RHUC2	612076	AD/AR	13	22
23	***SLC34A1***	solute carrier family 34 (sodium phosphate), member 1	NM_003052.4	Hypophosphatemic nephrolithiasis /osteoporosis-1, NPHLOP1 / Fanconi renotubular syndrome 2	612286 / 613388	AD/AR	13	23

24	***SLC34A3***	solute carrier family 34 (sodium phosphate), member 3	NM_001177316.1	Hypophosphatemic rickets with hypercalciuria	241530	AR	12	24
25	***SLC3A1***	solute carrier family 3 (cystine, dibasic and neutral amino acid transporters, activator of cystine, dibasic and neutral amino acid transport), member 1	NM_000341.3	Cystinuria, type A	220100	AR	10	25
26	***SLC4A1***	solute carrier family 4, anion exchanger, member 1 (erythrocyte membrane protein band 3, Diego blood group)	NM_000342.3	Primary distal renal tubular acidosis, dominant / recessive	179800 / 611590	AD/AR	19	26
27	***SLC7A9***	solute carrier family 7 (glycoproteinassociated amino acid transporter light chain, bo,+ system), member 9	NM_014270.4	Cystinuria, type B	220100	AD/AR	12	27
28	***SLC9A3R1***	solute carrier family 9, subfamily A (NHE3, cation proton antiporter 3), member 3 regulator 1	NM_004252.4	Hypophosphatemic nephrolithiasis/osteoporosis-2, NPHLOP2	612287	AD	6	28
29	***VDR***	vitamin D (1,25- dihydroxyvitamin D3) receptor	NM_000376.2	Idiopathic hypercalciuria	277440	AD	11	29
30	***XDH***	xanthine dehydrogenase	NM_000379.3	Xanthinuria, type 1	278300	AR	36	30

AR, autosomal recessive; AD, autosomal dominant; XR, X-linked recessive
Genes in which mutations were detected are underlined.

REFERENCES

1. Reed, B.Y. *et al.* Identification and Characterization of a Gene with Base Substitutions Associated with the Absorptive Hypercalciuria Phenotype and Low Spinal Bone Density. *The Journal of Clinical Endocrinology & Metabolism* **87**, 1476-1485 (2002).
2. Purdue, P.E., Allsop, J., Isaya, G., Rosenberg, L.E. & Danpure, C.J. Mistargeting of peroxisomal L-alanine:glyoxylate aminotransferase to mitochondria in primary hyperoxaluria patients depends upon activation of a cryptic mitochondrial targeting sequence by a point mutation. *Proceedings of the National Academy of Sciences* **88**, 10900-10904 (1991).
3. Hidaka, Y. *et al.* Human adenine phosphoribosyltransferase. Identification of allelic mutations at the nucleotide level as a cause of complete deficiency of the enzyme. *J Clin Invest* **80**, 1409-1415 (1987).
4. Smith, A.N. *et al.* Mutations in ATP6N1B, encoding a new kidney vacuolar proton pump 116-kD subunit, cause recessive distal renal tubular acidosis with preserved hearing. *Nat Genet* **26**, 71-75 (2000).
5. Karet, F.E. *et al.* Mutations in the gene encoding B1 subunit of H+-ATPase cause renal tubular acidosis with sensorineural deafness. *Nat Genet* **21**, 84-90 (1999).
6. P J Venta, R.J.W., T M Johnson, W S Sly, and R E Tashian. Carbonic anhydrase II deficiency syndrome in a Belgian family is caused by a point mutation at an invariant histidine residue (107 His----Tyr): complete structure of the normal human CA II gene. *American journal of human genetics* **49**(1991).
7. Pearce, S.H.S. *et al.* A Familial Syndrome of Hypocalcemia with Hypercalciuria Due to Mutations in the Calcium-Sensing Receptor. *New England Journal of Medicine* **335**, 1115-1122 (1996).
8. Lloyd, S.E. *et al.* A common molecular basis for three inherited kidney stone diseases. *Nature* **379**, 445-449 (1996).
9. Simon, D.B. *et al.* Mutations in the chloride channel gene, CLCNKB, cause Bartter's syndrome type III. *Nat Genet* **17**, 171-8 (1997).
10. Simon, D.B. *et al.* Paracellin-1, a renal tight junction protein required for paracellular Mg2+ resorption. *Science* **285**, 103-6 (1999).
11. Konrad, M. *et al.* Mutations in the Tight-Junction Gene Claudin 19 (CLDN19) Are Associated with Renal Magnesium Wasting, Renal Failure, and Severe Ocular Involvement. *The American Journal of Human Genetics* **79**, 949-957 (2006).
12. Schlingmann, K.P. *et al.* Mutations in CYP24A1 and Idiopathic Infantile Hypercalcemia. *New England Journal of Medicine* **365**, 410-421 (2011).
13. Jaureguiberry, G. *et al.* Nephrocalcinosis (Enamel Renal Syndrome) Caused by Autosomal Recessive FAM20A Mutations. *Nephron Physiology* **122**, 1-6 (2012).
14. Cramer, S.D., Ferree, P.M., Lin, K., Milliner, D.S. & Holmes, R.P. The Gene Encoding Hydroxypyruvate Reductase (GRHPR) is Mutated in Patients with Primary Hyperoxaluria Type II. *Hum Mol Genet* **8**, 2063-2069 (1999).

