Supplemental Table 1. Allele frequency of *CYP21A2* mutations

g.DNA	Protein	Number of alleles	% of total	Mutation group
	Gene deletion/ Chimeric genes	94	30.72	Null
g.92C>T	P30L	9	2.94	C
g.658 A/C>G	I2G	75	24.51	A
g.711-718del	D8bp (G110del8nt)	5	1.63	Null
g.1004T>A	I172N	44	14.38	B
g.1385T>A, g.1388T>A, g.1394T>A	e6 cluster	1	0.33	Null
g.1688G>T	V281L	22	7.19	C
g.1999C>T	Q318X	9	2.94	Null
g.2113C>T	R356W	15	4.90	Null
g.2584C>T	P453S	6	1.96	C
Multiple mutations on one allele				
	I2G+P453S	1	0.33	A
	I2G+D8bp	2	0.65	Null
	I172N+P453S	2	0.65	B
	e6+V281L	1	0.33	Null
	V281L+P453S	1	0.33	C
Rare mutations				
g.188A>T	H62L+P453S	2	0.65	B
g.752C>T	**R124C**	**1**	**0.33**	**B**
g.803C>T	**Q141X**	**1**	**0.33**	**Null**
g.1769C>T	L308F	1	0.33	B
g.2047delG	**V334*fsX28***	**1**	**0.33**	**Null**
g.2350G>C	**IVS9 +1G>C**	**1**	**0.33**	**Null**
g.2503C>T	R426C	1	0.33	Null
g.2504G>A	R426H	1	0.33	Null
g.2530C>T	R435C	1	0.33	B
g.2675G>C	R483P	1	0.33	B
g.2674dupC	**R483P*fsX40***	**1**	**0.33**	**Null**
	Alleles without mutation	7	2.29	
	total	306	100.00	

Novel mutations are shown in bold font type.

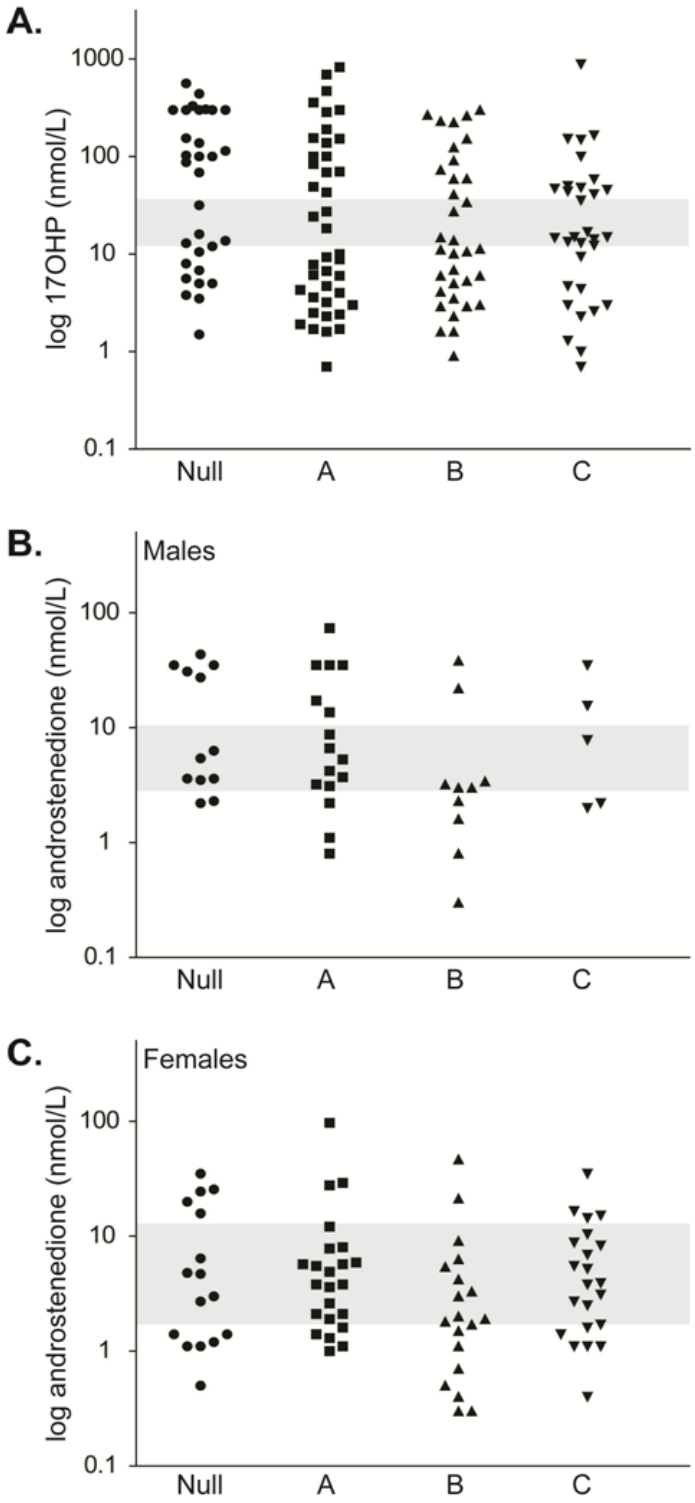
Supplemental Table 2. Mineralocorticoid replacement by mutation group and renin levels

