

S1. List of subjects and associated information included in analyses.

Sample	Type	Normal tissue	Tumor reads	Normal reads	Aligner	Sequencer	Sequencing center	Somatic total	Somatic coding	Somatic nonsyn	Somatic truncations	MSI	CIMP	Expression	Hyper-mutated	Anatomic Location	Tumor Stage
2806	AML	Solid	172,035	126,563	maq-0.7.1-9	Illumina	BI	0	0	0	0						
2811	AML	Solid	107,019	221,785	maq-0.7.1-9	Illumina	BI	2	1	1	0						
2819	AML	Solid	101,693	191,303	maq-0.7.1-9	Illumina	BI	1	1	0	0						
2842	AML	Solid	36,288		maq-0.7.1-9	Illumina	BI	1	1	1	0						
2907	AML	Solid	938,570	1,615,228	bwa-0.6.1	Illumina	WUGSC	0	0	0	0						
2908	AML	Solid	173,212	24,065	maq-0.7.1-9	Illumina	BI	2	1	1	0						
2909	AML	Solid	120,558	365,373	maq-0.7.1-9	Illumina	BI	0	0	0	0						
2934	AML	Solid	80,226	690,759	maq-0.7.1-9	Illumina	BI	0	0	0	0						
2936	AML	Solid	69,173	27,401	maq-0.7.1-9	Illumina	BI	0	0	0	0						
2939	AML	Solid	106,640	683,217	maq-0.7.1-9	Illumina	BI	2	2	1	0						
2943	AML	Solid	60,088	925,131	maq-0.7.1-9	Illumina	BI	0	0	0	0						
2955	AML	Solid	28,435	46,061	maq-0.7.1-9	Illumina	BI	1	1	1	0						
2965	AML	Solid	1,330,548	1,081,376	bwa-0.6.1	Illumina	WUGSC	0	0	0	0						
2966	AML	Solid	1,224,716	1,481,882	bwa-0.6.1	Illumina	WUGSC	0	0	0	0						
2967	AML	Solid	1,443,960	674,316	bwa-0.6.1	Illumina	WUGSC	1	1	1	1						
2968	AML	Solid	1,981,152	657,432	bwa-0.6.1	Illumina	WUGSC	0	0	0	0						
2969	AML	Solid	1,036,304	392,900	bwa-0.6.1	Illumina	WUGSC	0	0	0	0						
2970	AML	Solid	1,385,202	498,452	bwa-0.6.1	Illumina	WUGSC	1	1	1	0						
2971	AML	Solid	1,508,504	845,468	bwa-0.6.1	Illumina	WUGSC	0	0	0	0						
2972	AML	Solid	2,122,386	2,219,176	bwa-0.6.1	Illumina	WUGSC	0	0	0	0						
2973	AML	Solid	1,710,206	436,514	bwa-0.6.1	Illumina	WUGSC	0	0	0	0						
2974	AML	Solid	1,294,446	654,344	bwa-0.6.1	Illumina	WUGSC	1	1	1	0						
2975	AML	Solid	1,838,636	601,524	bwa-0.6.1	Illumina	WUGSC	0	0	0	0						
2977	AML	Solid	1,216,098	1,180,616	bwa-0.6.1	Illumina	WUGSC	0	0	0	0						
2978	AML	Solid	1,532,348	1,686,062	bwa-0.6.1	Illumina	WUGSC	2	1	1	0						
2981	AML	Solid	1,758,286	327,208	bwa-0.6.1	Illumina	WUGSC	0	0	0	0						
2983	AML	Solid	2,508,752	830,970	bwa-0.6.1	Illumina	WUGSC	1	0	0	0						

2985	AML	Solid	1,224,660	835,614	bwa-0.6.1	Illumina	WUGSC	0	0	0	0						
2986	AML	Solid	1,618,540	2,443,610	bwa-0.6.1	Illumina	WUGSC	0	0	0	0						
2987	AML	Solid	508,310	1,793,657	bwa-0.5.5	Illumina	WUGSC	0	0	0	0						
2989	AML	Solid	1,497,450	1,667,752	bwa-0.6.1	Illumina	WUGSC	0	0	0	0						
2995	AML	Solid	1,350,964	1,401,700	bwa-0.6.1	Illumina	WUGSC	0	0	0	0						
2996	AML	Solid	1,360,262	1,281,124	bwa-0.6.1	Illumina	WUGSC	2	2	2	0						
3000	AML	Solid	976,972	1,026,600	bwa-0.6.1	Illumina	WUGSC	0	0	0	0						
3002	AML	Solid	1,504,574	3,458,808	bwa-0.6.1	Illumina	WUGSC	0	0	0	0						
3005	AML	Solid	1,093,376	1,790,734	bwa-0.6.1	Illumina	WUGSC	0	0	0	0						
3009	AML	Solid	1,618,940	2,233,820	bwa-0.6.1	Illumina	WUGSC	5	5	3	1						
2670	COAD	Blood	140,467	489,330	bwa-0.5.9	Illumina	Harvard	0	0	0	0	MSS	Cluster3	CIN	NO	NA	NA
2671	COAD	Blood	132,367	392,543	bwa-0.5.9	Illumina	Harvard	1	1	1	0	Not Tested	NA	NA	NA	Sigmoid Colon	Stage IV
2672	COAD	Blood	130,102	160,892	bwa-0.5.9	Illumina	Harvard	3	3	2	0	MSI-H	CIMP.H	MSI/CIMP	YES	Transverse Colon	Stage IIIB
2674	COAD	Blood	97,391	179,869	bwa-0.5.9	Illumina	Harvard	1	0	0	0	MSS	Cluster4	MSI/CIMP	NO	Sigmoid Colon	Stage IV
2676	COAD	Blood	115,178	239,964	bwa-0.5.9	Illumina	Harvard	3	2	2	0	MSI-H	CIMP.H	MSI/CIMP	YES	Cecum	Stage IIB
2678	COAD	Blood	163,222	478,762	bwa-0.5.9	Illumina	Harvard	0	0	0	0	MSS	Cluster3	Invasive	NO	Transverse Colon	Stage IIIB
2679	COAD	Blood	46,175	170,985	bwa-0.5.9	Illumina	Harvard	2	1	1	1	Not Tested	NA	NA	NA	Ascending Colon	Stage IIB
2680	COAD	Blood	110,680	446,579	bwa-0.5.9	Illumina	Harvard	1	0	0	0	Not Tested	NA	NA	NA	Hepatic Flexure	Stage II
2681	COAD	Blood	65,333	450,746	bwa-0.5.9	Illumina	Harvard	0	0	0	0	Not Tested	NA	NA	NA	Cecum	Stage IIA
2682	COAD	Blood	108,648	562,538	bwa-0.5.9	Illumina	Harvard	0	0	0	0	Not Tested	NA	NA	NA	Cecum	Stage IV
2683	COAD	Blood	103,486	541,486	bwa-0.5.9	Illumina	Harvard	3	3	1	0	MSI-L	CIMP.L	CIN	NO	Ascending Colon	Stage IV
2684	COAD	Blood	14,926	157,163	bwa-0.5.9	Illumina	Harvard	0	0	0	0	Not Tested	NA	NA	NA	Cecum	Stage I
3509	COAD	Solid	113,991	230,765	bwa-0.5.9	Illumina	Harvard	1	1	1	1	Not Tested	NA	NA	NA	Sigmoid Colon	Stage II
3510	COAD	Solid	167,823	503,988	bwa-0.5.9	Illumina	Harvard	0	0	0	0	Not Tested	NA	NA	NA	Transverse Colon	Stage II
3514	COAD	Blood	138,541	795,875	bwa-0.5.9	Illumina	Harvard	0	0	0	0	MSS	Cluster3	MSI/CIMP	NO	Ascending Colon	Stage I
3516	COAD	Blood	108,072	236,502	bwa-0.5.9	Illumina	Harvard	1	1	1	0	MSI-H	CIMP.H	MSI/CIMP	YES	Ascending Colon	Stage III
3529	COAD	Solid	245,602	817,109	bwa-0.5.9	Illumina	Harvard	0	0	0	0	MSI-L	Cluster4	CIN	NO	Sigmoid Colon	Stage IIIC
3534	COAD	Blood	3,840,670	999,542	bwa-0.5.9	Illumina	BCM	3	2	1	0	MSS	Cluster3	CIN	NO	Ascending Colon	Stage IIA
3548	COAD	Blood	161,551	315,369	bwa-0.5.9	Illumina	Harvard	2	1	1	1	MSS	Cluster3	CIN	NO	Cecum	Stage IIIC
3549	COAD	Blood	98,156	414,253	bwa-0.5.9	Illumina	Harvard	0	0	0	0	MSS	CIMP.L	CIN	NO	Cecum	Stage I
3553	COAD	Blood	249,536	245,326	bwa-0.5.9	Illumina	Harvard	1	1	1	1	MSI-L	Cluster4	CIN	NO	Sigmoid Colon	Stage I

