Supplementary Table 1: Clinicopathological features of all patients from each CRC cohorts

Characteristics		**CRC** **Testing cohort** n=24	**CRC** **Validation cohort** n=50	**CRC** **Clinical evaluation cohort** n=220
Gender	Male	14	30	129
	Female	10	20	91
Age (y)	Mean (SD)	-	66.3 (12.1)	67.2 (11.8)
	Median (Min-Max)	-	67 (33–91)	69 (12–91)
Tumor location	Colon	19	31	155
	Rectum	5	19	65
Histological type	Differentiated	23	47	198
	Undifferentiated	1	3	22
TNM stage	I	3	8	40
	II	8	16	61
	III	10	15	53
	IV	3	11	66

Supplementary Table 2: Primer sequences for PCR

Primers for RNA editing site-specific quantitative PCR (RESSqPCR)

Gene	Primer sequence
Wild-type AZIN1	Forward: CATTCAGCTCAGGAAGAAGACATCT Reverse: AATACAAGGAAGATGAGCCTCTGTTTAC
Edited AZIN1	Forward: ACTGAATGACATCATGTAATAAATGGCT Reverse: GAGCTTGATCAAATTGTGGCAG

Primers for qRT-PCR

Gene	Primer sequence
ADAR1	Forward: CCCTTCAGCCACATCCTTC Reverse: GCCATCTGCTTTGCCACTT
ADAR2	Forward: CTGACACGCTCTTCAATGGTT Reverse: GGCGCAGTTCGTTCAAGAT
OCT4	Forward: ACATCAAAGCTCTGCAGAAAGAACT Reverse: CTGAATACCTTCCCAAATAGAACCC
SOX2	Forward: CGCCGCCCCCAGCAGACTTCACAT Reverse: TGCACCCCTCCCATTTCCCTCGTT
GAPDH	Forward: CTGCACCACCAACTGCTTAG Reverse: GTCTTCTGGGTGGCAGTGAT

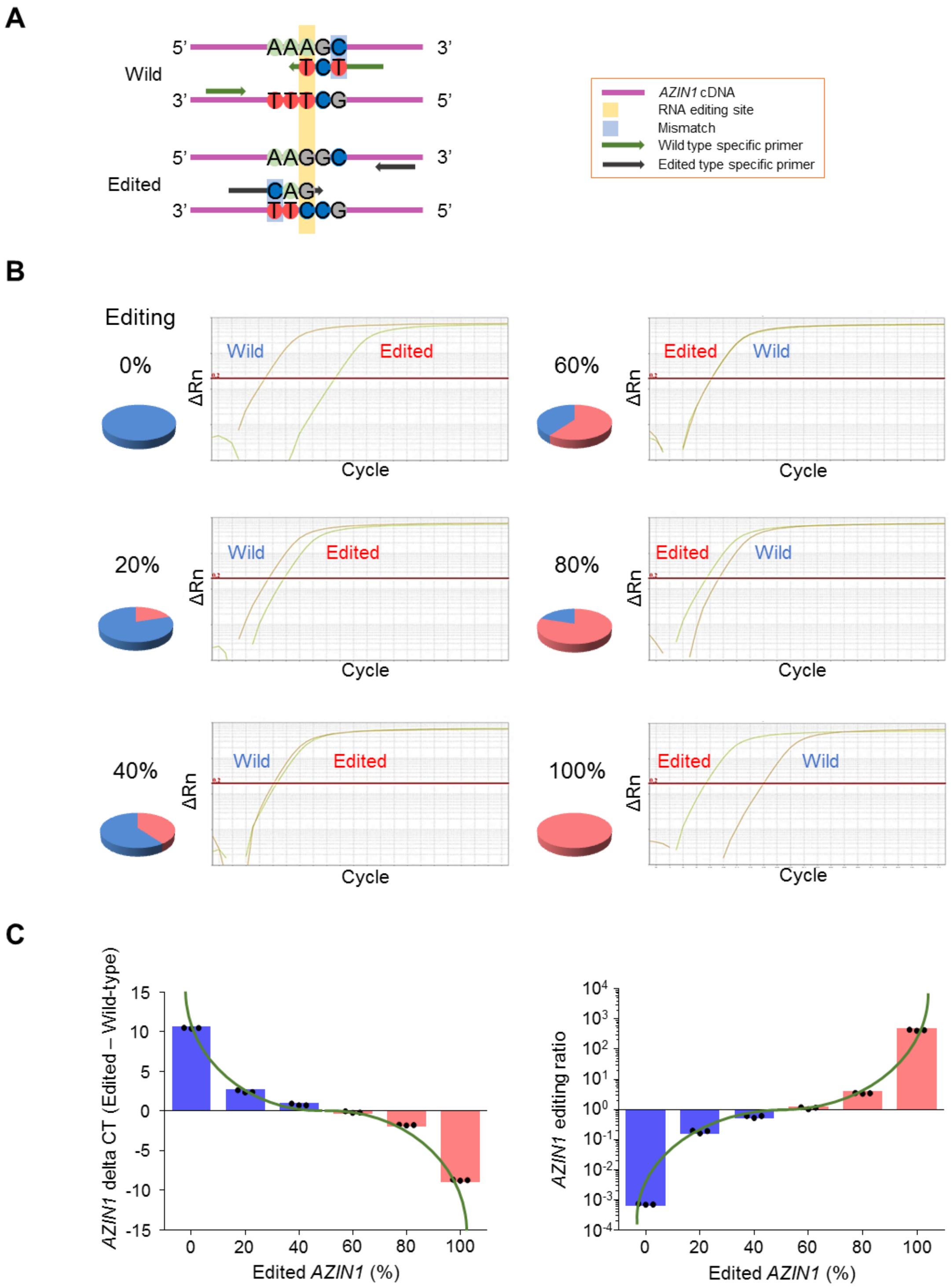
Supplementary Table 3: Clinicopathological variables and expression status of ADAR1 in the clinical evaluation cohort

