

SUPPLEMENTARY TABLES

Table S1. Clinical and biochemical data for CPA with and without *PRKAR1B* CNV

	Patients with <i>PRKAR1B</i> CNV	Patients without <i>PRKAR1B</i> CNV
N	3	18
Gender (F/M)	3/0	15/3
Age (years) ^a	47.74 ± 3.35	39.54 ± 5.03
Midnight serum cortisol (nmol/L) ^a	304.98 ± 131.10	365.70 ± 76.17
Morning serum cortisol (nmol/L) ^a	347.76 ± 85.56	451.26 ± 59.89
Post-LDDST serum cortisol (nmol/L)	474.72 ± 0.00	488.24 ± 108.46
Post-HDDST serum cortisol (nmol/L)	452.64 ± 0.00	308.56 ± 57.13
UFC (nmol/day) ^a	241.36 ± 238.88	342.52 ± 102.67
Change of UFC (%) ^b	1.30	61.96
Urine 17-OHS (μg/g creatinine/24h) ^a	15.00 ± 4.80	8.88 ± 1.56
Pre-Liddle urine 17-OHS (μg/g creatinine/24h)	15.20 ± 5.00	9.23 ± 2.16
Post-Liddle urine 17-OHS (μg/g creatinine/24h)	14.65 ± 10.45	12.80 ± 1.96
ACTH (pg/mL) ^a	<0.05	0.07 ± 0.02
Size of tumor (cm)	4.00 ± 1.00	3.38 ± 0.39

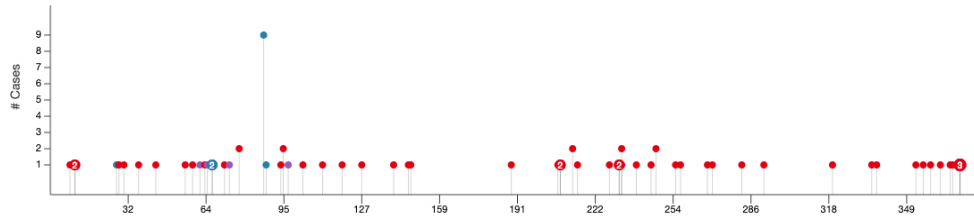
Data are presented as mean ± SEM or percentage; ^aAt the time of diagnosis; ^bPercentage of change Pre- and Post-Liddle test; CPA, cortisol-producing adrenal adenomas; CNV, copy number variants; F, females; M, males; LDDST, low-dose dexamethasone suppression test; HDDST, high-dose dexamethasone suppression test; UFC, urinary free cortisol; 17-OHS, 17-hydroxycorticosteroid; ACTH, adrenocorticotropin hormone; To convert serum cortisol *nmol/L* to *μg/dL*, divide by 27.588; UFC *nmol/day* to *μg/24h*, divide by 2.76; Urine 17-OHS *μg/g creatinine* to *mmol/mol creatinine*, multiply by 0.000312; ACTH *pg/mL* to *pmol/L*, multiply by 0.22.

Table S2. *In silico* analyses of *PRKAR1B* variants

Patient ID	Gene	Transcript	dbSNP ID	HGVS coding	HGVS Protein	Allele Frequency ^a	SIFT ^b	Polyphen2 ^c	Mutation Taster ^d	Mutation Assessor ^e	FATHMM ^f
CAR757.03	PRKAR1B	NM_001164760.2	rs61732492	c.118A>G	p.I40V	0.013545	Tolerated	Benign	Damaging	Predicted non-functional (neutral)	Tolerated
CAR762.03	PRKAR1B	NM_001164760.2	rs183383238	c.200C>T	p.A67V	0.00019396	Damaging	Benign	Damaging	Predicted non-functional (neutral)	Damaging
CAR521.01	PRKAR1B	NM_001164760.2	rs376485407	c.898G>A	p.A300T	0.0000648	Damaging	Probably damaging	Damaging	Predicted functional (medium)	Damaging

^aAllele Frequency extracted from gnomAD version 2.0.1; *In silico* analyses done using the prediction tools: ^bSorting Tolerant From Intolerant, ^cPolymorphism Phenotyping v2, ^dMutationTaster, ^eMutation Assessor, ^fFunctional Analysis through Hidden Markov Models v2.3

