Supplementary Material

# Supplementary Figures and Tables

## Supplementary table S1. Genetic causes of secondary hypercalcemia and hypocalcemia with hypercalciuria, nephrolithiasis and/or nephrocalcinosis.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gene** | **Gene product** | **Phenotype** | **OMIM phenotype number** | **Inheritance** | **Description** |
| 7q11.23 | N/A | Williams-Beuren syndrome | 194050 | AD | Facial dysmorphism, cardiovascular issues, social problems, hypertension, syndromal infantile hypercalcemia, NC |
| *PIK3C2A* | Phosphatidylinositol-4-phosphate 3-kinase catalytic subunit type 2 alpha | Oculoskeleto-dental syndrome (1) | [618440](https://www.omim.org/entry/618440) | AR | Congenital cataract, short stature, skeletal anomalies, dysmorphic facies, dental anomalies, developmental delay, stroke, hearing loss, glaucoma, hypercalcemia, hypercalciuria, NC (3 cases) |
| ? *PCSK1* | ? Proprotein convertase, subtilisin/kexin type 1 | Blue diaper syndrome (2, 3) | [211000](https://www.omim.org/entry/211000?search=Blue%20diaper%20syndrome&highlight=blue%20diaper%20syndrome%20syndromic) | ? AR,  ? XLR | Disorder of intestinal tryptophan transport, bluish colored diaper from incanduria, hypercalcemia, NC |
| *SI* | Sucrase-isomaltase | Congenital sucrase-isomaltase deficiency (4, 5) | [222900](https://www.omim.org/entry/222900) | AR | Absence of sucrase and most of maltase digestive activity, isomaltase activity absent to normal, unabsorbed disaccharides with osmotic-fermatative diarrhea, vomiting, flatulence, abdominal pain, cases with NL and NC (possibly due to hypercalcemia with dehydration) |
| *SLC5A1* | Solute carrier family 5 (sodium/glucose cotransporter) member 1 | Glucose/galactose malabsorption (6) | [606824](https://www.omim.org/entry/606824) | AR | Defect in glucose/ galactose intestinal transport, neonatal watery diarrhea, dehydration, hypercalcemia, hypercalciuria, NC, NL |

AD, autosomal dominant; AR, autosomal recessive; NC, nephrocalcinosis; NL, nephrolithiasis; XLR, X-linked recessive.

## Supplementary table S2. Genetic causes of secondary proximal tubulopathy with hypercalciuria and nephrolithiasis and/or nephrocalcinosis.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gene** | **Gene product** | **Phenotype** | **OMIM phenotype number** | **Inheritance** | **Description** |
| *ALDOB* | Fructose-bisphosphate aldolase B (PT) | Hereditary fructose intolerance (7, 8) | [229600](https://www.omim.org/entry/229600) | AR | Recurrent vomiting, abdominal pain, hypoglycemia, liver failure, poor growth, possible proximal RTA, NC in 2 cases, NL in 1 case |
| *ATP7B* | Copper-transporting ATPase beta polypeptide | Wilson disease (9) | [277900](https://www.omim.org/entry/277900) | AR | Intracellular hepatic copper build-up, hepatic and neurologic abnormalities, hypercalciuria, NC, NL |
| *CTNS* | Cystinosin, lysosomal cystine transporter (PT) | Nephropathic cystinosis (10) | [219800](https://www.omim.org/entry/219800) | AR | Lysosomal storage disorder, accumulation of cystine in cells, poor growth, hypophosphatemic/ calcipenic rickets, ESKD, Fanconi renotubular syndrome, hypercalciuria, hyperphosphaturia, NC, NL |
| *FAH* | Fumaryl-acetoacetate hydrolase (PT) | Tyrosinemia type 1 (11) | [276700](https://www.omim.org/entry/276700) | AR | Deficiency of fumaryl-acetoacetase (tyrosine degradation enzyme), liver disease, Fanconi renotubular syndrome, hypophosphatemic rickets, NC |
| *LCT* | Lactase-phlorizin hydrolase | Congenital lactase deficiency (12) | [223000](https://www.omim.org/entry/223000) | AR | Vomiting, diarrhea, failure to thrive, dehydration, disacchariduria, RTA, amino aciduria, metabolic acidosis, hypercalcemia, hypercalciuria, NC |
| *RRM2B* | Ribonucleotide reductase regulatory TP53 inducible subunit M2B | Mitochondrial DNA depletion syndrome 8A (encephalo-myopathic type with renal tubulopathy) (13) | [612075](https://www.omim.org/entry/612075) | AR | Neonatal hypotonia, lactic acidosis, neurologic deterioration, proximal tubulopathy, NC |
| *TRNT1* | Mitochondrial CCA-adding tRNA nucleotidyl-transferase | Sideroblastic anemia with B-cell immune-deficiency, periodic fevers, developmental delay (14) | [616084](https://www.omim.org/entry/616084) | AR | SNHL, retinitis pigmentosa, cardiomyopathy, Fanconi renotubular syndrome, NC, few cases of NL |
| *VIPAS39* | VPS33b-interacting protein | Arthrogryposis, renal dysfunction, and cholestasis 2 (15) | [613404](https://www.omim.org/entry/613404) | AR | Joint contractures, cholestasis, failure to thrive, ichthyosis, Fanconi renotubular syndrome, NC |
| *VPS33B* | Homolog of yeast vacuolar protein sorting 33 b | Arthrogryposis, renal dysfunction, and cholestasis 1 (15) | [208085](https://www.omim.org/entry/208085) | AR | Joint contractures, cholestasis, failure to thrive, ichthyosis, Fanconi renotubular syndrome, NC |

