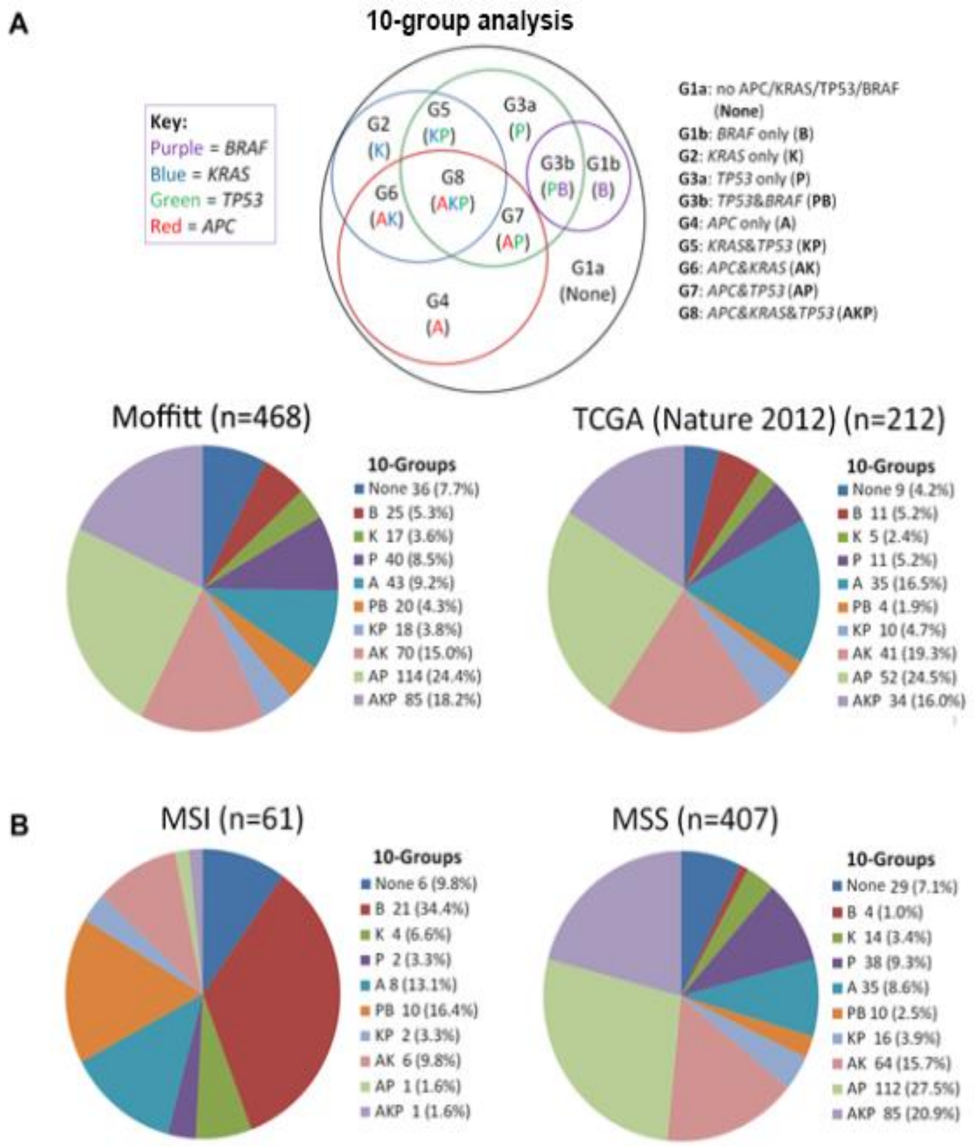
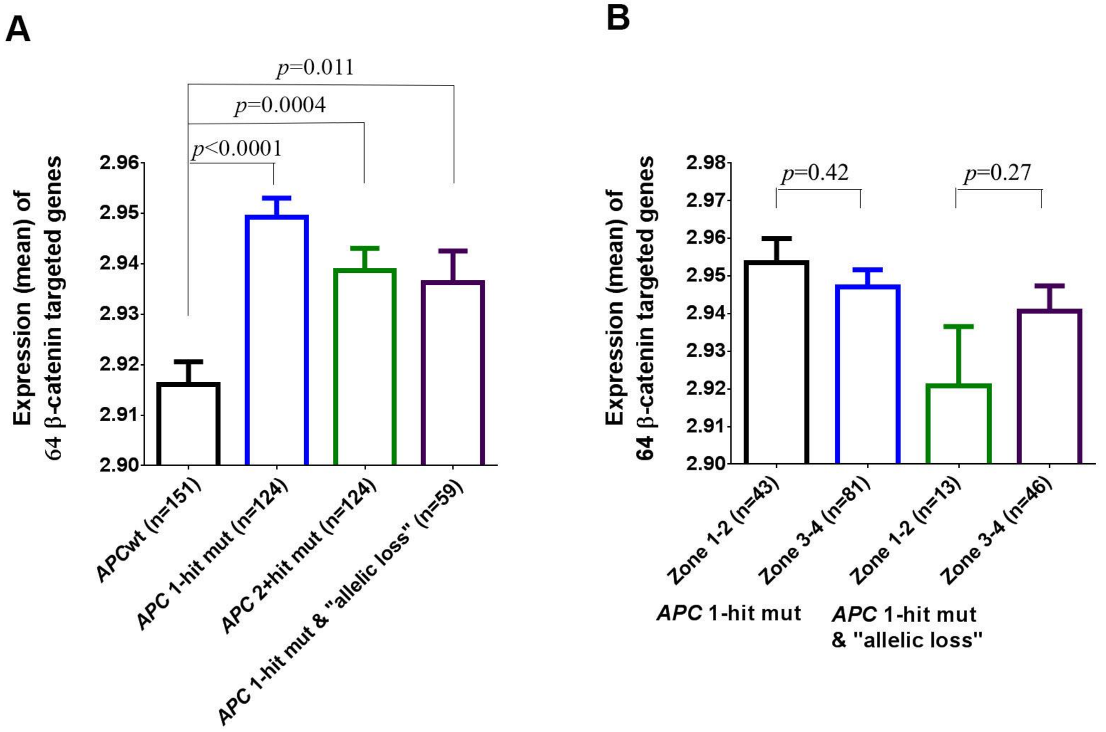
SUPPLEMENTARY FIGURES

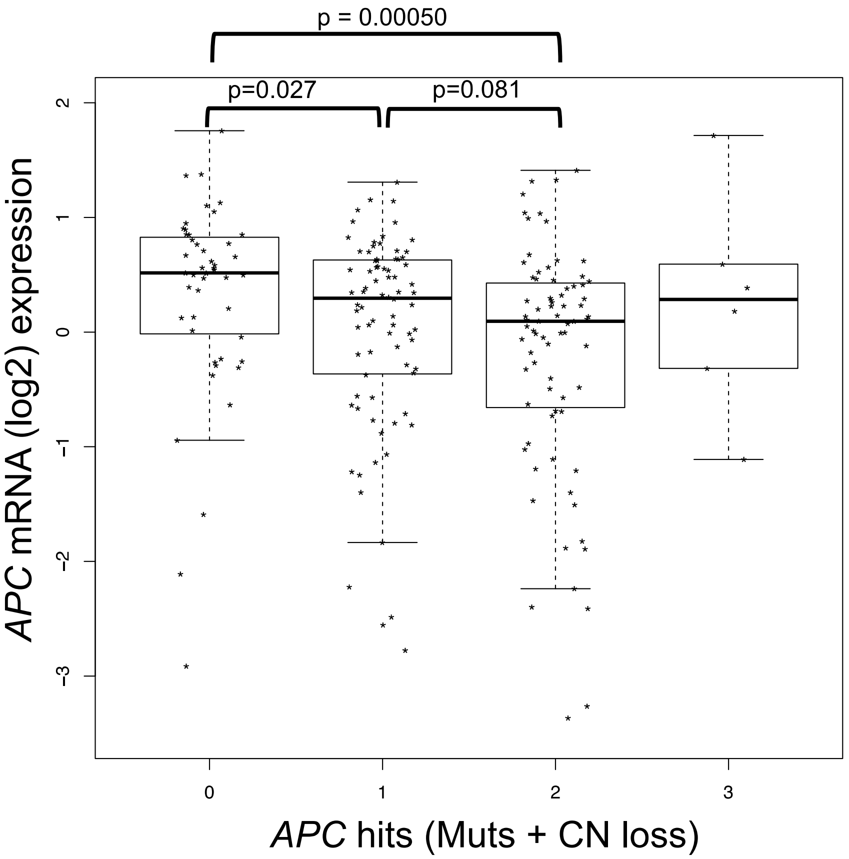


Supplementary Figure 1. The 10-group analysis of colorectal cancer. 10 groups were formed according to the pairwise, statistically significant, positive or negative correlations between somatic mutations of four driver genes *APC*, *KRA*S, *TP53* and *BRAF*. Presence or absence of *APC*, *KRAS*, and *TP53* mutations would define eight possible combinatorial groups; *BRAF*-mutated tumors only comprise two additional significant groups (i.e. *BRAF* only and *TP53* &

