

Supplementary Data

Racial/ethnic and sex differences in somatic cancer gene mutations among patients with early-onset colorectal cancer

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Supplementary Tables

Table S1. Clinical and demographic characteristics of the colorectal cancer (CRC) patient study population by race/ethnicity and age at sequencing: AACR Project GENIE.

Characteristic	Total		Age at Colorectal Cancer (CRC) Sequencing															
			Early-Onset CRC (<50 years)						Late-Onset CRC (50+ years)									
	Total		Total		NHW		NHB		API		Total		NHW		NHB		API	
Characteristic	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Total	6903		2016	29.2	1666	82.6	166	8.2	184	9.1	4887	70.8	4190	85.7	369	7.6	328	6.7
Age at Sequencing																		
<30 Years	108	1.6	108	5.4	88	5.3	11	6.6	9	4.9								
30-39 Years	550	8.0	550	27.3	450	27.0	46	27.7	54	29.3								
40-49 Years	1358	19.7	1358	67.4	1128	67.7	109	65.7	121	65.8								
50-59 Years	1875	27.2									1875	38.4	1560	37.2	173	46.9	142	43.3
60-69 Years	1808	26.2									1808	37.0	1561	37.3	123	33.3	124	37.8
70-79 Years	889	12.9									889	18.2	780	18.6	61	16.5	48	14.6
80+ Years	315	4.6									315	6.4	289	6.9	12	3.3	14	4.3
Mean, Years (std)	57.0	(13.1)	41.4	(6.3)	41.5	(6.3)	40.9	(6.1)	41.0	(6.1)	63.4	(9.2)	63.6	(9.3)	61.9	(8.6)	61.9	(8.9)
Sex																		
Female	3181	46.1	942	46.7	756	45.4	90	54.2	96	52.2	2239	45.8	1916	45.7	164	44.4	159	48.5
Male	3722	53.9	1074	53.3	910	54.6	76	45.8	88	47.8	2648	54.2	2274	54.3	205	55.6	169	51.5
Tumor Mutational Burden (TMB) Status*																		
Non-hypermutated	6250	90.5	1832	90.9	1511	90.7	157	94.6	164	89.1	4418	90.4	3771	90.0	342	92.7	305	93.0
Hypermutated	653	9.5	184	9.1	155	9.3	9	5.4	20	10.9	469	9.6	419	10.0	27	7.3	23	7.0
Histological Subtype/Site																		
Colon Adenocarcinoma	4481	64.9	1220	60.5	1003	60.2	112	67.5	105	57.1	3261	66.7	2815	67.2	266	72.1	180	54.9
Rectal Adenocarcinoma	1352	19.6	454	22.5	382	22.9	31	18.7	41	22.3	898	18.4	751	17.9	62	16.8	85	25.9
Colorectal Adenocarcinoma	910	13.2	300	14.9	249	14.9	19	11.4	32	17.4	610	12.5	517	12.3	35	9.5	58	17.7
Colorectal Mucinous Adenocarcinoma	160	2.3	42	2.1	32	1.9	4	2.4	6	3.3	118	2.4	107	2.6	6	1.6	5	1.5
Sample Type																		
Primary Tumor	4664	67.6	1407	69.8	1163	69.8	114	68.7	130	70.7	3257	66.6	2796	66.7	228	61.8	233	71.0
Metastasis	2027	29.4	543	26.9	450	27.0	48	28.9	45	24.5	1484	30.4	1278	30.5	126	34.1	80	24.4
Unknown	212	3.1	66	3.3	53	3.2	4	2.4	9	4.9	146	3.0	116	2.8	15	4.1	15	4.6

*Predicted by tumor mutational burden (TMB) at a cutoff of $10^{1.25}$.

Abbreviations: NHW, non-Hispanic white; NHB, non-Hispanic black; API, Asian or Pacific Islander; N, number; std, standard deviation.

Table S2. Baseline mutation probability, comparison and heterogeneity of non-silent somatic gene mutations among patients with early-onset and late-onset non-hypermutated colorectal cancer. Genes ranked by false discovery rate (FDR).

Gene Symbol	Baseline mutation probability	Baseline mutation probability by age at cancer sequencing				P	FDR
		Early-Onset CRC	Late-Onset CRC	OR*	95% CI*		
<i>TP53</i>	0.76	0.80	0.74	1.39	1.22 -	1.60	1.39E-06
<i>LRP1B</i>	0.08	0.15	0.06	2.96	1.53 -	5.73	0.001
<i>TCF7L2</i>	0.08	0.10	0.08	1.38	1.12 -	1.69	0.002
<i>KDR</i>	0.02	0.02	0.03	0.56	0.37 -	0.85	0.006
<i>FBXW7</i>	0.11	0.12	0.11	1.27	1.06 -	1.52	0.009
<i>FLT4</i>	0.02	0.02	0.03	0.64	0.42 -	0.98	0.04
<i>AMER1</i>	0.05	0.03	0.05	0.69	0.48 -	1.00	0.048
<i>WRN</i>	0.02	0.01	0.03	0.51	0.26 -	1.03	0.06
<i>SMAD3</i>	0.03	0.04	0.03	1.43	0.98 -	2.10	0.07
<i>DOCK8</i>	0.04	0.06	0.04	1.64	0.96 -	2.79	0.07
<i>BRAF</i>	0.08	0.07	0.09	0.84	0.68 -	1.04	0.11
<i>PIK3CG</i>	0.02	0.01	0.02	0.63	0.35 -	1.11	0.11
<i>PTEN</i>	0.03	0.04	0.03	1.27	0.94 -	1.72	0.12
<i>RNF43</i>	0.04	0.03	0.04	0.77	0.55 -	1.08	0.13
<i>AXIN2</i>	0.03	0.02	0.03	0.72	0.47 -	1.11	0.14
<i>CTNNB1</i>	0.04	0.03	0.04	0.80	0.59 -	1.08	0.14
<i>MGA</i>	0.03	0.02	0.03	0.72	0.46 -	1.13	0.15
<i>SMAD4</i>	0.15	0.15	0.15	1.11	0.95 -	1.30	0.18
<i>ROS1</i>	0.03	0.03	0.03	1.26	0.89 -	1.78	0.18
<i>PTPRT</i>	0.05	0.04	0.05	0.80	0.56 -	1.14	0.21
<i>ERBB3</i>	0.03	0.03	0.03	0.81	0.58 -	1.14	0.22
<i>ATM</i>	0.06	0.05	0.06	0.86	0.67 -	1.10	0.22
<i>KAT6A</i>	0.03	0.04	0.03	1.38	0.81 -	2.36	0.24
<i>SMAD2</i>	0.03	0.03	0.03	1.20	0.88 -	1.64	0.25
<i>MED12</i>	0.03	0.02	0.03	0.79	0.53 -	1.19	0.26
<i>AR</i>	0.02	0.02	0.02	0.79	0.52 -	1.20	0.26
<i>RIF1</i>	0.04	0.03	0.05	0.71	0.38 -	1.35	0.30
<i>MTOR</i>	0.03	0.02	0.03	0.83	0.59 -	1.19	0.32
<i>IKZF1</i>	0.02	0.02	0.02	0.81	0.53 -	1.23	0.33
<i>PREX2</i>	0.03	0.03	0.04	0.80	0.50 -	1.27	0.34
<i>GLI2</i>	0.05	0.05	0.05	1.21	0.79 -	1.85	0.37
<i>CARD11</i>	0.03	0.03	0.03	0.86	0.61 -	1.20	0.37