AR, autosomal recessive; ESKD, end stage kidney disease; NC, nephrocalcinosis; NL, nephrolithiasis; PT, proximal tubule; RTA, renal tubular acidosis; SNHL, sensorineural hearing loss.

## Supplementary table S3. Genetic causes of hyperaldosteronism and pseudohyperaldosteronism with hypercalciuria and nephrolithiasis and/or nephrocalcinosis.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gene** | **Gene product** | **Phenotype** | **OMIM phenotype number** | **Inheritance** | **Description** |
| *CACNA1H* | Calcium voltage-gated channel subunit alpha-1 H | Familial HA type IV (16, 17) | [617027](https://www.omim.org/entry/617027) | AD | Hypertension, HA, hypokalemia, possibly NC, NL |
| *CLCN2* | Chloride voltage-gated channel 2 | Familial HA type II (16, 17) | [605635](https://www.omim.org/entry/605635) | AD | Hypertension, HA, hypokalemia, possibly NC, NL |
| *CYP11B1* | Cytochrome P450 family 11 subfamily B member 1 | Glucocorticoid-remediable aldosteronism / Familial HA type I (16, 17) | [103900](https://www.omim.org/entry/103900) | AD | Hypertension, low plasma renin activity, HA, abnormal adrenal steroid production, responsive to dexamethasone treatment, possibly NC, NL |
| *KCNJ5* | Potassium inwardly rectifying channel subfamily J member 5 | Familial HA type III (16, 17) | [613677](https://www.omim.org/entry/613677) | AD | HA, hypertension, high levels of hybrid steroids 18-oxocortisol and 18-hydroxycortisol, require adrenalectomy to control hypertension, possibly NL, NC |
| *WNK4* | WNK lysine deficient protein kinase 4 (DCT, CD) | Pseudo-hyperaldosteronism type IIB / Gordon syndrome (18) | [614491](https://www.omim.org/entry/614491) | AD | Hypocalcemia, decreased bone mineral density, hypercalciuria, NL |

AD, autosomal dominant; CD, collecting duct; DCT, distal convoluted tubule; HA, hyperaldosteronism; NC, nephrocalcinosis; NL, nephrolithiasis.