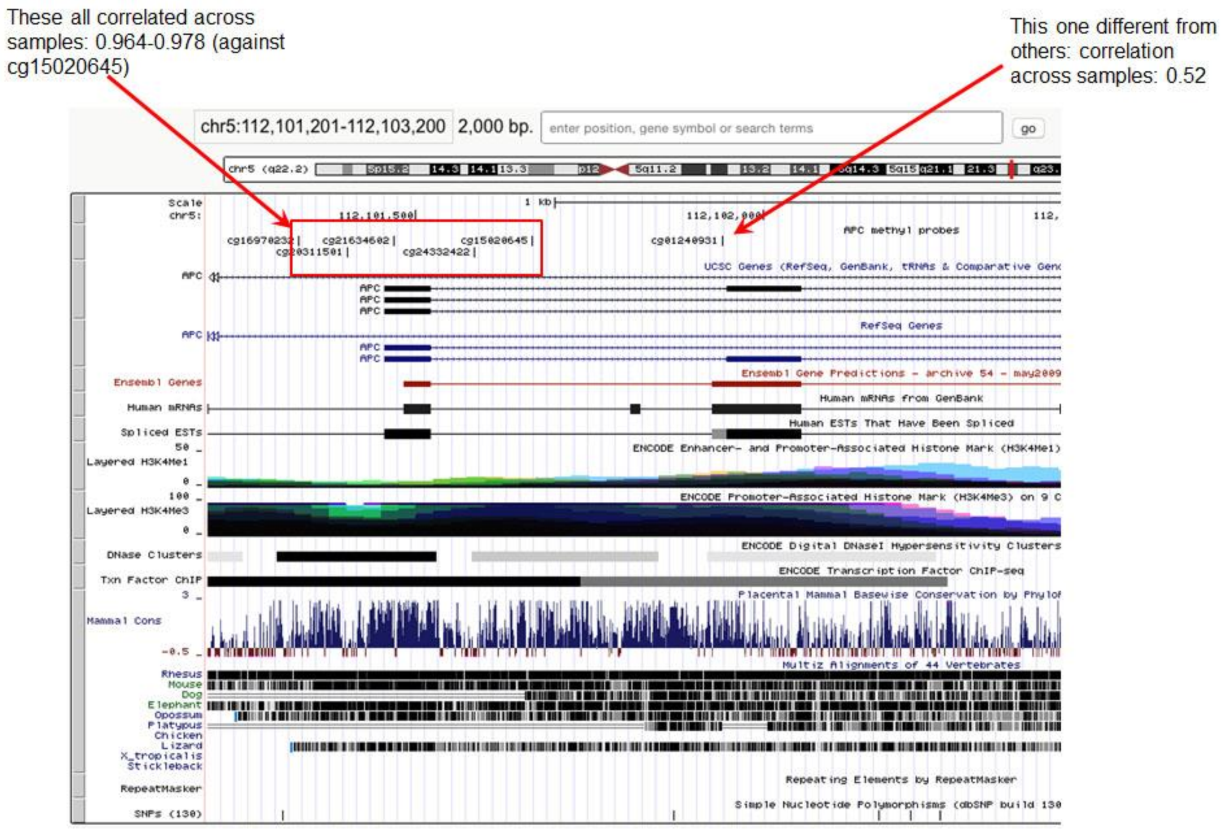
BRAF), given its strong anti-associations with *KRAS* (with which it did not co-occur), and *APC*. Notably, a significant relationship between *BRAF* and *TP53* was also reported by another group [1]. "None" – a group of tumors not having the four driver mutations in our analysis. (**A)** The distribution of *APC*, *KRAS*, *TP53* and/or *BRAF* mutations in each group in the Moffitt (n = 468) and TCGA (n = 212) [2] datasets. (**B)** The mutation distribution in each group in the Moffitt MSI (n = 61) and MSS (n = 407) tumors.



Supplementary Figure 2. Expression of β-catenin targeted genes in *APC* groups (n=458, 10 samples without suitable microarray data were excluded from 468 CRCs). (**A**) The mean mRNA (log2) expression of 64 β-catenin targeted genes [3] relative to each of four *APC* subgroups. (**B**) Comparison of expression of WNT targets between zone 1-2 mutations and zone 3-4 mutations in *APC* one mutation tumors without or with inferred allelic loss. Error bars represent standard errors (SEM). *p* values were obtained from two-tailed, unequal variance Welch *t* test.



Supplementary Figure 3. *APC* mRNA expression by derived hits in TCGA CRCs [2] for which 209 samples had data of mutation, CNA and RNAseq expression. The mean of log2 rpkm was used for mRNA expression of *APC*. CN loss represents copy number loss. *p* values were obtained by the exact Wilcoxon rank sum test. The bolded horizontal lines indicate the median value, the top and bottom box edge indicate the third and first quartiles, respectively, and the whiskers indicate the most extreme data point no more than 1.5 times the interquartile range.



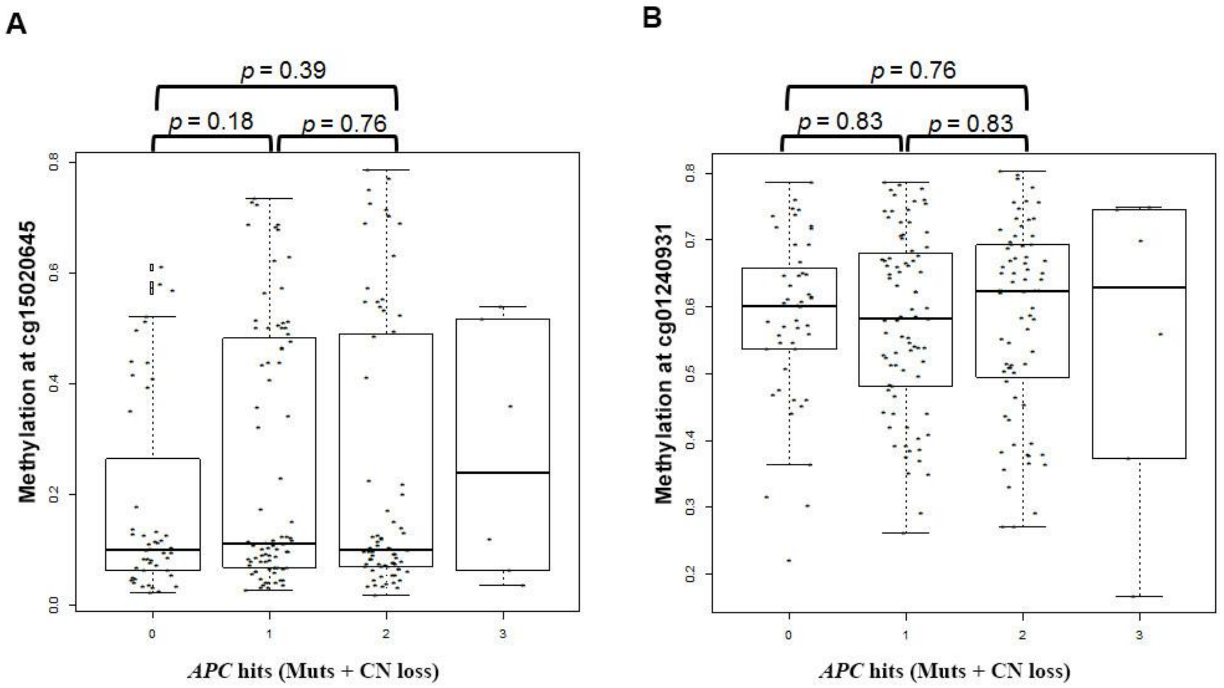
These all correlated across samples: 0.964-0.978 (against cg15020645)

This one different from others: correlation across samples: 0.52

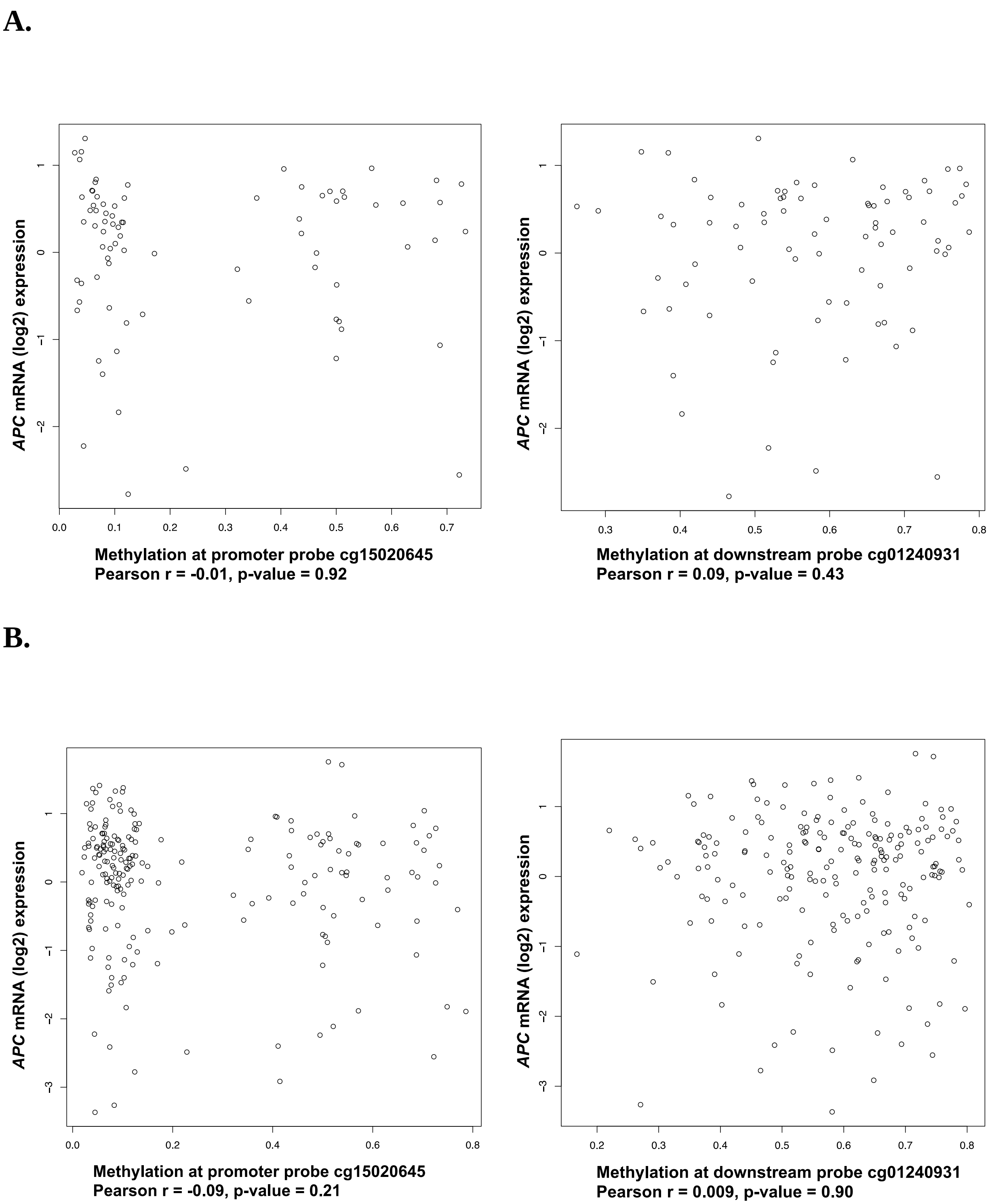
chr5:112,101,201-112,103,200 2,000 bp.

Supplementary Figure 4. *APC* methylation probes used in TCGA CRCs [2].

A UCSC Genome browser (http://genome.ucsc.edu/) illustrating the location of 6 APC methylation probes relative to the gene model itself. Note that 5 probes localize to the gene start, and 1 probe is localized further into the gene body.

