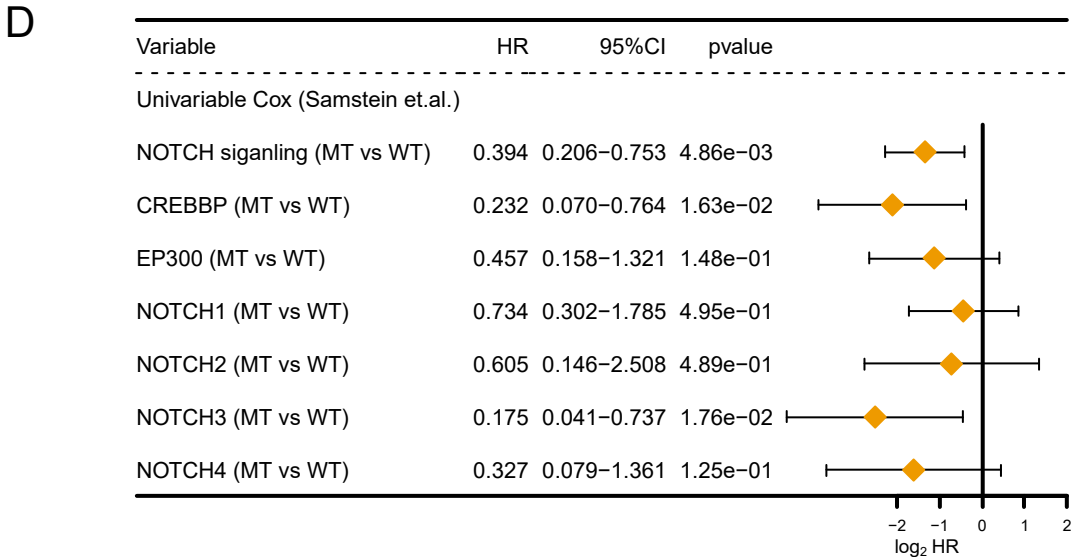
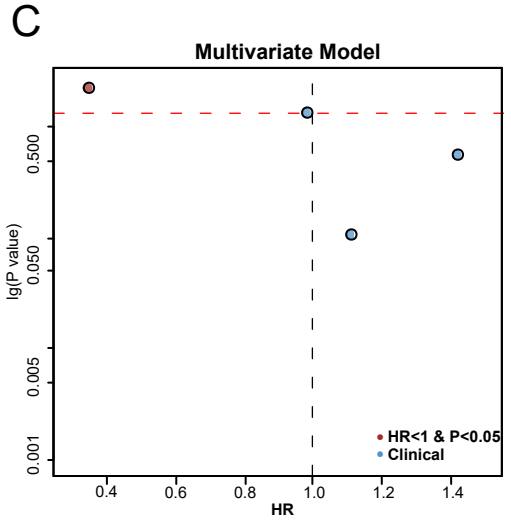
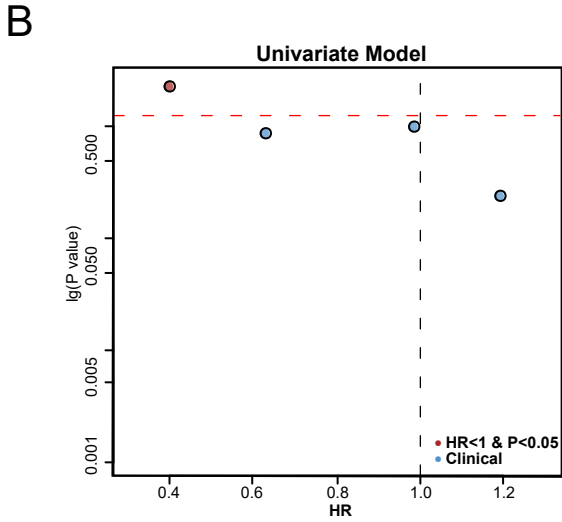