<i>BRCA2</i>	0.04	0.03	0.04	0.87	0.64	-	1.18	0.38	0.85
<i>APC</i>	0.74	0.74	0.74	1.06	0.93	-	1.21	0.39	0.85
<i>FANCM</i>	0.03	0.03	0.03	0.76	0.41	-	1.42	0.39	0.85
<i>KRAS</i>	0.45	0.43	0.46	0.95	0.85	-	1.07	0.41	0.86
<i>ASXL1</i>	0.02	0.02	0.03	0.86	0.59	-	1.25	0.43	0.86
<i>ARID1B</i>	0.04	0.04	0.04	1.13	0.84	-	1.52	0.43	0.86
<i>PTPRS</i>	0.04	0.04	0.04	1.15	0.80	-	1.66	0.45	0.87
<i>SMARCA4</i>	0.02	0.02	0.03	0.87	0.59	-	1.28	0.48	0.89
<i>FAT1</i>	0.04	0.04	0.04	1.11	0.81	-	1.52	0.50	0.89
<i>NOTCH1</i>	0.03	0.02	0.03	0.88	0.62	-	1.27	0.50	0.89
<i>PIK3C2B</i>	0.03	0.03	0.02	1.20	0.71	-	2.03	0.50	0.89
<i>EPHA3</i>	0.03	0.02	0.03	0.89	0.60	-	1.31	0.55	0.90
<i>EPHA5</i>	0.03	0.03	0.03	0.89	0.60	-	1.31	0.55	0.90
<i>PRKDC</i>	0.05	0.05	0.05	1.12	0.76	-	1.65	0.56	0.90
<i>SETD2</i>	0.02	0.02	0.02	0.89	0.60	-	1.32	0.56	0.90
<i>KMT2A</i>	0.02	0.03	0.02	1.11	0.78	-	1.58	0.58	0.91
<i>PIK3CA</i>	0.17	0.16	0.18	0.96	0.82	-	1.12	0.59	0.91
<i>GRIN2A</i>	0.03	0.03	0.03	1.12	0.73	-	1.72	0.60	0.91
<i>NOTCH3</i>	0.03	0.03	0.03	0.92	0.64	-	1.30	0.63	0.94
<i>NRAS</i>	0.05	0.04	0.05	0.94	0.72	-	1.23	0.66	0.96
<i>TSC2</i>	0.02	0.02	0.02	0.92	0.62	-	1.38	0.70	0.96
<i>KMT2C</i>	0.03	0.03	0.03	0.92	0.60	-	1.42	0.71	0.96
<i>BCOR</i>	0.02	0.02	0.02	0.93	0.64	-	1.36	0.72	0.96
<i>POLE</i>	0.02	0.02	0.02	1.07	0.72	-	1.59	0.74	0.96
<i>BCORL1</i>	0.02	0.02	0.02	1.09	0.62	-	1.90	0.76	0.96
<i>EP300</i>	0.03	0.02	0.03	0.95	0.66	-	1.36	0.77	0.96
<i>COL7A1</i>	0.09	0.09	0.09	1.06	0.70	-	1.60	0.79	0.96
<i>NF1</i>	0.02	0.02	0.03	0.95	0.66	-	1.37	0.79	0.96
<i>ATR</i>	0.02	0.02	0.02	1.05	0.71	-	1.56	0.80	0.96
<i>SETBP1</i>	0.02	0.02	0.02	0.92	0.50	-	1.70	0.80	0.96
<i>ERBB4</i>	0.04	0.03	0.04	0.96	0.71	-	1.32	0.82	0.96
<i>KMT2B</i>	0.02	0.02	0.03	0.94	0.53	-	1.66	0.83	0.96
<i>EPHB1</i>	0.03	0.03	0.03	1.05	0.68	-	1.61	0.84	0.96
<i>PIK3R1</i>	0.03	0.03	0.03	0.97	0.69	-	1.36	0.84	0.96
<i>ERBB2</i>	0.03	0.03	0.03	1.03	0.74	-	1.45	0.85	0.96
<i>ATRX</i>	0.03	0.03	0.03	0.98	0.70	-	1.36	0.88	0.98
<i>SOX9</i>	0.10	0.10	0.10	1.01	0.84	-	1.23	0.90	0.98
<i>KMT2D</i>	0.06	0.05	0.06	0.98	0.77	-	1.26	0.90	0.98
<i>CITA</i>	0.02	0.02	0.02	0.97	0.53	-	1.78	0.92	0.98
<i>ARID1A</i>	0.06	0.05	0.06	1.01	0.79	-	1.29	0.93	0.98
<i>ARID2</i>	0.02	0.02	0.02	1.01	0.69	-	1.48	0.95	0.99
<i>CREBBP</i>	0.03	0.03	0.03	1.01	0.72	-	1.42	0.96	0.99

<i>ALK</i>	0.03	0.03	0.03	0.99	0.71	-	1.39	0.97	0.99
<i>POLQ</i>	0.05	0.05	0.05	1.00	0.60	-	1.67	1.00	1.00

Abbreviations: CRC, colorectal cancer; OR, odds ratio; CI, confidence interval; FDR, false discovery rate.

*ORs, 95% CIs, P and FDR values were calculated for genes from models adjusted for patient race/ethnicity, sex, histology and site, sequencing assay, sample type and tumor mutational burden.

Table S3. Racial/ethnic patterns in baseline mutation probability, comparison and heterogeneity of all non-silent somatic gene mutations among patients with early-onset and late-onset non-hypermutated colorectal cancer.