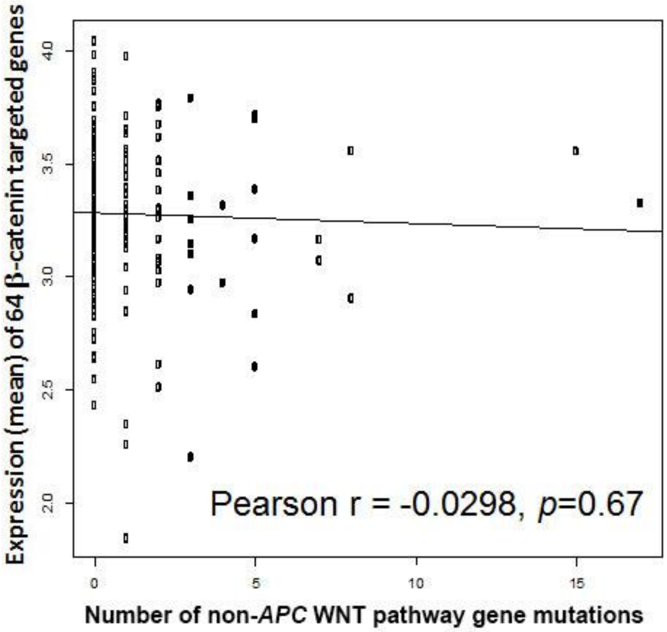


Supplementary Figure 5. ***APC*** **methylation by derived hits in TCGA CRCs** [2]. (**A**) *APC* probe cg15020645 (promoter region). (**B**) *APC* probe cg01240931 (within gene). CN loss represents copy number loss. *p* values were obtained by exact Wilcoxon rank sum test. The bolded horizontal lines indicate the median value, the top and bottom box edge indicate the third and first quartiles, respectively, and the whiskers indicate the most extreme data point no more than 1.5 times the interquartile range.

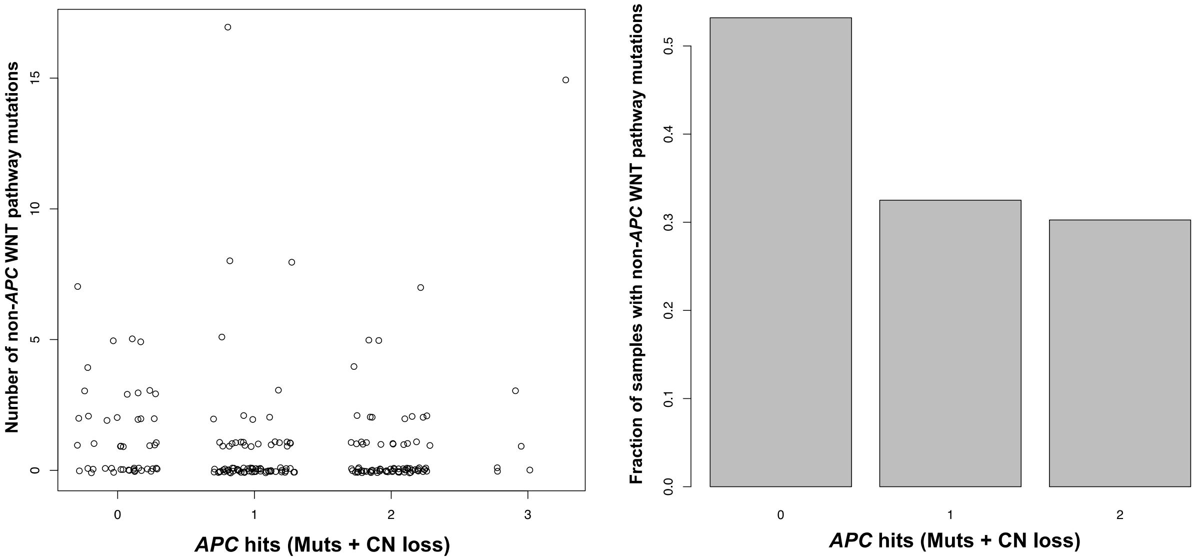


Supplementary Figure 6. ***APC* expression versus methylation in TCGA CRCs** [2].

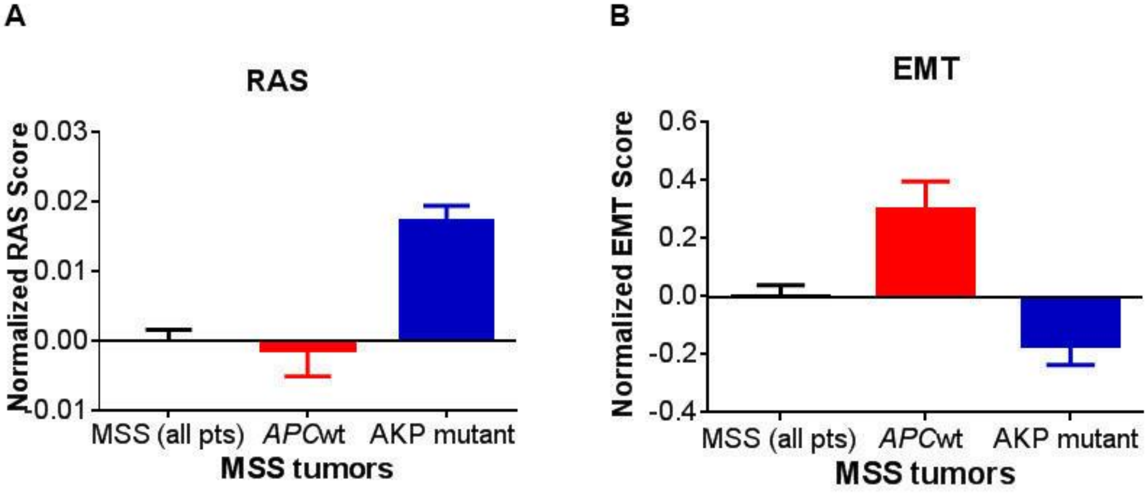
(A) 1-hit samples. (B) All samples. No significant correlation was observed for either probe in either 1-hit or all samples.



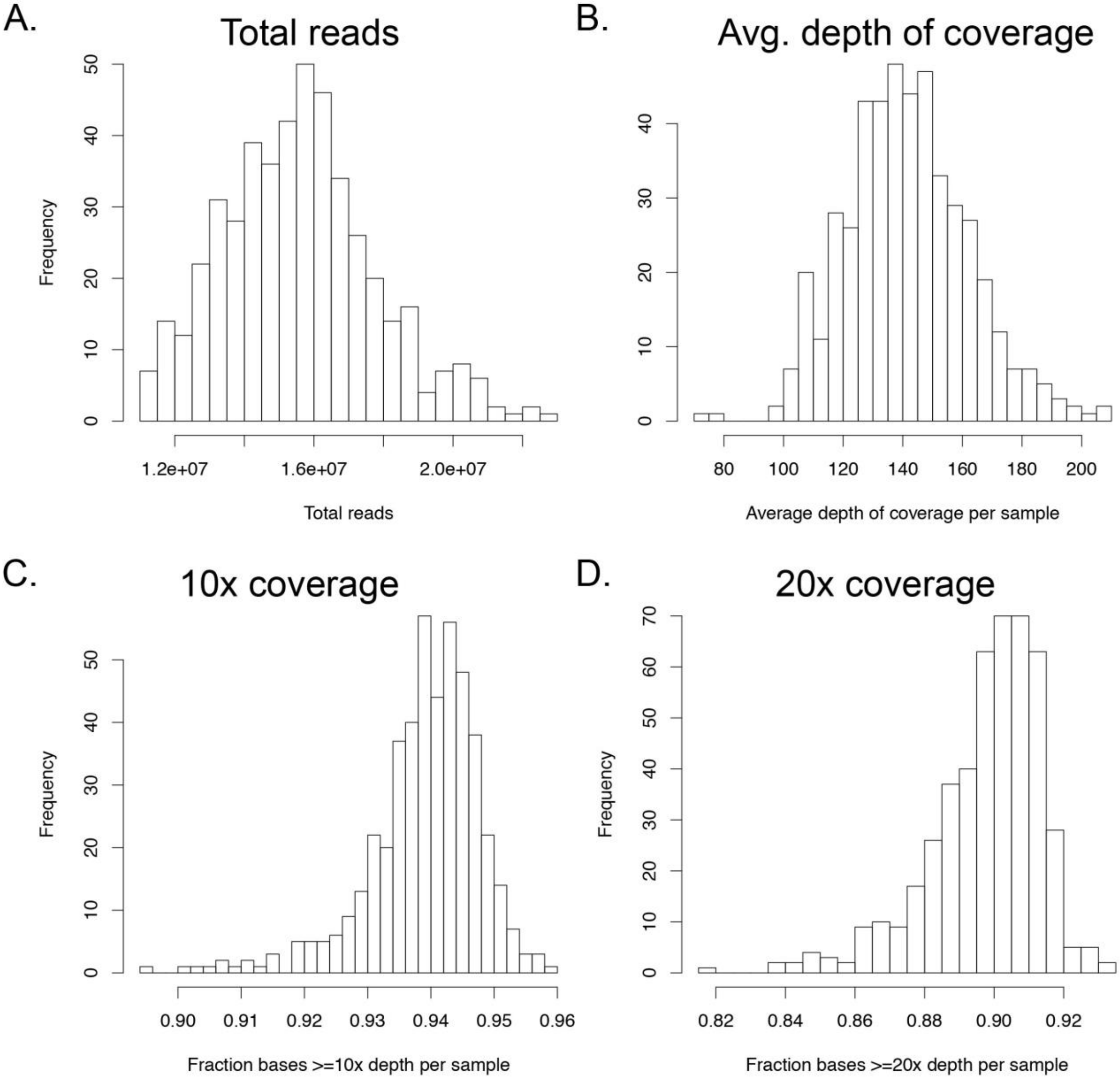
Supplementary Figure 7. Correlation of the expression of the 64 β-catenin targeted genes [3] versus the number of non-*APC* WNT pathway gene mutations (63 genes examined) in TCGA CRCs [2]. The mean of log2 rpkm was used for mRNA expression of the 64 genes.



Supplementary Figure 8. non-*APC* WNT pathway gene mutations (63 genes examined) across derived hits in TCGA CRCs [2]. Left: Number of non-*APC* WNT pathway mutations observed in each *APC* hit class. Right: Fraction of samples with non-*APC* WNT pathway mutations in each *APC* hit class.