	Mutation group				Significance of Mutation group	Significance of Paired Comparisons					
	Null	A	B	C		Null vs A	Null vs B	Null vs C	A vs B	A vs C	B vs C
Renin in Patients Not on Fludrocortisone											
No fludrocortisone, renin within reference range	0 (0%)	2 (22.2%)	11 (52.4%)	16 (72.7%)	0.023	.	.	.	.	.	.
No fludrocortisone, high renin (1 or 2 fold above reference range)	2 (100%)	7 (77.8%)	9 (42.9%)	4 (18.2%)	0.003**	1.000	0.217	0.046	0.118	0.003	0.104
No fludrocortisone, renin lower than mid reference range	0 (0%)	0 (0%)	1 (4.8%)	2 (9.1%)	0.902	.	.	.	.	.	.
Renin in Patients on Fludrocortisone											
Fludrocortisone, high renin (1 or 2 fold above reference range)	19 (79.2%)	21 (70.0%)	5 (41.7%)	1 (11.1%)	0.001**	0.540	0.058	0.001***	0.158	0.005	0.178
Fludrocortisone, renin mid to upper reference range	2 (8.3%)	8 (26.7%)	6 (50.0%)	6 (66.7%)	0.002**	0.158	0.011	0.002***	0.169	0.047	0.660
Fludrocortisone, low – renin lower than mid reference range	3 (12.5%)	1 (3.3%)	1 (8.3%)	2 (22.2%)	0.241	.	.	.	.	.	.

*Significant at the 5% level, **Significant at the Bonferroni adjusted level of 1.67%, *** Significant at the Bonferroni adjusted level of 0.28%

Supplemental Table 3. Female fertility and attempted pregnancy

Mutation group	**Null**	**A**	**B**	**C**
Patients (n)	19	24	25	29
Patients with at least one child (n)	1	2	8	13
Never tried (n)	15 (79.9%)	19 (79.2%)	12 (48.0%)	11 (37.9%)
Patients , < 30 yrs (n)	8	9	3	10
Never tried < 30 yrs (n)	8 (100%)	8 (89%)	3 (100%)	6 (60%)



Supplemental Figure 1

Serum levels of 17OHP (A) androstenedione (B, C for males and females, respectively) in samples from CAH patients in the morning after intake of the usual glucocorticoid morning dose by mutation group. The *shaded areas* represent recommended target range (Merke DP, Bornstein SR 2005 Congenital adrenal hyperplasia. Lancet 365:2125-213634). The majority of patients were outside these therapeutic target ranges for 17OHP; however normal androstenedione concentrations were more frequently achieved.