Variable		n	ADAR1 expression High (n=106)	 Low (n=114)	p *value*
Gender	Male	129	71	58	**0.016***
	Female	91	35	56	
Age (y)	<69[#]	109	56	53	0.35
	≧69	111	50	61	
Location	Colon	155	76	79	0.7
	Rectum	65	30	35	
Histological type	Differentiated	198	95	103	0.86
	Undifferentiated	22	11	11	
Pathological T category	pT1/2	50	19	31	0.1
	pT3/4	170	87	83	
Lymph vessel invasion	Absent	21	8	13	0.33
	Present	199	98	101	
Vascular invasion	Absent	51	25	26	0.89
	Present	169	81	88	
Lymph node metastasis	Absent	122	54	68	0.2
	Present	98	52	46	
Hepatic metastasis	Absent	174	76	98	**0.0095***
	Present	46	30	16	
Distant metastasis	Absent	154	66	88	**0.016***
	Present	66	40	26	
UICC TNM classification	Stage I	40	15	25	**0.025***
	Stage II	61	28	33	
	Stage III	53	23	30	
	Stage IV	66	40	26	

[#] The median age at surgery is 69 years in this cohort.

* $p<0.05$

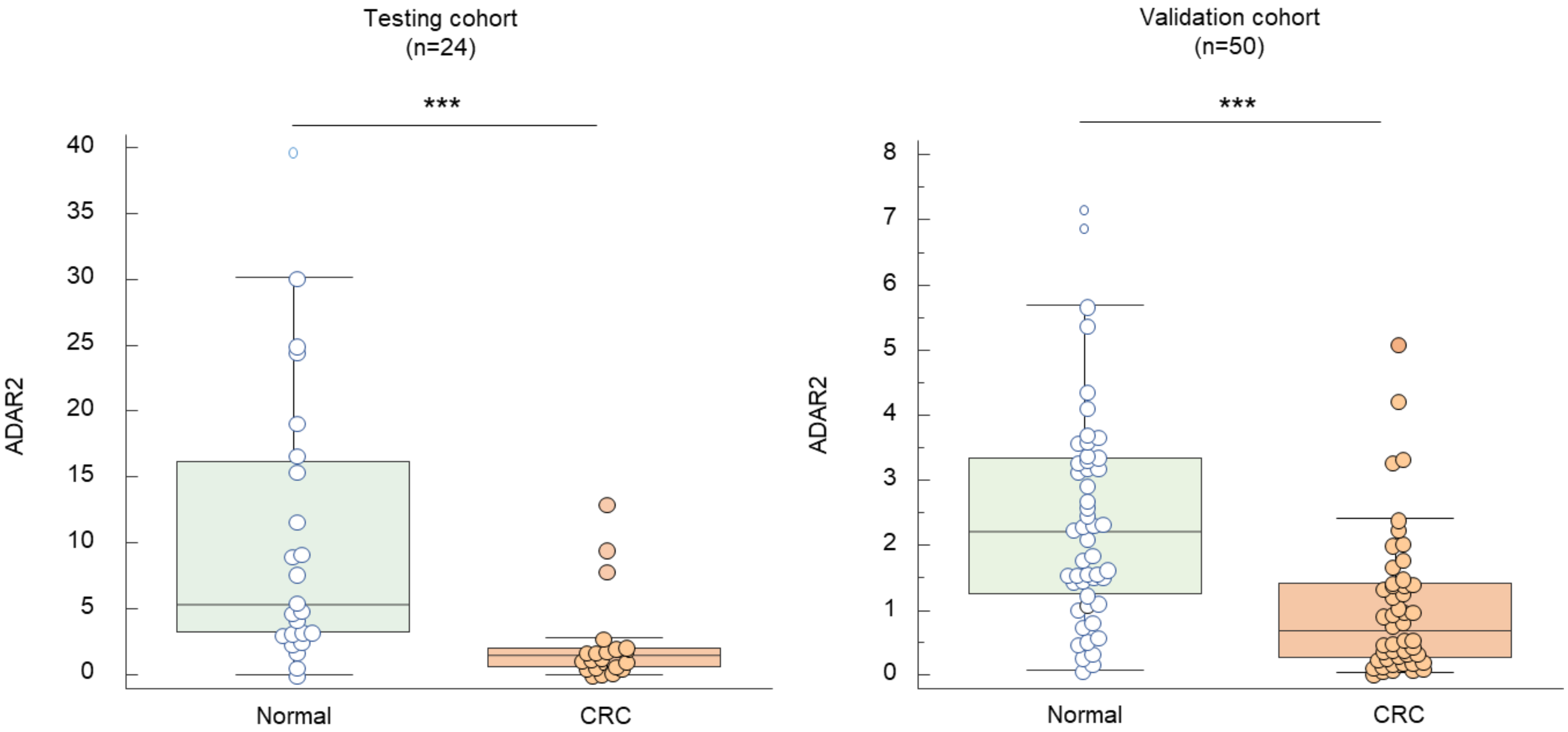
Supplementary Figure 1



Supplementary Figure 1: RESSq-PCR can efficiently discriminate between wild-type and edited *AZIN1* RNA.

(A) Primer design for *AZIN1* RNA edited site-specific quantitative PCR (RESSq-PCR) **(B, C)** The reliability of RESSq-PCR for assessment of *AZIN1* RNA editing levels was examined using predetermined mixtures of oligonucleotides derived from wild-type or edited *AZIN1* sequences, ranging from 0 to 100%.