Supplementary Figure 9. Comparison of the RAS_AZ [4] (A) or EMT [5] (B) signature scores between MSS tumors containing wild type *APC* (n=156) and the AKP (*APC*, *KRAS*, *TP53*) triple mutant (n=85). The scores were normalized by the average scores of all 407 MSS tumors (from total 468 all patient samples) which were used as references and set to be zero. Error bars represent standard errors (SEM). The two-tailed, unequal variance Welch *t* test was used to assess the statistical significance of comparison, $p<0.0001$ for both RAS/MAKP and EMT scores as compared between *APC*wt and AKP mutant groups.



Supplementary Figure 10. Sequencing metrics. (**A**) Distribution of total sequenced reads across sample. (**B**) Distribution of average final depth of coverage. (**C**) Distribution of fraction targeted bases covered by >=10 reads (**D**) >=20 reads.

SUPPLEMENTARY TABLES (Supplementary Tables 2 and 8 are attached as separate EXCEL files)

Supplementary Table 1. List of 1321 genes in targeted gene sequencing

ABCA1	ABCA3	ABCB1	ABCC2	ABCC3	ABCC4	ABL1	ABL2
ACAP1	ACVR1B	ACVR2A	ADA	ADAM17	ADAM29	ADAM33	ADAMTS18
ADAMTS20	ADAMTSL3	ADCY1	ADCY9	ADH7	ADHFE1	ADORA2A	ADORA2B
ADRA1A	ADRB3	AFF4	AKAP6	AKAP9	AKT1	AKT1S1	AKT2
AKT3	ALK	ALOX12B	ALOX15	ALPK2	ALPK3	ALS2	ANAPC5
ANKRD32	ANO1	APAF1	APBB1IP	APC	APC2	APEX1	APOB
AR	ARAF	ARAP3	AREG	ARFRP1	ARHGAP26	ARHGAP29	ARHGAP6
ARHGEF11	ARHGEF12	ARID1A	ARID3A	ARNT	ARRB1	ASXL1	ATG10
ATG12	ATG16L1	ATG16L2	ATG2B	ATG4D	ATG5	ATG9B	ATM
ATOH1	ATP8B1	ATR	ATRX	AURKA	AURKB	AURKC	AXIN1
AXIN2	AXL	AZI2	BAD	BAI1	BAI2	BAI3	BAK1
BAP1	BARD1	BAT1	BAX	BAZ1A	BBC3	BCAT1	BCL10
BCL11A	BCL2	BCL2A1	BCL2L1	BCL2L11	BCL2L14	BCL2L15	BCL2L2
BCL3	BCL6	BCL9	BCL9L	BCORL1	BCR	BECN1	BID
BIK	BIRC2	BIRC3	BIRC5	BIRC6	BIRC7	BLM	BMF
BMI1	BMP2	BMP4	BMPR1A	BMPR1B	BMPR2	BMX	BNIP3
BOK	BPTF	BRAF	BRCA1	BRCA2	BRD2	BRD3	BRIP1
BTG2	BTK	BTRC	BUB1	C10orf137	C12orf63	C1orf144	C9orf96
CA12	CA9	CABLES1	CAD	CALCR	CALCRL	CARD11	CASC5
CASK	CASP2	CASP8	CASP9	CAV1	CBFA2T3	CBL	CBLB
CBLC	CBX4	CBX7	CBX8	CCBP2	CCDC63	CCDC82	CCKAR
CCKBR	CCL18	CCL2	CCL8	CCNA1	CCNA2	CCND1	CCND2
CCND3	CCNDBP1	CCNE1	CCNE2	CCR3	CCR5	CD14	CD22
CD248	CD33	CD34	CD4	CD44	CD79A	CD79B	CD8A
CDC25A	CDC25B	CDC25C	CDC42	CDC42BPA	CDC42BPB	CDC6	CDC7
CDC73	CDH1	CDH11	CDH2	CDH20	CDH5	CDK1	CDK12
CDK19	CDK2	CDK4	CDK5	CDK6	CDK7	CDK8	CDK9
CDKL2	CDKN1A	CDKN1B	CDKN1C	CDKN2A	CDKN2B	CDKN2C	CDKN2D
CDKN3	CDS1	CEBPA	CELSR1	CELSR2	CENPF	CEP110	CES3
CHD5	CHD8	CHEK1	CHEK2	CHIC2	CHKA	CHKB	CHRNA3
CHRNA5	CHRNB4	CHUK	CIC	CLSPN	CLTC	CLU	CMAS
CNTD2	CNTN1	COL11A1	COL14A1	COL1A1	COL7A1	CREBBP	CRHR1
CRKL	CRLF2	CSDA	CSF1R	CSK	CSMD3	CSNK1G2	CTDP1
CTNNA1	CTNNB1	CTNND2	CTSH	CUBN	CX3CR1	CXCR4	CXorf30
CYB5D2	CYLD	CYP1B1	CYP2C19	CYP2C8	CYP2D6	CYP3A4	CYP3A5
DAB2	DAXX	DBF4	DBF4B	DBN1	DCC	DCLK3	DCLRE1C
DDB1	DDB2	DDIT3	DDR1	DDR2	DDX1	DDX10	DDX11
DGKA	DGKB	DGKG	DGKZ	DIP2C	DIS3	DKK1	DLC1
DLG1	DLL1	DLL3	DLL4	DNAH8	DNAJC24	DNMT1	DNMT3A
DNMT3B	DNTT	DOK1	DOT1L	DPYSL4	DTX1	DUSP1	DUSP10
DUSP14	DUSP2	DUSP4	DUSP5	DUSP6	DUSP9	DYRK2	E2F1
E2F3	E4F1	ECT2	EEF2K	EGF	EGFL6	EGFR	EGLN1
EIF2AK1	EIF4E	ELK1	ELK3	ELP2	ENPP2	EP300	EP400
EPHA1	EPHA10	EPHA2	EPHA3	EPHA4	EPHA5	EPHA6	EPHA7
EPHA8	EPHB1	EPHB2	EPHB3	EPHB4	EPHB6	EPO	ERBB2
ERBB3	ERBB4	ERC1	ERCC2	ERCC3	ERCC4	ERCC5	ERCC6
EREG	ERG	ERGIC3	ERN1	ERN2	ERRFI1	ESR1	ESR2
ETS1	ETS2	ETV1	ETV4	ETV5	ETV6	EVC2	EWSR1
EXOC2	EXOC4	EXT1	EXT2	EZH2	F2RL2	FADD	FAM123B
FAM46A	FANCA	FANCB	FANCC	FANCD2	FANCE	FANCF	FANCG
FANCL	FANCM	FAS	FASLG	FASN	FBXL6	FBXO10	FBXO32
FBXW7	FCGR3A	FEN1	FER	FES	FGF10	FGF19	FGF2
FGF3	FGF4	FGFR1	FGFR2	FGFR3	FGFR4	FH	FHIT
FIGF	FKTN	FLI1	FLNB	FLT1	FLT3	FLT4	FN1
FOS	FOSL1	FOXL2	FOXM1	FOXO1	FOXO3	FOXP3	FOXP4
FPR3	FRMD7	FSCB	FSCN1	FURIN	FUT4	FYN	FZD10
G3BP2	GAB1	GAB2	GAB3	GABARAPL1	GABPA	GADD45G	GATA1
GEN1	GLI1	GLI3	GLP1R	GLS	GNA11	GNAQ	GNAS
GOLIM4	GPC5	GPR124	GPR81	GPR84	GRB10	GRB2	GRIN2A

