Supplementary Table

Supplementary Table 1
Mutation spectrum of the 372 affected offspring of von Hippel-Lindau disease patients

Mutation site	Alteration of Protein	Family NO.	Patient NO.
c.4C>G	p.Pro2Ala	1	3
c.160delA		1	3
c.176insAGCAdelTCCTGCGCT		1	1
c.193T>C	p.Ser65Pro	1	8
c.194C>T	p.Ser65Leu	4	23
c.194C>G	p.Ser65Trp	1	3
c.205insG		1	2
c.208G>T	p.Glu70stop	1	5
c.224delTCT		1	5
c.226delTTC		3	7
c.233A>G	p.Asn78Ser	4	19
c.239delGTCCGCG		1	7
c.240T>G	p.Ser80Arg	1	3
c.241delC		1	2
c.245G>C	p.Arg82Leu	1	3
c.256C>T	p.Pro86Ser	4	7
c.257C>T	p.Pro86Leu	1	1
c.262T>C	p.Ser88Arg	1	3
c.263G>A	p.Trp88stop	1	2
c.263G>C	p.Trp88Ser	1	9
c.266T>C	p.Leu89Pro	2	10
c.265delC		1	1
c.269A>T	p.Asn90Ile	3	10
c.280G>T	p.Glu94stop	1	3
c.288insA		1	2
c.292T>A	p.Tyr98Asn	1	4
c.293A>C	p.Tyr98Ser	1	7
c.329delA		1	1
c.337C>T		2	5
c.340delG		1	3
c.341ins CCCGATAGGTCACCTTTGGCTCTTCAGAGATGC		1	3
c.349T>G	p.Trp117Gly	1	4
c.381delGCTTinsC		1	2
c.388G>C	p.Val130Leu	1	2
c.395delA		1	4
c.404T>A	p.Leu135stop	1	2

c.406delT		1	2
c.414A > G	p.Pro138Pro	1	1
c.425delT		1	3
c.426insG		1	3
c.433delCAGCC		1	3
c.433C > T	p.Gln145stop	1	9
c.436insGG		1	1
c.452T>G	p.Ile151Ser	1	2
c.462delA		1	3
c.464delTGTAT		1	1
c.464delT		1	4
c.464-1G>C		1	8
c.464-1G>A		1	1
c.468insACTC		1	4
c.480delG		1	3
c.481C>T	p.Arg161stop	3	6
c.482G>A	p.Arg161Gln	2	5
c.485G>A	p.Cys162Tyr	1	2
c.486C>G	p.Cys162Trp	3	6
c.486C>A	p.Cys162stop	1	5
c.499C>T	p.Arg167Trp	10	20
c.499C > G	p.Arg167Gly	1	1
c.500G>A	p.Arg167Gln	7	19
c.506T > C	p.Leu169Pro	1	1
c.509T>A	p.Val170Asp	3	10
c.530_536delGACTGGA		1	1
c.533T>G	p.Leu178Arg	1	1
c.565-570delGAAGAC		1	1
Deletion		17	67

Supplementary Table 2 Age at the onset of VHL-related lesions in different generation

Lesion	Mean ± SD	Median (range)
Generation 2	249	
CHB (66.7%)	32.0 ± 10.7	31.0 (11-66)
RA (19.7%)	28.3 ± 11.3	27.0 (8-55)
RCC (49.0%)	38.9 ± 10.9	37.5 (18-74)
PCL (42.2%)	36.2 ± 11.5	35.0 (10-66)
PHEO (15.7%)	33.1 ± 12.3	34.0 (8-66)
GS (4.4%)	24.1 ± 15.5	20.0 (4-56)
Generation 3	109	
CHB (49.5%)	21.8 ± 8.2	21.5 (10-50)
RA (21.1%)	18.0 ± 6.0	17.0 (2-27)
RCC (35.8%)	28.5 ± 6.6	27.0 (14-44)

PCL (39.4%)	27.4 ± 6.73	28.0 (14-44)
PHEO (10.1%)	27.0 ± 9.5	26.0 (9-44)
GS (11.9%)	19.15 ± 5.2	19.0 (8-26)
Generation 4	14	
RA (14.3%)	16.5 ± 0.7	16.5 (16-17)
PCL (21.4%)	23.3 ± 6.5	23.0 (17-30)

Supplementary Table 3
Univariate and multivariate analysis for risk factors of RCC-specific survival

Variables	univariate analysis P value
Generation (3 and 4 vs 2)	0.321
Mutation (truncating mutation vs missense mutation)	0.054
Classification (VHL type 2 vs VHL type 1)	0.449
Gender (female vs male)	0.842
Mutation region	0.684
Onset age (≤ 28 vs >28)	0.351
First symptom (haemangioblastoma vs abdomen)	0.581

Supplementary table legends

Supplementary Table 1 Mutation spectrum of the 372 affected offspring of von Hippel-Lindau disease patients.

Supplementary Table 2 Age at the onset of VHL-related lesions in different generation.

Supplementary Table 3 Univariate and multivariate analysis for risk factors of RCC-specific survival.