

Supplementary Figures and Tables:

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A



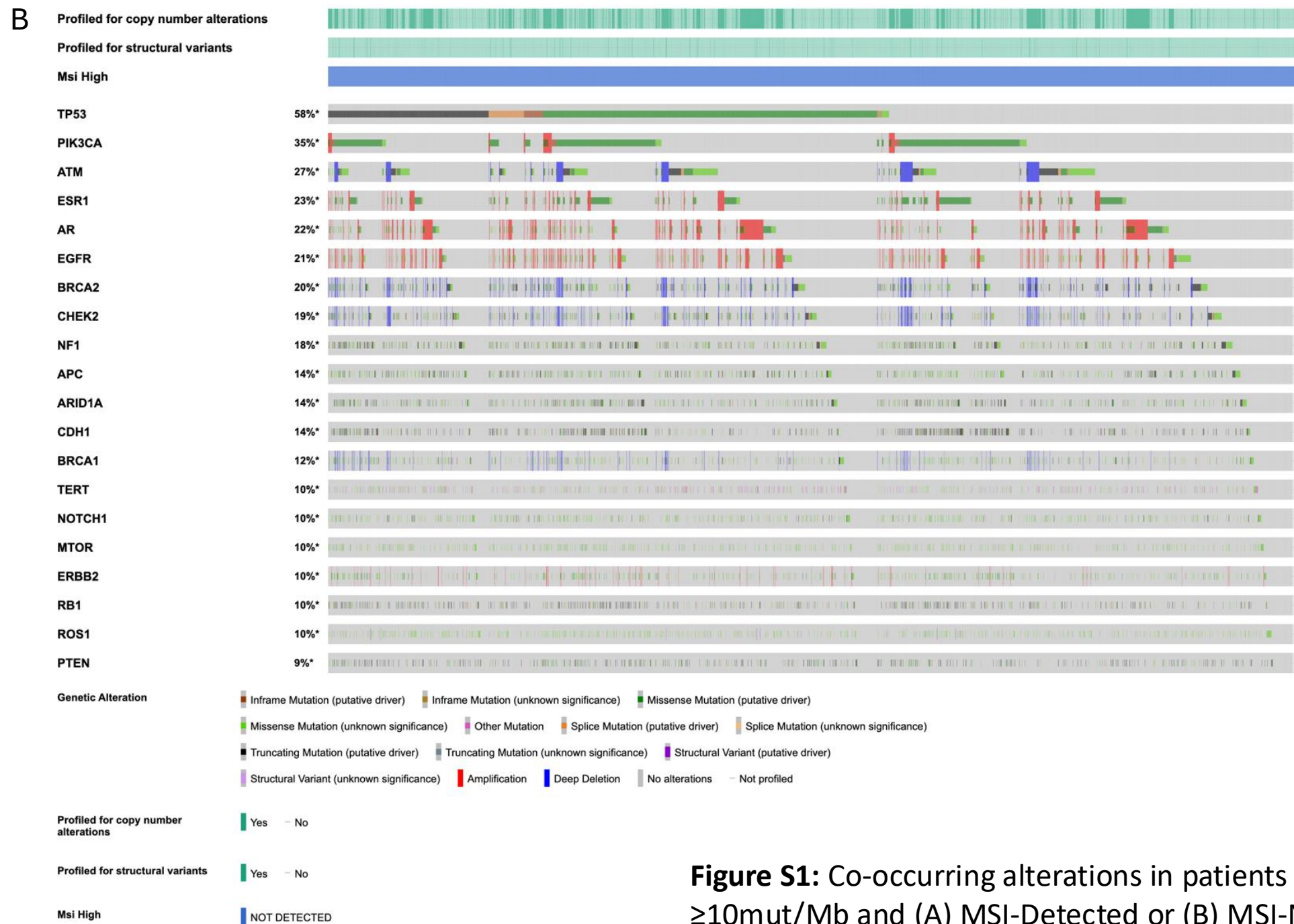


Figure S1: Co-occurring alterations in patients with a bTMB ≥ 10 mut/Mb and (A) MSI-Detected or (B) MSI-Not Detected.

