Supplementary data

Supplementary Table 1. European recommendations for blood pressure classification stages adapted to age

Children			Adults				
Category*	0–15 years SBP and/or DBP percentile	16 years and older SBP and/or DBP values (mmHg)	Category*	Systolic (mmHg)		Diastolic (mmHg)	Categories used in this study
Normal	<90th	<130/85	Normal	120-129	and/or	80-84	1
High-normal	≥90th to <95th percentile	130–139/85–89	High Normal	130-139	and/or	85-89	2
Hypertension	≥95th percentile	≥ 140/90	Grade 1 Hypertension	140-159	and/or	90-99	3
Stage 1 hypertension	95th percentile to the 99th percentile and 5mmHg	140–159/90–99	Grade 2 Hypertension	160-179	and/or	100-109	4
Stage 2 hypertension	>99th percentile plus 5mmHg	160–179/100–109	Grade 3 hypertension	≥180	and/or	≥110	5

Systolic Blood Pressure (SBP); Diastolic Blood Pressure (DBP). *Lurbe E 2016; Williams B 2018

Supplementary Table 2.

List of the 64 pathogenic variants detected in the 4 genes of patients with familial hyperkalemic hypertension

Gene	Mutation		ACMG criteria	ACMG class	Literature
	cDNA level	Protein level			
CUL3	c.1207-26A>G	p.?	PS3 PM1 PM2 PP3 PP5	5	Boyden et al, 2012; Ostrosky-Frid et al, 2
	c.1207-17_1207 10delinsAAGAT	p.?	PM1 PM2 PP1 PP3	4	This publication
	c.1207-3C>A,	p.?	PS2 PS4 PM1 PM2 PM6 PP3 PP5	5	Boyden et al, 2012
	c.1207-2A>G;	p.?	PVS1 PS2 PM1 PM2 PM6 PP3 PP4	5	This publication
	c.1207-1G>A		PVS1 PS2 PS3 PM1 PM2 PM6 PP3 PP5	5	Boyden et al, 2012; Araki Y et al, 2015
	c. 1207-1_1207delinsAG	p.?	PM1 PM2 PM6 PP5	4	This publication
	c.1236G>A	p.(Leu412=)	PS2 PS3 PM1 PM2 PM6 PP5	5	Boyden et al, 2012
	c.1377+1G>A	p.?	PVS1 PM1 PM2 PP3 PP5	5	Glover et al, 2014
	c.1377+2T>C	p.?	PVS1 PS2 PM1 PM2 PM6 PP3	5	This publication
	c.1377+3A>T	p.?	PS2 PM1 PM2 PM6	4	This publication
	c.1377+4A>G	p.?	PS2 PM1 PM2 PM6	4	This publication
KLHL3 Dominant	c.233C>T	p.(Met78Thr)	PM2 PM5 PP2 PP3 PP5	4	Hureaux 2029
	c.234G>A	p.(Met78Ile)	PM2 PM5 PP2 PP3 PP5	4	Hureaux 2019
	c.444T>A	p.(His148Gln)	PM1 PM2 PP2 PP5	4	Hureaux et al, 2019
	c.491G>T	p.(Cys164Phe)	PS3 PS4 PM2 PP2 PP3 PP5	5	Ohta et al, 2013
	c.683G>A	p.(Arg228His)	PM5 PM2 PP2 PP3	4	This publication
	c.922G>A;	p.(Gly308Ser)	PM2 PP1 PP2 PP3 PP5	4	Hureaux et al, 2019
	c.1079G>A	p.(Arg360Gln)	PM1 PM2 PP2 PP3	4	This publication
	c.1081G>A	p.(Val361Met)	PM1 PM2 PP2 PP3 PP5	4	Louis dit Picard et al, 2012
	c.1084C>T	p.(Arg362Trp)	PM1 PM2 PP2 PP3 PP5	4	Louis-dit-Picard et al, 2012
	c.1156A>G	p.(Thr386Ala)	PS2 PM1 PM2 PP2 PP3	5	This publication
	c.1205T>C	p.(Phe402Ser)	PM1 PM2 PP1 PP2 PP3 PP5	4	Hureaux et al, 2019
	c.1229C>T	p.(Ser410Leu)*	PS3 PM2 PP2 PP3 PP5	4	Boyden et al, 2012; Mori et al, 2013
	c.1295G>A	p.(Ser432Asn)	PS3 PM1 PM2 PP2 PP3	5	Boyden et al, 2012; Ohta et al, 2013
	c.1297A>G	p.(Ser433Gly)	PS2 PS3 PM1 PM2 PM5 PP2 PP3 PP5	5	Louis-dit-Picard et al, 2012; Ishizawa et a 2016
	c.1298G>A	p.(Ser433Asn)	PS2 PS3 PM1 PM2 PM5 PP2 PP3 PP5	5	Boyden et al, 2012; Lifton et al.2012, Oh 2013, Shibata et al, 2014
	c.1300G>A	p.(Val434Met)	PM1 PM2 PP1 PP2 PP3 PP5	4	Hureaux et al, 2019
	c.1442G>A	p.(Ser481Asn)	PM1 PM2 PP2 PP3	4	This publication
	c.1480G>A	p.(Ala494Thr)	PS3 PM2 PP1 PP2 PP3 PP5	4	Boyden et al, 2012; Ohta 2013, Glover et 2014
	c.1492C>T	p.(His498Tyr)	PM2 PM5 PP1 PP2 PP3 PP5	4	Kelly et al, 2016
	c.1493A>G	p.(His498Arg)	PM1 PM2 PM5 PP2	4	This publication
	c.1499G>T	p.(Gly500Val)*	PM1 PM2 PP2 PP3 PP5	4	Louis-dit-Picard et al, 2012 (in Dominan form); Glover et al, 2014
	c.1582C>T	p.(Arg528Cys)	PS3 PM1 PM2 PM5 PP2 PP5	5	Boyden et al, 2012; Ohta 2013, Wu et al.
	c.1583G>A	p.(Arg528His)	PS2 PS3 PS4 PM2 PM5 PP2 PP3 PP5	5	Louis dit Picard et al, 2012 and Boyden e 2012;Ohta 213; Mori et al, 2013;Susa K Sasaki et al, 2017
	c.1587C>A	p.(Asn529Lys)	PS3 PM1 PM2 PP2 PP3 PP5	4	Louis-dit-Picard et al, 2012; Ohta 2013, Schumacher et al, 2014