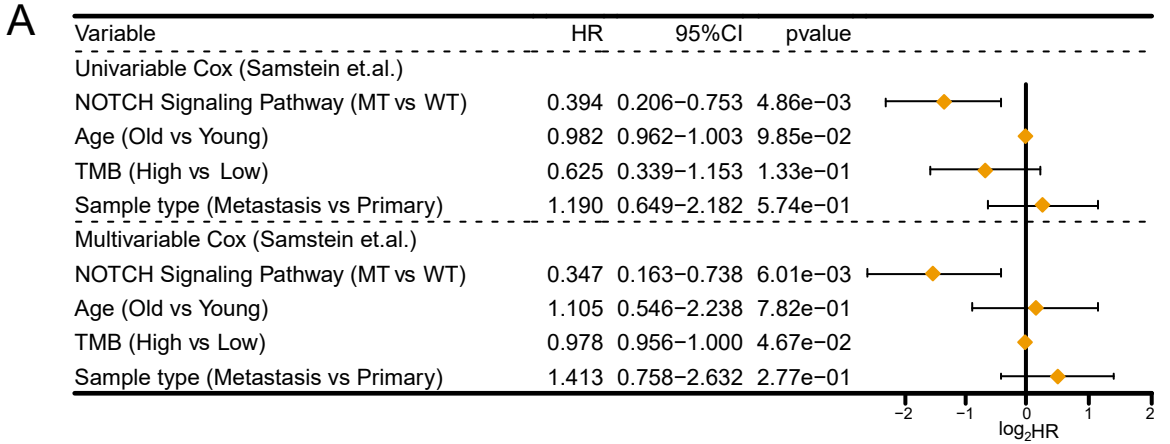
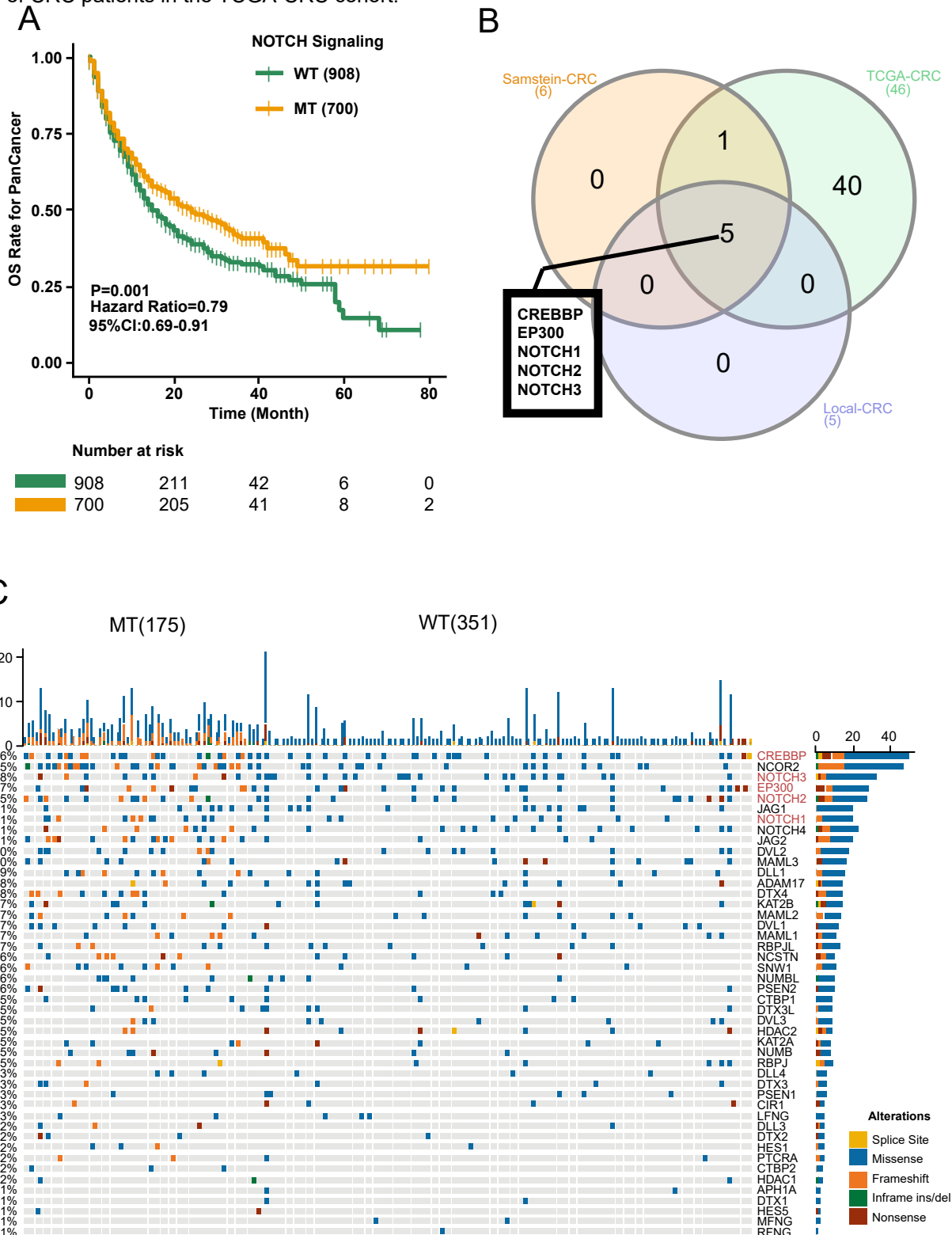