GRK5 *GRM1* *GRM3* *GRM5* *GRM6* *GRM7* *GRM8* *GSK3A*
GSK3B *GSPT1* *GSTP1* *GSTT1* *GSX2* *GTPBP4* *GUCY1A2* *GUCY2F*
HAPLN1 *HCCS* *HCRTR2* *HDAC1* *HDAC2* *HDAC4* *HDAC9* *HDLBP*
HECW1 *HECW2* *HERC1* *HERC3* *HERC6* *HES1* *HES4* *HES5*
HES6 *HES7* *HEY1* *HEY2* *HEYL* *HGF* *HIF1A* *HIP1*
HIPK2 *HLA-A* *HMGA1* *HMGA2* *HNF1A* *HOXA3* *HOXA9* *HOXD13*
HRAS *HRK* *HSD11B1* *HSD17B2* *HSF1* *HSP90AA1* *HSP90AB1* *HSPA2*
HUS1 *ICK* *ID1* *IDH1* *IDH2* *IGF1* *IGF1R* *IGF2*
IGF2R *IGFBP1* *IGFBP2* *IGFBP3* *IGFBP4* *IGFBP5* *IGFBP6* *IGFBP7*
IGFBPL1 *IKBIP* *IKBKAP* *IKBKB* *IKBKE* *IKBKG* *IKZF1* *IKZF3*
IL12A *IL12B* *IL1B* *IL21R* *ILF3* *ILK* *ING4* *INHBA*
INPP4A *INPP4B* *INPP5A* *INPPL1* *INSR* *INSRR* *IQGAP1* *IRAK2*
IRAK3 *IRAK4* *IRF4* *IRS1* *IRS2* *IRS4* *ITCH* *ITGA10*
ITGA9 *ITGAL* *ITGAV* *ITGB2* *ITGB3* *ITGB4* *ITK* *ITPA*
ITPR1 *ITPR2* *ITPR3* *ITSN2* *JAG1* *JAG2* *JAK1* *JAK2*
JAK3 *JUN* *JUNB* *KAT2B* *KCNH8* *KDM1A* *KDM4C* *KDM5A*
KDM5C *KDM6A* *KDR* *KEAP1* *KIAA0182* *KIAA1409* *KIF16B* *KISS1*
KIT *KLF6* *KNTC1* *KRAS* *KSR1* *KSR2* *KTN1* *LAMC1*
LAMP1 *LARGE* *LATS1* *LATS2* *LCK* *LCP1* *LDHA* *LDHB*
LEF1 *LGALS7* *LGR5* *LHCGR* *LIG3* *LIG4* *LMO2* *LPHN1*
LPHN2 *LPHN3* *LRP1* *LRP1B* *LRP5* *LRP6* *LRRC10* *LRRC7*
LRRK2 *LRRN3* *LTA* *LTBP1* *LTBR* *LTF* *LTK* *LYN*
MACF1 *MAG* *MAGI1* *MAGI2* *MAGI3* *MAMDC4* *MAN1B1* *MAP1LC3A*
MAP1LC3B *MAP1LC3C* *MAP2K1* *MAP2K2* *MAP2K4* *MAP2K6* *MAP2K7* *MAP3K1*
MAP3K11 *MAP3K14* *MAP3K2* *MAP3K5* *MAP3K6* *MAP3K8* *MAP3K9* *MAP4K4*
MAPK1 *MAPK10* *MAPK13* *MAPK3* *MAPK7* *MAPK8* *MAPK8IP2* *MAPK8IP3*
MAPK9 *MAPKAP1* *MAPT* *MARK1* *MARK4* *MAS1* *MAS1L* *MAST4*
MCHR2 *MCL1* *MCM3AP* *MCPH1* *MDC1* *MDK* *MDM2* *MDM4*
MECOM *MEF2C* *MELK* *MEN1* *MERTK* *MET* *MEX3B* *MGA*
MGC42105 *MGMT* *MICAL1* *MINK1* *MITF* *MKNK1* *MKNK2* *MKRN3*
MLH1 *MLH3* *MLL* *MLL2* *MLL3* *MLL4* *MLLT6* *MMP16*
MMP2 *MMP8* *MMP9* *MN1* *MOS* *MPL* *MRE11A* *MS4A1*
MSH2 *MSH3* *MSH4* *MSH6* *MSN* *MST1R* *MTHFR* *MTM1*
MTMR3 *MTOR* *MUC1* *MUC16* *MUC4* *MUTYH* *MYB* *MYBL1*
MYBL2 *MYC* *MYCL1* *MYCN* *MYD88* *MYEOV* *MYH1* *MYH11*
MYH9 *MYLK2* *MYO1B* *MYST4* *N4BP2* *NBN* *NCAM1* *NCDN*
NCK1 *NCK2* *NCOA2* *NCOA7* *NEDD4L* *NEIL3* *NEK10* *NEK11*
NEK2 *NEK7* *NEK8* *NEK9* *NF1* *NF2* *NFATC3* *NFKB1*
NFKB2 *NFKBIB* *NFKBID* *NFKBIE* *NFKBIZ* *NGFR* *NIN* *NIPBL*
NKD2 *NKX2-1* *NLE1* *NLK* *NLRP1* *NLRP3* *NLRP5* *NLRP8*
NMUR2 *NOS1* *NOS2* *NOTCH1* *NOTCH2* *NOTCH3* *NOTCH4* *NOV*
NPM1 *NPY2R* *NPY5R* *NQO1* *NR0B1* *NRARP* *NRAS* *NRBP1*
NRG2 *NRK* *NRP2* *NTRK1* *NTRK2* *NTRK3* *NUAK1* *NUAK2*
NUMB *NUMBL* *NUP153* *NUP214* *NUP98* *OBSCN* *ODZ1* *OR8G1*
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PDIA4 *PDK1* *PDK3* *PDPK1* *PDZRN4* *PEA15* *PER1* *PERP*
PES1 *PFKFB1* *PFKFB2* *PFKFB3* *PFKFB4* *PGR* *PHB* *PHF14*
PHF20 *PHLPP1* *PHLPP2* *PHOX2B* *PIAS1* *PIK3C2A* *PIK3C2B* *PIK3C2G*
PIK3C3 *PIK3CA* *PIK3CB* *PIK3CD* *PIK3CG* *PIK3R1* *PIK3R2* *PIK3R3*
PIM1 *PIM2* *PKHD1* *PKM2* *PKMYT1* *PKN3* *PLA2G4A* *PLAG1*
PLAGL1 *PLAT* *PLAU* *PLCB1* *PLCB4* *PLCG1* *PLCG2* *PLCH1*
PLD1 *PLD2* *PLXNB3* *PMAIP1* *PML* *PMS2* *POLE* *POLL*
POLM *POLN* *POLQ* *POU1F1* *PPARA* *PPARG* *PPARGC1A* *PPM1D*
PPM1H *PPM1L* *PPP1CC* *PPP1R3A* *PPP2R1A* *PPP2R2B* *PPP2R3A* *PRDM16*
PRDM5 *PREX1* *PREX2* *PRKAA1* *PRKAA2* *PRKAB1* *PRKAB2* *PRKACA*
PRKACB *PRKACG* *PRKAG1* *PRKAG2* *PRKAG3* *PRKAR1A* *PRKCA* *PRKCD*
PRKCE *PRKCG* *PRKCH* *PRKCI* *PRKCZ* *PRKD1* *PRKD2* *PRKDC*
PRRC2C *PSEN1* *PSEN2* *PTCH1* *PTCH2* *PTEN* *PTGFR* *PTGS2*
PTK2 *PTK2B* *PTP4A3* *PTPN1* *PTPN11* *PTPN12* *PTPN13* *PTPN14*
PTPN21 *PTPN22* *PTPN3* *PTPN5* *PTPN6* *PTPN9* *PTPRC* *PTPRD*
PTPRF *PTPRG* *PTPRJ* *PTPRS* *PTPRT* *PTPRU* *PXN* *PYGO2*
RAC1 *RAD18* *RAD21* *RAD50* *RAD51* *RAD51C* *RAD54B* *RAF1*
RALA *RALB* *RALGAPA1* *RAP1A* *RAP1GDS1* *RAPGEF2* *RAPH1* *RARA*
RASA1 *RASA2* *RASA3* *RASGRF1* *RASGRF2* *RASGRP1* *RASSF1* *RB1*
RB1CC1 *RBBP4* *RBL1* *RBL2* *RBP2* *RBPJ* *RECQL4* *REG4*
REL *RELA* *RELB* *RET* *REV1* *REV3L* *RFC1* *RFC4*
RFC5 *RFX2* *RGL1* *RGL2* *RHEB* *RHOBTB2* *RICTOR* *RIF1*

RING1 RIPK1 RIPK4 RNF123 RNF213 ROBO1 ROBO2 ROCK1
ROCK2 ROR1 ROR2 ROS1 RPL10 RPL36A RPS6 RPS6KA1
RPS6KA2 RPS6KA3 RPS6KA4 RPS6KA5 RPS6KA6 RPS6KB1 RPS6KB2 RPTOR
RRAS2 RRM2B RUNX1 RUNX1T1 RYK SDHB SDHC SDHD
SENP6 SERPINB5 SESN2 SETD2 SFN SFRP1 SFRP2 SGK1
SGK2 SGK3 SGK494 SH3GLB1 SHC1 SIK1 SIRT1 SIRT6
SIX4 SKP2 SLC17A5 SLC19A1 SLC22A2 SLC2A1 SLC2A3 SLC2A4
SLC4A4 SLC6A18 SLC6A2 SLCO1B3 SMAD2 SMAD3 SMAD4 SMAD7
SMARCA4 SMARCB1 SMC6 SMG1 SMO SMYD2 SNAI1 SNAI2
SNAI3 SNX13 SOCS1 SOD2 SORL1 SOS1 SOS2 SOX10
SOX11 SOX2 SPEG SPEN SPO11 SPOP SPRED1 SPRY1
SPRY2 SPTAN1 SRC SRF SRPK2 SRSF6 STAT1 STAT3
STAT4 STAT5A STAT5B STIL STIM1 STK11 STK19 STK32B
STK32C STK33 STK36 STMN1 STMN3 STON2 STYK1 SUFU
SULT1A1 SUZ12 SYK SYNE1 SYNE2 TAB3 TACR3 TAF15
TAF1L TAL1 TANK TBCK TBK1 TBKBP1 TBX22 TCF12
TCF3 TCF4 TCF7L2 TDG TEC TECTA TEK TERT
TET2 TEX14 TFDP1 TFE3 TFEB TGFB1 TGFB2 TGFB3
TGFBR1 TGFBR2 THBS1 THEM4 THRAP3 TIAM1 TICAM1 TICAM2
TK1 TLE4 TLN1 TLR2 TLR3 TLR4 TLR7 TMEFF2
TMEM132B TMEM161A TMPRSS2 TMPRSS6 TNF TNFAIP3 TNFRSF10A TNFRSF10B
TNFRSF11A TNFRSF1A TNFRSF8 TNFSF11 TNK2 TNKS TNKS2 TNNI3K
TNPO1 TNPO3 TOP1 TOP2A TOP2B TOPBP1 TP53 TP53AIP1
TP53BP1 TP63 TP73 TPD52 TPMT TPO TRADD TRAF1
TRAF2 TRAF3 TRAF4 TRAF5 TRAF6 TRAF7 TRIB3 TRIM24
TRIM28 TRIM33 TRIM36 TRIM37 TRIM47 TRIO TRIP11 TRRAP
TSC1 TSC2 TSHR TSPAN31 TTBK2 TTK TTN TUBD1
TWF2 TWIST1 TYK2 UBA1 UBASH3B UBP1 UBR4 UBR5
UGT1A1 UHRF1BP1L ULK1 ULK2 ULK3 UMPS UPP1 USP24
USP28 USP33 USP34 USP42 USP43 USP5 USP54 USP6NL
USP7 USP8 USP9X UVRAG VAV1 VEGFA VEGFC VEPH1
VHL VPS13B VRTN WEE1 WHSC1 WIF1 WNK1 WNK2
WNK4 WNT1 WNT10B WNT2 WNT2B WNT4 WNT9B WRN
WSB1 WT1 WWP2 XBP1 XIAP XPA XPC XRCC1
XRCC2 XRCC3 XRCC5 XRCC6 YWHAQ ZAP70 ZBTB16 ZC3H12B
ZEB1 ZEB2 ZMYM2 ZMYM4 ZNF148 ZNF217 ZNF384 ZNF442
ZNF831

Supplementary Table 2. Comparison of Moffitt and TCGA Non-Silent Mutation Rates

	Moffitt		TCGA		Pct	Fisher
Gene	Pts	(%)	Pts	(%)	Diff	p-value
KRAS	190	(41)	90	(42)	-1	.67
TP53	277	(59)	111	(52)	7	.11
*HLA-A**	84	(18)	4	(2)	16	$1.4\text{x}10^{-10}$
APC	329	(70)	162	(76)	-6	.12
SMAD4	55	(12)	29	(14)	-2	.53
FBXW7	57	(12)	35	(17)	-5	.11
*MUC4**	242	(52)	5	(2)	50	$1.1\text{x}10^{-43}$
BRAF	60	(13)	22	(10)	-3	.45
TCF7L2	45	(10)	30	(14)	-4	.087
PIK3CA	71	(15)	43	(20)	-5	.12
GNAS	45	(10)	23	(11)	-1	.68
TAF1L	56	(12)	18	(8)	4	.19
CSMD3	84	(18)	31	(15)	3	.32
LRP1B	95	(20)	37	(17)	3	.40
*OBSCN**	148	(32)	15	(7)	25	$1.1\text{x}10^{-13}$
*SYNE1**	157	(34)	45	(21)	13	.0011
*TTN**	321	(69)	78	(37)	32	$9.5 \text{ x } 10^{-15}$
*CBX4**	28	(6)	1	(0.5)	6	.0003
*ITGB4**	45	(10)	4	(2)	8	.0002
ADAMTS18	43	(9)	12	(6)	3	.13
FAM123B	46	(10)	24	(11)	-1	.59
*MUC16**	187	(40)	35	(17)	23	$4.8 \text{ x } 10^{-10}$

Note: TCGA data based on 212 samples [2].

