

**Table S1. All shared variants detected by WES, performed for III-2, IV-1 and IV-2.**

<b>Gene</b>	<b>Transcript</b>	<b>cDNA</b>	<b>Protein</b>	<b>gnomAD frequency</b>	<b>Considerations</b>
PRSS56	NM_001195129.1	c.318G>C	p.(Val106=)	5/73820	no predicted effect on splicing
MYO1G	NM_033054.2	c.831T>G	p.(Ala277=)	0	no predicted effect on splicing
SLC25A16	NM_152707.3	c.908G>A	p.(Gly303Asp)	1/250544	no co-segregation in IV-3
PRDM10	NM_020228.2	c.2030G>A	p.(Cys677Tyr)	1/208488	co-segregation, conserved amino acid
SMEK1/PPP4R3A	NM_001284280.1	c.2426C>T	p.(Thr809Met)	9/282842	no co-segregation in III-4
CARHSP1	NM_014316.3	c.184G>A	p.(Val62Ile)	42/282518	high frequency in gnomAD

**Table S2. Genes analyzed in the hereditary cancer gene panel in patient IV-3**

A2ML1	CD27	DNAJC21	FANCL	KRAS	NOP10	PTPN11	RPS28	SPRED1
ACD	CD70	EGFR	FANCM	LHCGR	NPM1	RAD50	RPS29	SQSTM1
AIP	CDC73	EGLN1	FAS	LIG4	NRAS	RAD51C	RPS7	STK11
AKT1	CDH1	EGLN2	FASLG	LIG4	NSD1	RAD51D	RTEL1	SUFU
ALK	CDH23	ELANE	FBXW7	LZTR1	NTHL1	RAF1	RUNX1	TERC
AMH	CDK4	ELP1	FH	MAD2L2	PALB2	RB1	SAMD9	TERF2IP
AMHR2	CDKN1A	EPCAM	FLCN	MAP2K1	PARN	RECQL4	SAMD9L	TERT
ANKRD26	CDKN1B	ERCC1	G6PC3	MAP2K2	PAX5	REST	SBDS	TG
APC	CDKN1C	ERCC2	GALNT12	MAX	PDGFB	RET	SDHA	THPO
ARMC5	CDKN2A	ERCC3	GATA2	MCM8	PDGFRA	RHBDF2	SDHAF2	TINF2
ASXL1	DKN2B	ERCC4	GDNF	MCM9	PHOX2B	RIT1	SDHB	TMEM127
ATM	CDKN2C	ERCC5	GFI1	MDH2	PIK3CA	RNASEL	SDHC	TNFRSF11A
ATR	CEBPA	ERCC6	GPC3	MEN1	PMS2	RNF43	SDHD	TP53
AXIN2	CHEK2	ESR2	GPR161	MET	PMS2CL	RPL11	SEMA4A	TRIM28
BAP1	CREBBP	ETV6	GREM1	MITF	POLD1	RPL15	SFTPA1	TRIM37
BARD1	CTC1	EXT1	GRHL2	MLH1	POLE	RPL18	SFTPA2	TRIP13
BLM	CTLA4	EXT2	HAVCR2	MPL	POLH	RPL27	SH2B3	TSC1
BMPR1A	CTNNA1	EZH2	HAX1	MRE11	POT1	RPL35A	SH2D1A	TSC2
BRAF	CTR9	FAN1	HNF1A	MSH2	POU6F2	RPL5	SHOC2	USB1
BRCA1	CYLD	FANCA	HOXB13	MSH3	PPM1D	RPS10	SLX4	VHL
BRCA2	DDB2	FANCB	IDH1	MSH6	PRF1	RPS15A	SMAD4	WAS
BRIP1	DDX11	FANCC	IDH2	MTAP	PRKAR1A	RPS17	SMAD9	WRAP53
BUB1	DDX41	FANCD2	IKZF1	MUTYH	PRKN	RPS19	SMARCA4	WRN
BUB1B	DICER1	FANCE	IPMK	NBN	PRSS1	RPS20	SMARCB1	WT1
BUB3	DIS3L2	FANCF	TK	NF1	PTCH1	RPS24	SMARCE1	XPA
CARD11	DKC1	FANCG	KIF1B	NF2	PTCH2	RPS26	SOS1	XPC
CBL	DLST	FANCI	KIT	NHP2	PTEN	RPS27	SPINK1	

**Table S3. Overlap of gene expression changes upon FLCN loss or PRDM10Cys677Tyr induction in RPTECs as indicated in figure 4F.**  
Asterisks indicate genes of potential interest overlapping between FLCN<sup>KO</sup> and PRDM10Cys677Tyr cell lines.

