Supplementary Material

Prevalence of Mendelian kidney disease among patients with high-risk *APOL1* genotypes undergoing commercial genetic testing in the United States

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Supplementary Figure 1. Comparison of self-reported or designated race/ethnicity with genomic ancestry derived from HGDP and 1KG.

Supplementary Figure 2. Population Stratification of individuals harboring *APOL1* risk alleles.

Supplementary Figure 3. Flowchart of patients in the overall cohort included in this study.

Supplementary Figure 4. Most common genes among all patients with Mendelian kidney diseases stratified by *APOL1* genotype included in this study.

Supplementary Table 1. Comprehensive list of 343 genes implicated in Mendelian kidney diseases.

Supplementary Table 2. Distribution of global ancestry proportions across five continental populations in genetic clusters from principal component analysis.

Supplementary Table 3. Comparative analysis of self-reported or designated race/ethnicity and genetic clusters derived from principal component analysis.

Supplementary Table 4. Global ancestry proportions in five continental populations based on self-reported or designated race/ethnicity.

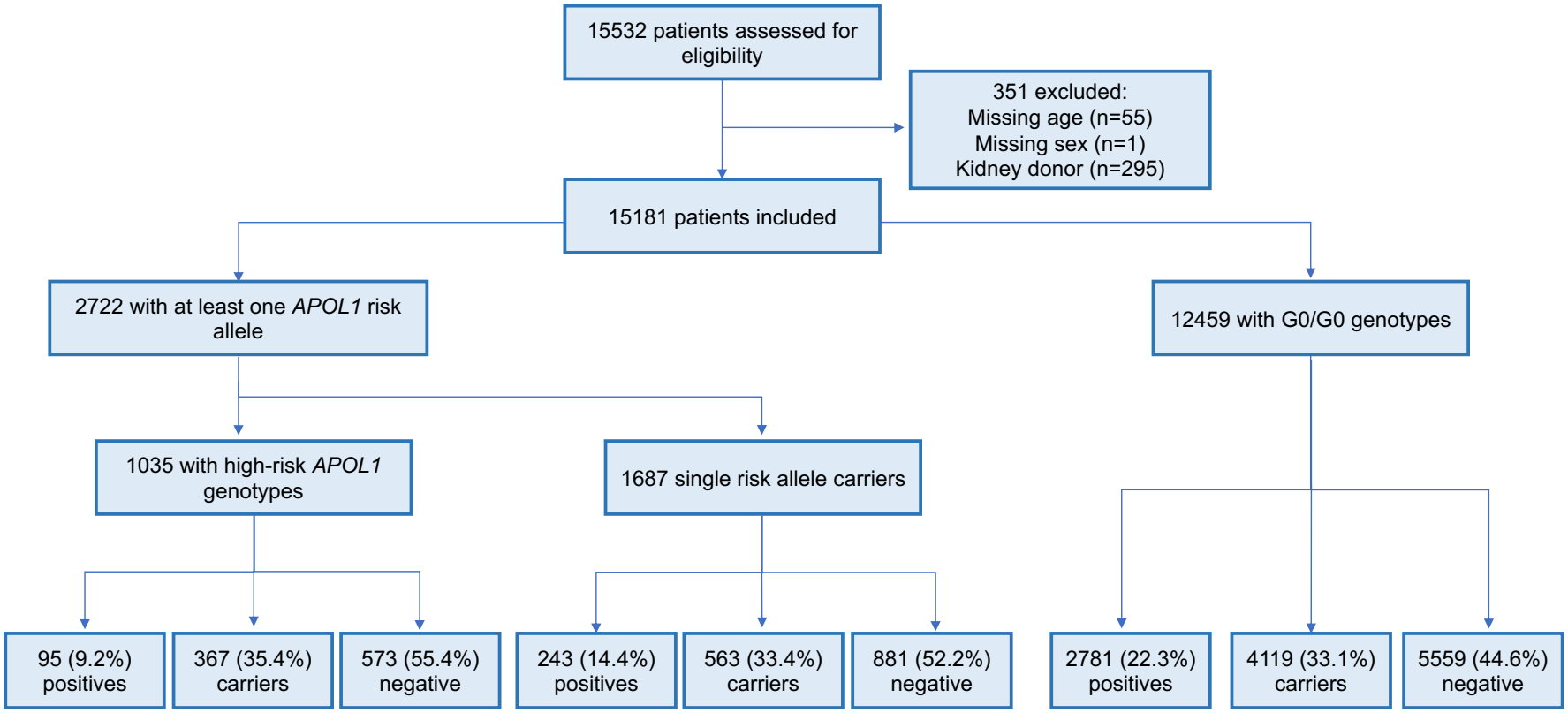
Supplementary Table 5. Demographic data of patients stratified by presence of *APOL1* risk alleles in the overall cohort.

Supplementary Table 6. Prevalence of disease category across *APOL1* high-risk genotype and *APOL1* low-risk genotypes among the in patients with recent African ancestry.

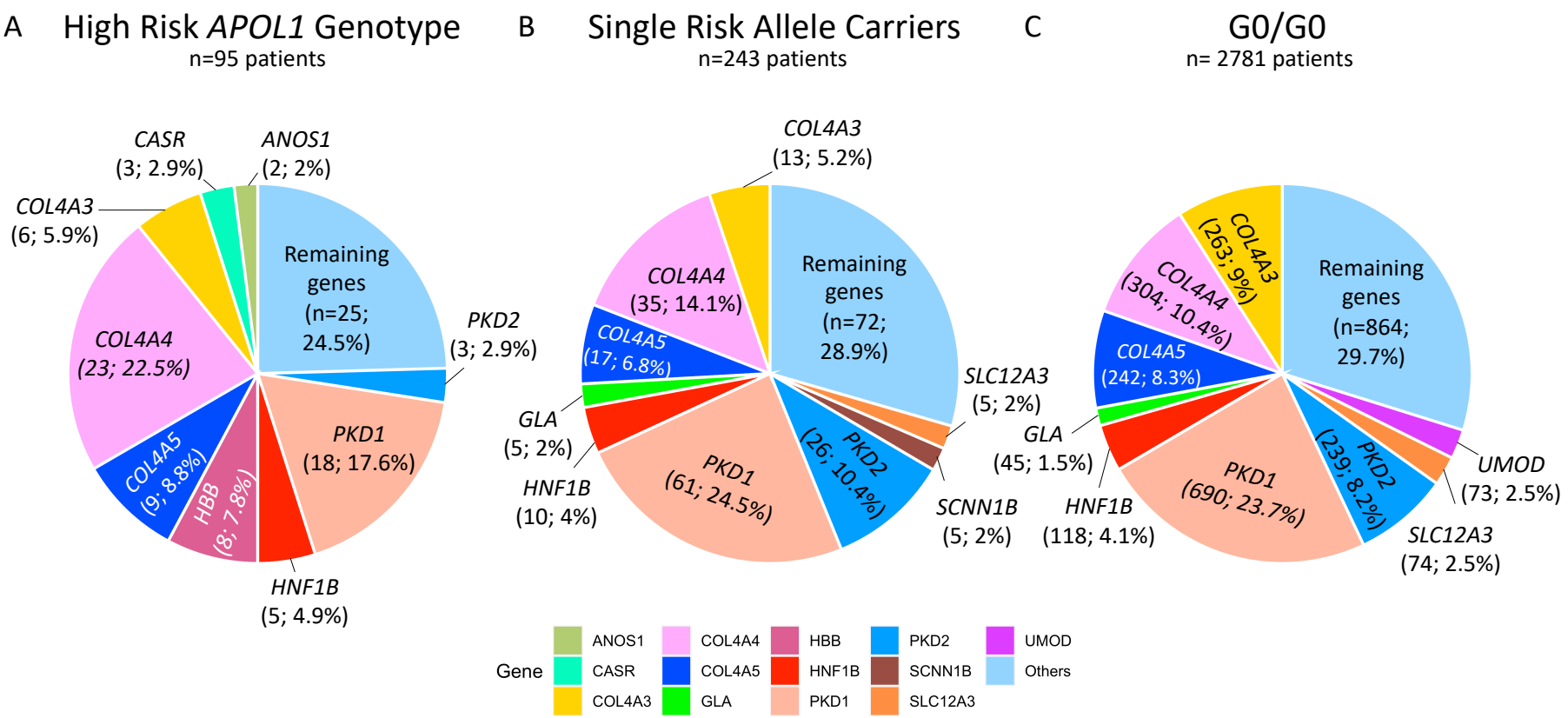
Supplementary Table 7. Frequency of Mendelian kidney disease stratified by *APOL1* genotype in the overall cohort.

