

Supplementary Table S1.

Overview of 251 patients with COQ2, COQ6 and COQ8B(ADCK4) enrolled in the study: genotype and phenotype characteristics.

COQ2

Drovandi S. et al CoQ10 deficiency associated glomerulopathy: Clinical spectrum and genotype-phenotype associations.

	ID (reference if already published)	Genotypes			Baseline features											Follow-up				
		Gene	Variant(s) CMA / AA modification	Status (Comp. Het/Hom)	Gender	Country of origin/ethnicity	Consanguinity	other siblings affected (dead*)	Reason for genetic testing	Age at 1 st clinical manifestation (years)	Age at Kidney disease onset (years)	Initial proteinuria	Initial GFR (ml/min/1.73mq)	Hypertension	Oedema	Histopathology (kidney)	Age at ESRD (years) (Hemodialysis- Peritoneal dialysis, if available)	Age at kidney transplant (years)	Age at last observation or death* (years)	Follow-up (years)
1	S1.S2.Survey update	COQ2	c.890A>G p.(Tyr29/Cys)	Hom	M	North Africa	yes (cousins)	1	Phenotype	1.0	1.0	4.3 (g/24h)	>90	no	yes	FSGS	1.5 (PD)	3.0	20.0	19.0
2	S1.S2.Survey update	COQ2	c.890A>G p.(Tyr29/Cys)	Hom	F	North Africa	yes (cousins)	1	Family screening	1.0	1.0	55 g/m2/24h	>90	no	yes	FSGS mitochondrial proliferation	16 (PD)	17.0	18.0	17.0
3	S3.Survey update	COQ2	c.590G>A p.(Arg179His) c.683A>G p.(Asn28Ser)	Comp. Het	M	Eastern Europe	no	0	Phenotype	1.5	1.5	Nephrotic range	<15	no	yes	collapsing glomerulopathy dysmorphic mitochondria	1.6(PD)	6.0	6	4.5
4	S3	COQ2	c.437G>A p.(Ser146Asn)	Hom	M	Southern Italy	yes	1*	Phenotype	birth	0 (5days)	n/a	n/a	yes	yes	crescents, dysmorphic mitochondria	0 (3 w PD)	n/a	0.5*	0.5
5	S4	COQ2	c.1198delT p.(Asn401fsTer415)	Hom	F	France	no	1*	Phenotype	birth	0.0	n/a	n/a	no	yes	n/a	0.0	n/a	0.04*	0.04
6	S4.S6	COQ2	c.1198delT p.(Asn401fsTer415)	Hom	M	France	no	1*	Phenotype	birth	0.0	n/a	n/a	no	no	n/a	0.0	n/a	1 day*	1 day
7	S5	COQ2	c.905C>T p.(Ala302Val)	Hom	M	Turkey	yes (first degree)	1	Phenotype	birth	n	n	n	no	yes	n/a	n/a	n/a	0.5*	0.5
8	S5	COQ2	c.905C>T p.(Ala302Val)	Hom	F	Turkey	yes (first degree)	1	Phenotype	birth	n	n	n	no	yes	n/a	n/a	n/a	0.4*	0.4
9	S6	COQ2	c.437G>A p.(Ser146Asn) Reported as: c.326G>A	Hom	M	n/a	n/a	0	Phenotype	0.16	0.4	0.5 --> 5 g/L	n/a	yes	yes	FSGS, dysmorphic mitochondria	0.4	n/a	0.5*	0.5
10	S7	COQ2	c.437G>A p.(Ser146Asn) c.1159C>T p.(Arg387Ter)	Comp. Het	F	n/a	n/a	0	Phenotype	birth	n	n/a	n/a	no	no	n/a	0.0	n/a	0.16*	0.16
11	S8	COQ2	c.545T>G p.(Met182Arg)	Hom	F	n/a	yes	2	Phenotype	birth	0.0	500mg/g	n/a	no	no	n/a	n/a	n/a	0*(23h)	0.0
12	S9	COQ2	c.1169G>C p.(Gly390Ala)	Hom	F	Southern Italy	n/a	0 (1 cousin affected)	NS -gene panel	18.0	18.0	n/a	n/a	no	yes	FSGS, dysmorphic mitochondria	19 (HD)	20.0	37.0	19.0
13	S9	COQ2	c.1169G>C p.(Gly390Ala)	Hom	F	Southern Italy	n/a	0 (1 cousin affected)	NS -gene panel	16.0	16.0	n/a	n	no	yes	FSGS, dysmorphic mitochondria	17 (HD)	18.0	23.0	7.0
14	S10	COQ2	c.973A>G p.(Thr325Ala) c.1159C>T p.(Arg387Ter)	Comp. Het	M	Asian-American	n/a	0	NS -gene panel	0.75	0.75	197 mg/mg	72	no	yes	FSGS, mitochondrial podocyte proliferation	n/a	n/a	2.4	1.6
15	S10	COQ2	c.683A>G p.(Asn28Ser) c.881C>T p.(Thr294Ile)	Comp. Het	M	Caucasian	n/a	0	NS -gene panel	10.0	10.0	40 mg/mg	45	no	yes	FSGS, dysmorphic mitochondria	11(HD)	13.0	13.0	3
16	S10	COQ2	c.176dupT p. (Ala60ArgfsTer33) c.683A>G p.(Asn28Ser)	Comp. Het	M	Mixed european ancestry	n/a	0	NS -gene panel	2.0	2.0	22.5 mg/mg	100	no	yes	FSGS, dysmorphic mitochondria	n/a	n/a	3.0	1.0
17	S11	COQ2	c.683A>G p.(Asn28Ser) c.701delT p.(Leu234fsTer247)	Comp. Het	F	Caucasian	n/a	0	NS -gene panel	2.0	2.0	n/a	n/a	no	yes	n/a	2.5 (PD)	n/a	4.0	2.0
18	S12	COQ2	c.683A>G p.(Asn28Ser)	Hom	F	Eastern Europe	no	1	NS -gene panel	3.0	3.0	1900 mg/mmol	n/a	n/a	yes	FSGS	3.5 (HD)	n/a	6.0	3.0
19	S12	COQ2	c.683A>G p.(Asn28Ser)	Hom	F	Eastern Europe	no	1	NS -gene panel	3.0	3.0	400 mg/mmol	n/a	n/a	yes	FSGS	n/a	n/a	3.4	0.4
20	S13	COQ2	c.832T>C p.(Cys278Arg) + ARSB c.1213>G>A hom (MPS IV)	Hom	F	Chinese	yes (cousins)	1.2*	NS -gene panel	0.5	0.5	5.657g/24h	n/a	no	yes	FSGSc, tubular- interstitial lesion	0.5 (PD)	n/a	0.5*	2w
21	S14	COQ2	c.683A>G p.(Asn28Ser)	Hom	M	Caucasian	n/a	n/a	NS -gene panel	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
22	S14	COQ2	c.518G>A p.(Arg173His) c.683A>G p.(Asn28Ser)	Comp. Het	M	European	no	n/a	NS -gene panel	n/a	2.5	n/a	n/a	n/a	n/a	FSGS	n/a	n/a	n/a	n/a
23	S14	COQ2	c.683A>G p.(Asn28Ser) c.856C>T p.(Leu286Phe)	Comp. Het	F	European	no	n/a	NS -gene panel	n/a	1.25	n/a	n/a	n/a	n/a	FSGS	n/a	n/a	n/a	n/a
24	S14	COQ2	c.890T>C p.(Tyr29/Cys)	Hom	M	Arabic	yes	n/a	NS -gene panel	n/a	0.4	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
25	PodNet	COQ2	c.374T>C p.(Leu125Ser)	Hom	M	Eastern Europe	no	1*	NS -gene panel	0.56	0.56	16.3g/m2/24h	no	no	yes	n/a	0.66 (PD)	2.3	9.3	8.7

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		Gene	Variant(s) cDNA (AA modification)	Status (Comp., Het/Hom)	Gender	Country of origin/ethnicity	Consanguinity	other siblings affected (deu*)	Reason for genetic testing	Age at 1 st clinical manifestation (years)	Age at kidney disease onset (years)	Initial proteinuria	Initial GFR (ml/min/1.73m ²)	Hypertension	Oedema	Histopathology (kidney)	Age at ESRD (years) (Hemodialysis- Peritoneal dialysis, if available)	Age at kidney transplant (years)	Age at last observation or death* (years)	Follow-up (years)
26	PodoNet	COQ2	c.683A>G p.(Asn228Ser) c.1115A>G p.(Asp372Gly)	Comp. Het	M	Eastern Europe	no	1	NS -gene panel	0.9	0.9	6.5g/m2/24h	n/a	yes	yes	GGs	1.9(PD)	n/a	3.8	2.9
27	PodoNet	COQ2	c.287_288insC p. (Ala97Arg/Leu56) c.683A>G p.(Asn228Ser)	Comp. Het	F	Ukraine (Slavian)	no	1	NS -gene panel	1.4	1.58	0.16->16.5g /m2/24h	n/a	no	no	n/a	2.5(PD)	n/a	4.0	2.4
28	PodoNet	COQ2	c.1115A>G p.(Asp372Gly)	Hom	M	Poland	no	1	NS -gene panel	1.66	1.86	15.9g/m2/ 24h	n/a	no	yes	PSGS	3.1 (PD)	4.3	18.0	16.34
29	PodoNet	COQ2	c.683A>G p.(Asn228Ser) c.733T>G p.(Tyr245Asp)	Comp. Het	M	Poland	no	0	NS -gene panel	2.4	2.4	n/a	n/a	no	yes	n/a	n/a	n/a	2.6	0.2
30	PodoNet	COQ2	c.571-1G>A c.683A>G p.(Asn228Ser)	Comp. Het	F	Eastern Europe/Tajikistan/ German	no	2.1*	Phenotype (sibling affected) and ML features	2.0	2.0	n/a	n/a	no	yes	FSGS, dysmorphic mitochondria	n/a	n/a	6.7	4.7
31	PodoNet	COQ2	c.424C>G p.(Pro142Ala) c.539A>G p.(Asn180Ser)	Comp. Het	M	Colombia	n/a	0	NS -gene panel	n/a	1.9	10g/m2/24h	n/a	yes	yes	diffuse mesangial sclerosis	n/a	n/a	2.1	n/a
32	S15	COQ2	c.518G> p.(Arg173His) c.973A>G p.(Thr325Ala)	Comp. Het	M	Chinese	no	2.1*	NS -gene panel	0.9	0.9	22.87 mg/mg	>90	n/a	n/a	n/a	n/a	n/a	1.2	0.3
33	S16	COQ2	c.437G>A p.(Ser146Asn)	Hom	M	Turkey	n/a	1*	Phenotype	Birth (2 days)	Birth (2 days)	4 mg/mg	n/a	n/a	n/a	LM negative. EM dysmorphic mitochondria	n/a	n/a	0.4*	0.4
34	S16	COQ2	c.437G>A p.(Ser146Asn)	Hom	F	Turkey	n/a	1*	Phenotype (sibling affected)	Birth	Birth	8.04 mg/mg	n/a	n/a	n/a	n/a	2.5	n/a	2.6*	2.6
35	S16	COQ2	c.437G>A p.(Ser146Asn)	Hom	F	Turkey	n/a	1*	NS-gene panel (post-mortem)	0.25	0.25	139 mg/m2/h	n/a	n/a	n/a	visceral epithelial hypertrophy, tubulo-interstitial lesions	0.25 (PD)	n/a	0.5*	0.25
36	S16	COQ2	c.437G>A p.(Ser146Asn)	Hom	M	Turkey	n/a	1*	Phenotype (sibling affected)	Birth (5days)	Birth (5days)	8.9 mg/mg	n/a	n/a	n/a	n/a	n/a	n/a	1.2*	1.2
37	S17	COQ2	c.590G>A p.(Arg197His) c.683A>G p.(Asn228Ser)	Comp. Het	F	Netherlands	no	0	NS-gene panel	2.5	2.5	6g/L	>90	yes	yes	cfSGS	2.5	3.0	8.7	6.2
38	S17	COQ2	c.683A>G p.(Asn228Ser)	Hom	F	Netherlads	yes	0	NS-gene panel	1.8	1.8	33.8 g/10 mmol	n/a	n/a	yes	cfSGS	n/a	n/a	7.3	5.5
39	Survey	COQ2	c.518G>A p.(Arg173His) c.683A>G p.(Asn228Ser)	Comp. Het	M	Mixed ancestry (Caucasian)	no	0	NS-gene panel	1.7	1.7	Nephrotic range	60-GFR<90	no	yes	cfSGS + interstitial fibrosis	n/a	n/a	n/a	n/a
40	Survey	COQ2	c.437G>A p.(Ser146Asn) c.683A>G p.(Asn228Ser)	Comp. Het	M	Caucasian (Algerian)	yes	0	NS-gene panel	0.9	0.9	Nephrotic range	>90	yes	yes	n/a	n/a	n/a	1.1	0.2
41	Survey	COQ2	c.778+1G>A c.992_993delinsGC p.(Gly331Glu)	Comp. Het	F	Caucasian (Turkey)	no	0	NS-gene panel	0.5	0.5	Nephrotic range	>90	no	yes	MCD	n/a	n/a	2.0	1.5
42	Survey	COQ2	c.683A>G p.(Asn228Ser) c.550G>T p.(Asp184Tyr)	Comp. Het	M	Caucasian	no	0	NS-gene panel	1	1	Nephrotic range	>90	n/a	yes	FSGS	5.0	6.0	20.0	19.0
43	Survey	COQ2	c.683A>G p.(Asn228Ser) c.517C>T p.(Arg173Gly)	Comp. Het	M	Caucasian (Slovenia)	no	n/a	NS-gene panel	9	11	Sub nephrotic range	>90	n/a	n/a	FSGS	16.7 (PD)	21.0	21.0	12.0
44	Survey	COQ2	c.518G>A p.(Arg173His) c.683A>G p.(Asn228Ser)	Comp. Het	F	Caucasian (Turkey)	no	0	NS-gene panel	2	2	28 mg/mg	>90	yes	yes	FSGS	n/a	n/a	3.0	1.0
45	Survey	COQ2	n/a	Comp. Het	F	Caucasian (Iran)	yes	1	Phenotype	13	13	Sub nephrotic range	<15	yes	yes	n/a	n/a	n/a	15.0	2.0
46	MitoNET	COQ2	c.437G>A p.(Ser146Asn) c.590G>A p.(Arg197His)	Comp. Het	M	Georgian	no	0	Phenotype	0.2	0.3	5600 g/mol crea	>90	no	yes	n/a	n/a	n/a	5.2*	5.0

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S18	COQ2	c.288dupC p. (Ala97Arg16Ter56) c.376C>G p.(Arg126Gly)	Comp. Het	M	Ashkenazi Jewish (USA)	no	2	Phenotype	n/a	n/a	n/a	n/a	n/a	n/a	GGS	n/a	n/a	25.0	n/a
S18	COQ2	c.288dupC p. (Ala97Arg16Ter56) c.376C>G p.(Arg126Gly)	Comp. Het	M	Ashkenazi Jewish (USA)	no	2	Family screening	n/a	n/a	n/a	n/a	n/a	n/a	Mesangial sclerosis	n/a	5.0	32.0	n/a
S18	COQ2	c.288dupC p. (Ala97Arg16Ter56) c.376C>G p.(Arg126Gly)	Comp. Het	F	Ashkenazi Jewish (USA)	no	2	Family screening	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	10.0	28.0	n/a
Survey	COQ2	c.437G>A p.(Ser146Asn) c.683A>G p.(Asn285Ser)	Comp. Het	M	Caucasian (Norway)	no	0	Phenotype	4	4	Nephrotic range	>90	yes	yes	FSGS	6.0	6.5	16.0	12.0
Survey	COQ2	c.659C>T p.(Ala220Val) c.1158C>G p.(Asn386Lys)	Comp. Het	F	Caucasian (France)	no	1	Phenotype	0.3	0.3	Nephrotic range	>90	yes	no	FSGS	n/a	n/a	2.1	1.9
Survey	COQ2	c.313_329dup p. (Ala111Ser16Ter67) c.683A>G p.(Asn285Ser)	Comp. Het	F	Caucasian (France)	no	0	NS-gene panel	0.7	0.7	Nephrotic range	15<GFR<30	yes	yes	GGS	2.4	5.2	37.0	36.3
Survey	COQ2	c.223_249delins AlaGln p. (Arg75Lys16Ter90) c.644G>A p.(Gly215Glu)	Comp. Het	F	African descent	yes	0	NS-gene panel	27.0	27.0	Nephrotic range	>90	no	yes	MCD	29.4	31.4	31.4	4.4
Survey	COQ2	c.683A>G p.(Asn285Ser)	Hom	F	Algeria	yes	0	NS-gene panel	13.3	13.3	Nephrotic range	>90	yes	yes	FSGS NOS+TIF	n/a	n/a	14.0	0.7
Survey	COQ2	c.890A>G p.(Tyr297Cys) c.1239G>A p.(Lys413=)	Comp. Het	M	Algeria	yes	0	NS-gene panel	0.5	0.5	Nephrotic range	>90	n/a	yes	n/a	0.8	n/a	2.2	1.7
Survey	COQ2	n/a	Hom	F	Arabic	yes	0	NS-gene panel	1.0	1.0	Nephrotic range	30<GFR<60	yes	yes	Diffuse mesangial sclerosis	1.0	n/a	4.0	3.0
Survey	COQ2	c.571-1G>A c.890A>G p.(Tyr297Cys)	Comp. Het	M	Arabic	no	0	Phenotype	0.3	0.3	Nephrotic range	>90	no	no	n/a	n/a	n/a	1*	1.0
MitoNET	COQ2	c.215C>T p.(Pro72Leu) Reported as: c.65C>T c.1031delG p.(Gly344Val16Ter2) Reported as: c.881delG	Comp. Het	F	Japan	n/a	n/a	Phenotype	1.6	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	3.0	1.4
MitoNET	COQ2	c.349G>C p.(Ala117Pro) Reported as: c.199G>C c.912+1delG	Comp. Het	F	Japan	n/a	1	Phenotype	1.6	1.6	Nephrotic range	<15	n/a	n/a	n/a	1.6	n/a	1.6	0.0
MitoNET	COQ2	c.349G>C p.(Ala117Pro) Reported as: c.199G>C c.912+1delG	Comp. Het	F	Japan	n/a	1	Phenotype	0.9	0.9	Nephrotic range	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
CCGKDD	COQ2	c.778+1G>A c.973A>G p.(Thr325Ala)	Comp. Het	M	Chinese	no	n/a	Research	1.8	1.8	Nephrotic syndrome	>90	no	yes	n/a	9.9	14.2	14.8	13.0
CCGKDD	COQ2	c.778+27>C Reported as: c.628+27>C c.973A>G p.(Thr325Ala)	Comp. Het	M	Chinese	no	n/a	NS-gene panel	0.9	0.9	90 mg/kg/ 24h	55	no	yes	n/a	n/a	n/a	0.9*	0.0
CCGKDD	COQ2	c.518G>A p.(Arg173His) c.973A>G p.(Thr325Ala)	Comp. Het	M	Chinese	no	n/a	NS-gene panel	0.8	0.8	21.3mg/kg/24h	229	no	yes	n/a	n/a	n/a	2.3	1.5