	c.1643C>A	p.(Ser548Tyr)	PM1 PM2 PP1 PP2 PP3	4	This publication
KLHL3 Recessive	c.14+1G>A	p.?	PVS1 PM2 PM3 PP3	5	This publication
	c.228del	p.(Cys76Trpfs*16)	PVS1 PM1 PM2 PP1 PP3	5	This publication
	c.682C>G	p.(Arg228Gly)	PM2 PM3 PM5 PP2 PP3 PP5	4	Louis-dit-Picard et al, 2012
	c.830T>C	p.(Leu277Pro)	PM1 PM2 PM3 PP2 PP3	4	This publication
	c.1045G>A	p.(Val349Met)	PM1 PM2 PP2 PP3	4	This publication
	c.1150C>T	p.(Arg384Trp)	PM1 PM2 PM5 PP1 PP2 PP3 PP5	4	Louis-dit-Picard et al, 2012
	c.1192G>A	p.(Ala398Thr)	PM1 PM2 PM5 PP1 PP2 PP3	4	Louis-dit-Picard et al, 2012
	c.1277C>T	p.(Pro426Leu)	PM1 PM2 PP1 PP2 PP5	4	Louis-dit-Picard et al, 2012
	c.1291C>T	p.(Arg431Trp)	PM1 PM2 PM5 PP1 PP2 PP3	4	This publication
	c.1360del	p.(Arg454Alafs*4)	PVS1 PM1 PM2 PP1 PP3	5	This publication
	c.1535del	p.(Pro512Leufs*12)	PVS1 PM2 PP3	5	This publication
	c.1579C>T	p(Arg527Trp)	PM1 PM2 PP2 PP3	4	This publication
	c.1580G>A	p.(Arg527Gln)	PM1 PM2 PM3 PP2 PP3	4	This publication
WNK1	c.1888G>A	p.(Gluy630Lys)	PM1 PM2 PP1 PP3	4	This publication
	c.1891G>A	p.(Glu631Lys)	PS3 PM1 PM2 PP1 PP5	5	Louis-dit-Picard et al, 2020
	c.1900G>A	p.(Ala634Thr)	PS3 PM1 PM2 PM5 PP5	5	Louis-dit-Picard et al, 2020
	c.1901C>G	p.(Ala634Gly)	PM1 PM2 PM5 PP1 PP3	4	This publication
	c.1903G>A	p.(Asp635Asn)	PS3 PM1 PM2 PM5 PP5	5	Louis-dit-Picard et al, 2020
	c.1905T>A	p.(Asp635Glu)	PS3 PM1 PM2 PM5 PP1 PP5	5	Louis-dit-Picard et al, 2020
	c.1906C>G	p.(Gln636Glu)	PS3 PM1 PM2 PM5 PP1 PP4 PP5	5	Louis-dit-Picard et al, 2020
	c.1907A>G	p.(Gln636Arg)	PS3 PM1 PM2 PM5 PP1 PP4 PP5	5	Louis-dit-Picard et al, 2020
	Intron 1 large deletion of 21 Kb		PVS1, PM2	4	This publication
	Intron 1 large deletion of 23 Kb		PVS1, PM2	4	This publication
	Intron 1 large deletion of 41 Kb		PVS1,PS3, PM2	5	Wilson FH et al, 2001
WNK4	c.1682C>A	p.(Pro561Gln)	PM1 PM2 PM5 PP1 PP3	4	This publication
	c.1682C>G	p.(Pro561Arg)	PM1 PM2 PM5 PP1 PP5	4	Mori et al, 2017
	c.1690G>A	p.(Asp564Asn)	PM1 PM2 PM5 PP1 PP5	4	Sakoh et al, 2019
	c.3553C>T	p.(Arg1185Cys)	PM1 PM2 PP1 PP3 PP5	4	Wilson et al, 2001

A total of 64 different pathogenic or probably pathogenic variants were found in the 4 genes responsible for FHHt in our French cohort: 11 in *CUL3*; 25 in *KLHL3* Dominant form; 13 in *KLHL3* Recessive form; 11 in *WNK1* and 4 in *WNK4*. Among them, 25 mutations (39%) are newly described. 2 *KLHL3* Dominant variants are also described in Recessive form in literature (marked with an asterisk).