Supplementary Figure 1. Univariate and multivariate Cox regression analysis results in the ICI-treated cohort.

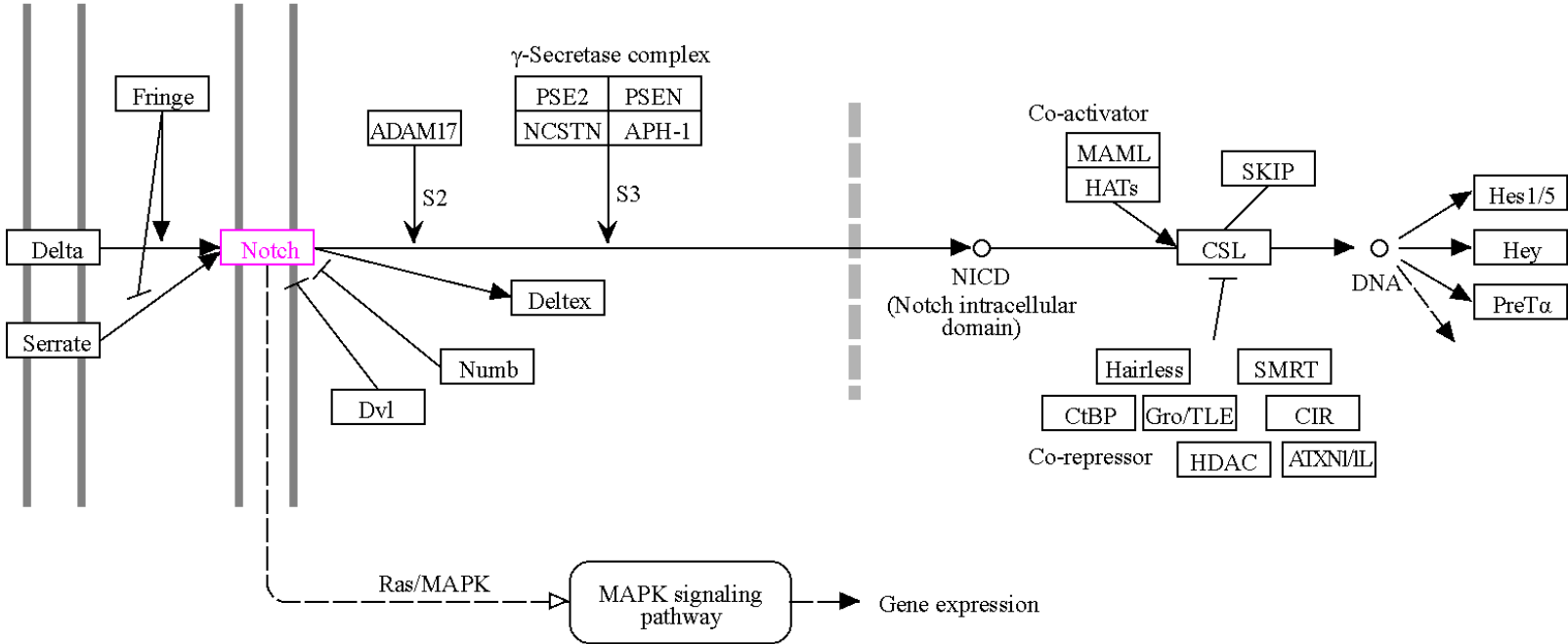


Supplementary Figure 2. (A) KM survival curves for OS rate among patients in the OSR cohort. **(B)** Shared genes in the NOTCH pathway gene set among the 3 cohorts. **(C)** Genomic profiles of CRC patients in the TCGA-CRC cohort.