Supplementary Figure 1: Comparison of self-reported or designated race/ethnicity with genomic ancestry derived from HGDP and 1KG. *Left Panel:* Each point represents an individual. Open circles in transparent colors represent individuals from HGDP and 1KG used as the reference panel, while cross points in darker (opaque) colors represent the self-reported race/ethnicity of individuals from our cohort. PC1 and PC2 represent the first two principal components of ancestry informative markers. The genetic diversity across the samples includes five major continental populations: European, African, Admixed American, Central-South Asian, and East Asian, alongside the self-reported race/ethnicity of participants in our study. There is excellent qualitative overlap between the self-reported race/ethnicity and the expected genetic ancestry. *Right Panel:* UMAP visualization based on the first 10 principal components. The sample coloring corresponds to the participants' self-reported race/ethnicity, providing insights into the clustering patterns relative to self-identified groups.

Supplementary Figure 2: Population Stratification of individuals harboring *APOL1* risk alleles. *Left Panel:* This panel shows the global ancestry structure of individuals with high-risk *APOL1* genotypes, represented by black points, illustrating their distribution across the diverse population groups in 1KGP and HGDP Samples. *Right Panel:* Single risk allele carriers for *APOL1* are represented by black points. It is clear in both panels that individuals with high-risk *APOL1* genotypes and single risk allele carriers have recent African ancestry (transparent purple points).



Supplementary Figure 3: Flowchart of patients in the overall cohort included in this study. Positive samples refer to the number of patients with Mendelian kidney disease. Carriers were defined as patients harboring heterozygous P/LP (pathogenic/likely pathogenic) variants in genes associated with a recessive inheritance pattern. The remaining samples were considered negative.



Supplementary Figure 4: **Most common genes among the overall cohort of patients with Mendelian kidney diseases stratified by *APOL1* genotype included in this study.** Proportional representation (n, %) of most common genes in patients with (a) high-risk *APOL1* genotypes, (b) single-risk allele carriers and (c) G0/G0 patients.

Supplementary Table 1: Comprehensive list of 343 genes implicated in Mendelian kidney diseases. Detailed information about each of the 343 genes associated with Mendelian kidney diseases studied. This includes the gene name, associated disease, inheritance pattern, and disease category. We also detail the presence of pathogenic or likely pathogenic (P/LP) variants. The inheritance patterns are categorized as autosomal recessive (AR), autosomal dominant (AD), X-linked (XL), and unknown (UK). Disease categories are defined as follows: Cystic & Tubulointerstitial Diseases (CTI), Glomerular Diseases (G), Tubulopathies and Tubular Diseases (T), Congenital Anomalies of the Kidney and Urinary Tract & Structural Diseases (CS), and Complement-related Kidney Diseases (CR).

Gene	Disease Name	Inheritance	Disease Category	P/LP variants
ABCC6	Pseudoxanthoma elasticum and/or Generalized arterial calcification of infancy	AR	T	Yes
ABCC8	ABCC8-related disorders	AD;AR	T; G	Yes
ACE	Renal Tubular Dysgenesis	AR	CS	Yes
ACTB	ACTB-Related Disorders	AD	CS	No
ACTN4	Focal Segmental Glomerulosclerosis	AD		Yes
ADA2	Adenosine Deaminase 2 Deficiency (DADA2); Sneddon syndrome	AR	G	Yes
ADAMTS13	Familial Thrombotic Thrombocytopenic Purpura	AR	CR	Yes
AGPAT2	Lipodystrophy congenital generalized, type 1	AR	G	Yes
AGT	Renal Tubular Dysgenesis	AR	CS	Yes
AGTR1	Renal Tubular Dysgenesis	AR	CS	Yes
AGXT	Primary hyperoxaluria type 1	AR	T	Yes
AHI1	Joubert Syndrome 3	AR	CTI	Yes
ALG1	Congenital Disorder of Glycosylation, Type 1K	AR	G	Yes
ALG8	Congenital disorder of glycosylation type Ih	AR	CTI	Yes
ALG9	Polycystic Kidney and Liver Disease (AD); Congenital Disorder of Glycosylation, type 2 (AR); Gillessen Kaesbach Nishimura syndrome (GIKANIS) (AR)	AD;AR	CTI	Yes
ALMS1	Alstrom syndrome	AR	CTI	Yes
ALPL	Hypophosphatasia	AD;AR	T	Yes
AMN	Megaloblastic Anemia 1, Norwegian Type	AR	T	Yes
ANKS6	Nephronophthisis 16	AR	CTI	Yes
ANOS1	Isolated Gonadotropin-Releasing Hormone (GnRH) Deficiency	XL	CS	Yes
AP2S1	Familial Hypocalciuric Hypercalcemia, Type 3	AD	T	No
APOA1	Familial Visceral Amyloidosis (AD); Primary Hypoalphalipoproteinemia (AR)	AD;AR	G	Yes
APOC2	Hyperlipoproteinemia, type Ib	AR	G	Yes
APOPT1	Mitochondrial Complex 4 deficiency	AR	T	Yes
APRT	Adenine Phosphoribosyltransferase Deficiency	AR	T	Yes
AQP2	Diabetes insipidus, nephrogenic	AD;AR	T	Yes
ARL6	Bardet-Biedl Syndrome 3 (AR); Retinitis Pigmentosa 55 (AR)	AR	CTI	Yes
ATP6V0A4	ATP6V0A4-Distal Renal Tubular Acidosis (AR)	AR	T	Yes

Gene	Disease Name	Inheritance	Disease Category	P/LP variants
ATP6V1B1	ATP6V1B1-Distal Renal Tubular Acidosis (ATP6V1B1-dRTA)	AR	T	Yes
ATP7B	Wilson disease	AR	T	Yes
AVP	Diabetes insipidus, Neurohypophyseal	AD	T	Yes
AVPR2	Diabetes Insipidus, Nephrogenic	XL	T	Yes
B2M	Familial Visceral Amyloidosis (AD); Immunodeficiency 43 (AR)	AD;AR	G	Yes
BBS1	Bardet-Biedl syndrome 1	AR	CS; CTI	Yes
BBS10	Bardet-Biedl syndrome 10	AR	CS; CTI	Yes
BBS12	Bardet-Biedl syndrome 12	AR	CS; CTI	Yes
BBS2	Bardet-Biedl syndrome 2 (AR); Retinitis Pigmentosa 74 (AR)	AR	CS; CTI	Yes
BBS4	Bardet-Biedl Syndrome 4	AR	CS; CTI	Yes
BBS5	Bardet-Biedl Syndrome 5	AR	CS; CTI	Yes
BBS7	Bardet-Biedl syndrome 7	AR	CS; CTI	Yes
BBS9	Bardet-Biedl syndrome 9	AR	CTI	Yes
BCS1L	BCS1L-Related Disorders (AR)	AR	T	Yes
BICC1	Renal Dysplasia, Cystic	UK	CS; CTI	No
BMP4	Congenital Anomalies of the Kidney and Urinary Tract; Microphthalmia, syndromic 6	AD	CS	No
BMPR2	Pulmonary Hypertension, Familial Primary with or without Hereditary Hemorrhagic Telangiectasia & Pulmonary venoocclusive disease 1	AD	T	Yes
BRAF	Noonan Syndrome (AD); Noonan Syndrome with Multiple Lentigines (AD); Cardiofaciocutaneous Syndrome (AD)	AD	CS	No
BSCL2	BSCL2-related conditions	AD;AR	G	Yes
BSND	Bartter Syndrome, Type 4a (AR)	AR	T	Yes
C3	Atypical Hemolytic Uremic Syndrome (AD); C3 Glomerulopathy (AD); C3 deficiency (AR)	AD;AR	CR	Yes
CA2	Osteopetrosis with Renal Tubular Acidosis	AR	T	Yes
CACNA1H	Familial Hyperaldosteronism, Type IV (AD)	AD	T	No
CACNA1S	Hypokalemic Periodic Paralysis Type 1 (AD); Malignant Hyperthermia Susceptibility (AD); Dihydropyridine receptor congenital myopathy (AR)	AD;AR		Yes
CASR	CASR-related conditions	AD;AR	T	Yes
CAV1	Lipodystrophy, Familial Partial, type 7 (AD); Pulmonary Hypertension, Primary, 3 (AD); Lipodystrophy, Congenital Generalized, Type 3 (AR)	AD;AR	T	Yes
CD151	Nephropathy with Pretibial Epidermolysis Bullosa and Deafness	AR	G	Yes
CD2AP	Focal Segmental Glomerulosclerosis 3 (AR); Susceptibility to Focal Segmental Glomerulosclerosis (AD)	AD;AR	G	Yes