A

Profiled for copy number alterations

Profiled for structural variants

Msi High

TP53

72%

AR

57%

ARID1A

57%

NOTCH1

54%

APC

48%

PIK3CA

45%

ATM

44%

BRCA2

44%

MTOR

43%

NF1

40%

EGFR

40%

PTEN

38%

MSH6

34%

MSH2

32%

BRAF

31%

TERT

31%

MET

30%

ERBB2

29%

RB1

28%

ALK

28%

Genetic Alteration



Profiled for copy number alterations

Yes — No

Profiled for structural variants

Yes — No

Msi High

DETECTED

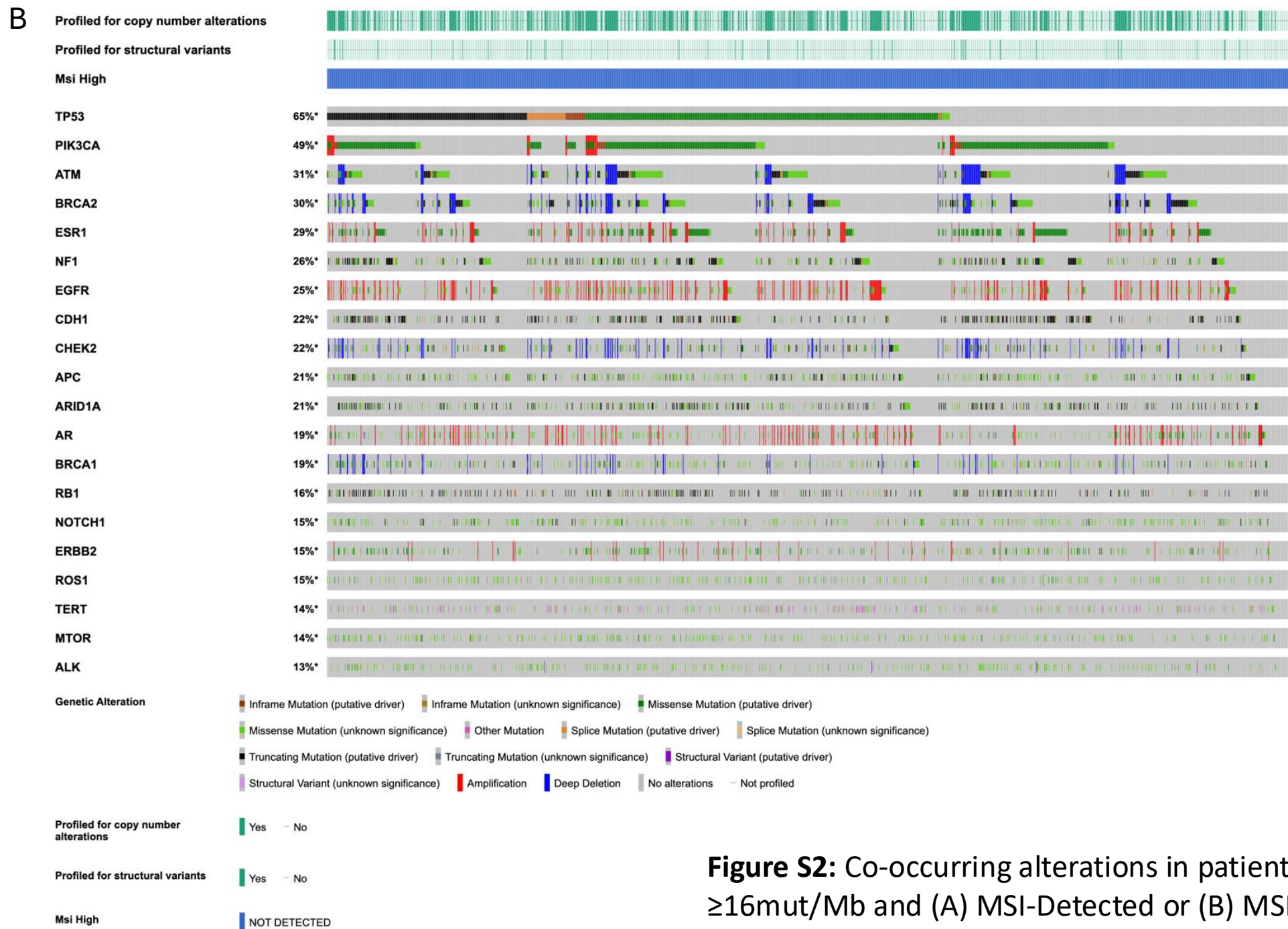


Figure S2: Co-occurring alterations in patients with a bTMB $\geq 16\text{mut/Mb}$ and (A) MSI-Detected or (B) MSI-Not Detected.