Supplementary Figure 3. The signalling principle of the NOTCH signalling pathway.

NOTCH SIGNALING PATHWAY



Supplementary Table 1. Solid Tumour Clinical 680 Genes Full List.

Schedule 1: Solid Tumor Clinical 680 Genes Full List

<i>ABCB1</i> (NM_000927)	<i>KMT2B</i> (NM_014727)
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<i>AREG</i> (NM_001657)	<i>KIF1B</i> (NM_015074)
<i>ATR</i> (NM_001184)	<i>KLF4</i> (NM_004235)
<i>ABCC1</i> (NM_004996)	<i>KMT2C</i> (NM_170606)
<i>ACVR1</i> (NM_001105)	<i>KRT15</i> (NM_002275)
<i>ALK</i> (NM_004304)	<i>KDM6A</i> (NM_021140)
<i>ATRIP</i> (NM_130384)	<i>KIF5B</i> (NM_004521)
<i>ARID1A</i> (NM_006015)	<i>KLLN</i> (NM_001126049)
<i>ABCC11</i> (NM_032583)	<i>KMT2D</i> (NM_003482)
<i>ADCY2</i> (NM_020546)	<i>KRT5</i> (NM_000424)
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<i>ARID1B</i> (NM_020732)	<i>LBR</i> (NM_002296)
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<i>ADH1B</i> (NM_000668)	<i>LRP2</i> (NM_004525)
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<i>AURKA</i> (NM_003600)	<i>LIG4</i> (NM_002312)
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TSHR (NM_000369)
TCEB1 (NM_005648)
TGFBR2 (NM_001024847)
TNFRSF19 (NM_018647)
TPMT (NM_000367)
TSPAN31 (NM_005981)
TERC (NR_001566)
TMEM127 (NM_017849)
TNFSF11 (NM_033012)
TRAF1 (NM_005658)
TTK (NM_001166691)
TERT (NM_198253)
TMPRSS2 (NM_001135099)
TNFSF8 (NM_001244)
TRAM2-AS1 (NR_103446)
TUBB1 (NM_030773)
TET1 (NM_030625)
TNF (NM_000594)
TOP1 (NM_003286)
TREX2 (NM_080701)
TYMS (NM_001071)
TET2 (NM_017628)
TNFAIP3 (NM_006290)
TOP2A (NM_001067)
TSC1 (NM_000368)
U2AF1 (NM_006758)
UBE2A (NM_003336)
UBE2I (NM_003345)
UBE2V2 (NM_003350)
UGT1A1 (NM_000463)
UGT1A4 (NM_007120)
UGT1A6 (NM_001072)
UGT1A9 (NM_021027)
VEGFA (NM_001025366)
VEGFC (NM_005429)
VHL (NM_000551)
WAS (NM_000377)
WIF1 (NM_007191)
WNK2 (NM_006648)
WNT5B (NM_032642)
WRN (NM_000553)
WT1 (NM_024426)
XPB1 (NM_005080)
XPA (NM_000380)
XPC (NM_004628)

IFNL2(NM_172138) *XPO1*(NM_003400)
IKBKE(NM_001193321) *XRCC1*(NM_006297)
IL23R(NM_144701) *XRCC2*(NM_005431)
IRF4(NM_001195286) *XRCC4*(NM_022406)
JUN(NM_002228) *YAP1*(NM_006106)
KCNJ5(NM_000890) *YES1*(NM_005433)
KDR(NM_002253) *ZBTB16*(NM_006006)
KIT(NM_000222) *ZNF367*(NM_153695)
KMT2A(NM_001197104) *ZNF423*(NM_001271620)
KRAS(NM_004985) *ZNF750*(NM_024702)
KDM5A(NM_001042603) *KEAP1*(NM_012289) *ZRSR2*(NM_005089)
KLC1(NM_001130107)

Note: The detection range covers the entire coding region of 528 genes and the adjacent introns \pm 20bp, and part of the region of 152 genes. Gene names followed the rules of the HUGO Gene Nomenclature Committee (HGNC); gene transcripts were selected using the Locus Reference Genomic.

Supplementary Table 2. Baseline characteristics of 109 CRC patients (ICI-treated CRC cohort).