3555	COAD	Blood	193,719	119,868	bwa-0.5.9	Illumina	Harvard	2	1	1	0	MSS	CIMP.L	MSI/CIMP	YES	Hepatic Flexure	Stage IIA
3558	COAD	Blood	177,912	515,731	bwa-0.5.9	Illumina	Harvard	2	1	1	0	MSS	CIMP.L	Invasive	NO	Sigmoid Colon	NA
3664	COAD	Blood	181,258	400,386	bwa-0.5.9	Illumina	Harvard	1	0	0	0	MSS	CIMP.H	MSI/CIMP	NO	Cecum	Stage II
3666	COAD	Blood	240,336	382,297	bwa-0.5.9	Illumina	Harvard	3	3	3	1	MSS	Cluster4	Invasive	NO	Cecum	Stage III
3672	COAD	Blood	114,652	129,619	bwa-0.5.9	Illumina	Harvard	0	0	0	0	MSI-H	CIMP.H	MSI/CIMP	YES	Transverse Colon	Stage III
3675	COAD	Blood	217,808	541,740	bwa-0.5.9	Illumina	Harvard	2	2	2	0	Not Tested	CIMP.L	NA	NA	Hepatic Flexure	Stage II
3681	COAD	Blood	156,095	463,061	bwa-0.5.9	Illumina	Harvard	0	0	0	0	MSS	CIMP.L	MSI/CIMP	NO	Cecum	Stage III
3685	COAD	Blood	134,991	449,190	bwa-0.5.9	Illumina	Harvard	0	0	0	0	MSS	Cluster4	Invasive	NO	Sigmoid Colon	Stage II
3688	COAD	Blood	143,522	82,192	bwa-0.5.9	Illumina	Harvard	3	2	2	0	MSS	Cluster4	CIN	NO	Sigmoid Colon	Stage IV
3692	COAD	Blood	110,024	231,482	bwa-0.5.9	Illumina	Harvard	0	0	0	0	MSS	Cluster4	Invasive	NO	Splenic Flexure	Stage IV
3693	COAD	Blood	108,218	348,057	bwa-0.5.9	Illumina	Harvard	2	2	2	2	MSS	Cluster4	CIN	NO	Sigmoid Colon	Stage IV
3715	COAD	Blood	93,318	112,830	bwa-0.5.9	Illumina	Harvard	7	7	6	1	MSI-H	CIMP.H	MSI/CIMP	YES	Ascending Colon	Stage II
3807	COAD	Solid	424,159	426,668	bwa-0.5.9	Illumina	Harvard	2	0	0	0	MSS	Cluster4	MSI/CIMP	NO	Sigmoid Colon	Stage IIIC
3808	COAD	Solid	413,591	420,815	bwa-0.5.9	Illumina	Harvard	1	0	0	0	MSI-L	Cluster3	MSI/CIMP	NO	Cecum	Stage IIA
3810	COAD	Solid	469,400	329,459	bwa-0.5.9	Illumina	Harvard	2	1	1	1	MSS	Cluster4	MSI/CIMP	NO	Sigmoid Colon	Stage IIA
3812	COAD	Blood	137,004	534,804	bwa-0.5.9	Illumina	Harvard	1	0	0	0	MSS	Cluster4	MSI/CIMP	NO	Sigmoid Colon	Stage IIA
3861	COAD	Blood	193,657	651,699	bwa-0.5.9	Illumina	Harvard	3	2	2	0	Not Tested	CIMP.L	Invasive	NA	Cecum	Stage IIA
3947	COAD	Blood	199,154	336,480	bwa-0.5.9	Illumina	Harvard	0	0	0	0	MSI-H	CIMP.H	MSI/CIMP	YES	Ascending Colon	Stage IIB
3955	COAD	Blood	47,892	42,494	bwa-0.5.9	Illumina	BCM	0	0	0	0	MSS	Cluster4	CIN	NO	Descending Colon	Stage IIIB
3956	COAD	Blood	98,515	588,418	bwa-0.5.9	Illumina	Harvard	0	0	0	0	MSS	Cluster3	CIN	NO	Cecum	Stage IIA
3966	COAD	Blood	92,390	113,225	bwa-0.5.9	Illumina	Harvard	2	1	1	0	MSI-H	CIMP.L	MSI/CIMP	YES	Hepatic Flexure	Stage IIA
3968	COAD	Blood	65,276	376,180	bwa-0.5.9	Illumina	Harvard	3	3	3	0	Not Tested	Cluster3	CIN	NA	Sigmoid Colon	Stage I
3970	COAD	Blood	68,156	241,363	bwa-0.5.9	Illumina	Harvard	3	2	2	1	Not Tested	Cluster3	NA	NA	Sigmoid Colon	Stage IIA
3994	COAD	Blood	97,264	437,069	bwa-0.5.9	Illumina	Harvard	2	0	0	0	MSS	CIMP.H	MSI/CIMP	NO	Transverse Colon	Stage IIIB
4070	COAD	Blood	29,878	142,820	bwa-0.5.9	Illumina	Harvard	0	0	0	0	MSS	Cluster3	CIN	NO	Cecum	Stage IIIC
4071	COAD	Blood	33,575	214,010	bwa-0.5.9	Illumina	Harvard	3	3	3	1	MSS	Cluster3	CIN	NO	NA	Stage I
4308	COAD	Blood	103,810	748,569	bwa-0.5.9	Illumina	Harvard	1	1	1	1	Not Tested	NA	NA	NA	Sigmoid Colon	Stage IIIB
4313	COAD	Blood	52,903	180,955	bwa-0.5.9	Illumina	Harvard	1	1	1	0	Not Tested	NA	NA	NA	Descending Colon	Stage I
4315	COAD	Blood	126,020	293,581	bwa-0.5.9	Illumina	Harvard	2	2	2	1	Not Tested	NA	NA	NA	Cecum	Stage IIA
4614	COAD	Blood	95,422	145,883	bwa-0.5.9	Illumina	Harvard	1	0	0	0	Not Tested	NA	NA	NA	NA	Stage IVA
4615	COAD	Blood	71,521	158,197	bwa-0.5.9	Illumina	Harvard	0	0	0	0	Not Tested	NA	NA	NA	NA	Stage IIIB

4681	COAD	Blood	99,508	573,380	bwa-0.5.9	Illumina	Harvard	0	0	0	0	Not Tested	NA	NA	NA	Ascending Colon	Stage IIA
4682	COAD	Blood	60,584	684,231	bwa-0.5.9	Illumina	Harvard	1	1	1	1	Not Tested	NA	NA	NA	Sigmoid Colon	Stage IVA
4684	COAD	Blood	118,020	460,228	bwa-0.5.9	Illumina	Harvard	2	2	2	1	Not Tested	NA	NA	NA	NA	Stage IVA
4744	COAD	Blood	69,400	270,124	bwa-0.5.9	Illumina	Harvard	1	1	1	0	Not Tested	NA	NA	NA	Cecum	Stage I
4746	COAD	Blood	87,067	465,179	bwa-0.5.9	Illumina	Harvard	2	2	1	1	Not Tested	NA	NA	NA	Sigmoid Colon	Stage I
4747	COAD	Blood	277,924	714,931	bwa-0.5.9	Illumina	Harvard	1	1	1	1	Not Tested	NA	NA	NA	Cecum	Stage IVA
4748	COAD	Blood	91,371	564,672	bwa-0.5.9	Illumina	Harvard	3	2	2	0	Not Tested	NA	NA	NA	Transverse Colon	Stage IIIB
4750	COAD	Blood	122,492	634,810	bwa-0.5.9	Illumina	Harvard	1	0	0	0	Not Tested	NA	NA	NA	NA	Stage IIIA
4752	COAD	Blood	112,385	401,114	bwa-0.5.9	Illumina	Harvard	1	1	1	0	Not Tested	NA	NA	NA	Ascending Colon	Stage IIA
4951	COAD	Blood	114,412	489,930	bwa-0.5.9	Illumina	Harvard	1	0	0	0	Not Tested	NA	NA	NA	Ascending Colon	Stage IIA
5256	COAD	Blood	147,563	193,095	bwa-0.5.9	Illumina	Harvard	3	1	0	0	Not Tested	NA	NA	NA	Hepatic Flexure	Stage IIA
A00N	COAD	Blood	252,882	208,397	bwa-0.5.9	Illumina	Harvard	1	1	1	0	MSI-L	Cluster4	MSI/CIMP	YES	Cecum	Stage IIB
A00Q	COAD	Blood	271,031	201,040	bwa-0.5.9	Illumina	Harvard	1	0	0	0	Not Tested	CIMP.L	CIN	NO	Sigmoid Colon	Stage IIIB
A00R	COAD	Blood	319,832	83,397	bwa-0.5.9	Illumina	Harvard	1	1	1	0	MSI-H	CIMP.L	MSI/CIMP	YES	Cecum	Stage I
A00U	COAD	Blood	144,810	119,509	bwa-0.5.9	Illumina	Harvard	1	0	0	0	MSS	CIMP.L	Invasive	NO	Ascending Colon	Stage IIIB
A00W	COAD	Blood	140,715	136,034	bwa-0.5.9	Illumina	Harvard	2	2	2	1	MSS	Cluster3	Invasive	NO	Sigmoid Colon	Stage I
A00Z	COAD	Blood	128,834	67,501	bwa-0.5.9	Illumina	Harvard	3	2	2	1	MSS	Cluster4	CIN	NO	Sigmoid Colon	Stage IIA
A010	COAD	Blood	333,269	130,309	bwa-0.5.9	Illumina	Harvard	1	0	0	0	MSI-L	Cluster4	MSI/CIMP	NO	Transverse Colon	Stage IIB
A01C	COAD	Blood	147,640	143,524	bwa-0.5.9	Illumina	Harvard	0	0	0	0	Not Tested	Cluster4	CIN	NA	Ascending Colon	Stage IIIA
A01D	COAD	Blood	128,335	155,052	bwa-0.5.9	Illumina	Harvard	2	2	2	0	MSS	CIMP.L	MSI/CIMP	NO	Sigmoid Colon	Stage IIIC
A01G	COAD	Blood	684,297	111,839	bwa-0.5.9	Illumina	Harvard	1	1	1	0	MSI-L	CIMP.L	Invasive	NO	Cecum	Stage IIA
A01I	COAD	Blood	188,685	247,173	bwa-0.5.9	Illumina	Harvard	2	2	2	1	MSS	CIMP.L	Invasive	NO	Sigmoid Colon	Stage I
A01K	COAD	Blood	274,403	97,841	bwa-0.5.9	Illumina	Harvard	0	0	0	0	MSS	Cluster3	MSI/CIMP	NO	Sigmoid Colon	Stage IIIC
A01P	COAD	Solid	344,626	83,882	bwa-0.5.9	Illumina	Harvard	1	0	0	0	MSI-H	CIMP.H	NA	YES	Ascending Colon	Stage IIIB
A01Q	COAD	Blood	380,306	199,916	bwa-0.5.9	Illumina	Harvard	1	0	0	0	MSI-H	CIMP.L	MSI/CIMP	YES	Ascending Colon	Stage II
A01R	COAD	Solid	349,112	96,374	bwa-0.5.9	Illumina	Harvard	1	1	1	0	MSI-H	CIMP.L	NA	YES	Ascending Colon	Stage IIIC
A01S	COAD	Solid	413,372	146,205	bwa-0.5.9	Illumina	Harvard	0	0	0	0	MSI-L	Cluster4	NA	NO	Sigmoid Colon	Stage IIIB
A01T	COAD	Solid	365,609	141,869	bwa-0.5.9	Illumina	Harvard	2	2	2	0	MSS	Cluster3	NA	NO	Sigmoid Colon	Stage IIIB
A02K	COAD	Blood	99,831	167,601	bwa-0.5.9	Illumina	Harvard	0	0	0	0	Not Tested	Cluster3	NA	NA	Ascending Colon	Stage IV
A02O	COAD	Solid	152,611	64,890	bwa-0.5.9	Illumina	Harvard	0	0	0	0	MSS	CIMP.H	NA	NO	Transverse Colon	Stage II
A02R	COAD	Blood	381,712	56,234	bwa-0.5.9	Illumina	Harvard	5	3	1	0	Not Tested	CIMP.H	MSI/CIMP	NA	Cecum	Stage IIA

