

**Table S3. The tumor location, tumor volume and stage were not associated with gender and age.** Fisher's exact test was used for p value calculation between two groups. Chi-square test was used for p value calculation among three groups.

Features	Gender		p value	Age		p value	
	Male	Female		≥ 50	< 50		
Tumor location	Left-side colon	23 (63.89%)	13 (36.11%)	0.161	25 (69.44%)	11 (30.56%)	0.302
	Right-side colon	13 (41.94%)	18 (58.06%)		21 (67.74%)	10 (32.26%)	
	Rectal	39 (59.09%)	27 (40.91%)		53 (80.30%)	13 (19.70%)	
Tumor volume	≥ 5 cm	27 (50.94%)	26 (49.06%)	0.367	39 (73.58%)	14 (26.42%)	1.000
	< 5 cm	46 (60.53%)	30 (39.47%)		57 (75.00%)	19 (25.00%)	
Stage	0~II	35 (56.45%)	27 (43.55%)	>0.999	49 (79.03%)	13 (20.97%)	0.320
	III~IV	40 (56.34%)	31 (43.66%)		50 (70.42%)	21 (29.58%)	
MS status	MSS	67 (55.37%)	54 (44.63%)	0.550	97 (80.17%)	24 (19.83%)	< 0.001
	MSI	8 (66.67%)	4 (33.33%)		2 (16.67%)	10 (83.33%)	

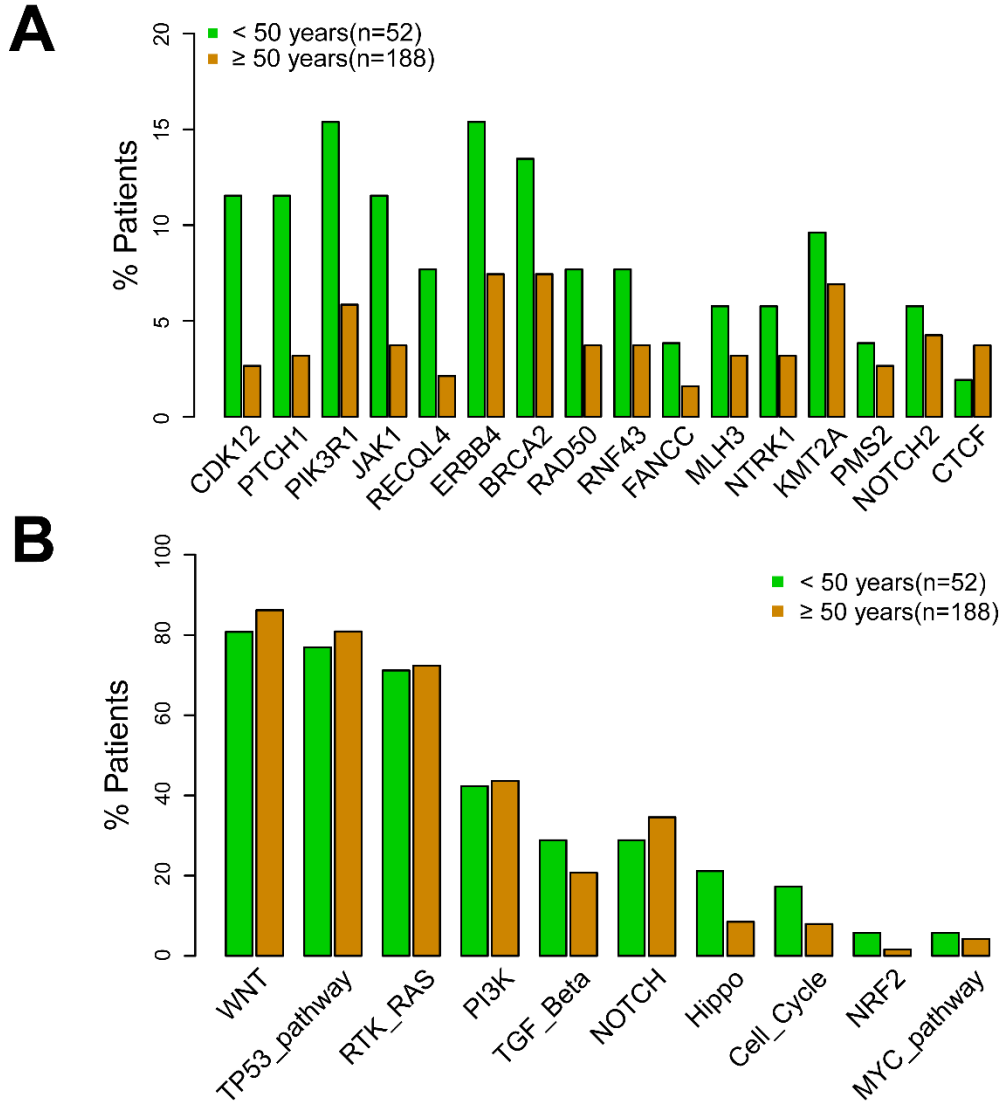
**Table S4. The distribution of *KRAS* G12 and G13 mutations in tumors of different anatomic locations.**

Locations	KRAS G13	KRAS G12	P value
Right-side colon	9 (39.13%)	10 (43.48%)	0.014
Left-side colon	1 (5.88%)	13 (76.47%)	
Rectal	5 (16.13%)	24 (77.42%)	