ACMG criteria description: **PVS: very strong evidence of pathogenicity**. **PVS1**: null variant (nonsense, frameshift, canonical +/−1 or 2 splice sites, initiation codon, single or multi-exon deletion) in a gene where loss of function is a known mechanism of disease. **PS: strong evidence of pathogenicity**. **PS1**: same amino acid change as a previously established pathogenic variant regardless of nucleotide change. **PS2**: de novo (both maternity and paternity confirmed) in a patient with the disease and no family history **PS3**: well-established in vitro or in vivo functional studies supportive of a damaging effect on the gene or gene product. **PS4**: the prevalence of the variant in affected individuals is significantly increased compared to the prevalence in controls. **PM: moderate evidence of pathogenicity. PM1**: Located in a mutational hot spot and/or critical and well-established functional domain without benign variation. **PM2**: absent from controls (or at extremely low frequency if recessive) in gnomAD database. **PM3**: detected in trans with a pathogenic variant (the phase was determined). **PM4**: protein length changes due to in-frame deletions/insertions in a non-repeat region or stop-loss variants. **PM5**: Novel missense change at an amino acid residue where a different missense change determined to be pathogenic has been seen before. **PM6**: Assumed de novo, but without confirmation of paternity and maternity. **PP: supporting evidence of pathogenicity. PP1**: co-segregation with disease in multiple affected family members in a gene definitively known to cause the disease. **PP2**: Missense variant in a gene that has a low rate of benign missense variation and in which missense variants. **PP3**: Multiple lines of computational evidence support a deleterious effect on the gene or gene product. **PP4**: Patient's phenotype or family history is highly specific for a disease with a single genetic aetiology. **PP5**: Reputable source recently reports variant as pathogenic but the evidence is not available to the laboratory to perform an independent evaluation.

Supplementary Table 3a.

Criteria of pathogenicity of new missense variants

Gene	Mutation		Allelic frequency in gnomAD* (%)	*In silico* prediction				Familial segregation
				SIFT	Poly-Phen-2	Mutation Taster	CADD score	
	cDNA level	Protein level						
KLHL3 Dominant	c.683G>A	p.(Arg228His)	0.00040	Deleterious	Probably Damaging	Disease causing	31	No
	c.1079G>A	p.(Arg360Gln)	Absent	Deleterious	Probably Damaging	Disease causing	32	No
	c.1156A>G	p.(Thr386Ala)	Absent	Deleterious	Probably Damaging	Disease causing	26.2	Yes, *de novo*
	c.1442G>A	p.(Ser481Asn)	Absent	Deleterious	Probably Damaging	Disease causing	23.7	No
	c.1493A>G	p.(His498Arg)	Absent	Deleterious	Benign	Disease causing	26.9	No
	c.1643C>A	p.(Ser548Tyr)	0.00080	Deleterious	Probably Damaging	Disease causing	28.4	Yes
KLHL3 Recessive	c.830T>C	p.(Leu277Pro)	Absent	Deleterious	Probably Damaging	Disease causing	26	Yes
	c.1045G>A	p.(Val349Met)	Absent	Deleterious	Probably Damaging	Disease causing	24.2	No
	c.1291C>T	p.(Arg431Trp)	0.00040	Deleterious	Probably Damaging	Disease causing	11.73	Yes
	c.1579C>T	p(Arg527Trp)	0.0016	Deleterious	Probably Damaging	Disease causing	14.32	No
	c.1580G>A	p.(Arg527Gln)	Absent	Deleterious	Probably Damaging	Disease causing	32	Yes
WNK1	c.1888G>A	p.(Gluy630Lys)	Absent	Deleterious	Probably Damaging	Disease causing	29.6	Yes
	c.1901C>G	p.(Ala634Gly)	Absent	Deleterious	Possibly Damaging	Disease causing	24.2	No
WNK4	c.1682C>A	p.(Pro561Gln)	Absent	Deleterious	Probably Damaging	Disease causing	25.3	Yes