Non-Hispanic White (NHW)										Non-Hispanic Black (NHB)										Asian or Pacific Islander (API)										
Gene Symbol	Baseline mutation probability by age at cancer sequencing									Baseline mutation probability by age at cancer sequencing									Baseline mutation probability by age at cancer sequencing									Mutation frequency	Heterogeneity	
	Baseline mutation probability	Early-Onset CRC	Late-Onset CRC	OR*	95% CI*	P	FDR	Baseline mutation probability	Early-Onset CRC	Late-Onset CRC	OR*	95% CI*	P	FDR	Baseline mutation probability	Early-Onset CRC	Late-Onset CRC	OR*	95% CI*	P	FDR	P	Cochran's Q test	P-Hett						
TP53	0.75	0.79	0.74	1.39	1.20 - 1.61	1.36E-05	0.001	0.74	0.77	0.72	1.31	0.80 - 2.14	0.29	0.995	0.80	0.84	0.78	1.66	0.97 - 2.84	0.06	0.60	0.25	0.49	0.78						
LRP1B	0.08	0.18	0.04	4.75	2.21 - 10.23	6.77E-05	0.003	0.07	0.00	0.09	-	- -	-	-	0.11	0.10	0.13	-	- -	-	-	2.45E-10	-	-						
TCF7L2	0.09	0.10	0.08	1.45	1.17 - 1.80	0.0008	0.02	0.07	0.06	0.07	0.80	0.32 - 1.97	0.62	0.999	0.08	0.08	0.07	1.36	0.63 - 2.93	0.43	0.96	0.14	1.60	0.45						
SMAD3	0.03	0.04	0.03	1.76	1.14 - 2.71	0.01	0.18	0.04	0.01	0.06	0.25	0.03 - 2.05	0.20	0.995	0.04	0.06	0.04	1.65	0.58 - 4.67	0.35	0.93	0.07	3.16	0.21						
FLT4	0.02	0.01	0.03	0.53	0.32 - 0.87	0.01	0.18	0.02	0.01	0.03	0.19	0.02 - 2.06	0.17	0.995	0.03	0.05	0.02	3.45	1.05 - 11.37	0.04	0.51	0.0006	9.19	0.01						
KDR	0.02	0.02	0.03	0.58	0.37 - 0.92	0.02	0.23	0.03	0.01	0.03	0.30	0.05 - 1.84	0.19	0.995	0.03	0.02	0.03	0.73	0.16 - 3.31	0.69	0.99	0.91	0.60	0.74						
FBXW7	0.11	0.11	0.10	1.26	1.04 - 1.54	0.02	0.23	0.10	0.10	0.10	0.90	0.45 - 1.80	0.76	0.999	0.14	0.17	0.12	1.86	1.03 - 3.38	0.04	0.51	0.04	2.53	0.28						
RNF43	0.04	0.03	0.04	0.67	0.45 - 0.98	0.04	0.35	0.02	0.03	0.02	1.60	0.40 - 6.36	0.50	0.995	0.05	0.06	0.05	1.35	0.54 - 3.36	0.52	0.99	0.046	3.09	0.21						
BRAF	0.09	0.07	0.09	0.79	0.63 - 0.99	0.04	0.35	0.04	0.04	0.04	1.21	0.42 - 3.53	0.72	0.999	0.06	0.07	0.05	1.15	0.49 - 2.71	0.75	0.99	0.27	1.23	0.54						
APC	0.74	0.75	0.74	1.15	1.00 - 1.33	0.06	0.39	0.78	0.76	0.79	0.94	0.56 - 1.58	0.82	0.999	0.69	0.59	0.74	0.53	0.34 - 0.83	0.006	0.43	0.00001	10.58	0.005						
RIF1	0.04	0.03	0.04	0.77	0.39 - 1.53	0.45	0.85	0.03	0.03	0.02	1.88	0.09 - 37.61	0.68	0.999	0.09	0.04	0.12	0.01	0.00 - 0.58	0.03	0.51	0.83	4.67	0.10						
PICK3CA	0.17	0.16	0.18	1.01	0.86 - 1.20	0.88	0.93	0.20	0.19	0.21	1.00	0.58 - 1.70	0.99	0.999	0.13	0.07	0.16	0.47	0.23 - 0.94	0.03	0.51	0.003	4.49	0.11						
MTOR	0.03	0.02	0.03	0.73	0.50 - 1.08	0.12	0.58	0.02	0.03	0.02	0.99	0.27 - 3.65	0.98	0.999	0.01	0.02	0.01	8.65	1.15 - 64.90	0.04	0.51	0.98	5.65	0.06						
FAT1	0.04	0.04	0.04	0.93	0.66 - 1.32	0.68	0.92	0.04	0.06	0.03	2.35	0.76 - 7.28	0.14	0.995	0.02	0.05	0.01	4.37	1.02 - 18.71	0.047	0.51	0.32	6.07	0.048						
ATRX	0.03	0.02	0.03	0.84	0.58 - 1.24	0.39	0.76	0.03	0.06	0.02	3.29	1.09 - 9.95	0.035	0.995	0.04	0.04	0.04	1.16	0.40 - 3.38	0.78	0.99	0.03	5.29	0.07						
CREBBP	0.03	0.03	0.03	0.94	0.64 - 1.38	0.75	0.92	0.03	0.05	0.02	3.12	0.94 - 10.37	0.06	0.995	0.03	0.02	0.03	0.81	0.23 - 2.88	0.74	0.99									
PIK3R1	0.03	0.03	0.03	1.05	0.73 - 1.52	0.78	0.92	0.04	0.03	0.05	0.29	0.08 - 1.08	0.07	0.995	0.01	0.01	0.01	0.78	0.10 - 6.17	0.82	0.99									
COL7A1	0.08	0.09	0.08	1.18	0.76 - 1.83	0.47	0.85	0.12	0.03	0.16	0.16	0.02 - 1.55	0.11	0.995	0.09	0.12	0.07	4.39	0.37 - 51.61	0.24	0.79									
EP300	0.03	0.02	0.03	0.89	0.60 - 1.33	0.58	0.89	0.03	0.04	0.02	2.69	0.78 - 9.25	0.12	0.995	0.02	0.01	0.02	0.38	0.06 - 2.46	0.31	0.93									
PTEN	0.03	0.04	0.03	1.28	0.91 - 1.80	0.15	0.58	0.06	0.07	0.05	1.97	0.84 - 4.62	0.12	0.995	0.02	0.02	0.02	0.67	0.12 - 3.85	0.66	0.99									
NOTCH1	0.03	0.02	0.03	0.71	0.47 - 1.08	0.11	0.58	0.03	0.04	0.03	2.25	0.70 - 7.26	0.18	0.995	0.03	0.04	0.02	2.33	0.65 - 8.31	0.19	0.79									
AMER1	0.05	0.04	0.05	0.74	0.50 - 1.10	0.13	0.58	0.06	0.03	0.07	0.43	0.12 - 1.48	0.18	0.995	0.02	0.01	0.03	0.37	0.04 - 3.31	0.38	0.93									
GLI2	0.05	0.05	0.05	1.09	0.68 - 1.74	0.73	0.92	0.04	0.07	0.01	8.42	0.33 - 213.97	0.20	0.995	0.13	0.16	0.12	1.67	0.43 - 6.45	0.46	0.97									
KMT2B	0.03	0.02	0.03	0.81	0.43 - 1.53	0.52	0.89	0.02	0.03	0.01	4.36	0.46 - 41.61	0.20	0.995	0.02	0.02	0.02	1.50	0.23 - 9.70	0.67	0.99									
ERBB2	0.03	0.03	0.03	0.96	0.66 - 1.39	0.83	0.92	0.02	0.03	0.02	2.22	0.64 - 7.62	0.21	0.995	0.02	0.02	0.02	1.10	0.27 - 4.50	0.90	1.00									
BCOR	0.02	0.02	0.03	0.92	0.60 - 1.39	0.68	0.92	0.01	0.01	0.02	0.25	0.03 - 2.38	0.23	0.995	0.03	0.04	0.03	1.64	0.55 - 4.90	0.38	0.93									
KMT2A	0.02	0.02	0.02	1.00	0.67 - 1.50	0.98	0.98	0.02	0.03	0.01	2.27	0.52 - 9.95	0.28	0.995	0.03	0.04	0.03	2.09	0.69 - 6.35	0.19	0.79									
PRKDC	0.05	0.05	0.04	1.32	0.87 - 1.99	0.19	0.63	0.04	0.06	0.03	2.29	0.50 - 10.53	0.29	0.995	0.08	0.00	0.13	-	- -	-	-									
ARID1B	0.04	0.04	0.04	1.15	0.84 - 1.59	0.38	0.76	0.04	0.03	0.05	0.52	0.15 - 1.75	0.29	0.995	0.02	0.03	0.01	3.98	0.83 - 19.18	0.09	0.72									
KMT2C	0.03	0.02	0.03	0.89	0.54 - 1.46	0.64	0.91	0.04	0.06	0.03	2.02	0.53 - 7.78	0.30	0.995	0.03	0.02	0.04	0.44	0.08 - 2.49	0.35	0.93									
NF1	0.03	0.02	0.03	0.89	0.60 - 1.31	0.55	0.89	0.02	0.03	0.01	2.15	0.49 - 9.50	0.31	0.995	0.02	0.02	0.02	1.60	0.35 - 7.33	0.55	0.99									
PREX2	0.03	0.02	0.04	0.67	0.39 - 1.15	0.14	0.58	0.03	0.02	0.03	2.60	0.38 - 18.01	0.33	0.995	0.03	0.05	0.02	3.34	0.70 - 16.05	0.13	0.79									
ASXL1	0.02	0.02	0.03	0.84	0.56 - 1.26	0.39	0.76	0.02	0.02	0.02	0.38	0.05 - 2.82	0.35	0.995	0.02	0.02	0.02	1.37	0.37 - 5.09	0.64	0.99									
SMARCA4	0.02	0.02	0.03	0.89	0.59 - 1.35	0.59	0.89	0.03	0.02	0.04	0.53	0.13 - 2.10	0.37	0.995	0.01	0.01	0.01	2.26	0.26 - 19.76	0.46	0.97									
SMAD2	0.03	0.03	0.03	1.29	0.91 - 1.82	0.15	0.58	0.05	0.04	0.06	0.62	0.22 - 1.77	0.37	0.995	0.03	0.03	0.02	1.74	0.48 - 6.37	0.40	0.93									
KAT6A	0.03	0.03	0.03	1.31	0.72 - 2.37	0.38	0.76	0.02	0.04	0.02	3.18	0.24 - 41.56	0.38	0.995	0.06	0.06	0.06	1.94	0.28 - 13.36	0.50	0.99									
NOTCH3	0.03	0.03	0.03	0.93	0.63 - 1.36	0.71	0.92	0.03	0.04	0.04	1.38	0.55 - 3.44	0.49	0.995	0.05	0.05	0.06	1.03	0.42 - 2.54	0.95	1.00									
POLQ	0.05	0.05	0.05	1.22	0.71 - 2.11	0.47	0.85	0.06	0.03	0.08	0.36	0.04 - 3.68	0.39	0.995	0.09	0.03	0.12	0.26	0.03 - 2.50	0.24	0.79									
AXIN2	0.02	0.02	0.03	0.82	0.52 - 1.29	0.39	0.76	0.03	0.02	0.04	0.51	0.11 - 2.48	0.41	0.995	0.02	0.01	0.03	0.27	0.03 - 2.36	0.24	0.79									
ERBB4	0.04	0.04	0.04	1.02	0.74 - 1.41	0.91	0.93	0.02	0.01	0.03	0.51	0.10 - 2.63	0.42	0.995	0.02	0.02	0.03	0.78	0.17 - 3.57	0.74	0.99									
SETBP1	0.02	0.02	0.02	0.92	0.48 - 1.76	0.80	0.92	0.03	0.04	0.02	2.27	0.25 - 20.55	0.47	0.995	0.01	0.00	0.01	-	- -	-	-									
BRCA2	0.04	0.04	0.04	0.91	0.65 - 1.28	0.59	0.89	0.05	0.05	0.06	0.70	0.27 - 1.81	0.47	0.995	0.04	0.03	0.04	0.46	0.13 - 1.62	0.23	0.79									
CTNNB1	0.04	0.04	0.04	0.71	0.50 - 1.01	0.055	0.39	0.05	0.06	0.04	1.38	0.55 - 3.44	0.49	0.995	0.05	0.05	0.06	1.03	0.42 - 2.54	0.95	1.00									
ARID1A	0.06	0.05	0.06	1.03	0.79 - 1.35	0.82	0.92	0.05	0.06	0.05	1.37	0.54 - 3.46	0.51	0.995	0.06	0.05	0.07	0.84	0.34 - 2.08	0.71	0.99									
ROS1	0.03	0.03	0.03	1.22	0.83 - 1.78	0.31	0.76	0.02	0.02	0.02	0.60	0.13 - 2.78	0.51	0.995	0.03	0.04	0.02	2.14	0.65 - 7.05	0.21	0.79									
EPHA3	0.03	0.03	0.03	0.97	0.63 - 1.50	0.91	0.93	0.03	0.03	0.03	1.56	0.41 - 5.98	0.51	0.995	0.03	0.01	0.05	0.17	0.02 - 1.40	0.10	0.72									
AR	0.02	0.02	0.02	0.79	0.50 - 1.25	0.32	0.76	0.02	0.01	0.02	0.56	0.09 - 3.43	0.53	0.995	0.02	0.02	0.03	1.												