Variant details provided according to cDNA NM_015697.8; protein NP_056512.5 (421 aa)

COQ6

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1	S19	COQ6	c.763G>A p.(Gly255Arg)	Hom	n/a	Lebanon	yes	n/a	NS-gene panel	birth	6.4	Nephrotic range	n/a	n/a	n/a	FSGS	9.3	n/a	n/a	n/a	
2	S19	COQ6	c.763G>A p.(Gly255Arg)	Hom	n/a	Lebanon	yes	n/a	NS-gene panel	birth	0.3	Nephrotic range	n/a	n/a	n/a	n/a	1.7	n/a	17.5*	17.5	
3	S19	COQ6	c.763G>A p.(Gly255Arg)	Hom	n/a	Lebanon	yes	n/a	NS-gene panel	1.2	1.2	Nephrotic range	n/a	n/a	n/a	FSGS	1.4	n/a	6.5*	5.3	
4	S19	COQ6	n/a	Hom	n/a	Lebanon	yes	n/a	NS-gene panel	birth	0.5	Nephrotic range	n/a	n/a	n/a	FSGS	3.0	n/a	5*	5.0	
5	S19	COQ6	c.763G>A p.(Gly255Arg)	Hom	n/a	Turkey	yes	0	NS-gene panel	0.3	0.3	Nephrotic range	n/a	n/a	n/a	diffuse mesangial sclerosis	0.4	n/a	n/a*	n/a	
6	S19	COQ6	c.763G>A p.(Gly255Arg)	Hom	n/a	Turkey	yes	1	NS-gene panel	birth	0.3	Nephrotic range	n/a	n/a	n/a	n/a	0.4	n/a	n/a	n/a	
7	S19	COQ6	c.763G>A p.(Gly255Arg)	Hom	n/a	Turkey	yes	1	NS-gene panel	0.2	0.2	ProtU 40 mg/mg	n/a	n/a	n/a	n/a	n/a	n/a	1.25	1.0	
8	S19	COQ6	c.763G>A p.(Gly255Arg)	Hom	n/a	Turkey	yes	n/a	NS-gene panel	6.0	6.0	Nephrotic range	n/a	n/a	n/a	FSGS	6.5	n/a	n/a	n/a	
9	S19	COQ6	c.763G>A p.(Gly255Arg)	Hom	n/a	Turkey	yes	n/a	NS-gene panel	2.5	2.5	Nephrotic range	n/a	n/a	n/a	FSGS	n/a	n/a	n/a	n/a	
10	S19	COQ6	c.1058C>A p.(Ala353Asp)	Hom	n/a	Turkey	yes	n/a	NS-gene panel	2.5	2.5	Nephrotic range	n/a	n/a	n/a	FSGS	3.4	n/a	n/a*	n/a	
11	S19	COQ6	c.1341G>A p.(Trp447Ter) c.1383del p.(Ile462fs)	Comp. Het	F	Turkey	no	0	NS-gene panel	3.4	3.4	Nephrotic range	n/a	no	yes	FSGS	7.2(PD)	n/a	7.6	4.2	
12	S14	COQ6	c.1154A>C p.(Asp385Ala) c.1235A>G p.(Tyr412Cys)	Comp. Het	M	European	no	n/a	NS-gene panel	n/a	4.5	n/a	n/a	n/a	n/a	MPGN	n/a	n/a	n/a	n/a	
13	S9	COQ6	c.782C>T p.(Pro261Leu)	Hom	M	Southern Italy	n/a	0	NS-gene panel	0.6	0.6	n/a	n/a	n/a	n/a	MPGN and C3 deposits	1.6 (PD)	n/a	1.6	1.0	
14	S20	COQ6	c.1078C>T p.(Arg360Trp)	Hom	M	Chinese	no	0	n/a	0.8	0.8	ProtU 7.2 mg/mg	n	n/a	yes	n/a	n/a	n/a	n/a	n/a	
15	S21	COQ6	c.189_191del p.(Lys64del) c.782C>T p.(Pro261Leu)	Comp. Het	M	Korean	n/a	0	Phenotype	n/a	3.8	ProtU 34mg/mg	72	n/a	n/a	cFSGS mitochondrial proliferation	6.0	11.4	n/a	n/a	
16	S21	COQ6	c.189_191del p.(Lys64del) c.686A>C p.(Gln229Pro)	Comp. Het	F	Korean	n/a	0	Phenotype	n/a	1.9	ProtU 57.6 mg/mg	14	n/a	n/a	FSGS, mitochondrial proliferation	2.6	n/a	n/a	n/a	
17	S21	COQ6	c.189_191del p.(Lys64del) c.782C>T p.(Pro261Leu)	Comp. Het	F	Korean	n/a	0	Phenotype	n/a	3.9	ProtU 5.1 mg/mg	16	n/a	n/a	cFSGS mitochondrial proliferation	4.0	6.3	n/a	n/a	
18	S21	COQ6	c.189_191del p.(Lys64del) c.782C>T p.(Pro261Leu)	Comp. Het	F	Korean	n/a	0	Phenotype	n/a	2.6	ProtU 27.5 mg/mg	167	n/a	n/a	cFSGS mitochondrial proliferation	4.6	7.25	n/a	n/a	
19	S21	COQ6	c.189_191del p.(Lys64del) c.782C>T p.(Pro261Leu)	Comp. Het	F	Korean	n/a	1*	Phenotype	n/a	1.25	ProtU 12.5 mg/mg	70	n/a	n/a	FSGS, mitochondrial proliferation	1.4	6.4	n/a	n/a	
20	S21	COQ6	c.189_191del p.(Lys64del) c.782C>T p.(Pro261Leu)	Comp. Het	M	Korean	n/a	0	Phenotype	n/a	2	ProtU 13.6mg/mg	89	n/a	n/a	FSGS, mitochondrial proliferation	3.6	5	n/a	n/a	
21	S22	COQ6	c.804del p.(Leu269TrpfsTer13) c.1078C>T p.(Arg360Trp)	Comp. Het	F	Poland	no	0	NS-gene panel	2.4	2.4	2.11 g/L	n/a	no	no	FSGS/MCD	n/a	n/a	6.8	4.4	
22	S23	COQ6	c.1058C>A p.(Ala353Asp) + COQ8B c.512A>G p.(His174Arg) het	Hom.	F	Turkey	yes (cousins)	1	NS-gene panel	7.0	7	158 mg/m2/h	n/a	n/a	n/a	FSGS	7	7.6	10.0	3.0	
23	S23	COQ6	c.1058C>A p.(Ala353Asp)	Hom	M	Turkey	yes (cousins)	1	Family screening	10.0	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	17.0	7.0	

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Genotypes				Baseline features												Follow-up			
ID (reference if already published)	Gene	Variant(s) CDNA / (AA modification)	Status (Comp. Het/Hom)	Gender	Country of origin/ethnicity	Consanguinity	other siblings affected (dead*)	Reason for genetic testing	Age at 1 st clinical manifestation (years)	Age at Kidney disease onset (years)	Initial proteinuria	Initial GFR (ml/min/1.73mq)	Hypertension	Oedema	Histopathology (kidney)	Age at ESRD (years) (Hemodialysis- Peritoneal dialysis . if available)	Age at kidney transplant (years)	Age at last observation or death* (years)	Follow-up (years)
S24	COQ6	c.1078C>T p.(Arg360Trp)	Hom	F	Chinese	n/a	0	NS-gene panel	birth	0.16	3.28g/m2/24h	n/a	n/a	yes	n/a	n/a	n/a	2.0	2.0
S25	COQ6	c.1058C>A p.(Ala353Asp)	Hom	M	Turkey	yes	1	Phenotype	5.0	5	n/a	ESRD	yes	no	Pannephritis glomerular fibrosis	5(PD)	6	20.0	15.0
S25	COQ6	c.1058C>A p.(Ala353Asp)	Hom	M	Turkey	yes	1	Phenotype (family screening)	4.0	5	n/a	n/a	no	no	SFGS	n/a	n/a	8.0	4.0
PodoNet	COQ6	c.1058C>A p.(Ala353Asp)	Hom	F	Kazakhstan	no	0	NS-gene panel	1.0	1	3.75g/m2/24h	n/a	no	no	MCD	2.75 (PD)	4.5	6.1	5.1
PodoNet	COQ6	c.1058C>A p.(Ala353Asp)	Hom	F	Kazakhstan	no	0	NS-gene panel	1.2	1.2	n/a	n/a	no	no	FSGS	1.6(PD)	3.5	9.5	8.3
PodoNet	COQ6	c.1058C>A p.(Ala353Asp)	Hom	F	Kazakhstan	no	0	NS-gene panel	1.2	1.2	18g/m2/24h	n/a	no	yes	n/a	1.5(PD)	3.5	5.3	4
PodoNet	COQ6	c.1058C>A p.(Ala353Asp)	Hom	M	Kazakhstan	no	1*	NS-gene panel	2.3	2.3	3.66 g/m2/24h	n/a	yes	yes	FSGS	n/a	n/a	3.8	1.5
PodoNet	COQ6	c.1058C>A p.(Ala353Asp)	Hom	M	Kazakhstan	no	0	NS-gene panel	4.5	4.5	n/a	n/a	no	no	FSGS	n/a	n/a	10	5.5
PodoNet	COQ6	c.1058C>A p.(Ala353Asp)	Hom	M	Iran	yes (second cousins)	0	NS-gene panel	11.6	11.6	2g/m2/24h	n/a	yes	yes	FSGS	n/a	n/a	13.1	1.5
PodoNet	COQ6	c.1235A>G p.(Tyr412Cys)	Hom	F	Russia	no	0	EM features	0.6	0.6	0.86 g/L	n/a	no	no	FSGS	n/a	n/a	15	14.4
PodoNet	COQ6	c.1078C>T p.(Arg360Trp) c.1235A>G p.(Tyr412Cys)	Comp. Het	F	Russia	no	0	EM features	birth	1.3	n/a	n/a	no	yes	Mitochondrial cytopathy	n/a	n/a	8	8
PodoNet	COQ6	c.983C>A p.(Ala328Asp)	Hom	M	Kazakhstan	n/a	1*	Family screening	2.3	2.3	n/a	n/a	no	no	FSGS	n/a	n/a	3.1	0.8
S26	COQ6	c.782C>T p.(Pro261Leu) + large deletion including part of the COQ6 gene	Comp. Het	M	Japan	n/a	n/a	NS-gene panel	0.9	0.9	50g/g Crea	n/a	n/a	yes	MCD dysmorphic mitochondria	n/a	n/a	1.4	0.5
S27	COQ6	c.1078C>T p.(Arg360Trp)	Hom	M	Chinese	no	n/a		0.9	0.9	1.04 g/24h	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Survey	COQ6	c.1343G>A p.(Gly448Asp) Reported as: c.572G>A	Hom	M	Arab	yes	0	NS-gene panel	1.25	1.25	Nephrotic range	>90	no	yes	GGs	2	5.5	16	14.75
Survey	COQ6	c.782C>T p.(Pro261Leu)	Hom	F	Caucasian (Iran)	yes	1	NS-gene panel	1	1	Nephrotic range	>90	no	no	FSGS	n/a	n/a	7	6
Survey	COQ6	c.782C>T p.(Pro261Leu)	Hom	M	Caucasian (Iran)	yes	1	Family history	0.5	0.5	Nephrotic range	>90	n/a	n/a	FSGS	n/a	n/a	3	2.5
MitoNET	COQ6	c.1079G>T p.(Arg360Leu) c.1237G>T p.(Glu413Ter)	Comp. Het	M	Caucasian (Germany)	no	2	Phenotype	3	28	n/a	<15	n/a	n/a	n/a	28	28	39	36
MitoNET	COQ6	c.1079G>T p.(Arg360Leu) c.1237G>T p.(Glu413Ter)	Comp. Het	M	Caucasian (Germany)	no	2	Family history	3	7	n/a	<15	n/a	n/a	n/a	7	9	39	36
MitoNET	COQ6	c.1079G>T p.(Arg360Leu) c.1237G>T p.(Glu413Ter)	Comp. Het	F	Caucasian (Germany)	no	2	Family history	5	18	n/a	n/a	n/a	n/a	n/a	38	n/a	42	36
Survey	COQ6	c.1235A>G p.(Tyr412Cys)	Hom	F	Caucasian (Germany)	no	0	NS-gene panel	1	2	Nephrotic range	60<GFR<90	yes	yes	Mitochondrial abnormalities	n/a	n/a	15	14
Survey	COQ6	c.1058C>A p.(Ala353Asp)	Hom	M	Caucasian (Turkey)	yes	1	Phenotype	5.5	5.5	Nephrotic range	15<GFR<30	no	no	GGs	5.5	6.7	6.7	1.2
Survey	COQ6	c.1058C>A p.(Ala353Asp)	Hom	M	Caucasian (Turkey)	yes	1	Phenotype	4.5	4.5	Nephrotic range	>90	no	no	SFGS	n/a	n/a	6.2	1.7
Survey	COQ6	c.799_807del p.(Ser267_Leu269del) c.1058C>A p.(Ala353Asp)	Comp. Het	M	Caucasian (Turkey)	no	n/a	NS-gene panel	0.6	0.6	Nephrotic range	30<GFR<60	no	no	n/a	2.7	n/a	2.7	2.1
CCGKDD	COQ6	c.1078C>T p.(Arg360Trp) Reported as: c.1003C>T	Hom	M	Chinese	yes	n/a	Research	1.7	1.7	Nephrotic range (437 mg/kg/d)	121	no	yes	FSGS	n/a	n/a	1.9	0.2

Variant details provided according to cDNA NM_182476.3; protein NP_872282.1

COQ8B

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	Genotypes				Baseline features												Follow-up			
	ID (reference if already published)	Gene	Variant(s) CDNA / (AA modification)	Status (Comp. Het/Hom)	Gender	Country of origin/ethnicity	Consanguinity	Positive family history	Reason for genetic testing	Age at 1 st clinical manifestation (years)	Age at Kidney disease onset (years)	Initial proteinuria	Initial GFR (ml/min/1.73m ²)	Hypertension	Oedema	Histopathology (kidney)	Age at ESRD (years) (Hemodialysis- Peritoneal dialysis, if available)	Age at kidney transplant (years)	Age at last observation or death* (years)	Follow-up (years)
1	S28	COQ8B	c.1339dupG p.(Glu447GlyfsTer10)	Hom	M	n/a	n/a	yes	NS-gene panel	14.0	14.0	2.1 g/d	73	n/a	yes	FSGS	17.7	n/a	17.7	3.7
2	S28	COQ8B	c.1339dupG p.(Glu447GlyfsTer10)	Hom	F	n/a	n/a	yes	NS-gene panel	n/a	7.3	0.78 g/d	>75	n/a	yes	FSGS	12.6	n/a	12.6	5.3
3	S28	COQ8B	c.1339dupG p.(Glu447GlyfsTer10)	Hom	F	n/a	n/a	yes	NS-gene panel	17.0	17.0	n/a	n/a	n/a	yes	n/a	18.0	n/a	18.0	1.0
4	S28	COQ8B	c.1339dupG p.(Glu447GlyfsTer10)	Hom	F	n/a	n/a	yes	NS-gene panel	27.0	27.0	n/a	n/a	yes	yes	n/a	31.0	n/a	31.0	4.0
5	S28	COQ8B	c.1339dupG p.(Glu447GlyfsTer10)	Hom	F	n/a	n/a	yes	NS-gene panel	7.0	7.0	5-6 mg/m2/d	n/a	n/a	n/a	n/a	n/a	n/a	12.3	5.3
6	S28.S34 Survey update	COQ8B	c.1339dupG p.(Glu447GlyfsTer10)	Hom	F	Turkey	n/a	yes	NS-gene panel	25.7	25.7	3.6g/d	63	yes	yes	FSGS	35.4	n/a	37.0	11.3
7	S28.S34	COQ8B	c.1339dupG p.(Glu447GlyfsTer10)	Hom	M	Turkey	n/a	yes	NS-gene panel	16.7	16.7	300 mg/dL in spot urine	4.9	n/a	n/a	n/a	16.7	16.7	25.3	8.6
8	S28.S34	COQ8B	c.1339dupG p.(Glu447GlyfsTer10)	Hom	M	Turkey	n/a	yes	NS-gene panel	n/a	13.5	6.76 g/d	120	n/a	n/a	FSGS/GGS	16.6	n/a	22.3	8.8
9	S28	COQ8B	not tested	n/a	M	n/a	n/a	yes	NS-gene panel	n/a	22.0	n/a	<15	n/a	n/a	n/a	22.0	n/a	22.0	0.0
10	S28	COQ8B	c.293T>G p.(Leu98Arg)	Hom	F	n/a	n/a	yes	NS-gene panel	n/a	5.9	1.39 g/m2/d	>75	n/a	n/a	FSGS	n/a	n/a	14.3	8.4
11	S28	COQ8B	c.293T>G p.(Leu98Arg)	Hom	M	n/a	n/a	yes	NS-gene panel	n/a	13.3	2 g/m2/d	>75	n/a	yes	FSGS	14.0	n/a	14.0	0.7
12	S28	COQ8B	c.532C>T p.(Arg178Trp)	Hom	M	n/a	n/a	yes	NS-gene panel	n/a	14.3	1.5 g/d	7.5	yes	n/a	FSGS	14.3	n/a	14.3	0.0
13	S28	COQ8B	c.532C>T p.(Arg178Trp)	Hom	M	n/a	n/a	yes	NS-gene panel	n/a	9.8	2.5 g/d	2.5	yes	yes	FSGS	9.8	n/a	9.8	0.0
14	S28.S34 Survey update	COQ8B	c.293T>G p.(Leu98Arg)	Hom	F	Turkey	n/a	yes	NS-gene panel	n/a	13.5	3+	64	n/a	yes	FSGS/GGS	16.1	16.0	20.3	6.8
15	S28.S34.S38.Surve y update	COQ8B	c.293T>G p.(Leu98Arg)	Hom	F	Turkey	yes	yes	NS-gene panel	27.0	27.0	0.38 g/d	136	n/a	n/a	n/a	n/a	n/a	30.0	3.0
16	S28	COQ8B	c.1339dupG p.(Glu447GlyfsTer10)	Hom	M	n/a	n/a	yes	NS-gene panel	14.9	14.9	1.3 g/m2/d	3.5	n/a	n/a	n/a	14.9	n/a	14.9	0.0
17	S28	COQ8B	c.1339dupG p.(Glu447GlyfsTer10)	Hom	F	n/a	n/a	yes	NS-gene panel	10.0	13.2	0.36 g/mmol uAlbCr	12	yes	n/a	n/a	13.2	n/a	13.2	0.0
18	S28	COQ8B	c.1339dupG p.(Glu447GlyfsTer10)	Hom	M	n/a	n/a	yes	NS-gene panel	18.0	18.0	n/a	n/a	n/a	n/a	n/a	18.0	n/a	18.0	0.0
19	S28 Survey update	COQ8B	c.1339dupG p.(Glu447GlyfsTer10)	Hom	M	n/a	n/a	yes	NS-gene panel	9.0	9.0	0.044 g/mmol uAlbCr	142	n/a	n/a	n/a	n/a	n/a	9.3	0.3
20	S28	COQ8B	c.748G>A p.(Asp250Asn)	Hom	M	n/a	n/a	yes	NS-gene panel	16.9	16.9	2.64 g/m2/d	28	yes	n/a	FSGS	17.4	n/a	17.4	0.5
21	S28	COQ8B	c.748G>A p.(Asp250Asn)	Hom	F	n/a	n/a	yes	NS-gene panel	13.4	13.4	0.13g/m2/d	15	yes	yes	FSGS	13.7	n/a	13.7	0.3
22	S28	COQ8B	c.645delT p.(Phe215LeufsTer14)	Hom	M	n/a	n/a	no	NS-gene panel	15.1	15.1	0.18g/m2/d	9.5	yes	yes	FSGS	15.8	n/a	15.8	0.7
23	S28	COQ8B	c.1199_1200dup p.(His400AsnfsTer11)	Hom	M	n/a	n/a	no	NS-gene panel	10.8	10.8	n/a	n/a	n/a	yes	FSGS- tip lesion	15.9	n/a	15.9	5.1
24	S28 Survey update	COQ8B	c.929C>T p.(Pro310Leu) c.1493_1494delinsAA p.(Ala498Glu)	Comp. Het	F	Caucasian	no	no	NS-gene panel	n/a	5.1	0.3 g/d	57	n/a	n/a	FSGS-NOS	13.6	14.6	27.5	22.4
25	S28 Survey update	COQ8B	c.645del p.(Phe215LeufsTer14)	Hom	M	Caucasian	no	no	NS-gene panel	14.2	14.2	0.56 g/mmol uPCr	4	yes	yes	FSGS NOS	15.2	n/a	15.2	1.0
26	S28 Survey update	COQ8B	c.1339dup p.(Glu447GlyfsTer10)	Hom	M	Caucasian (Kurdish)	yes	no	NS-gene panel	17.6	17.6	'nephrotic-range'	<15	no	no	cFSGS	18.0	n/a	18.0	0.4
27	S29	COQ8B	c.101G>A p.(Trp34Ter) c.954_956dup p.(Thr339dup)	Comp. Het	n/a	European	n/a	no	NS-gene panel	10.0	10.0	n/a	n/a	n/a	n/a	FSGS	12.0	n/a	14.0	4.0
28	S29	COQ8B	c.532C>T p.(Arg178Trp)	Hom	n/a	Arab	n/a	yes	NS-gene panel	7.0	7.0	n/a	n/a	n/a	n/a	GS	7.0	10.0	10.0	3.0
29	S29	COQ8B	c.532C>T p.(Arg178Trp)	Hom	n/a	Arab	n/a	yes	NS-gene panel	13.0	13.0	n/a	n/a	n/a	n/a	FSGS	n/a	15.0	15.0	2.0
30	S29	COQ8B	c.857A>G p.(Asp286Gly) c.1447G>T p.(Glu483Ter)	Comp. Het	n/a	n/a	n/a	yes	NS-gene panel	14.0	14.0	n/a	n/a	n/a	n/a	FSGS	15.0	18.0	18.0	4.6
31	S29	COQ8B	c.857A>G p.(Asp286Gly) c.1447G>T p.(Glu483Ter)	Comp. Het	n/a	n/a	n/a	yes	NS-gene panel	3.0	3.0	n/a	n/a	n/a	n/a	FSGS	n/a	n/a	n/a	0.0
32	S29	COQ8B	c.857A>G p.(Asp286Gly) c.1447G>T p.(Glu483Ter)	Comp. Het	n/a	n/a	n/a	yes	NS-gene panel	9.0	9.0	n/a	n/a	n/a	n/a	FSGS	n/a	n/a	n/a	0.0
33	S29	COQ8B	c.958C>T p.(Arg320Trp)	Hom	n/a	Tunisia	n/a	yes	NS-gene panel	12.0	12.0	n/a	n/a	n/a	n/a	FSGS	17.0	17.0	17.0	5.0
34	S29 Survey update	COQ8B	c.958C>T p.(Arg320Trp)	Hom	F	Tunisia	yes	yes	NS-gene panel	20.5	20.5	n/a	<15	yes	no	n/a	22.6	n/a	22.6	2.1
35	S29 Survey update	COQ8B	c.1027C>T p.(Arg343Trp)	Hom	F	Morocco	yes	yes	NS-gene panel	20.0	20.0	n/a	<15	yes	yes	n/a	20.0	n/a	36.0	16.0
36	S29 Survey update	COQ8B	c.1027C>T p.(Arg343Trp)	Hom	F	Morocco	yes	yes	NS-gene panel	birth	18.0	n/a	n/a	yes	no	cFSGS	19.0	n/a	34.0	16.0
37	S29	COQ8B	c.1199_1200dup p.(His400AsnfsTer11)	Hom	n/a	Turkey	n/a	yes	NS-gene panel	n/a	0.5	n/a	n/a	n/a	n/a	FSGS	n/a	n/a	5.0	4.5