Supplementary Table 3b

Criteria of pathogenicity of new splice-site variants

Gene	Mutation		Allelic frequency in gnomAD* (%)	*In silico* prediction**				Familial segregation
				MaxEntScan	NNSPLICE	Human Splicing Finder	SPiP Risk	
	cDNA level	Protein level						
CUL3	c.1207-2A>G;	p.?	Absent	-100.0%	-100.0%	-100.0%	98.67%	Yes, *de novo*
	c. 1207-1_1207delinsAG	p.?	Absent	-100.0%	-100.0%	-100.0%	98.67%	Yes, *de novo*
	c.1377+2T>C	p.?	Absent	-100.0%	-100.0%	-100.0%	97.46%	Yes, *de novo* in one family and inherited from th
	c.1377+3A>T	p.?	Absent	Creation of new splice site	Creation of new splice site	Creation of new splice site	96.95%	Yes, *de novo*
	c.1377+4A>G	p.?	Absent	Creation of new splice site	Creation of new splice site	Creation of new splice site	96.95%	Yes, *de novo*
KLHL3 Recessive	c.14+1G>A	p.?	Absent	-100.0%	-100.0%	-100.0%	97.46%	

** expressed as the decrease percentage compared with normal score

Supplementary Table 4a. Basic clinical and biochemical characteristics of the 19 *CUL3* patients (index cases and affected relatives).

Patient Id	Age at onset (years)	Sex (M/F)	HBP Grade	Na+ mmol/L	K+ mmol/L	Cl- mmol/L	HCO3- mmol/L	GFR ml/min/1.73m^2 (MDRD/Schwartz)	Renin (pg/mL)	Aldo (pg/mL)
08001	1.5	F	2	na	6.9	115	12	na	na	na
09001	33	M	3	142	7.3	104	14.6	103	na	93
09002	na	M	3	na	7.7	114	na	na	na	na
25001	15	F	3	140	5.8	111	19	100	2.9	544
27001	2	M	3	na	9.6	113	12	na	na	na
44001	0.7	M	1	136	7.4	111	16.2	na	na	94
59001	6	M	3	137	8.7	114	16	117	19.0	537
62001	9	M	3	137	7.1	111	17	129	0.6	110
78001	4	F	3	141	7.4	118	15.5	85	na	na
103001	2	M	3	137	6.8	122	na	100	na	na
103011	na	F	na	na	na	na	na	na	na	na
109001	12	F	3	135	7.7	117	15.7	132	0.7	30
127001	5	F	3	135	6.8	113	17	197	2.9	6
132001	22	F	3	138	5.3	106	21.3	128	na	507
132011	na	F	na	na	na	na	na	na	na	na
146-001	4	F	3	140	6.8	112	16	na	0.6	164
154001	15	M	na	na	na	na	na	na	na	na
155001	1	F	2	138	6.8	116	15.5	na	2.5	15
182001	10	M	na	na	na	na	na	na	na	na
Median	**5.5**	**-**	**3**	**138**	**7.1**	**113**	**16**	**117**	**2.5**	**102**

na: not available

Supplementary Table 4b: Growth clinical and biological data of *CUL3* patients (index cases and affected relatives)

Patient Id	clinical findings	Sex	Age at work-up	Weight (Kg)	Z-score weight	height (cm)	Z-score height	BMI (Kg/m2)	Total Calcium (mmol/l)	Ionized Calcium (mmol/l)	Phosphate (mmol/l)	Calcium/creat (mmol/mmol)
08001	Growth retardation	F	1.5	9	-1.5	70	-4	18.3	na	na	na	na
09001	Muscles fatigue and episodes of paralysis	M	43	61	-1	161	-2	23.5	na	na	na	na
09002	Sharp T waves on ECG	M	17	48	-2.5	159	-2	18.9	na	na	na	na
25001		F	15	49	-1	151	-2	21.4	na	na	na	na
27001		M	2	10.8	-2.5	91	1	13	na	na	na	na
44001	Growth retardation	M	0.9	9	-1	74	0	16.4	na	na	na	na
59001		M	6	20.5	0	121	0.5	14	na	na	na	na
62001	Developmental and behavioral disorder	M	9	26	-1	128	-1	15.8	2.54	na	2.1	na
78001		F	4	16	0	100	-1	16	na	na	na	na
103001	na	M	2	9	-3	83	-2	13	2.55	1.23	1.48	na
103011	na	F	na	na	na	na	na	na	na	na	na	na
109001	Growth retardation, dyshidrotic eczema on hands	F	12	28.3	-2.5	135	-5	15.5	2.2	na	1.85	na
127001	Growth and developmental retardation	F	6.5	17.6	-2	111	-2	14.2	2.33	1.19	na	na
132001		F	24	55	0	150	-2	24.4	na	na	1.23	0.24
132011	na	F	na	na	na	na	na	na	na	na	na	na
146001	Growth retardation since 18 months	F	5	na	na	na	na	na	2.31	na	1.57	na
154001	na	M	16	na	na	na	na	na	na	na	na	na
155001	Growth retardation	F	1	na	na	na	na	na	2.42	na	1.81	na
182001	Growth retardation	M	13	33	-2	133	-3	18.6	na	na	na	0.22
Median			6.5	23.3	-1.3	125	-2	16.6	2.4	1.2	1.7	0.2

na: not available.

