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Supplemental Data

Molecular Basis of DFNB73: Mutations of *BSND*

Can Cause Nonsyndromic Deafness or Bartter Syndrome

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Table S1. Clinical and biochemical features of carriers and p.I12T homozygotes

Feature	Reference ranges	Family (individual)								
		DF067 (IV:1)	DF067 (V:2)	DF067 (V:5)	DF393 (V:2)	DF393 (V:8)	DF393 (V:3)	DF815 (V:12)	DF815 (VI:10)	DF815 (VI:8)
genotypes		T[a]/T	T/T	T/+	T/T	T/T	T/+	T/T	T/T	T/+
present age (y)		45	16	21	20	14	12	42	16	8
hearing loss		deaf	deaf	normal	deaf	deaf	normal	deaf	deaf	normal
Other Symptoms of BSIV[b]		no	no	no	no	no	no	no	no	no
S[c] Na (mmol/L)	136-148	143	142	140	139	143	141	141	141	140
S K (mmol/L)	3.6-5.0	3.49	3.83	3.98	4.12	3.69	4.36	4.02	4.14	4.7
S Cl (mmol/L)	95-108	104	103	101	101	104	102	102	103	104
S HCO_3 (mmol/ L)	22-29	25	24.3	27.2	NA	NA	27.2	28.1	25.6	22.5
S Mg (mg/dl)	1.9-2.5	NA[f]	NA	NA	2.35	2.22	2.4	NA	NA	NA
S Ca (mg/dl)	8.6-10.5	9.29	9.09	9.41	9.85	9.37	9.69	NA	NA	NA
S Creatinine (mg/dl)	0.7-1.2	0.6	0.67	0.77	0.82	0.75	1.28	1.06	0.93	0.54
P[d] Renin (ng/ml/hr)	0.15-2.33	4.5	11.05	8.7	20.3	7.0	3.75	NA	NA	NA
S Aldosterone (ng/dl)	4-31	9.3	12.8	41.5	13.4	14.0	22.6	NA	NA	NA
S Osmolality (mosm/Kg)	273-304	NA	NA	NA	304	324	332	NA	NA	NA
U[e] Na (mmol/ L)	30-150	9.0	58	NA	63	95	83	115.5	68	103
U K (mmol/ L)	20-67	NA	NA	NA	NA	NA	NA	NA	NA	NA
U Cl (mmol/ L)	46-168	NA	NA	NA	57	102	137	NA	NA	NA
U Mg (mg/dl)		NA	NA	NA	6.64	11.14		NA	NA	NA
U Ca (mg/dl)					13.9	2.96	5.49		50.32	55.42
(mg/24hrs)	100-320	32.0	29.20	NA				56.35		
U osmolality (mosm/Kg)	50-1400	NA	NA	NA	290	314	657	NA	NA	NA
nephrocalcinosis		NA	NA	NA	absent	absent	[g]	NA	NA	NA

[a] p.I12T, [b]Other Symptoms of BSIV (polyhydramnion, premature birth, low birth weight, failure to thrive, polyuria, polydypsia, nocturnal enuresis), [c]Serum (S), [d]Plasma (P), [e] Urinary (U) values were determined from spot samples, [f]Not available (NA). [g]Left renal stone with hydronephrosis

Figure S1. Representative pure-tone audiograms of affected members of family PKDF815 Pure-tone response thresholds are shown for p.I12T homozygotes (A) or for a p.I12T/E4X compound heterozygote (B). Filled and open circles represent the right and left ears, respectively. The carriers of mutant alleles have normal hearing.