A02W	COAD	Blood	272,246	170,592	bwa-0.5.9	Illumina	Harvard	3	2	2	1	MSI-L	Cluster4	CIN	NO	Sigmoid Colon	Stage I
A02Y	COAD	Blood	81,809	75,534	bwa-0.5.9	Illumina	Harvard	2	2	2	1	MSS	CIMP.L	NA	NO	Cecum	Stage I
A03J	COAD	Solid	191,734	77,877	bwa-0.5.9	Illumina	Harvard	2	2	2	1	MSS	CIMP.L	NA	NO	Sigmoid Colon	Stage I
124	GBM	Blood	735,485	3,678,908	maq-0.7.1	Illumina	WUGSC	0	0	0	0						
145	GBM	Blood	616,095	2,531,599		Illumina		1	0	0	0						
152	GBM	Blood	547,708	1,351,130	bwa-0.6.1	Illumina	BI	0	0	0	0						
155	GBM	Blood	248,934	997,705		Illumina		1	1	0	0						
185	GBM	Blood	2,495,527	438,618	maq-0.7.1-9	Illumina	BI	0	0	0	0						
188	GBM	Blood	353,330	4,094,026		Illumina		0	0	0	0						
208	GBM	Blood	1,007,442	3,052,700	bwa-0.6.1	Illumina	WUGSC	1	0	0	0						
214	GBM	Blood	569,976	3,269,556	bwa-0.6.1	Illumina	WUGSC	0	0	0	0						
648	GBM	Blood	849,233	2,505,503		Illumina		0	0	0	0						
686	GBM	Blood	899,363	677,474	maq-0.7.1-9	Illumina	BI	0	0	0	0						
692	GBM	Blood	1,356,559	1,382,680	maq-0.7.1-9	Illumina	BI	1	1	1	0						
742	GBM	Blood	515,275	1,027,343	maq-0.7.1-9	Illumina	BI	2	1	1	0						
744	GBM	Blood	2,070,086	2,505,432	maq-0.7.1-9	Illumina	BI	0	0	0	0						
745	GBM	Blood	1,139,184	869,798	maq-0.7.1-9	Illumina	BI	0	0	0	0						
786	GBM	Blood	442,108	889,101		Illumina		1	1	1	0						
821	GBM	Blood	1,868,105	1,049,624	maq-0.7.1-9	Illumina	BI	0	0	0	0						
827	GBM	Blood	6,399,542	2,482,402	maq-0.7.1-9	Illumina	BI	0	0	0	0						
828	GBM	Blood	3,740,829	3,356,113	maq-0.7.1-9	Illumina	BI	0	0	0	0						
846	GBM	Blood	2,911,590	308,719	maq-0.7.1-9	Illumina	BI	0	0	0	0						
861	GBM	Blood	1,915,409	390,903	maq-0.7.1-9	Illumina	BI	0	0	0	0						
877	GBM	Blood	526,398	4,234,560	bwa-0.6.1	Illumina	WUGSC	0	0	0	0						
878	GBM	Blood	856,902	1,247,005	maq-0.7.1-9	Illumina	BI	0	0	0	0						
881	GBM	Blood	1,849,078	1,849,078	bwa-0.6.1	Illumina	WUGSC	0	0	0	0						
882	GBM	Blood	1,736,721	539,630	maq-0.7.1-9	Illumina	BI	0	0	0	0						
1063	GBM	Blood	1,211,202	173,109	bwa-0.5.5	Illumina	WUGSC	0	0	0	0						
1086	GBM	Blood	324,025	1,048,922		Illumina		1	1	1	0						
1401	GBM	Blood	487,324	3,426,534		Illumina		0	0	0	0						
1438	GBM	Blood	218,731	1,869,566		Illumina		0	0	0	0						

1454	GBM	Blood	879,776	757,931		Illumina		0	0	0	0
1459	GBM	Blood	658,334	1,253,705		Illumina		1	0	0	0
1460	GBM	Blood	322,484	7,598,177		Illumina		0	0	0	0
1830	GBM	Blood	1,199,840	227,564	maq-0.7.1-9	Illumina	BI	0	0	0	0
723	OV	Blood	625,804	4,007,870	bwa-0.6.1	Illumina	WUGSC	1	0	0	0
751	OV	Blood	995,290	8,655,131		Illumina		1	1	1	0
886	OV	Blood	3,300,408	7,394,468	maq-0.7.1-9	Illumina	BI	1	1	1	0
890	OV	Blood	892,872	6,483,156	bwa-0.6.1	Illumina	WUGSC	0	0	0	0
931	OV	Solid	7,181,621	9,189,433	maq-0.7.1-9	Illumina	BI	0	0	0	0
934	OV	Solid	12,292,397	16,522,869	maq-0.7.1-9	Illumina	BI	0	0	0	0
970	OV	Blood	2,653,231	1,672,579	maq-0.7.1-9	Illumina	BI	0	0	0	0
975	OV	Blood	3,968,254	1,776,148	maq-0.7.1-9	Illumina	BI	1	1	0	0
979	OV	Blood	3,450,254	4,195,613	maq-0.7.1-9	Illumina	BI	1	0	0	0
980	OV	Blood	1,182,558	2,003,830	bwa-0.6.1	Illumina	WUGSC	0	0	0	0
982	OV	Blood	1,111,850	4,549,218		Illumina		0	0	0	0
1027	OV	Blood	3,336,360	4,600,122	maq-0.7.1-9	Illumina	BI	1	1	1	1
1103	OV	Blood	2,758,670	5,467,896	bwa-0.6.1	Illumina	WUGSC	1	1	1	0
1122	OV	Blood	3,779,247	2,408,549	maq-0.7.1-9	Illumina	BI	0	0	0	0
1313	OV	Blood	3,607,159	3,227,209	maq-0.7.1-9	Illumina	BI	0	0	0	0
1319	OV	Blood	1,529,069	4,808,996		Illumina		2	1	1	0
1320	OV	Blood	2,357,769	2,683,044	maq-0.7.1-9	Illumina	BI	0	0	0	0
1326	OV	Blood	4,417,521	7,733,555	maq-0.7.1-9	Illumina	BI	1	1	1	0
1328	OV	Blood	6,281,769	4,329,508	maq-0.7.1-9	Illumina	BI	0	0	0	0
1329	OV	Blood	4,122,734	1,339,973	maq-0.7.1-9	Illumina	BI	0	0	0	0
1331	OV	Blood	1,229,285	1,274,134	maq-0.7.1-9	Illumina	BI	4	4	4	0
1341	OV	Blood	3,376,907	1,956,714	maq-0.7.1-9	Illumina	BI	1	1	1	0
1342	OV	Solid	2,720,176	3,868,275	maq-0.7.1-9	Illumina	BI	0	0	0	0
1356	OV	Solid	1,973,456	3,003,360	maq-0.7.1-9	Illumina	BI	0	0	0	0
1357	OV	Solid	1,993,710	3,107,402	maq-0.7.1-9	Illumina	BI	0	0	0	0
1371	OV	Solid	2,543,798	2,803,608	bwa-0.6.1	Illumina	BI	0	0	0	0
1411	OV	Blood	830,522	8,423,464	bwa-0.6.1	Illumina	WUGSC	1	1	1	0