Gene	Disease Name	Inheritance	Disease Category	P/LP variants
CDC73	CDC73-related Disorders (AD)	AD	T	Yes
CDKN1C	Beckwith-Wiedemann Syndrome (AD); IMAGe Syndrome (AD)	AD	T	No
CEL	Maturity-Onset Diabetes of the Young, Type 8	AD	G	Yes
CEP164	Senior-Loken Syndrome; Nephronophthisis 15	AR	CTI	Yes
CEP290	CEP290-Related Ciliopathies	AR	CTI	Yes
CFH	Atypical Hemolytic Uremic Syndrome (AD); C3 Glomerulopathy (AD); Complement Factor H Deficiency (AR)	AD;AR	CR	Yes
CFHR5	Atypical Hemolytic Uremic Syndrome (AD); C3 Glomerulopathy (AD); Complement Factor H Deficiency (AR)	AD;AR	CR	No
CFI	Atypical Hemolytic Uremic Syndrome (AD); C3 Glomerulopathy (AD); Complement Factor I Deficiency (AR)	AD;AR	CR	Yes
CHD7	CHARGE syndrome	AD	CS	Yes
CHRM3	Prune-Belly Syndrome (AR)	AR	CS	No
CHRNA3	Bladder Dysfunction, Autonomic, with Impaired Pupillary Reflex and Secondary Congenital Anomalies of the Kidney and Urinary Tract	AR	CS	Yes
CISD2	Wolfram Syndrome 2	AR	G	No
CLCN2	Hyperaldosteronism (AD); CLCN2-related leukoencephalopathy (AR)	AD;AR	T	Yes
CLCN5	Dent disease 1	XL	T	Yes
CLCNKB	Bartter Syndrome, Type 3/4B (AR); Gitelman syndrome (AR)	AR	T	Yes
CLDN16	Hypomagnesemia 3, Renal	AR	T	Yes
CLDN19	Hypomagnesemia 5, Renal, with Ocular Involvement	AR	T	Yes
CNNM2	Renal hypomagnesemia (AD/AR)	AD;AR	T	Yes
COL4A1	COL4A1-Related Disorders	AD	CTI	Yes
COL4A3	COL4A3-related Alport syndrome	AD;AR	G	Yes
COL4A4	COL4A4-related Alport syndrome	AD;AR	G	Yes
COL4A5	Alport syndrome, X-linked	XL	G	Yes
COQ2	Coenzyme Q10 Deficiency, Primary 1	AR	G	Yes
COQ6	Coenzyme Q10 Deficiency, Primary 6	AR	G	Yes
COX10	Mitochondrial Complex 4 deficiency	AR	T	Yes
COX20	Mitochondrial Complex 4 deficiency	AR	T	Yes
COX6B1	Mitochondrial Complex 4 deficiency	AR	T	No
CPLANE1	Orofaciodigital Syndrome 6 (AR); Joubert syndrome with Oral-Facial-Digital features (AR)	AR	CTI	Yes
CPT2	Carnitine Palmitoyltransferase II Deficiency (AR)	AR	G; T	Yes
CREBBP	Rubinstein-Taybi Syndrome, Type 1 (AD); Menke-Hennekam Syndrome (AD)	AD	T	No
CTNS	Cystinosis	AR	CTI	Yes

Gene	Disease Name	Inheritance	Disease Category	P/LP variants
CUBN	Proteinuria, chronic benign; Megaloblastic Anemia 1, FinnishType	AR	G	Yes
CUL3	Pseudohypoaldosteronism, Type 2E	AD	T	Yes
CYP11A1	Congenital adrenal insufficiency (CYP11A1-deficiency)	AR	T	Yes
CYP11B1	Familial hyperaldosteronism type I (AD); Adrenal hyperplasia, congenital, due to 11-beta-hydroxylase deficiency (AR)	AD;AR	T	Yes
CYP11B2	Corticosterone methyloxidase deficiency	AR	T	Yes
CYP17A1	17-Alpha-Hydroxylase/7,20-Lyase Deficiency	AR	T	Yes
CYP24A1	CYP24A1-related hypercalcemia (AR)	AR	T	Yes
CYP27B1	Vitamin D-Dependent Rickets, Type 1A	AR	T	Yes
CYP2R1	Rickets due to Defect in Vitamin D 25-hydroxylation	AR	T	Yes
DCDC2	Nephronophthisis 19	AR	CTI	Yes
DGKE	Atypical Hemolytic Uremic Syndrome	AR	G	Yes
DHCR7	Smith-Lemli-Opitz syndrome	AR	CS	Yes
DLC1	Nephrotic Syndrome	UK	G	No
DMP1	Hypophosphatemic Rickets	AR	T	Yes
DNASE1L3	Systemic Lupus Erythematosus 16	AR	T	Yes
EBP	Chondrodysplasia Punctata (XL); MEND syndrome (XL)	XL	T	No
EIF2AK3	Wolcott-Rallison Syndrome	AR	G	Yes
ELP1	Familial Dysautonomia, Hereditary Sensory and Autonomic Neuropathy Type 3	AR	G	Yes
ENPP1	Hypophosphatemic Rickets (AR); Generalized arterial calcification of infancy (AR); Cole disease (AD)	AD;AR	T	Yes
EYA1	Branchiootorenal Spectrum Disorders (AD)	AD	CS	Yes
FAM20A	Amelogenesis Imperfecta, Type 1G	AR	T	Yes
FAN1	Interstitial Nephritis, Karyomegalic	AR	CTI	Yes
FANCA	Fanconi Anemia, Group A (AR)	AR	CS	Yes
FANCB	Fanconi Anemia, Group B	XL	CS	No
FANCC	Fanconi Anemia, Group C (AR)	AR	CS	Yes
FANCD2	Fanconi Anemia, Group D2	AR	CS	Yes
FANCE	Fanconi Anemia, Group E	AR	CS	Yes
FANCF	Fanconi Anemia, Group F	AR	CS	Yes
FANCG	Fanconi Anemia, Group G	AR	CS	Yes
FANCI	Fanconi Anemia, Group I	AR	CS	Yes
FANCL	Fanconi Anemia, Group L	AR	CS	Yes
FASTKD2	Mitochondrial Complex 4 deficiency	AR	T	Yes
FGA	Hereditary Renal Amyloidosis (AD); Congenital Fibrinogen Deficiency (AR)	AD;AR	G	Yes
FGF10	Lacrimo-auriculo-dento-digital (LADD) Syndrome	AD	CS	No

Gene	Disease Name	Inheritance	Disease Category	P/LP variants
FGF23	Hypophosphatemic Rickets (AD); Tumoral Calcinosis, Hyperphosphatemic (AR)	AD;AR	T	Yes
FGFR1	FGFR1-related conditions	AD	CS	Yes
FGFR2	FGFR2-related conditions	AD	CS	Yes
FLCN	Birt-Hogg-Dubé syndrome (AD); Primary Spontaneous Pneumothorax (AD)	AD	CTI	Yes
FN1	Glomerulopathy With Fibronectin Deposits 2 (AD); Corner Fracture Type Spondylometaphyseal Dysplasia (AD)	AD	G	Yes
FOXC1	Axenfeld-Rieger Syndrome, Type 3	AD	CS	Yes
FOXC2	Lymphedema-Distichiasis Syndrome with Renal Disease and Diabetes Mellitus	AD	G	Yes
FOXI1	Hereditary Distal Renal Tubular Acidosis (AR)	AR	T	No
FOXP3	IPEX syndrome (including type 1 diabetes)	XL	G	Yes
FRAS1	Fraser Syndrome	AR	CS	Yes
FREM1	FREM1-related conditions	AD;AR	CS	Yes
FREM2	Fraser Syndrome	AR	CS	Yes
FXYD2	Hypomagnesemia 2, Renal	AD	T	No
G6PC	Glycogen storage disease, type 1a	AR	T	Yes
GALNT3	Hyperphosphatemic Familial Tumoral Calcinosis	AR	T	Yes
GANAB	Polycystic Kidney and/or Polycystic Liver Disease	AD	CTI	Yes
GATA3	Hypoparathyroidism, Sensorineural Deafness, and Renal Dysplasia	AD	CS	Yes
GATM	Cerebral creatine deficiency syndrome 3 (AR); Fanconi renotubular syndrome 1 (AD)	AD;AR	T	Yes
GCK	Maturity-onset diabetes of the young, type 2 (AD); Late onset, non insulin dependent diabetes mellitus (AD); Permanent neonatal diabetes mellitus 1 (AR); Familial hyperinsulinemic hypoglycemia 3 (AD)	AD;AR	G	Yes
GCM2	Familial Isolated Hypoparathyroidism (AD/AR); Familial Isolated Hyperparathyroidism (AD)	AD;AR	T	Yes
GLA	Fabry disease	XL	G	Yes
GLI3	GLI3-Related Disorders	AD	CS	Yes
GLIS2	Nephronophthisis 7	AR	CTI	No
GLIS3	Diabetes Mellitus, Neonatal, With Congenital Hypothyroidism	AR	G; CTI	Yes
GNA11	Autosomal Dominant Hypocalcemia 2 (AD); Hypocalciuric hypercalcemia, type II (AD)	AD	T	No
GNAS	GNAS-Related Disorders	AD	T	Yes
GPC3	Simpson-Golabi-Behmel Syndrome, Type 1	XL	CS	Yes
GRHPR	Hyperoxaluria, Primary, Type 2	AR	T	Yes
GRIP1	Fraser Syndrome	AR	CS	Yes