	NOTCH Signaling MT (N=52)	NOTCH Signaling WT (N=57)	Overall (N=109)	p value
factor(Gender)				
Female	23 (44.2%)	25 (43.9%)	48 (44.0%)	1
Male	29 (55.8%)	32 (56.1%)	61 (56.0%)	
factor(SAMPLE_TYPE)				
Metastasis	30 (57.7%)	29 (50.9%)	59 (54.1%)	0.5667
Primary	22 (42.3%)	28 (49.1%)	50 (45.9%)	
factor(Drug_Type)				
Combination	3 (5.8%)	7 (12.3%)	10 (9.2%)	0.2565
CTLA4	1 (1.9%)	0 (0%)	1 (0.9%)	
PD-1/PDL-1	48 (92.3%)	50 (87.7%)	98 (89.9%)	
TMB				
Mean (SD)	48.4 (44.9)	7.37 (5.89)	26.9 (37.3)	1.4e-07*
Median [Min, Max]	45.4 [1.97, 204]	6.14 [1.97, 44.8]	7.90 [1.97, 204]	
Age				
Mean (SD)	55.8 (13.4)	52.9 (13.7)	54.3 (13.5)	0.22
Median [Min, Max]	58.5 [25.0, 82.0]	53.0 [19.0, 81.0]	56.0 [19.0, 82.0]	

Supplementary Table 3. Baseline characteristics of CRC patients (TCGA-CRC cohort).

	NOTCH Signaling MT (N=175)	NOTCH Signaling WT (N=351)	Overall (N=526)	P value
factor(Gender)				
female	92 (52.6%)	158 (45.0%)	250 (47.5%)	0.1153
male	83 (47.4%)	193 (55.0%)	276 (52.5%)	
factor(TNM_Stage)				
I	29 (16.6%)	59 (16.8%)	88 (16.7%)	0.006791*
II	81 (46.3%)	109 (31.1%)	190 (36.1%)	
III	45 (25.7%)	107 (30.5%)	152 (28.9%)	
IV	17 (9.7%)	59 (16.8%)	76 (14.4%)	
Missing	3 (1.7%)	17 (4.8%)	20 (3.8%)	
factor(Ethnicity)				
hispanic or latino	2 (1.1%)	3 (0.9%)	5 (1.0%)	1
not hispanic or latino	113 (64.6%)	219 (62.4%)	332 (63.1%)	
Missing	60 (34.3%)	129 (36.8%)	189 (35.9%)	
factor(Disease)				
COAD	137 (78.3%)	256 (72.9%)	393 (74.7%)	0.2021
READ	38 (21.7%)	95 (27.1%)	133 (25.3%)	
Age				
Mean (SD)	66.3 (13.5)	66.0 (12.5)	66.1 (12.8)	0.7
Median [Min, Max]	68.0 [33.0, 90.0]	68.0 [31.0, 90.0]	68.0 [31.0, 90.0]	

Supplementary Table 4. Baseline characteristics of 103 CRC patients (Local-CRC cohort).

	NOTCH Signaling MT (N=27)	NOTCH Signaling WT (N=75)	Overall (N=103)	p value
factor(MSI_Status)				
MSI-H	1 (3.7%)	5 (6.7%)	6 (5.8%)	
MSI-L	1 (3.7%)	4 (5.3%)	5 (4.9%)	0.8739
MSS	25 (92.6%)	60 (80.0%)	86 (83.5%)	
Missing	0 (0%)	6 (8.0%)	6 (5.8%)	
TMB				
Mean (SD)	9.63 (19.8)	6.55 (14.3)	7.37 (15.9)	
Median [Min, Max]	4.61 [0, 99.3]	3.29 [0, 87.5]	3.95 [0, 99.3]	0.01451*
Missing	0 (0%)	0 (0%)	1 (1.0%)	

Supplementary Table 5. The genes in NOTCH pathway.

KEGG_NOTCH_SIGNALING_PATHWAY

ADAM17	JAG1
APH1A	JAG2
CIR1	KAT2A
CREBBP	KAT2B
CTBP1	LFNG
CTBP2	MAML1
DLL1	MAML2
DLL3	MAML3
DLL4	MFNG
DTX1	NCOR2
DTX2	NCSTN
DTX3	NOTCH1
DTX3L	NOTCH2
DTX4	NOTCH3
DVL1	NOTCH4
DVL2	NUMB
DVL3	NUMBL
EP300	PSEN1
HDAC1	PSEN2
HDAC2	PSENE1
HES1	PTCRA
HES5	RBPJ
	RBPJL
	RFNG
	SNW1