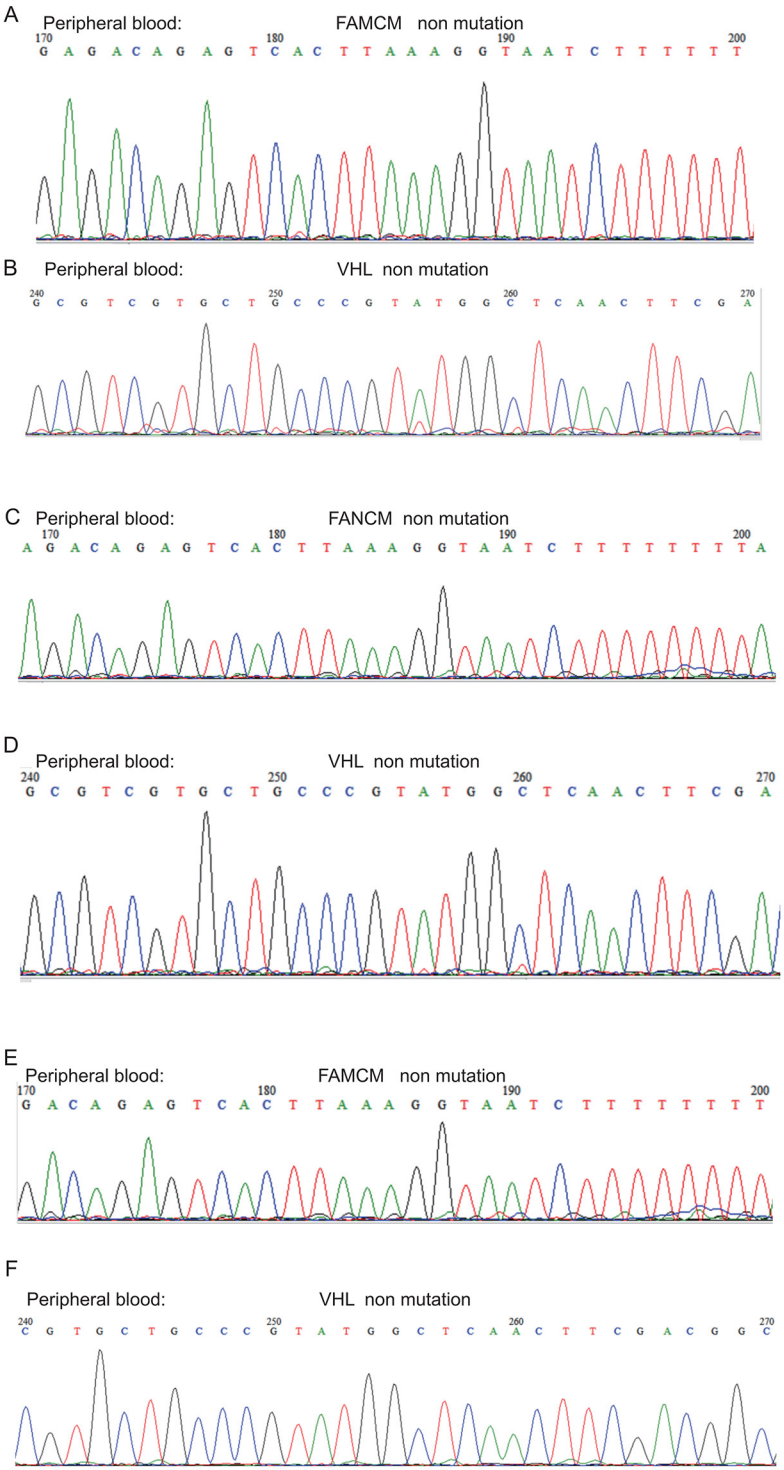

Figure S1 Sanger sequencing chromatograms of *FANCM* and *VHL* for patient RCC88's parents and brother. Genetic testing of DNA samples collected from RCC88's father (A,B), mother (C,D), and brother (E,F) revealed that none of them harbored *FANCM* or *VHL* mutations. RCC, renal cell carcinoma.

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Table S1 Genes related to germline cancer predisposition