UP (n=446)					DOWN(n=473)				
ACP5*	ENPP1	GLYATL2	CENPN	TIGD6	CDH1*	SERPING1	SLC30A2	SEPP1	OSBPL10
NPR1	ARHGEF6	RACGAP1	E2F8	ZNF367	KCNJ1	FOLR1	DNAH5	KSR1	CERK
ATP6V0D2	THSD1	SNCG	TUBA1C	CALB2	SLC3A1	IGSF10	PNMAL1	ARID5B	MIR3936
ALDH1A3	FANCI	NCAPG2	CCNE2	NT5DC2	CDH3*	TESC	AMBP	SLC17A1	MACC1
HS3ST3A1	TRPC4	LIG1	RIMS2	IGFBP6	MUC1	ASS1	LRRC49	GJB1	LACTB2
SLC37A2	MEIS2	ZNF219	KCNT2	RNASEH2A	FILIP1L	SLITRK2	RASSF10	CDHR1	ELMO2
PREX1	CATSPER1	MMP16	ANXA6	SEC24D	AIF1L	KCNH3	LOC647859	CAMSAP3	CASC1
SRPX	CCND1*	TRAM2	BRIP1	FAM72A	BCAM	DNER	FAM84A	BBOX1	FAM13B
TNFAIP8L3	ADRA1B	MCM4	ABAT	KIF14	PDK4	TSPAN1	TRIM17	SYT16	OSMR
SIGLEC15	FAM115C	C11orf82	CEP78	SIX1	CMTM4	CEACAM19	CACNA1H	RINL	ATP8A1
PTGIS	FBN2	BRCA2	FAM72D	MCM10	ABCB1	BCL3	RNF152	APBB1IP	C1orf186
PDPN	MAPRE2	SPTBN4	NOG	LYPD1	PTH1R	SERPINF2	DEPTOR	INTS10	CHCHD10
ANPEP	RAD51AP1	AURKA	TTK	KIF2C	TFCP2L1	ADH6	NHLRC4	SPRY4	C2CD4B
NOS1	PITPNM3	SH3BGRL3	CDCA2	SMAGP	TMPRSS4	SLC44A3	DNAJB13	SLC44A2	LINC00488
NID1	KCNK6	PCDHGC3	KCNQ5	C17orf53	ERBB4	ADAMTS9	FAM189A1	SERPINA5	BHLHE40
CPEB1	GOLGA7B	ABCA13	FAM72B	SMG9	TMEM37	SCN7A	IVNS1ABP	AQP3	TNFSF10
CNIH3	CD276	AMTN	PGM5P2	CENPO	SHROOM2	PDE7B	COL28A1	NCOA7	CASR
RGL1	C7orf58	TUBB	AP1S1	CENPF	LOC90246	LOC723809	GABARAPL1	KLHDC2	PKP4
DAAM2	KIF18A	CFL2	MKI67	LOC730101	CCL2*	TNFAIP2	HS6ST1	KCNQ1OT1	FGFR2
CTSL2	FBLN7	FAM114A1	DYNC1I1	PRC1	PHACTR3	C3orf25	LTB	RPS6KL1	RERG
C11orf41	CD97	TYMS	CDCA8	NUF2	MECOM	WWC1	VWA7	DKFZP586I1420	ZNF331
MLPH	CDC6	STK10	KIF23	MPV17	AFAP1	EFHC2	PTPN14	PID1	TSNAXIP1
MDGA1	CYBRD1	MAP6	KRT79	LOC100505702	KCNIP4	LPHN1	DDX5	CCDC40	IQCE
ZNF114	CDC45	CHEK1	ATG16L1	PDZD4	DOK5	GABRP	PABPC4L	SPP1	TMEM176B
LCP1	VWDE	FAM111B	CDCA3	EPB41L4A	CASZ1	CLDN2	AMIGO1	SAT1	LRP6