Table S3. Somatic variants of *PRKAR1B* in different tissues



Tissue	Variant Type	Protein Change	DNA Change (hg38)	Gene
Bladder	Stop Gained	Q371*	chr7:g.550465G>A	PRKAR1B
Bladder	Missense	E257Q	chr7:g.584508C>G	PRKAR1B
Bladder	Missense	R232W	chr7:g.596160G>A	PRKAR1B
Brain	Missense	A270V	chr7:g.579338G>A	PRKAR1B
Brain	Missense	L66V	chr7:g.680708A>C	PRKAR1B
Breast	Missense	K367N	chr7:g.550475C>G	PRKAR1B
Bronchus and Lung	Missense	Q371K	chr7:g.550465G>T	PRKAR1B
Bronchus and Lung	Missense	G319A	chr7:g.551406C>G	PRKAR1B
Bronchus and Lung	Stop Gained	Q64*	chr7:g.680714G>A	PRKAR1B
Bronchus and Lung	Missense	Q28K	chr7:g.711424G>T	PRKAR1B
Bronchus and Lung; Pancreas	Missense	E247K	chr7:g.584538C>T	PRKAR1B
Bronchus and Lung; Prostate gland	Missense	R335W	chr7:g.550573G>A	PRKAR1B
Bronchus and Lung; Skin	Missense	S77F	chr7:g.680674G>A	PRKAR1B
Cervix uteri	Missense	A127V	chr7:g.677289G>A	PRKAR1B
Cervix uteri	Stop Gained	S73*	chr7:g.680686G>C	PRKAR1B
Cervix uteri	Missense	S71L	chr7:g.680692G>A	PRKAR1B
Colon	Missense	E103K	chr7:g.680597C>T	PRKAR1B
Colon	Stop Gained	R97*	chr7:g.680615G>A	PRKAR1B
Colon	Missense	R94H	chr7:g.680623C>T	PRKAR1B
Colon	Missense	V36I	chr7:g.711400C>T	PRKAR1B
Corpus uteri	Missense	R368M	chr7:g.550473C>A	PRKAR1B
Corpus uteri	Missense	L359M	chr7:g.550501G>T	PRKAR1B
Corpus uteri	Missense	A337T	chr7:g.550567C>T	PRKAR1B
Corpus uteri	Missense	M245I	chr7:g.584542C>T	PRKAR1B
Corpus uteri	Missense	T239M	chr7:g.584561G>A	PRKAR1B
Corpus uteri	Missense	R233H	chr7:g.596156C>T	PRKAR1B
Corpus uteri	Missense	R233C	chr7:g.596157G>A	PRKAR1B
Corpus uteri	Missense	R232Q	chr7:g.596159C>T	PRKAR1B
Corpus uteri	Missense	R228Q	chr7:g.596171C>T	PRKAR1B
Corpus uteri	Missense	G208C	chr7:g.596232C>A	PRKAR1B
Corpus uteri	Splice Acceptor substitution	X184_splice	chr7:g.596305C>A	PRKAR1B
Corpus uteri	Missense	H140Y	chr7:g.677251G>A	PRKAR1B
Corpus uteri	Missense	R95H	chr7:g.680620C>T	PRKAR1B
Corpus uteri	Frameshift Insertion	N88Efs*56	chr7:g.680643_680644insG	PRKAR1B
Corpus uteri	Frameshift Deletion	L66Wfs*26	chr7:g.680707delA	PRKAR1B
Corpus uteri	Missense	R63G	chr7:g.680717T>C	PRKAR1B
Corpus uteri	Stop Gained	E61*	chr7:g.680723C>A	PRKAR1B
Corpus uteri	Missense	E58D	chr7:g.711332C>A	PRKAR1B
Corpus uteri	Missense	V30I	chr7:g.711418C>T	PRKAR1B
Corpus uteri	Missense	E10D	chr7:g.711476C>A	PRKAR1B
Corpus uteri	Missense	P8H	chr7:g.711483G>T	PRKAR1B
Corpus uteri; Brain	Missense	A213V	chr7:g.596216G>A	PRKAR1B
Corpus uteri; Stomach; Colon	Frameshift Deletion	P87Rfs*5	chr7:g.680644delG	PRKAR1B
Esophagus	Splice Donor substitution	X147_splice	chr7:g.677228C>A	PRKAR1B
Esophagus	Missense	E55K	chr7:g.711343C>T	PRKAR1B
Other and unspecified parts of tongue	Missense	D291N	chr7:g.579276C>T	PRKAR1B
Other and unspecified parts of tongue	Missense	V215M	chr7:g.596211C>T	PRKAR1B
Ovary	Missense	I255M	chr7:g.584512G>C	PRKAR1B
Ovary	Missense	Y207F	chr7:g.596234T>A	PRKAR1B
Ovary	Missense	S147R	chr7:g.607452A>C	PRKAR1B
Ovary	Splice Acceptor deletion	X60_splice	chr7:g.680691delTGACTTTTGCCCG GCCAAATCTGCCTGTTTCTTCC	PRKAR1B
Pancreas	Missense	V111M	chr7:g.680573C>T	PRKAR1B
Prostate gland	Missense	I282T	chr7:g.579302A>G	PRKAR1B
Prostate gland	Missense	R146S	chr7:g.677231C>G	PRKAR1B
Rectum	Missense	E356K	chr7:g.550510C>T	PRKAR1B
Skin	Missense	Q371R	chr7:g.550464T>C	PRKAR1B
Skin	Missense	S363F	chr7:g.550488G>A	PRKAR1B
Skin	Missense	P353L	chr7:g.550518G>A	PRKAR1B
Skin	Missense	P119S	chr7:g.677314G>A	PRKAR1B
Skin	Missense	P43L	chr7:g.711378G>A	PRKAR1B
Stomach	Missense	A268V	chr7:g.579344G>A	PRKAR1B
Stomach	Missense	G208S	chr7:g.596232C>T	PRKAR1B
Stomach	Missense	I818R	chr7:g.596292C>T	PRKAR1B
Stomach	Frameshift Insertion	I27Dfs*53	chr7:g.711427_711428insC	PRKAR1B
Stomach	Missense	E10A	chr7:g.711477T>G	PRKAR1B