Supplementary Table S1. Published or potential transcription factor binding sites flanking the transcription start site of *Cnr1* (–212 to +140) in the human CB1 promoter. Two methylated CpG sites are located at transcription binding sites (-113 and +81) and three methylated CpG sites are located GAGA Box (the transcription start site) (1). Using Transcription Element Search Software (see Supplementary Footnotes), we found that a number of methylated CpG sites are located in the core sequence of the transcription factor binding sites (potential transcription factor binding sites).

Position	Transcription factor binding sites (1)	Potential Transcription factor binding sites
-179		T-Ag
-176		
-174		T-Ag, ER
-171		ER
-138		
-134		
-129		
-113	SP1, ZF9, MAZF, MZF1	SP1, ZF9, MAZF, MZF1
-111		AP-2, MIG1
-100		Sp1, E2F-1
-97		Sp1, E2F-1, MIG1, ADR1
-85		E2F1, T-Ag, CUP
-82		CUP, Adf-1, T-Ag
-79		Adf-1, T-Ag, AP-4
-47	PDX1, XBP1, MAX, ARNT, BMALL, PAX8	PDX1, XBP1, MAX, ARNT, BMALL, PAX8
-36		
-34	GAGA Box	GAGA Box
-12	GAGA Box	GAGA Box, NHP-1
+9	GAGA Box	GAGA Box
+11		
+15		
+24		T-Ag, Sp1
+36		GAGA
+38		GAGA, Ttk_88K
+42		Ttk_88K
+47		T-Ag
+52		T-Ag, F-ACT1
+55		F-ACT1, SIF, Zmhoxla
+59		Zmhoxla, GCF
+63		GCF
+71		CAC-binding_protein
+77		

+81	ZF9	ZF9
+89		AP2
+92		AP2
+101		Ttk_88K, RAV1, Sp1, GCF, ER
+108		
+110		Ttk_88K

Supplementary Figure legends

Fig. S1. CB2 expression in human colorectal tumors and CB1 expression in adenomas of *Apc*$^{Min/+}$ mice. (A-B) CB2 expression was measured by quantitative real-time PCR in 19 sets of paired human tumors and adjacent normal tissues (A) and in 10 CRC cell lines (B). In (A), the relative expression of CB2 is the average of triplicate samples normalized against the transcript levels of *hβ-actin*; in (B), data are the means ± SE of the relative expression from three independent experiments. (C) The levels of CB1 mRNA in intestinal adenoma and adjacent normal tissues from *Apc*$^{Min/+}$ mice were analyzed by quantitative real-time PCR. The relative expression of CB1 is the averages of triplicates samples against the transcript levels of *mGAPDH*. Data are represented as the mean ± SE of the relative expression from eight mice.

Fig. S2. Methylation status of the CB1 promoter in 5-aza-dC-treated CRC cell lines. After treatment of cells with 5-aza-dC, the methylation status of all 39 of the CpG sites in the *Cnr1* promoter region (-212 to +140) in three CRC cell lines was determined by bisulphite sequencing PCR as described in Fig. 2.

Fig. S3. Activation of CB1 induces apoptosis and downregulates survivin. (A) 5-aza-dC-treated HCT-116 cells as described in Fig. 1D were treated with R-1 and the apoptotic rate was measured. (B-C) LS-174T cells (B) and 5-aza-dC-treated HCT-116 cells (C)

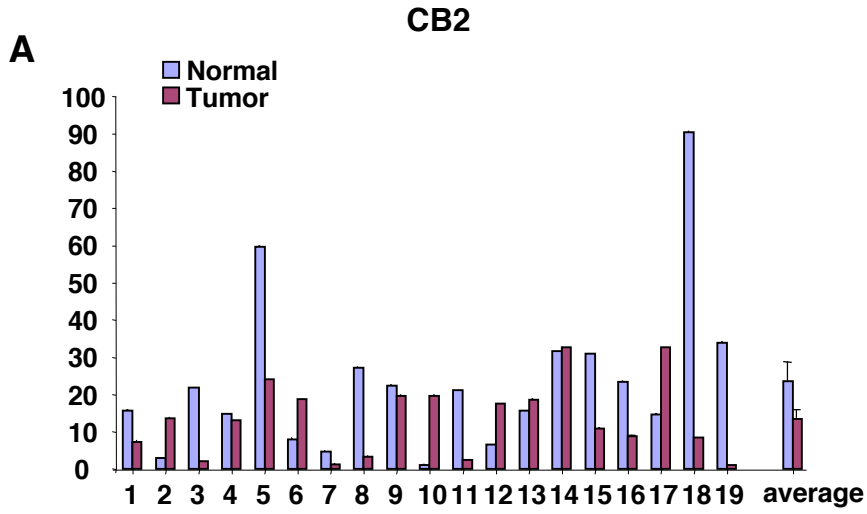
were treated with R-1 and survivin levels were measured by western blotting. (D) SW-480 cells were treated with R-1 and the levels of phosphorylated survivin, cdc-2, and β-actin were assessed by western blotting.