## Supplementary table S4. Genetic causes of hyperparathyroidism and hypoparathyroidism with hypercalciuria and nephrolithiasis and/or nephrocalcinosis.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gene** | **Gene product** | **Phenotype** | **OMIM phenotype number** | **Inheritance** | **Description** |
| *CDC73* | Cell division cycle 73 | Familial primary hyperparathyroidism (19, 20) | 145000 | AD | Overproduction of PTH, hypercalcemia, hypercalciuria, NL, NC |
| *GCM2* | Glial cells missing transcription factor 2 | Hyperparathyroidism 4 (19, 20) | [617343](https://www.omim.org/entry/617343) | AD | Overproduction of PTH, hypercalcemia, hypercalciuria, NL, NC |
| *GATA3* | GATA-binding protein 3 | Hypoparathyroidism, sensorineural deafness, renal dysplasia (21) | [146255](https://www.omim.org/entry/146255) | AD | Hypoparathyroidism, SNHL, may have CAKUT, NS, hematuria, proteinuria, CKD, ESKD, RTA, hypercalciuria, NC |
| *MEN1* | Menin 1 | MEN type I (19, 20) | [131100](https://www.omim.org/entry/131100) | AD | Overproduction of PTH, hypercalcemia, hypercalciuria, NL, NC |
| *RET* | Rearranged during transfection protooncogene | MEN type IIA (19, 20) | [171400](https://www.omim.org/entry/171400) | AD | Overproduction of PTH, hypercalcemia, hypercalciuria, NL, NC |
| *CDKN1B* | Cyclin-dependent kinase inhibitor 1B | MEN type IV (19, 20) | [610755](https://www.omim.org/entry/610755) | AD | Overproduction of PTH, hypercalcemia, hypercalciuria, NL, NC |

AD, autosomal dominant; CAKUT, congenital anomalies of the kidney and urinary tract; CKD, chronic kidney disease; ESKD, end stage kidney disease; MEN, multiple endocrine neoplasia; NC, nephrocalcinosis; NL, nephrolithiasis; NS, nephrotic syndrome; PTH, parathyroid hormone; RTA, renal tubular acidosis; SNHL, sensorineural hearing loss.