* Genes that have substantially lower frequencies (*p*<0.01 in TCGA)

Supplementary Table 3. Demographic features of 10 groups of CRC

Frequencies and percentages of right tumor, stages, MSI, metastasis, and "developing" metastasis in 10 groups

								Stage %		Devel.
Group	Name	N	Md Age	% Right	No. MSI (%)	Mets (%)	1-2	3	4	Mets
1a	None	35	65	43	6 (17)	10 (29)	51	26	23	6
1b	B	25	**77** ↑	**84** ↑	**21 (84)** ↑	**3 (12)** ↓	64	24	12	0
2	K	18	67	50	4 (22)	9 (50)	39	22	39	11
3a	P	40	69	41	2 (5)	9 (22)	47	42	**11** ↓	12
3b	BP	20	**75** ↑	60	**10 (50)** ↑	6 (30)	55	15	30	0
4*	A	43	68	37	8 (19)	10 (23)	56	30	14	9
5	KP	18	70	50	2 (11)	8 (44)	33	39	28	17
6	AK	70	66	44	6 (9)	25 (36)	51	23	26	10
7*	AP	113	**60** ↓	**21**↓	**1 (1)** ↓	41 (36)	39	36	25	12
8	AKP	86	65	45	**1 (1)** ↓	**44 (51)** ↑	24	47	29	22
Total		468	66	41	61 (13)	165 (35)	43	33	24	11

Percentages of each of 10 groups and MSI by Primary Location

					Group^					
Location	N	B/BP	None	K/KP	P	A	AK	AP	AKP	MSI
Cecum	65	8	3	9	8	11	22	**12** ↓	**28** ↑	15
Ascend Rt	100	**25** ↑	8	10	9	8	10	**11** ↓	19	**31** ↑
Transverse	26	12	**19** ↑	8	8	4	27	19	4	**31** ↑
Descend Lt	32	3	3	9	9	6	22	28	19	9
Sigmoid	131	6	6	6	10	9	11	**34** ↑	18	**4** ↓
Rectosig	40	2	2	2	12	8	18	**42** ↑	12	**2** ↓
Rectum	70	**3** ↓	**14** ↑	9	3	14	16	24	17	**6** ↓
Overall	464	10	8	8	8	9	15	24	17	13

Notes:
A = *APC*, K = *KRAS*, P = *TP53*, B = *BRAF.* None = none of the 4 genes are mutated.
* Groups 4 and 7 include 3 and 5 patients with BRAF(*V600E*) mutations, respectively.
^ Groups B and BP, and K and KP were combined together, as their location distrubutions were similar, and their counts were rather low when separated.
AKP muts represents the number of partnering mutations (A, K or P).
There is significantly higher or lower observation than expectation: ↑(↓) for p<0.05; ↑↑(↓↓) for p<0.01; ↑↑↑(↓↓↓) for p<0.001; based on individual chi-square (X^2) contribution from the table cell;
Devel. Mets = Percent of non-stage 4 patients in class who had distant metastasis at tissue collection.

Overall, the median age was 66, 41% had right-sided tumors, 13% were MSI and 35% had distant metastases. The *BRAF* groups (B, BP) (10%) were older, had more right-sided tumors, and higher MSI rates. Only 8 tumors had *BRAF* and *APC* mutations (5 also had *TP53* mutations) and were thus placed into groups 4 and 7; three and one of them were MSI-H, respectively. Group 7 (AP) tumors (24%) were younger, had higher left-sided and MSS rates, while Group 8 (AKP) tumors (18%) were more often MSS and distantly metastatic.

Supplementary Table 4. Association between *KRAS* and *TP53* by *APC* mutation status

A. *APC*mut tumors (N=312)

		*TP53*wt	*TP53*mut	Total
	Group	AK	AKP	
*KRAS*mut	Observed	70	85	155
	Expected	56.1	98.9	
	Group	A	AP	
*KRAS*wt	Observed	43	114	157
	Expected	56.9	100.1	
Total		113	199	312

Pearson r = - 0.18; Fisher p-value = 0.0005

B. *APC*wt tumors (N=156)

		*TP53*wt	*TP53*mut	Total
	Group	K	KP	
*KRAS*mut	Observed	17	18	35
	Expected	17.5	17.5	
	Group	B, Unk	P, BP	
*KRAS*wt	Observed	61	60	121
	Expected	60.5	60.5	
Total		78	78	156

Pearson r = -0.02; Fisher p-value = 0.71

Notes: A = *APC*, K = *KRAS*, P = *TP53*, B = *BRAF*, Unk = tumors with unknown drivers
AKP = mutations in *APC*, *KRAS*, and *TP53;*
The negative association between *KRAS* and *TP53*, however, appears to be induced by the mathematics of the 2×2 table, which requires that the under-representation of *APC*-only tumors be matched in the AKP group.

Supplementary Table 5. *APC* truncation mutation profiles and related other gene mutations

barcode	zone1-2	Zone3-4	Biallelic_loss	msi_high	WNT_ pathway	CTNN	WNT	FAM123B	MACF1	TCF7L2	AXIN1	CDH1	GSK3B	WIF1	TCF4
DS-40207	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-48717	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-48788	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-48888	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-49422	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-49449	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-49454	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-49513	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-49664	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-49843	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-49844	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-50544	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-50587	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-50607	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-50712	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-50740	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-51020	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-51043	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-51610	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-51652	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-51809	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-51948	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-51995	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-53059	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-53114	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-53116	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-53211	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-53230	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-53303	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-53317	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-53324	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-53359	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-53460	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-53489	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-53528	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-53679	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

DS-53750	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-53783	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-53800	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-53957	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-54043	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-54051	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-54054	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-54730	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-54783	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-54833	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-55343	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-55398	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-56069	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-56330	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-56334	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-56551	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-56604	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-57046	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-57048	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-57055	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-57433	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-57616	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-58510	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-58532	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-59213	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-67098	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-67931	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-52005	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0
DS-52925	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0
DS-53117	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0
DS-54038	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0
DS-54189	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0
DS-48894	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0
DS-51972	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0
DS-52367	0	0	0	0	1	0	0	0	0	0	0	0	1	0	0
DS-50597	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0
DS-50631	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0
DS-50925	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0
DS-51754	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0
DS-54223	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0
DS-54289	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0
DS-54405	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0
DS-54718	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0

DS-54926	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0
DS-56142	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0
DS-56635	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0
DS-57052	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0
DS-59550	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0
DS-59556	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0
DS-59974	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0
DS-48937	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0
DS-58843	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0
DS-57472	0	0	0	0	1	0	0	0	0	1	0	1	0	0	0
DS-48055	0	0	0	0	1	0	0	0	0	1	1	0	0	0	0
DS-56979	0	0	0	0	1	0	0	0	1	1	0	0	0	0	1
DS-48957	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0
DS-51877	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0
DS-53682	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0
DS-33635	0	0	0	0	1	0	0	1	1	0	0	0	0	0	0
DS-67984	0	0	0	0	1	0	0	1	1	0	0	0	0	0	0
DS-48893	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0
DS-52126	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0
DS-52847	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0
DS-53053	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0
DS-53168	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0
DS-54564	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0
DS-49315	0	0	0	0	1	0	1	0	1	0	0	0	0	0	0
DS-50620	0	0	0	0	1	0	1	0	1	0	0	0	0	0	0
DS-55411	0	0	0	0	1	0	1	0	1	0	0	0	0	0	0
DS-49208	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0
DS-53516	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0
DS-54031	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0
DS-54362	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0
DS-56796	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0
DS-58478	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0
DS-48639	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
DS-50754	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
DS-53382	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
DS-51155	0	0	0	1	1	0	0	0	0	0	0	1	0	0	0
DS-51783	0	0	0	1	1	0	0	0	0	0	0	1	0	0	0
DS-53730	0	0	0	1	1	0	0	0	0	0	0	0	0	1	0
DS-51711	0	0	0	1	1	0	0	0	0	0	0	1	0	1	0
DS-48913	0	0	0	1	1	0	0	0	1	0	0	0	0	0	0
DS-51827	0	0	0	1	1	0	0	0	1	0	0	0	0	0	0
DS-54750	0	0	0	1	1	0	0	0	1	0	0	0	0	0	0
DS-56351	0	0	0	1	1	0	0	0	1	0	0	0	0	0	0

DS-56820	0	0	0	1	1	0	0	0	1	0	0	0	0	0	0
DS-51215	0	0	0	1	1	0	0	0	1	0	0	1	0	0	0
DS-51893	0	0	0	1	1	0	0	0	1	0	0	0	1	0	0
DS-50760	0	0	0	1	1	0	0	1	1	0	0	0	0	0	0
DS-50817	0	0	0	1	1	0	0	1	1	0	0	0	0	0	0
DS-48658	0	0	0	1	1	0	0	1	1	0	1	0	0	0	1
DS-51942	0	0	0	1	1	0	0	1	0	1	0	1	0	0	0
DS-49669	0	0	0	1	1	0	1	0	0	0	0	0	0	0	0
DS-53687	0	0	0	1	1	0	1	0	0	0	0	0	0	0	0
DS-55390	0	0	0	1	1	0	1	0	0	0	0	0	0	0	0
DS-49665	0	0	0	1	1	0	1	0	0	0	0	0	0	0	1
DS-56326	0	0	0	1	1	0	1	0	0	0	0	1	0	0	0
DS-48712	0	0	0	1	1	0	1	0	1	0	0	0	0	0	0
DS-53232	0	0	0	1	1	0	1	0	1	0	0	0	0	0	0
DS-48909	0	0	0	1	1	0	1	0	1	0	0	1	0	0	0
DS-52929	0	0	0	1	1	0	1	0	1	0	1	0	0	0	0
DS-53945	0	0	0	1	1	0	1	1	1	0	0	0	0	0	0
DS-48645	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0
DS-49373	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0
DS-51584	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0
DS-51798	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0
DS-51982	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0
DS-53731	0	0	0	1	1	1	0	0	0	0	0	1	0	0	0
DS-50258	0	0	0	1	1	1	0	0	1	0	0	0	0	0	0
DS-50698	0	0	0	1	1	1	0	0	1	0	0	0	0	0	0
DS-51671	0	0	0	1	1	1	0	0	1	0	0	0	0	0	0
DS-67027	0	0	0	1	1	1	0	0	1	0	0	0	0	0	0
DS-49496	0	0	0	1	1	1	0	0	1	0	1	0	0	0	0
DS-49521	0	0	0	1	1	1	0	1	0	0	1	0	1	0	0
DS-51886	0	0	0	1	1	1	1	0	0	0	0	0	0	0	0
DS-52095	0	0	0	1	1	1	1	0	0	1	0	0	0	0	0
DS-49127	0	0	0	1	1	1	1	0	1	1	0	0	0	0	0
DS-52864	0	0	0	1	1	1	1	0	1	1	0	0	0	0	0
DS-56888	0	0	0	1	1	1	1	0	1	1	0	0	1	0	0
DS-40203	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-48595	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-48682	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-48795	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-50692	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-50851	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-51018	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-51803	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-51941	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0