PTPRS	0.04	0.05	0.04	1.27	0.85 - 1.90	0.24	0.73	0.04	0.04	0.04	0.78	0.19 - 3.15	0.72	0.999	0.05	0.04	0.06	0.59	0.17 - 2.02	0.40	0.93
KRAS	0.44	0.42	0.45	0.94	0.83 - 1.07	0.37	0.76	0.57	0.57	0.57	1.08	0.70 - 1.66	0.72	0.999	0.41	0.40	0.42	0.93	0.61 - 1.43	0.75	0.99
FANCM	0.03	0.02	0.03	0.67	0.33 - 1.36	0.27	0.76	0.04	0.04	0.04	0.74	0.12 - 4.64	0.75	0.999	0.02	0.06	0.00	-	-	-	-
EPHB1	0.03	0.03	0.03	1.18	0.73 - 1.90	0.49	0.87	0.04	0.03	0.04	0.82	0.22 - 3.04	0.77	0.999	0.02	0.01	0.03	0.23	0.03 - 2.10	0.20	0.79
CARD11	0.03	0.03	0.03	0.91	0.63 - 1.30	0.61	0.89	0.02	0.03	0.02	1.22	0.30 - 4.95	0.78	0.999	0.03	0.01	0.05	0.27	0.06 - 1.30	0.10	0.72
IKZF1	0.02	0.02	0.02	0.79	0.49 - 1.25	0.31	0.76	0.02	0.02	0.02	0.83	0.21 - 3.32	0.79	0.999	0.02	0.02	0.02	1.02	0.19 - 5.38	0.98	1.00
ATR	0.02	0.02	0.02	1.05	0.68 - 1.62	0.84	0.92	0.02	0.02	0.02	0.85	0.19 - 3.77	0.83	0.999	0.02	0.03	0.02	1.43	0.34 - 6.01	0.63	0.99
POLE	0.02	0.02	0.02	0.98	0.62 - 1.54	0.94	0.95	0.03	0.03	0.03	0.87	0.21 - 3.54	0.85	0.999	0.03	0.04	0.02	1.87	0.47 - 7.41	0.37	0.93
PTPRT	0.05	0.04	0.05	0.83	0.55 - 1.24	0.36	0.76	0.04	0.04	0.04	1.11	0.32 - 3.88	0.87	0.999	0.06	0.03	0.07	0.50	0.16 - 1.61	0.25	0.79
GRIN2A	0.03	0.03	0.03	1.16	0.72 - 1.85	0.54	0.89	0.02	0.02	0.02	0.87	0.16 - 4.73	0.87	0.999	0.02	0.02	0.03	1.20	0.27 - 5.32	0.81	0.99
SMAD4	0.15	0.15	0.15	1.13	0.95 - 1.34	0.16	0.59	0.15	0.15	0.14	1.04	0.59 - 1.85	0.89	0.999	0.13	0.14	0.13	0.95	0.52 - 1.75	0.88	1.00
KMT2D	0.06	0.05	0.06	1.03	0.78 - 1.34	0.85	0.92	0.05	0.05	0.05	0.94	0.37 - 2.41	0.90	0.999	0.04	0.03	0.05	0.67	0.22 - 2.11	0.50	0.99
SOX9	0.10	0.09	0.10	1.03	0.83 - 1.27	0.81	0.92	0.08	0.08	0.08	0.96	0.45 - 2.04	0.91	0.999	0.11	0.11	0.11	1.22	0.82 - 2.41	0.56	0.99
DOCK8	0.04	0.06	0.04	1.68	0.95 - 2.97	0.08	0.49	0.06	0.07	0.06	1.10	0.16 - 7.69	0.93	0.999	0.04	0.08	0.02	-	-	-	-
MGA	0.03	0.02	0.03	0.81	0.51 - 1.29	0.38	0.76	0.01	0.00	0.02	-	-	-	-	0.02	0.01	0.03	0.27	0.03 - 2.45	0.25	0.79
ARID2	0.03	0.02	0.03	1.08	0.73 - 1.59	0.72	0.92	0.01	0.01	0.01	-	-	-	-	0.02	0.01	0.02	0.23	0.02 - 2.13	0.19	0.79
PIK3C2B	0.03	0.02	0.03	0.96	0.54 - 1.73	0.90	0.93	0.01	0.04	0.00	-	-	-	-	0.03	0.04	0.03	-	-	-	-
WRN	0.02	0.01	0.03	0.53	0.26 - 1.11	0.09	0.54	0.02	0.00	0.03	-	-	-	-	0.02	0.02	0.01	1.70	0.09 - 33.63	0.73	0.99
PIK3CG	0.02	0.02	0.03	0.72	0.40 - 1.30	0.28	0.76	0.01	0.00	0.02	-	-	-	-	0.01	0.00	0.02	-	-	-	-
BCORL1	0.02	0.03	0.02	1.35	0.75 - 2.43	0.31	0.76	0.01	0.00	0.01	-	-	-	-	0.05	0.02	0.06	0.69	0.05 - 9.27	0.78	0.99

Abbreviations: CRC, colorectal cancer; OR, odds ratio; CI, confidence interval; FDR, false discovery rate.