Supplementary Table 5: Growth parameters for all familial hyperkalemic hypertension genotypes

	WNK1 ac.m (n=29)	*WNK1* int1del (n=23)	*WNK4* (n=10)	*KLHL3* AD (n=56)	*KLHL3* AR (n=16)	*CUL3* (n=19)	Kruskal-Wallis test
n with avail. Data	21	19	6	32	6	14	
Age at work-up	27[6;46]	36[17;49]^{i3}	38[13;43]	33[19;52]^{n3}	9[4;26]	7[2;16]^{i3n3}	< 0.0001
Weight (Kg)	51[33;61]^{c1}	68[57;79]^{i3}	67[66;98]^{l2}	69[57;81]^{c1n3}	61[19;66]	23[10;48]^{i3l2n3}	< 0.0001
Height (cm)	157[133;166]	169[160;175]^{i3}	162[110;170]	160[151;169]^{n1}	155[114;163]	125[89;150]^{i3n1}	0.0002
BMI (Kg/m^2)	19.5[18.0;22.6]^{c2}	21.9[18.9;28.4]^{i1}	28.4[23.7;37.3]^{l2}	26.1[22.3;30.9]^{c2n3}	24.5[15.0;25.4]	16.2[14.2;19.5]^{i1l2n3}	< 0.0001
Z-score weight	0.0[-1.7;+0.3]^{c1}	0.7[0.0;+1.3]^{i3}	0.7[0.0;+2.1]^{l2}	1.3[0.0;+1.7]^{c1n3}	0.0[0.0;+0.2]	-1.3[-2.5; and -0.8]^{i3l2n3}	< 0.0001
Z-score height	-1.0[-2.0;and + 0.3]	0.0[-0.5;and +1.0]^{g2i2}	0.0[-0.9;0.0]	-1.5[-2.0;-1.0]^{g2}	-1.5[-2.5; and +0.4]	-2.0[-2.3;-0.8]^{i2}	0.0011
Growth failure	28% (6/21)	11% (2/19)	0% (0/6)	34% (11/32)	50% (3/6)	71% (10/14)	

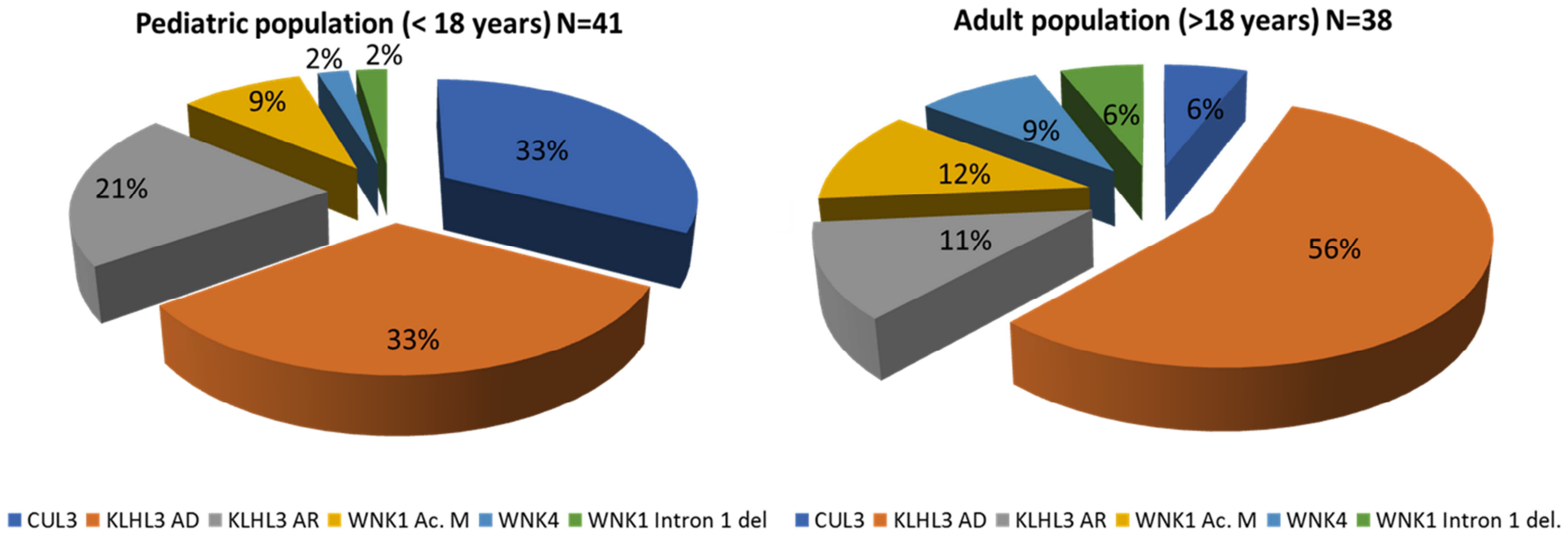
Values are given in median [IQR].
Growth failure is defined by a Z-score of height and/or of weight inferior or equal to -2 standard deviation. Statistical significance is given by superscript after square brackets as follow: *WNK1* ac.m vs *KLHL3* AD: c; *WNK1* int1del vs *KLHL3* AD: g; *WNK1* int1del vs *CUL3*:i; *WNK4* vs *CUL3*: l; *KLHL3* AD vs *CUL3* : n. * is 1, ** is 2 and *** is 3.

