

Table S1 List of DNA Damage Repair Pathway Genes

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)	Translation Synthesis (TLS)	Nucleotide pools (NP)	Others
ALKBH1	CCNH	EXO1	APITD1	BARD1	DCLRE1C	ALKBH2	HLTF	NUDT1	AEN
APEX1	CDK7	HMGB1	BARD1	BLM	DNTT	ALKBH3	MAD2L2	NUDT15	ATM
APEX2	CETN2	LIG1	BLM	BRCA1	FAM175A	ASCC3	PCNA	NUDT18	ATR
APLF	CUL3	MLH1	BRCA1	BRCA2	LIG4	MGMT	POLB	RRM1	ATRIP
APTX	CUL4A	MLH3	BRCA2	BRIP1	MRE11A		POLH	RRM2	ATRX
FEN1	CUL5	MSH2	BRE	DMC1	NBN		POLI		BABAM1
HMGB1	DDB1	MSH3	BRIP1	DNA2	NHEJ1		POLK		BCAS2
HMGB2	DDB2	MSH6	ERCC1	EID3	PARG		POLM		BRCC3
LIG1	ERCC1	PCNA	ERCC4	EME1	PARP1		POLN		CDC25A
LIG3	ERCC2	PMS1	FAAP100	EME2	PARP3		POLQ		CDC25B
MBD4	ERCC3	PMS2	FAAP20	ERCC1	PNKP		RAD18		CDC25C
MPG	ERCC4	POLD1	FAAP24	EXO1	POLB		REV1		CDC5L
MUTYH	ERCC5	POLD2	FAN1	FANCM	POLL		REV3L		CHAF1A
NEIL1	ERCC6	POLD3	FANCA	FEN1	POLM		SHPRH		CHEK1
NEIL2	ERCC8	POLD4	FANCB	GEN1	PRKDC		UBE2A		CHEK2
NEIL3	GTF2H1	RFC1	FANCC	H2AFX	RAD50		UBE2B		CLK2
NTHL1	GTF2H2	RFC2	FANCD2	HELQ	RIF1		UBE2N		DCLRE1A
OGG1	GTF2H3	RFC3	FANCE	HFM1	RNF168		UBE2V2		DCLRE1B
PARG	GTF2H4	RFC4	FANCF	INO80	RNF8		USP1		DUT
PARP1	GTF2H5	RFC5	FANCG	KAT5	TP53BP1		WDR48		ENDOV
PARP2	LIG1	RPA1	FANCI	LIG1	XRCC4				EXO5
PARP3	MMS19	RPA2	FANCL	MRE11A	XRCC5				GADD45A
PARP4	MNAT1	RPA3	FANCM	MUS81	XRCC6				GADD45G
PCNA	PCNA	RPA4	HELQ	NBN					HERC2
PNKP	POLD1		HES1	NFATC2IP					HUS1
POLB	POLD2		MAD2L2	NSMCE1					IDH1
POLD1	POLD3		PALB2	NSMCE2					MDC1
POLD2	POLD4		RAD51	NSMCE3					MORF4L1
POLD3	POLE		RAD51C	NSMCE4A					MPLKIP
POLD4	POLE2		RMI1	PALB2					MRPL40
POLE	POLE3		RMI2	PARG					NABP2
POLE2	POLE4		SLX1A	PARP1					PER1
POLE3	RAD23A		SLX4	PARP2					PLK3
POLE4	RAD23B		STRA13	PARPBP					PLRG1
POLK	RBX1		TELO2	PAXIP1					POLA1
POLL	RFC1		TOP3A	PCNA					POLG
RFC1	RFC2		TOP3B	POLD1					PRPF19
RFC2	RFC3		UBE2T	POLD2					PTEN
RFC3	RFC4		USP1	POLD3					RAD1
RFC4	RFC5		WDR48	POLD4					RAD17
RFC5	RPA1		XRCC2	POLH					RAD9A
SMUG1	RPA2			POLQ					RAD9B
TDG	RPA3			PPP4C					RIF1
TDP1	RPA4			PPP4R1					RNF169
UNG	TCEA1			PPP4R2					RNF4