*ORs, 95% CIs, P and FDR values were calculated for genes from models adjusted for patient sex, histology and site, sequencing assay, sample type and tumor mutational burden.

†P-values were derived from Cochran's Q test for heterogeneity across the racial/ethnic groups. Only genes with significant associations for non-silent somatic mutations between early-onset and late-onset non-hypermutated CRC cases in at least one racial/ethnic group were tested.

Table S4. Baseline mutation probability, comparison and heterogeneity of non-silent somatic gene mutations among patients with early-onset and late-onset non-hypermutated colorectal cancer by sex.

Gene Symbol	Female						Male						Mutation frequency	Heterogeneity			
	Baseline mutation probability by age at cancer sequencing						Baseline mutation probability by age at cancer sequencing										
	Baseline mutation probability	Early-Onset CRC	Late-Onset CRC	OR*	95% CI*	P	FDR	Baseline mutation probability	Early-Onset CRC	Late-Onset CRC	OR*	95% CI*	P	FDR			
TP53	0.75	0.80	0.73	1.54	1.26 - 1.88	2.73E-05	0.002	0.76	0.79	0.75	1.29	1.07 - 1.55	0.007	0.51	0.45	1.57	0.21
BRAF	0.09	0.06	0.10	0.58	0.42 - 0.81	0.002	0.057	0.08	0.08	0.07	1.16	0.87 - 1.54	0.32	0.81	0.03	9.35	0.002
EP300	0.02	0.01	0.03	0.30	0.13 - 0.67	0.004	0.09	0.03	0.04	0.03	1.59	1.04 - 2.43	0.03	0.64	0.00003	12.71	0.0004
KDR	0.03	0.01	0.03	0.43	0.23 - 0.82	0.01	0.16	0.02	0.02	0.03	0.67	0.38 - 1.18	0.17	0.75	0.74	1.04	0.31
LRP1B	0.09	0.17	0.06	3.55	1.34 - 9.38	0.01	0.16	0.07	0.13	0.05	2.21	0.80 - 6.09	0.12	0.75	0.026	0.43	0.51
WRN	0.03	0.01	0.03	0.17	0.04 - 0.72	0.02	0.17	0.02	0.02	0.02	1.06	0.46 - 2.46	0.89	0.95	0.006	4.63	0.03
SMAD2	0.03	0.04	0.03	1.71	1.09 - 2.68	0.02	0.17	0.03	0.03	0.04	0.89	0.57 - 1.39	0.61	0.95	0.21	4.11	0.04
TCF7L2	0.09	0.11	0.09	1.41	1.06 - 1.88	0.02	0.17	0.08	0.09	0.07	1.40	1.04 - 1.87	0.025	0.63	0.16	0.00	0.97
AXIN2	0.02	0.01	0.03	0.36	0.15 - 0.85	0.02	0.17	0.03	0.03	0.03	1.00	0.60 - 1.66	0.99	0.99	0.003	4.02	0.04
APC	0.73	0.74	0.72	1.21	1.00 - 1.47	0.049	0.35	0.75	0.73	0.76	0.93	0.78 - 1.12	0.45	0.81	0.61	3.79	0.05
KRAS	0.49	0.50	0.49	1.08	0.91 - 1.27	0.40	0.73	0.41	0.36	0.43	0.83	0.71 - 0.98	0.02	0.63	1.72E-09	4.73	0.03
FBXW7	0.12	0.12	0.11	1.26	0.98 - 1.63	0.08	0.41	0.10	0.11	0.10	1.27	0.99 - 1.63	0.06	0.68			
FLT4	0.02	0.02	0.02	0.75	0.41 - 1.40	0.37	0.73	0.02	0.02	0.03	0.58	0.33 - 1.04	0.07	0.68			
TSC2	0.02	0.02	0.02	1.54	0.88 - 2.71	0.13	0.47	0.02	0.01	0.02	0.57	0.31 - 1.06	0.08	0.68			
POLQ	0.05	0.02	0.06	0.36	0.12 - 1.04	0.06	0.37	0.05	0.07	0.04	1.77	0.94 - 3.35	0.08	0.68			
ERBB2	0.03	0.02	0.03	0.59	0.32 - 1.08	0.09	0.42	0.03	0.04	0.03	1.45	0.95 - 2.21	0.09	0.68			
SMAD3	0.03	0.03	0.03	1.32	0.73 - 2.37	0.36	0.73	0.03	0.04	0.03	1.56	0.93 - 2.60	0.09	0.68			
MGA	0.02	0.02	0.03	0.87	0.46 - 1.66	0.68	0.91	0.03	0.02	0.03	0.61	0.33 - 1.13	0.11	0.75			
SETD2	0.02	0.02	0.02	1.29	0.71 - 2.32	0.40	0.73	0.03	0.02	0.03	0.65	0.37 - 1.15	0.14	0.75			
PIK3CG	0.02	0.01	0.02	0.73	0.31 - 1.71	0.47	0.77	0.02	0.01	0.03	0.56	0.25 - 1.22	0.14	0.75			
PRKDC	0.05	0.05	0.05	0.93	0.53 - 1.63	0.79	0.91	0.04	0.05	0.04	1.47	0.85 - 2.52	0.17	0.75			
KMT2B	0.03	0.03	0.02	1.75	0.79 - 3.89	0.17	0.55	0.02	0.01	0.03	0.53	0.22 - 1.30	0.17	0.75			
ARID1A	0.06	0.07	0.06	1.26	0.89 - 1.76	0.19	0.58	0.05	0.04	0.06	0.78	0.54 - 1.12	0.18	0.75			
SMAD4	0.16	0.16	0.16	1.05	0.84 - 1.32	0.66	0.91	0.14	0.15	0.14	1.15	0.93 - 1.44	0.20	0.81			
PREX2	0.04	0.03	0.04	0.97	0.51 - 1.83	0.93	0.95	0.03	0.02	0.04	0.63	0.31 - 1.30	0.21	0.81			
ATM	0.06	0.06	0.07	0.92	0.65 - 1.31	0.65	0.91	0.06	0.05	0.06	0.81	0.57 - 1.15	0.23	0.81			
SMARCA4	0.02	0.02	0.02	1.13	0.64 - 1.99	0.67	0.91	0.03	0.02	0.03	0.72	0.42 - 1.24	0.24	0.81			
MTOR	0.03	0.02	0.03	0.86	0.51 - 1.46	0.58	0.88	0.03	0.02	0.03	0.76	0.47 - 1.24	0.27	0.81			
CTNNB1	0.04	0.03	0.04	0.82	0.53 - 1.27	0.38	0.73	0.04	0.03	0.04	0.79	0.52 - 1.21	0.28	0.81			
KMT2D	0.06	0.05	0.06	0.80	0.55 - 1.17	0.25	0.67	0.05	0.06	0.05	1.19	0.85 - 1.67	0.32	0.81			
AMER1	0.05	0.04	0.06	0.67	0.40 - 1.11	0.12	0.47	0.04	0.03	0.04	0.77	0.45 - 1.31	0.33	0.81			
ROS1	0.03	0.03	0.02	1.31	0.78 - 2.21	0.31	0.73	0.03	0.03	0.03	1.26	0.79 - 2.00	0.34	0.81			
FANCM	0.04	0.04	0.04	0.85	0.38 - 1.90	0.69	0.91	0.02	0.02	0.03	0.61	0.22 - 1.68	0.34	0.81			