1853	OV	Blood	33,784	66,714	maq-0.7.1-9	Illumina	BI	3	1	1	0						
2689	READ	Blood	192,339	365,448	bwa-0.5.9	Illumina	Harvard	3	2	2	1	MSS	CIMP.L	CIN	NO	Rectosigmoid Jctn	Stage IV
2691	READ	Blood	147,431	646,677	bwa-0.5.9	Illumina	Harvard	0	0	0	0	MSS	CIMP.L	Invasive	NO	Rectum	Stage I
2692	READ	Blood	109,187	557,574	bwa-0.5.9	Illumina	Harvard	1	1	1	0	MSS	Cluster4	CIN	NO	NA	Stage IIA
3574	READ	Blood	196,810	804,305	bwa-0.5.9	Illumina	Harvard	2	2	1	0	MSS	Cluster3	CIN	NO	Rectum	Stage II
3582	READ	Blood	65,609	454,831	bwa-0.5.9	Illumina	Harvard	1	1	1	0	MSS	Cluster4	CIN	NO	Rectum	Stage IV
3727	READ	Blood	153,648	233,853	bwa-0.5.9	Illumina	Harvard	1	1	0	0	MSS	Cluster3	CIN	NO	Rectum	Stage III
3728	READ	Blood	148,840	309,071	bwa-0.5.9	Illumina	Harvard	1	0	0	0	Not Tested	Cluster4	MSI/CIMP	NA	Rectum	Stage IIIB
3878	READ	Blood	252,365	114,455	bwa-0.5.9	Illumina	Harvard	3	2	2	0	MSS	CIMP.L	MSI/CIMP	NO	Rectum	Stage I
3881	READ	Blood	82,762	223,718	bwa-0.5.9	Illumina	Harvard	0	0	0	0	MSS	CIMP.L	MSI/CIMP	NO	Rectum	Stage IIA
3882	READ	Blood	77,646	219,073	bwa-0.5.9	Illumina	Harvard	3	1	1	0	MSS	Cluster4	CIN	NO	Rectum	Stage I
3885	READ	Blood	86,403	202,070	bwa-0.5.9	Illumina	Harvard	2	2	1	0	Not Tested	CIMP.L	Invasive	NA	Rectum	Stage IIIB
3887	READ	Blood	195,402	378,819	bwa-0.5.9	Illumina	Harvard	1	1	1	0	MSS	Cluster4	CIN	NO	Rectum	Stage IIA
3890	READ	Blood	74,731	575,360	bwa-0.5.9	Illumina	Harvard	1	1	1	1	MSS	Cluster3	CIN	NO	Rectum	Stage I
3892	READ	Blood	194,150	488,521	bwa-0.5.9	Illumina	Harvard	0	0	0	0	MSS	Cluster4	Invasive	YES	Rectum	Stage I
3893	READ	Blood	189,743	709,627	bwa-0.5.9	Illumina	Harvard	2	1	1	0	MSS	Cluster4	CIN	NO	Rectum	Stage IIIB
3894	READ	Blood	205,805	836,827	bwa-0.5.9	Illumina	Harvard	1	1	1	0	MSS	Cluster3	CIN	NO	Rectum	Stage IIA
3896	READ	Blood	200,174	613,616	bwa-0.5.9	Illumina	Harvard	2	1	1	1	MSS	Cluster3	CIN	NO	Rectum	Stage I
3898	READ	Blood	75,714	228,272	bwa-0.5.9	Illumina	Harvard	3	2	1	0	MSS	Cluster3	CIN	NO	Rectum	Stage IIA
3902	READ	Blood	201,227	571,816	bwa-0.5.9	Illumina	Harvard	2	1	0	0	MSS	CIMP.L	MSI/CIMP	NO	Rectum	Stage IIA
3909	READ	Blood	296,465	585,506	bwa-0.5.9	Illumina	Harvard	1	1	1	1	MSS	Cluster3	CIN	NO	Rectum	Stage IIIB
3913	READ	Solid	214,071	252,715	bwa-0.5.9	Illumina	Harvard	2	2	1	0	MSS	Cluster4	CIN	NO	Rectosigmoid Jctn	Stage IV
3999	READ	Blood	189,195	1,033,940	bwa-0.5.9	Illumina	Harvard	3	2	2	2	MSS	Cluster3	CIN	NO	Rectum	Stage IIIC
4001	READ	Blood	253,010	666,963	bwa-0.5.9	Illumina	Harvard	2	1	1	1	MSI-L	Cluster4	CIN	NO	Rectum	Stage IIA
4005	READ	Blood	103,111	407,831	bwa-0.5.9	Illumina	Harvard	1	0	0	0	MSS	Cluster3	CIN	NO	Rectum	Stage IV
4007	READ	Blood	133,301	375,788	bwa-0.5.9	Illumina	Harvard	1	0	0	0	MSI-L	CIMP.L	CIN	NO	Rectum	Stage IV
4008	READ	Blood	107,024	829,455	bwa-0.5.9	Illumina	Harvard	0	0	0	0	MSS	Cluster3	CIN	NO	Rectum	Stage IIA
4015	READ	Blood	121,772	394,662	bwa-0.5.9	Illumina	Harvard	3	3	3	1	MSS	Cluster4	CIN	NO	Rectum	Stage IIA
A002	READ	Blood	109,920	180,002	bwa-0.5.9	Illumina	Harvard	0	0	0	0	MSS	Cluster3	MSI/CIMP	YES	Rectum	Stage I
A008	READ	Blood	85,766	143,303	bwa-0.5.9	Illumina	Harvard	0	0	0	0	MSS	Cluster4	Invasive	NO	Rectum	Stage I
A00C	READ	Blood	120,417	166,263	bwa-0.5.9	Illumina	Harvard	1	1	1	1	MSS	Cluster3	Invasive	NO	Rectum	Stage IIIB

A00H	READ	Blood	115,632	92,171	bwa-0.5.9	Illumina	Harvard	3	2	2	1	MSS	Cluster4	Invasive	NO	Rectum	Stage IIA
A00Y	READ	Blood	186,017	93,726	bwa-0.5.9	Illumina	Harvard	1	1	1	0	MSS	Cluster3	Invasive	NO	Rectum	Stage IIA
A011	READ	Blood	130,704	161,785	bwa-0.5.9	Illumina	Harvard	1	0	0	0	MSS	CIMP.L	Invasive	NO	Rectum	Stage IIA
A014	READ	Blood	116,655	200,986	bwa-0.5.9	Illumina	Harvard	2	2	2	1	MSS	Cluster4	CIN	NO	Rectum	Stage I
A015	READ	Blood	279,064	64,840	bwa-0.5.9	Illumina	Harvard	2	1	1	0	Not Tested	Cluster3	Invasive	NO	Rectum	Stage I
A016	READ	Blood	400,265	117,621	bwa-0.5.9	Illumina	Harvard	4	2	1	1	Not Tested	Cluster3	CIN	NO	Rectum	Stage IV
A01J	READ	Blood	191,669	82,362	bwa-0.5.9	Illumina	Harvard	2	2	2	0	Not Tested	Cluster4	CIN	NA	Rectum	Stage IIA
A01L	READ	Blood	237,214	71,236	bwa-0.5.9	Illumina	Harvard	4	4	2	1	MSS	Cluster3	Invasive	NO	Rectum	Stage IIIB
A01N	READ	Blood	148,819	83,080	bwa-0.5.9	Illumina	Harvard	0	0	0	0	Not Tested	Cluster4	CIN	NA	Rectum	Stage IV
A01W	READ	Solid	192,201	92,532	bwa-0.5.9	Illumina	Harvard	1	0	0	0	MSS	NA	NA	NO	Rectum	Stage IIA
A01Y	READ	Solid	215,695	53,081	bwa-0.5.9	Illumina	Harvard	0	0	0	0	MSS	NA	NA	NO	Rectum	Stage IIA
A020	READ	Solid	239,340	64,873	bwa-0.5.9	Illumina	Harvard	1	1	1	0	MSS	NA	NA	NO	Rectum	Stage IIIB
A032	READ	Blood	171,207	98,267	bwa-0.5.9	Illumina	Harvard	0	0	0	0	MSS	Cluster4	CIN	NO	Rectum	Stage IIIB

Abbreviations: MSI, microsatellite instability MSS, microsatellite stable; MSI-H, microsatellite instability-high; MSI-L microsatellite instability-low.

S2. Inherited mtDNA variants and somatic mtDNA mutations found in 226 tumors.

Tumor	Sample	Region	Variant type	aa change	Pos	Locus	FI	Score	Ref	Obs	Tumor heteroplasmy	Normal heteroplasmy	Δ heteroplasmy	MT depth tumor	MT depth normal	MtDB Fr
COAD	2676	Noncoding	Noncoding SNV		591	tRNA Phe			C	T	86.80%	0.00%	86.80%	718	329	0.00%
COAD	3534	Noncoding	Noncoding SNV		709	12S rRNA			G	A	91.60%	0.25%	91.35%	7,932	4,073	16.42%
COAD	3812	Noncoding	Noncoding SNV		777	12S rRNA			G	A	58.70%	0.00%	58.70%	1,773	447	0.00%
READ	3896	Noncoding	Noncoding SNV		777	12S rRNA			G	A	76.40%	0.43%	75.97%	1,370	467	0.00%
COAD	2680	Noncoding	Noncoding SNV		822	12S rRNA			G	A	16.00%	0.00%	16.00%	1,249	533	0.00%
OV	723	Noncoding	Noncoding SNV		888	12S rRNA			T	C	90.50%	1.00%	89.50%	7,920	3,741	0.00%
COAD	A00Q	Noncoding	Noncoding SNV		930	12S rRNA			G	A	86.50%	0.39%	86.11%	511	760	2.26%
READ	A016	Noncoding	Noncoding SNV		1,097	12S rRNA			G	A	45.80%	0.32%	45.48%	236	943	0.00%
GBM	742	Noncoding	Noncoding SNV		1,227	12S rRNA			G	A	72.00%	1.32%	70.68%	1,933	2,497	0.00%
GBM	208	Noncoding	Noncoding SNV		1,415	12S rRNA			G	A	34.00%	0.00%	34.00%	7,864	4,764	0.04%
READ	3728	Noncoding	Noncoding SNV		1,420	12S rRNA			T	C	74.90%	0.83%	74.07%	896	240	0.11%
COAD	3970	Noncoding	Noncoding SNV		1,604	tRNA Val			G	A	34.60%	0.00%	34.60%	633	207	0.00%
COAD	4614	Noncoding	Noncoding SNV		1,604	tRNA Val			G	A	91.90%	0.47%	91.43%	371	215	0.00%
COAD	3810	Noncoding	Noncoding SNV		1,623	tRNA Val			G	A	78.80%	0.49%	78.31%	1,417	1,014	0.00%
READ	4007	Noncoding	Noncoding SNV		1,641	tRNA Val			G	A	88.60%	0.25%	88.35%	1,059	405	0.00%
READ	A01W	Noncoding	Noncoding SNV		1,664	tRNA Val			G	C	87.20%	0.00%	87.20%	257	523	0.00%
COAD	3807	Noncoding	Noncoding SNV		1,766	16S rRNA			T	C	28.60%	0.65%	27.95%	1,338	1,385	0.11%
COAD	3808	Noncoding	Noncoding SNV		1,858	16S rRNA			G	A	69.00%	0.15%	68.85%	1,147	1,301	0.00%
AML	2908	Noncoding	Noncoding SNV		1,870	16S rRNA			A	G	28.20%	0.00%	28.20%	595	97	0.00%
GBM	1459	Noncoding	Noncoding SNV		1,966	16S rRNA			G	A	85.10%	2.68%	82.42%	5,904	2,405	0.00%
READ	3878	Noncoding	Noncoding SNV		1,969	16S rRNA			G	A	65.00%	0.32%	64.68%	671	317	0.00%
COAD	3688	Noncoding	Noncoding SNV		2,011	16S rRNA			G	A	93.20%	0.85%	92.35%	410	118	0.00%
COAD	2674	Noncoding	Noncoding SNV		2,177	16S rRNA			T	C	68.70%	0.00%	68.70%	457	297	0.04%
COAD	A01P	Noncoding	Noncoding SNV		2,222	16S rRNA			T	C	51.20%	0.25%	50.95%	295	1,210	0.04%
READ	3898	Noncoding	Noncoding SNV		2,299	16S rRNA			T	C	74.80%	0.00%	74.80%	781	249	0.00%
COAD	A02W	Noncoding	Noncoding SNV		2,377	16S rRNA			G	A	75.60%	0.00%	75.60%	430	759	0.00%
COAD	A010	Noncoding	Noncoding SNV		2,385	16S rRNA			T	C	17.60%	0.00%	17.60%	335	983	0.00%
COAD	3807	Noncoding	Noncoding SNV		2,400	16S rRNA			C	A	92.60%	0.37%	92.23%	1,414	1,362	0.00%
AML	2978	Noncoding	Noncoding SNV		2,669	16S rRNA			A	T	69.20%	5.00%	64.20%	2,515	5,962	0.00%
READ	A015	Noncoding	Noncoding SNV		2,690	16S rRNA			G	A	71.40%	0.12%	71.28%	199	867	0.00%
COAD	3966	Noncoding	Noncoding SNV		2,700	16S rRNA			G	A	11.90%	0.00%	11.90%	335	258	0.00%
AML	2811	Noncoding	Noncoding SNV		2,777	16S rRNA			G	A	25.00%	4.31%	20.69%	552	1,114	0.00%
COAD	3548	Noncoding	Noncoding SNV		2,810	16S rRNA			G	A	89.10%	0.00%	89.10%	994	489	0.00%
READ	3893	Noncoding	Noncoding SNV		2,831	16S rRNA			G	A	11.50%	0.75%	10.75%	1,962	531	0.63%