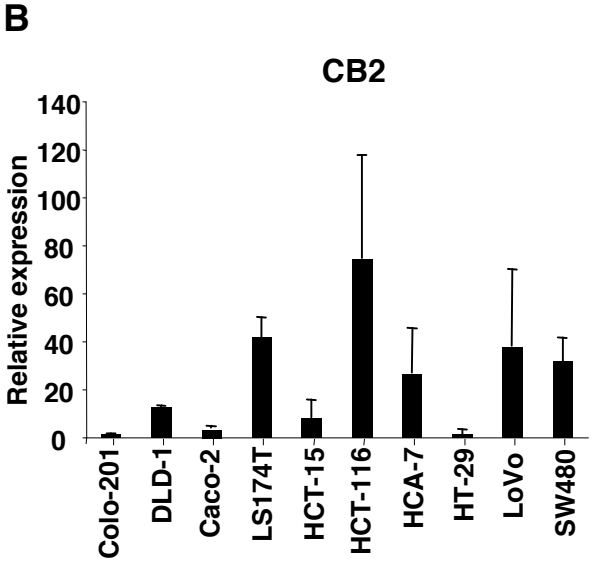
Supplementary Footnotes:

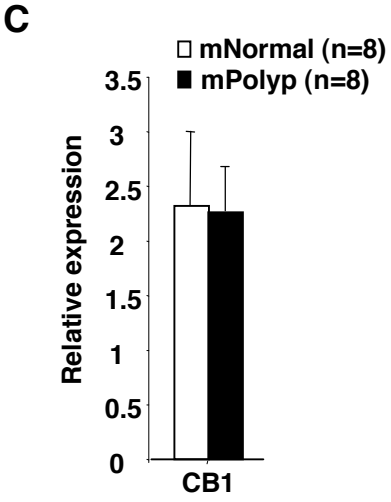
Web Transcription Element Search Software: http://www.cbil.upenn.edu/tess

Supplementary References:

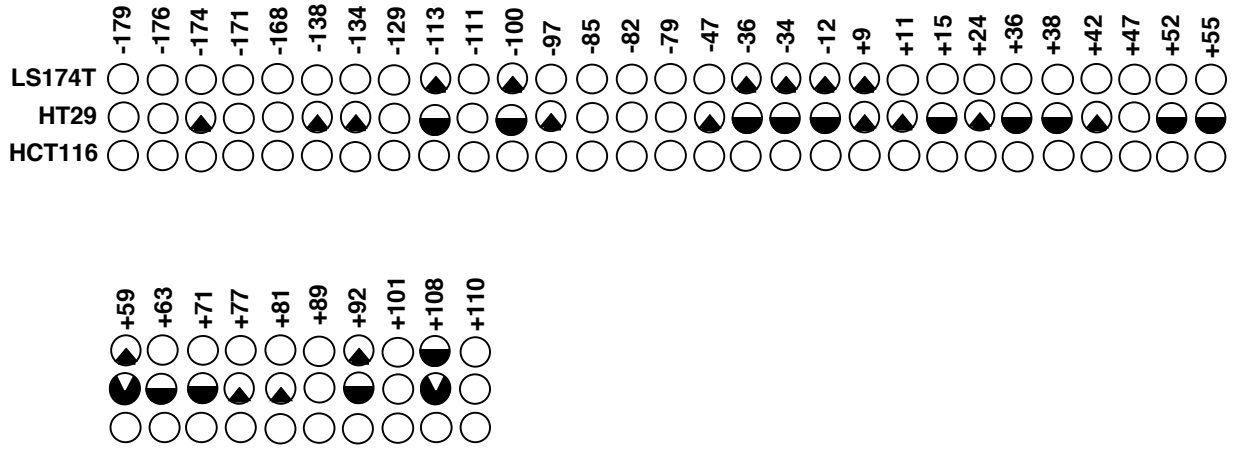
1. McCaw EA, Hu H, Gomez GT, Hebb AL, Kelly ME, and Denovan-Wright EM. Structure, expression and regulation of the cannabinoid receptor gene (CB1) in Huntington's disease transgenic mice. Eur J Biochem 2004; 271:4909-20.