<i>ATR</i>	0.02	0.03	0.02	1.53	0.88	- 2.67	0.13	0.47	0.02	0.02	0.02	0.76	0.43	- 1.35	0.35	0.81
<i>PTEN</i>	0.04	0.04	0.04	1.35	0.89	- 2.05	0.16	0.54	0.03	0.03	0.03	1.24	0.79	- 1.96	0.35	0.81
<i>NRAS</i>	0.05	0.05	0.05	1.07	0.73	- 1.58	0.73	0.91	0.04	0.04	0.05	0.84	0.57	- 1.23	0.37	0.81
<i>FAT1</i>	0.04	0.04	0.04	1.07	0.67	- 1.70	0.78	0.91	0.04	0.04	0.04	1.21	0.79	- 1.86	0.38	0.81
<i>ALK</i>	0.03	0.03	0.03	1.19	0.75	- 1.88	0.45	0.77	0.03	0.02	0.03	0.80	0.48	- 1.34	0.39	0.81
<i>ASXL1</i>	0.02	0.02	0.02	0.98	0.56	- 1.72	0.95	0.96	0.03	0.02	0.03	0.80	0.48	- 1.33	0.39	0.81
<i>DOCK8</i>	0.05	0.08	0.04	1.87	0.91	- 3.83	0.09	0.42	0.04	0.04	0.03	1.41	0.64	- 3.15	0.40	0.81
<i>ARID2</i>	0.02	0.02	0.02	1.32	0.76	- 2.29	0.32	0.73	0.02	0.02	0.03	0.79	0.46	- 1.37	0.40	0.81
<i>CIITA</i>	0.02	0.02	0.01	1.91	0.69	- 5.30	0.21	0.60	0.03	0.02	0.03	0.71	0.32	- 1.59	0.41	0.81
<i>BCOR</i>	0.03	0.02	0.03	0.69	0.39	- 1.21	0.19	0.58	0.02	0.02	0.02	1.24	0.73	- 2.10	0.42	0.81
<i>PTPRS</i>	0.05	0.04	0.05	1.13	0.65	- 1.97	0.65	0.91	0.04	0.05	0.04	1.22	0.75	- 2.00	0.43	0.81
<i>BRCA2</i>	0.04	0.03	0.04	0.84	0.54	- 1.33	0.46	0.77	0.04	0.03	0.04	0.85	0.55	- 1.29	0.44	0.81
<i>RIF1</i>	0.04	0.03	0.04	0.67	0.24	- 1.84	0.44	0.77	0.04	0.03	0.05	0.73	0.31	- 1.68	0.46	0.81
<i>MED12</i>	0.03	0.03	0.04	0.80	0.47	- 1.36	0.40	0.73	0.02	0.02	0.02	0.79	0.42	- 1.50	0.47	0.82
<i>NOTCH1</i>	0.03	0.02	0.03	0.93	0.55	- 1.60	0.80	0.91	0.03	0.02	0.03	0.84	0.51	- 1.38	0.49	0.83
<i>EPHA3</i>	0.03	0.03	0.03	0.93	0.53	- 1.64	0.80	0.91	0.03	0.02	0.03	0.86	0.49	- 1.51	0.60	0.95
<i>CARD11</i>	0.03	0.02	0.03	0.80	0.47	- 1.34	0.39	0.73	0.03	0.03	0.03	0.90	0.58	- 1.41	0.65	0.95
<i>IKZF1</i>	0.02	0.02	0.02	0.77	0.43	- 1.40	0.39	0.73	0.02	0.02	0.02	0.87	0.48	- 1.58	0.65	0.95
<i>KMT2C</i>	0.03	0.03	0.03	1.03	0.54	- 1.99	0.92	0.95	0.03	0.03	0.03	0.87	0.48	- 1.58	0.65	0.95
<i>GLI2</i>	0.05	0.07	0.05	1.67	0.91	- 3.05	0.10	0.44	0.05	0.04	0.05	0.87	0.47	- 1.61	0.67	0.95
<i>KMT2A</i>	0.02	0.02	0.02	1.10	0.64	- 1.91	0.73	0.91	0.03	0.03	0.03	1.11	0.69	- 1.78	0.67	0.95
<i>SOX9</i>	0.11	0.10	0.11	1.09	0.83	- 1.44	0.52	0.83	0.10	0.09	0.10	0.94	0.72	- 1.24	0.68	0.95
<i>EPHA5</i>	0.03	0.02	0.03	0.75	0.39	- 1.43	0.38	0.73	0.03	0.03	0.03	1.11	0.67	- 1.83	0.69	0.95
<i>PIK3CA</i>	0.19	0.17	0.20	0.97	0.78	- 1.20	0.77	0.91	0.16	0.14	0.16	0.96	0.77	- 1.19	0.69	0.95
<i>PIK3R1</i>	0.03	0.03	0.03	0.96	0.61	- 1.53	0.88	0.95	0.02	0.02	0.03	0.91	0.55	- 1.52	0.73	0.95
<i>ARID1B</i>	0.03	0.03	0.03	1.18	0.74	- 1.88	0.50	0.80	0.04	0.04	0.04	1.07	0.73	- 1.58	0.73	0.95
<i>AR</i>	0.02	0.02	0.03	0.73	0.40	- 1.33	0.30	0.73	0.02	0.02	0.02	0.91	0.50	- 1.65	0.75	0.95
<i>POLE</i>	0.02	0.02	0.02	1.10	0.60	- 2.01	0.77	0.91	0.03	0.02	0.03	1.09	0.64	- 1.86	0.75	0.95
<i>GRIN2A</i>	0.03	0.03	0.03	1.11	0.61	- 2.02	0.73	0.91	0.02	0.02	0.02	1.10	0.59	- 2.06	0.76	0.95
<i>COL7A1</i>	0.10	0.10	0.10	1.04	0.58	- 1.85	0.90	0.95	0.07	0.07	0.08	1.10	0.60	- 2.01	0.76	0.95
<i>BCORL1</i>	0.03	0.04	0.03	1.21	0.62	- 2.37	0.58	0.88	0.01	0.01	0.01	0.86	0.30	- 2.50	0.78	0.95
<i>KAT6A</i>	0.04	0.05	0.03	1.62	0.78	- 3.36	0.20	0.58	0.03	0.03	0.02	1.11	0.49	- 2.51	0.80	0.95
<i>ERBB3</i>	0.03	0.02	0.03	0.63	0.37	- 1.10	0.10	0.44	0.03	0.03	0.04	0.95	0.61	- 1.47	0.81	0.95
<i>RNF43</i>	0.04	0.03	0.05	0.60	0.36	- 1.00	0.05	0.35	0.03	0.03	0.03	0.95	0.60	- 1.51	0.83	0.95
<i>ATRX</i>	0.04	0.04	0.05	0.96	0.64	- 1.45	0.86	0.95	0.02	0.02	0.02	0.94	0.53	- 1.67	0.83	0.95
<i>CREBBP</i>	0.03	0.03	0.03	1.01	0.61	- 1.66	0.97	0.97	0.03	0.03	0.03	0.96	0.60	- 1.53	0.85	0.95
<i>PTPRT</i>	0.04	0.03	0.05	0.57	0.32	- 1.03	0.06	0.37	0.05	0.05	0.05	0.96	0.61	- 1.52	0.86	0.95
<i>NOTCH3</i>	0.03	0.02	0.03	0.78	0.45	- 1.37	0.39	0.73	0.03	0.03	0.03	1.04	0.66	- 1.65	0.87	0.95
<i>PIK3C2B</i>	0.03	0.03	0.02	1.39	0.65	- 2.95	0.39	0.73	0.03	0.02	0.03	1.06	0.50	- 2.26	0.88	0.95
<i>ERBB4</i>	0.03	0.03	0.04	0.98	0.61	- 1.57	0.93	0.95	0.04	0.03	0.04	0.98	0.64	- 1.49	0.93	0.96
<i>SETBP1</i>	0.02	0.02	0.02	0.76	0.27	- 2.14	0.60	0.89	0.03	0.03	0.03	1.03	0.48	- 2.21	0.94	0.96
<i>EPHB1</i>	0.03	0.03	0.03	1.08	0.57	- 2.03	0.82	0.91	0.03	0.03	0.03	0.98	0.54	- 1.78	0.95	0.96
<i>NF1</i>	0.03	0.02	0.03	0.91	0.53	- 1.55	0.73	0.91	0.02	0.02	0.02	1.02	0.61	- 1.69	0.95	0.96