## Supplementary table S5. Other genetic causes of hypercalciuria and nephrolithiasis and/or nephrocalcinosis.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gene** | **Gene product** | **Phenotype** | **OMIM phenotype number** | **Inheritance** | **Description** |
| *ADCY10* | Adenylyl cyclase 10 | Susceptibility to absorptive hypercalciuria / Familial idiopathic hypercalciuria (22) | [143870](https://www.omim.org/entry/143870) | AD | Hypercalciuria, recurrent NL |
| *ALPL* | Bio-mineralization associated alkaline phosphatase (PT) | Infantile Hypophosphatasia (23) | [241500](https://www.omim.org/entry/241500) | AR | First 6 months of life PPi inhibits bone mineralization, failure to thrive, hyporexia, muscle weakness, delayed motor development, rickets, hypercalciuria, NC, sometimes NL |
| Childhood Hypophosphatasia (24) | [241510](https://www.omim.org/entry/241510) | AR | After 6 months old PPi inhibits bone mineralization, rickets, short stature, muscle weakness, delayed motor development, may have hypercalciuria, NC |
| Adult Hypophosphatasia (25) | [146300](https://www.omim.org/entry/146300) | AD/AR | In adults PPi inhibits bone mineralization, osteomalacia, pseudofractures, fractures, muscle/joint pain, cases of NC (uncertain if due to treatment) |
| *CDKN1C* | Cyclin-dependent kinase inhibitor 1C | IMAGE Syndrome (26) | [614732](https://www.omim.org/entry/614732) | AD | IUGR, metaphyseal dysplasia, congenital adrenal hypoplasia, genital anomalies, craniosynostosis, cleft palate, scoliosis, hypercalciuria, hypocalcemia, NC |
| *CDKN1C* | Cyclin-dependent kinase inhibitor 1c | Beckwith-Wiedemann syndrome (27) | [130650](https://www.omim.org/entry/130650) | AD | Rapid growth in first few years, hemihypertrophy, macroglossia, hypoglycemia, abdominal wall defects, visceromegaly, Wilms tumor, hepatoblastoma, CAKUT, hypercalciuria, NC, NL |
| *ICR1* | H19/IGF2-imprinting control region |
| *KCNQ1OT1* | KCNQ1-opposite strand / antisense transcript 1 |
| *CFTR* | Cystic fibrosis transmembrane conductance regulator | Cystic fibrosis (28) | [219700](https://www.omim.org/entry/219700) | AR | COPD, exocrine pancreatic insufficiency, high NaCl in sweat, hypercalciuria, NC |
| *CLDN2* | Claudin-2, integral membrane tight junction protein (PT) | Obstructive azoospermia with NL (29) | [301060](https://www.omim.org/entry/301060) | XLR | Male infertility, hypercalciuria, NL |
| *FAM20A* | Family with sequence similarity 20 member A | Amelogenesis imperfecta type IG / Enamel-renal syndrome (30) | [204690](https://www.omim.org/entry/204690) | AR | Hypoplastic enamel, pulp stones, delayed/failed eruption of secondary dentition, gingival overgrowth, NC of unclear etiology |
| *GEMIN4* | Gem nuclear organelle associated protein 4 | Neuro-developmental disorder with microcephaly, cataracts, renal abnormalities (31) | [617913](https://www.omim.org/entry/617913) | AR | Complex severe neurodevelopmental disorder, microcephaly, cataracts, GERD, seizures, hyporeflexia, CAKUT, hypertension, tubulopathy, NL, NC |
| *GNAS* | GNAS complex locus | Somatic mosaic McCune-Albright syndrome (32, 33) | [174800](https://www.omim.org/entry/174800) | Mosaic | Postzygotic somatic mutation early in development, monoclonal population of mutated cells, polyostotic fibrous dysplasia, cafe-au-lait spots, peripheral precocious puberty, thyrotoxicosis, pituitary gigantism, Cushing syndrome, NC mostly related to hypercalciuria |
| *MPV17* | Mitochondrial inner membrane protein MPV17 | Mitochondrial DNA depletion syndrome 6 (34) | [256810](https://www.omim.org/entry/256810) | AR | Infantile progressive liver failure, progressive neurologic issues, eye abnormalities, hypoparathyroidism, tubulopathy, NC |
| *PIGT* | Phosphatidyl-inositol glycan anchor biosynthesis class T | Multiple congenital anomalies-hypotonia-seizures syndrome 3 (35, 36) | [615398](https://www.omim.org/entry/615398) | AR | Neonatal hypotonia, seizures, dysmorphic features, variable congenital anomalies including CAKUT, hypercalciuria with NC (5 cases) |
| *PIK3R1* | Phospho-inositide-3-kinase regulatory subunit 1 | SHORT syndrome (37) | [269880](https://www.omim.org/entry/269880) | AD | Short stature, joint hyperextensibility, hernias, eye anomalies, teething delay, dysmorphic facies, partial lipodystrophy, insulin resistance, hearing deficits, hypercalciuria with NC |
| *VDR* | 1,25-dihydroxy-vitamin D3 receptor | Idiopathic hypercalciuria (38, 39) | N/A | AD | Hypercalciuria, NL |

AD, autosomal dominant; AR, autosomal recessive; CAKUT, congenital anomalies of the kidney and urinary tract; COPD, chronic obstructive pulmonary disease; GERD, gastroesophageal reflux disease; IUGR, Intrauterine growth restriction; NaCl, sodium chloride; NC, nephrocalcinosis; NL, nephrolithiasis; PPi, inorganic pyrophosphate; PT, proximal tubule; XLR, X-linked recessive.