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38	S29	COQBB	c.1356_1362del p.(Gln452Hisfs)	Hom	n/a	Indian	n/a	yes	NS-gene panel	16.0	16.0	n/a	n/a	n/a	n/a	cFSGS	n/a	n/a	18.0	2.0
39	S29	COQBB	c.1356_1362del p.(Gln452Hisfs)	Hom	n/a	Indian	n/a	yes	NS-gene panel	21.0	21.0	n/a	n/a	n/a	n/a	cFSGS	n/a	n/a	22.0	1.0
40	S27	COQBB	c.748G>A p.(Asp250Asn) reported as: c.625C>G	Hom	F	Chinese	no	n/a	NS-gene panel	11.7	11.7	65mg/kg/24h	75	no	no	FSGS	n/a	n/a	12.0	2.3
41	S30	COQBB	c.241G>T p.(Glu81Ter) c.1468C>T p.(Arg490Cys)	Comp. Het	M	Chinese	n/a	no	NS-gene panel	11.0	11.0	n/a	n/a	n/a	n/a	FSGS	n/a	n/a	12.0	1.0
42	S30	COQBB	c.488C>T p.(Arg150Ter) c.748G>C p.(Asp250His)	Comp. Het	F	Chinese	n/a	yes	NS-gene panel	8.0	8.0	n/a	n/a	n/a	n/a	FSGS	11.8	n/a	11.8	3.8
43	S30	COQBB	c.532C>T p.(Arg178Trp) c.748G>C p.(Asp250His)	Comp. Het	F	Chinese	n/a	yes	NS-gene panel	9.2	9.2	n/a	n/a	n/a	n/a	Sclerosing GN	11.0	n/a	11.0	1.8
44	S30	COQBB	c.737G>A p.(Ser246Asn)	Hom	F	Chinese	n/a	yes	NS-gene panel	8.2	8.2	n/a	n/a	n/a	n/a	FSGS	n/a	n/a	9.2	1.0
45	S30	COQBB	c.737G>A p.(Ser246Asn)	Hom	F	Chinese	n/a	yes	NS-gene panel	17.4	17.4	n/a	n/a	n/a	n/a	MpGN	n/a	n/a	18.9	1.5
46	S30	COQBB	c.748G>C p.(Asp250His)	Hom	F	Chinese	n/a	yes	NS-gene panel	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	0.0
47	S30	COQBB	c.748G>C p.(Asp250His)	Hom	F	Chinese	n/a	yes	NS-gene panel	1.7	1.7	n/a	n/a	n/a	n/a	FSGS	6.0	n/a	6.0	4.3
48	S30	COQBB	c.748G>C p.(Asp250His) c.1093C>G p.(Gln365Glu)	Comp. Het	F	Chinese	n/a	yes	NS-gene panel	6.0	6.0	n/a	n/a	n/a	n/a	FSGS	n/a	n/a	12.0	6.0
49	S31	COQBB	c.532C>T p.(Arg178Trp) c.748G>C p.(Asp250His)	Comp. Het	F	Chinese	no	n/a	WES	n/a	0.75	413.4 mg/d	117.6	no	no	n/a	n/a	n/a	5.8	5.05
50	S31	COQBB	c.737G>A p.(Ser246Asn) Reported as: c.614C>T c.748G>A p.(Asp250Asn) Reported as: c.625C>G	Comp. Het	F	Chinese	no	n/a	WES	9.0	9.0	2148.7 mg/d	n/a	no	yes	FSGS	14.2	n/a	14.2	5.2
51	S32	COQBB	c.449G>A p.(Arg150Gln) c.759C>A p.(Asn253Lys)	Comp. Het	F	Korean	n/a	yes	NS-gene panel	8.2	8.2	Prot/Crea 4.19 mg/mg	81.4	n/a	n/a	FSGS NOS, dysmorphic mitochondria	15.0	n/a	15.0	6.8
52	S32	COQBB	c.449G>A p.(Arg150Gln) c.759C>A p.(Asn253Lys)	Comp. Het	M	Korean	n/a	yes	NS-gene panel	n/a	5.0	Prot/Crea 2.47 mg/mg	68.5	n/a	n/a	n/a	10.2	n/a	10.2	5.2
53	S32	COQBB	c.449G>A p.(Arg150Gln) c.759C>A p.(Asn253Lys)	Comp. Het	F	Korean	n/a	n/a	NS-gene panel	n/a	10.7	Prot/Crea 2.54 mg/mg	64.5	n/a	n/a	cFSGS, dysmorphic mitochondria	13.8	n/a	13.8	3.1
54	S32	COQBB	c.737G>A p.(Ser246Asn)	Hom	F	Korean	n/a	n/a	NS-gene panel	n/a	10.0	Prot/Crea 8.6 mg/ mg	74.8	n/a	n/a	FSGS NOS, dysmorphic mitochondria	12.5	n/a	12.5	2.5
55	S32	COQBB	c.737G>A p.(Ser246Asn) c.1468C>T p.(Arg490Cys)	Comp. Het	F	Korean	n/a	n/a	Family screening	7.0	7.0	Prot/Crea 3.32mg/ mg	82.6	n/a	n/a	cFSGS, dysmorphic mitochondria	10.6	n/a	17.0	10.0
56	S32	COQBB	c.737G>A p.(Ser246Asn)	Hom	F	Korean	n/a	n/a	NS-gene panel	12.7	12.7	Prot/Crea 2.45 mg/mg	97.4	n/a	n/a	FSGS NOS, dysmorphic mitochondria	n/a	n/a	13.7	1.0
57	S33	COQBB	c.748G>C p.(Asp250His) c.1339G>A p.(Glu447GlyfsTer10)	Hom	F	Chinese	yes	yes	NS-gene panel	birth	9.0	174 mg/kg/d	n/a	n/a	yes	FSGS, mesangial proliferation	11.0	n/a	13.0	4.0
58	S33	COQBB	c.748G>C p.(Asp250His) c.1339G>A p.(Glu447GlyfsTer10)	Hom	M	Chinese	yes	yes	NS-gene panel	2.0	2.0	190 mg/kg/d	n/a	yes	yes	FSGS, mesangial proliferation	n/a	n/a	4.7	2.7
59	S34	COQBB	c.1199dupA p.(His400GlnfsTer11)	Hom	M	Turkey	yes	yes	NS-gene panel	18.0	18.0	n/a	12	n/a	n/a	n/a	n/a	n/a	29*	11.0
60	S34 Survey update	COQBB	c.1199dupA p.(His400GlnfsTer11)	Hom	M	Turkey	yes	yes	single gene	n/a	12.0	7.8 mg/mg	48	n/a	n/a	n/a	13.0	13.5	18.0	6.0
61	S34 S38 Survey update	COQBB	c.1199dupA p.(His400GlnfsTer11)	Hom	F	Turkey	yes	yes	single gene	2.0	2.0	n/a	183	n/a	n/a	n/a	n/a	n/a	5.2	3.2

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Genotypes				Baseline features														Follow-up			
ID (reference if already published)	Gene	Variant(s) cDNA / (AA modification)	Status (Comp. Het/Hom)	Gender	Country of origin/ethnicity	Consanguinity	Positive family history	Reason for genetic testing	Age at 1 st clinical manifestation (years)	Age at kidney disease onset (years)	Initial proteinuria	Initial GFR (ml/min/1.73m ²)	Hypertension	Oedema	Histopathology (kidney)	Age at ESRD (years) (Hemodialysis- Peritoneal dialysis - if available)	Age at kidney transplant (years)	Age at last observation or death* (years)	Follow-up (years)		
S34.S38.Survey update	COQ8B	c.1199dupA p.(His400GlnTer11)	Hom	M	Turkey	yes	yes	single gene	7.0	7.0	n/a	141	n/a	n/a	n/a	n/a	n/a	n/a	9.2	2.2	
S34.Survey update	COQ8B	c.1199dupA p.(His400GlnTer11)	Hom	F	Turkey	n/a	yes	single gene	13.0	13.0	910 mg/m2/d	40	n/a	n/a	n/a	n/a	16.0	16.0	22.4	9.4	
S34.Survey update	COQ8B	c.1199dupA p.(His400GlnTer11)	Hom	M	Turkey	n/a	yes	single gene	5.0	5.0	3.7 mg/m2/d	35	n/a	n/a	n/a	n/a	13.0	13.0	18.0	13.0	
S34	COQ8B	c.1339dupG p.(Glu447GlyTer10)	Hom	F	Turkey	n/a	n/a	single gene	12.0	12.0	4.3 mg/m2/d	138	n/a	n/a	n/a	n/a	n/a	n/a	14.8*	2.8	
S34	COQ8B	c.1199dupA p.(His400GlnTer11)	Hom	F	Turkey	yes	yes	single gene	n/a	17.7	1.38 mg/m2/d	9	n/a	n/a	n/a	n/a	17.7	n/a	21.1*	3.4	
S34	COQ8B	c.1199dupA p.(His400GlnTer11)	Hom	M	Turkey	yes	yes	single gene	4.2	4.2	129 mg/m2/d	184	n/a	n/a	n/a	n/a	17.5	n/a	18.3	14.1	
S34	COQ8B	c.1199dupA p.(His400GlnTer11)	Hom	F	Turkey	yes	yes	single gene	22.6	22.6	1.63 mg/m2/d	n/a	n/a	n/a	n/a	n/a	23.0	n/a	26.0	3.4	
S34.S38.Survey update	COQ8B	c.1199dupA p.(His400GlnTer11)	Hom	F	Turkey	yes	yes	single gene	7.7	7.7	1.58 mg/m2/d	136	n/a	n/a	n/a	n/a	n/a	n/a	13.0	5.3	
S34.S38.Survey update	COQ8B	c.1199dupA p.(His400GlnTer11)	Hom	M	Turkey	yes	yes	single gene	23.7	23.7	177 mg/m2/d	111	n/a	n/a	n/a	n/a	n/a	n/a	25.0	1.3	
S34.Survey update	COQ8B	c.1339dupG p.(Glu447GlyTer10)	Hom	F	Turkey	n/a	yes	WES	birth	12.4	956 mg/m2/d	14	n/a	n/a	n/a	n/a	12.5	n/a	19.0	6.6	
S34.Survey update	COQ8B	c.1339dupG p.(Glu447GlyTer10)	Hom	F	Turkey	n/a	yes	WES	9.6	9.6	3.6 mg/m2/d	30	n/a	n/a	n/a	n/a	10.5	n/a	16.8	7.2	
S34.Survey update	COQ8B	c.1339dupG p.(Glu447GlyTer10)	Hom	F	Turkey	n/a	yes	WES	20.3	20.3	725 mg/m2/d	9	n/a	n/a	n/a	n/a	20.5	n/a	25.3	5.0	
S34.Survey update	COQ8B	c.1430G>A p.(Arg477Gln)	Hom	F	Turkey	n/a	n/a	single gene	n/a	17.8	419 mg/m2/d	55	n/a	n/a	n/a	n/a	19.0	n/a	20.3	2.5	
S34.S38.Survey update	COQ8B	c.1430G>A p.(Arg477Gln)	Hom	F	Turkey	yes	n/a	single gene	9.0	9.0	1.5 mg/m2/d	91	n/a	n/a	n/a	n/a	n/a	n/a	19.3	10.3	
S34.Survey update	COQ8B	c.1339dupG p.(Glu447GlyTer10)	Hom	F	Turkey	n/a	yes	single gene	16.4	16.4	7.5 mg/m2/d	32	n/a	n/a	n/a	n/a	17.0	17.0	18.0	1.6	
S34.Survey update	COQ8B	c.1339dupG p.(Glu447GlyTer10)	Hom	M	Turkey	n/a	yes	single gene	n/a	6.4	900 mg/m2/d	54	n/a	n/a	n/a	n/a	11.0	11.0	26.5	20.1	
S34.S38.Survey update	COQ8B	c.1339dupG p.(Glu447GlyTer10)	Hom	M	Turkey	no	yes	single gene	23.5	24.0	1.06 mg/m2/d	140	n/a	n/a	n/a	n/a	n/a	n/a	26.0	2.5	
S34.Survey update	COQ8B	c.293T>G p.(Lys98Arg)	Hom	M	Turkey	yes	yes	single gene	n/a	9.0	27.3 mg/m2/d	7	n/a	n/a	n/a	n/a	9.0	n/a	18.0	9.0	
S34.Survey update	COQ8B	c.293T>G p.(Lys98Arg)	Hom	M	Turkey	yes	yes	single gene	n/a	9.6	1.188 mg/m2/d	5	n/a	n/a	n/a	n/a	9.6	16.0	16.0	6.4	
S34.S38.Survey update	COQ8B	c.293T>G p.(Lys98Arg)	Hom	M	Turkey	yes	yes	single gene	32.2	32.2	947 mg/m2/d	58	n/a	n/a	n/a	n/a	n/a	n/a	40.0	7.8	
S35	COQ8B	c.648G>A p.(Ala217Thr) c.748G>T p.(Asp250Tyr)	Comp. Het	M	Caucasian	no	no	NS-gene panel	n/a	5.0	Prot/Crea 2.6g/g	100	no	no	FSGS	10.0	10.5	10.5	5.5		
S36	COQ8B	c.532C>T p.(Arg178Trp)	Hom	F	Japanese	n/a	no	Phenotype (dysmorphic mitochondria)	30.0	30.0	Prot/Crea 1.85 g/g	82	no	no	FSGS, dysmorphic mitochondria	n/a	n/a	33.5	3.5		
S37	COQ8B	c.748G>A p.(Asp250Asn) Reported as: c.625C>G c.1041C>A p.(Cys347Ter) Reported as: 918C>A	Comp. Het	M	Chinese	no	yes	NS-gene panel	10.0	10.0	Prot/Crea 1.54 g/g	138	no	no	FSGS, dysmorphic mitochondria	n/a	n/a	14.3	4.3		
S37	COQ8B	n/a	n/a	F	Chinese	no	yes	n/a	12.0	12.0	2.64 g/24h	10	yes	yes	chronic sclerosing GN, dysmorphic mitochondria	12.0	n/a	12.5*	0.5		
PodoNet	COQ8B	c.1339dup p.(Glu447GlyTer10)	Hom	M	Turkey (Persian/Kurdish)	yes	n/a	NS-gene panel	11.8	11.8	Prot/Crea 4.17 g/g	>90	yes	yes	n/a	n/a	n/a	n/a	16.6	4.8	
PodoNet	COQ8B	c.3671G>T	Hom	F	Caucasian (Serbia)	no	n/a	NS-gene panel	5.3	5.3	Prot/Crea 7.32g/g	n/a	n/a	n/a	MPGN	n/a	n/a	n/a	5.8	0.5	
PodoNet	COQ8B	c.719A>G p.(Tyr240Cys)	Hom	M	Caucasian (Russia)	yes	yes	NS-gene panel	2.0	2.0	Subnephrotic	60<GFR<90	no	no	n/a	n/a	n/a	n/a	9.5	7.5	
PodoNet	COQ8B	c.271C>T p.(Arg91Cys)	Hom	M	Caucasian (Russia)	no	no	NS-gene panel	1.4	1.4	2.2 g/m2/day	60<GFR<90	no	no	n/a	n/a	n/a	n/a	41.*	2.7	
Survey	COQ8B	n/a	Hom	M	Caucasian (Turkey)	yes	no	NS-gene panel	n/a	1.2	Nephrotic range	>90	no	yes	FSGS	13.7	n/a	13.7	12.5		
S39.MitoNET	COQ8B	1447G>T p.(Glu483Ter)	Hom	M	Caucasian (Turkey)	yes	yes	Family screening	24.0	24.0	n/a	n/a	n/a	n/a	n/a	FSGS	24.0	28.0	55.0	31.0	
S39.MitoNET	COQ8B	1447G>T p.(Glu483Ter)	Hom	F	Caucasian (Turkey)	yes	yes	NS-gene panel	32.0	32.0	Nephrotic range	60<GFR<90	no	no	FSGS	n/a	n/a	n/a	33.0	1.0	
Survey	COQ8B	c.439T>C p.(Cys147Arg) c.645del p.(Phe 215LeufsTer14)	Comp. Het	F	Caucasian (France)	no	no	WES-CKD cause screening	4.0	5.5	Subnephrotic	<15	yes	no	Chronic sclerosing GN	7.0	10.0	10.5	5.0		
Survey	COQ8B	c.439T>C p.(Cys147Arg) c.1035>T>C	Comp. Het	M	Caucasian (Spain)	no	no	NS-gene panel	1.5	6.6	Nephrotic range	<15	yes	no	GGs, tubular atrophy, TMA secondary to hypertension	6.6	6.9	14.0	7.4		
Survey	COQ8B	c.538C>T p.(Arg180Cys)	Hom	M	Pacific Islander	no	yes	CKD-cause screening	11.9	11.9	n/a	<15	yes	no	GGs, interstitial fibrosis and tubular atrophy	11.9	12.0	14.3	2.4		