Abbreviations: CRC, colorectal cancer; OR, odds ratio; CI, confidence interval; FDR, false discovery rate.

*ORs, 95% CIs, P and FDR values were calculated for genes from models adjusted for patient race/ethnicity, histology and site, sequencing assay, sample type and tumor mutational burden.

†P-values were derived from Cochran's Q test for heterogeneity by sex. Only genes with significant associations for non-silent somatic mutations between early-onset and late-onset non-hypermutated CRC cases in at least one sex-specific group were tested.

Table S5. Read depth for clinical-grade targeting sequencing data from tumor tissues and case counts by early-onset and late-onset groups and sequencing center.

Participating GENIE Center	Center Abbreviation	Number of Panels/ Pipelines per Center	Read depth*	Early-Onset CRC (No. Patients)	Late-Onset CRC (No. Patients)
Memorial Sloan Kettering Cancer Center	MSK	4	750X	1124	2636
Dana-Farber Cancer Institute	DFCI	3	350X	674	1660
Duke Cancer Institute, Duke University Health System	DUKE	3	750X-1000X	63	182
Johns Hopkins Sidney Kimmel Comprehensive Cancer Center	JHU	2	500X	49	171
Vanderbilt-Ingram Cancer Center	VICC	4	1000X	56	150
University of California, San Francisco	UCSF	2	500X	34	64
The University of Texas MD Anderson Cancer Center	MDA	3	250X	8	14
The Herbert Irving Comprehensive Cancer Center, Columbia University	COLU	3	1000X	2	5
Providence Cancer Institute	PROV	3	--	0	3
Princess Margaret Cancer Centre, University Health Network	UHN	5	500X	6	2

*Read depth as provided by each participating center. This includes mean (MSK, DFCI, JHU, VICC, UCSF, COLU and UHN), range (DUKE) or minimum (MDA) read depth coverage.

Supplementary Figures

Figure S1. Mutation rates among 6,903 tumor samples from colorectal cancer patients across racial/ethnic groups for (A) Asian or Pacific Islander [API], (B) Non-Hispanic Black [NHB], and (C) Non-Hispanic White [NHW] individuals. Non-hypermutated tumors were defined using a cutoff (red line) of 17.78+ mutations/Mb.

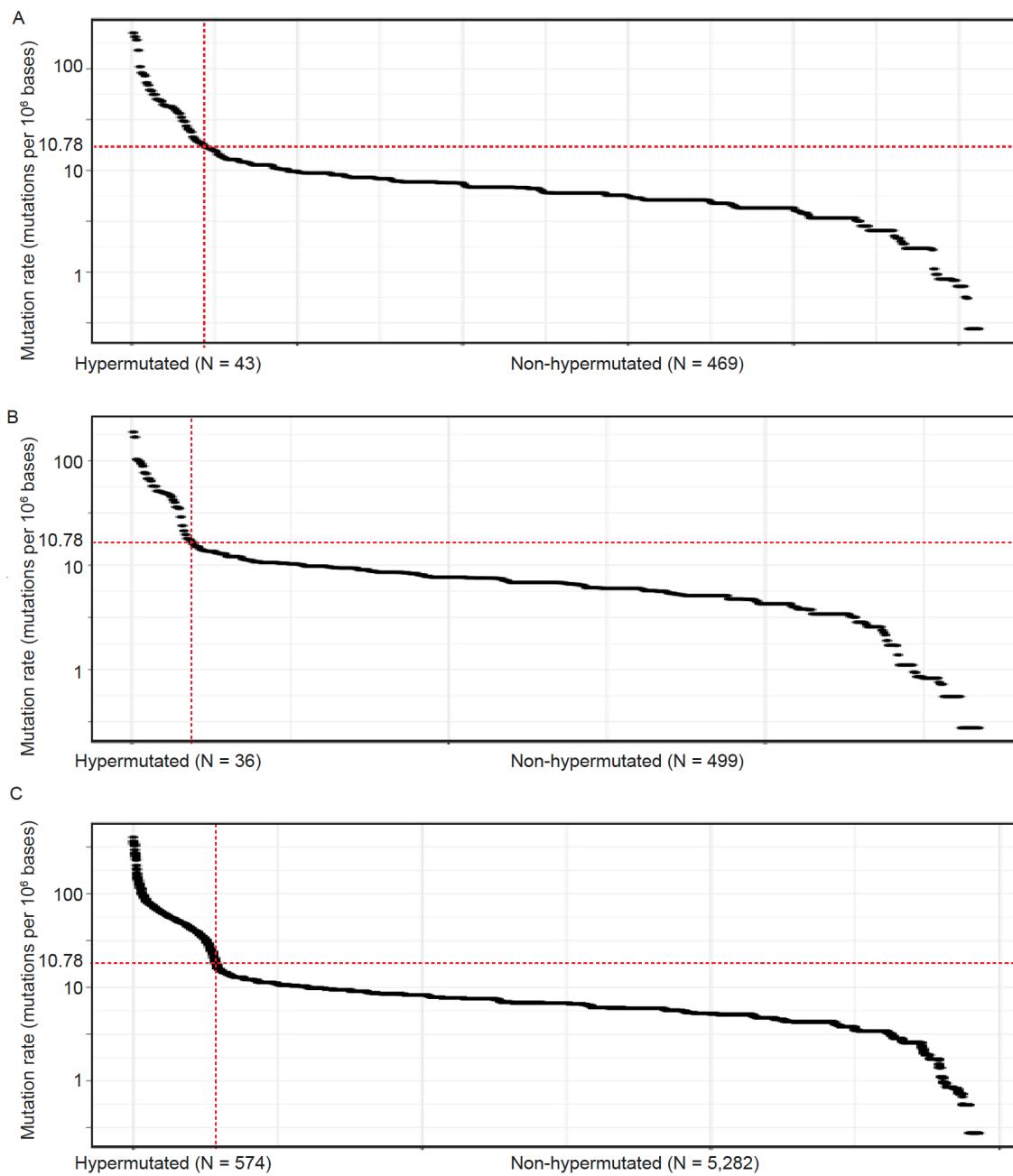


Figure S2. Adjusted mutation rates in 653 hypermutated colorectal tumors: AACR GENIE.