Gene	Disease Name	Inheritance	Disease Category	P/LP variants
GSN	Amyloidosis, Finnish Type	AD	G	Yes
HBB	Beta-Hemoglobinopathies (AD/AR); Sickle cell disease (AR)	AD;AR	G; T	Yes
HGD	Alkaptonuria	AR	T	Yes
HNF1A	HNF1A-MODY (Maturity-Onset Diabetes of the Young)	AD	CTI	Yes
HNF1B	HNF1B-Related Disorders	AD	CTI; CS	Yes
HNF4A	Fanconi Renotubular Syndrome 4, with or without Maturity-Onset Diabetes of the Young (MODY), Type 1 (AD); MODY, Type 1 (AD); Congenital Hyperinsulinism (AD); Diabetes Mellitus, Type 2 (AD)	AD	G	Yes
HOGA1	Primary Hyperoxaluria, Type 3	AR	T	Yes
HOXA13	Hand-Foot-Uterus Syndrome	AD	CS	Yes
HPRT1	HPRT1-Related Disorders (XL)	XL	T	No
HPS1	Hermansky-Pudlak syndrome 1	AR	G	Yes
HPSE2	Urofacial Syndrome (AR)	AR	CS	Yes
HSD11B2	Apparent Mineralocorticoid Excess	AR	T	Yes
HSD3B2	Congenital adrenal hyperplasia due to 3-beta-hydroxysteroid dehydrogenase 2 deficiency	AR	T	Yes
IFT122	Cranioectodermal Dysplasia, Type 1	AR	CTI	Yes
IFT140	Retinitis pigmentosa 80; Short-Rib Thoracic Dysplasia 9 with or without Polydactyly	AR	CTI	Yes
IFT172	Short-Rib Thoracic Dysplasia 10 With Or Without Polydactyly (AR); Bardet-Biedl syndrome 20 (AR); Retinitis Pigmentosa 71 (AR)	AR	CTI	Yes
IFT43	Cranioectodermal Dysplasia, Type 3	AR	CTI	Yes
INF2	Focal Segmental Glomerulosclerosis 5; Charcot-Marie-Tooth Disease E	AD	G	Yes
INS	Diabetes mellitus, insulin-dependent, 2 (AD); Diabetes mellitus, permanent neonatal 4 (AD/AR); Maturity-onset diabetes of the young, type 10 (AD); Hyperproinsulinemia (AD)	AD;AR	G	Yes
INVS	Nephronophthisis 2; Senior-Loken syndrome	AR	CTI	Yes
IQCB1	Senior-Loken Syndrome 5	AR	CTI	Yes
ITGA3	Interstitial Lung Disease with Nephrotic Syndrome and Epidermolysis Bullosa	AR	G	Yes
ITGA6	Junctional Epidermolysis Bullosa- Pyloric Atresia Syndrome	AR	CS	Yes
ITGB4	Junctional Epidermolysis Bullosa-Pyloric Atresia Syndrome	AD;AR	G	Yes
JAG1	Alagille Syndrome, Type 1	AD	CS	Yes
KANSL1	Koolen-De Vries Syndrome	AD	CS	Yes
KAT6B	Genitopatellar syndrome; SBBYSS syndrome	AD	CS	No
KCNA1	Episodic Ataxia Type 1	AD	T	No
KCNJ1	Bartter syndrome	AR	T	Yes

Gene	Disease Name	Inheritance	Disease Category	P/LP variants
KCNJ10	Seizures, Sensorineural Deafness, Ataxia, Mental Retardation, and Electrolyte Imbalance (SeSAME Syndrome)	AR	T	Yes
KCNJ11	KCNJ11-Related Diabetes (AD); Familial Hyperinsulinism (AD/AR)0	AD;AR	G	Yes
KCNJ5	Familial Hyperaldosteronism Type 3	AD	T	No
KCNK3	Pulmonary Hypertension, Primary 4	AD	T	No
KCTD1	Scalp-Ear-Nipple Syndrome	AD	CS	No
KLHL3	Pseudohypoaldosteronism, Type 2D	AD;AR	T	Yes
KRAS	Cardiofaciocutaneous Syndrome (AD); Noonan Syndrome (AD)	AD	CS	No
LAMB2	Nephrotic Syndrome, Type 5, with or without Ocular Abnormalities; Pierson Syndrome	AR	G	Yes
LCAT	Complete LCAT Deficiency (AR); Partial LCAT Deficiency (AR)	AR	G	Yes
LDHA	Glycogen Storage Disease, Type 11	AR	T	Yes
LMNA	LMNA-Related Disorders	AD;AR	G	Yes
LMX1B	Nail-Patella Syndrome (AD); Focal Segmental Glomerulosclerosis 10 (AD)	AD	G	Yes
LPIN1	Myoglobinuria, Acute Recurrent	AR	G	Yes
LRP2	Donnai-Barrow Syndrome	AR	T	Yes
LRP4	Cenani-Lenz Syndactyly Syndrome	AR	CS	Yes
LRP5	LRP5-Related Disorders	AD;AR	CTI	Yes
LYZ	Amyloidosis, Familial Visceral, Renal	AD	G	No
LZTFL1	Bardet-Biedl Syndrome, Type 17	AR	CTI	Yes
MAFB	Multicentric Carpotarsal Osteolysis with or without Nephropathy	AD	G	Yes
MAGI2	Nephrotic Syndrome 15	AR	G	Yes
MEFV	Familial Mediterranean fever	AR	G	Yes
MKKS	Bardet-Biedl Syndrome, Type 6 (AR); McKusick-Kaufman syndrome (AR)	AR	CTI	Yes
MMACHC	Methylmalonic aciduria and homocystinuria, cblC type	AR	CR	Yes
MNX1	Currarino Syndrome	AD	CS	Yes
MOCOS	Xanthinuria, Type II	AR	T	Yes
MUT	Methylmalonic Aciduria, Type mut0 (AR)	AR	G; T	Yes
MVK	Mevalonate Kinase Deficiency	AR	G	Yes
MYCN	Feingold Syndrome 1 (AD)	AD	CS	No
MYH9	MYH9-Related Disorders (AD)	AD	G	Yes
MYO1E	Focal Segmental Glomerulosclerosis, 6	AR	G	Yes
NEK8	Nephronophthisis 9; Renal-Hepatic-Pancreatic Dysplasia	AR	CTI	Yes
NEUROD1	Maturity-Onset Diabetes of the Young 6	AD	G	Yes
NF1	Neurofibromatosis, Type 1	AD	G; T	Yes
NLRP3	Cryopyrin-Associated Periodic Syndromes (CAPS) (AD)	AD	G	No

Gene	Disease Name	Inheritance	Disease Category	P/LP variants
NOTCH2	Acroosteolysis Dominant Type; Alagille syndrome 2; Hajdu- Cheney Syndrome	AD	CS; CTI	Yes
NPHP1	Nephronophthisis 1, Juvenile; Senior-Loken Syndrome; Joubert Syndrome 4	AR	CTI	Yes
NPHP3	NPHP3-related conditions	AR	CTI	Yes
NPHP4	Nephronophthisis 4; Senior-Loken syndrome 4	AR	CTI	Yes
NPHS1	Congenital Nephrotic Syndrome, Finnish Type	AR	G	Yes
NPHS2	Congenital nephrotic syndrome, type 2	AR	G	Yes
NR0B1	Congenital Adrenal Hypoplasia with Hypogonadotropic Hypogonadism	XL	T	Yes
NR3C1	Glucocorticoid Resistance, Generalized	AD	T	Yes
NR3C2	Pseudohypoaldosteronism Type I, Autosomal Dominant Hypertension, Early-Onset	AD	T	Yes
NSD1	Sotos Syndrome	AD	CS	Yes
NSDHL	CHILD syndrome (XLD); CK syndrome (XLR)	XL	CS	Yes
OCRL	Dent disease 2; Lowe Syndrome	XL	T	Yes
OFD1	OFD1-Related Conditions (XL)	XL	CTI	Yes
OPLAH	5-Oxoprolinase Deficiency	AR	T	Yes
PAX2	PAX2-Related Disorders (AD)	AD	CS; G	Yes
PBX1	Congenital Anomalies of the Kidney and Urinary Tract syndrome with or without Hearing Loss, Abnormal Ears, or Developmental Delay (CAKUTHED)	AD	CS	Yes
PCBD1	BH4-Deficient Hyperphenylalaninemia D (AR); Juvenile-Onset Diabetes Mellitus (AR)	AR	G; T	Yes
PDSS1	Coenzyme Q10 Deficiency, Primary, 2	AR	G	Yes
PDSS2	Coenzyme Q10 Deficiency, Primary, 3	AR	G	Yes
PDX1	PDX1-familial monogenic diabetes, Pancreatic agenesis 1	AD;AR	G	Yes
PET100	Mitochondrial Complex 4 deficiency	AR	T	Yes
PGK1	Phosphoglycerate kinase 1 deficiency	XL	T	No
PHEX	Hypophosphatemic Rickets	XL	T	Yes
PKD1	Polycystic Kidney Disease 1	AD	CTI	Yes
PKD2	Polycystic Kidney Disease 2	AD	CTI	Yes
PKHD1	Autosomal Recessive Polycystic Kidney Disease	AR	CTI	Yes
PLCE1	Nephrotic Syndrome, Type 3	AR	G	Yes
PLG	Congenital Plasminogen Deficiency (AR)	AR	CR	Yes
PMM2	Congenital Disorder of Glycosylation, Type 1A; Hyperinsulinemic Hypoglycemia and Polycystic Kidney Disease	AR	G	Yes
PPP3CA	Arthrogryposis, Cleft Palate, Craniosynostosis, and Impaired Intellectual Development	AD	T	No
PRKCSH	Polycystic Liver Disease 1	AD	CTI	Yes
PRODH	Hyperprolinemia, Type 1	AR	CS; G; T	Yes

