

Supplementary Tables 1. List of genes included in DNA damage response (DDR) gene set

Base Excision Repair (BER)	Nucleotide Excision Repair (NER) - includes TC-NER and GC-NER	Mismatch Repair (MMR)	Fanconi Anemia (FA)	Homology-dependent recombination (HDR)	Non-homologous End Joining (NHEJ)	Direct Repair (DR)	Translesion Synthesis (TLS)	Nucleotide pools (NP)
APLF	LIG1	LIG1	XRCC2	LIG1	DNTT	ASCC3	POLB	NUDT1
APTX	PCNA	EXO1	APITD1	MRE11A	LIG4	ALKBH2	POLM	NUDT15
LIG1	POLD1	HMGB1	BARD1	NBN	MRE11A	ALKBH3	UBE2A	NUDT18
LIG3	POLD2	MLH1	BLM	PARG	NBN	MGMT	PCNA	RRM1
PARG	POLD3	MLH3	BRCA1	PARP1	NHEJ1		HLTF	RRM2
PARP1	POLD4	MSH2	BRCA2	PARPBP	PARG		MAD2L2	
PARP3	RFC1	MSH3	BRE	RAD50	PARP1		POLH	
PNKP	RFC2	MSH6	BRIP1	TP53BP1	PARP3		POLI	
POLB	RFC3	PCNA	ERCC1	XRCC2	PNKP		POLK	
POLL	RFC4	PMS1	ERCC4	XRCC3	POLB		POLN	
XRCC1	RFC5	PMS2	FAAP100	EXO1	POLL		POLQ	
HMGB1	RPA1	POLD1	FAAP24	PCNA	POLM		RAD18	

PCNA	RPA2	POLD2	FAAP20	POLD1	PRKDC		REV1	
POLD1	RPA3	POLD3	FAN1	POLD2	RAD50		REV3L	
POLD2	RPA4	POLD4	FANCA	POLD3	RNF168		SHPRH	
POLD3	CCNH	RFC1	FANCB	POLD4	RNF8		UBE2B	
POLD4	CDK7	RFC2	FANCC	RFC1	TP53BP1		UBE2N	
RFC1	CETN2	RFC3	FANCD2	RFC2	XRCC4		UBE2V2	
RFC2	CUL3	RFC4	FANCE	RFC3	XRCC5		USP1	
RFC3	CUL4A	RFC5	FANCF	RFC4	XRCC6		WDR48	
RFC4	CUL5	RPA1	FANCG	RFC5	DCLRE1C			
RFC5	DDB1	RPA2	FANCI	RPA1	FAM175A			
ALKBH1	DDB2	RPA3	FANCL	RPA2	RIF1			
APEX1	ERCC1	RPA4	FANCM	RPA3				
APEX2	ERCC2		HELQ	RPA4				
FEN1	ERCC3		HES1	BARD1				
HMGB2	ERCC4		MAD2L2	BLM				
MBD4	ERCC5		PALB2	BRCA1				

MPG	ERCC6		RAD51	BRCA2				
MUTYH	ERCC8		RAD51C	BRIP1				
NEIL1	GTF2H1		RMI1	DMC1				
NEIL2	GTF2H2		RMI2	DNA2				
NEIL3	GTF2H3		SLX1A	EID3				
NTHL1	GTF2H4		SLX4	EME1				
OGG1	GTF2H5		STRA13	EME2				
PARP2	MMS19		TELO2	ERCC1				
PARP4	MNAT1		TOP3A	FANCM				
POLE	POLE		TOP3B	FEN1				
POLE2	POLE2		UBE2T	GEN1				
POLE3	POLE3		USP1	H2AFX				
POLE4	POLE4		WDR48	HELQ				
POLK	RAD23A			HFM1				
SMUG1	RAD23B			INO80				
TDG	RBX1			KAT5				

TDP1	TCEA1			MUS81				
UNG	TCEB1			NFATC2IP				
WRN	TCEB2			NSMCE1				
	UVSSA			NSMCE2				
	XAB2			NSMCE3				
	XPA			NSMCE4A				
	XPC			PALB2				
				PARP2				
				PAXIP1				
				POLH				
				POLQ				
				PPP4C				
				PPP4R1				
				PPP4R2				
				PPP4R4				
				RAD51				

				RAD51B				
				RAD51C				
				RAD51D				
				RAD52				
				RAD54B				
				RAD54L				
				RBBP8				
				RDM1				
				RECQL				
				RECQL4				
				RECQL5				
				RMI1				
				RMI2				
				RTEL1				
				SHFM1				
				SLX1A				

				SLX1B				
				SLX4				
				SMARCAD1				
				SMC5				
				SMC6				
				SPO11				
				SWSAP1				
				TOP3A				
				TOP3B				
				UIMC1				
				WRN				
				ZSWIM7				

