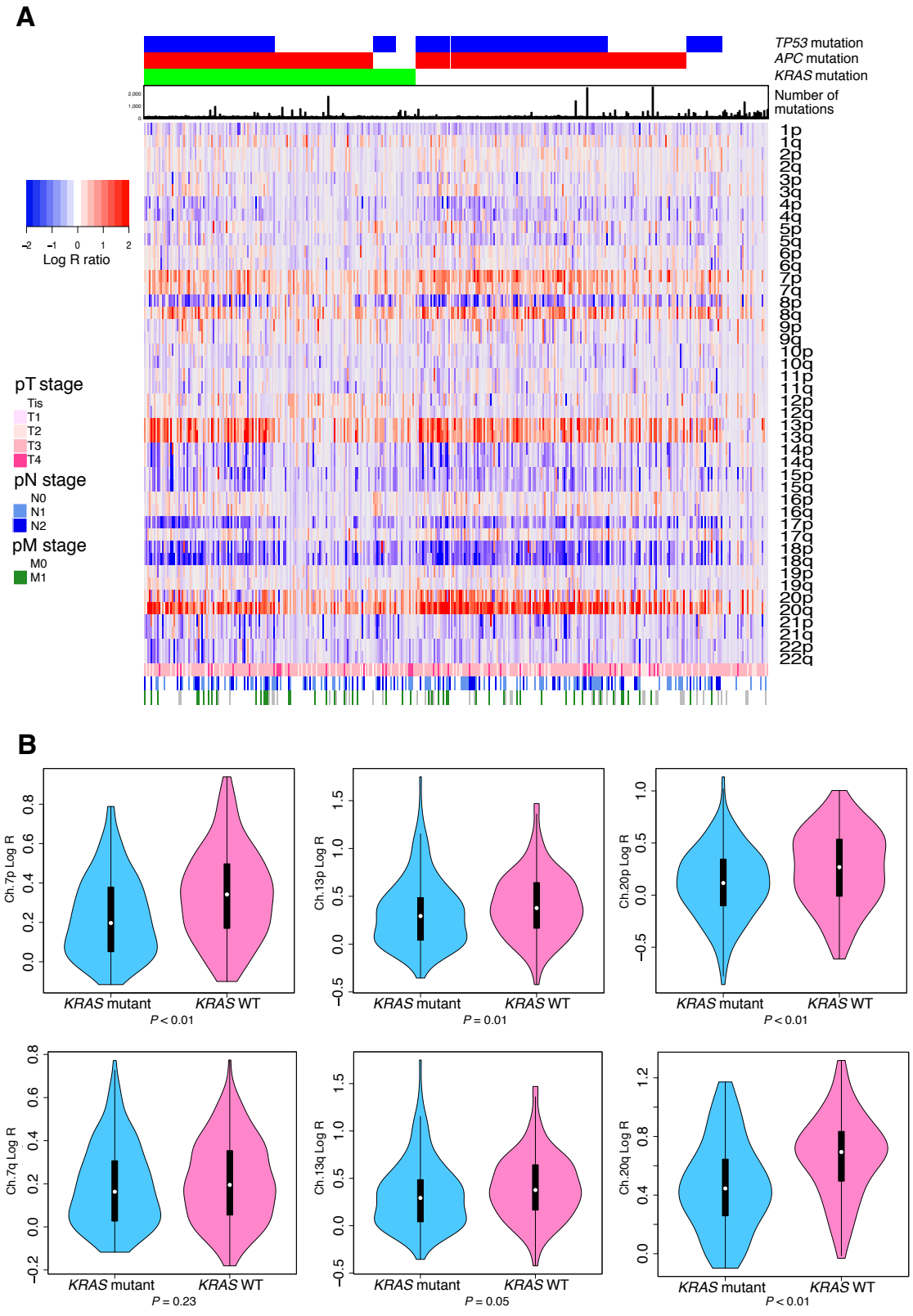

Supplementary Figure 1 Associations of major driver genes of colorectal cancer and copy number

alterations in The Cancer Genome Atlas (TCGA) dataset

A) Associations of mutations in *KRAS*, *TP53*, and *APC*, and copy number alterations. B) Comparison of copy number alterations between *KRAS*-mutant and *KRAS*-wild-type cases.