15. Hamilton, A.J. *et al.* The HNF4A R76W mutation causes atypical dominant Fanconi syndrome in addition to a β cell phenotype. *Journal of Medical Genetics* **51**, 165-169 (2014).
16. Belostotsky, R. *et al.* Mutations in DHDPSL Are Responsible For Primary Hyperoxaluria Type III. *The American Journal of Human Genetics* **87**, 392-399 (2010).
17. Davidson BL, T.S., Van Antwerp M, Gibbs DA, Watts RW, Kelley WN, Palella TD. Identification of 17 independent mutations responsible for human hypoxanthine-guanine phosphoribosyltransferase (HPRT) deficiency. *American journal of human genetics* **48**(1991).
18. Simon, D.B. *et al.* Genetic heterogeneity of Bartter's syndrome revealed by mutations in the K+ channel, ROMK. *Nat Genet* **14**, 152-6 (1996).
19. Reilly DS, L.R., Ledbetter DH, Nussbaum RL. Tightly linked flanking markers for the Lowe oculocerebrorenal syndrome, with application to carrier assessment. *American Journal of Human Genetics* **42**(1988).
20. Simon, D.B. *et al.* Bartter's syndrome, hypokalaemic alkalosis with hypercalciuria, is caused by mutations in the Na-K-2Cl cotransporter NKCC2. *Nat Genet* **13**, 183-8 (1996).
21. Enomoto, A. *et al.* Molecular identification of a renal urate-anion exchanger that regulates blood urate levels. *Nature* **417**, 447-452 (2002).
22. Matsuo, H. *et al.* Mutations in Glucose Transporter 9 Gene SLC2A9 Cause Renal Hypouricemia. *The American Journal of Human Genetics* **83**, 744-751 (2008).
23. Prié, D. *et al.* Nephrolithiasis and Osteoporosis Associated with Hypophosphatemia Caused by Mutations in the Type 2a Sodium□Phosphate Cotransporter. *New England Journal of Medicine* **347**, 983-991 (2002).
24. Lorenz-Depiereux, B. *et al.* Hereditary Hypophosphatemic Rickets with Hypercalciuria Is Caused by Mutations in the Sodium-Phosphate Cotransporter Gene SLC34A3. *The American Journal of Human Genetics* **78**, 193-201 (2006).
25. Calonge, M.J. *et al.* Cystinuria caused by mutations in rBAT, a gene involved in the transport of cystine. *Nat Genet* **6**, 420-425 (1994).
26. Bruce, L.J. *et al.* Familial distal renal tubular acidosis is associated with mutations in the red cell anion exchanger (Band 3, AE1) gene. *J Clin Invest* **100**, 1693-1707 (1997).
27. Feliubadalo, L. *et al.* Non-type I cystinuria caused by mutations in SLC7A9, encoding a subunit (bo,+AT) of rBAT. *Nat Genet* **23**, 52-57 (1999).
28. Karim, Z. *et al.* NHERF1 Mutations and Responsiveness of Renal Parathyroid Hormone. *New England Journal of Medicine* **359**, 1128-1135 (2008).
29. Scott, P. *et al.* Suggestive Evidence for a Susceptibility Gene Near the Vitamin D Receptor Locus in Idiopathic Calcium Stone Formation. *Journal of the American Society of Nephrology* **10**, 1007-1013 (1999).
30. Ichida, K. *et al.* Identification of two mutations in human xanthine dehydrogenase gene responsible for classical type I xanthinuria. *J Clin Invest* **99**, 2391-2397 (1997).

Supplemental Table 2. Clinical characteristics of individuals with identified monogenic disease causes.