READ	3882	Noncoding	Noncoding SNV		2,844	16S rRNA			G	A	53.10%	0.00%	53.10%	554	82	0.00%
COAD	5256	Noncoding	Noncoding SNV		2,860	16S rRNA			G	A	96.40%	0.52%	95.88%	578	384	0.00%
COAD	3994	Noncoding	Noncoding SNV		3,019	16S rRNA			G	A	88.20%	0.01%	88.19%	1,312	197	0.00%
COAD	3664	Noncoding	Noncoding SNV		3,022	16S rRNA			G	A	93.50%	0.00%	93.50%	1,270	541	0.00%
GBM	145	Noncoding	Noncoding SNV		3,036	16S rRNA			G	A	43.10%	0.00%	43.10%	7,929	3,385	0.00%
COAD	5256	Noncoding	Noncoding SNV		3,132	16S rRNA			G	A	12.30%	0.21%	12.09%	595	481	0.00%
READ	3902	Noncoding	Noncoding SNV		3,179	16S rRNA			G	A	32.50%	0.33%	32.17%	1,798	601	0.00%
COAD	3558	Noncoding	Noncoding SNV		3,203	16S rRNA			A	G	87.00%	0.36%	86.64%	1,695	548	0.30%
OV	751	Coding	Nonsynonymous SNV	L8P	3,329	ND1	medium	3.065	T	C	95.10%	1.04%	94.06%	7,881	2,589	0.00%
GBM	786	Coding	Nonsynonymous SNV	I13T	3,344	ND1	low	1.085	T	C	83.10%	0.00%	83.10%	3,869	834	0.00%
COAD	4315	Coding	Nonsynonymous SNV	G36D	3,413	ND1	high	3.83	G	A	59.70%	0.00%	59.70%	762	282	0.00%
COAD	A00N	Coding	Nonsynonymous SNV	E59K	3,481	ND1	high	3.83	G	A	85.70%	1.27%	84.43%	596	864	0.00%
COAD	3534	Coding	Synonymous SNV	E59E	3,483	ND1			G	A	39.60%	0.29%	39.31%	7,909	3,817	0.15%
COAD	A00R	Coding	Nonsynonymous SNV	A78T	3,538	ND1	high	3.745	G	A	56.00%	0.12%	55.88%	216	829	0.00%
AML	2974	Coding	Nonsynonymous SNV	A82T	3,550	ND1	medium	3.425	G	A	54.00%	8.00%	46.00%	848	4,246	0.00%
READ	A00Y	Coding	Nonsynonymous SNV	A112P	3,640	ND1	medium	3.28	G	C	90.60%	0.00%	90.60%	255	506	0.00%
READ	3887	Coding	Nonsynonymous SNV	S152L	3,761	ND1	high	3.815	C	T	92.80%	0.00%	92.80%	1,159	572	0.00%
COAD	3675	Coding	Nonsynonymous SNV	G158S	3,778	ND1	high	3.83	G	A	95.40%	0.00%	95.40%	1,681	716	0.00%
COAD	3666	Coding	Nonsynonymous SNV	A182T	3,850	ND1	medium	2.285	G	A	92.20%	0.28%	91.92%	1,098	708	0.00%
READ	3885	Coding	Nonsynonymous SNV	A182T	3,850	ND1	medium	2.285	G	A	18.90%	0.00%	18.90%	639	91	0.00%
COAD	A02Y	Coding	Truncating	W185X	3,860	ND1	high	5	G	A	75.40%	0.00%	75.40%	114	497	0.00%
COAD	A02R	Coding	Synonymous SNV	W185W	3,861	ND1			A	G	52.30%	0.21%	52.09%	130	974	0.00%
OV	886	Coding	Nonsynonymous SNV	S188P	3,868	ND1	high	3.83	T	C	60.20%	0.22%	59.98%	7,916	23,037	0.00%
OV	1319	Coding	Nonsynonymous SNV	A191T	3,877	ND1	high	3.83	G	A	92.20%	2.37%	89.83%	7,609	3,171	0.00%
AML	3009	Coding	Synonymous SNV	E204E	3,918	ND1			G	A	26.10%	1.00%	25.10%	2,833	5,750	0.55%
COAD	3861	Coding	Nonsynonymous SNV	G218D	3,959	ND1	high	3.83	G	A	39.80%	0.80%	39.00%	1,705	501	0.00%
AML	2996	Coding	Nonsynonymous SNV	F270L	4,114	ND1	high	3.83	T	C	56.30%	1.00%	55.30%	2,901	5,509	0.00%
COAD	3534	Coding	Nonsynonymous SNV	R281H	4,148	ND1	high	3.83	G	A	80.70%	0.03%	80.67%	7,906	3,195	0.00%
READ	A01L	Coding	Synonymous SNV	F293F	4,185	ND1			C	T	90.80%	0.00%	90.80%	142	529	0.11%
READ	4005	Noncoding	Noncoding SNV		4,286	tRNA Ile			T	C	35.40%	0.33%	35.07%	1,162	307	0.00%
COAD	3861	Noncoding	Noncoding SNV		4,309	tRNA Ile			G	A	21.20%	0.17%	21.03%	2,015	587	0.00%
COAD	A02R	Noncoding	Noncoding indel		4,318	tRNA Ile			C	CC	76.09%	0.00%	76.09%	92	760	0.00%
COAD	2679	Noncoding	Noncoding SNV		4,431	tRNA Met			C	T	67.90%	1.79%	66.11%	427	112	0.00%
AML	3009	Coding	Synonymous SNV	I1I	4,472	ND2			T	C	95.40%	3.00%	92.40%	2,771	7,345	0.00%
GBM	1086	Coding	Nonsynonymous SNV	I98T	4,762	ND2	medium	2.645	T	C	44.60%	0.06%	44.54%	5,084	1,632	0.00%
READ	3582	Coding	Nonsynonymous SNV	L128P	4,852	ND2	high	3.64	T	C	93.40%	0.00%	93.40%	1,177	191	0.00%
READ	3878	Coding	Nonsynonymous SNV	S140P	4,887	ND2	high	3.78	T	C	64.80%	0.54%	64.26%	770	368	0.00%
OV	975	Coding	Synonymous SNV	L153L	4,928	ND2			T	C	47.70%	0.61%	47.09%	7,623	7,376	0.52%
OV	1411	Coding	Nonsynonymous SNV	G165S	4,962	ND2	high	3.785	G	A	40.40%	0.00%	40.40%	7,872	3,075	0.00%

