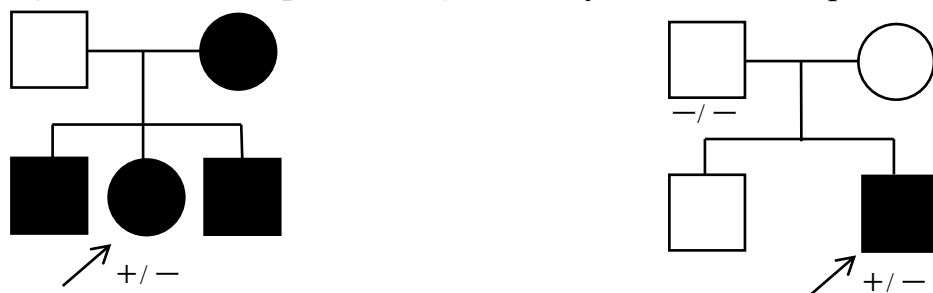


(A) Family 8 c.1739C>A, p.Thr580Lys Family 9 c.1939T>C, p.Ser647Pro (C)



(B)

	580				
KCC3-SLC12A6	S	F	F	S	T
KCC1-SLC12A4	S	F	F	S	T
KCC2-SLC12A5	S	F	F	S	T
KCC4-SLC12A7	S	F	F	S	T

	647				
L	S	M	F	F	
L	S	M	F	F	
L	S	M	F	F	
L	S	M	F	F	

	580				
SLC12A6_Human	S	F	F	S	T
SLC12A6_Mouse	S	F	F	S	T
SLC12A6_Cat	S	F	F	S	T
SLC12A6_Dog	S	F	F	S	T
SLC12A6_Cow	S	F	F	S	T
SLC12A6_Frog	S	F	F	S	T

	647				
L	S	M	F	F	
L	S	M	F	F	
L	S	M	F	F	
L	S	M	F	F	
L	S	M	F	F	
L	S	M	F	F	

(D)

Nucleotide change	c.1739C>A		c.1939T>C		
Amino Acid change	p.Thr580Lys		p.Ser647Pro		
Zygoty	Heterozygous		Heterozygous		
Allele frequency-gnomAD	0		0		
Allele frequency-jMorp	0		0		
Our control	-		-		
SIFT/Prediction	0	Damaging	0	Damaging	
PROVEAN/Prediction	-4.57	Deleterious	-3.9	Deleterious	
Polyphen2/Prediction	0.998	Damaging	1	Damaging	
MutationAssesor/Prediction	4.025	Damaging	4.27	Damaging	
FATHMM/Prediction	-5.25	Damaging	-5.12	Damaging	
Condel/prediction	0.73	Damaging	0.746	Damaging	
Dynamut	$\Delta\Delta G$ /Prediction	-0.269kcal/mol	Destabilizing	-0.403kcal/mol	Destabilizing
	$\Delta\Delta G$ (ENCOM)/Prediction	-0.02kcal/mol	Destabilizing	-0.134kcal/mol	Destabilizing
iMutant	RI/Stability	5	Decrease	5	Decrease
ACMG	Population Data	PS4_Supporting PM2		PS4_Supporting PM2	
	In silico Data	PP3		PP3	
	De novo Data				
	Other Data				
	Criteria	Uncertain Significance		Uncertain Significance	

	This report	
	Family 7	Family 8
Mutation	c.1739C>A	c.1939T>C
	p.Thr580Lys	p.Ser647Pro
Ethnicity	Japanese	Japanese
Onset age	38	3
Exam age	63	37
Genotype	AD	Sporadic
Distal weakness	+	+
Distal atrophy	+	+
distal leg MMT	3	0-1
Sensory disturbance	+	+
DTR	Absent	Absent
Cognitive impairment	—	—
Other symptom	CK335	—
Median CMAP (mV)	7.94	NE
Median MNCV (m/s)	50.6	NE
Median SNAP (μ V)	3.4	NE
Median SCV (m/s)	18.5	NE
Tibial CMAP (mV)	5.8	NE
Tibial MNCV (m/s)	34.4	NE
Sural SNAP (μ V)	NE	NE
Sural SCV (m/s)	NE	NE
Brain MRI	leukoaraiosis	NA

(E)

CMTNS parameter/Pt	Family 7	Family 8
Sensory symptoms	NA	3
Motor symptoms legs	NA	4
Motor symptoms arms	NA	NA
Pinprick sensibility	NA	3
Vibration	NA	NA
Strength legs	4	4
Strength arms	4	4
Ulnar CMAP	0	3
Ulnar SNAP	3	4