PLAT	LRP4	FOXP2	XRCC2	ACOT11	TSPAN8	HUNK	SGK223	C1orf226	GNE
KIAA1211	SLC20A1	OSBP2	MND1	KLHL4	EDN1	PLCB1	KCNQ1	TEX2	DNAI1
CD109	CD3EAP	F13A1	PLOD1	UST	SLC12A1	MAOB	GRB7	TRPS1	EPS8L1
SFTA1P	VGF	TUBA1B	FNDC4	NEIL3	AGR2	LOC100130417	ZC3H12B	LOC100507651	CTSC
SPOCD1	CCDC15	CLSPN	LOC154761	CENPI	TC2N	PKHD1	LGALS9	LOC388630	VAV3
SHOX2	PPAPDC1A	FOXM1	SEMA3E	CCDC86	RBBP8	SFRP1	NLGN4X	LRRC48	NOSTRIN
PCDH7	BACE2	CALM1	FHOD1	POC1A	SCNN1A	TMEM45B	DCDC5	RAP1GAP	CCDC160
GLI2	CAMK4	NCAPD2	ADTRP	KIF4A	PCDH1	RHOB	C7orf41	ICOSLG	HES1
SLC14A1	LIMA1	TLR6	POLE2	GCAT	PCDP1	CDH16	PDE4D	TMEM133	ABCA3
APBA2	RGS17	KIAA1462	GSG2	BASP1	TRIB2	EPB41L4B	FABP3	GDF7	C10orf10
ITGAX	MLF1IP	RNF125	TUBB3	FAM214B	C19orf21	AR	C10orf107	GABARAPL3	TTC28
HS3ST3B1	HJURP	HRK	PKM2	PTPLA	LEFTY1	SUCNR1	ENTPD2	SLC29A4	SRSF5
ECM1	RASGRF2	JARID2	Mar-04	CCNB2	EFEMP1	RORC	PTGER2	ACMSD	MITF
LOC100287314	COL6A3	DPF3	STK32C	GIN51	ZPLD1	TMEM173	LONRF2	MAGIX	PHACTR4
FRMD5	C10orf114	PADI1	GFRA1	LEF1	OCLN	SULT1E1	TNFRSF11B	RNF19A	COL18A1
LHFPL2	C8orf34	WFDC3	MAP3K4	FAM189A2	TNS1	PCK1	B4GALT1	CCDC107	CYB561
NGEF	LAPTM5	KIF15	PKMYT1	ZNF845	LINC00473	ADSSL1	FLRT3	LNX1	LOC100129534
CD163L1	ZIC2	ANLN	LOC100128164	IMPDH1	NUAK2	PBLD	ZNRF3	RAPGEF3	IRX3
TNNT1	ITGA11	TBX3	PAQR4	COL13A1	PAPLN	TLE2	PDE6B	HS3ST1	DIP2C
JPH1	DLX2	MELK	PPP1R14B	SPAG5	NR1H4	SEMA6A	ZNF618	UBD	PDGFA
EVI2A	EXO1	CCDC69	NCAPG	ESPL1	GPR143	FAM20A	CNKS3	LOC100131089	PLEKHG1
MTIL	PMP22	MME	GGCT	SOWAHD	CHDH	IFITM1	SLC6A13	BSPRY	MAOA
ABCG2	TRIP13	NCAPH	PLK1	ARHGAP31	CDKN1C	ZNF467	C10orf108	SEMA3B	MIDN
KRT19	TNFRSF11A	ACOT7	DACT1	COTL1	PCSK6	FAAH2	FAM149A	TPPP	DZIP1
HHAT	DCN	GLI3	WDR76	LOC100192378	SAMD12	CHL1	EFNA5	C12orf39	BCL2L15
ADAMTS12	PBK	GIN52	TTF2		KCNK5	ALDH1A2	MRPL33	STK17B	LMBRD1
GPR115	DSCC1	MCM2	STIL		ARHGEF16	SLC40A1	TRIB1	G0S2	COL24A1
OSBPL1A	CENPA	AURKB	SLC17A7		C21orf62	RHPN2	STAT3	PPP1R13B	C9orf71
TP73	FABP5	STMN1	LOC100506343		ATP1B1	SASH1	RASAL1	INSR	NLK