Supplementary Figure 2

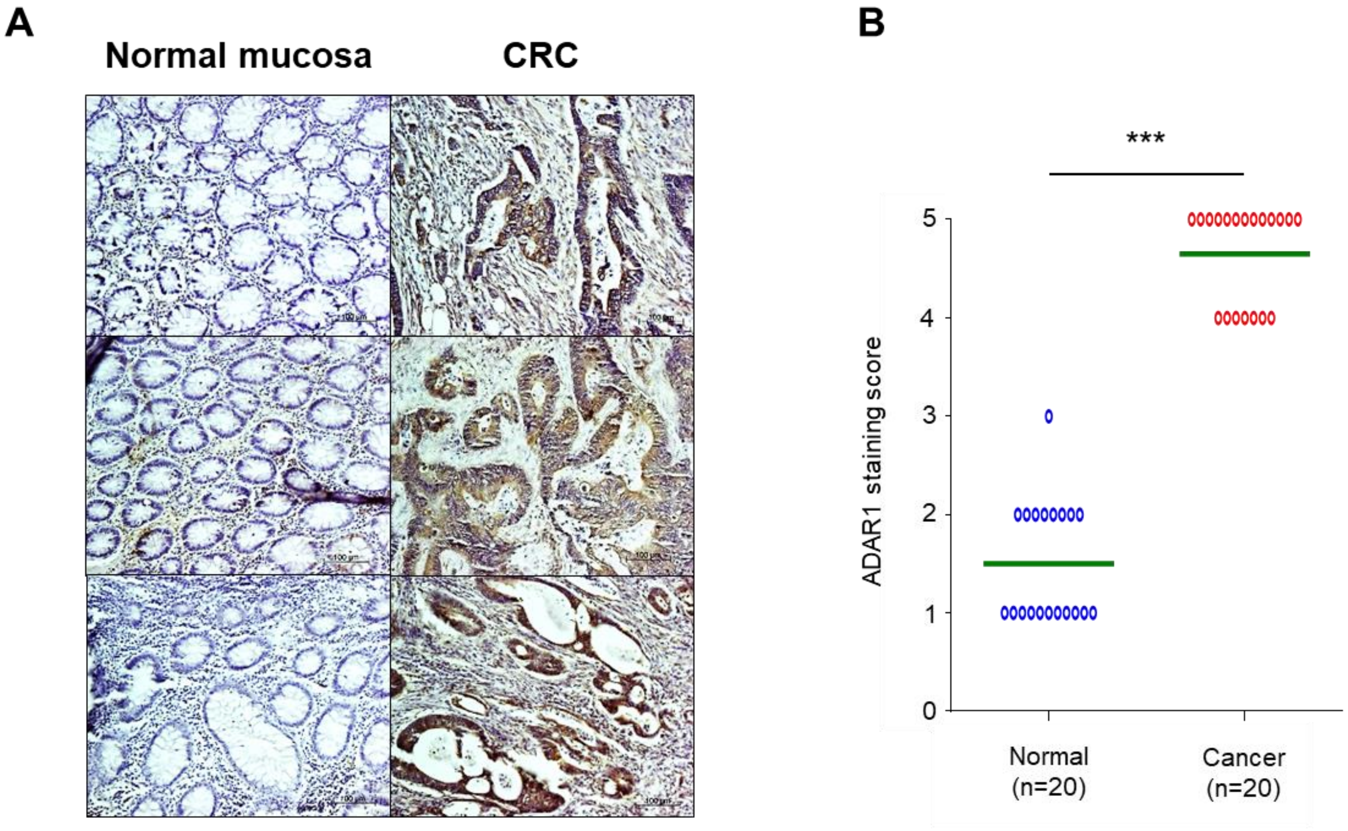

Testing cohort (n=24)

Validation cohort (n=50)

Supplementary Figure 2: Decreased levels of ADAR2 in CRC

The expression level of ADAR2 was significantly downregulated in CRC tissues compared with normal mucosa ($p<0.0001$ in both cohorts). ***$p<0.001$, Wilcoxon's signed rank test.