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Genotypes				Baseline features												Follow-up			
ID (reference if already published)	Gene	Variant(s) cDNA / (AA modification)	Status (Comp. Het/Hom)	Gender	Country of origin/ethnicity	Consanguinity	Positive family history	Reason for genetic testing	Age at 1 st clinical manifestation (years)	Age at Kidney disease onset (years)	Initial proteinuria	Initial GFR (ml/min/1.73m ²)	Hypertension	Oedema	Histopathology (kidney)	Age at ESRD (years) (Hemodialysis- Peritoneal dialysis - if available)	Age at kidney transplant (years)	Age at last observation or death* (years)	Follow-up (years)
Survey	COQ8B	c.1345C>T p.(Arg490Cys) c.449G>A p.(Arg150Gln)	Comp. Het	F	Chinese	no	yes	Research	19.0	19.0	Nephrotic range	>90	no	no	FSGS	21.7	n/a	26.0	7.0
Survey	COQ8B	c.289+1G>T c.748G>A p.(Asp250Asn) Reported as: c.625C>G	Comp. Het	F	Chinese	no	yes	Research	12.0	12.0	Nephrotic range	<15	yes	yes	GGs	12.0	n/a	24.3	12.3
Survey	COQ8B	c.289+1G>T c.748G>C p.(Asp250His)	Comp. Het	M	Chinese	no	yes	Research	11.0	11.0	Nephrotic range	n/a	no	no	Minor GN abnormalities	n/a	n/a	20.0	9.0
S17	COQ8B	c.532C>T p.(Arg178Trp)	Hom	F	Netherlands	yes	no	CKD-cause screening	n/a	4.0	1g/L	>90	n/a	n/a	n/a	14.8	15.8	21.4	17.4
Survey	COQ8B	c.645del p.(Phe215Leu&Ter14)	Hom	M	Turkey	yes	yes	NS-gene panel	9.2	9.2	Nephrotic range	60<GFR<90	no	no	n/a	17.8	n/a	17.8	8.6
Survey	COQ8B	c.645del p.(Phe215Leu&Ter14)	Hom	M	Turkey	yes	yes	NS-gene panel	8.6	8.6	Nephrotic range	<15	yes	yes	GGs	8.6	n/a	8.6	0.0
S29.Survey update	COQ8B	c.645del p.(Phe215Leu&Ter14) c.1430G>A p.(Arg477Gln)	Comp. Het	F	Algerian	no	yes	NS-gene panel	2.0	2.0	Nephrotic range	>90	yes	yes	FSGS	13.8	15.2	15.2	13.2
S29.Survey update	COQ8B	c.645del p.(Phe215Leu&Ter14) c.1430G>A p.(Arg477Gln)	Comp. Het	M	Algerian	no	yes	NS-gene panel	2.4	2.4	Nephrotic range	>91	yes	no	FSGS	12.5	13.6	13.6	11.2
Survey	COQ8B	c.645del p.(Phe215Leu&Ter14)	Hom	F	Caucasian (France)	no	no	NS-gene panel	32.0	32.0	Nephrotic range	>92	yes	no	FSGS NOS+TF	n/a	n/a	32.8	0.8
Survey	COQ8B	c.1430G>A p.(Arg477Gln)	Hom	M	Turkey	yes	yes	NS-gene panel	15.0	15.0	Nephrotic range	15<GFR<30	yes	no	FSGS	15.0	16.0	16.0	1.0
Survey	COQ8B	c.1199del p.(His400Gln&Ter11)	Hom	F	Caucasian (Turkey)	yes	yes	NS-gene panel	17.0	17.0	Nephrotic range	60<GFR<90	yes	no	n/a	n/a	n/a	18.2	1.2
CCGDD	COQ8B	c.1A>G p.(Met1Val) c.748G>C p.(Asp250His)	Comp. Het	M	Chinese	no	n/a	Research	n/a	4.1	208mg/kg/24h	>90	yes	yes	FSGS	6.0	n/a	10.0	5.9
S40	COQ8B	c.449G>A p.(Arg150Gln) c.737G>A p.(Ser246Asn)	Comp. Het	M	Chinese	no	no	Research	2.3	2.3	n/a	>90	no	no	n/a	8.0	n/a	12.0	9.7
S40	COQ8B	c.532C>T p.(Arg178Trp) c.737G>A p.(Ser246Asn)	Comp. Het	M	Chinese	no	no	Research	n/a	10.0	40.8mg/kg/24h	5	yes	no	n/a	10.0	11.0	15.0	5.0
CCXGDD	COQ8B	c.737G>A p.(Ser246Asn)	Hom	F	Chinese	no	n/a	Research	5.2	5.2	196mg/kg/24h	57	no	yes	FSGS	10.0	n/a	11.0	5.8
CCXGDD	COQ8B	c.748G>C p.(Asp250His) c.1488C>T p.(Arg490Cys)	Comp. Het	M	Chinese	no	n/a	Research	11.0	11.0	n/a	13	yes	yes	n/a	11.0	n/a	13*	2.0
CCXGDD	COQ8B	c.737G>A p.(Ser246Asn) c.1488C>T p.(Arg490Cys)	Comp. Het	M	Chinese	no	n/a	Research	5.0	5.0	n/a	4	yes	yes	GGs	5.0	12.0	12.0	7.0
S40	COQ8B	c.748G>C p.(Asp250His)	Hom	M	Chinese	no	yes	NS-gene panel	5.0	5.0	91mg/kg/24h	83	no	no	FSGS	n/a	n/a	5.0	0.0
S40	COQ8B	c.748G>C p.(Asp250His)	Hom	F	Chinese	no	yes	NS-gene panel	13.0	13.0	135mg/kg/24h	24	no	yes	n/a	n/a	n/a	13.0	0.0
S40	COQ8B	c.748G>C p.(Asp250His)	Hom	M	Chinese	yes	no	Research	10.3	10.3	81mg/kg/24h	5	yes	yes	n/a	10.3	12.7	14.9	4.6
CCXGDD	COQ8B	c.532C>T p.(Arg178Trp) c.748G>C p.(Asp250His)	Comp. Het	F	Chinese	no	n/a	NS-gene panel	6.0	6.0	79mg/kg/24h	31	no	no	n/a	6.7	n/a	6.7	0.7
S40	COQ8B	c.737G>A p.(Ser246Asn)	Hom	M	Chinese	no	no	NS-gene panel	7.5	7.5	Nephrotic range	15.6	no	yes	FSGS	7.9	8.7	14.1	6.6
S40	COQ8B	c.748G>C p.(Asp250His)	Hom	F	Chinese	yes	yes	Research	n/a	9.9	100mg/kg/24h	5.6	yes	yes	diffuse endocapillary proliferative GN	9.9	16.0	18.3	8.4
S40	COQ8B	c.748G>C p.(Asp250His)	Hom	M	Chinese	yes	yes	NS-gene panel	n/a	1.9	92mg/kg/24h	110	no	no	SFGS	n/a	n/a	10.1	8.2
S40	COQ8B	c.551A>G p.(Asp184Gly) c.737G>A p.(Ser246Asn)	Comp. Het	M	Chinese	no	no	NS-gene panel	3.1	3.1	Nephrotic range	>90	no	no	FSGS	8.3	n/a	9.6	6.5

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121	S40	COQ8B	c.532C>T p.(Arg178Trp) c.737G>A p.(Ser246Asn)	Comp. Het	M	Chinese	no	no	Research	6.6	6.6	165mg/kg/24h	5.02	no	yes	GGs	6.6	8.6	10.3	3.7
122	S40	COQ8B	c.737G>A p.(Ser246Asn)	Hom	F	Chinese	no	no	NS-gene panel	3.0	3.0	3.94 mg/mg	125	no	no	FSGS	n/a	n/a	7.1	4.1
123	CKXGDD	COQ8B	c.737G>A p.(Ser246Asn) c.748G>C p.(Asp250His)	Comp. Het	M	Chinese	no	n/a	Research	5.5	5.5	n/a	7.6	yes	yes	GGs	5.5	6.3	8.4	2.9
124	CKXGDD	COQ8B	c.532C>T p.(Arg178Trp) c.748G>C p.(Asp250His)	Comp. Het	M	Chinese	no	n/a	Research	1.8	1.8	n/a	149	no	no	n/a	4.6	n/a	6.0	4.2
125	CKXGDD	COQ8B	c.1468C>T p.(Arg490Cys) c.737G>A p.(Ser246Asn)	Comp. Het	M	Chinese	no	n/a	Research	birth	10.0	2+;28mg/kg/24h	1.09	yes	no	n/a	10.0	11.9	11.9	1.9
126	CKXGDD	COQ8B	c.737G>A p.(Ser246Asn)	Hom	M	Chinese	no	n/a	NS-gene panel	1.0	1.0	3+;pro/ur 15.9	227	no	yes	n/a	n/a	n/a	5.0	4.0
127	CKXGDD	COQ8B	c.449G>A p.(Asp155Gln) c.748G>C p.(Asp250His)	Comp. Het	F	Chinese	no	n/a	NS-gene panel	1.0	1.0	146.79mg/kg/24h	303.15	no	yes	FSGS	n/a	n/a	3.0	2.0
128	CKXGDD	COQ8B	c.737G>A p.(Ser246Asn) c.748G>C p.(Asp250His)	Comp. Het	M	Chinese	no	n/a	NS-gene panel	6.0	6.0	n/a	n/a	no	no	MPGN	n/a	n/a	n/a	n/a
129	CKXGDD	COQ8B	c.1468C>T p.(Arg490Cys) c.737G>A p.(Ser246Asn)	Comp. Het	M	Chinese	no	n/a	Research	5.0	5.0	100mg/kg/24h	4.7	no	yes	n/a	5.0	n/a	12.0	7.0
130	CKXGDD	COQ8B	c.538C>T p.(Arg180Cys)	Hom	F	Chinese	yes	n/a	NS-gene panel	3.0	3.0	1+;	>90	no	no	FSGS	10.4	n/a	12.0	9.0
131	S41	COQ8B	c.271C>T p.(Arg91Cys) c.737G>A p.(Ser246Asn)	Comp. Het	M	Chinese	no	no	NS-gene panel	3.0	3.0	590 mg/24 h. 33 mg/kg	189.5	no	no	EM mitochondrial abnormalities	n/a	n/a	3.6	6.6
132	S40	COQ8B	c.538C>T p.(Arg180Cys)	Hom	F	Chinese	yes	no	n/a	4.4	4.4	n/a	n/a	n/a	n/a	FSGS	11.5	n/a	11.5	7.1
133	S40	COQ8B	c.737G>A p.(Ser246Asn) c.748G>C p.(Asp250His)	Comp. Het	F	Chinese	no	no	n/a	9.3	9.3	n/a	n/a	n/a	n/a	FSGS	13.5	n/a	13.5	4.2
134	S40	COQ8B	c.737G>A p.(Ser246Asn) c.748G>C p.(Asp250His)	Comp. Het	M	Chinese	no	no	n/a	n/a	7.0	n/a	n/a	n/a	n/a	MPGN	n/a	n/a	n/a	n/a
135	S40	COQ8B	c.737G>A p.(Ser246Asn) c.936_938del p.(Val313del)	Comp. Het	F	Chinese	no	no	n/a	3.6	3.6	n/a	n/a	n/a	n/a	FSGS	9.4	n/a	9.4	5.8
136	S40	COQ8B	c.748G>C p.(Asp250His)	Hom	M	Chinese	yes	no	n/a	3.3	3.3	n/a	n/a	n/a	n/a	n/a	3.9	n/a	3.9	0.6
137	S40	COQ8B	c.748G>C p.(Asp250His)	Hom	F	Chinese	no	no	n/a	11.7	11.7	n/a	n/a	n/a	n/a	MPGN	13.9	n/a	13.9	2.2
138	S40	COQ8B	c.748G>C p.(Asp250His) c.1468C>T p.(Arg490Cys)	Comp. Het	F	Chinese	no	no	n/a	n/a	11.1	n/a	n/a	n/a	n/a	n/a	11.1	n/a	11.1	0.0
139	S40	COQ8B	c.893+2T>A c.1035+3A>G	Comp. Het	M	Chinese	no	no	n/a	15.0	15.0	n/a	n/a	n/a	n/a	FSGS	17.2	n/a	17.2	2.2
140	S40	COQ8B	c.893+2T>A c.1035+3A>G Reported as: c.770+2T>A c.912+3A>G	Comp. Het	M	Chinese	no	no	n/a	16.0	16.0	n/a	n/a	n/a	n/a	n/a	17.6	n/a	17.6	1.6

Variant details provided according to cDNA NM_024876.4; protein NP_079152.3

Abbreviations:

n/a	non available/ non applicable
Comp. Het.	compound heterozygote
Hom	homozygote
F	female
M	male
NS	nephrotic syndrome
FSGS	focal segmental glomerulosclerosis
cFSGS	collapsing Focal segmental glomerulosclerosis
NOS	non otherwise specified
GGs	global glomerulosclerosis
MCD	minimal change disease
MPGN	membranoproliferative glomerulonephritis
DMS	difuse Mesangial Sclerosis
PD	peritoneal dialysis
HD	hemodialysis
uAlbCrea	urine albumin to creatinine ratio
W	weeks
GFR	glomerular filtration rate

Supplementary Table S2.

Variant reporting. Annotations (current reference sequence COQ2: NM_015697.8, NP_001345850.1; COQ6: NM_182476.3, NP_872282.1 and COQ8B: NM_024876.4, NP_079152.3.), ACMG classification, population frequency and references. Number of cases among our study population.

COQ2

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COQ2	variant type	cDNA NM_015697.8	protein NP_056512.5 (421 aa)	protein NP_001345850.1 (371 aa)	rsID (dbSNPs)	ClinVar (UniProt*) Variation ID	ClinVar status	Significance (According to ACMG 2015)	AutoPVS1	Allele frequency GnomAD ver. 2.1.1 exomes	Allele frequency GnomAD ver. 3.1.1 genomes	Max. population GnomAD ver. 2.1.1 exomes	N° cases	N° homozygotes	N° heterozygotes	Ethnicity	References	Published / novel
1	truncating	c.176dup	p.Ala60ArgfsTer33	p.Ala10ArgfsTer33	rs1198292264	-	-	Pathogenic PVS1 PM2 PM3 PP3	VeryStrong	-	-	-	1	0	1	Mixed european ancestry	S10	published
2	missense	c.215C>T	p.Pro72Gln	p.Pro22Gln	rs765747895	-	-	Unknown significance PM2 PM3 PP2 BP4		-	-	-	1	0	1	Japan	MitoNET	novel
3	truncating	c.223_249delinsAAG GA	p.Arg75LysfsTer90	p.Arg25LysfsTer90	-	-	-	Pathogenic PVS1 PM2 PP3	VeryStrong	-	-	-	1	0	1	Caucasian(France)	Survey	novel
4	truncating	c.288dup	p.Ala97ArgfsTer56	p.Ala47ArgfsTer56	rs759310292	631951	Conflicting interpretations of pathogenicity: Likely benign(1); Uncertain significance(1)	Pathogenic PVS1 PM2 PM3 PP1	VeryStrong	0.000295	0.00007896	Ashkenazi Jews 0.00374	4	0	4	Eastern Europe,Ashkenazi Jewish (USA)	S18,PodoNet	published
5	truncating	c.313_329dup	p.Ala111SerfsTer67	p.Ala61SerfsTer67	rs1466843900	-	-	Pathogenic PVS1 PM2 PM3 PP3	VeryStrong	0.00000733	0.00002628	European Non- Finnish 0.00002	1	0	1	Caucasian(France)	Survey	novel
6	missense	c.349G>C	p.Ala117Pro	p.Ala67Pro	-	-	-	Likely pathogenic PM2 PM3 PP1 PP2	n/a	-	-	-	2	0	2	Japan	MitoNET	novel
7	missense	c.374T>C	p.Leu125Ser	p.Leu75Ser	-	-	-	Uncertain Significance PM2 PP2 PP3	n/a	-	-	-	1	1	0	Eastern Europe	PodoNet	novel
8	missense	c.376C>G	p.Arg126Gly	p.Arg76Gly	rs868158482	-	-	Likely pathogenic PM2 PM3 PP1 PP2 PP3	n/a	0.00001	-	Asian 0.00004	3	0	3	Ashkenazi Jewish (USA)	S18	published
9	missense	c.424C>G	p.Pro142Ala	p.Pro92Ala	rs1025584033	-	-	Uncertain Significance PM2 PP2 PP3	n/a	0.00000516	0.00003288	Latino 0.0000396	1	0	1	Colombia	PodoNet	novel
10	missense	c.437G>A	p.Ser146Asn	p.Ser96Asn	rs121918233	1440 *VAR_068161	pathogenic	Pathogenic PS3 PS4 PM2 PP1 PP2 PP3 PP5	n/a	0.00001649	0.00001972	European Non- Finnish 0.00003669	10	6	4	Italy /NA/turkey/ mixed (China+French West Indies+Magreb)/Ca ucasian (Norway)/Caucasia n(Georgia)	S3,S6,S7,S16,Mito NET, Survey	published
11	missense	c.517C>T	p.Arg173Cys	p.Arg123Cys	rs758103492	-	-	Likely pathogenic PM2 PM3 PP2 PP3	n/a	0.00000831	-	East Asian 0.00006	1	0	1	Slovenia	Survey	novel
12	missense	c.518G>A	p.Arg173His	p.Arg123His	rs752363398	-	-	Pathogenic PS4 PM2 PM3 PP2 PP3	n/a	0.00009117	0.00002628	Ashkenazi Jews 0.00132	5	0	5	Europe, China, mixed(China+Frenc h West Indies+Magreb), Turkey	S14,S15,Survey, CCGKDD	published
13	missense	c.539A>G	p.Asn180Ser	p.Asn130Ser	-	-	-	Uncertain Significance PM2 PP2 PP3	n/a	-	-	-	1	0	1	Colombia	PodoNet	novel
14	missense	c.545T>G	p.Met182Arg	p.Met132Arg	rs1057519348	375338 *VAR_076913	pathogenic	Likely Pathogenic PS3 PM2 PP2 PP3 PP5	n/a	-	-	-	1	0	1	NA	S8	published
15	missense	c.550G>T	p.Asp184Tyr	p.Asp134Tyr	-	-	-	Likely pathogenic PM2 PM3 PP2 PP3	n/a	-	-	-	1	0	1	Italy	Survey	novel
16	truncating	c.571-1G>A	n/a	n/a	-	-	-	Pathogenic PVS1 PM2 PM3 PP3	VeryStrong	-	-	-	2	0	2	Eastern Europe/Tajikistan/ Arabic	Survey,PodoNet	novel
17	missense	c.590G>A	p.Arg197His	p.Arg147His	rs121918231	1438 *VAR_068162	pathogenic	Pathogenic PS3 PM2 PM3 PP2 PP3 PP5	n/a	0.000008041	0.00002630	East Asian 0.00005572	4	0	4	Eastern Europe/Belgium/ Caucasian (Norway)/ Caucasian(Georgia)	S3,S17,MitoNET, Survey	published
18	missense	c.644G>A	p.Gly215Glu	p.Gly165Glu	rs200791648	-	-	Likely pathogenic PM2 PM3 PP2 PP3	n/a	0.00003216	0.0001381	African 0.000388	1	0	1	Caucasian(France)	Survey	novel
19	missense	c.659C>T	p.Ala220Val	p.Ala170Val	-	-	-	Uncertain Significance PM2 PP2 PP3	n/a	-	-	-	1	0	1	Caucasian(France)	Survey	novel