Gene	Disease Name	Inheritance	Disease Category	P/LP variants
PROKR2	Hypogonadotropic hypogonadism 3 with or without anosmia	AD;AR	CS	Yes
PRPS1	Phosphoribosylpyrophosphate synthetase superactivity	XL	T	No
PTH1R	Metaphyseal Chondrodysplasia, Murk Jansen Type (AD); Failure of tooth eruption, primary (AD); Chondrodysplasia, Blomstrand type (AR); Eiken syndrome (AR)	AD;AR	CTI	Yes
PTPN11	Noonan Syndrome (AD); Noonan Syndrome with Multiple Lentigines (AD)	AD	CS	Yes
PTPRO	Nephrotic Syndrome, Type 6	AR	G	Yes
RAD51C	Fanconi Anemia, Group O	AR	CS	Yes
REN	Autosomal Dominant Tubulointerstitial Kidney Disease (ADTKD-REN) (AD); Renal Tubular Dysgenesis (REN-dRTD) (AR)	AD;AR	CTI	Yes
RET	Multiple endocrine neoplasia 2A/2B; Familial medullary thyroid carcinoma	AD	CS	Yes
RMND1	Combined Oxidative Phosphorylation Deficiency 11	AR	CS	Yes
ROBO2	Congenital Anomalies of the Kidney and Urinary Tract	AD	CS	No
ROR2	Brachydactyly, type B1 (AD), Robinow Syndrome (AR)	AR	T	Yes
RPGRIP1L	Ciliopathies, RPGRIP1L-Related	AR	CTI	Yes
RPL11	Diamond-Blackfan Anemia 7	AD	CS	Yes
RPL35A	Diamond-Blackfan Anemia 5	AD	CS	No
RPL5	Diamond-Blackfan Anemia 6	AD	CS	No
RPS10	Diamond-Blackfan Anemia 9	AD	CS	No
RPS17	Diamond-Blackfan Anemia 4	AD	CS	No
RPS19	Diamond-Blackfan Anemia 1	AD	CS	No
RPS24	Diamond-Blackfan Anemia 3	AD	CS	No
RPS26	Diamond-Blackfan Anemia 10	AD	CS	No
RPS7	Diamond-Blackfan Anemia 8	AD	CS	No
RRM2B	RRM2B Mitochondrial DNA Maintenance Defects (RRM2B-MDMDs) (AD/AR)	AD;AR	T	Yes
SALL1	Townes-Brocks syndrome 1	AD	CS	Yes
SALL4	SALL4-Related Disorders (AD)	AD	CS	No
SARS2	Hyperuricemia, Pulmonary Hypertension, Renal Failure, And Alkalosis Syndrome (HUPRA Syndrome) (AR)	AR	T	Yes
SCARB2	Action Myoclonus-Renal Failure (AMRF) Syndrome	AR	G	Yes
SCN4A	SCN4A-Related Disorders	AD;AR	T	Yes
SCNN1A	Pseudohypoaldosteronism, Type 1	AR	T	Yes
SCNN1B	Liddle Syndrome 1 (AD); Pseudohypoaldosteronism, Type 1 (AR)	AD;AR	T	Yes

Gene	Disease Name	Inheritance	Disease Category	P/LP variants
SCNN1G	Liddle Syndrome 2 (AD); Pseudohypoaldosteronism, type 1 (AR)	AD;AR	T	Yes
SCO1	Mitochondrial Complex 4 deficiency	AR	T	Yes
SDCCAG8	Senior Loken Syndrome, Type 7; Bardet-Biedl Syndrome 16	AR	CTI	Yes
SEC63	Polycystic Liver Disease 2	AD	T	Yes
SEMA3E	CHARGE syndrome	UK	CS	No
SI	Sucrase-Isomaltase Deficiency	AR	T	Yes
SIX1	Branchiootorenal Spectrum Disorders (AD)	AD	CS	No
SIX5	Branchiootorenal Spectrum Disorders (AD)	AD	CS	No
SLC12A1	Bartter syndrome	AR	T	Yes
SLC12A3	Gitelman syndrome	AR	T	Yes
SLC16A12	Juvenile cataract with microcornea	AD	T	No
SLC22A12	Hypouricemia, Renal 1	AR	T	Yes
SLC26A1	Nephrolithiasis, Calcium Oxalate	AR	T	No
SLC2A2	Fanconi-Bickel Syndrome	AR	T	Yes
SLC2A9	Renal Hypouricemia 2	AD;AR	T	Yes
SLC34A1	Hypophosphatemic Nephrolithiasis/Osteoporosis 1 (AD) & Infantile Hypercalcemia 2 (AR)	AD;AR	T	Yes
SLC34A3	Hypophosphatemic Rickets with Hypercalciuria	AR	T	Yes
SLC37A4	Glycogen Storage Disease, Type 1B/1C (AR)	AR	G; T	Yes
SLC3A1	Cystinuria	AD;AR	T	Yes
SLC4A1	SLC4A1-associated Distal Renal Tubular Acidosis (AD/AR); Ovalocytosis, SA Type (AD); Cryohydrocytosis (AD); Spherocytosis, Type 4 (AD)	AD;AR	T	Yes
SLC4A4	Renal Tubular Acidosis, Proximal, with Ocular Abnormalities	AR	T	Yes
SLC5A1	Glucose-Galactose Malabsorption	AR	T	Yes
SLC5A2	Renal Glucosuria	AD;AR	T	Yes
SLC6A19	Hyperglycinuria (AD); Hartnup Disorder (AR); Iminoglycinuria (Complex)	AD;AR	T	Yes
SLC7A7	Lysinuric protein intolerance	AR	T	Yes
SLC7A9	Cystinuria	AD;AR	T	Yes
SLX4	Fanconi Anemia, Group P	AR	CS	Yes
SMAD9	Pulmonary Hypertension, Primary 2	AD	T	Yes
SMARCAL1	Schimke immunoosseous dysplasia	AR	G	Yes
SMC1A	Cornelia de Lange Syndrome (XL); Developmental and Epileptic Encephalopathy 85, with or without Midline Brain Defects (DEE85)	XL	CS	Yes
SOX17	Vesicoureteral Reflux 3	AD	CS	Yes
SOX18	SOX18-Related Disorders (AD/AR)	AD;AR	G; ?	No
SRCAP	Floating-Harbor Syndrome	AD	CS; T	Yes
STAR	Lipoid Adrenal Hyperplasia	AR	CS	Yes
STX16	Pseudohypoaldosteronism	AD	T	No
TACO1	Mitochondrial Complex 4 deficiency	AR	T	Yes

Gene	Disease Name	Inheritance	Disease Category	P/LP variants
TFAP2A	Branchiooculofacial Syndrome	AD	CS	No
THBD	Atypical Hemolytic Uremic Syndrome	AD	CR	Yes
TMEM67	TMEM67-related conditions	AR	CTI	Yes
TNS2	Nephrotic Syndrome	UK	G	No
TP53RK	Galloway-Mowat Syndrome	AR	G	No
TP63	P63-Related Conditions	AD	CS	Yes
TRIM32	Limb-girdle muscular dystrophy, type 2H (AR)	AR	CTI	Yes
TRPC6	Focal Segmental Glomerulosclerosis 2	AD	G	Yes
TRPM6	Hypomagnesemia 1, Intestinal	AR	T	Yes
TSC1	Tuberous sclerosis	AD	CTI	Yes
TSC2	Tuberous sclerosis	AD	CTI	Yes
TTC21B	Nephronophthisis 12; Short-rib thoracic dysplasia 4 with or without polydactyly	AR	CTI; G	Yes
TTC8	Bardet-Biedl Syndrome 8	AR	CTI	Yes
TXNL4A	Burn-McKeown syndrome	AR	CS	Yes
UMOD	Autosomal Dominant Tubulointerstitial Kidney Disease (ADTKD-UMOD) (AD)	AD	CTI	Yes
UPK3A	Renal Hypodysplasia	UK	CS	No
UQCC2	Mitochondrial Complex 3 Deficiency, Nuclear Type 7	AR	T	Yes
VDR	Vitamin D-dependent Rickets, Type 2A	AR	T	Yes
VHL	Von Hippel-Lindau Syndrome (AD); Familial Erythrocytosis 2 (AR)	AD	CTI	Yes
WAS	Wiskott-Aldrich Syndrome (XL); X-Linked Thrombocytopenia (XL); X-Linked Severe Congenital Neutropenia (XL)	XL	G	No
WDPCP	Bardet-Biedl Syndrome 15	AR	CTI	Yes
WDR19	WDR19-related conditions (see note below)	AR	CTI	Yes
WDR72	Amelogenesis Imperfecta with or without Distal Renal Tubular Acidosis - WDR72	AR	T	Yes
WDR73	Galloway-Mowat Syndrome	AR	G	Yes
WFS1	Wolfram Syndrome Spectrum Disorder (AD/AR)	AD;AR	CS; T	Yes
WNK1	Pseudohypoaldosteronism, Type 2C (AD); Autosomal recessive Neuropathy, hereditary sensory and autonomic, type II (AR)	AD;AR	T	Yes
WNK4	Pseudohypoaldosteronism, Type 2B	AD	T	Yes
WNT4	Mullerian Aplasia and Hyperandrogenism	AD	CS	No
WNT5A	Robinow Syndrome 1	AD	CS	No
WT1	WT1-Related Disorders	AD	CS; G	Yes
XDH	Xanthinuria, Type I	AR	T	Yes
XPNPEP3	Nephronophthisis-Like Nephropathy 1	AR	CTI	Yes
XRCC4	Short Stature, Microcephaly, and Endocrine Dysfunction	AR	CS	Yes