Supplementary Table 6: Response to hydrochlorothiazide

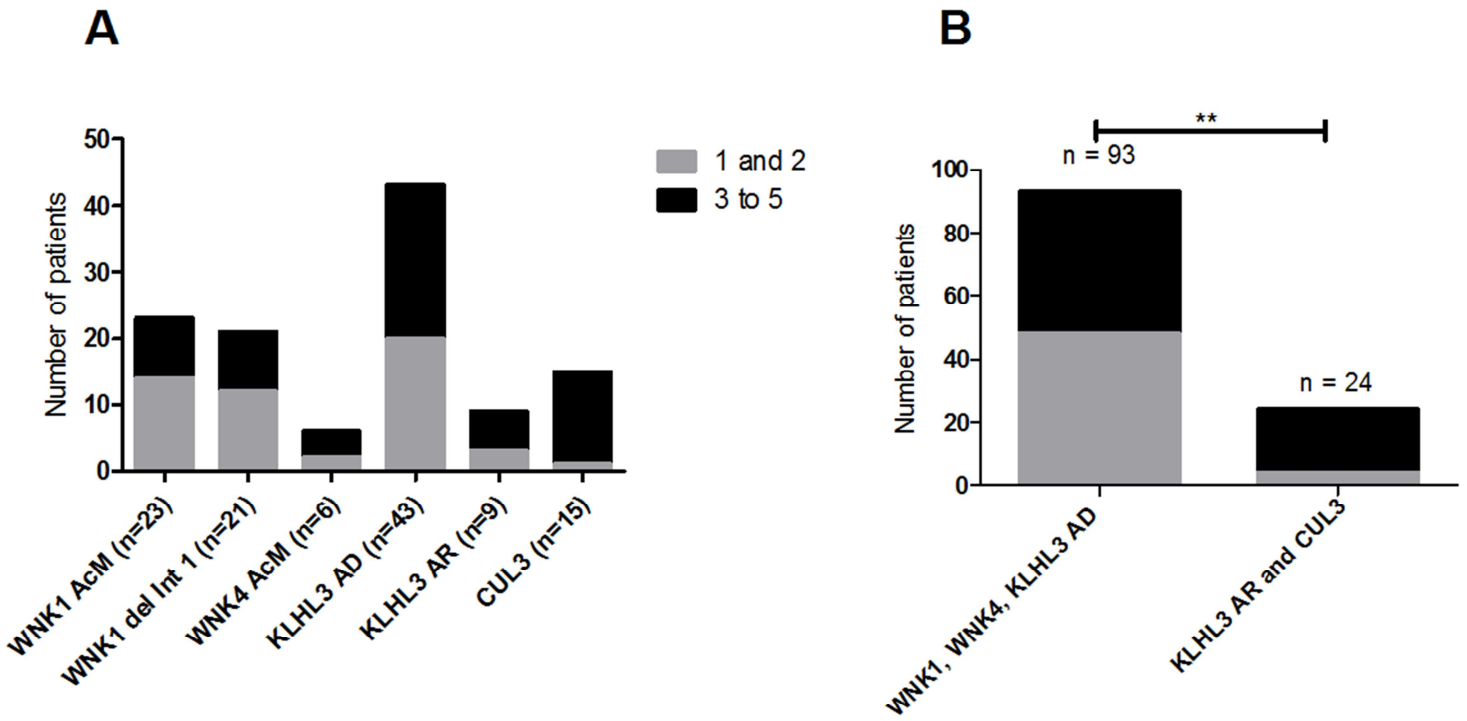
Parameters	*WNK1* acidic motif (n=29)	*KLHL3* AD (n=56)	*KLHL3* AR (n=16)	*CUL3* (n=19)	*P* Value (Kruskal-Wallis test)
Delta of SBP (mmHg)	0.5[0.0;13.0]	13.5[2.2 ;30.5]	24.0[19.0;28.0]	21.5[17.5;44.3]	0.0394
number of values	4	10	5	10	
Delta of DBP (mmHg)	7.5[1.5;21.8]	10.0[1.8;30.3]	3.0[1.5;24.5]	17.0[10.0;31.3]	0.2421
number of values	4	10	5	10	
Delta of K+ (mmol/l)	1.6[1.4;1.8]^{m1}	1.9[0.5;2.4]^{n2}	2.2[1.5;3.5]	3.3[2.0;4.0]^{m1n2}	0.0049
number of values	7	15	9	12	
Delta of Cl- (mmol/l)	6.0[5.5;9.0]	3.5[2.0;5.0]	11.0[4.5;13.5]	7.0[2.8;16.3]	0.1409
number of values	5	4	8	10	
Delta of HCO3- (mmol/l)	4.5[4.0;6.7]^{m1}	6.0[5.0;7.0]	7.6[4.9;9.0]	12.5[7.3;15.3]^{m1}	0.0139
number of values	4	7	9	10	

Values are given in median [interquartile 25%; interquartile 75%]. *WNK1* intron 1 deletion and *WNK4* groups were excluded due to lack of data. Statistical significance is given by superscript after square brackets as follow: *WNK1* acidic motif vs *CUL3*: m; *KLHL3 AD* vs *CUL3*: n. * is 1, ** is 2.