## Supplementary table S6. Other genetic causes of hyperoxaluria with nephrolithiasis and/or nephrocalcinosis.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gene** | **Gene product** | **Phenotype** | **OMIM phenotype number** | **Inheritance** | **Description** |
| *PEX1 (40)* | Peroxisomal biogenesis factor 1 | Peroxisome biogenesis disorder A (Zellweger) | [214100](https://www.omim.org/entry/214100) | AR | Absence of peroxisomes, severe neurologic dysfunction, craniofacial abnormalities, liver dysfunction, hyperoxaluria with NL and NC with *PEX1*, likely *PEX5*, possibly *PEX3, PEX6, PEX 10, PEX 12, PEX13, PEX14, PEX16, PEX19, PEX26* |
| *PEX3 (41)* | Peroxisomal biogenesis factor 3 | [614882](https://www.omim.org/entry/614882) |
| *PEX5 (42)* | Peroxisomal biogenesis factor 5 | [214110](https://www.omim.org/entry/214110) |
| *PEX6 (40)* | Peroxisomal biogenesis factor 6 | [614862](https://www.omim.org/entry/620152) |
| *PEX10 (41)* | Peroxisomal biogenesis factor 10 | [614870](https://www.omim.org/entry/614870) |
| *PEX12 (41)* | Peroxisomal biogenesis factor 12 | [614859](https://www.omim.org/entry/614859) |
| *PEX13 (41)* | Peroxisomal biogenesis factor 13 | [614883](https://www.omim.org/entry/614883) |
| *PEX14 (40)* | Peroxisomal biogenesis factor 14 | [614887](https://www.omim.org/entry/614887) |
| *PEX16 (41)* | Peroxisomal biogenesis factor 16 | [614876](https://www.omim.org/entry/614876) |
| *PEX19 (40)* | Peroxisomal biogenesis factor 19 | [614886](https://www.omim.org/entry/614886) |
| *PEX26 (41)* | Peroxisomal biogenesis factor 26 | [614872](https://www.omim.org/entry/614872) |
| *PEX1 (42)* | Peroxisomal biogenesis factor 1 | Peroxisome biogenesis disorder B (NALD and IRD) | [601539](https://www.omim.org/entry/601539) | AR | Milder phenotype than Zellweger, hyperoxaluria with NL and NC with *PEX1* and *PEX3*, likely *PEX5*, possibly *PEX6, PEX7, PEX10, PEX11, PEX12, PEX13, PEX16, PEX26* |
| *PEX3 (43)* | Peroxisomal biogenesis factor 3 | [617370](https://www.omim.org/entry/617370) |
| *PEX5 (42)* | Peroxisomal biogenesis factor 5 | [202370](https://www.omim.org/entry/202370) |
| *PEX6 (41)* | Peroxisomal biogenesis factor 6 | [614863](https://www.omim.org/entry/612075) |
| *PEX7 (41)* | Peroxisomal biogenesis factor 7 | [614879](https://www.omim.org/entry/614879) |
| *PEX10 (41)* | Peroxisomal biogenesis factor 10 | [614871](https://www.omim.org/entry/614871) |
| *PEX11 (41)* | Peroxisomal biogenesis factor 11 | [614920](https://www.omim.org/entry/614920) |
| *PEX12 (40)* | Peroxisomal biogenesis factor 12 | [266510](https://www.omim.org/entry/266510) |
| *PEX13 (40)* | Peroxisomal biogenesis factor 13 | [614885](https://www.omim.org/entry/614885) |
| *PEX16 (40)* | Peroxisomal biogenesis factor 16 | [614877](https://www.omim.org/entry/614877) |
| *PEX26 (40)* | Peroxisomal biogenesis factor 26 | [614873](https://www.omim.org/entry/614873) |

AR, autosomal recessive; IRD, infantile Refsum disease; NALD, neonatal adrenoleukodystrophy; NC, nephrocalcinosis; NL, nephrolithiasis.