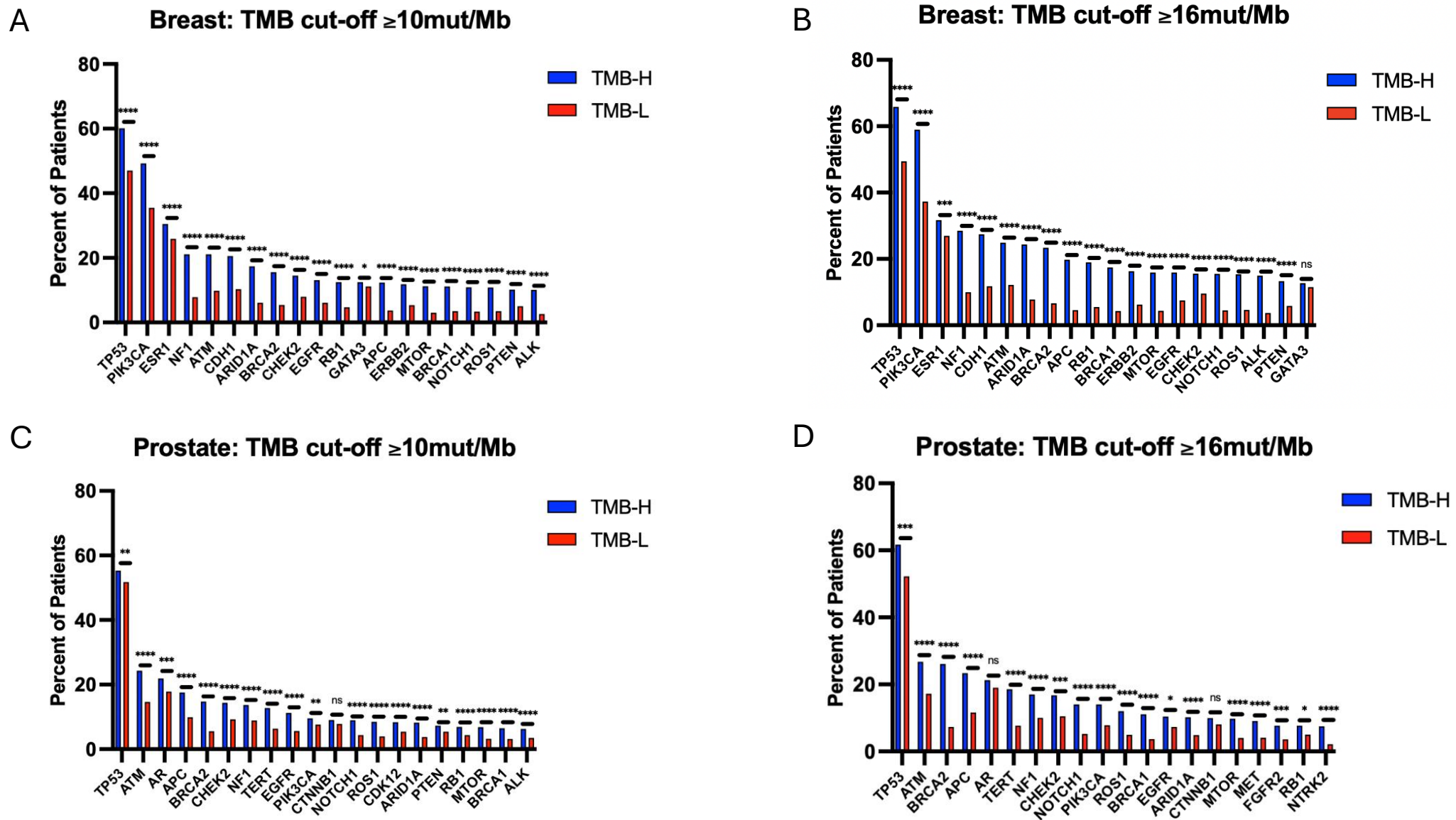


Figure S3: Genomic Landscape in cohort of breast cancer with bTMB ≥ 10 (A) and bTMB ≥ 16 (B); prostate cancer in with bTMB ≥ 10 (C) and bTMB ≥ 16 (D). Patients with MSI-Detected have been removed.

Table S1: Source data for Figure 2.

PFS (days)	TMB16 (1=yes, 0=no, 99=unknown)	Progression (1=yes, 0=no, 99=unknown)	TMB20 (1=yes, 0=no, 99=unknown)	MSI (1=yes, 0=no, 99=unknown)
51	0	1	0	0
78	0	1	0	0
507	0	1	0	0
133	1	1	0	0
309	1	1	1	1
39	1	1	1	1
42	1	0	0	0
0	1	0	1	1
364	1	0	0	1
120	0	1	0	0
72	0	1	0	0
421	1	1	0	0
151	1	1	1	0
23	1	1	1	1
150	0	1	0	99
686	0	0	0	99
122	0	1	0	99
623	1	0	0	99
346	0	1	0	99
0	0	0	0	99
533	1	0	1	1
364	1	1	1	1
49	0	0	0	0
84	1	1	1	0
63	0	1	0	0
63	1	1	0	0
478	1	1	1	0
91	1	1	1	0
62	1	0	0	0
20	1	1	1	0
52	1	1	1	0
805	0	0	0	0
0	1	1	0	0
63	0	0	0	0
22	1	0	1	0
85	1	1	0	0
126	1	1	1	0
93	0	1	0	0
0	0	1	0	0
211	0	1	0	0
0	1	1	1	0
96	0	99	0	0
84	0	0	0	0
39	1	1	1	1
461	1	0	1	1
79	0	1	0	0
40	0	1	0	99
83	1	1	0	99

3A

Gene	bTMB-H*	bTMB-L*	p value
TP53	58.94	49.15	3.63E-29
PIK3CA	34.36	23.08	2.27E-46
ATM	23.38	11.98	5.77E-67
