

## A Affymetrix Discovery set

CIT CCMST		C2 (n=83)	C4 (n=46)	C3 (n=56)	C6 (n=45)	C5 (n=118)	C1 (n=95)
dMMR	2.1e-42	68%	12%	7%	0%	1%	1%
CIMP+	1.1e-23	59%	34%	18%	3%	3%	4%
CIN+	1.7e-15	44%	73%	65%	83%	95%	95%
BRAF mut	4.1e-19	40%	22%	6%	0%	1%	0%
KRAS mut	1.1e-12	28%	50%	87%	28%	27%	42%
TP53 mut	7.3e-03	41%	45%	35%	59%	71%	59%
Proximal Location	5e-17	72%	57%	59%	16%	21%	26%
TNM 4 vs 1,2,3	5.3e-04	5%	31%	13%	2%	15%	13%
Stem Cell up (Merlos et al)	2.1e-16	42%	91%	16%	47%	65%	32%
Crypt Bottom up (Kosinski et al)	1.7e-33	27%	96%	4%	67%	33%	5%
Normal-like GEP	1.3e-21	33%	30%	11%	82%	17%	7%
BRAFm-like (Popovici et al)	7.6e-37	69%	50%	38%	2%	3%	1%
Serrated CRC (Laiho et al)	2.9e-15	66%	74%	52%	56%	24%	21%

## B Affymetrix Validation set

CIT CCMST		C2 (n=218)	C4 (n=74)	C3 (n=149)	C6 (n=81)	C5 (n=257)	C1 (n=250)
dMMR	1.5e-49	80%	22%	21%	16%	5%	5%
CIMP+	6.5e-05	48%	11%	21%	0%	6%	0%
CIN+	1.3e-07	40%	67%	39%	100%	97%	94%
BRAF mut	1.5e-06	33%	0%	0%	0%	0%	0%
KRAS mut	0.033	24%	46%	68%	33%	25%	38%
TP53 mut	9.5e-06	13%	60%	12%	87%	66%	65%
Proximal Location	2.2e-08	76%	46%	62%	29%	33%	36%
TNM 4 vs 1,2,3	0.031	6%	13%	13%	16%	19%	21%
Stem Cell up (Merlos et al)	1.1e-25	37%	88%	25%	68%	64%	46%
Crypt Bottom up (Kosinski et al)	1.8e-14	15%	50%	17%	19%	14%	9%
Normal-like GEP	4.6e-39	15%	11%	20%	70%	9%	9%
BRAFm-like (Popovici et al)	2.6e-95	77%	50%	46%	10%	4%	3%
Serrated CRC (Laiho et al)	2.1e-50	82%	62%	54%	59%	28%	18%

## C TCGA Validation dataset

CIT CCMST		C2 (n=36)	C4 (n=7)	C3 (n=20)	C6 (n=6)	C5 (n=38)	C1 (n=45)
dMMR	2.1e-13	74%	17%	18%	0%	0%	0%
CIMP+	2.4e-11	61%	29%	15%	0%	5%	0%
CIN+	5.8e-03	14%	0%	0%	100%	71%	78%
BRAF mut	5.8e-10	48%	14%	5%	0%	0%	0%
KRAS mut	3.8e-03	29%	57%	74%	17%	29%	27%
TP53 mut	0.017	35%	29%	26%	67%	63%	62%
Proximal Location	1.2e-05	86%	57%	65%	50%	42%	27%
TNM 4 vs 1,2,3	0.33	9%	29%	10%	0%	24%	16%
Stem Cell up (Merlos et al)	1e-06	42%	86%	30%	100%	76%	24%
Crypt Bottom up (Kosinski et al)	1.3e-08	28%	71%	0%	0%	3%	2%
Normal-like GEP	0.023	6%	0%	0%	33%	3%	4%
BRAFm-like (Popovici et al)	7.3e-05	25%	29%	5%	0%	0%	0%
Serrated CRC (Laiho et al)	8.6e-09	78%	86%	70%	33%	18%	22%

Figure S3