Supplementary Table 1 Clinicopathological characteristics of pT1 colorectal carcinomas with recurrence or distant metastasis after endoscopic resection

No.	Morphological type	Age (years)	Sex	Tumour size (mm)	Tumour location	Histological grade	SM depth (μm)	Ly	V	Tumour budding*	Resection	Months to recurrence	Metastasis site
1	Depressed (IIa + IIc)	38	Female	18	Rb	Well	4,750	1	1	0	Endoscopic	7.2	Distant LN
2	Depressed (IIa + IIc)	47	Male	23	Ra	Mod	6,400	2	1	0	Surgical	23.5	Lung
3	Depressed (IIa + IIc)	53	Male	15	Rs	Por	2,200	3	1	2	Surgical	27.4	Lung
4	Depressed (IIa + IIc)	65	Male	22	TC	Mod/muc	3,000	1	0	0	Surgical	0†	Liver
5	Depressed (IIa + IIc)	84	Female	21	Ra	Mod/por	3,700	1	0	0	Endoscopic	16.0	Peripheral LN
6	Depressed (Is + IIc)	56	Male	12	Rs	Mod	3,250	1	2	2	Surgical	0†	Liver
7	Flat (LST-G)	61	Female	20	Rb	Mod	5,000	0	1	2	Surgical	25.1	Lung
8	Flat (LST-G)	70	Female	30	AC	Mod/por	5,200	0	0	0	Surgical	21.7	Liver
9	Flat (LST-NG)	68	Male	23	Rb	Por	350	1	0	0	Endoscopic	54.0	Liver
10	Protruded (Isp)	43	Male	25	Rs	Mod/por	2,500	0	0	0	Surgical	13.4	Lung
11	Protruded (Ip)	82	Female	18	SC	Well	4,000	1	0	2	Endoscopic	37.5	Lung

* Counted as numbers of isolated single cells or small clusters (< 5 cells) in the stroma at the invasive tumour margin within a 20x microscopic field, and categorized as grade 1 (< 5 budding foci), grade 2 (5–9), and grade 3 (≥ 10).

† In these cases, liver metastases were identified at the time of diagnosis of colorectal carcinoma.

AC, ascending colon; LN, lymph node; LST-G, laterally spreading tumour-granular type; LST-NG, laterally spreading tumour-nongranular type; Ly, lymphatic invasion; Mod, moderately differentiated adenocarcinoma; Muc, mucinous carcinoma; Por, poorly differentiated adenocarcinoma; SC, sigmoid colon; SM, submucosal; TC, transverse colon; V, vascular invasion; Well, well-differentiated adenocarcinoma.

Supplementary Table 2 Clinicopathological characteristics of pT1 colorectal carcinomas submitted for whole-exome sequencing

	Morphological type			
Characteristic*	**Total (n=27)**	**Depressed (n=19)**	**Protruded (n=8)**	**p value‡**
Age, years	69 (62-78)	71 (68-80)	51 (49-69)	0.01
Sex				0.33
Female	14 (52%)	11 (58%)	3 (38%)	
Male	13 (48%)	8 (42%)	5 (62%)	
Tumour size, mm	15 (14-20)	15 (14-20)	21 (15-24)	0.06
Tumour location				0.18
Proximal colon	14 (52%)	12 (63%)	2 (25%)	
Distal colon	6 (22%)	3 (13%)	3 (38%)	
Rectum	7 (26%)	4 (21%)	3 (38%)	
Histological grade				0.08
Well or moderately differentiated	23 (85%)	15 (79%)	8 (100%)	
Poorly differentiated or mucinous	4 (15%)	4 (21%)	0	
Adenoma component				0.02
Absent	25 (93%)	19 (100%)	6 (75%)	
Present	2 (7%)	0	2 (25%)	
SM depth				0.11
< 1000 μm	1 (4%)	0	1 (12%)	
≥ 1000 μm	26 (96%)	19 (100%)	7 (88%)	
Lymphatic invasion				0.77
Absent	18 (67%)	13 (68%)	5 (63%)	
Present	9 (33%)	6 (32%)	3 (37%)	
Vascular invasion				0.71

Absent	12 (44%)	8 (42%)	4 (50%)	
Present	15 (56%)	11 (58%)	4 (50%)	
Tumour budding†				0.41
Grade 1	21 (88%)	14 (74%)	7 (88%)	
Grade 2-3	6 (12%)	5 (26%)	1 (12%)	

* Data are expressed as number of patients (%) or median (interquartile range).

† Counted as numbers of isolated single cells or small clusters (< 5 cells) in the stroma at the invasive tumour margin within a 20x microscopic field, and categorized as grade 1 (< 5 budding foci), grade 2 (5–9), grade 3 (≥ 10).

‡ To compare characteristics between subgroups, we used the Fisher's exact test for categorical variables, and the Wilcoxon rank-sum test for continuous variables.