ESR1	20.11	14.96	5.44E-15
NF1	19.36	8.31	1.21E-77
BRCA2	16.62	5.48	9.65E-98
APC	16.19	6.45	2.09E-72
ARID1A	16.15	5.08	2.23E-100
AR	15.55	9.57	2.25E-25
CHEK2	14.57	8.52	7.47E-28
CDH1	14.21	6.53	1.22E-48
EGFR	13.57	5.91	2.01E-51
NOTCH1	12.53	3.8	6.84E-80
TERT	11.4	4.7	3.61E-47
MTOR	11.3	3.12	1.92E-79
RB1	11.26	4.53	1.4E-48
ROS1	10.81	3.73	2.23E-58
PTEN	10.62	5.24	4.75E-31
BRCA1	10.13	3.34	7.1E-58
ERBB2	10.06	4.05	5.48E-43
*numbers are percentages			

3B

Gene	bMSI-H*	bMSI-Not Detected*	p-value
TP53	71.38	58.22	0.000006896
ARID1A	56.55	13.81	8.16E-60
AR	54.48	13.29	5.88E-57
NOTCH1	53.45	10.16	1.55E-68
APC	47.24	14.39	1.43E-37
PIK3CA	43.45	33.83	0.001145
MTOR	42.07	9.52	4.13E-44
ATM	41.38	22.34	3.09E-12
BRCA2	40	15.27	1.02E-22
NF1	38.97	18.22	1.3E-15
PTEN	37.93	9.04	3.19E-37
EGFR	34.14	12.38	2.39E-20
MSH6	33.79	3.77	1.77E-56
MSH2	31.38	2.06	7.41E-67
TERT	30.69	10.28	4.24E-20
MET	30	7.27	3.7E-28
BRAF	29.31	5.91	2.27E-32
ERBB2	28.62	8.98	3.27E-20
ALK	27.93	8.62	4.41E-20
RB1	27.59	10.32	2.42E-15
*numbers are percentages			

Table S2: Source data and p-values for Figure 3A-B.