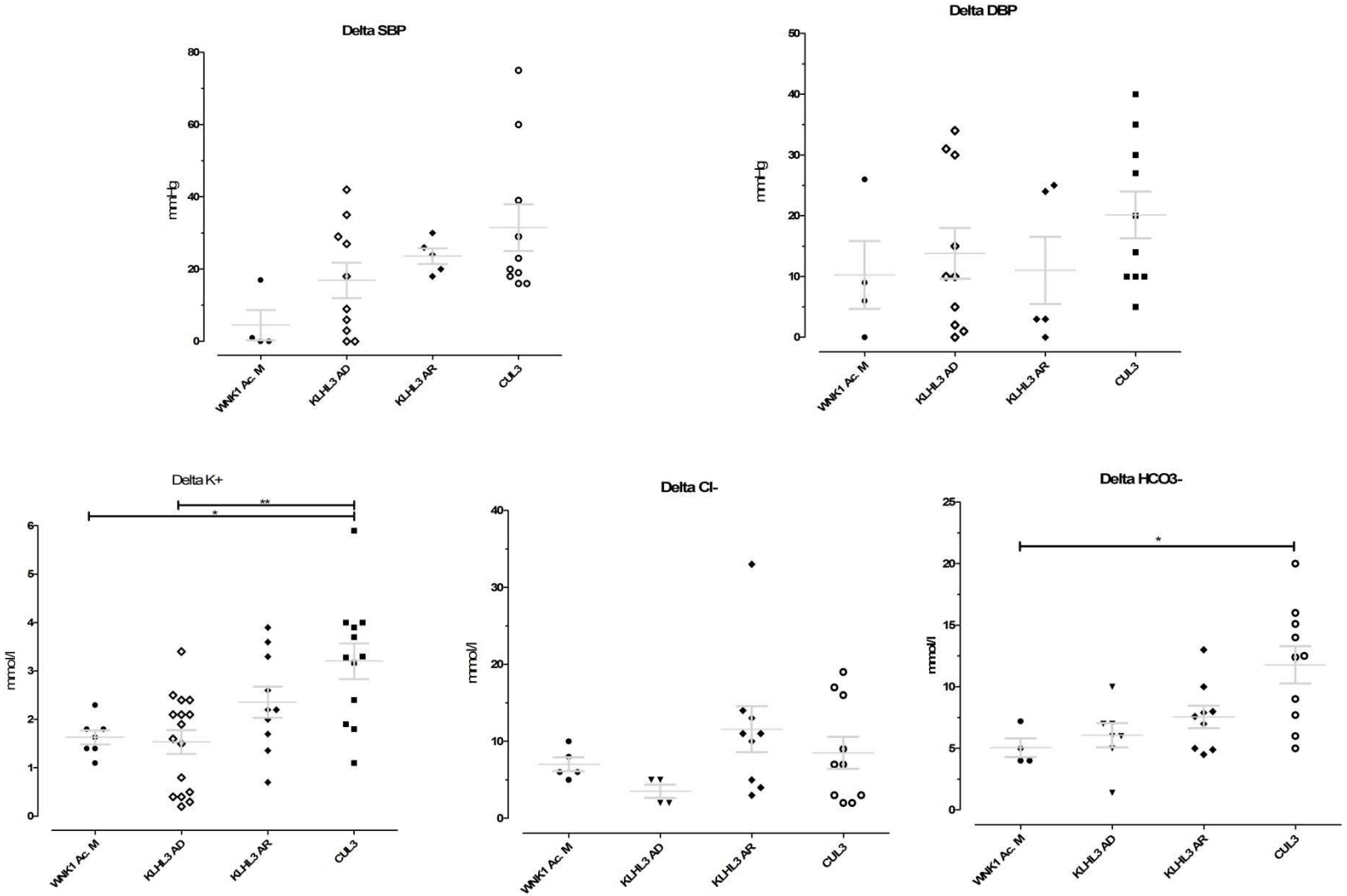
Supplementary Figure 1. Genotype distribution of pediatric and adult populations with familial hyperkalemic hypertension.