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COQ2	variant type	cDNA NM_015697.8	protein NP_056512.5 (421 aa)	protein NP_001345850.1 (371 aa)	rsID (dbSNPs)	ClinVar (UniProt*) Variation ID	ClinVar status	Significance (According to ACMG 2015)	AutoPVS1	Allele frequency GnomAD ver. 2.1.1 exomes	Allele frequency GnomAD ver. 3.1.1 genomes	Max. population GnomAD ver. 2.1.1 exomes	N° cases	N° homozygotes	N° heterozygotes	Ethnicity	References	Published /novel
20	missense	c.683A>G	p.Asn228Ser	p.Asn178Ser	rs121918232	1439 *VAR_068163	uncertain significance	Pathogenic P53 P54 PM2 PP2 PP3 PP5	n/a	0.0001249	0.00008540	European Non- Finnish 0.0002266 Other 0.0002813	22	5	17	Caucasian/Mixed european ancestry/ Eastern europe/Poland/Taji kistan/mixed (China+French West Indies+Magreb)/Alg eria/Turkey/Italy/Si ovenia/Caucasin(Fr ance)	S3,S10,S11,S12,S1 4, PodoNet, S17,Survey	published
21	truncating	c.701delT	p.Leu234fsTer14	p.Leu184ArgfsTer1 4	rs1458437821	-	-	Pathogenic PVS1 PM2 PM3 PP3	VeryStrong	0.000004144	0.000006573	European Non- Finnish 0.0000913	1	0	1	Caucasian	S11	published
22	missense	c.733T>G	p.Tyr245Asp	p.Tyr195Asp	-	-	-	Likely pathogenic PM2 PM3 PP2 PP3	n/a	-	-	-	1	0	1	Poland	PodoNet	novel
23	truncating	c.778+1G>A	n/a	n/a	rs745504932	-	-	Pathogenic PVS1 PM2 PP3	VeryStrong	0.000004167	-	East Asian 0.00006	2	0	2	Turkey/China	Survey,CCGKDD	novel
24	truncating	c.778+2T>C	n/a	n/a	-	-	-	Pathogenic PVS1 PM2 PM3 PP3	VeryStrong	-	-	-	1	0	1	China	CCGKDD	novel
25	missense	c.832T>C	p.Cys278Arg	p.Cys228Arg	-	-	-	Uncertain Significance PM2 PP2 PP3	n/a	-	-	-	1	1	0	China	S13	published
26	missense	c.856C>T	p.Leu286Phe	p.Leu236Phe	rs776124921	-	-	Likely pathogenic PM2 PM3 PP2 PP3	n/a	0.000008043	-	European Non- Finnish 0.0000177	1	0	1	Europe	S14	published
27	missense	c.881C>T	p.Thr294Ile	p.Thr244Ile	rs376333414	-	-	Likely pathogenic PM2 PM3 PP2 PP3	n/a	0.000008071	0.00001315	South Asian 0.0000328	1	0	1	Caucasian	S10	published
28	missense	c.890A>G	p.Tyr297Cys	p.Tyr247Cys	rs121918230	1436 *VAR_025701	pathogenic	Pathogenic P53 P54 PM2 PM3 PP2 PP3 PP5	n/a	0.000004062	-	South Asian 0.00003314	5	3	2	North Africa/ Arabic/Algerian	S1,S2,S14, Survey	published
29	missense	c.905C>T	p.Ala302Val	p.Ala252Val	rs762616589	375339 *VAR_076914	pathogenic	Pathogenic P53 PM2 PP1 PP2 PP3 PP5	n/a	-	-	-	2	2	0	Turkey	S5	published
30	truncating	c.912+1del	n/a	n/a	-	-	-	Pathogenic PVS1 PM2 PP1 PP3	VeryStrong	-	-	-	2	0	2	Japan	MitoNET	novel
31	missense	c.973A>G	p.Thr325Ala	p.Thr275Ala	rs769971059	-	-	Pathogenic P54 PM2 PM3 PP2 PP3	n/a	0.00005607	0.00001971	East Asian 0.000634	5	0	5	Asian/American/ China	S10,S15,CCGKDD	published
32	missense	c.992_993delinsGC	p.Gly331Ser	p.Gly281Ser	novel	-	-	Likely pathogenic PM2 PM3 PM4 PP2 PP3	n/a	-	-	-	1	0	1	Turkey	Survey	novel
33	truncating	c.1031del	p.Gly344ValfsTer2	p.Gly294ValfsTer2	-	-	-	Pathogenic PVS1 PM2 PP3	VeryStrong	-	-	-	1	0	1	Japan	MitoNET	novel
34	missense	c.1115A>G	p.Asp372Gly	p.Asp322Gly	novel	-	-	Likely pathogenic PM2 PM3 PP2 PP3	n/a	-	-	-	2	1	1	Eastern Europe/Poland	PodoNet	novel
35	missense	c.1158C>G	p.Asn386Lys	p.Asn336Lys	novel	-	-	Uncertain Significance PM2 PP2 PP3	n/a	-	-	-	1	0	1	Caucasian(France)	Survey	novel
36	truncating	c.1159C>T	p.Arg387Ter	p.Arg337Ter	rs751185256	60538	pathogenic / risk factor	Pathogenic PVS1 PM2 PM3 PP3 PP5	Moderate	0.00001212	0.00001318	Latino 0.00002937	2	0	2	Asian/American/ NA	S1,S7	published
37	missense	c.1169G>C	p.Gly390Ala	p.Gly340Ala	rs752608037	*VAR_078121	-	Likely pathogenic P53 PM2 PP2 PP3	n/a	0.00002424	0.0001644	Latino 0.000147	2	2	0	Italy	S9	published
38	truncating	c.1197del	p.Asn401fsTer15	p.Asn351fsTer15	rs750710187	375340	pathogenic	Pathogenic PVS1 PM2 PP5	Moderate	0.00001217	0.00001316	European Non- Finnish 0.00002675	2	2	0	France	S4,S6	published
39	truncating	c.1239G>A	p.Lys413=	p.Lys363=	novel	-	-	Uncertain Significance PM2 PP3 PP5	n/a	-	-	-	1	0	1	Algeria	Survey	novel

COQ6

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COQ6	variant type	cDNA NM_182476.3	protein NP_872282.1	Protein NP_872286.2	rsID (dbSNPs)	ClinVar (UniProt*) Variation ID	ClinVar status	Significance (According to ACMG 2015)	AutoPVS1	Allele frequency GnomAD ver. 2.1.1 exomes	Allele frequency GnomAD ver. 3.1.1 genomes	Max. population	N° cases	N° homozygotes	N° heterozygotes	Ethnicity	References	Published /novel
1	truncating	c.189_191del	p.Lys64del	p.Lys39del	rs746839544	-	-	Likely pathogenic PM2 PM3 PM4 PP3	n/a	0.00001193	-	East Asian 0.0001631	6	0	6	Korea	S21	published
2	missense	c.686A>C	p.Gln229Pro	p.Gln204Pro	rs1446126959	-	-	Likely pathogenic PM2 PM3 PP3	n/a	-	-	-	1	0	1	Korea	S21	published
3	missense	c.763G>A	p.Gly255Arg	p.Gly230Arg	rs1057519350	375342 *VAR_068216	pathogenic	Pathogenic PS1 PS4 PM1 PM2 PP3 PP5	n/a	-	-	-	6	6	0	Lebanon/Turkey	S19	published
4	missense	c.782C>T	p.Pro261Leu	p.Pro236Gln	rs371260604	807582 *VAR_078122	pathogenic	Pathogenic PS4 PM1 PM2 PM3 PP3 PP5	n/a	0.00006718	0.0001051	East Asian 0.0001002 Other 0.0002769	9	3	6	Italy/ Korea/Japan/Iran	S9,S21,S26, Survey	published
5	truncating	c.799_807del	p.Ser267_Leu269del	p.Ser242_Leu244del	-	-	-	Likely pathogenic PM2 PM3 PM4 PP3	n/a	-	-	-	1	0	1	Turkey	Survey	novel
6	truncating	c.804del	p.Leu269TrpfsTer13	p.Leu244TrpfsTer13	-	-	-	Pathogenic PVS1 PM2 PM3 PP3	VeryStrong	-	-	-	1	0	1	Poland	S22	published
7	missense	c.983C>A	p.Ala328Asp	p.Ala303Asp	-	-	-	Uncertain Significance PM2 BP4	n/a	-	-	-	1	1	0	Russia	PodoNet	novel
8	missense	c.1058C>A	p.Ala353Asp	p.Ala328Asp	rs397514479	31595	pathogenic	Pathogenic PS4 PM1 PM2 PM3 PP1 PP3 PP5	n/a	-	-	-	16	15	1	Turkey/ Kazakhstan/Iran	S19,S23,S25,Podo Net, Survey	published
9	missense	c.1078C>T	p.Arg360Trp	p.Arg335Trp	rs778856227	-	-	Pathogenic PS4 PM1 PM2 PM3 PM5 PP3	n/a	0.00001193	-	European Non- Finnish 0.00002637	7	5	2	Poland/China/ Russia	S20,S22,S24,S27, PodoNet,CCGKDD	published
10	missense	c.1079G>T	p.Arg360Leu	p.Arg335Leu	rs367817034	807583	Likely pathogenic	Pathogenic PS4 PM1 PM2 PP3 PP5	n/a	-	-	-	3	0	3	Caucasian (Germany)	MitoNET	novel
11	missense	c.1154A>C	p.Asp385Ala	p.Asp360Ala	-	-	-	Likely pathogenic PM1 PM2 PM3 PP3	n/a	-	-	-	1	0	1	European	S14	published
12	missense	c.1235A>G	p.Tyr412Cys	p.Tyr387Cys	rs374270071	375343	pathogenic	Pathogenic PS4 PM1 PM2 PM3 PP3 PP5	n/a	0.000007953	0.00001314	European Non- Finnish 0.00001758	4	2	2	European/Russia/ Germany	S14, PodoNet,Survey	published
13	truncating	c.1237G>T	p.Glu413Ter	p.Glu388Ter	rs1594816203	807584	pathogenic	Pathogenic PVS1 PM2 PM3 PP1 PP3 PP5	VeryStrong	-	-	-	3	0	3	Caucasian (Germany)	MitoNET	novel
14	truncating	c.1341G>A	p.Trp447Ter	p.Trp422Ter	rs1057519351	375344	pathogenic	Pathogenic PVS1 PM2 PM3 PP3 PP5	Moderate	-	-	-	1	0	1	Turkey	S19	published
15	missense	c.1343G>A	p.Gly448Asp	p.Gly423Asp	rs1350331121	-	-	Uncertain Significance PM2 PP3	n/a	-	0.000006572	Genomes v3.1.1 African/African- American 0.00002413	1	1	0	Arab	Survey	novel
16	truncating	c.1383del	p.Ile462fs	p.Ile437fs	rs1057519352	375345	pathogenic	Pathogenic PVS1 PM2 PM3 PP3 PP5	Moderate	-	-	-	1	0	1	Turkey	S19	published