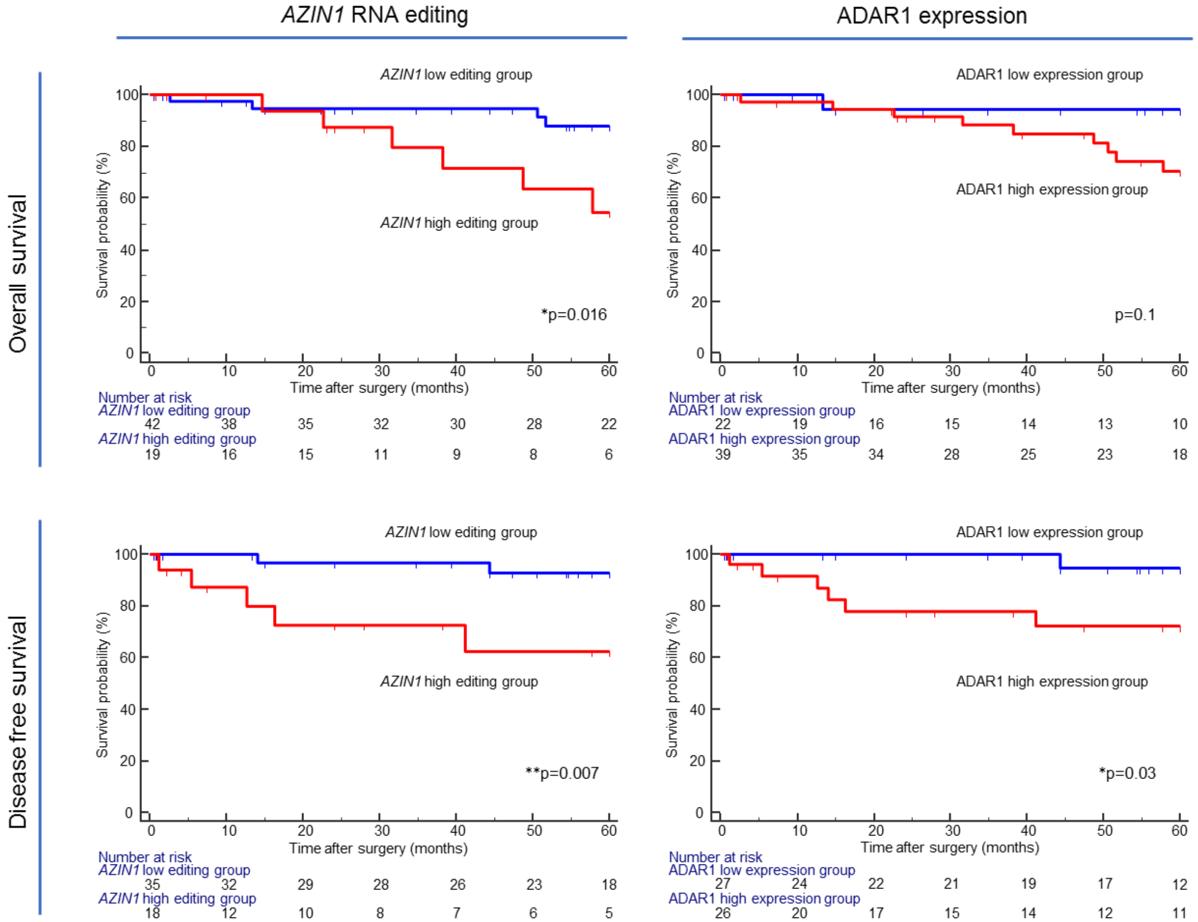
Supplementary Figure 3



Supplementary Figure 3: Increased levels of ADAR1 protein in CRC tissues.

(A) Immunohistochemical analysis of ADAR1 protein in CRC tissues and normal mucosa. **(B)** Staining scores used to determine the level of ADAR1 expression in the tissues ($p<0.001$). ***$p<0.001$, Wilcoxon rank sum test.