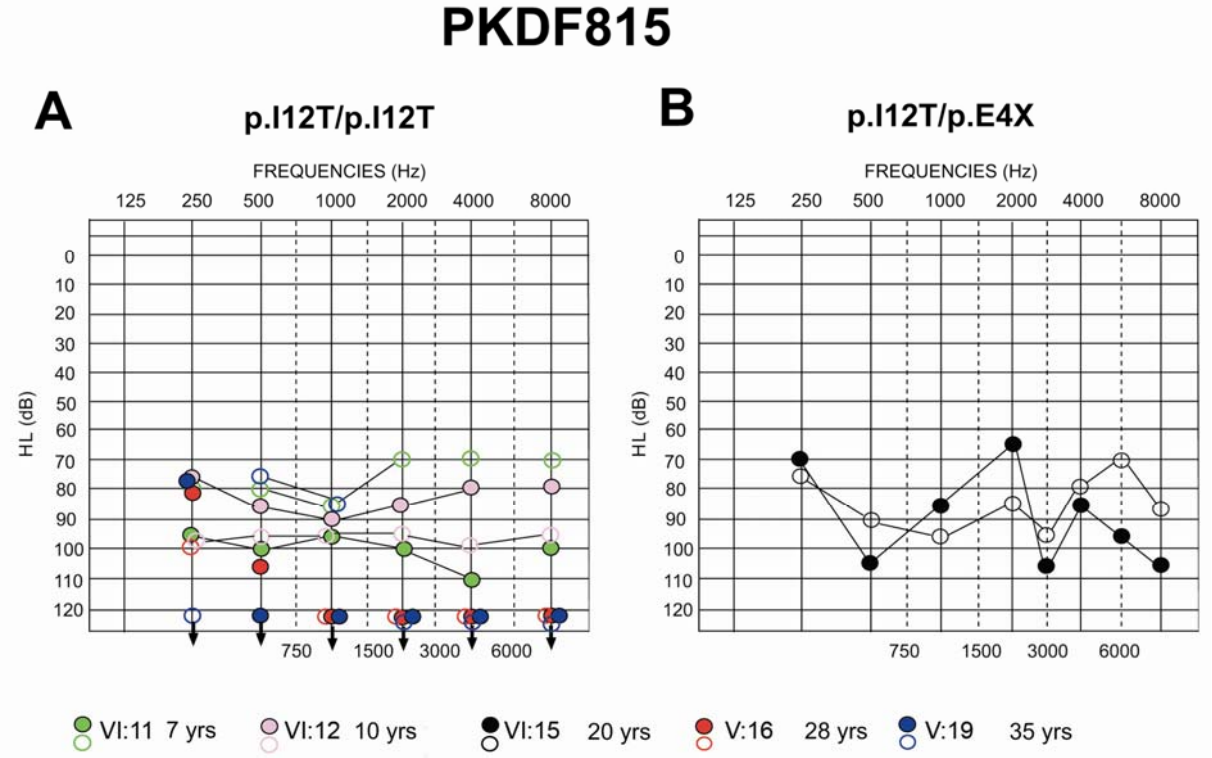

Figure S2. p.I12T reduces ClC-K/barttin current amplitudes also at low [Cl⁻] Mean current amplitudes ± SEM, n = 8–10, of ClC-Ka/barttin channels for wild-type and p.I12T barttin at low chloride concentrations (30/30 mM Cl_{ext}/Cl_{int}).

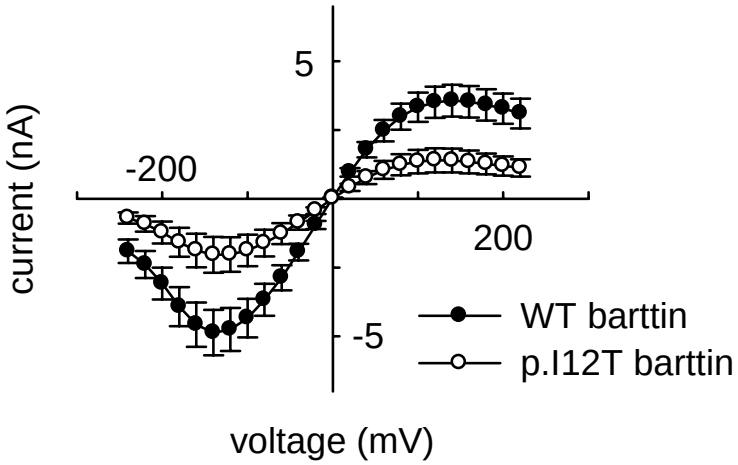

Figure S3. Noise analysis of ClC-Ka/barttin for WT and p.I12T barttin

(A) Representative whole-cell recording from ClC-Ka/WT barttin channels used for stationary noise analysis. (B) Plot of the variance, normalized by the product of the mean current (I) and the electrical driving force ($V-V_r$), versus the macroscopic conductance $I/(V-V_r)$ from the cell shown in (A) after filtering with 2 or 10 kHz. Solid lines give linear fits to the data. (C,D) Representative stationary noise analyses for WT or p.I12T barttin at 150/124mM Cl_{ext}/Cl_{int} (C) or at 30/30mM Cl_{ext}/Cl_{int} (D). (E,F) Mean unitary current conductances (E) and voltage dependences of the absolute open probability (F) of ClC-Ka/barttin channels for WT and p.I12T barttin obtained for high and low chloride concentrations. Data points represent mean values ± SEM, n = 7-12.