TMCC3	TGM5	FAXC	CDA		ARHGEF38	SMTNL2	LPCAT1	CXCL3	PHYHD1
C1orf187	MEF2C	CHAF1A	POLQ		WDR66	CPAMD8	ILDR1	PER2	AP2A2
BACH2	LHFP	FXYD6	GCNT4		NINL	IER5L	PTAFR	PPP1R3B	DAG1
ANKH	SLC43A1	E2F1	SKA1		FOSL2	KCTD1	DLG3	FAM154B	RERE
POSTN	OXTR	VIM	FGF12		CLCN5	SAMD11	CHSY1	ADH1C	SESTD1
CDCA7L	BDH1	CHAF1B	C6orf115		SOWAHC	MT1F	TNFRSF19	EPAS1	ATP6V1A
RTN4RL2	BUB1B	FAH	PORCN		ETS2	LRRRC8B	RNF208	HS6ST2	RCBTB2
APOBEC3B	CCNE1	ZWINT	MCC		SUSD4	LOC100422737	SMAD6	CGN	SPRY2
ANK2	BLM	CCNA2	CDC25C		GLUL	BCR	TMPRSS3	NME9	FZD4
DTL	DRAP1	SGOL1	CALCR		RNF180	C1orf201	CRIM1	ARHGAP24	C1orf228
RGS20	NET1	LACTB	FGD3		SERPINA3	FGL2	TMEM176A	ABCA4	C11orf54
EMR2	METTL7B	GPR63	NDC80		C2CD4A	THSD7B	PAPPA2	COLEC12	MORN3
FIBCD1	XYLB	FAM40B	FEN1		NR3C2	UBXN10	PGBD5	TLR1	SST
BCHE	ADAMTSL1	SHC4	SGOL2		MAL	ZDHHC15	SLC45A4	FBXO36	CCDC64
MPP1	UHRF1	TIMELESS	DOCK10		CXCL14	RHOV	CDKL1	TBL1X	THEM4
VSTM2L	ORC6	AP1S2	FBXO5		CYP26B1	ZNF204P	EMID2	PITPNM1	MFHAS1
MCF2	ERCC6L	RRM1	ADCY3		AFF1	HOXD8	CPT1A	LYNX1	KIAA0664L3
MCOLN2	HLA-DRB1	CDT1	WDHD1		RASL11A	RASD1	HIP1	DUSP4	ACVR1B
C9orf125	TIAM1	WDR62	DPYSL3		IRF2BPL	DAPK1	GPC4	CTAGE4	TTC40
PTTG1	NANS	PADI3	HMMR		SOX9	CFI	ACPP	NCEH1	RAB17
PARD6G	PDE4DIP	TK1	KIF11		B3GNT2	CFB	MMS22L	PTGER4	TRAM1
ZIC5	BEST3	RMI2	MAGI2		MEST	SLC6A12	CDC42SE2	CD7	LOC402160
PPP1R3C	ITGA5	BIRC5	PRR11		MPZL2	CXorf26	ACSM3	VLDLR	TCTN1
C19orf33	NRIP3	LMNB2	C1orf21		BZRAP1	BCRP2	CSGALNACT1	RUNDC3B	
FLI1	TLR4	ALOXE3	HLX		HNF1A	CLMN	IFITM2	EFNA1	
SPOCK1	MAD2L1	RAB7L1	GRIN2D		CYS1	KIAA1671	LOC100507218	SLC48A1	
PAX6	GINS4	SCN3B	KPNA2		ABLIM1	FAM110C	BCRP3	HGD	
TCF4	RAD51	ESCO2	KIFC1		TLR5	APOL4	FCGR2A	COG2	
LRRRC8E	COL5A1	RAD54L	DLX1		TSPAN7	ABP1	NR4A1	RIC3	

LUM	FXYD5	SARDH	DLGAP5		WFDC2	SLC22A5	WDR72	ZBTB46	
SLC7A8	MTHFD1	ARHGAP11A	CENPH		RNF150	NLGN4Y	FIBIN	PHF15	
RBM20	SH3KBP1	APOBEC3C	SLC28A3		LLGL2	GPC3	HAP1	FOXO1	
BRCA1	KCNN4	BEND6	AOX1		C1orf106	KIAA2022	TNF	TTC25	
HMGA1	GPR85	E2F2	KIAA1524		ID4	LEFTY2	HIST1H2AC	IFITM3	
HECW2	CASC5	MYBL2	SMC2		C6orf223	LOC100302650	KLHDC7A	PRUNE2	
CKAP2L	LMNB1	SHCBP1	CORO2B		KCNK2	SHISA2	LRG1	H3F3B	
E2F7	TACC3	CENPW	XDH		MGAT4A	BLNK	SLC17A3	FOXJ1	
UBASH3B	INCENP	TMEM45A	PCDH18		ARRDC4	PLSCR1	TNS3	DGCR5	
EGF	EFHD2	TOB2P1	TCF19		PDZD2	HAVCR1	PTGER3	MED9	
GPM6A	NDST3	BTC	CEP55		CACNA1D	TNFSF13	AKIRIN1	LZTS1	
FMOD	C3orf55	ST8SIA5	TUBB2A		PVR	MARVELD2	EPCAM	IQCH	
AFF3	TPX2	MYH16	DEPDC1B		IPCEF1	SGK2	KYNU	CNTD2	
BUB1	TRPM3	INPP4B	LRP1		BCL2	DOC2B	KCNC4	SLC16A4	
PDGFRB*	ORC1	SKA3	SHISA4		ITM2A	ACSL4	ARL14	GUCY1A3	
RAI14	RAB3B	SIPA1L1	DSN1		SOSTDC1	RSPH1	INADL	OBSL1	