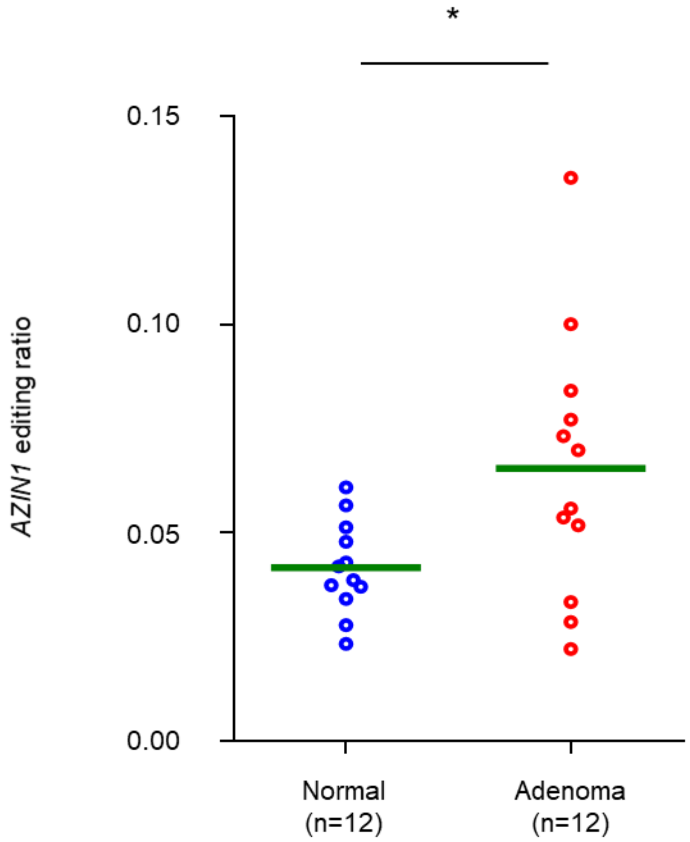
Supplementary Figure 4



Supplementary Figure 4: Increased levels of edited *AZIN1* RNA and ADAR1 expression levels both correlate with shorter OS and DFS in Stage II CRC patients

Kaplan-Meier survival analysis in Stage II CRC patients based on *AZIN1* RNA editing status and expression status of ADAR1 in primary CRC tissues. *p<0.05, **p<0.01, Log-rank test.