Supplementary Table 2: Distribution of global ancestry proportions across five continental populations in genetic clusters from principal component analysis. Cross-referencing between genetic clusters identified through principal component analysis (PCA) using the first 10 principal components and the global ancestry proportions for each continental population determined by admixture analysis. For each sample assigned to a genetic cluster, we present the median proportions and interquartile ranges of ancestry. The results demonstrate a high correlation between PCA-based clustering and admixture proportions for each cluster.

Genetic Cluster	N	Global Ancestry Proportions				
		African	European	Admixed_American	East Asian	Central-South Asian
Admixed American	2313	0.05 [0.02-0.09]	0.44 [0.34-0.54]	0.37 [0.26-0.48]	0.06 [0.01-0.11]	0 [0-0.08]
African	3678	0.7 [0.63-0.76]	0.22 [0.15-0.29]	0.01 [0-0.06]	0.01 [0-0.05]	0 [0-0.04]
Central-South Asian	368	0 [0-0.02]	0.33 [0.26-0.43]	0.03 [0-0.08]	0.3 [0.22-0.36]	0.29 [0.24-0.34]
East Asian	769	0 [0-0]	0.04 [0-0.09]	0.06 [0-0.13]	0.87 [0.78-0.93]	0 [0-0]
European	7458	0 [0-0.02]	0.82 [0.75-0.88]	0.01 [0-0.06]	0.01 [0-0.07]	0.1 [0.02-0.15]

Supplementary Table 3: Comparative analysis of self-reported or designated race/ethnicity and genetic clusters derived from principal component analysis. Cross-referencing between the self-reported or self-designated race/ethnicity and the assigned genetic clusters derived from principal component analysis. We show the number of samples for each self-reported or designated race/ethnicity group, and their intersection with the genetic clusters assigned in the ancestry analysis. The term "Multiple" refers to samples with more than one self-reported race and ethnicity category. Samples excluded from the cluster analysis are listed in the 'unclustered samples' column. Overall, we observed a high overlap between the self-reported or self-designated race/ethnicity and the genetic clusters assigned to each sample.

Self-reported race & ethnicity	No. of Unique Samples	Genetic Cluster					
		Admixed American	African	Central-South Asian	East Asian	European	Unclustered Samples*
African American	2893	15	2718	2	0	26	132
European American	5563	138	51	9	20	5110	235
East Asian	213	0	1	12	192	2	6
Hispanic	1912	1540	115	0	17	179	61
Mediterranean	70	0	1	7	1	58	3
Multiple**	241	31	53	8	23	116	10
Other	445	41	54	49	107	180	14
South-East Asian	302	1	0	135	147	8	11
Unknown	3542	547	685	146	262	1779	123

*No. of Samples excluded during PCA filtering steps due to missing the minimum number of single-nucleotide variants after quality control.
**The term 'Multiple' refers to samples with more than one self-reported race and ethnicity category.

Supplementary Table 4: Global ancestry proportions in five continental populations based on self-reported or designated race/ethnicity. Distribution of the global ancestry proportions for five continental populations as determined by admixture analysis across the self-reported or designated race/ethnicity in this study. We show the median and interquartile ranges of these proportions within each race/ethnicity group. Notably, individuals who self-reported or designated as African American showed a high proportion of recent African ancestry. Similar trends were observed in other race/ethnicity groups. These results underscore the reliability of self-reported or designated race/ethnicity in reflecting genetic ancestry within our cohort.

Self-reported race & ethnicity	N	Genetic Cluster				
		African	European	Admixed American	East Asian	Central-South Asian
African American	2761	0.71 [0.64-0.77]	0.21 [0.15-0.28]	0.02 [0-0.05]	0.01 [0-0.05]	0 [0-0.04]
European American	5328	0 [0-0.01]	0.83 [0.76-0.89]	0.01 [0-0.06]	0.01 [0-0.07]	0.09 [0.01-0.14]
East Asian	207	0 [0-0]	0.01 [0-0.06]	0.06 [0.01-0.12]	0.89 [0.81-0.94]	0 [0-0]
Hispanic	1851	0.06 [0.02-0.12]	0.45 [0.34-0.55]	0.35 [0.19-0.47]	0.05 [0-0.11]	0 [0-0.08]
Mediterranean	67	0.02 [0-0.06]	0.68 [0.59-0.76]	0.02 [0-0.08]	0.03 [0-0.1]	0.15 [0.09-0.23]
Multiple*	231	0.03 [0.01-0.22]	0.58 [0.32-0.77]	0.03 [0-0.13]	0.05 [0-0.11]	0.05 [0-0.13]
Other	431	0.01 [0-0.06]	0.46 [0.14-0.71]	0.04 [0-0.11]	0.11 [0.02-0.44]	0.05 [0-0.18]
South-East Asian	291	0 [0-0.01]	0.2 [0.04-0.35]	0.04 [0-0.11]	0.51 [0.3-0.87]	0.05 [0-0.28]
Unknown	3419	0.01 [0-0.11]	0.65 [0.28-0.83]	0.03 [0-0.12]	0.03 [0-0.1]	0.04 [0-0.13]

*The term 'Multiple' refers to samples with more than one self-reported race and ethnicity category.

Supplementary Table 5: Demographic data of patients stratified by presence of *APOL1* risk alleles in the overall cohort. Details of the main characteristics of our study cohort (n=15,181), including the distribution of gender, age, self-reported race/ethnicity, and genetic cluster. Data are stratified by *APOL1* risk allele status—categorized as High-Risk *APOL1* Genotype, Single Risk Allele Carriers, and G0/G0—and by Mendelian kidney disease status (Positive, Carrier, and Negative) within each group. Both raw numbers and row proportions (in parentheses) are provided for each category.

Category	All Patients	High-Risk *APOL1* Genotype				Single Risk Allele Carriers				G0/G0			
		All	Positive*	Carrier	Negative	All	Positive	Carrier	Negative	All	Positive	Carrier	Negative
No. of Samples	15181	1035 (6.8)	95 (9.2)	367 (35.5)	573 (55.4)	1687 (11.1)	243 (14.4)	563 (33.4)	881 (52.2)	12459 (82.1)	2781 (22.3)	4119 (33.1)	5559 (44.6)
Gender & Age													
Female	7606	472 (6.2)	54 (11.4)	152 (32.2)	266 (56.4)	798 (10.5)	133 (16.7)	248 (31.1)	417 (52.3)	6336 (83.3)	1536 (24.2)	2054 (32.4)	2746 (43.3)
Male	7575	563 (7.4)	41 (7.3)	215 (38.2)	307 (54.5)	889 (11.7)	110 (12.4)	315 (35.4)	464 (52.2)	6123 (80.8)	1245 (20.3)	2065 (33.7)	2813 (45.9)
Median Age yr [IQR]	47 [30-62]	45 [32-57]	37 [22-52]	46 [35-57]	45 [32-57]	46 [31-60]	40 [22-53]	47 [31-63]	48 [33-61]	47 [29-63]	40 [24-57]	50 [32-65]	48 [31-64]
Self-reported race & ethnicity													
African American	2960	815 (27.5)	73 (9)	293 (36)	449 (55.1)	1158 (39.1)	154 (13.3)	404 (34.9)	600 (51.8)	987 (33.3)	150 (15.2)	320 (32.4)	517 (52.4)
East Asian	230									230 (100)	62 (27)	64 (27.8)	104 (45.2)
European American	5718	9 (0.2)	1 (11.1)	3 (33.3)	5 (55.6)	47 (0.8)	13 (27.7)	12 (25.5)	22 (46.8)	5662 (99)	1289 (22.8)	2061 (36.4)	2312 (40.8)
Hispanic	1989	41 (2.1)	2 (4.9)	17 (41.5)	22 (53.7)	136 (6.8)	26 (19.1)	39 (28.7)	71 (52.2)	1812 (91.1)	409 (22.6)	446 (24.6)	957 (52.8)