DS-52121	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-52681	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-52756	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-52771	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-52790	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-52838	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-52882	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-52940	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-53052	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-53156	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-53453	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-53505	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-53835	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-54072	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-54148	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-54195	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-54327	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-54393	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-54429	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-54452	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-54556	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-54569	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-54679	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-55324	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-55383	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-56094	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-56803	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-56894	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-56962	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-57013	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-57035	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-57927	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-58258	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-67827	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-67949	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-69689	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-87910	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-67980	0	1	0	0	1	0	0	0	0	0	0	0	0	1	0
DS-53132	0	1	0	0	1	0	0	0	0	0	0	0	0	1	1
DS-51050	0	1	0	0	1	0	0	0	1	0	0	0	0	0	0
DS-53298	0	1	0	0	1	0	0	0	1	0	0	0	0	0	0
DS-53482	0	1	0	0	1	0	0	0	1	0	0	0	0	0	0
DS-67030	0	1	0	0	1	0	0	0	1	0	0	0	0	0	0

DS-48833	0	1	0	0	1	0	0	0	0	1	0	0	0	0	0
DS-49498	0	1	0	0	1	0	0	0	0	1	0	0	0	0	0
DS-50536	0	1	0	0	1	0	0	0	0	1	0	0	0	0	0
DS-51766	0	1	0	0	1	0	0	0	0	1	0	0	0	0	0
DS-52569	0	1	0	0	1	0	0	0	0	1	0	0	0	0	0
DS-53728	0	1	0	0	1	0	0	0	0	1	0	0	0	0	0
DS-48670	0	1	0	0	1	0	0	0	1	1	0	0	0	0	0
DS-50521	0	1	0	0	1	0	0	1	0	0	0	0	0	0	0
DS-50626	0	1	0	0	1	0	0	1	0	0	0	0	0	0	0
DS-52871	0	1	0	0	1	0	0	1	0	0	0	0	0	0	0
DS-52888	0	1	0	0	1	0	0	1	0	0	0	0	0	0	0
DS-53129	0	1	0	0	1	0	0	1	0	0	0	0	0	0	0
DS-54674	0	1	0	0	1	0	0	1	0	0	0	0	0	0	0
DS-54751	0	1	0	0	1	0	0	1	0	0	0	0	0	0	0
DS-56668	0	1	0	0	1	0	0	1	1	0	0	0	0	0	0
DS-53095	0	1	0	0	1	0	1	0	0	0	0	0	0	0	0
DS-53143	0	1	0	0	1	0	1	0	0	0	0	0	0	0	0
DS-68849	0	1	0	0	1	0	1	0	0	0	0	0	0	0	0
DS-49826	0	1	0	0	1	0	1	0	1	0	0	0	0	0	0
DS-67953	0	1	0	0	1	0	1	0	1	0	0	0	0	0	0
DS-53295	0	1	0	0	1	0	1	1	0	0	0	0	0	0	0
DS-48649	0	1	0	0	1	1	0	0	0	0	0	0	0	0	0
DS-49425	0	1	0	0	1	1	0	0	0	0	0	0	0	0	0
DS-56858	0	1	0	0	1	1	0	0	0	0	0	0	0	0	0
DS-57955	0	1	0	0	1	1	0	0	0	0	0	0	0	0	0
DS-59932	0	1	0	0	1	1	0	0	0	0	0	0	0	0	0
DS-51875	0	1	0	0	1	1	0	0	0	0	1	0	0	0	0
DS-58341	0	1	0	0	1	1	0	0	1	0	0	0	0	0	0
DS-50648	0	1	0	0	1	1	0	1	0	0	0	0	0	0	0
DS-53972	0	1	0	1	1	0	0	0	1	0	0	0	0	0	0
DS-51086	0	1	0	1	1	1	0	1	0	0	0	0	0	0	1
DS-52912	0	1	0	1	1	1	1	0	0	0	1	0	0	0	1
DS-44878	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-48592	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-48921	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-49637	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-49730	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-50529	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-51087	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-51527	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-51878	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-51923	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-51977	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0

DS-52111	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-52151	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-52359	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-52889	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-53661	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-54062	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-54129	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-54255	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-54355	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-54724	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-54737	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-54845	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-56118	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-56176	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-56348	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-56384	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-56964	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-57008	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-57026	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-58141	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-58440	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-60341	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-61202	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-48808	0	1	1	0	1	0	0	0	1	0	0	0	0	0	0
DS-53115	0	1	1	0	1	0	0	0	1	0	0	0	0	0	0
DS-53121	0	1	1	0	1	0	0	0	1	0	0	0	0	0	0
DS-48655	0	1	1	0	1	0	0	0	0	1	0	0	0	0	0
DS-49417	0	1	1	0	1	0	0	0	0	1	0	0	0	0	0
DS-50772	0	1	1	0	1	0	0	1	0	0	0	0	0	0	0
DS-54439	0	1	1	0	1	0	0	1	0	1	0	0	0	0	0
DS-50723	0	1	1	0	1	0	1	0	0	0	0	0	0	0	0
DS-67162	0	1	1	0	1	0	1	0	0	0	0	0	0	0	0
DS-51121	0	1	1	0	1	0	1	0	1	0	1	0	0	0	0
DS-55407	0	1	1	0	1	0	1	1	0	0	0	0	0	0	0
DS-53969	0	1	1	0	1	1	0	0	0	0	0	0	0	0	0
DS-54782	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-54928	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-67065	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-50931	0	2	0	0	1	0	0	1	0	0	0	0	0	0	0
DS-50573	0	2	0	0	1	0	1	0	0	0	0	0	0	0	0
DS-60296	0	2	0	0	1	1	0	0	0	0	0	0	0	0	0
DS-49796	0	2	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-53494	0	2	1	0	0	0	0	0	0	0	0	0	0	0	0

DS-48823	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-50568	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-50796	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-51630	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-52022	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-52131	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-52369	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-53385	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-53481	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-53736	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-54009	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-54089	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-54391	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-54697	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-55379	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-56101	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-56310	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-56626	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-56683	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-56842	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-58234	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-67013	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-70294	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-52210	1	0	0	0	1	0	0	0	0	0	0	1	0	0	0
DS-52853	1	0	0	0	1	0	0	0	0	0	0	0	1	0	0
DS-47369	1	0	0	0	1	0	0	0	1	0	0	0	0	0	0
DS-53246	1	0	0	0	1	0	0	0	1	0	0	0	0	0	0
DS-48764	1	0	0	0	1	0	0	0	0	1	0	0	0	0	0
DS-50827	1	0	0	0	1	0	0	0	0	1	0	0	0	0	0
DS-53272	1	0	0	0	1	0	0	0	0	1	0	0	0	0	0
DS-54041	1	0	0	0	1	0	0	0	0	1	0	0	0	0	0
DS-58275	1	0	0	0	1	0	0	0	0	1	0	0	0	0	0
DS-60252	1	0	0	0	1	0	0	0	0	1	0	0	0	0	0
DS-67994	1	0	0	0	1	0	0	0	0	1	0	0	0	0	0
DS-51676	1	0	0	0	1	0	0	1	0	0	0	0	0	0	0
DS-48607	1	0	0	0	1	1	0	0	0	0	0	0	0	0	0
DS-49325	1	0	0	0	1	1	0	0	0	0	0	0	0	0	0
DS-52942	1	0	0	0	1	1	0	0	0	0	0	0	1	0	0
DS-67955	1	0	0	0	1	1	0	1	1	1	0	0	0	0	0
DS-53424	1	0	0	0	1	1	1	0	0	0	0	0	0	0	0
DS-48929	1	0	0	1	1	0	1	0	1	0	0	0	0	0	0
DS-48789	1	0	0	1	1	1	0	0	0	0	0	0	0	0	0
DS-50855	1	0	0	1	1	1	0	0	0	1	0	0	0	0	0

DS-51220	1	0	0	1	1	1	0	1	0	0	0	0	0	0	0
DS-49718	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-50725	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-50739	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-51821	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-53191	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-54015	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-54589	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-56678	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-55384	1	0	1	0	1	0	0	0	1	0	0	0	0	0	0
DS-67956	1	0	1	0	1	0	0	0	1	0	0	0	0	0	0
DS-51932	1	0	1	0	1	0	0	1	0	0	0	0	0	0	0
DS-67844	1	0	1	0	1	0	1	1	1	0	0	1	0	0	0
DS-52320	1	0	1	0	1	1	0	0	0	0	0	0	0	0	0
DS-44604	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-44863	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-48739	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-48827	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-48857	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-49395	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-49435	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-49441	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-49459	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-50652	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-50685	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-50687	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-50788	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-50812	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-50890	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-51088	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-51769	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-51797	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-51997	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-51998	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-52837	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-52992	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-53055	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-53138	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-53139	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-53189	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-53408	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-53644	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-53664	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0