## Supplementary table S7. Other genetic metabolic disorders with nephrolithiasis and/or nephrocalcinosis.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gene** | **Gene product** | **Phenotype** | **OMIM phenotype number** | **Inheritance** | **Description** |
| *CLPB* | Caseinolytic mitochondrial matrix peptidase chaperone subunit B | 3-methyl-glutaconic aciduria type VIIB (44) | [616271](https://www.omim.org/entry/616271) | AR | Cataracts, neurologic deficits, neutropenia, NC in at least 2 cases |
| *FUT8* | Fucosyl-transferase 8 | Congenital disorder of glycosylation with defective fucosylation 1 (45) | [618005](https://www.omim.org/entry/618005) | AR | Poor growth, failure to thrive, hypotonia, skeletal anomalies, delayed psychomotor development, ID, NC |
| *G6PC* | Glucose-6-phosphatase catalytic subunit 1 (PT) | Glycogen storage disease type 1A (46) | [232200](https://www.omim.org/entry/232200) | AR | Glycogen accumulation, severe hypoglycemia, hepatomegaly, growth retardation, delayed puberty, lactic acidemia, hyperlipidemia, hyperuricemia, gout, nephropathy, NL, hypercalciuria, NC |
| *HGD* | Homogentisate 1,2-dioxygenase (PT) | Alkaptonuria (47) | [203500](https://www.omim.org/entry/203500) | AR | Homogentisic acid accumulation, darkened urine, connective tissue pigmentation, joint/spine arthritis, cardiac valves destruction, NL |
| *OPLAH* | 5-oxoprolinase, ATP-hydrolysing | 5-oxoprolinase deficiency (48) | 260005 | AD/AR | Inborn error of glutathione metabolism, excessive excretion of 5-oxo-L-proline, NL |
| *SLC1A1* | Solute carrier family 1 member 1 (PT) | Dicarboxylic aminoaciduria (49) | [222730](https://www.omim.org/entry/222730) | AR | Incomplete glomerular anionic amino acid reabsorption, elevated urinary glutamate/aspartate, NL |
| *SLC36A2* | Solute carrier family 36 member 2 (PT) | Hyper-glycinuria (50) | [138500](https://www.omim.org/entry/138500) | AD | Glycinuria, oxalate NL |
| *SLC6A19* | Solute carrier family 6 member 19 (PT) | Hartnup disorder (51) | [234500](https://www.omim.org/entry/234500) | AR | Aminoaciduria, pellagra-like light-sensitive rash, cerebellar ataxia, emotional instability, hyperuricosuria, uric acid NL |

AD, autosomal dominant; AR, autosomal recessive; ESKD, end stage kidney disease; ID, intellectual disability; NC, nephrocalcinosis; NL, nephrolithiasis.

## Supplementary table S8. Genetic disorders with polycystic kidney disease with nephrolithiasis and/or nephrocalcinosis.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gene** | **Gene product** | **Phenotype** | **OMIM phenotype number** | **Inheritance** | **Description** |
| *ALG5* | ALG5 dolichyl-phosphate beta-glucosyltransferase | AD PKD 7 (52) | [620056](https://www.omim.org/entry/620056) | AD | NL (usually uric acid or calcium oxalate), abnormal transport of ammonium, low urine pH, hypocitraturia, some with distal RTA |
| *DNAJB11* | DnaJ heat shock protein family (Hsp40) member B11 | AD PKD 6 with or without polycystic liver disease (52) | [618061](https://www.omim.org/entry/618061) | AD | NL (usually uric acid or calcium oxalate), abnormal transport of ammonium, low urine pH, hypocitraturia, some with distal RTA |
| *GANAB* | Glucosidase II alpha subunit | AD PKD 3 (52) | [600666](https://www.omim.org/entry/600666) | AD | NL (usually uric acid or calcium oxalate), abnormal transport of ammonium, low urine pH, hypocitraturia, some with distal RTA |
| *PKD1* | Polycystin 1, transient receptor potential channel interacting | AD PKD 1 (52) | 173900 | AD | NL (usually uric acid or calcium oxalate), abnormal transport of ammonium, low urine pH, hypocitraturia, some with distal RTA |
| *PKD2* | Polycystin 2, transient receptor potential cation channel | AD PKD 2 (52) | [613095](https://www.omim.org/entry/613095) | AD | NL (usually uric acid or calcium oxalate), abnormal transport of ammonium, low urine pH, hypocitraturia, some with distal RTA |
| *PKHD1* | PKHD1 ciliary IPT domain containing fibrocystin/polyductin | AR PKD 4 with or without hepatic disease (53) | [263200](https://www.omim.org/entry/263200) | AR | Multifactorial NL, NC, medullary sponge kidney |

AD, autosomal dominant; AR, autosomal recessive; NC, nephrocalcinosis; NL, nephrolithiasis; PKD, polycystic kidney disease; RTA, renal tubular acidosis.