Boxplots of adjusted mutation rates between early-onset and late-onset cases with hypermutated CRC (left), and by sex for early-onset (middle) and late-onset (right) cases with hypermutated colorectal tumors. The residual of adjusted mutation rates and *P*-values were derived from models adjusted for race/ethnicity, sex, site and histology, sequencing assay, and sample type, as appropriate.

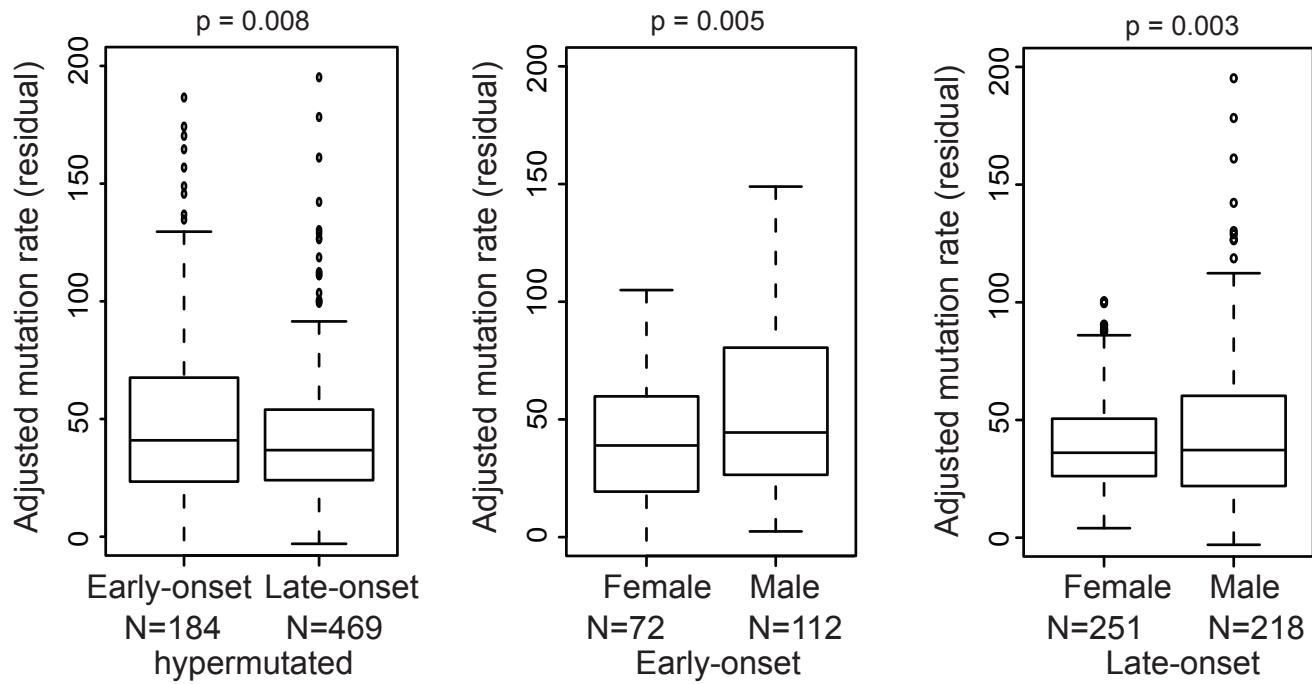


Figure S3. Tumor mutational burden (TMB) across sequencing assay/platform for early-onset and late-onset non-hypermutated colorectal cancer cases: AACR Project GENIE. TMB is defined by number of mutations per Mb. Sequencing assays/platforms with greater than 5 early-onset non-hypermutated colorectal cancer cases are presented with frequency counts (a total of 14 early-onset non-hypermutated cases excluded).

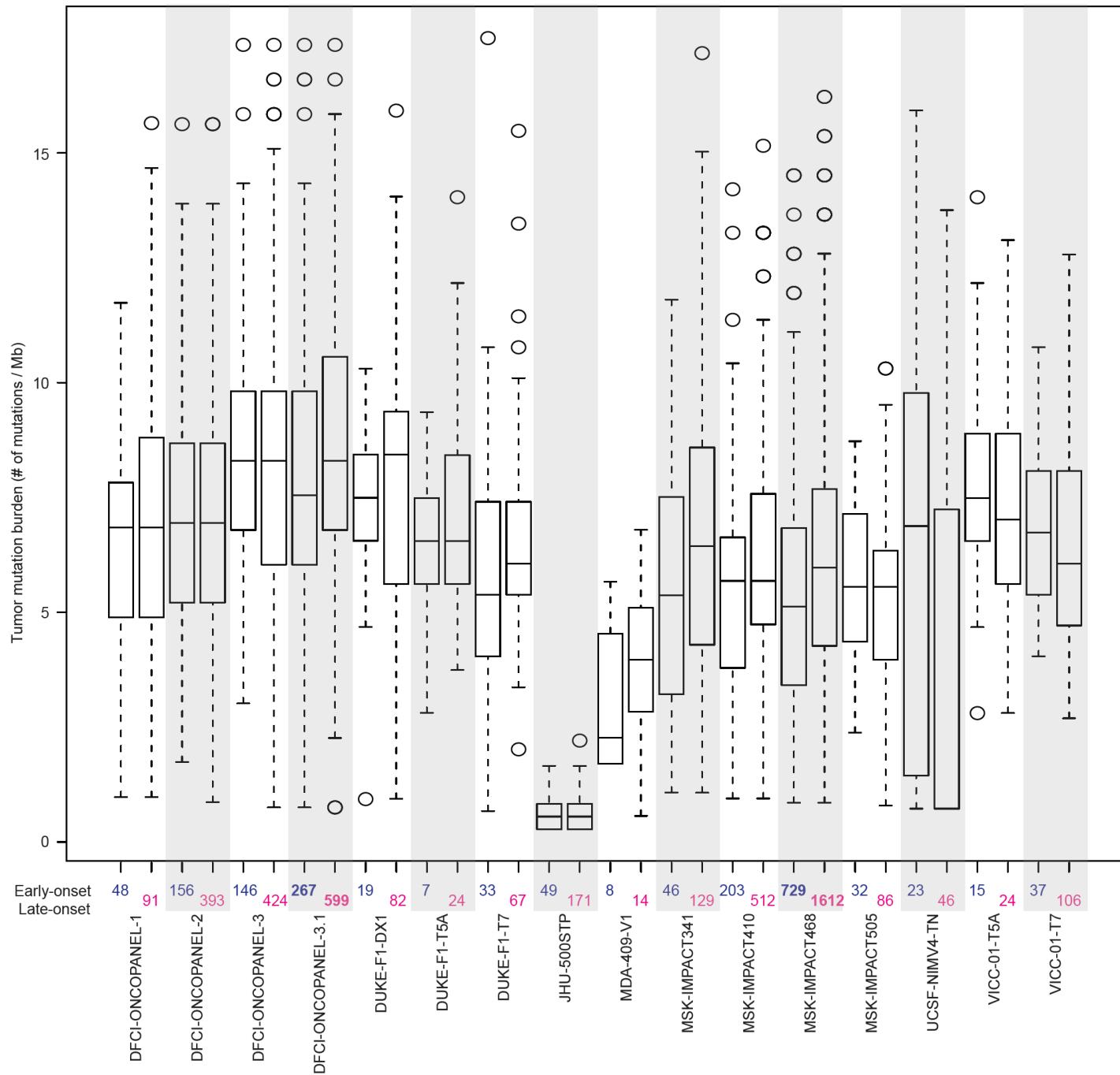


Figure S4. Frequency of non-silent somatic mutations in commonly assayed and mutated genes between early-onset and late-onset non-hypermutated CRC cases (mutation frequency >10%).