COQ8B

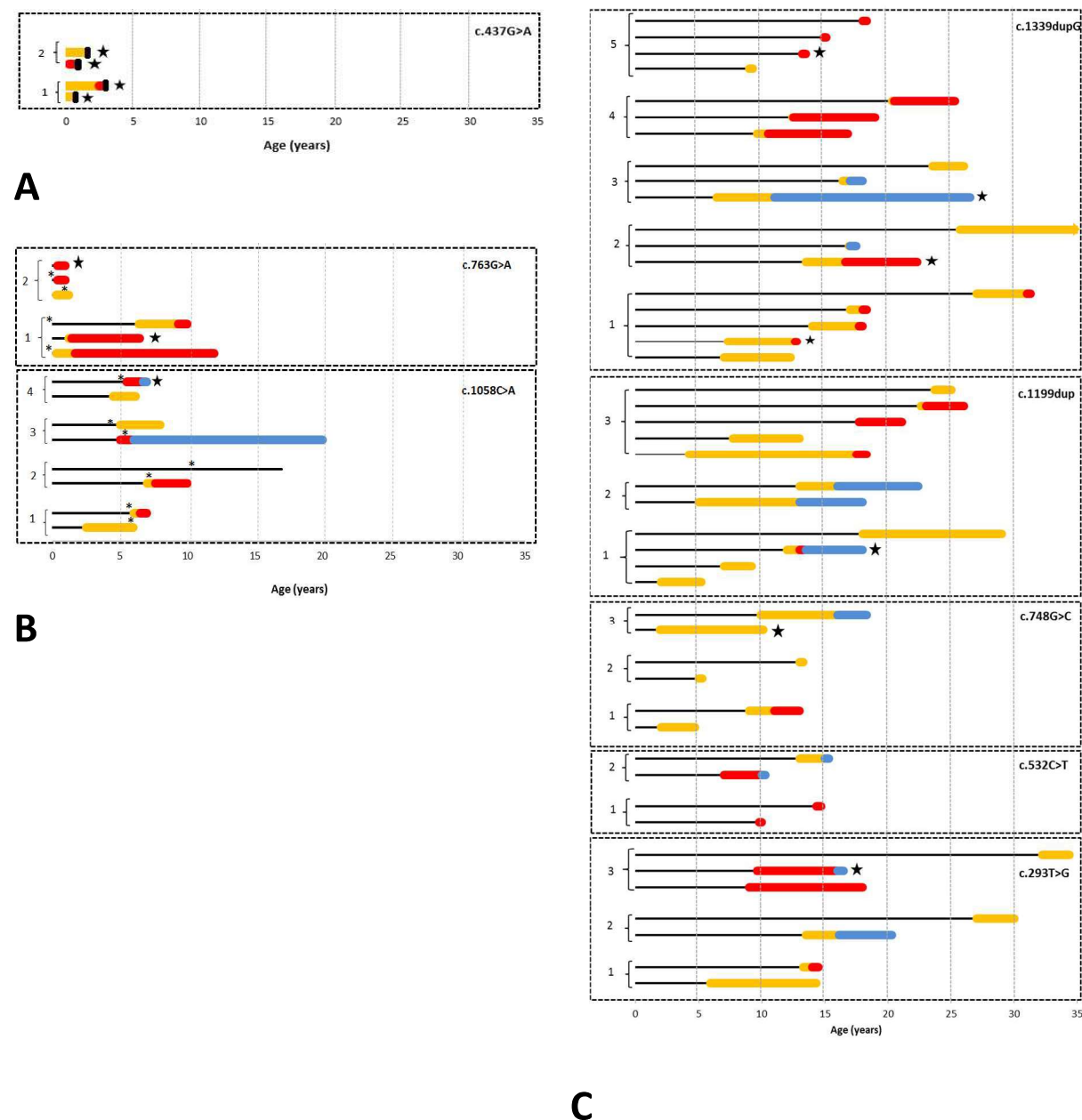
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COQ8B	variant type	cDNA NM_024876.4	Protein NP_079152.3	rsID (dbSNPs)	ClinVar (UniProt*) Variation ID	ClinVar status	Significance (According to ACMG 2015)	AutoPVS1	Allele frequency GnomAD ver. 2.1.1 exomes	Allele frequency GnomAD ver. 3.1.1 genomes	Max. population	N° cases	N° homozygotes	N° heterozygotes	Ethnicity	References	Published /novel
1	truncating	c.1A>G	p.Met1Val	rs766623669	-	-	Pathogenic PVS1 PM2 PM3 PP3	Moderate	-	-	-	1	0	1	Chinese	CCGKDD	novel
2	truncating	c.101G>A	p.Trp34Ter	rs1057519345	375334	Pathogenic	Pathogenic PVS1 PM2 PM3 PP3 PP5	VeryStrong	-	0.000006572	Genomes v3.1.1 European (non- Finnish) 0.00001470	1	0	1	European	S29	published
3	truncating	c.241G>T	p.Glu81Ter	rs1291233620	-	-	Pathogenic PVS1 PM2 PP3	n/a	0.00003186	0.000006571	East Asian 0.0006410	1	0	1	Chinese	S30	published
4	missense	c.271C>T	p.Arg91Cys	rs754975339	-	-	Uncertain Significance PM2 PM3 PP3	n/a	0.00001193	-	Southern European 0.00008694	2	1	1	Caucasian (Russia); Chinese	S41,PodoNet	published
5	truncating	c.289+1G>T	n/a	rs750128167	-	-	Pathogenic PVS1 PM2 PM3 PP3	VeryStrong	0.00001989	0.00001315	European (non- Finnish) 0.00003518	2	0	2	Chinese	Survey	novel
6	missense	c.293T>G	p.Leu98Arg	-	-	-	Likely Pathogenic PS4 PM2 PP1 PP3 PP5	n/a	-	-	-	7	7	0	Turkey	S28,S34,S38	published
7	truncating	c.367+1G>T	n/a	rs143411357	-	-	Pathogenic PVS1 PM2 PP3	VeryStrong	0.000003982	-	Bulgarian 0.0003748	1	1	0	Serbia	PodoNet	novel
8	missense	c.439T>C	p.Cys147Arg	-	-	-	Likely pathogenic PM1 PM2 PM3 PP2 PP3	n/a	-	-	-	2	0	2	Caucasian	Survey	novel
9	truncating	c.448C>T	p.Arg150Ter	rs1253068939	-	-	Pathogenic PVS1 PM2 PM3 PP3	VeryStrong	0.000008007	0.000006572	-	1	0	1	Chinese	S30	published
10	missense	c.449G>A	p.Arg150Gln	rs757644020	-	-	Pathogenic PS4 PM1 PM2 PM3 PP1 PP3	n/a	0.00001602	-	Korean 0.0002619	6	1	5	Korean/Chinese	CCGKDD, Survey, S32	published
11	missense	c.532C>T	p.Arg178Trp	rs398122978	91845	Pathogenic/Likely pathogenic	Pathogenic PS4 PM1 PM2 PM3 PP1 PP3 PP5	n/a	0.00002422	0.00003285	Asian 0.00010	12	6	6	Arab/Chinese/ Japanese/ Caucasian (Netherlands)	CCGKDD,S28,S29,S 30,S31,S36,S17	published
12	missense	c.538C>T	p.Arg180Cys	rs866812916	-	-	Likely pathogenic PS4 PM1 PM2 PP3	n/a	-	-	-	3	3	0	Pacific islander/Chinese	CCGKDD, Survey, S40	published
13	missense	c.551A>G	p.Asp184Gly	-	-	-	Likely pathogenic PM1 PM2 PM3 PP3	n/a	-	-	-	1	0	1	Chinese	S40	published
14	truncating	c.645del	p.Phe215fs	rs764587648	375336	Pathogenic	Pathogenic PVS1 PS4 PM2 PM3 PP3 PP5	VeryStrong	0.00002841	0.00003285	European 0.000031	8	5	3	Caucasian/France/ Turkey	Survey,S28,S29	published
15	missense	c.649G>A	p.Ala217Thr	rs116013644	-	-	Likely Pathogenic PM1 PM2 PM3 PP3	n/a	0.0001178	0.0001577	Southern European 0.0004425	1	0	1	Caucasian	S35	published
16	missense	c.719A>G	p.Tyr240Cys	-	-	-	Likely Pathogenic PM1 PM2 PP3	n/a	-	-	-	1	1	0	Caucasian (Russia)	PodoNet	novel
17	missense	c.737G>A	p.Ser246Asn	rs200841458	-	-	Pathogenic PS4 PM1 PM2 PM3 PP1 PP3 PP5	n/a	0.00006005	0.00004599	Korean 0.002619	24	8	16	Chinese/Korean	CCGKDD, S30,S31,S32,S40,S 41	published
18	missense	c.748G>A	p.Asp250Asn	rs769834604	-	-	Pathogenic PS4 PM1 PM2 PM3 PM5 PP1 PP3	n/a	0.000004011	-	East Asian 0.0007725	6	3	3	Chinese	Survey,S28,S27,S3 1,S37	published
19	missense	c.748G>C	p.Asp250His	rs769834604	-	-	Pathogenic PS4 PM1 PM2 PM3 PM5 PP3	n/a	0.00004413	0.00002628	East Asian 0.0007523	25	10	15	Caucasian/Chinese	CCGKDD, Survey, S28,S30,S31,S33,S 40	published
20	missense	c.748G>T	p.Asp250Tyr	-	-	-	Likely Pathogenic PM1 PM2 PM5 PP3	n/a	-	-	-	1	0	1	Caucasian	S35	published
21	missense	c.759C>A	p.Asn253Lys	rs781023923	-	-	Likely Pathogenic PM1 PM2 PM3 PP3	n/a	0.00000401	-	East Asian 0.0000544	3	0	3	Korean	S32	published
22	truncating	c.893+2T>A	n/a	rs759259550	-	-	Pathogenic PVS1 PM2 PP3	n/a	0.0000119	-	East Asian 0.000163	2	0	2	Chinese	S40	published
23	missense	c.857A>G	p.Asp286Gly	rs398122979	91846	Pathogenic	Likely Pathogenic PM1 PM2 PM3 PP1 PP3 PP5	n/a	0.000012	0.00001972	European 0.000022	3	0	3		S29	published
24	missense	c.929C>T	p.Pro310Leu	-	-	-	Likely Pathogenic PM2 PM3 PP3	n/a	-	-	-	1	0	1	Caucasian	S28	published
25	in-frame deletion	c.936_938del	p.Val313del	-	-	-	Likely Pathogenic PM2 PM3 PM4 PP3	n/a	-	-	-	1	0	1	Chinese	S40	published
26	in-frame duplication	c.954_956dup	p.Thr319dup	rs1057519346	-	-	Likely Pathogenic PM2 PM3 PM4 PP3 PP5	n/a	-	-	-	1	0	1	European	S29	published
27	missense	c.958C>T	p.Arg320Trp	rs369573693	91848	Pathogenic	Likely Pathogenic PM2 PP1 PP3 PP5	n/a	0.00001993	0.00002627	African 0.00012	2	2	0	Tunisian	S29	published
28	missense	c.1027C>T	p.Arg343Trp	rs398122981	91849	Pathogenic	Likely Pathogenic PM2 PP1 PP3 PP5	n/a	0.000004001	-	Asian 0.00002	2	2	0	Maroccan	S29	published

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COQ8B	variant type	cDNA NM_024876.4	Protein NP_079152.3	rsID (dbSNPs)	ClinVar (UniProt*) Variation ID	ClinVar status	Significance (According to ACMG 2015)	AutoPVS1	Allele frequency GnomAD ver. 2.1.1 exomes	Allele frequency GnomAD ver. 3.1.1 genomes	Max. population	N° cases	N° homozygotes	N° heterozygotes	Ethnicity	References	Published /novel
29	<i>truncating</i>	c.1035+2T>C	n/a	-	974475	Pathogenic	Pathogenic PVS1 PM2 PP3 PP5	VeryStrong	-	-	-	1	0	1	Caucasian	Survey	novel
30	<i>truncating</i>	c.1035+3A>G	n/a	rs368182892	-	-	Uncertain Significance PM2 PM3 BP4	n/a	0.00002802	0.00007885	African 0.000371	2	0	2	Chinese	S40	published
31	<i>truncating</i>	c.1041C>A	p.Cys347Ter	-	-	-	Likely Pathogenic PVS1 PM2 PM3 PP3	VeryStrong	-	-	-	1	0	1	Chinese	S37	published
32	<i>missense</i>	c.1093C>G	p.Gln365Glu	-	-	-	Likely Pathogenic PM1 PM2 PM3 PP3	n/a	-	-	-	1	0	1	Chinese	S30	published
33	<i>truncating</i>	c.1199dup	p.His400fs	rs398122982	91850	Pathogenic	Pathogenic PVS1 PS4 PM2 PM3 PP1 PP3	VeryStrong	0.000003976	-	Other 0.0002	14	14	0	Turkey	Survey,S28,S29,S3 4	published
34	<i>truncating</i>	c.1339dup	p.Glu447GlyfsTer1 0	rs759968901	-	-	Pathogenic PVS1 PS4 PM2 PM3 PP1 PP3	Strong	0.00002427	0.00001320	Swedish 0.00007670	21	21	0	Turkey/Kurdish	PodoNet,S28,S34,S 38	published
35	<i>missense</i>	c.1345C>T	p.Arg449Cys	rs750037594	-	-	Uncertain Significance PM2 PM3 PP3	n/a	0.00005843	0.00003288	Ashkenazi Jewish 0.0002116	1	0	1	Chinese	Survey	novel
36	<i>truncating</i>	c.1356_1362del	p.Gln452fs	rs398122983	91851	Pathogenic	Pathogenic PVS1 PM2 PP1 PP3 PP5	VeryStrong	-	-	-	2	2	0	Indian	S29	published
37	<i>missense</i>	c.1430G>A	p.Arg477Gln	rs1057519347	375337	Pathogenic	Pathogenic PS4 PM2 PM3 PP1 PP3 PP5	n/a	0.000004133	-	European 0.000008	5	3	2	Turkey/Algerian	Survey,S29,S34,S3 8	published
38	<i>truncating</i>	c.1447G>T	p.Glu483Ter	rs398122980	91847	Pathogenic	Pathogenic PVS1 PM2 PM3 PP1 PP3 PP5	Strong	0.00005162	0.00001315	East Asian 0.0003763	5	2	3	Turkey	Survey,S29,S39	published
39	<i>missense</i>	c.1468C>T	p.Arg490Cys	rs750037594	-	-	Likely pathogenic PS4 PM2 PM3 PP3	n/a	0.00005843	0.00003288	Ashkenazi Jewish 0.0002116	7	0	7	Chinese/Korean	CCGKDD,S30,S31,S 32,S40	published
40	<i>missense</i>	c.1493_1494delins AA	p.Ala498Glu	-	-	-	Likely Pathogenic PM2 PM3 PP3	n/a	-	-	-	1	0	1	Caucasian	S28	published

Supplementary Figure S1. Intrafamilial and interfamilial phenotypic variability in homozygous individuals (variants carried by at least 2 members of two different families).



Legend:
Synopsis of clinical disease course. Families with the same variant are grouped with dotted outline, family members are grouped with brace. The black line denotes the time before first clinical disease manifestation, the yellow bars denote the period with proteinuria/chronic kidney disease (CKD), the red bars show dialysis periods, and the blue bars show transplantation periods. The symbols denote the time of sensorineural deafness diagnosis (*) and patients with neurological symptoms (☆).

A) Families with disease-causing variants in *COQ2* gene.

B) Families with disease-causing variants in *COQ6* gene.

C) Families with disease-causing variants in *COQ8B* gene.

Supplementary Table S3.A Genotype-phenotype correlations in subgroups of patients carrying common *COQ2* variants (homozygous state in at least 5 individuals or reported in at least 5 different families). Numbers represent % (number of affected patients/informative number of patients) and median (interquartile range) as appropriate. P values of Fisher's exact test are italicized

	<i>COQ2</i>	c.437G>A rs121918233	<i>P- Value</i>	c.683A>G rs121918232	<i>P- Value</i>
Total number of patients with homozygous variants (females)	63 (30)	6 (2)	-	5 (4)	-
First disease manifestation					
Age at first symptoms [years]	1 (0.3-2)	0 (0-0.2)	-	3 (2.7-5.6)	-
Onset < 6 months of age	21.8 (12/55)	100 (6/6)	<0.0001	0 (0/4)	0.5658
Onset >2 years of age	78.2 (43/55)	0 (0/6)	<0.0001	25 (1/4)	0.0292
Kidney involvement	93.6 (59/63)	100 (6/6)	>0.9999	100 (5/5)	>0.9999
Kidney disease presentation					
Age at first kidney disease manifestation [years]	1 (0.5-2)	Birth (0-0.2)	-	3 (2.7-5.6)	-
Nephrotic range proteinuria	85.7 (36/42)	60 (3/5)	0.1414	100 (3/3)	>0.9999
Non-nephrotic-range proteinuria	14.3 (6/42)	40 (2/5)	0.1414	0 (0/3)	>0.9999
Hypertension	28.6 (12/42)	33.3 (2/6)	>0.9999	100 (1/1)	0.2857
Oedema	86.6 (39/45)	33.3 (2/6)	0.0014	100 (3/3)	>0.999
Microhematuria	6.8 (4/59)	0 (0/6)	>0.9999	-	-
Chronic kidney disease (stage 2-4)	18.7 (6/32)	0 (0/6)	0.5645	0 (0/1)	>0.9999
End-stage kidney disease	9.4 (3/32)	50 (3/6)	0.0040	0 (0/1)	>0.9999
Renal histopathological findings					
Focal segmental glomerulosclerosis	69.4 (25/36)	25 (1/4)	0.0756	100 (4/4)	0.2904
FSGS, not otherwise specified	76 (19/25)	100 (1/1)	>0.9999	75 (3/4)	>0.9999
FSGS, collapsing subtype	24 (6/25)	0 (0/1)	>0.9999	25 (1/4)	>0.9999
FSGS, tip-lesion	0 (0/25)	0 (0/1)	>0.9999	0 (0/4)	>0.9999
Global glomerulosclerosis	11.1 (4/36)	0 (0/4)	>0.9999	0 (0/4)	>0.9999
Mesangioproliferative glomerulonephritis	11.1 (4/36)	0 (0/4)	>0.9999	0 (0/4)	>0.9999
Minimal change disease	5.6 (2/36)	0 (0/4)	>0.9999	0 (0/4)	>0.9999
Dysmorphic mitochondria	30.5 (11/36)	75 (3/4)	0.0756	0 (0/4)	0.2904
Extra-renal features					
Any extrarenal involvement	77.9 (46/59)	100 (6/6)	0.3220	75 (3/4)	>0.9999
Intrauterine abnormalities/preterm delivery	13.6 (8/59)	50 (3/6)	0.0279	0 (0/4)	>0.9999
Infantile multisystemic disease/multi organ failure	22 (13/59)	100 (6/6)	<0.0001	0 (0/4)	0.5664
Neurological findings	47 (28/59)	100 (6/6)	0.0084	0 (0/4)	0.1141
Encephalopathy/seizures	42 (25/59)	100 (6/6)	0.0039	-	-
Developmental delay/cognitive impairment	5 (3/59)	16.6 (1/6)	0.2794	-	-
Retinopathy/ocular abnormalities	20.3 (12/59)	0 (0/6)	0.3302	0 (0/4)	0.5725
Hearing abnormalities	1.7 (1/59)	0 (0/6)	>0.9999	0 (0/4)	>0.9999
Myopathy	20.3 (12/59)	33.3 (2/6)	0.5915	25 (1/4)	>0.9999
Cardiovascular abnormalities	15.2 (9/59)	16.6 (1/6)	>0.9999	0 (0/4)	>0.9999
Liver dysfunction	13.6 (8/59)	33.3 (2/6)	0.1832	0 (0/4)	>0.9999
Growth retardation	11.8 (7/59)	0 (0/6)	>0.9999	50 (2/4)	0.0653
Facial/body dysmorphisms	3.4 (2/59)	0 (0/6)	>0.9999	0 (0/4)	>0.9999
Clinical outcome (status at last follow-up)					
Median follow-up time [years]	1.5 (0.3-4.4)	0.4 (0.3-1)	-	1.8 (0.6-3.2)	-
Deceased	25.4 (16/63)	100 (6/6)	<0.0001	0 (0/5)	0.3172
Median age at death [years]	0.5 (0.3-0.9)	0.5 (0.5-1)	-	-	-
End-stage renal disease	50.8 (32/63)	66.6 (4/6)	0.6719	20 (1/5)	0.1962
Median age at ESKD [years]	2.4 (0.7-5.7)	0.3 (0.2-0.9)	-	3.5	-
Median time from 1 st manifestation to ESKD [years]	0.5 (0-1.65)	0 (0-0.6)	-	0.5	-
Kidney transplantation	26.9 (17/63)	-	-	-	-
Median age at kidney transplantation [years]	8.3 (5.2-17.2)	-	-	-	-
Probability of ESKD at age 5 yrs [%]	47.6	100	-	33.4	-
Probability of ESKD at age 18 yrs [%]	80.8	100	-	33.4	-

Supplementary Table S3.B Genotype-phenotype correlations in subgroups of patients carrying common *COQ6* variants (homozygous state in at least 5 individuals or reported in at least 5 different families). Numbers represent % (number of affected patients/informative number of patients) and median (interquartile range) as appropriate. P values of Fisher's exact test are italicized.