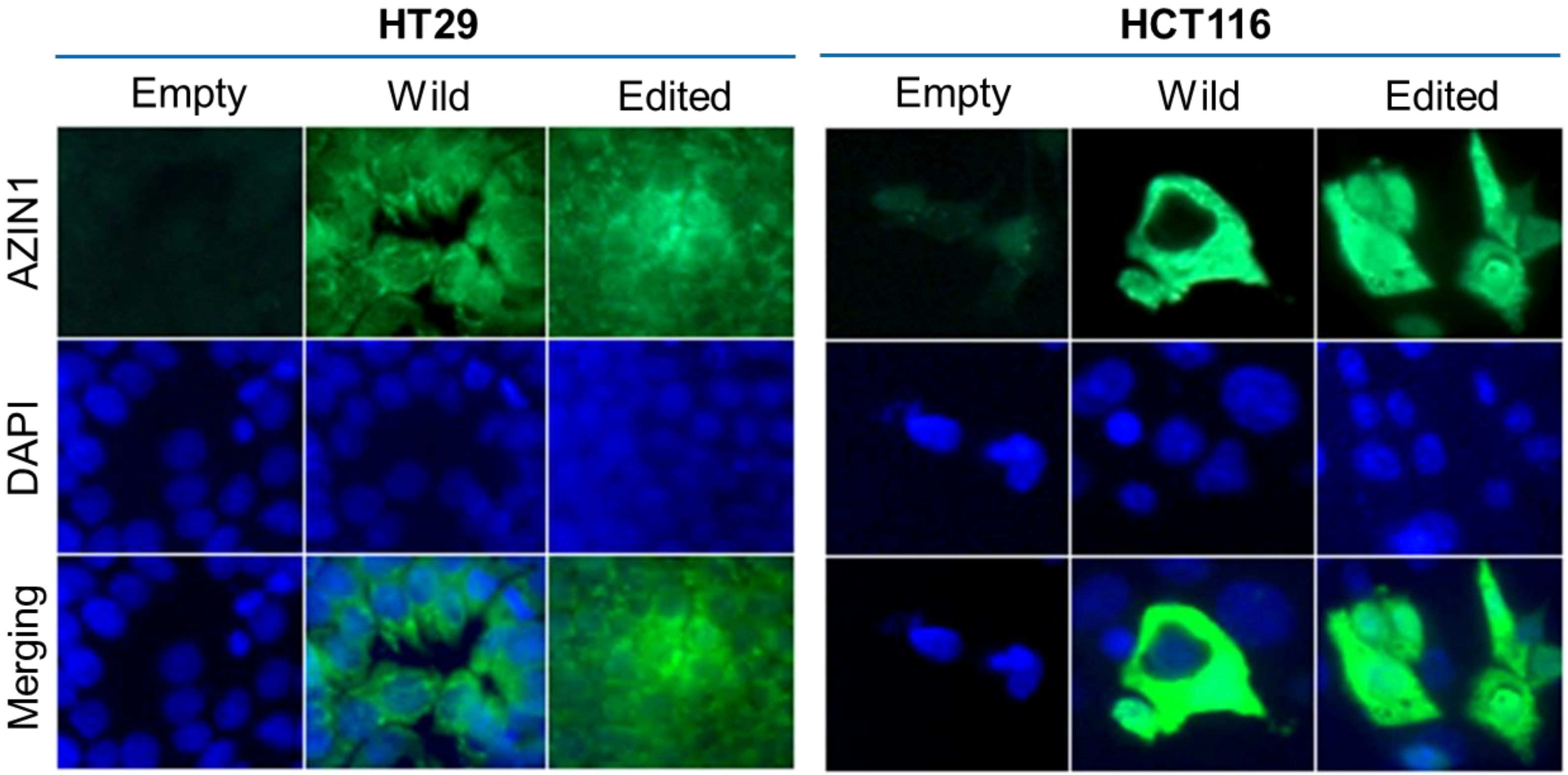
Supplementary Figure 5



Supplementary Figure 5: Increased levels of edited *AZIN1* RNA in colorectal adenoma.

RESSq-PCR analysis to determine edited *AZIN1* RNA levels in colorectal adenoma compared with adjacent normal mucosa (p=0.016). *p<0.05, Wilcoxon rank sum test.

Supplementary Figure 6



Supplementary Figure 6: Immunofluorescence analysis of CRC cell lines transfected with empty, wild-type, or edited *AZIN1* vector.

Wild-type *AZIN1* is mainly located in cytoplasm, while edited *AZIN1* is seen in both nucleus and cytoplasm in immunofluorescence staining (x400, green: *AZIN1*, blue: DAPI).