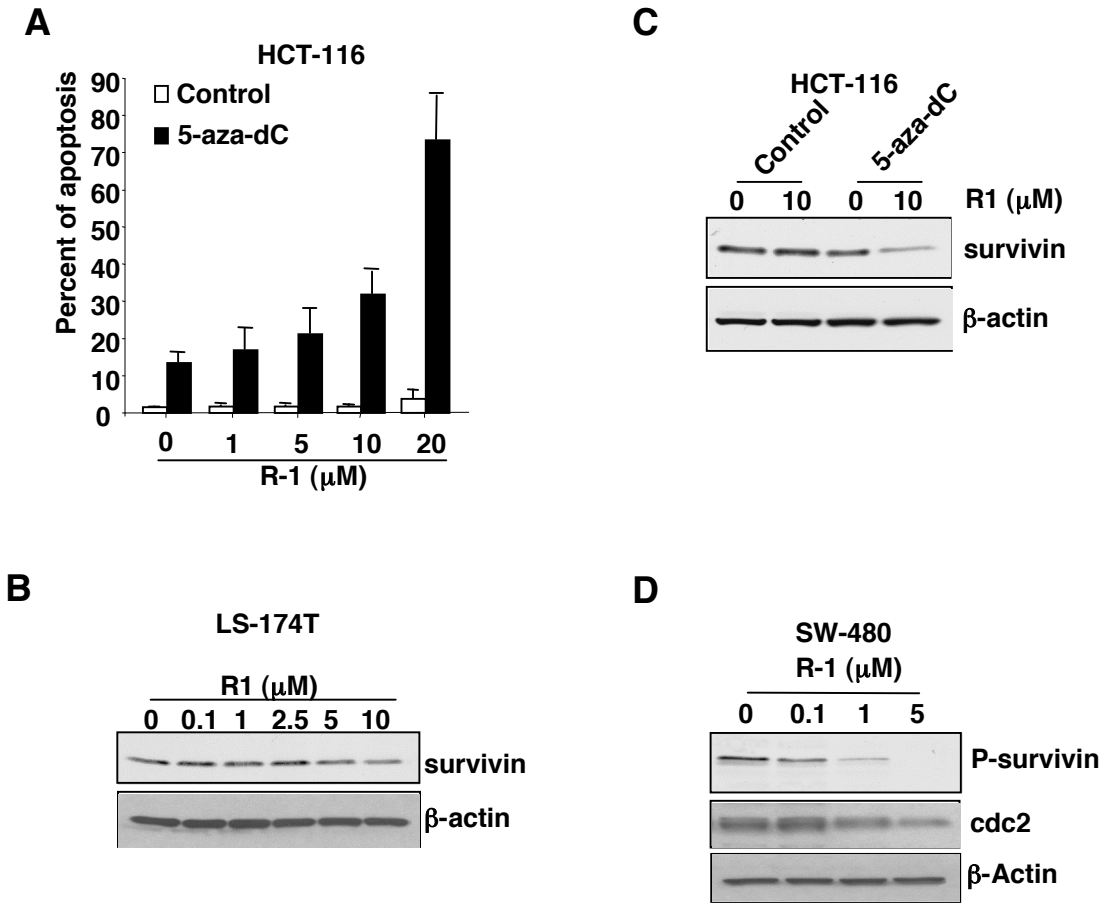




Supplementary Fig. S1



Supplementary Fig. S2



Supplementary Fig. S3