AKT1	*BRIP1*	*CYLD*	*FANCC*	*HRAS*	*MTAP*	*PMS2*	*SDHAF2*	*TEK*
AKT2	*BTK*	*DDR2*	*FANCG*	*IDH1*	*MUTYH*	*PRKAR1A*	*SDHB*	*TERC*
ALK	*CBL*	*DICER1*	*FANCI*	*IDH2*	*MYC*	*PTCH1*	*SDHC*	*TERT*
APC	*CDC73*	*DNMT3A*	*FANCL*	*JAK1*	*MYD88*	*PTEN*	*SDHD*	*TP53*
AR	*CDH1*	*EGFR*	*FANCM*	*JAK2*	*NBN*	*PTPN11*	*SF3B1*	*TSC1*
ARAF	*CDK4*	*EP300*	*FAS*	*KIT*	*NF1*	*RAD50*	*SH2D1A*	*TSC2*
ATM	*CDKN1B*	*EPCAM*	*FBXW7*	*KRAS*	*NF2*	*RAD51*	*SHOC2*	*U2AF1*
AXIN2	*CDKN2A*	*ERBB2*	*FGFR1*	*MAP2K1*	*NOTCH2*	*RAD51C*	*SLX4*	*VHL*
B2M	*CEBPA*	*ERBB3*	*FH*	*MAP2K2*	*NPM1*	*RAF1*	*SMAD4*	*WT1*
BAP1	*CFTR*	*ERCC2*	*FLCN*	*MEN1*	*NRAS*	*RB1*	*SMARCA4*	*XIAP*
BCL10	*CHEK2*	*ERCC3*	*FLT3*	*MET*	*NSD1*	*RECQL4*	*SMARCB1*	*XPO1*
BLM	*CREBBP*	*ERCC4*	*FLT4*	*MLH1*	*NTHL1*	*RET*	*SMO*	
BMPR1A	*CSF3R*	*ERCC5*	*GATA2*	*MRE11*	*PALB2*	*RIT1*	*SOS1*	
BRAF	*CTLA4*	*ETV6*	*GNAS*	*MSH2*	*PHOX2B*	*RTEL1*	*STAT3*	
BRCA1	*CTNNB1*	*EZH2*	*H3F3A*	*MSH3*	*PIK3CA*	*RUNX1*	*STK11*	
BRCA2	*CXCR4*	*FANCA*	*HNF1A*	*MSH6*	*PLCG2*	*SDHA*	*SUFU*	

Table S2 Clinical characteristics of patients with RCC and pathogenic mutations

Patient ID	Sex	Age at diagnosis (years)	Mutation gene	Histology	Family history	Recurrence or metastasis
RCC15	Male	21	*VHL*	ccRCC	Maternal aunt: VHL	0
RCC16	Male	44	*VHL*	ccRCC	0	0
RCC19	Male	44	*VHL, RAD51C*	ccRCC	Mother: glioma	0
RCC40	Male	36	*MUTYH*	ccRCC	0	0
RCC63	Male	39	*FANCI*	Unclassified	Father: gastric cancer	0
RCC68	Male	56	*FLCN*	Unclassified	Father: gastric cancer	0
RCC88	Male	29	*VHL, FANCM*	ccRCC	0	1: metastasis
RCC93	Male	24	*RAD50*	MiT family translocation RCC	0	0
RCC96	Female	36	*FLCN*	chRCC	0	0
RCC109	Male	62	*NBN*	ccRCC	0	0
RCC115	Male	37	*SDHB*	chRCC	0	0
RCC121	Female	32	*FH*	pRCC	Mother: endometrial carcinoma	1: metastasis
RCC122	Male	24	*FH*	pRCC	Father: RCC	0

RCC, renal cell carcinoma; ccRCC, clear cell renal cell carcinoma; VHL, von Hippel-Lindau; MiT, microphthalmia; chRCC, chromophobe renal cell carcinoma; pRCC, papillary renal cell carcinoma.

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Table S3 Detail on pathogenic mutations

Study ID	Gene 1	Variant 1	Protein 1	Transcript NM_#S	Pathogenicity
RCC15	*VHL*	c.340G>C	p.Gly114Arg	NM_000551	P
RCC16	*VHL*	c.345C>G	p.His115Gln	NM_000551	P
RCC19	*VHL*	c.517_527delGAGAATTACAG	p.Glu173fs	NM_000551	P
RCC19	*RAD51C*	c.904+2T>C	#	NM_058216	P
RCC40	*MUTYH*	c.1214C>T	p.Pro405Leu	NM_001128425	P
RCC63	*FANCI*	c.158-2A>G	#	NM_001113378	P
RCC68	*FLCN*	c.1379_1380delTC	p.Leu460fs	NM_001353229	P
RCC88	*VHL*	c.264G>A	p.W88*	NM_000551	P
RCC88	*FANCM*	c.4515+1G>C	#	NM_020937	LP
RCC93	*RAD50*	c.2165dupA	p.E723fs	NM_005732	P
RCC96	*FLCN*	c.1285dupC	p.H429fs	NM_001353229	P
RCC109	*NBN*	c.235-1G>C	#	NM_002485	LP
RCC115	*SDHB*	c.725G>A	p.R242H	NM_003000	P
RCC121	*FH*	c.A563T	p.N188I	NM_000143	P
RCC122	*FH*	c.191dupA	p.N64fs	NM_000143	P

#, frameshift mutation; *, nonsense mutation; RCC, renal cell carcinoma; P, pathogenic; LP, likely pathogenic.

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