Suplementary Figure 2. Blood pressure and familial hyperkalemic hypertension genotypes

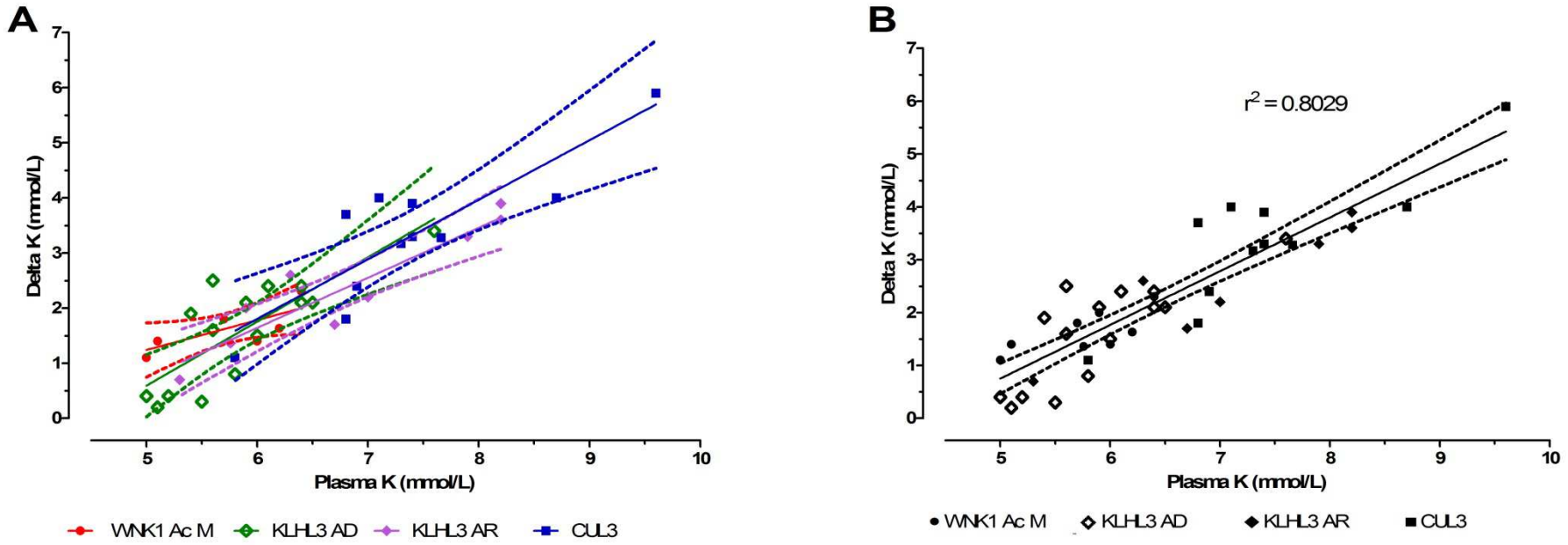


Supplementary figure 3: Response to hydrochlorothiazide



Response to hydrochlorothiazide: “Delta analyses” of Cl-, HCO3-, SBP and DBP: graphical representation of available data. “Delta analyses” correspond to the difference (increase or decrease of clinical and biochemical parameters) before and after HCTZ treatment. We observed a significant difference with higher response to treatment in *CUL3* patients for kalemia (P = 0.0049) and bicarbonates (P = 0.0139). Median and Interquartile in grey bars.

Supplementary Figure 4. Delta of K+ under hydrochlorothiazide treatment *versus* basal kalemia



Linear regression analysis of Delta of K+ versus basal kalemia. A. The slopes of the different groups are not significantly different. B. A global significant association exists between the basal plasma K^+ values and the decrease observed in hydrochlorothiazide ($P < 0.0001$).

Reporting checklist for cross sectional study.

Based on the STROBE cross sectional guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the STROBE cross sectionalreporting guidelines, and cite them as:

von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies.

		Reporting Item	Page Number
Title and abstract			
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	2
Abstract	#1b	Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	#3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	#4	Present key elements of study design early in the paper	5-7
Setting	#5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data	5-6

		collection	
Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of selection of participants.	5
	#7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-7
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for for exposed and unexposed groups if applicable.	6
Bias	#9	Describe any efforts to address potential sources of bias	16
Study size	#10	Explain how the study size was arrived at	5
Quantitative variables	#11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	5-6-7
Statistical methods	#12a	Describe all statistical methods, including those used to control for confounding	5-6-7
Statistical methods	#12b	Describe any methods used to examine subgroups and interactions	5-6-7
Statistical methods	#12c	Explain how missing data were addressed	5-6-7
Statistical methods	#12d	If applicable, describe analytical methods taking account of sampling strategy	n/a
Statistical methods	#12e	Describe any sensitivity analyses	5-6-7
Results			
Participants	#13a	Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for for exposed and unexposed groups if applicable.	7
Participants	#13b	Give reasons for non-participation at each stage	7
Participants	#13c	Consider use of a flow diagram	n/a

Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable.	7-8-9
Descriptive data	#14b	Indicate number of participants with missing data for each variable of interest	6-9-22
Outcome data	#15	Report numbers of outcome events or summary measures. Give information separately for exposed and unexposed groups if applicable.	9 to13 and 22
Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	n/a
Main results	#16b	Report category boundaries when continuous variables were categorized	5-13
Main results	#16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	#17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	10-13
Discussion			
Key results	#18	Summarise key results with reference to study objectives	12 & 15
Limitations	#19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	15
Interpretation	#20	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	13-17
Generalisability	#21	Discuss the generalisability (external validity) of the study results	16-17
Other Information			
Funding	#22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17