Category	All Patients	High-Risk *APOL1* Genotype				Single Risk Allele Carriers				G0/G0			
		All	Positive*	Carrier	Negative	All	Positive	Carrier	Negative	All	Positive	Carrier	Negative
Mediterranean	93					1 (1.1)			1 (100)	92 (98.9)	16 (17.4)	33 (35.9)	43 (46.7)
Other	570	23 (4)	2 (8.7)	12 (52.2)	9 (39.1)	25 (4.4)	4 (16)	11 (44)	10 (40)	522 (91.6)	123 (23.6)	162 (31)	237 (45.4)
South-East Asian	330					2 (0.6)			2 (100)	328 (99.4)	76 (23.2)	90 (27.4)	162 (49.4)
Unknown	3542	161 (4.5)	18 (11.2)	50 (31.1)	93 (57.8)	341 (9.6)	50 (14.7)	107 (31.4)	184 (54)	3040 (85.8)	707 (23.3)	1014 (33.4)	1319 (43.4)
Genetic cluster													
Admixed American	2313	27 (1.2)		8 (29.6)	19 (70.4)	141 (6.1)	25 (17.7)	38 (27)	78 (55.3)	2145 (92.7)	476 (22.2)	552 (25.7)	1117 (52.1)
African	3678	944 (25.7)	91 (9.6)	345 (36.5)	508 (53.8)	1453 (39.5)	198 (13.6)	496 (34.1)	759 (52.2)	1281 (34.8)	213 (16.6)	406 (31.7)	662 (51.7)
Central-South Asian	368					2 (0.5)	1 (50)		1 (50)	366 (99.5)	78 (21.3)	107 (29.2)	181 (49.5)
East Asian	769					1 (0.1)		1 (100)		768 (99.9)	175 (22.8)	207 (27)	386 (50.3)
European	7458	4 (0.1)	1 (25)	1 (25)	2 (50)	37 (0.5)	10 (27)	10 (27)	17 (45.9)	7417 (99.5)	1766 (23.8)	2715 (36.6)	2936 (39.6)
Unclustered Samples***	595	60 (10.1)	3 (5)	13 (21.7)	44 (73.3)	53 (8.9)	9 (17)	18 (34)	26 (49.1)	482 (81)	73 (15.1)	132 (27.4)	277 (57.5)

*Positive refers to patients with a molecular diagnosis of Mendelian kidney disease

***No. of Samples excluded during PCA filtering steps due to missing the minimum number of single-nucleotide variants after quality control

Supplementary Table 6: Prevalence of disease category across *APOL1* high-risk genotype and *APOL1* low-risk genotypes among the in patients with recent African ancestry. Comparative analysis of the frequency of Mendelian kidney diseases between *APOL1* high-risk and low-risk genotypes in patients of recent African ancestry. We aggregated positive cases by disease category and performed a proportion test, stratifying by the presence of high-risk *APOL1* genotypes. P-values were adjusted using the Bonferroni method in R to control for multiple testing.

Disease Category	Prevalence of disease categories by *APOL1* risk alleles among African ancestry				Prevalence of disease categories by Mendelian status among African ancestry			
	High Risk Genotype	Low Risk Genotypes	*P*	P adjusted	High Risk Genotype	Low Risk Genotypes	*P*	P adjusted
	N=944	N=2734			N=91	N=411		
Complement-related Kidney Diseases	1 (0.11)	7 (0.26)	0.39338	1.00000	1 (1.1)	7 (1.7)	0.67705	0.90288
CAKUT & Structural Diseases	12 (1.27)	39 (1.43)	0.72499	1.00000	12 (13.19)	39 (9.49)	0.29075	0.87225
Cystic & Tubulointerstitial Diseases	29 (3.07)	206 (7.53)	0.00000	0.00001	29 (31.87)	206 (50.12)	0.00159	0.00636
Glomerular Diseases	49 (5.19)	144 (5.27)	0.92775	1.00000	49 (53.85)	144 (35.04)	0.00085	0.00423
Tubulopathy and Tubular Diseases	19 (2.01)	72 (2.63)	0.28976	1.00000	19 (20.88)	72 (17.52)	0.45144	0.90288

Supplementary Table 7: Frequency of Mendelian kidney disease stratified by *APOL1* genotype in the overall cohort. Comprehensive overview of the frequency of positive cases for Mendelian kidney diseases across the genes harboring P/LP variants, within our cohort (n=15,181). It details the counts and relative frequencies of these cases, both in the overall population and stratified by *APOL1* genotype categories: High-Risk *APOL1* Genotype, Single Risk Allele Carriers, and G0/G0.

Gene	Inheritance	Total	Percentage (%)	High Risk *APOL1* Genotype		Single Risk Allele Carriers		G0/G0	
				N	%	N	%	N	%
PKD1	AD	769	5.07	18	1.74	61	3.62	690	5.54
COL4A4	AD;AR	362	2.38	23	2.22	35	2.07	304	2.44
COL4A3	AD;AR	282	1.86	6	0.58	13	0.77	263	2.11
COL4A5	XL	268	1.77	9	0.87	17	1.01	242	1.94
PKD2	AD	268	1.77	3	0.29	26	1.54	239	1.92
HNF1B	AD	133	0.88	5	0.48	10	0.59	118	0.95
SLC12A3	AR	79	0.52	0	0	5	0.3	74	0.59
UMOD	AD	77	0.51	0	0	4	0.24	73	0.59
GLA	XL	50	0.33	0	0	5	0.3	45	0.36
SLC7A9	AD;AR	46	0.3	0	0	2	0.12	44	0.35
NPHP1	AR	36	0.24	0	0	1	0.06	35	0.28
CLCN5	XL	35	0.23	0	0	4	0.24	31	0.25
ABCC8	AD;AR	31	0.2	1	0.1	2	0.12	28	0.22
CFI	AD;AR	29	0.19	0	0	4	0.24	25	0.2
COL4A1	AD	29	0.19	2	0.19	0	0	27	0.22
HBB	AD;AR	28	0.18	8	0.77	4	0.24	16	0.13
PAX2	AD	28	0.18	0	0	3	0.18	25	0.2
NPHS2	AR	26	0.17	0	0	0	0	26	0.21
TSC2	AD	22	0.14	0	0	0	0	22	0.18
CASR	AD;AR	19	0.13	3	0.29	1	0.06	15	0.12
SLC2A9	AD;AR	19	0.13	0	0	2	0.12	17	0.14
SLC3A1	AD;AR	19	0.13	1	0.1	0	0	18	0.14
INF2	AD	18	0.12	0	0	0	0	18	0.14
CFH	AD;AR	17	0.11	1	0.1	1	0.06	15	0.12
GANAB	AD	16	0.11	0	0	0	0	16	0.13
HNF1A	AD	17	0.11	0	0	0	0	17	0.14
PRKCSH	AD	15	0.1	1	0.1	1	0.06	13	0.1
SLC4A1	AD;AR	15	0.1	0	0	2	0.12	13	0.1
TRPC6	AD	15	0.1	1	0.1	1	0.06	13	0.1
PKHD1	AR	14	0.09	0	0	1	0.06	13	0.1
CLCNKB	AR	12	0.08	1	0.1	0	0	11	0.09
FLCN	AD	12	0.08	1	0.1	1	0.06	10	0.08
WT1	AD	12	0.08	1	0.1	1	0.06	10	0.08
ALG9	AD;AR	10	0.07	0	0	0	0	10	0.08
ALPL	AD;AR	10	0.07	1	0.1	0	0	9	0.07