	<i>COQ6</i>	c.763G>A rs1057519350 <i>P- Value</i>	c.782C>T rs371260604 <i>P- Value</i>	c.1058C>A rs397514479 <i>P- Value</i>	c.1078C>T rs778856227 <i>P- Value</i>
Total number of patients with homozygous variants (females)	48 (16)	6 (NA) -	4 (1)* -	15 (4) -	4 (1) -
First disease manifestation					
Age at first symptoms [years]	1.2 (0.6-3.4)	0 (0.1-0.3) -	0.7 (0.5-0.9) -	4.5 (2.4-5.7) -	0.8 (0.6-1.1) -
Onset < 15 months of age	51.2 (21/41)	100 (6/6) <i>0.0207</i>	100 (4/4) <i>0.1069</i>	20 (3/15) <i>0.0036</i>	66.6 (3/4) <i>0.6060</i>
Kidney involvement	97.9 (47/48)	100 (6/6) <i>>0.9999</i>	100 (4/4) <i>>0.9999</i>	93 (14/15) <i>0.3125</i>	100 (4/4) <i>>0.9999</i>
Kidney disease presentation					
Age at first kidney disease manifestation [years]	2 (0.9-4.5)	0.3 (0.3-0.9) -	0.7 (0.5-0.9) -	4.5 (2.3-5.3) -	0.8 (0.6-1.1) -
Nephrotic range proteinuria	86.1 (31/36)	100 (6/6) <i>0.5638</i>	66.6 (2/3) <i>0.3704</i>	85 (6/7) <i>>0.9999</i>	75 (3/4) <i>0.4658</i>
Non-nephrotic-range proteinuria	13.9 (5/36)	0 (0/6) <i>0.5638</i>	33.3 (1/3) <i>0.3704</i>	14.3 (1/7) <i>>0.9999</i>	25 (1/4) <i>0.4658</i>
Asymptomatic proteinuria	18.7 (9/48)	0 (0/6) <i>0.5777</i>	0 (0/4) <i>>0.9999</i>	26.6 (4/15) <i>0.4321</i>	0 (0/4) <i>>0.9999</i>
Hypertension	21 (4/19)	- -	- -	33.3 (3/9) <i>0.3034</i>	0 (0/2) <i>>0.9999</i>
Oedema	47.8 (11/23)	- -	100 (1/1) <i>0.4783</i>	30 (3/10) <i>0.2138</i>	100 (3/3) <i>0.0932</i>
Microhematuria	8.5 (4/47)	- -	- -	- -	25 (1/4) <i>0.3081</i>
Chronic kidney disease (stage 2-4)	36.8 (7/19)	- -	33.3 (1/3) <i>>0.9999</i>	33.3 (1/3) <i>>0.9999</i>	0 (0/1) <i>>0.9999</i>
End-stage kidney disease	21 (4/19)	- -	0 (0/3) <i>>0.9999</i>	33.3 (1/3) <i>0.5304</i>	0 (0/1) <i>>0.9999</i>
Renal histopathological findings					
Focal segmental glomerulosclerosis	72.2 (26/36)	66.6 (2/3) <i>>0.9999</i>	75 (3/4) <i>>0.9999</i>	76.9 (10/13) <i>0.7160</i>	50 (1/2) <i>0.4841</i>
FSGS, not otherwise specified	88.4 (23/26)	100 (2/2) <i>>0.9999</i>	100 (3/3) <i>>0.9999</i>	100 (10/10) <i>0.2615</i>	100 (1/1) <i>>0.9999</i>
FSGS, collapsing subtype	11.5 (3/26)	0 (0/2) <i>>0.9999</i>	0 (0/3) <i>>0.9999</i>	0 (0/10) <i>0.2615</i>	0 (0/1) <i>>0.9999</i>
FSGS, tip-lesion	0 (0/26)	0 (0/2) <i>>0.9999</i>	0 (0/3) <i>>0.9999</i>	0 (0/10) <i>>0.9999</i>	0 (0/1) <i>>0.9999</i>
Global glomerulosclerosis	8.3 (3/36)	0 (0/3) <i>>0.9999</i>	0 (0/4) <i>>0.9999</i>	15.4 (2/13) <i>0.5394</i>	0 (0/2) <i>>0.9999</i>
Mesangioproliferative glomerulonephritis	5.6 (2/36)	0 (0/3) <i>>0.9999</i>	0 (0/4) <i>>0.9999</i>	0 (0/13) <i>0.5254</i>	0 (0/2) <i>>0.9999</i>
Minimal change disease	5.6 (2/36)	0 (0/3) <i>>0.9999</i>	25 (1/4) <i>0.2127</i>	7.7 (1/13) <i>>0.9999</i>	0 (0/2) <i>>0.9999</i>
Dysmorphic mitochondria	25 (9/36)	0 (0/3) <i>0.5576</i>	50 (2/4) <i>0.2552</i>	0 (0/13) <i>0.0136</i>	50 (1/2) <i>0.4429</i>
Extra-renal features					
Any extrarenal involvement	89.1 (41/46)	100 (6/6) <i>>0.9999</i>	75 (3/4) <i>0.3794</i>	85.7 (12/14) <i>0.6327</i>	100 (4/4) <i>>0.9999</i>
Intrauterine abnormalities/preterm delivery	2.2 (1/46)	0 (0/6) <i>>0.9999</i>	0 (0/4) <i>>0.9999</i>	0 (0/14) <i>>0.9999</i>	0 (0/4) <i>>0.9999</i>
Infantile multisystemic disease/multi organ failure	0 (0/46)	0 (0/6) <i>>0.9999</i>	0 (0/4) <i>>0.9999</i>	0 (0/14) <i>>0.9999</i>	0 (0/4) <i>>0.9999</i>
Neurological findings	21.7 (10/46)	33.3 (2/6) <i>0.5975</i>	0 (0/4) <i>0.5625</i>	14.3 (2/14) <i>0.6994</i>	75 (3/4) <i>0.0278</i>
Encephalopathy/seizures	8.7 (4/46)	33.3 (2/6) <i>0.0767</i>	-	7.1 (1/14) <i>>0.9999</i>	25 (1/4) <i>0.3141</i>
Developmental delay/cognitive impairment	13 (6/46)	0 (0/6) <i>0.5785</i>	-	7.1 (1/14) <i>0.6506</i>	75 (3/4) <i>0.3141</i>
Retinopathy/ocular abnormalities	17.4 (8/46)	0 (0/6) <i>0.5713</i>	0 (0/4) <i>>0.9999</i>	21.4 (3/14) <i>0.6848</i>	0 (0/4) <i>>0.9999</i>
Hearing abnormalities	73.9 (34/46)	83.3 (5/6) <i>>0.9999</i>	50 (2/4) <i>0.2758</i>	78.6 (11/14) <i>0.7294</i>	50 (2/4) <i>0.2758</i>
Myopathy	8.7 (4/46)	0 (0/6) <i>>0.9999</i>	25 (1/4) <i>0.3141</i>	0 (0/14) <i>0.2979</i>	50 (2/4) <i>0.03227</i>

Cardiovascular abnormalities	8.7 (4/46)	0 (0/6)	>0.9999	25 (1/4)	0.3141	0 (0/14)	0.2979	50 (2/4)	0.03227
Liver dysfunction	2.2 (1/46)	0 (0/6)	>0.9999	0 (0/4)	>0.9999	0 (0/14)	>0.9999	25 (1/4)	0.0870
Growth retardation	8.7 (4/46)	16.6 (1/6)	0.4400	0 (0/4)	>0.9999	0 (0/14)	0.2979	50 (2/4)	0.0327
Facial/body dysmorphisms	4.3 (2/46)	16.6 (1/6)	0.2464	0 (0/4)	>0.9999	0 (0/14)	>0.9999	25 (1/4)	0.1681
Clinical outcome(last follow-up)									
Median follow-up time [years]	1.7 (0-5.4)	0.5 (0-4.2)	-	0.25 (0-1.6)	-	3 (1.3-5.3)	-	1.1 (0.1-3.5)	-
Deceased	10.4 (5/48)	50 (3/6)	0.0104	0 (0/4)	>0.9999	6.6 (1/15)	>0.9999	0 (0/4)	>0.9999
Median age at death [years]	6.5 (5.75-12)	12 (9.2-14.7)	-	-	-	-	-	-	-
End-stage renal disease	56.2 (27/48)	83.3 (5/6)	0.2115	25 (1/4)	0.3055	53.3 (8/15)	>0.9999	0 (0/4)	0.0308
Median age at ESKD [years]	3.4 (1.6-6.2)	1.4 (0.4-1.7)	-	3.6	-	4.2 (2.4-5.7)	-	-	-
ESKD< 2years of age	33.3 (9/27)	80 (4/5)	0.0297	0 (0/1)	>0.9999	25 (2/8)	0.6758	-	-
Median time from 1 st manifestation to ESKD [years]	0.95 (0.3-2)	0.2 (0.1-1.4)	-	1.6	-	0.5 (0.4-0.9)	-	-	-
Kidney transplantation	29.2 (14/48)	0 (0/6)	0.1611	25 (1/4)	>0.9999	40 (6/15)	0.3153	0 (0/4)	0.3071
Median age at kidney transplantation [years]	6.35 (5.1-7.5)	-	-	5	-	5.2 (3.7-6.5)	-	-	-
Probability of ESKD at age 5 yrs [%]	47.8	77.8	-	50	-	36.6	-	0	-
Probability of ESKD at age 18 yrs [%]	72.3	100	-	50	-	63	-	0	-

* Included patient with c.782 variant+ deletion

Supplementary Table S3.C Genotype-phenotype correlations in subgroups of patients carrying common *COQ8B* variants (homozygous state in at least 5 individuals or reported in at least 5 different families). Numbers represent % (number of affected patients/informative number of patients) and median (interquartile range) as appropriate. P values of Fisher's exact test are italicized.

	COQ8B	c.293T>G n/a	P- Value	c.532C>T rs398122978	P- Value	c.645delT rs764587648	P- Value
Total number of patients with homozygous variants (females)	140 (65)	7 (3)	-	6 (2)	-	5 (1)	-
First disease manifestation							
Age at first symptoms [years]	9.1 (3.9-15)	NA	-	NA	-	9.2 (8.6-15.1)	-
Kidney involvement	100(140/140)	100 (7/7)	>0.9999	100 (6/6)	>0.9999	100 (5/5)	>0.9999
Kidney disease presentation							
Age at first kidney disease manifestation [years]	9.9(5.3-14.4)	13.3 (9.3-20.2)	-	11.4 (7.7-13.9)	-	14.2 (9.2-15.1)	-
Onset<5 years of age	23.5 (33/140)	0 (0/7)	<i>0.1986</i>	16.6 (1/6)	>0.9999	0 (0/5)	<i>0.5916</i>
Onset>10 years of age	47.1 (66/140)	57.1 (4/7)	<i>0.7068</i>	50 (3/6)	>0.9999	60 (3/5)	<i>0.6665</i>
Nephrotic range proteinuria	71.7 (86/120)	57.1 (4/7)	<i>0.4029</i>	50 (3/6)	0.3497	80 (4/5)	>0.9999
Non-nephrotic-rangeproteinuria	28.3 (34/120)	42.9 (3/7)	<i>0.4029</i>	50 (3/6)	0.3497	20 (1/5)	>0.9999
Asymptomatic proteinuria	23.6 (33/140)	28.6 (2/7)	<i>0.6679</i>	16.6 (1/6)	>0.9999	40 (2/5)	<i>0.3366</i>
Hypertension	39 (32/82)	0 (0/4)	<i>0.1522</i>	66.6 (2/3)	0.5574	80 (4/5)	<i>0.0733</i>
Oedema	40.2 (33/82)	50 (2/4)	>0.9999	0 (0/3)	0.2696	60 (3/5)	<i>0.3872</i>
Microhematuria	18 (13/72)	0 (0/4)	>0.9999	0 (0/3)	>0.9999	20 (1/5)	>0.9999
Chronic kidney disease (stage 2-4)	32.3 (33/102)	28.6 (2/7)	>0.9999	16.6 (1/6)	0.6610	60 (3/5)	<i>0.3254</i>
End-stage kidney disease	33.3 (34/102)	28.6 (2/7)	>0.9999	50 (3/6)	0.3975	20 (1/5)	<i>0.6625</i>
Renal histopathological findings							
Focal segmental glomerulosclerosis	77.1 (64/83)	66.6 (2/3)	<i>0.5465</i>	80 (4/5)	>0.9999	75 (3/4)	>0.9999
FSGS, not otherwise specified	89 (57/64)	100 (2/2)	>0.9999	100 (4/4)	>0.9999	100 (3/3)	>0.9999
FSGS, collapsing subtype	9.4 (6/64)	0 (0/2)	>0.9999	0 (0/4)	>0.9999	0 (0/3)	>0.9999
FSGS, tip-lesion	1.5 (1/64)	0 (0/2)	>0.9999	0 (0/4)	>0.9999	0 (0/3)	>0.9999
Global glomerulosclerosis	15.6 (13/83)	33.3 (1/3)	<i>0.4042</i>	20 (1/5)	0.5831	25 (1/4)	<i>0.5010</i>
Mesangioproliferative glomerulonephritis	7.2 (6/83)	0 (0/3)	>0.9999	0 (0/5)	>0.9999	0 (0/4)	>0.9999
Minimal change disease	0 (0/83)	0 (0/3)	>0.9999	0 (0/5)	>0.9999	0 (0/4)	>0.9999
Dysmorphic mitochondria	10.8 (9/83)	0 (0/3)	>0.9999	20 (1/5)	<i>0.4452</i>	0 (0/4)	>0.9999
Extra-renal features							
Any extrarenal involvement	29.3 (41/140)	71.4 (5/7)	<i>0.0228</i>	50 (3/6)	<i>0.3584</i>	20 (1/5)	>0.9999
Intrauterine abnormalities/preterm delivery	0.7 (1/140)	0 (0/7)	>0.9999	16.6 (1/6)	<i>0.0429</i>	0 (0/5)	>0.9999
Neurological findings	12.1 (17/140)	14.3 (1/7)	>0.9999	16.6 (1/6)	<i>0.5471</i>	0 (0/5)	>0.9999
Encephalopathy/seizures	7.1 (10/140)	0 (0/7)	>0.9999	0 (0/6)	>0.9999	-	-
Developmental delay/cognitive impairment	5 (7/140)	14.3 (1/7)	<i>0.3073</i>	16.6 (1/6)	<i>0.2692</i>	-	-
Retinopathy/ocular abnormalities	5 (7/140)	0 (0/7)	>0.9999	33.3 (2/6)	0.0293	20 (1/5)	<i>0.2292</i>
Cardiovascular abnormalities	7.1 (10/140)	14.3 (1/7)	>0.9999	0 (0/6)	>0.9999	0 (0/5)	>0.9999
Growth retardation	3.6 (5/140)	0 (0/7)	>0.9999	0 (0/6)	>0.9999	20 (1/5)	<i>0.1685</i>
Facial/body dysmorphisms	1.4 (2/140)	0 (0/7)	>0.9999	0 (0/6)	>0.9999	0 (0/5)	>0.9999
Clinical outcome (status at last follow-up)							
Median follow-up time [years]	3.9 (1.35-6.9)	6.8 (4.7-8.1)	-	2.5 (0.5-3.3)	-	0.8 (0.7-1)	-
Deceased	4.3 (6/140)	0 (0/7)	>0.9999	0 (0/6)	>0.9999	0 (0/5)	>0.9999
Median age at death [years]	13.9 (12.6-19.5)	-	-	-	-	-	-
End-stage renal disease	66.4 (93/140)	57.1 (4/7)	<i>0.6872</i>	66.6 (4/6)	>0.9999	80 (4/5)	<i>0.6636</i>
Median age at ESKD [years]	13 (10-16.7)	11.8 (9.4-14.5)	-	12 (9.1-14.4)	-	15.5 (13.5-16.3)	-
Median time from 1 st manifestation to ESKD [years]	1 (0-4.2)	0.35 (0-1.2)	-	0 (0-2.7)	-	0.8 (0.5-2.9)	-
Kidney transplantation	26.4 (37/140)	28.6 (2/7)	>0.9999	50 (3/6)	<i>0.1885</i>	0 (0/5)	<i>0.3252</i>
Median age at kidney transplantation [years]	15.1 (11-16)	16	-	15 (12.5-15.4)	-	-	-
Probability of ESKD at age 5 yrs [%]	3.1	0	-	0	-	0	-
Probability of ESKD at age 18 yrs [%]	74.2	62	-	66.7	-	80	-

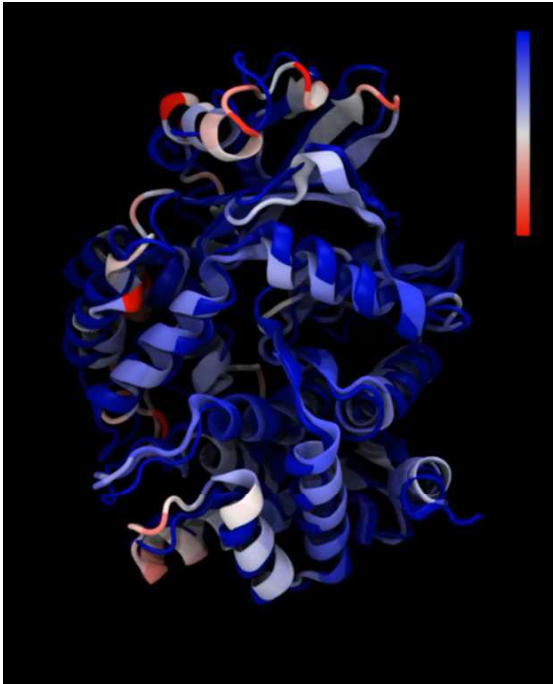
	COQ8B	c.737G>A rs200841458	P- Value	c.748G>C rs769834604	P- Value	c.1199dup rs398122982	P- Value	c.1339dupG rs759968901	P- Value
Total number of patients with homozygous variants (females)	140 (65)	8 (6)	-	10 (6)	-	14 (6)	-	21(11)	-
First disease manifestation									
Age at first symptoms [years]	9.1 (3.9-15)	7.5 (4.1-10.4)	-	1.7 (0-3.5)	-	10.8 (6-17.5)	-	14 (9.3-17.8)	-
Kidney involvement	100(140/140)	100 (8/8)	>0.9999	100 (10/10)	>0.9999	100 (14/14)	>0.9999	100 (21/21)	>0.9999
Kidney disease presentation									
Age at first kidney disease manifestation [years]	9.9 (5.3-14.4)	7.8 (4.6-10.6)	-	4.1 (1.9-9.6)	-	11.4 (5.5-17.5)	-	14 (11.8-17.6)	-
Onset<5 years of age	23.5 (33/140)	25 (2/8)	>0.9999	60 (6/10)	0.0116	21.4 (3/14)	>0.9999	0 (0/21)	0.0038
Onset>10 years of age	47.1 (66/140)	37.5 (3/8)	0.7223	10 (1/10)	0.0191	57.1 (8/14)	0.5743	76.2 (16/21)	0.0044
Nephrotic range proteinuria	71.7 (86/120)	87.5 (7/8)	0.4381	100 (8/8)	0.1035	61.5 (8/13)	0.5146	55.6 (10/18)	0.1532
Non-nephrotic-range proteinuria	28.3 (34/120)	12.5 (1/8)	0.4381	0 (0/8)	0.1035	38.4 (5/13)	0.5146	44.4 (8/18)	0.1532
Asymptomatic proteinuria	23.6 (33/140)	12.5 (1/8)	0.6804	30 (3/10)	0.7000	0 (0/14)	0.0404	19 (4/21)	0.7823
Hypertension	39 (32/82)	0 (0/4)	0.1522	33.3 (2/6)	>0.9999	50 (1/2)	>0.9999	28.6 (4/14)	0.5493
Oedema	40.2 (33/82)	75 (3/4)	0.2979	66.6 (4/6)	0.2137	50 (1/2)	>0.9999	42.8 (6/14)	>0.9999
Microhematuria	18 (13/72)	0 (0/4)	>0.9999	40 (2/5)	0.2193	0 (0/2)	>0.9999	38.4 (5/13)	0.0497
Chronic kidney disease (stage 2-4)	32.3 (33/102)	50 (3/6)	0.3856	50 (2/4)	0.5931	28.5 (4/14)	>0.9999	29.4 (5/17)	>0.9999
End-stage kidney disease	33.3 (34/102)	0 (0/6)	0.1748	25 (1/4)	>0.9999	21.4 (3/14)	0.3754	35.3 (6/17)	>0.9999
Renal histopathological findings									
Focal segmental glomerulosclerosis	77.1 (64/83)	85.7 (6/7)	>0.9999	71.4 (5/7)	0.6569	50 (1/2)	0.4076	80 (4/5)	>0.9999
FSGS, not otherwise specified	89 (57/64)	100 (6/6)	>0.9999	100 (5/5)	>0.9999	100 (1/1)	>0.9999	75 (3/4)	0.3783
FSGS, collapsing subtype	9.4 (6/64)	0 (0/6)	>0.9999	0 (0/5)	>0.9999	0 (0/1)	>0.9999	25 (1/4)	0.3323
FSGS, tip-lesion	1.5 (1/64)	0 (0/6)	>0.9999	0 (0/5)	>0.9999	0 (0/1)	>0.9999	0 (0/4)	>0.9999
Global glomerulosclerosis	15.6 (13/83)	0 (0/7)	0.5895	0 (0/7)	0.5895	0 (0/2)	>0.9999	20 (1/5)	0.5831
Mesangioproliferative glomerulonephritis	7.2 (6/83)	14.3 (1/7)	0.4208	28.6 (2/7)	0.0782	0 (0/2)	>0.9999	0 (0/5)	>0.9999
Dysmorphic mitochondria	10.8 (9/83)	28.6 (2/7)	0.1650	0 (0/7)	>0.9999	0 (0/2)	>0.9999	0 (0/5)	>0.9999
Extra-renal features									
Any extrarenal involvement	29.3 (41/140)	0 (0/8)	0.1048	50 (5/10)	0.1571	21.4 (3/14)	0.7576	28.6 (6/21)	>0.9999
Intrauterine abnormalities/preterm delivery	0.7 (1/140)	0 (0/8)	>0.999	0 (0/10)	>0.9999	0 (0/14)	>0.9999	0 (0/21)	>0.9999
Neurological findings	12.1 (17/140)	0 (0/8)	0.5956	10 (1/10)	>0.9999	14.3 (2/14)	0.6793	19 (4/21)	0.2873
Encephalopathy/seizures	7.1 (10/140)	-	-	10 (1/10)	0.5356	7.1 (1/14)	>0.9999	14.3 (3/21)	0.1734
Developmental delay/cognitive impairment	5 (7/140)	-	-	0 (0/10)	>0.9999	7.1 (1/14)	0.5299	4.8 (1/21)	>0.9999
Retinopathy/ocular abnormalities	5 (7/140)	0 (0/8)	>0.9999	10 (1/10)	0.4118	0 (0/14)	>0.9999	0 (0/21)	0.5942
Cardiovascular abnormalities	7.1 (10/140)	0 (0/8)	>0.9999	20 (2/10)	0.1518	7.1 (1/14)	>0.9999	14.3 (3/21)	0.1734
Growth retardation	3.6 (5/140)	0 (0/8)	>0.9999	0 (0/10)	>0.9999	0 (0/14)	>0.9999	4.8 (1/21)	0.5620
acial/body dysmorphisms	1.4 (2/140)	0 (0/8)	>0.9999	0 (0/10)	>0.9999	0 (0/14)	>0.9999	0 (0/21)	>0.9999
Clinical outcome (status at last follow-up)									
Median follow-up time [years]	3.9 (1.35-6.9)	3.2 (1.3-4.5)	-	2.4 (0.1-4.2)	-	4.8 (3.2-8.5)	-	4 (1-6.6)	-
Deceased	4.3 (6/140)	0 (0/8)	>0.9999	0 (0/10)	>0.9999	14.3 (2/14)	0.1106	4.8 (1/21)	>0.9999
Median age at death [years]	13.9 (12.6-19.5)	-	-	-	-	25 (23-27)	-	14.8	-
End-stage renal disease	66.4 (93/140)	37.5 (3/8)	0.1182	50 (5/10)	0.3032	50 (7/14)	0.2321	76.2 (16/21)	0.4525
Median age at ESKD [years]	13 (10-16.7)	10 (8.9-11.2)	-	9.9 (6-11)	-	16 (14.4-17.6)	-	16.8 (13-18)	-
ESKD<12 years of age	44 (41/93)	66.6 (2/3)	0.5810	80 (4/5)	0.1658	0 (0/7)	0.0165	12.5 (2/16)	0.0055
Median time from 1 st manifestation to ESKD [years]	1 (0-4.2)	2.5 (1.4-3.6)	-	2 (0.6-2.2)	-	3 (0.7-6.5)	-	0.75 (0-3.7)	-
Kidney transplantation	26.4 (37/140)	25 (2/8)	>0.9999	20 (2/10)	>0.9999	21.4 (3/14)	0.7606	14.2 (3/21)	0.2816
Median age at kidney transplantation [years]	15.1 (11-16)	8.7	-	16	-	13.5 (13.2-14.7)	-	16.7 (13.8-16.8)	-
Probability of ESKD at age 5 yrs [%]	3.1	0	-	0	-	0	-	0	-
Probability of ESKD at age 18 yrs [%]	74.2	58.4	-	100	-	59.1	-	75.6	-