Supplementary Tables 4. DMG Gene list of two cohorts

The retrospective dMMR/MSI-H cohort DMG gene			TCGA MSI-H cohort DMG gene		
gene	<i>p</i>	HR	gene	<i>p</i>	HR
<i>ABCB11</i>	0.00000	18.2	<i>CREBBP</i>	0.93	1.05
<i>ABL1</i>	0.00004	10.5	<i>KIF21A</i>	0.50	1.53
<i>ARHGEF16</i>	0.00000	14.2	<i>KMT2E</i>	0.65	1.32
<i>C5orf42</i>	0.00023	17.7	<i>MKI67</i>	0.04	3.18
<i>CCDC88C</i>	0.00028	8.65	<i>OTOG</i>	0.66	0.746
<i>CEP350</i>	0.00003	11.2	<i>POLQ</i>	0.57	1.48
<i>CHD4</i>	0.00029	10.6	<i>SEMA5A</i>	0.22	0.291
<i>CREBBP</i>	0.004	7.22	<i>SON</i>	0.10	3.91e−09
<i>CTAGE1</i>	0.00039	8.38	<i>SPEF2</i>	0.87	1.12
<i>DHX9</i>	0.00007	10.4	<i>STAB2</i>	0.75	0.822
<i>DMD</i>	0.00021	8.93	<i>TCHH</i>	0.03	3.18
<i>DNAH6</i>	0.00022	11	<i>TPR</i>	0.003	4.89
<i>FAM124A</i>	0.00028	8.65	<i>UNC13C</i>	0.94	1.05
<i>FBN1</i>	0.00078	7.62	<i>USH2A</i>	0.73	0.82
<i>GREB1L</i>	0.00025	10.9	<i>ZNF236</i>	0.17	2.2
<i>KIAA1109</i>	0.00237	1.68E+09			
<i>KIF21A</i>	0.002	8.24			
<i>KMT2E</i>	0.003	7.56			
<i>MKI67</i>	0.003	7.66			
<i>NBAS</i>	0.00001	15			
<i>NWD2</i>	0.00068	7.93			
<i>OTOG</i>	0.002	8.24			
<i>PARP14</i>	0.00045	9.92			
<i>POLQ</i>	0.00073	7.75			
<i>SDE2</i>	0.00001	11.8			
<i>SEMA5A</i>	0.00030	8.74			
<i>SH3TC2</i>	0.00000	17.1			

<i>SLX4</i>	0.00090	7.58			
<i>SON</i>	0.002	8.12			
<i>SPEF2</i>	0.001	7.49			
<i>STAB2</i>	0.001	8.94			
<i>SZT2</i>	0.001	13.9			
<i>TCHH</i>	0.003	7.78			
<i>TMC3</i>	0.00004	11			
<i>TPR</i>	0.003	7.6			
<i>UNC13C</i>	0.00017	9.49			
<i>USH2A</i>	0.003	7.56			
<i>VPS13D</i>	0.00016	11.4			
<i>VWF</i>	0.00027	10.7			
<i>ZBED9</i>	0.00016	9.21			
<i>ZNF236</i>	0.001	7.06			

Supplementary Table 5. Multivariate Cox analysis in the retrospective dMMR/MSI-H cohort.

PFS	Multivariate Cox analysis		
	Hazard ratio	95% CI	<i>p value</i>
TMB	1.01 (<i>MKI67</i>)	0.97-1.05 (<i>MKI67</i>)	0.459 (<i>MKI67</i>)
	1.01 (<i>TPR</i>)	0.98-1.04 (<i>TPR</i>)	0.290 (<i>TPR</i>)
	1.01 (<i>TCHH</i>)	0.98-1.03 (<i>TCHH</i>)	0.257 (<i>TCHH</i>)
	1.008 (<i>MKI67_TPR</i>)	0.98-1.03 (<i>MKI67_TPR</i>)	0.554 (<i>MKI67_TPR</i>)
	1.01 (<i>TPR_TCHH</i>)	0.99-1.04 (<i>TPR_TCHH</i>)	0.191(<i>TPR_TCHH</i>)
<i>MKI67</i>	2.35	0.24-22.98	0.460
<i>TPR</i>	5.20	0.92-29.32	0.061
<i>TCHH</i>	5.46	0.99-29.90	0.050
<i>MKI67_TPR</i>	7.22	0.67-76.81	0.101
<i>TPR_TCHH</i>	8.32	0.97-70.93	0.052

dMMR/MSI: deficient mismatch repair/microsatellite instability-high; PFS: progression free survival; TMB: tumor mutational burden;

Supplementary Tables 6. Survival hazard ratio analysis

Cohort	Gene	Hazard ratio	low95	up95	<i>p value</i>
The retrospective dMMR/MSI-H cohort (n = 32)	<i>MKI67</i>	4.557	1.136	18.29	0.019*
	<i>TPR</i>	7.605	1.573	36.76	0.003**
	<i>TCHH</i>	7.776	1.608	37.62	0.003**
TCGA-MSI-H cohort (n = 45)	<i>MKI67</i>	2.092	0.6643	6.59	0.20
	<i>TPR</i>	4.043	1.31	12.48	0.009**
	<i>TCHH</i>	3.621	1.142	11.48	0.02*

dMMR/MSI: deficient mismatch repair/microsatellite instability-high;

p* value<0.05; *p* value<0.01; ****p* value<0.001