

Figure S1. Ingenuity Pathway Analysis (IPA). (A) and (B) IPA representative networks showing genes regulated by S15A with NF- $\kappa$ B as one of the critical nodes in these networks.

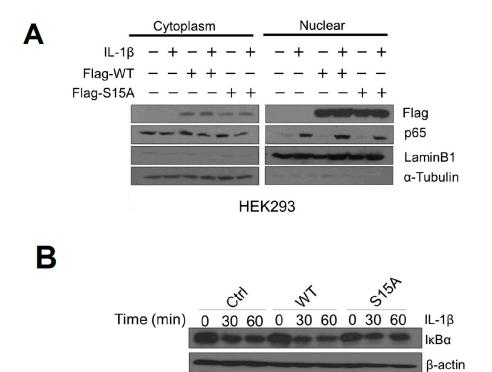


Figure S2. Effect of S15A mutant on PRMT5 subcellular localization, p65 nuclear translocation and IκB $\alpha$  degradation. (A) Cell fractionation assay, showing subcellular compartmentalization of Flag-PRMT5 and Flag-S15A in HEK293 cells. Western blot was probed with anti-FLAG, p65, LaminB1 and  $\alpha$ -tubulin antibodies. (B) Western blot, showing IL-1 $\beta$ -induced IκB $\alpha$  degradation pattern in WTPRMT5 and S15A HEK293 cells.

HEK293

ACCESSION NO.	TargetID	S15A-PRMT5 +IL- 1β/WT+IL-1β
NM_001115.1	ADCY8	0.45
NM_014391.2	ANKRD1	0.38
NM_020373.2	ANO2	0.15
XR_041624.1	C10ORF85	0.36
XR_041485.1	C13ORF29	0.27
XM_001726191.1	C190RF290S	0.00
NM_178342.2	C3ORF35	0.50
NM_018452.3	C6ORF35	0.32
NM_145028.3	C6ORF81	0.16
NM_152786.1	C9ORF43	0.33
NM_001742.2	CALCR	0.24
NM_175931.1	CBFA2T3	0.28
NM_138414.1	CCDC101	0.41
NM_015603.1	CCDC9	0.48
NM_004591.1	CCL20	0.37
NM_207007.2	CCL4L2	0.47
NM_145057.2	CDC42EP5	0.41
NM_000735.2	CGA	0.33
NM_000737.2	CGB	0.45
NM_024111.2	CHAC1	0.00
NM_015557.1	CHD5	0.27
NM_024944.2	CHODL	0.47
NM_138429.1	CLDN15	0.49
NM_080645.2	COL12A1	0.22
NM_002089.3	CXCL2	0.29
NM_016229.3	CYB5R2	0.36
NM_000779.2	CYP4B1	0.31
NR_024064.1	DAD1L	0.39
NM_006557.4	DMRT2	0.28
NR_024595.1	DNM1P35	0.06
NM_133637.1	DQX1	0.37
NM_004428.2	EFNA1	0.48
NM_007036.2	ESM1	0.22
NM_153606.2	FAM71A	0.50
NM_001012426.1	FOXP4	0.06
NM_000148.2	FUT1	0.35

NM_002068.1	GNA15	0.40
XM_935238.1	GOLGA8F	0.45
BX109627	HS.130639	0.46
Al801879	HS.144030	0.14
BU633914	HS.25555	0.27
AK026734	HS.287720	0.34
AF339771	HS.344872	0.19
CD695721	HS.538157	0.00
Al253067	HS.541845	0.20
U10515	HS.544238	0.46
AI628074	HS.545238	0.13
NM_130770.2	HTR3C	0.28
NM_172200.1	IL15RA	0.17
NM_001012633.1	IL32	0.49
NM_000564.2	IL5RA	0.50
NM_000584.2	IL8	0.48
NM_002195.1	INSL4	0.30
XM_934728.1	KIAA0565	0.09
NM_138343.2	KLC4	0.02
NM_002774.3	KLK6	0.34
NM_004139.2	LBP	0.29
NM_001010939.1	LIPJ	0.18
NM_033029.2	LMLN	0.15
XM_001724965.1	LOC100129268	0.13
XM_001716704.1	LOC100130288	0.15
XM_001718675.1	LOC100130705	0.50
XM_001714361.1	LOC100131999	0.18
XR_038987.1	LOC100132496	0.37
XM_001724630.1	LOC100132716	0.05
XM_001726146.1	LOC100132839	0.06
XM_001721522.1	LOC100134009	0.18
XM_001720931.1	LOC100134041	0.14
XM_001715304.1	LOC100134081	0.00
XM_001721704.1	LOC100134170	0.19
XM_001714134.1	LOC100134499	0.00
NM_178514.3	LOC283487	0.26
XM_944838.2	LOC285733	0.27
XM_939888.1	LOC339742	0.49
XM_370865.4	LOC388122	0.23

XM 374766.2	LOC399715	0.11
XM 495854.3	LOC440013	0.10
XM 001717499.1	LOC642076	0.04
NR 024495.1	LOC642826	0.40
XM 927139.1	LOC643869	0.14
XM 933938.2	LOC643872	0.38
XM 928663.1	LOC645649	0.03
XR 037491.1	LOC646808	0.46
XM 943707.1	LOC649431	0.33
XM_941853.1	LOC652416	0.00
XM_928640.1	LOC653651	0.39
XM_001126803.1	LOC728185	0.36
XR_015405.1	LOC728895	0.43
XM_001130993.1	LOC729675	0.23
XM_001714434.1	LOC730376	0.40
NM_002343.2	LTF	0.01
NM_012323.2	MAFF	0.44
NM_005204.2	MAP3K8	0.39
NM_052858.3	MARVELD3	0.33
NM_033290.1	MID1	0.33
NR_030209.1	MIR518E	0.31
NM_173855.3	MORN3	0.40
NM_013404.3	MSLN	0.21
NM_003828.2	MTMR1	0.45
NM_001005474.1	NFKBIZ	0.47
NM_001080379.1	PACRG	0.01
NM_000438.3	PAX3	0.27
NM_003706.1	PLA2G4C	0.41
NM_002658.2	PLAU	0.44
XM_940486.1	PLEKHA2	0.26
NM_014330.2	PPP1R15A	0.46
NM_022114.2	PRDM16	0.11
NM_000963.1	PTGS2	0.32
NM_000963.1	PTGS2	0.40
NM_001024455.2	RGAG4	0.43
NM_184237.1	RNPC2	0.48
NM_001007098.1	SCP2	0.40
NM_000450.1	SELE	0.22
NM_013386.3	SLC25A24	0.41

NR_003237.1	SNORD113-9	0.34
XM_291729.7	TAF3	0.38
NM_031898.1	TEKT3	0.16
NM_001001524.2	TM6SF2	0.10
NM_001097620.1	TMEM184A	0.08
NM_002160.2	TNC	0.45
NM_002160.1	TNC	0.44
NM_006290.2	TNFAIP3	0.28
NM_001561.4	TNFRSF9	0.50
NM_033229.2	TRIM15	0.41
NM_020810.2	TRMT5	0.21
NM_001080419.1	UNK	0.50
NM_030570.2	UPK3B	0.39
NM_001078.2	VCAM1	0.15
NM_206923.1	YY2	0.30
NM_145271.3	ZNF688	0.18

Figure S3. Full list of genes downregulated by the S15A-PRMT5 mutation. Fold change is represented as S15A-PRMT5 +IL-1 $\beta$ /WT+IL-1 $\beta$  ≤ 0.5