READ	A015	Coding	Nonsynonymous SNV	G188E	5,032	ND2	high	3.785	G	A	72.20%	0.19%	72.01%	237	1,078	0.00%
COAD	A00Z	Coding	Nonsynonymous SNV	S231P	5,160	ND2	high	3.705	T	C	86.50%	0.31%	86.19%	170	324	0.00%
COAD	A01D	Coding	Nonsynonymous SNV	R232H	5,164	ND2	neutral	0.455	G	A	19.20%	0.27%	18.93%	473	376	0.00%
READ	3999	Noncoding	Noncoding SNV		5,623	tRNA Ala			G	A	66.70%	0.50%	66.20%	2,083	404	0.00%
COAD	A00U	Noncoding	Noncoding indel		5,685	tRNA Asp			CACTT	C	59.72%	0.00%	59.72%	144	219	0.00%
READ	A00H	Noncoding	Noncoding SNV		5,853	tRNA Tyr			T	C	60.60%	0.00%	60.60%	259	272	0.00%
COAD	A02W	Coding	Nonsynonymous SNV	P107R	6,223	CO I	medium	2.86	C	G	77.00%	0.00%	77.00%	508	664	0.00%
COAD	3715	Coding	Nonsynonymous SNV	G134E	6,304	CO I	medium	2.86	G	A	74.20%	0.00%	74.20%	302	106	0.00%
COAD	3675	Coding	Nonsynonymous SNV	G160E	6,382	CO I	medium	2.86	G	A	50.80%	0.00%	50.80%	1,724	734	0.00%
COAD	2671	Coding	Nonsynonymous SNV	A192T	6,477	CO I	medium	2.86	G	A	27.80%	0.00%	27.80%	1,120	365	0.00%
COAD	3558	Coding	Nonsynonymous SNV	G225E	6,577	CO I	medium	2.86	G	A	85.80%	0.18%	85.62%	1,497	557	0.00%
OV	1331	Coding	Nonsynonymous SNV	G226E	6,580	CO I	medium	2.86	G	A	50.10%	0.06%	50.04%	7,638	8,108	0.00%
READ	3898	Coding	Nonsynonymous SNV	D227N	6,582	CO I	medium	2.86	G	A	95.00%	0.00%	95.00%	657	204	0.00%
GBM	692	Coding	Nonsynonymous SNV	G239D	6,619	CO I	medium	2.86	G	A	33.70%	0.57%	33.13%	7,763	7,162	0.00%
READ	3999	Coding	Truncating		6,692	CO I	high	5	AA	A	54.40%	0.50%	53.90%	2,751	378	0.00%
COAD	4313	Coding	Nonsynonymous SNV	E266K	6,699	CO I	medium	2.86	G	A	36.40%	0.00%	36.40%	590	172	0.00%
AML	2908	Coding	Nonsynonymous SNV	M273V	6,720	CO I	medium	2.86	A	G	32.90%	0.00%	32.90%	642	71	0.00%
OV	1103	Coding	Nonsynonymous SNV	A289T	6,768	CO I	medium	2.86	G	A	44.70%	0.00%	44.70%	7,888	6,726	0.00%
READ	4015	Coding	Nonsynonymous SNV	S322N	6,868	CO I	medium	2.86	G	A	79.80%	0.38%	79.42%	863	266	0.00%
READ	2689	Coding	Truncating	W340X	6,922	CO I	high	5	G	A	62.40%	0.00%	62.40%	933	501	0.00%
COAD	3688	Coding	Nonsynonymous SNV	D445N	7,236	CO I	medium	2.86	G	A	24.90%	0.00%	24.90%	386	140	0.00%
AML	2811	Coding	Nonsynonymous SNV	G457S	7,272	CO I	medium	2.86	G	A	55.50%	0.18%	55.32%	445	553	0.00%
COAD	3516	Coding	Nonsynonymous SNV	V482I	7,347	CO I	low	1.87	G	A	21.80%	0.37%	21.43%	616	268	0.04%
COAD	A02Y	Coding	Nonsynonymous SNV	E493K	7,380	CO I	high	3.865	G	A	80.60%	0.00%	80.60%	83	122	0.00%
AML	3009	Coding	Nonsynonymous SNV	V509L	7,428	CO I	medium	3.11	G	T	41.50%	2.00%	39.50%	2,192	5,329	0.00%
COAD	3555	Noncoding	Noncoding indel		7,466	tRNA Ser1			C	CC	77.02%	0.00%	77.02%	161	305	0.00%
COAD	4750	Noncoding	Noncoding indel		7,466	tRNA Ser1			C	CC	94.47%	0.00%	94.47%	868	171	0.00%
COAD	4951	Noncoding	Noncoding SNV		7,486	tRNA Ser1			G	A	46.00%	0.64%	45.36%	1,334	311	0.00%
COAD	A00Z	Noncoding	Noncoding SNV		7,552	tRNA Asp Acid			A	G	20.90%	0.00%	20.90%	196	359	0.00%
AML	2939	Coding	Synonymous SNV	F23F	7,654	CO II			T	C	31.40%	0.60%	30.80%	605	4,015	0.00%
AML	2955	Coding	Nonsynonymous SNV	D112N	7,919	CO II	medium	3.1	G	A	36.70%	5.32%	31.38%	166	263	0.00%
READ	A00H	Coding	Nonsynonymous SNV	G114S	7,925	CO II	medium	2.645	G	A	47.20%	0.00%	47.20%	286	329	0.00%
COAD	4748	Coding	Nonsynonymous SNV	G131S	7,976	CO II	medium	3.45	G	A	87.20%	0.00%	87.20%	1,535	229	0.00%
READ	3894	Coding	Nonsynonymous SNV	R134Q	7,986	CO II	medium	3.445	G	A	72.50%	0.00%	72.50%	2,262	479	0.00%
READ	A016	Coding	Synonymous SNV	G222G	8,251	CO II			G	A	40.70%	0.12%	40.58%	209	846	5.29%
READ	3913	Coding	Synonymous SNV	N62N	8,712	ATPase6			C	T	89.00%	0.14%	88.86%	833	706	0.00%
READ	A014	Coding	Nonsynonymous SNV	F78L	8,758	ATPase6	high	3.64	T	C	95.50%	0.19%	95.31%	286	515	0.00%
COAD	3715	Coding	Synonymous SNV	A80A	8,766	ATPase6			C	T	58.00%	0.00%	58.00%	274	116	0.04%
COAD	2676	Coding	Nonsynonymous SNV	A162T	9,010	ATPase6	high	3.675	G	A	89.70%	0.30%	89.40%	668	330	0.00%

COAD	A02R	Coding	Synonymous SNV	S176S	9,054	ATPase6			C	T	40.80%	0.06%	40.74%	211	1,351	0.07%
READ	3893	Coding	Nonsynonymous SNV	S219N	9,182	ATPase6	high	3.675	G	A	83.20%	0.00%	83.20%	1,951	546	0.15%
OV	1341	Coding	Nonsynonymous SNV	L220P	9,185	ATPase6	high	3.675	T	C	92.80%	0.19%	92.61%	7,899	12,381	0.00%
READ	A01L	Coding	Synonymous SNV	M1M	9,209	CO III			G	A	93.50%	0.64%	92.86%	216	625	0.00%
COAD	2679	Coding	Truncating	W16X	9,253	CO III	high	5	G	A	82.10%	0.00%	82.10%	565	132	0.00%
AML	2842	Coding	Nonsynonymous SNV	T28A	9,288	CO III	medium	3.285	A	G	85.60%	0.00%	85.60%	236	88	0.07%
COAD	3555	Coding	Nonsynonymous SNV	R63W	9,393	CO III	high	3.84	C	T	82.40%	0.00%	82.40%	193	302	0.00%
COAD	2683	Coding	Nonsynonymous SNV	E64K	9,396	CO III	high	3.84	G	A	94.90%	0.00%	94.90%	920	208	0.00%
GBM	742	Coding	Nonsynonymous SNV	S150N	9,655	CO III	high	3.835	G	A	73.80%	0.31%	73.49%	3,056	3,836	0.00%
COAD	3715	Coding	Nonsynonymous SNV	S150N	9,655	CO III	high	3.835	G	A	70.70%	0.00%	70.70%	352	114	0.00%
COAD	2672	Coding	Nonsynonymous SNV	E153K	9,663	CO III	high	3.82	G	A	81.30%	8.01%	73.29%	418	362	0.00%
COAD	4746	Coding	Nontruncating indel		9,756	CO III			T	TCTC	85.25%	0.00%	85.25%	868	180	0.00%
COAD	4748	Coding	Nonsynonymous SNV	G211D	9,838	CO III	high	3.84	G	A	83.30%	0.00%	83.30%	1,757	291	0.00%
COAD	2683	Coding	Synonymous SNV	A237A	9,917	CO III			C	T	96.50%	0.29%	96.21%	1,761	341	0.00%
COAD	2672	Coding	Nonsynonymous SNV	V248I	9,948	CO III	medium	3.49	G	A	78.50%	0.26%	78.24%	400	385	0.18%
AML	2939	Coding	Nonsynonymous SNV	V254A	9,967	CO III	high	3.795	T	C	69.30%	1.41%	67.89%	349	2,344	0.00%
COAD	A01Q	Noncoding	Noncoding SNV		10,000	tRNA Gly			G	A	16.20%	0.09%	16.11%	686	1,121	0.00%
AML	2983	Noncoding	Noncoding SNV		10,015	tRNA Gly			T	C	85.10%	3.00%	82.10%	4,739	13,177	0.00%
READ	A011	Noncoding	Noncoding SNV		10,031	tRNA Gly			T	C	19.70%	0.23%	19.47%	608	436	0.22%
READ	3878	Coding	Nonsynonymous SNV	A47T	10,197	ND3	high	4.005	G	A	63.30%	0.36%	62.94%	596	274	0.07%
COAD	3715	Coding	Nonsynonymous SNV	S101N	10,360	ND3	high	3.615	G	A	74.10%	0.00%	74.10%	386	135	0.00%
OV	979	Noncoding	Noncoding SNV		10,408	tRNA Arg			T	C	24.60%	0.11%	24.49%	991	896	0.00%
READ	4001	Noncoding	Noncoding SNV		10,412	tRNA Arg			T	C	66.90%	0.22%	66.68%	2,329	901	0.00%
OV	1853	Noncoding	Noncoding SNV		10,464	tRNA Arg			T	C	82.60%	0.00%	82.60%	23	73	0.00%
COAD	3509	Coding	Truncating		10,562	ND4L	high	5	A	AT	16.96%	0.00%	16.96%	572	291	0.00%
READ	3574	Coding	Nonsynonymous SNV	E34K	10,569	ND4L	medium	3.365	G	A	96.20%	0.16%	96.04%	2,420	626	0.00%
COAD	4744	Coding	Nonsynonymous SNV	M36T	10,576	ND4L	high	3.77	T	C	38.80%	0.00%	38.80%	971	233	0.00%
GBM	155	Coding	Synonymous SNV	S39S	10,586	ND4L			G	A	30.20%	0.00%	30.20%	4,895	3,467	1.29%
READ	3727	Coding	Synonymous SNV	A72A	10,685	ND4L			G	A	91.60%	0.93%	90.67%	664	107	0.81%
AML	3009	Coding	Nonsynonymous SNV	S82F	10,714	ND4L	high	4.12	C	T	26.80%	0.00%	26.80%	1,904	7,574	0.00%
COAD	4071	Coding	Nonsynonymous SNV	D88N	10,731	ND4L	medium	3.22	G	A	12.97%	0.00%	12.97%	699	111	0.00%
OV	1331	Coding	Nonsynonymous SNV	I34T	10,860	ND4	medium	3.23	T	C	38.80%	0.07%	38.73%	5,954	6,686	0.00%
READ	3913	Coding	Nonsynonymous SNV	S35T	10,863	ND4	medium	3	G	C	93.20%	0.30%	92.90%	793	657	0.00%
COAD	3968	Coding	Nonsynonymous SNV	F50S	10,908	ND4	low	0.935	T	C	90.30%	0.00%	90.30%	1,018	184	0.00%
READ	A00C	Coding	Truncating		10,947	ND4	high	5	C	CC	31.21%	0.00%	31.21%	330	273	0.00%
COAD	3715	Coding	Nonsynonymous SNV	I104T	11,070	ND4	low	1.49	T	C	58.90%	0.00%	58.90%	377	166	0.00%
COAD	A01T	Coding	Nonsynonymous SNV	Y119C	11,115	ND4	medium	3.405	A	G	31.50%	0.08%	31.42%	486	1,219	0.00%
READ	2692	Coding	Nonsynonymous SNV	E123K	11,126	ND4	medium	3.405	G	A	21.80%	0.00%	21.80%	1,711	342	0.00%
COAD	4752	Coding	Nonsynonymous SNV	M229T	11,445	ND4	medium	3.4	T	C	75.30%	0.00%	75.30%	1,112	311	0.00%