**Table S5. Clinicopathological features of the validation cohort.**

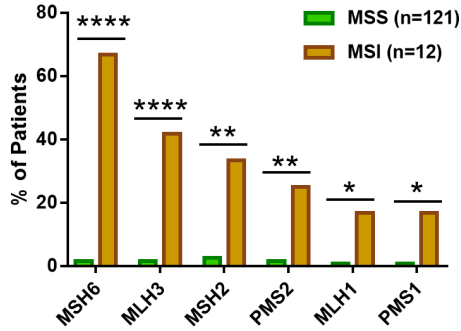
<b>Characteristics</b>	<b>No. (%)</b>
<b>No. of patients</b>	240
<b>Median age, years (range)</b>	60 (19, 84)
<b>Sex</b>	
<b>Female</b>	104 (43.3)
<b>Male</b>	136 (56.7)
<b>Primary tumor location</b>	
<b>Left-sided colon</b>	91 (37.92)
<b>Rectal</b>	62 (25.83)
<b>Right-sided colon</b>	87 (36.2)
<b>Pathological stage</b>	
<b>II</b>	112 (46.7)
<b>III</b>	128 (53.3)
<b>Histological type</b>	
<b>Adenocarcinoma</b>	212 (88.3)
<b>Mucinous/signet-ring carcinoma</b>	28 (11.7)
<b>Histological grade</b>	
<b>Moderate/well</b>	180 (75.0)
<b>Poor</b>	60 (25.0)
<b>MSI status</b>	
<b>MSI-H</b>	23 (9.6)
<b>MSI-L/MSS</b>	217 (90.4)

**Figure S1. The comparison of gene and pathway alterations in early- and late-onset patients.** (A) The comparison of somatic mutations between early- and late-onset CRC patients. (B) The comparison of pathway alterations between early- and late-onset CRC patients. \*:  $p < 0.05$ , \*\*:  $p < 0.01$ , \*\*\*:  $p < 0.001$ , \*\*\*\*:  $p < 0.0001$ .

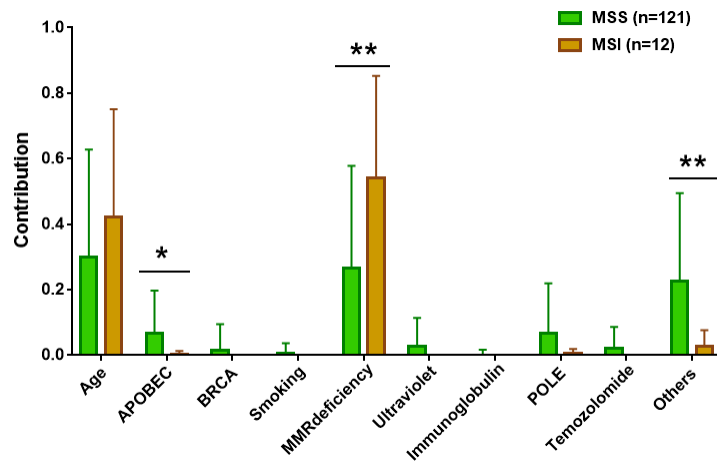


**Figure S2. The comparison of genetic alterations in MSS and MSI patients.** \*:  $p < 0.05$ , \*\*:  $p < 0.01$ , \*\*\*:  $p < 0.001$ , \*\*\*\*:  $p < 0.0001$ .

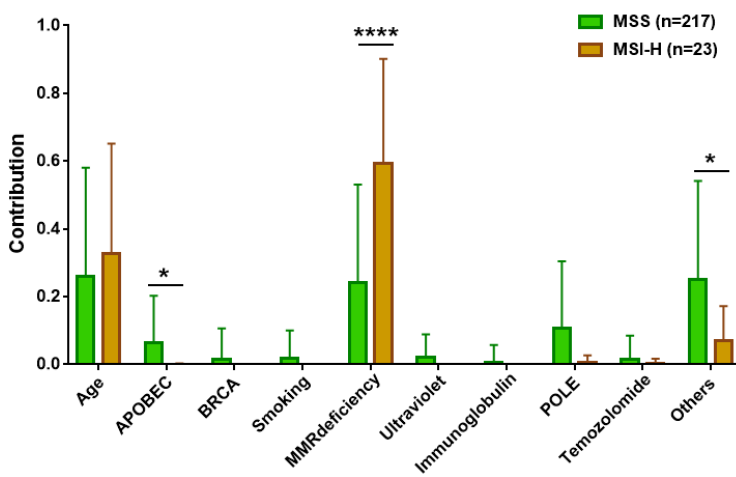
**A. Comparison of MRR genes in Our Cohort**



**B. Comparison of Mutation Signatures in Our Cohort**



**C. Comparison of Mutation Signatures in the Validation Cohort**



**Figure S3. The comparison of gene and pathway alterations among patients with different tumor anatomic locations.** (A) The comparison of somatic among patients with different tumor anatomic locations. (B) The comparison of pathway alterations among patients with different tumor anatomic locations. \*:  $p < 0.05$ , \*\*:  $p < 0.01$ , \*\*\*:  $p < 0.001$ , \*\*\*\*:  $p < 0.0001$ .