Gene	Inheritance	Total	Percentage (%)	High Risk *APOL1* Genotype		Single Risk Allele Carriers		G0/G0	
				N	%	N	%	N	%
NR3C2	AD	11	0.07	0	0	1	0.06	10	0.08
OFD1	XL	10	0.07	0	0	1	0.06	9	0.07
PROKR2	AD;AR	10	0.07	1	0.1	1	0.06	8	0.06
SEC63	AD	10	0.07	1	0.1	0	0	9	0.07
SMAD9	AD	11	0.07	2	0.19	2	0.12	7	0.06
WFS1	AD;AR	10	0.07	0	0	2	0.12	8	0.06
AVPR2	XL	9	0.06	0	0	1	0.06	8	0.06
CEL	AD	9	0.06	1	0.1	2	0.12	6	0.05
CUBN	AR	9	0.06	0	0	1	0.06	8	0.06
GATA3	AD	9	0.06	0	0	1	0.06	8	0.06
RET	AD	9	0.06	0	0	1	0.06	8	0.06
SCNN1B	AD;AR	9	0.06	0	0	5	0.3	4	0.03
CD2AP	AD;AR	7	0.05	1	0.1	0	0	6	0.05
CTNS	AR	7	0.05	0	0	0	0	7	0.06
FGA	AD;AR	8	0.05	0	0	0	0	8	0.06
HNF4A	AD	7	0.05	0	0	1	0.06	6	0.05
LMX1B	AD	7	0.05	0	0	1	0.06	6	0.05
NF1	AD	7	0.05	1	0.1	1	0.06	5	0.04
OCRL	XL	8	0.05	0	0	4	0.24	4	0.03
PBX1	AD	7	0.05	0	0	0	0	7	0.06
SALL1	AD	8	0.05	0	0	0	0	8	0.06
SLC5A2	AD;AR	7	0.05	1	0.1	0	0	6	0.05
CYP24A1	AR	6	0.04	0	0	0	0	6	0.05
JAG1	AD	6	0.04	0	0	0	0	6	0.05
NOTCH2	AD	6	0.04	0	0	4	0.24	2	0.02
NSD1	AD	6	0.04	0	0	0	0	6	0.05
PHEX	XL	6	0.04	0	0	2	0.12	4	0.03
AGXT	AR	5	0.03	0	0	0	0	5	0.04
ANOS1	XL	4	0.03	2	0.19	0	0	2	0.02
APOA1	AD;AR	4	0.03	0	0	0	0	4	0.03
APRT	AR	4	0.03	0	0	1	0.06	3	0.02
ATP6V0A4	AR	5	0.03	0	0	0	0	5	0.04
ATP7B	AR	4	0.03	0	0	0	0	4	0.03
C3	AD;AR	4	0.03	0	0	0	0	4	0.03
EYA1	AD	5	0.03	1	0.1	1	0.06	3	0.02
GCK	AD;AR	4	0.03	0	0	0	0	4	0.03
KLHL3	AD;AR	5	0.03	0	0	0	0	5	0.04
LMNA	AD;AR	5	0.03	0	0	0	0	5	0.04
MEFV	AR	4	0.03	0	0	0	0	4	0.03

Gene	Inheritance	Total	Percentage (%)	High Risk *APOL1* Genotype		Single Risk Allele Carriers		G0/G0	
				N	%	N	%	N	%
NPHP4	AR	4	0.03	0	0	0	0	4	0.03
PTPN11	AD	4	0.03	1	0.1	0	0	3	0.02
SLC12A1	AR	4	0.03	0	0	0	0	4	0.03
SLC34A1	AD;AR	4	0.03	0	0	0	0	4	0.03
VHL	AD	4	0.03	1	0.1	0	0	3	0.02
CDC73	AD	3	0.02	0	0	0	0	3	0.02
CNNM2	AD;AR	3	0.02	0	0	0	0	3	0.02
FAN1	AR	3	0.02	0	0	0	0	3	0.02
FGFR1	AD	3	0.02	1	0.1	0	0	2	0.02
FOXC1	AD	3	0.02	0	0	0	0	3	0.02
GNAS	AD	3	0.02	1	0.1	0	0	2	0.02
GRHPR	AR	3	0.02	0	0	0	0	3	0.02
INS	AD;AR	3	0.02	0	0	0	0	3	0.02
MYH9	AD	3	0.02	0	0	0	0	3	0.02
NPHS1	AR	3	0.02	0	0	0	0	3	0.02
NR3C1	AD	3	0.02	0	0	0	0	3	0.02
PDX1	AD;AR	3	0.02	0	0	0	0	3	0.02
REN	AD;AR	3	0.02	0	0	0	0	3	0.02
SCN4A	AD;AR	3	0.02	0	0	1	0.06	2	0.02
TSC1	AD	3	0.02	0	0	0	0	3	0.02
ABCC6	AR	1	0.01	0	0	0	0	1	0.01
ACTN4	AD	1	0.01	0	0	0	0	1	0.01
ADA2	AR	1	0.01	0	0	0	0	1	0.01
AQP2	AD;AR	2	0.01	0	0	0	0	2	0.02
ATP6V1B1	AR	2	0.01	0	0	0	0	2	0.02
AVP	AD	1	0.01	0	0	1	0.06	0	0
BBS1	AR	1	0.01	0	0	0	0	1	0.01
BBS10	AR	1	0.01	0	0	0	0	1	0.01
BBS2	AR	1	0.01	0	0	0	0	1	0.01
BBS9	AR	2	0.01	0	0	0	0	2	0.02
BMPR2	AD	2	0.01	0	0	0	0	2	0.02
BSCL2	AD;AR	1	0.01	0	0	0	0	1	0.01
CA2	AR	1	0.01	0	0	0	0	1	0.01
CACNA1S	AD;AR	1	0.01	0	0	0	0	1	0.01
CAV1	AD;AR	1	0.01	0	0	0	0	1	0.01
CEP290	AR	2	0.01	0	0	1	0.06	1	0.01
CHD7	AD	1	0.01	0	0	0	0	1	0.01
CLCN2	AD;AR	1	0.01	0	0	0	0	1	0.01
CLDN19	AR	1	0.01	0	0	0	0	1	0.01

Gene	Inheritance	Total	Percentage (%)	High Risk *APOL1* Genotype		Single Risk Allele Carriers		G0/G0	
				N	%	N	%	N	%
CPLANE1	AR	1	0.01	0	0	0	0	1	0.01
CUL3	AD	2	0.01	0	0	0	0	2	0.02
CYP11B1	AD;AR	1	0.01	0	0	1	0.06	0	0
CYP27B1	AR	1	0.01	0	0	0	0	1	0.01
FAM20A	AR	2	0.01	0	0	1	0.06	1	0.01
FANCC	AR	1	0.01	0	0	0	0	1	0.01
FGF23	AD;AR	1	0.01	0	0	0	0	1	0.01
FGFR2	AD	1	0.01	0	0	0	0	1	0.01
FN1	AD	2	0.01	0	0	0	0	2	0.02
FOXC2	AD	1	0.01	0	0	0	0	1	0.01
FOXP3	XL	2	0.01	0	0	1	0.06	1	0.01
G6PC	AR	2	0.01	0	0	0	0	2	0.02
GALNT3	AR	1	0.01	0	0	0	0	1	0.01
GLI3	AD	1	0.01	0	0	0	0	1	0.01
GPC3	XL	1	0.01	0	0	1	0.06	0	0
GSN	AD	1	0.01	0	0	0	0	1	0.01
HOGA1	AR	2	0.01	0	0	0	0	2	0.02
HOXA13	AD	1	0.01	0	0	0	0	1	0.01
HSD11B2	AR	1	0.01	0	0	0	0	1	0.01
IFT140	AR	2	0.01	0	0	0	0	2	0.02
IQCB1	AR	2	0.01	0	0	0	0	2	0.02
KANSL1	AD	1	0.01	0	0	0	0	1	0.01
KCNJ1	AR	2	0.01	0	0	0	0	2	0.02
KCNJ11	AD;AR	1	0.01	1	0.1	0	0	0	0
LRP5	AD;AR	1	0.01	0	0	0	0	1	0.01
MAFB	AD	1	0.01	0	0	0	0	1	0.01
MMACHC	AR	1	0.01	0	0	0	0	1	0.01
MNX1	AD	1	0.01	0	0	1	0.06	0	0
NEUROD1	AD	1	0.01	0	0	0	0	1	0.01
NPHP3	AR	1	0.01	0	0	0	0	1	0.01
NR0B1	XL	1	0.01	0	0	0	0	1	0.01
NSDHL	XL	1	0.01	0	0	0	0	1	0.01
PMM2	AR	1	0.01	0	0	0	0	1	0.01
PTH1R	AD;AR	2	0.01	0	0	0	0	2	0.02
RMND1	AR	1	0.01	0	0	0	0	1	0.01
RPL11	AD	1	0.01	0	0	0	0	1	0.01
RRM2B	AD;AR	1	0.01	0	0	0	0	1	0.01
SCARB2	AR	2	0.01	0	0	1	0.06	1	0.01
SCNN1A	AR	1	0.01	0	0	0	0	1	0.01

Gene	Inheritance	Total	Percentage (%)	High Risk *APOL1* Genotype		Single Risk Allele Carriers		G0/G0	
				N	%	N	%	N	%
SCNN1G	AD;AR	1	0.01	0	0	0	0	1	0.01
SDCCAG8	AR	2	0.01	0	0	0	0	2	0.02
SMC1A	XL	1	0.01	0	0	0	0	1	0.01
SOX17	AD	1	0.01	0	0	0	0	1	0.01
SRCAP	AD	1	0.01	0	0	0	0	1	0.01
THBD	AD	1	0.01	0	0	0	0	1	0.01
TMEM67	AR	1	0.01	0	0	0	0	1	0.01
TP63	AD	1	0.01	0	0	0	0	1	0.01
TRPM6	AR	1	0.01	0	0	0	0	1	0.01
TTC21B	AR	1	0.01	0	0	0	0	1	0.01
TXNL4A	AR	1	0.01	0	0	0	0	1	0.01
WDR19	AR	1	0.01	0	0	0	0	1	0.01
WNK4	AD	1	0.01	0	0	0	0	1	0.01