Gene[a]	Individual	Molecular Diagnosis	Compatible Urine / Serum Chemistry	Stone Analysis	Familial Inheritance
ADYC10	B580	Hypercalciuria	Y ☑ N ☐ n/a ☐	CaOx	AR ☐ AD ☑
ADYC10	B599	Hypercalciuria	Y ☑ N ☐ n/a ☐	n/a	AR ☐ AD ☑
SLC4A1	B280	dRTA Hypocalcemia	Y ☑ N ☐ n/a ☐ Y ☐ N ☑ n/a ☐	n/a	AR ☐ AD ☑
SLC9A3R1	B529	Hypophosphatemia Hyperphosphaturia	Y ☑ N ☐ n/a ☐ Y ☑ N ☐ n/a ☐	n/a	AR ☑ AD ☐
SLC34A1	B491	Hypophosphatemia	Y ☑ N ☐ n/a ☐	n/a	AR ☐ AD ☑
SLC34A1	B484	Hypophosphatemia	Y ☑ N ☐ n/a ☐	n/a	AR ☐ AD ☑
SLC34A1	B417	Hypophosphatemia	Y ☑ N ☐ n/a ☐	CaOx	AR ☐ AD ☑
SLC34A1	B610[b]	Hypophosphatemia	Y ☐ N ☑ n/a ☐	CaOx, CaPh	AR ☐ AD ☐
SLC34A1	B523	Hypophosphatemia	Y ☑ N ☐ n/a ☐	n/a	AR ☐ AD ☑
VDR	B481	Hypocalcemia Hypophosphatemia	Y ☐ N ☑ n/a ☐ Y ☑ N ☐ n/a ☐	n/a	AR ☑ AD ☐
VDR	B447	Hypocalcemia Hypophosphatemia	Y ☐ N ☑ n/a ☐ Y ☑ N ☐ n/a ☐	n/a	AR ☑ AD ☐
AGXT	B424	Hyperoxaluria	Y ☑ N ☐ n/a ☐	CaOx	AR ☑ AD ☐
ATP6V1B1	B482	dRTA Deafness	Y ☑ N ☐ n/a ☐ Y ☐ N ☐ n/a ☑	CaOx	AR ☑ AD ☐
ATP6V0A4	B329	Hypokalemia dRTA Metabolic acidosis	Y ☑ N ☐ n/a ☐ Y ☑ N ☐ n/a ☐ Y ☑ N ☐ n/a ☐	n/a	AR ☑ AD ☐
CLDN16	B604	Hypomagnesemia Hyperuricemia Hypermagnesiuria Hypercalciuria Hypocitraturia	Y ☑ N ☐ n/a ☐ Y ☐ N ☑ n/a ☐ Y ☑ N ☐ n/a ☐ Y ☑ N ☐ n/a ☐ Y ☑ N ☐ n/a ☐	n/a	AR ☑ AD ☐
CLDN19	A4592	Hypomagnesemia Hypercalciuria Hypermagnesuria	Y ☑ N ☐ n/a ☐ Y ☑ N ☐ n/a ☐ Y ☐ N ☐ n/a ☑	n/a	AR ☑ AD ☐
CYP24A1	B607	Hypercalcemia Hypercalciuria	Y ☑ N ☐ n/a ☐ Y ☑ N ☐ n/a ☐	n/a	AR ☑ AD ☐
CYP24A1	B540	Hypercalcemia Hypercalciuria	Y ☑ N ☐ n/a ☐ Y ☑ N ☐ n/a ☐	CaOx	AR ☑ AD ☐
SLC12A1	B446	Hypokalemia Hypercalciuria Hypochloremia Hyposthenuria Metabolic alkalosis	Y ☑ N ☐ n/a ☐ Y ☑ N ☐ n/a ☐ Y ☑ N ☐ n/a ☐ Y ☑ N ☐ n/a ☐ Y ☑ N ☐ n/a ☐	n/a	AR ☑ AD ☐
SLC3A1	B425	Cystinuria	Y ☑ N ☐ n/a ☐	cystine	AR ☑ AD ☐
SLC3A1	B458	Cystinuria	Y ☑ N ☐ n/a ☐	cystine	AR ☑ AD ☐

SLC3A1	B499	Cystinuria	Y ☑ N ☐ n/a ☐	cystine	AR ☑ AD ☐
OCRL	B422	Hypercalciuria Aminoaciduria pRTA Phosphoturia Proteinuria	Y ☑ N ☐ n/a ☐ Y ☑ N ☐ n/a ☐ Y ☑ N ☐ n/a ☐ Y ☑ N ☐ n/a ☐ Y ☑ N ☐ n/a ☐	n/a	XR ☑ AD ☐
OCRL	B199	Hypercalciuria Aminoaciduria pRTA Phosphoturia Proteinuria	Y ☑ N ☐ n/a ☐ Y ☐ N ☑ n/a ☐ Y ☐ N ☑ n/a ☐ Y ☐ N ☑ n/a ☐ Y ☐ N ☑ n/a ☐	CaOx	XR ☑ AD ☐

AD, autosomal dominant; AR, autosomal recessive; CaOx, calcium oxalate; CaPh, calcium phosphate; dRTA, distal renal tubular acidosis; N, no; n/a, not available; pRTA, proximal renal tubular acidosis; XR, X-linked recessive; Y, yes

[a]Autosomal dominant genes are underlined, autosomal recessive genes are not underlined, and X-linked recessive genes are double underlined.
[b]B610 is an adopted individual, and biological family information is unavailable.