Supplementary Table S4. Comparison of the subjects with *COQ8B* disease due to biallelic truncating variants (biallelic null alleles) to the rest of the *COQ8B* cohort. P values of Fisher's exact test are italicized.

	Non-Biallelic Truncating	Biallelic Truncating	<i>P- Value</i>
Total number of patients with homozygous variants (females)	90 (44)*	47 (20)	-
First disease manifestation			
Age at first symptoms [years]	7 (3-11)	14 (7.9-18)	-
Kidney involvement	100 (90/90)	100 (47/47)	>0.9999
Kidney disease presentation			
Age at first kidney disease manifestation [years]	8.6 (4.5-11.7)	14.2 (9.1-17.8)	-
Onset >10 years of age	30.7 (20/65)	50 (26/52)	0.0384
Nephrotic range proteinuria	73.7 (56/76)	65 (26/40)	0.3922
Non-nephrotic-range proteinuria	26.3 (20/76)	35 (14/40)	0.3922
Asymptomatic proteinuria	27.7 (25/90)	17 (8/47)	0.2080
Hypertension	39.3 (22/56)	39.1 (9/23)	>0.9999
Oedema	37.5 (21/56)	43.5 (10/23)	0.6230
Microhematuria	14 (7/50)	0 (0/6)	>0.9999
Chronic kidney disease (stage 2-4)	31.7 (20/63)	32.3 (11/34)	>0.9999
End-stage kidney disease	33.3 (21/63)	32.3 (11/34)	>0.9999
Renal histopathological findings			
Focal segmental glomerulosclerosis	76.2 (48/63)	88.2 (15/17)	0.5040
FSGS, not otherwise specified	93.7 (45/48)	73.3 (11/15)	0.0492
FSGS, collapsing subtype	6.3 (3/48)	17.6 (3/15)	0.1407
FSGS, tip-lesion	0 (0/48)	6.6 (1/15)	0.2381
Global glomerulosclerosis	15.8 (10/63)	11.7 (2/17)	>0.9999
Mesangioproliferative glomerulonephritis	6.3 (4/63)	5.8 (1/17)	>0.9999
Dysmorphic mitochondria	12.7 (8/63)	0 (0/17)	0.1919
Extra-renal features			
Any extrarenal involvement	33.3 (30/90)	21.3 (10/47)	0.1683
Intrauterine abnormalities/preterm delivery	1.1 (1/90)	0 (0/47)	>0.9999
Neurological findings	11.1 (10/90)	12.8 (6/47)	0.7844
Encephalopathy/seizures	6.6 (6/90)	8.5 (4/47)	0.7358
Developmental delay/cognitive impairment	6.6 (6/90)	4.2 (2/47)	0.7149
Retinopathy/ocular abnormalities	6.6 (6/90)	2.1 (1/47)	0.4217
Cardiovascular abnormalities	6.6 (6/90)	8.5 (4/47)	0.7358
Growth retardation	2.2 (2/90)	4.2 (2/47)	0.6068
Facial/body dysmorphisms	2.2 (2/90)	0 (0/47)	0.5459
Clinical outcome (status at last follow-up)			
Median follow-up time [years]	4.1 (2-7)	3.4 (1-6.3)	-
Deceased	2.2 (2/90)	6.4 (3/47)	0.3386
Median age at death [years]	8.5 (6.3-10.7)	21.1 (17.9-25)	-
End-stage renal disease	66.6 (60/90)	63.8 (30/47)	0.8499
Median age at ESKD [years]	11 (8.8-13.9)	16.8 (13.6-17.9)	-
ESKD> 14 years of age	25 (15/60)	73.3 (22/30)	<0.0001
Median time from 1 st manifestation to ESKD [years]	1.6 (0-4.4)	1 (0.1-3.9)	-
Kidney transplantation	33.3 (30/90)	14.9 (7/47)	-
Median age at kidney transplantation [years]	12.7 (10.2-15.9)	16 (13.2-16.8)	-
Probability of ESKD at age 5 yrs [%]	3.7	0	-
Probability of ESKD at age 18 yrs [%]	78.9	64.8	-

* Excluded 3 patients with unknown genotype

Supplementary Video S1. Comparison of the COQ8B homology model and COQ8A fragment crystal structure.

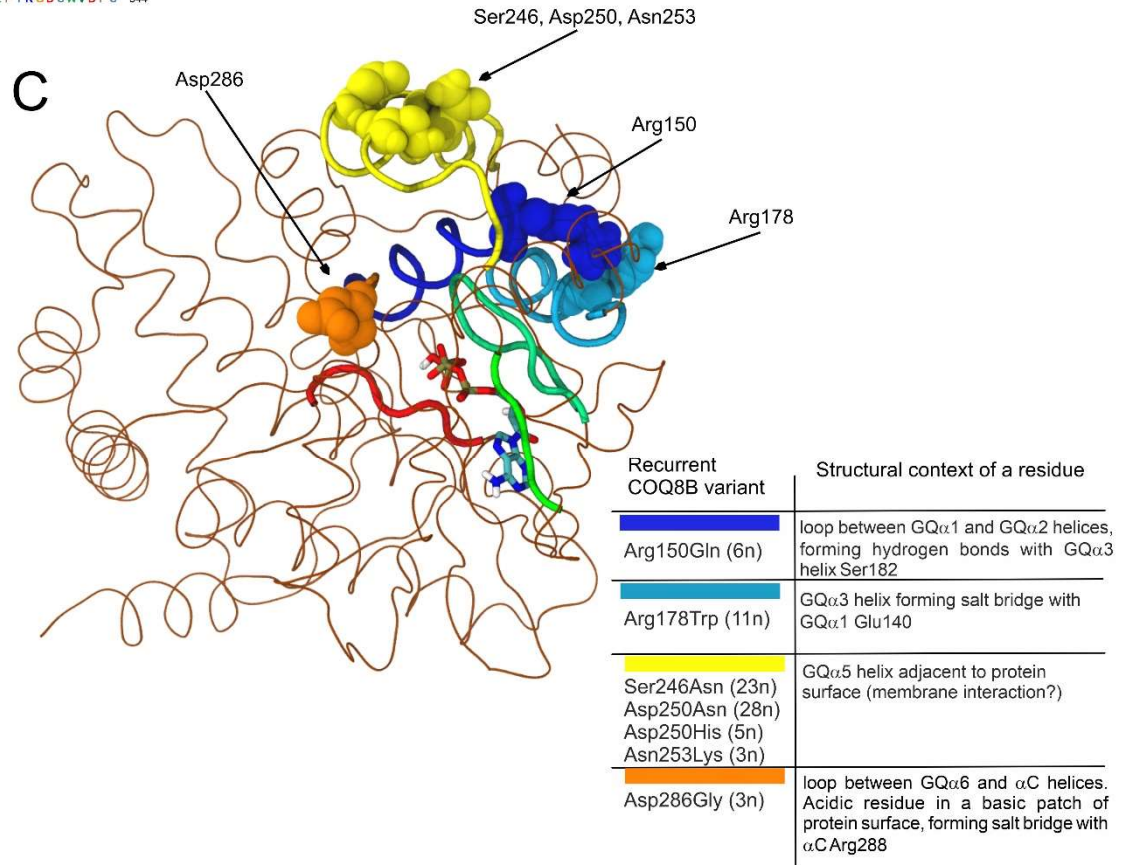
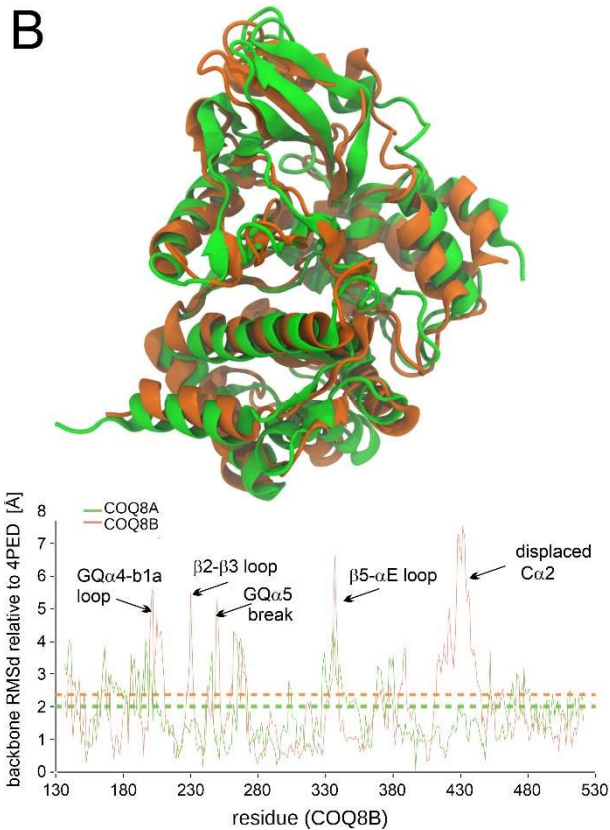
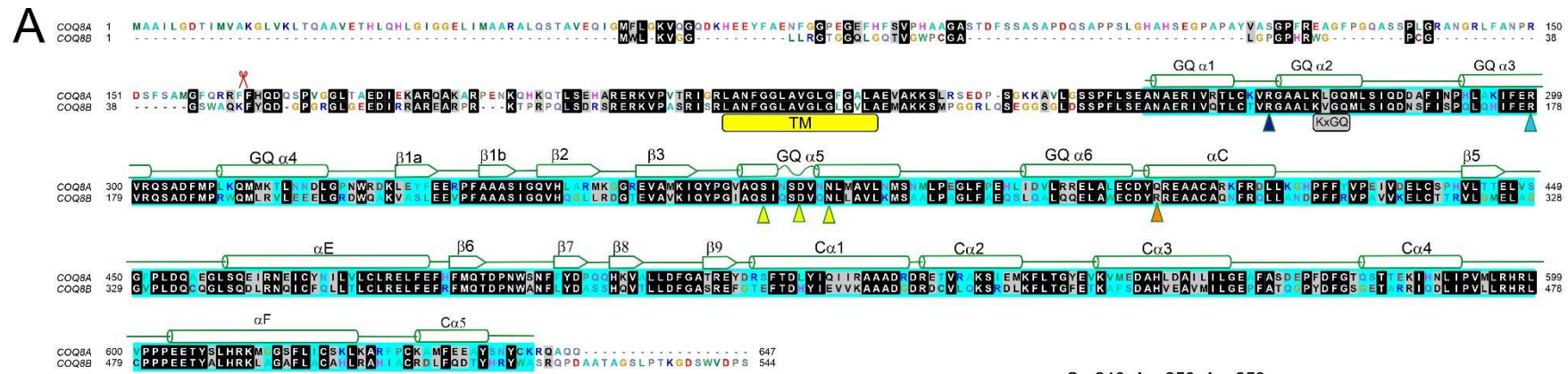


Supplementary Material S1. Structural aspects of the COQ8B protein.

No empirical data regarding COQ8B protein exist, however the catalytic domain of closely related COQ8A protein was successfully crystallized (S42,S43). The high sequence identity (61%, 235/385) and 76% similarity (195/385) between solved fragment of COQ8A and COQ8B, together with parallel enzymatic function and no gaps in the sequence alignment, allow for construction of COQ8B homology model with high probability of correct fold and spatial deviation of Ca coordinates better than 2.5 Å (S44). To analyze structural differences and similarities between COQ8A and COQ8B proteins, a homology model based on 4PED (1.6Å x-ray structure of human COQ8A without ligands) (S42) was obtained from SwissModel (S45) (created 13.11.2021) spanning residues 137 to 521. Both COQ8B model and COQ8A fragment crystal structure (after reverting selenomethionines to Met) were energy-minimized in GROMACS 2021.4 (S46) in OPLS/AA force field and subsequently subjected to 200 ns of molecular dynamics simulation in explicit solvent during which RMSD of Ca atoms converged (not shown). Final trajectory frames were energy-minimized and analyzed/visualized by VMD program (S47) (for comparison of those structures see Supplementary Video S1). The RMS deviation of backbone coordinates of final modelled structures relative to 4ped crystal structure were 2.008 Å for COQ8A and 2.368 Å for COQ8B as measured by ProFit (S48,S49). To visualize an active site, the ATP coordinates based on 5i35 (S43) COQ8A/ANP crystal structure were fitted into obtained models using DeepView 4.1 (S50) and energy-minimized.

The KxGQ functional motif, located in GQa2 helix protrudes into an active site, towards nucleotide γ -phosphate in 5i35.pdb structure. The variants that possibly influence the stability or orientation of GQa2 helix, e.g. by disturbing interactions with nearby elements, may therefore unfavorably alter the active site conformation, hampering enzymatic activity. This may probably be the case of variants in positions 150 and 178 located in the vicinity of this region. The variants located within GQa5 (positions 246,250,254) are not directly involved with active site interactions, being placed close to the protein surface. This may suggest their involvement in a not yet characterized protein-protein interaction within CoQ10 biosynthesis complex. It was however currently pointed out (S50) that COQ8A ATPase activity is released by membrane association via GQa1 and GQa4. Both these helices are located in direct proximity to GQa5 identified here as a hot spot for pathogenic variants of COQ8B. It may be further noted that the GQa5 helix with adjacent loops are relatively displaced between 4PED (ligand-free) and 5i35 (bound to non-hydrolysable ATP analog, ANP), which may indicate nucleotide-related conformational change and hence the role of this region in allosteric signaling.

In our modelling procedure, one of a few significant differences between COQ8B homology model and COQ8A structure after MD simulations, was an alternation within GQa5 helix. Whereas during simulation of COQ8A the whole helix, although curved within first turns of a helix, remained stable and highly similar to the 4ped crystal structure, COQ8B model developed a loss of one helix turn, effectively dividing the helix into a short N-terminal one, a turn and a remain of GQa5. This allows the speculation that the variants in GQa5 might be specific to COQ8B because of that structural difference. This hypothesis, however, needs further studies and both structural and biochemical evaluation.



Legend:**A). Sequence alignment between COQ8A and COQ8B proteins.**

Identical residues marked by black background, similar residues marked by grey background. Homology modeled region marked cyan. Above sequences, secondary structure assignment of homology model is depicted (naming of helices and strands follow the convention established in (S42), where helices belonging to the KxGQ motif-containing subdomain are prefixed with „GQ” and helices in C-terminal lobe insert are prefixed with „C”.

Marked is transmembrane helix (TM, yellow mark) and KxGQ motif (gray mark). The COQ8A N-terminal fragment cleavage site is marked by red scissors. The most frequently found pathogenic variants are marked with arrowheads below sequences (colors follow C panel conventions).

B) Comparison of COQ8A and COA8B structure models

Up, models of catalytic domain of COQ8A (green) and COQ8B (orange) superimposed.

This visualization is also available as an animation of 360 deg. rotation (Suppl. Video 1 (an mp4 file), colored by RMS deviation.

The high deviation regions specific for COQ8B are mostly labile external loops and the Ca2 helix which location was slightly skewed in COQ8B. The notable exception is the break within COQa5 helix.

Below, plot of residue-wise RMSD deviation from 4ped.pdb structure (residue numeration according to COQ8B protein). Dotted lines denote whole backbone RMSD values.

As expected, the structures of modelled fragments remain highly similar to the crystal structure and to each other (with RMSD of 2.8 Å between COQ8A and COQ8B). While molecular dynamics simulation introduced more uniform deviation from 4ped.pdb crystal structure for COQ8A, the homology model of COQ8B differ mostly locally in the 427-431 loop conformation resulting from skewing of Ca3 helix. Among COQ8B-related deviation peaks the solvent-exposed labile loops are indicated. The non-trivial structural difference seem to be the disruption of GQaC of COQ8B, helix, not present in COQ8A (neither in 4PED original crystal structure, nor after MD simulation).

C) Structural aspects of the selected COQ8B recurrent pathogenic missense variants.

Model of COQ8B with ATP modelled in active site (stick representation), with the functional motifs (as defined in S42) colored as follows: GQa1, (dark blue) GQa2 (light blue), A-rich loop (light green), VxxK motif, (green), ExD motif (orange), catalytic loop (red). The recurrent pathogenic variants (listed in table) are marked by spacefill representation in the color of appropriate region. Table lists COQ8B recurrent (reported in ≥ 3 non-related individuals) variants and their presumed structural roles.

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