## Supplementary table S9. Other genetic disorders with multifactorial etiologies of nephrolithiasis and/or nephrocalcinosis.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gene** | **Gene product** | **Phenotype** | **OMIM phenotype number** | **Inheritance** | **Description** |
| *CLDN10* | Claudin 10 (PT) | HELIX syndrome (54) | [617671](https://www.omim.org/entry/617671) | AR | Hypohidrosis, electrolyte imbalance, lacrimal gland dysfunction, ichthyosis, xerostomia, hypermagnesemia, abnormal renal absorption of cations, hypomagnesuria, hypocalciuria, NL |
| *EMC10* | ER membrane protein complex subunit 10 | Neuro-developmental disorder with dysmorphic facies and variable seizures (55, 56) | [619264](https://www.omim.org/entry/619264) | AR | Global developmental delay, seizures, dysmorphic facies, skeletal defects, CAKUT, NC (5 cases) |
| *HSD11B2* | Hydroxysteroid 11-beta- dehydrogenase 2 (CD) | Apparent mineralocorticoid excess (57) | [218030](https://www.omim.org/entry/218030) | AR | Decreased conversion of active cortisol to inactive cortisone, cortisol acts as a ligand for MR, sodium retention with hypernatremia, volume expansion, hypertension (low renin/aldosterone), metabolic alkalosis, hypokalemia, NC (possible chronic hypokalemia-induced interstitial nephritis) |
| *PAX2* | Paired box 2 | Papillorenal syndrome (58) | [120330](https://www.omim.org/entry/120330) | AD | CAKUT, FSGS, multiple cases of hyperuricemia, NL |
| *STRADA* | STE20 related adaptor alpha | Polyhydramnios, megalencephaly, and symptomatic epilepsy (59-61) | [611087](https://www.omim.org/entry/611087) | AR | No abnormal urine findings, NC in multiple cases, 1 case with concurrent NL |
| *ZNF687* | Zinc finger protein 687 | Paget disease of bone 6 (62) | [616833](https://www.omim.org/entry/616833) | AD | Polyostotic bone lesions primarily affecting axial skeleton, bone pain coronary artery disease, malignant giant cell tumor of bone, hearing loss, hypercalciuria, hyperoxaluria, NL |

AD, autosomal dominant; AR, autosomal recessive; CAKUT, congenital anomalies of the kidney ad urinary tract; CD, collecting duct; FSGS, focal segmental glomerulosclerosis; MR, mineralocorticoid receptor; NC, nephrocalcinosis; NL, nephrolithiasis