COAD	A03J	Coding	Nonsynonymous SNV	A233T	11,456	ND4	medium	3.4	G	A	46.10%	0.29%	45.81%	271	684	0.00%
COAD	A01I	Coding	Nonsynonymous SNV	G311S	11,690	ND4	medium	3.405	G	A	15.70%	1.01%	14.69%	814	595	0.00%
READ	A01L	Coding	Nonsynonymous SNV	I314T	11,700	ND4	neutral	0.1	T	C	43.30%	0.13%	43.17%	203	754	0.00%
READ	A01J	Coding	Nonsynonymous SNV	L315P	11,703	ND4	medium	3.405	T	C	48.90%	0.00%	48.90%	262	462	0.00%
AML	2819	Coding	Synonymous SNV	T350T	11,809	ND4			T	C	94.40%	1.19%	93.21%	465	759	0.00%
COAD	A01T	Coding	Nonsynonymous SNV	A356T	11,825	ND4	medium	2.315	G	A	30.80%	0.22%	30.58%	441	1,367	0.00%
COAD	3693	Coding	Truncating		11,867	ND4	high	5	C	CC	94.76%	0.42%	94.34%	782	240	0.00%
COAD	A00Z	Coding	Truncating		11,867	ND4	high	5	C	CC/CCC/CCCC	77.12%	0.00%	77.12%	118	329	0.00%
READ	A014	Coding	Truncating		11,867	ND4	high	5	C	CC	95.58%	0.17%	95.41%	294	606	0.00%
COAD	A02W	Coding	Truncating		11,867	ND4	high	5	C	CC	60.42%	0.00%	60.42%	379	580	0.00%
AML	2970	Coding	Nonsynonymous SNV	L398P	11,952	ND4	medium	3.355	T	C	41.00%	7.00%	34.00%	459	10,052	0.00%
COAD	3715	Coding	Nonsynonymous SNV	T413M	11,997	ND4	low	1.63	C	T	52.40%	0.00%	52.40%	382	132	0.00%
READ	3882	Coding	Nonsynonymous SNV	I453T	12,117	ND4	medium	2.165	T	C	92.20%	0.00%	92.20%	972	111	0.00%
COAD	2672	Coding	Synonymous SNV	G456G	12,127	ND4			G	A	37.40%	0.00%	37.40%	559	450	0.18%
READ	3885	Coding	Synonymous SNV	M3M	12,345	ND5			G	A	88.70%	0.00%	88.70%	638	100	0.00%
COAD	5256	Coding	Synonymous SNV	M3M	12,345	ND5			G	A	95.70%	0.00%	95.70%	629	460	0.00%
READ	3574	Coding	Synonymous SNV	L12L	12,370	ND5			C	T	13.40%	0.15%	13.25%	2,663	662	0.07%
READ	4001	Coding	Truncating		12,385	ND5	high	5	C	CC	79.73%	0.00%	79.73%	1,628	621	0.00%
COAD	4684	Coding	Truncating		12,385	ND5	high	5	C	CC	83.27%	0.00%	83.27%	1,076	308	0.00%
OV	1853	Coding	Nonsynonymous SNV	V24I	12,406	ND5	neutral	-0.71	G	A	74.10%	0.00%	74.10%	54	88	2.03%
OV	1027	Coding	Truncating		12,418	ND5	high	5	AA	A	35.58%	0.68%	34.90%	3,381	6,210	0.00%
AML	2967	Coding	Truncating		12,418	ND5	high	5	AA	A	46.02%	4.41%	41.60%	3477	6843	0.00%
AML	3009	Coding	Truncating		12,418	ND5	high	5	A	AA	44.33%	1.21%	43.12%	9422	6750	0.00%
COAD	3548	Coding	Truncating		12,418	ND5	high	5	A	AA	49.42%	0.80%	48.63%	692	377	0.00%
COAD	3553	Coding	Truncating		12,418	ND5	high	5	A	AA	85.34%	1.41%	83.93%	457	497	0.00%
COAD	3666	Coding	Truncating		12,418	ND5	high	5	AA	A	94.38%	1.37%	93.01%	960	511	0.00%
COAD	3810	Coding	Truncating		12,418	ND5	high	5	A	AA	81.07%	0.69%	80.38%	1009	725	0.00%
READ	3896	Coding	Truncating		12,418	ND5	high	5	A	AA	61.08%	0.41%	60.67%	1421	488	0.00%
READ	3909	Coding	Truncating		12,418	ND5	high	5	A	AA	76.69%	0.70%	76.00%	1373	717	0.00%
COAD	3970	Coding	Truncating		12,418	ND5	high	5	A	AA	40.33%	0.58%	39.75%	543	171	0.00%
READ	4015	Coding	Truncating		12,418	ND5	high	5	A	AA	84.69%	1.02%	83.68%	967	295	0.00%
COAD	4071	Coding	Truncating		12,418	ND5	high	5	A	AA	84.91%	1.22%	83.69%	477	82	0.00%
COAD	4308	Coding	Truncating		12,418	ND5	high	5	A	AA	73.19%	0.38%	72.81%	1794	265	0.00%
COAD	4315	Coding	Truncating		12,418	ND5	high	5	A	AA	74.54%	0.00%	74.54%	766	373	0.00%
COAD	4682	Coding	Truncating		12,418	ND5	high	5	A	AA	78.78%	0.64%	78.14%	1659	156	0.00%
COAD	4746	Coding	Truncating		12,418	ND5	high	5	A	AA	84.04%	0.00%	84.04%	1291	193	0.00%
COAD	4747	Coding	Truncating		12,418	ND5	high	5	A	AA	47.26%	0.14%	47.12%	1860	734	0.00%
READ	3902	Coding	Synonymous SNV	Y120Y	12,696	ND5			T	C	45.80%	0.16%	45.64%	2,001	629	0.30%
COAD	3693	Coding	Truncating	G148X	12,778	ND5	high	5	G	A	86.60%	0.00%	86.60%	1,089	312	0.00%

OV	1331	Coding	Nonsynonymous SNV	A236T	13,042	ND5	medium	2.835	G	A	33.50%	0.25%	33.25%	2,641	3,158	0.04%
COAD	A01G	Coding	Nonsynonymous SNV	A236T	13,042	ND5	medium	2.835	G	A	72.80%	0.15%	72.65%	331	2,026	0.04%
COAD	3970	Coding	Nonsynonymous SNV	V243I	13,063	ND5	medium	2.835	G	A	82.50%	0.00%	82.50%	773	208	0.00%
COAD	3966	Coding	Nonsynonymous SNV	A245T	13,069	ND5	medium	2.835	G	A	77.70%	0.00%	77.70%	341	285	0.00%
OV	1326	Coding	Nonsynonymous SNV	G281S	13,177	ND5	medium	2.835	G	A	44.00%	0.08%	43.92%	7,294	14,130	0.00%
COAD	A00W	Coding	Truncating		13,231	ND5	high	5	A	AA	12.95%	0.00%	12.95%	332	323	0.00%
COAD	A00W	Coding	Nonsynonymous SNV	L368P	13,439	ND5	medium	2.55	T	C	75.60%	0.19%	75.41%	532	540	0.00%
READ	4015	Coding	Nonsynonymous SNV	S423N	13,604	ND5	high	3.6	G	A	92.20%	0.30%	91.90%	1,066	331	0.00%
READ	2689	Coding	Nonsynonymous SNV	G433S	13,633	ND5	medium	3.185	G	A	16.40%	0.19%	16.21%	1,028	526	0.00%
READ	3890	Coding	Truncating	G460X	13,714	ND5	high	5	G	A	30.50%	0.00%	30.50%	1,632	236	0.00%
COAD	A01D	Coding	Nonsynonymous SNV	A464T	13,726	ND5	medium	2.4	G	A	81.90%	0.25%	81.65%	487	394	0.00%
COAD	3715	Coding	Truncating		13,754	ND5	high	5	CC	C	59.46%	0.56%	58.90%	222	178	0.00%
READ	A016	Coding	Truncating		13,763	ND5	high	5	C	CC	93.25%	0.00%	93.25%	237	902	0.00%
COAD	3968	Coding	Nonsynonymous SNV	S515Y	13,880	ND5	low	0.87	C	A	81.80%	0.80%	81.00%	1,220	251	0.74%
COAD	A03J	Coding	Truncating	G527X	13,915	ND5	high	5	G	A	77.00%	0.00%	77.00%	335	889	0.00%
COAD	2683	Coding	Synonymous SNV	M583M	14,085	ND5			A	G	96.90%	0.00%	96.90%	1,996	364	0.00%
COAD	3688	Coding	Nonsynonymous SNV	T598I	14,129	ND5	low	0.895	C	T	12.10%	0.00%	12.10%	536	137	0.15%
READ	3898	Coding	Synonymous SNV	V88V	14,410	ND6			G	A	94.20%	0.40%	93.80%	671	235	0.00%
OV	1331	Coding	Nonsynonymous SNV	M64V	14,484	ND6	high	4.13	T	C	78.10%	0.31%	77.79%	1,578	1,616	0.26%
AML	2996	Coding	Nonsynonymous SNV	I58V	14,502	ND6	low	1.405	T	C	57.30%	1.00%	56.30%	2,320	10,289	0.48%
READ	3999	Coding	Truncating		14,504	ND6	high	5	AA	A	16.40%	0.00%	16.40%	2,519	409	0.00%
COAD	A01I	Coding	Truncating		14,504	ND6	high	5	AA	A	96.17%	0.18%	95.99%	496	551	0.00%
READ	A01J	Coding	Nonsynonymous SNV	R5H	14,760	Cyt b	medium	2.68	G	A	47.50%	0.00%	47.50%	255	597	0.00%
COAD	2676	Coding	Nonsynonymous SNV	L10M	14,774	Cyt b	medium	2.69	C	A	11.10%	0.34%	10.76%	737	298	0.00%
AML	2978	Coding	Nonsynonymous SNV	G34D	14,847	Cyt b	low	1.73	G	A	25.00%	1.00%	24.00%	1,628	5,975	0.00%
COAD	A01R	Coding	Nonsynonymous SNV	C40Y	14,865	Cyt b	low	1.73	G	A	78.70%	0.21%	78.49%	244	939	0.00%
COAD	4684	Coding	Nonsynonymous SNV	A52T	14,900	Cyt b	low	1.73	G	A	88.90%	0.00%	88.90%	1,214	320	0.00%
COAD	A02R	Coding	Nonsynonymous SNV	C93Y	15,024	Cyt b	low	1.73	G	A	68.70%	0.09%	68.61%	182	1,149	0.04%
COAD	3968	Coding	Nonsynonymous SNV	A125P	15,119	Cyt b	low	1.7	G	C	28.70%	1.30%	27.40%	1,253	230	0.00%
READ	A00H	Coding	Truncating	G166X	15,242	Cyt b	high	5	G	A	75.10%	0.00%	75.10%	362	396	0.00%
COAD	4071	Coding	Nonsynonymous SNV	V170M	15,254	Cyt b	low	1.73	G	A	89.00%	0.00%	89.00%	626	89	0.00%
COAD	3666	Coding	Nonsynonymous SNV	G210E	15,375	Cyt b	high	3.775	G	A	42.90%	0.12%	42.78%	1,152	803	0.00%
COAD	3861	Coding	Nonsynonymous SNV	R282Q	15,591	Cyt b	low	1.845	G	A	78.60%	0.75%	77.85%	2,004	665	0.00%
READ	A01L	Coding	Truncating		15,594	Cyt b	high	5	CC	C	42.94%	0.00%	42.94%	163	548	0.00%
READ	A020	Coding	Nonsynonymous SNV	F317L	15,695	Cyt b	low	1.845	T	C	87.40%	0.00%	87.40%	223	841	0.00%
READ	3882	Noncoding	Noncoding SNV		15,897	tRNA Thr			G	A	93.50%	0.00%	93.50%	650	104	0.00%
COAD	3994	Noncoding	Noncoding SNV		15,926	tRNA Thr			C	T	88.40%	0.01%	88.39%	1,488	328	0.00%
READ	2689	Noncoding	Noncoding SNV		15,967	tRNA Pro			G	A	21.12%	0.31%	20.82%	913	654	0.00%
OV	1853	Noncoding	Noncoding SNV		15,995	tRNA Pro			G	A	37.70%	0.00%	37.70%	53	103	0.00%