DS-54307	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-54363	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-54503	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-54841	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-54925	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-55355	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-55388	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-56080	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-56293	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-56397	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-56421	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-56829	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-56830	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-56949	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-57041	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-58548	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-58694	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-60313	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-67914	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-69122	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-69164	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-53249	1	1	0	0	1	0	0	0	0	0	0	1	0	0	0
DS-56740	1	1	0	0	1	0	0	0	0	0	0	1	0	0	0
DS-50805	1	1	0	0	1	0	0	0	0	0	1	1	0	0	0
DS-51028	1	1	0	0	1	0	0	0	1	0	0	0	0	0	0
DS-57686	1	1	0	0	1	0	0	0	1	0	0	0	0	0	0
DS-60353	1	1	0	0	1	0	0	0	1	0	0	0	0	0	0
DS-49685	1	1	0	0	1	0	0	0	0	1	0	0	0	0	0
DS-52122	1	1	0	0	1	0	0	0	0	1	0	0	0	0	0
DS-52232	1	1	0	0	1	0	0	0	0	1	0	0	0	0	0
DS-56376	1	1	0	0	1	0	0	0	0	1	0	0	0	0	0
DS-56608	1	1	0	0	1	0	0	0	0	1	0	0	0	0	0
DS-57829	1	1	0	0	1	0	0	0	0	1	0	0	0	0	0
DS-48778	1	1	0	0	1	0	0	0	1	1	0	0	0	0	0
DS-56309	1	1	0	0	1	0	0	0	1	1	0	0	0	0	0
DS-50248	1	1	0	0	1	0	0	1	0	0	0	0	0	0	0
DS-51528	1	1	0	0	1	0	0	1	0	0	0	0	0	0	0
DS-51679	1	1	0	0	1	0	0	1	0	0	0	0	0	0	0
DS-53146	1	1	0	0	1	0	0	1	0	0	0	0	0	0	0
DS-56302	1	1	0	0	1	0	0	1	0	0	0	0	0	0	0
DS-87902	1	1	0	0	1	0	0	1	0	0	0	0	0	0	0
DS-49375	1	1	0	0	1	0	0	1	1	0	0	0	0	0	0
DS-51680	1	1	0	0	1	0	0	1	1	0	0	0	0	0	0

DS-40199	1	1	0	0	1	0	0	1	0	1	0	0	0	0	0
DS-54552	1	1	0	0	1	0	1	0	0	0	0	0	0	0	0
DS-68634	1	1	0	0	1	0	1	0	0	0	0	0	0	0	0
DS-50283	1	1	0	0	1	0	1	0	1	0	0	0	0	0	0
DS-56660	1	1	0	0	1	0	1	0	0	1	0	0	0	0	0
DS-54437	1	1	0	0	1	0	1	1	0	0	0	0	0	0	0
DS-50613	1	1	0	0	1	1	0	0	0	0	0	0	0	0	0
DS-51984	1	1	0	0	1	1	0	0	0	0	0	0	0	0	0
DS-52979	1	1	0	0	1	1	0	0	0	0	0	0	0	0	0
DS-53487	1	1	0	0	1	1	0	0	0	0	0	0	0	0	0
DS-53710	1	1	0	0	1	1	0	0	0	0	0	0	0	0	0
DS-55364	1	1	0	0	1	1	0	0	0	0	0	0	0	0	0
DS-55377	1	1	0	0	1	1	0	0	0	0	0	0	0	0	0
DS-56140	1	1	0	0	1	1	0	0	0	0	0	0	0	0	0
DS-56963	1	1	0	0	1	1	0	0	0	0	0	0	0	0	0
DS-57006	1	1	0	0	1	1	0	0	0	0	0	0	0	0	0
DS-61205	1	1	0	0	1	1	0	0	0	0	0	0	0	0	0
DS-53198	1	1	0	0	1	1	0	0	1	0	0	0	0	0	0
DS-51531	1	1	0	0	1	1	0	1	0	0	0	0	0	0	0
DS-50720	1	1	0	1	1	0	0	0	1	0	1	0	0	0	1
DS-50877	1	1	0	1	1	0	1	0	0	0	0	0	0	0	0
DS-55003	1	1	0	1	1	1	0	0	1	0	0	0	0	0	0
DS-54758	1	1	0	1	1	1	0	0	1	1	0	0	0	0	0
DS-51156	1	1	0	1	1	1	1	0	0	0	0	0	0	0	0
DS-54160	1	1	0	1	1	1	1	1	0	0	0	0	0	0	0
DS-48725	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-49116	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-49639	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-49716	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-50896	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-56647	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-68891	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0
DS-51202	1	1	1	0	1	0	1	0	0	1	0	0	0	0	0
DS-54013	1	2	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-49695	1	3	0	0	1	0	0	0	1	1	0	1	0	1	1
DS-56867	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-56998	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-57060	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS-51918	2	0	0	0	1	0	0	0	1	0	0	0	0	0	0
DS-53725	2	0	0	0	1	0	0	0	0	1	0	0	0	0	0
DS-52815	2	0	0	1	1	0	0	0	1	0	0	0	0	0	0
DS-51952	2	0	0	1	1	1	1	1	1	1	0	0	1	1	0
DS-49699	2	1	0	0	1	1	0	0	0	0	0	0	0	0	0

DS-50776	2	1	0	0	1	1	1	1	1	0	0	0	1	1	1
DS-59919	2	1	0	1	1	1	1	1	0	1	1	0	0	0	0

Note that 0 = “No” and 1 = “Yes”.

Supplementary Table 6. Counts of *APC* truncating mutations by sample using the TCGA COAD data.

No. of *APC* truncating mutations	**0**	**1**	**2**	**3**
***APC* copy number change**	0	0	0	0
No. of samples	46	74	38	3

No. of *APC* truncating mutations	**0**	**1**	**2**
***APC* copy number change**	-1	-1	-1
No. of samples	6	32	3

No. of *APC* truncating mutations	**0**	**2**	**0**
***APC* copy number change**	+1	+1	-2
No. of samples	1	5	1

Notes: 209 total samples with somatic mutation, CAN, and expression data; 60.3% of total have 0 or 1 hits. Data downloaded from: https://tcga-data.nci.nih.gov/docs/publications/coadread_2012/

Supplementary Table 7. Immunohistochemical staining (Allred scores) of β-catenin in 52 CRCs.

Barcode	Allred scores (nuclear)	Allred scores (cyto)	Allred scores (membranous)
DS-33635	4	7	7
DS-48055	0	7	7
DS-48893	3	8	8
Ds-49315	5	8	7
DS-50925	0	7	8
DS-51043	8	8	0
DS-51652	0	6	8
DS-51982	0	7	8
DS-53114	5	8	8
DS-53211	0	7	8
DS-54051	7	8	8
DS-54564	7	7	4
DS-54783	7	7	5
DS-56326	0	6	7
DS-47369	7	8	8
DS-48607	7	8	7
DS-48764	8	8	6
DS-49826	5	7	7
DS-51803	5	8	7
DS-51941	0	5	8
DS-52210	5	7	8
DS-52681	7	6	6
DS-52790	6	7	7
DS-52838	6	6	8
DS-52853	5	7	8
DS-53453	5	7	7
DS-54041	7	8	5
DS-58258	7	6	7
DS-67955	7	7	5
DS-67980	7	6	7
DS-70294	6	7	7
DS-40199	4	7	8
DS-44878	5	8	7
DS-48857	7	8	5
DS-49796	0	7	8
DS-50687	3	6	7
DS-51797	6	7	7
DS-51977	7	7	6

DS-51997	6	7	7
DS-52151	4	7	7
DS-52320	7	8	4
DS-53191	6	5	7
DS-54129	6	7	7
DS-54363	7	6	6
DS-54589	5	7	7
DS-56376	5	7	7
DS-56963	0	7	8
DS-58341	4	6	7
DS-60296	7	6	6
DS-60353	0	7	8
DS-49639	5	8	7
Ds-56293	2	7	8

Supplemental Table 8. Five-class classification and CMS classification (N=458)

	Classes	N	%CMS1	%CMS2	%CMS3	%CMS4	%NA	%Total
0	"*APC*wt"	151	34 ↑↑↑	8 ↓↓↓	12	28	18	100
1	"A(1), A(1)K, A(1)P"	138	6 ↓↓	36 ↑	13	24	21	100
2	"A(2), A(2)K, A(2)P"	83	13	35	18	17	17	100
3	"APC(1)KP"	45	9	33	11	27	20	100
4	"APC(2)KP"	41	5	24	20	27	24	100

Note:
1) A−*APC*, K−*KRAS,* P−*TP53*
Class 0: *APC* wild type**; Class 1:** *APC(1), APC(1)*/*KRAS*, *APC(1)*/*TP53*; **Class 2:** *APC(2), APC(2)*/*KRAS*, *APC(2)*/*TP53*; **Class 3:** *APC(1)/KRAS*/*TP53*; **Class 4**: *APC(2)/KRAS*/*TP53.* While A(1) or *APC* (1) represents one *APC* mutation, A(2) or *APC* (2) represents two *APC* mutations.
2)↑(↓) for *p*<0.05; ↑↑(↓↓) for *p*<0.01; ↑↑↑(↓↓↓) for *p*<0.001; based on individual chi-square contribution from the table cell.

Supplementary Table 9. Cox model predictors of overall survival of MSS tumors (N=399) (Models 1-4)

	Model	**1**	**Model**	**2**
Covariable	**HR**	**p-value**	**HR**	**p-value**
APC			0.47	0.0008
BRAF			2.23	0.012
2 *APC* muts			1.63	0.019
AKP			1.45	0.08
Metastasis	4.44	<.0001	4.54	<.0001
AGE(≥70)	1.10	<.0001	1.09	<.0001
LR χ2	75.7	<.0001	98.8	<.0001

	Model	**3**	**Model**	**4**	**Model**	**5**
Covariable	**HR**	**p-value**	**HR**	**p-value**	**HR**	**p-value**
APC			0.52	0.003	0.62	0.015
BRAF			1.55	0.23	1.50	0.26
2 *APC* muts			1.57	0.034		
AKP			1.37	0.14		
***APC*(2)KP**					2.03	0.007
CMS1	3.48	<.0001	2.39	0.012	2.55	0.007
CMS3	1.76	0.06	1.45	0.22	1.53	0.16
CMS4	1.34	0.22	1.24	0.37	1.24	0.37
CMS_NA	1.82	0.02	1.53	0.10	1.51	0.11
Metastasis	4.99	<.0001	4.86	<.0001	4.82	<.0001
AGE(≥70)	1.09	<.0001	1.09	<.0001	1.09	<.0001
LR χ2	92.6	<.0001	105.4	<.0001	105.1	<.0001

Supplementary References

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