## Supplementary table S10. Genetic disorders possibly associated with nephrolithiasis and/or nephrocalcinosis.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gene** | **Gene product** | **Phenotype** | **OMIM phenotype number** | **Inheritance** | **Description** |
| 19q13.11 | N/A | Proximal chromosome 19q13.11 deletion syndrome (63) | [617219](https://www.omim.org/entry/617219) | AD | Neurodevelopmental disorder, autism, feeding difficulties, growth retardation, kidney abnormalities (1 case with NL) |
| *AGPAT2* | 1-acylglycerol-3-phosphate O-acyltransferase 2 | Congenital generalized lipodystrophy type 1 (64) | [608594](https://www.omim.org/entry/608594) | AR | Near absence of adipose tissue, severe insulin resistance, NL (2 cases) |
| *AMMECR1* | AMMECR nuclear protein 1 | Midface hypoplasia, hearing impairment, elliptocytosis, NC (65) | [300990](https://www.omim.org/entry/300990) | XLR | 2 cases of this disease ever documented (2 half-brothers with NC, 1 with intermittent hypercalciuria) |
| *ATIC* | 5-aminoimidazole-4-carboxamide ribonucleotide formyltransferase/ IMP cyclohydrolase | AICA-ribosiduria due to ATIC deficiency (66) | [608688](https://www.omim.org/entry/608688) | AR | Global neurodevelopmental impairment, chorioretinal atrophy, growth impairment, scoliosis, coarse facies, epilepsy, aortic coarctation, chronic hepatic cytolysis, genital malformations, NC (1 case) |
| *ATP6V1E1* | V-ATPase H+ transporting V1 subunit E1 (alpha-IC, TAL, DCT) | AR cutis laxa type IIC (67) | [617402](https://www.omim.org/entry/617402) | AR | Skin wrinkling, sparse subcutaneous fat, dysmorphic progeroid facial features, hypotonia, cardiovascular involvement, NC (2 cases, brothers) |
| *BSCL2* | Seipin | Congenital generalized lipodystrophy type 2 (64) | [269700](https://www.omim.org/entry/269700) | AR | Near absence of adipose tissue, severe insulin resistance, hypertriglyceridemia, hepatic steatosis, NL (1 case) |
| *CHST14* | Carbohydrate sulfotransferase 14 | Ehlers-Danlos syndrome Musculo-contractural type 1 (68) | [601776](https://www.omim.org/entry/601776) | AR | Craniofacial dysmorphism, congenital thumb/finger contractures, clubfeet, kyphoscoliosis, hypotonia, hyperextensible thin skin, easy bruisability, atrophic scarring, wrinkled palms, joint hypermobility, ocular involvement, NL (1 case) |
| *FGF23* | Fibroblast growth factor 23 | Hyperphosphatemic familial tumoral calcinosis 2 (69) | [617993](https://www.omim.org/entry/617993) | AR | Progressive deposition of basic calcium phosphate crystals, increased renal phosphate absorption, hyperphosphatemia, NC (2 cases) |
| *GAD1* | Glutamate decarboxylase 1 | Developmental and epileptic encephalopathy 89 (70) | [619124](https://www.omim.org/entry/619124) | AR | Global developmental delay, ID, absent speech, axial hypotonia, spastic quadriparesis, seizures, joint contractures, foot deformities, dysmorphic facies, cleft palate, omphalocele, NL and NC (1 case) |
| *GNB2* | G protein subunit beta 2 | Neuro-developmental disorder with hypotonia and dysmorphic facies (71) | 619503 | AD | Global developmental delay, hypotonia, ID, dysmorphic facies, cardiac defects, joint contractures or hyperextensibility, dry skin, cryptorchidism, CAKUT, NC (1 case) |
| *IFIH1* | Interferon induced with helicase C domain 1 | Aicardi-Goutieres syndrome 7 (72) | [615846](https://www.omim.org/entry/615846) | AD | Inflammatory disorder, severe neurologic impairment, NC (1 case) |
| *MTM1* | Myotubularin 1 | X-linked centronuclear myopathy (73) | [310400](https://www.omim.org/entry/310400) | XLR | Congenital myopathy, slowly progressive weakness/wasting, pyloric stenosis, spherocytosis, gallstones, vitamin K-responsive bleeding diathesis, rapid linear growth, advanced bone age, NL (1 case), NC (1 case) |
| *MYL9* | Myosin light chain 9 | Megacystis-microcolon-intestinal hypoperistalsis syndrome 4 (74) | [619365](https://www.omim.org/entry/619365) | AR | Impaired smooth muscle contractility in bladder and intestines, bronchopulmonary dysplasia, recurrent NL (1 case) |
| *ROR2* | Receptor tyrosine kinase like orphan receptor 2 | AR Robinow syndrome 1 (75) | [268310](https://www.omim.org/entry/268310) | AR | Severe skeletal dysplasia, dysmorphic facies, short-limbed dwarfism, vertebral segmentation, genital hypoplasia, hypocitraturia with NC and NL (1 case) |
| *SLC45A1* | Solute carrier family 45 member 1 | Intellectual developmental disorder with neuropsychiatric features (76) | [617532](https://www.omim.org/entry/617532) | AR | ID, seizures, neuropsychiatric abnormalities, dysmorphic facies, NC (1 case) |
| *SRCAP* | Snf2 related CREBBP activator protein | Floating-Harbor Syndrome (77) | [136140](https://www.omim.org/entry/136140) | AD | Proportionate short stature, delayed bone age, delayed speech, dysmorphic facies, CAKUT, 2 cases of NC, 1 case with concurrent NL with hypercalciuria |
| *TMEM67* | Transmembrane protein 67 | COACH syndrome 1 (78) | [216360](https://www.omim.org/entry/216360) | AR | Cerebellar vermis hypo/aplasia, oligophrenia, ataxia, ocular coloboma, hepatic fibrosis, NL (1 case) |

AD, autosomal dominant; AR, autosomal recessive; CAKUT, congenital anomalies of the kidney and urinary tract; DCT, distal convoluted tubule; ID, intellectual disability; NC, nephrocalcinosis; NL, nephrolithiasis; TAL, thick ascending loop of Henle; XLR, X-linked recessive.

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