COAD	A02R	Noncoding	Noncoding SNV	16,390	D-loop	G	A	77.50%	0.13%	77.37%	178	1,567	3.32%
READ	A016	Noncoding	Noncoding SNV	16,399	D-loop	A	G	93.60%	0.80%	92.80%	280	1,244	2.04%
OV	1319	Noncoding	Noncoding SNV	16,465	D-loop	C	T	95.70%	0.00%	95.70%	5,707	4,443	0.21%
COAD	4748	Noncoding	Noncoding SNV	16,497	D-loop	A	G	23.20%	0.68%	22.52%	790	294	1.93%

Abbreviations: Pos, nucleotide position in mitochondrial genome (hg19); FI, functional impact predicted by

MutationAssessor; Score, functional impact score generated by MutationAssessor, MtDB Fr, frequency of reported variant in

MtDB; ND, NADH dehydrogenase; CO, cytochrome c oxidase; ATPase, ATP synthase

S3. Summary of tumor counts harboring various categories of somatic mutations.

Tumor type	# Pairs	# Tumors with Nonsyn only	# Tumors with Syn only	# Tumors with Nonsyn + Syn	# Tumors w/o coding somatic mutations	# Tumors with coding mutations alone	# Tumors w/o any somatic mutations
COAD	86	40	1	6	39	31	24
READ	43	21	2	6	14	17	9
OV	28	10	1	0	17	9	15
AML	37	9	1	2	25	9	24
GBM	32	4	1	0	27	4	24
Combined	226	84	6	14	122	70	96

Abbreviations: Nonsyn, nonsynonymous mutation; Syn, synonymous mutation; w/o, without

S4. Somatic truncating mutations.

Tumor	Sample	Pos	Locus	Ref	Obs	Homopolymer tract	MSI status	Tumor heteroplasmy	Normal heteroplasmy	Δ heteroplasmy
COAD	A02Y	3,860	ND1	G	A		MSS	75.40%	0.00%	75.40%
READ	3999	6,692	CO I	AA	A	A7	MSS	54.40%	0.50%	53.90%
READ	2689	6,922	CO I	G	A		MSS	62.40%	0.00%	62.40%
COAD	2679	9,253	CO III	G	A			82.10%	0.00%	82.10%
COAD	3509	10,562	ND4L	A	AT	No		16.96%	0.00%	16.96%
READ	A00C	10,947	ND4	C	CC	C6	MSS	31.21%	0.00%	31.21%
COAD	3693	11,867	ND4	C	CC	C6	MSS	94.76%	0.42%	94.34%
COAD	A00Z	11,867	ND4	C	CC/CCC/CCCC	C6	MSS	77.12%	0.00%	77.12%
COAD	A02W	11,867	ND4	C	CC	C6	MSI-L	60.42%	0.00%	60.42%
READ	A014	11,867	ND4	C	CC	C6	MSS	95.58%	0.17%	95.41%
COAD	4684	12,385	ND5	C	CC	C6		83.27%	0.00%	83.27%
READ	4001	12,385	ND5	C	CC	C6	MSI-L	79.73%	0.00%	79.73%
AML	3009	12,418	ND5	A	AA	A8		44.33%	1.21%	43.12%
COAD	3548	12,418	ND5	A	AA	A8	MSS	49.42%	0.80%	48.63%
COAD	3553	12,418	ND5	A	AA	A8	MSI-L	85.34%	1.41%	83.93%
COAD	3810	12,418	ND5	A	AA	A8	MSS	81.07%	0.69%	80.38%
COAD	3970	12,418	ND5	A	AA	A8		40.33%	0.58%	39.75%
COAD	4071	12,418	ND5	A	AA	A8	MSS	84.91%	1.22%	83.69%
COAD	4315	12,418	ND5	A	AA	A8		74.54%	0.00%	74.54%
COAD	4682	12,418	ND5	A	AA	A8		78.78%	0.64%	78.14%
COAD	4746	12,418	ND5	A	AA	A8		84.04%	0.00%	84.04%
COAD	4747	12,418	ND5	A	AA	A8		47.26%	0.14%	47.12%
READ	3896	12,418	ND5	A	AA	A8	MSS	61.08%	0.41%	60.67%
READ	3909	12,418	ND5	A	AA	A8	MSS	76.69%	0.70%	76.00%
READ	4015	12,418	ND5	A	AA	A8	MSS	84.69%	1.02%	83.68%
AML	2967	12,418	ND5	AA	A	A8		46.02%	4.41%	41.60%
COAD	3666	12,418	ND5	AA	A	A8	MSS	94.38%	1.37%	93.01%
COAD	4308	12,418	ND5	A	AA	A8		73.19%	0.38%	72.81%
OV	1027	12,418	ND5	AA	A	A8		35.58%	0.68%	34.90%
COAD	3693	12,778	ND5	G	A		MSS	86.60%	0.00%	86.60%
COAD	A00W	13,231	ND5	A	AA	A7	MSS	12.95%	0.00%	12.95%
READ	3890	13,714	ND5	G	A		MSS	30.50%	0.00%	30.50%
COAD	3715	13,754	ND5	CC	C	C5	MSI-H	59.46%	0.56%	58.90%
READ	A016	13,763	ND5	C	CC	C5		93.25%	0.00%	93.25%
COAD	A03J	13,915	ND5	G	A		MSS	77.00%	0.00%	77.00%
COAD	A01I	14,504	ND6	AA	A	A7	MSS	96.17%	0.18%	95.99%
READ	3999	14,504	ND6	AA	A	A7	MSS	16.40%	0.00%	16.40%
READ	A00H	15,242	Cyt b	G	A		MSS	75.10%	0.00%	75.10%
READ	A01L	15,594	Cyt b	CC	C	C5	MSS	42.94%	0.00%	42.94%

Abbreviations: Pos, position in mitochondrial genome; Ref, reference base; Obs, observed base; MSI, microsatellite instability

S5. AML and GBM tumors with reported IDH1 and IDH2 mutations.

Sample	Cancer	Somatic mtDNA mutations*	Gene	Codon	Ref aa	Obs aa	Ref nt	Obs nt	% Obs	Depth
2969	AML	0	IDH1	132	R	H	C	T	33%	30
2977	AML	0	IDH1	132	R	C	G	A	41%	32
827	GBM	0	IDH1	132	R	H	C	T	29%	1,438
1460	GBM	0	IDH1	132	R	H	C	T	30%	40
2907	AML	0	IDH2	140	R	Q	C	T	44%	27
2966	AML	0	IDH2	140	R	Q	C	T	45%	20
2973	AML	0	IDH2	140	R	Q	C	T	56%	27
2934	AML	0	IDH2	140	R	Q	C	T	46%	90
2936	AML	0	IDH2	140	R	Q	C	T	39%	61
3002	AML	0	IDH2	140	R	L	C	A	42%	24

Abbreviations: aa, amino acid; nt, nucleotide; % Obs, percent of aligned sequence

reads that exhibit the observed nucleotide *Somatic mtDNA mutations were found in

12 AML cases, none of which had mutant IDH. The p-value of this mutual exclusivity

is 0.028 (one-sided Fisher's exact test).

S6. Base changes observed in mtDNA somatic mutations.

Substitution	Somatic substitutions (%) n=196
G-to-A	118 (60%)
T-to-C	43 (22%)
C-to-T	15 (8%)
A-to-G	10 (5%)
G-to-C	4 (2%)
C-to-A	3 (1.5%)
G-to-T	1 (0.5%)
A-to-T	1 (0.5%)
C-to-G	1 (0.5%)
A-to-C	0 (0%)
T-to-A	0 (0%)
T-to-G	0 (0%)

S7. Distribution of each length of homopolymer tract within coding regions of the mitochondrial genome.