3C

Gene	bTMB-H*	bTMB-L*	p-value
TP53	65.75	50.72	9.34E-37
PIK3CA	47.13	24.02	1.03E-94
ATM	27.67	14.45	1.29E-44
NF1	27.57	9.99	3.43E-89
BRCA2	26.34	6.92	2.24E-126
ARID1A	25.9	6.5	4.97E-130
ESR1	24.96	15.56	1.19E-23
APC	24.52	7.74	2.58E-94
CDH1	21.43	7.43	2.26E-71
NOTCH1	20.64	4.84	6.00E-108
AR	19.02	10.65	2.33E-24
MTOR	18.33	4.2	4.58E-97
RB1	17.79	5.28	2.18E-71
EGFR	17.3	7.42	3.77E-40
BRCA1	17	4.05	2.86E-86
ROS1	16.17	4.79	1.15E-64
TERT	16.17	5.75	9.68E-51
ERBB2	16.02	4.7	9.65E-65
CHEK2	16.02	9.97	8.89E-15
PTEN	15.38	5.92	1.30E-42
*numbers are percentages			

3D

Gene	bMSI-H*	bMSI-Not Detected*	p-value
TP53	71.58	64.8	0.0142
ARID1A	57.19	20.8	2.71E-34
AR	55.09	13.14	5.76E-51
NOTCH1	54.39	15.14	2.11E-43
APC	48.07	20.69	5.3E-21
PIK3CA	43.86	47.66	0.13
MTOR	42.81	14.34	7.08E-26
ATM	41.75	25.37	2.1E-08
BRCA2	40.35	24.06	1.69E-08
NF1	39.65	25.6	1.213E-06
PTEN	38.25	11.66	2.97E-25
EGFR	34.39	14.51	2.13E-14
MSH6	34.39	6.06	2.83E-36
MSH2	31.58	4	2.27E-40
TERT	31.23	13.71	3.98E-12
MET	30.18	11.31	6.98E-15
BRAF	29.82	9.94	3.83E-17
ERBB2	29.12	13.89	9.63E-10
ALK	28.42	13.09	4.06E-10
RB1	28.07	16.11	2.243E-06
*numbers are percentages			

Table S3: Source data and p-values for Figure 3C-D.

HRR Genes	bTMB-10	bTMB-16	p Value	bTMB-10 MSI- Detected	bTMB-10 MSI- Not Detected	p Value	bTMB-16 MSI- Detected	bTMB-16 MSI- Not Detected	p Value
ATM	26.26%	32.53%	0.0018	43.17%	24.28%	3.63E-09	43.95%	26.76%	7.23E-06
BRCA1	8.25%	15.36%	3.54E-07	23.35%	6.48%	5.57E-14	23.77%	11.11%	2.41E-05
BRCA2	17.46%	31.02%	3.09E-13	40.53%	14.76%	1.81E-18	40.81%	26.08%	8.80E-05
CDK12	10.09%	13.25%	0.0267	24.67%	8.38%	9.00E-12	25.11%	7.26%	5.25E-10
CHEK2	14.42%	16.27%	0.2616	14.98%	14.35%	0.432	15.25%	16.78%	0.349
PALB2	5.02%	11.14%	1.12E-07	20.7%	3.19%	6.12E-20	21.08%	6.12%	2.13E-08
RAD51D	1.38%	3.31%	0.0025	5.29%	0.93%	2.00E-05	5.38%	2.27%	0.0323

Table S4: HRR genes by bTMB-H cutoffs and MSI status in patients with prostate cancer: bTMB-16 vs bTMB-10 groups.