Table S1 (continued)

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Base Excision Repair (BER)	Nucleotide Excision Repair (NER)-includes NER and GC-NER	Mismatch Repair (MMR)	Fanconi Anemia (FA)	Homology- dependent recombination (HDR)	Non- homologous End Joining (NHEJ)	Direct Repair (DR)	Translation Synthesis (TLS)	Nucleotide pools (NP)	Others
WRN	TCEB1			PPP4R4					RNMT
XRCC1	TCEB2			RAD50					RRM2B
	UVSSA			RAD51					SETMAR
	XAB2			RAD51B					SLX4
	XPA			RAD51C					SMARCA4
	XPC			RAD51D					SMARCC1
				RAD52					SOX4
				RAD54B					SPRTN
				RAD54L					SWI5
				RBBP8					TDP2
				RDM1					TOPBP1
				RECQL					TP53
				RECQL4					TREX1
				RECQL5					TREX2
				RFC1					TTK
				RFC2					TYMS
				RFC3					WEE1
				RFC4					YWHAB
				RFC5					YWHAE
				RMI1					YWHAG
				RMI2					
			RPA1						
			RPA2						
			RPA3						
			RPA4						
			RTEL1						
			SHFM1						
			SLX1A						
			SLX1B						
			SLX4						
			SMARCAD1						
			SMC5						
			SMC6						
			SPO11						
			SWSAP1						
			TOP3A						
			TOP3B						
			TP53BP1						
			UIMC1						
			WRN						
			XRCC2						
			XRCC3						
			ZSWIM7						

Table S2 Core DNA Damage Repair Genes

Base Excision Repair (BER)	Nucleotide Excision Repair (NER, including TC-NER and GC-NER)	Mismatch Repair (MMR)	Fanconi Anemia (FA)	Homologous Recombination (HR)	Non-homologous End Joining (NHEJ)	Direct Repair (DR)	Translation Synthesis (TLS)	Damage Sensor etc.
APEX1	CUL5	EXO1	FANCA	BARD1	LIG4	ALKBH2	POLN	ATM
APEX2	ERCC1	MLH1	FANCB	BLM	NHEJ1	ALKBH3	POLQ	ATR
FEN1	ERCC2	MLH3	FANCC	BRCA1	POLL	MGMT	REV1	ATRIP
PARP1	ERCC4	MSH2	FANCD2	BRCA2	POLM		REV3L	CHEK1
POLB	ERCC5	MSH3	FANCI	BRIP1	PRKDC		SHPRH	CHEK2
TDG	ERCC6	MSH6	FANCL	EME1	XRCC4			MDC1
TDP1	POLE	PMS1	FANCM	GEN1	XRCC5			RNMT
UNG	POLE3	PMS2	UBE2T	MRE11A	XRCC6			TOPBP1
	XPA			MUS81				TREX1
	XPC			NBN				
				PALB2				
				RAD50				
				RAD51				
				RAD52				
				RBBP8				
				SHFM1				
				SLX1A				
				TOP3A				
				TP53BP1				
				XRCC2				
				XRCC3				

Table S3 Clinically relevant fusions identified in LUAD

Fusion	No of Fusions	Frequency (%)
EML4&ALK	4	0.79
FGFR2&ATE1	1	0.20
WHSC1L1&FGFR1	1	0.20
CAPZA2&MET	1	0.20
TRIM24&NTRK2	1	0.20
TRIM33&RET	1	0.20
CLTC&ROS1	1	0.20
ROS1&FBXO9	1	0.20
CCDC6&RET	1	0.20
KRAS&SLC2A14	1	0.20
WHSC1L1&FGFR1	1	0.20

Table S4 Clinically relevant fusions identified in LUSC

Fusion	No of Fusions	Frequency (%)
FGFR2&CCAR2	1	0.20
FGFR3&TACC3	2	0.40
SMAD4&NRG1	1	0.20
THAP7&NRG1	1	0.20
WHSC1L1&NUTM1	1	0.20

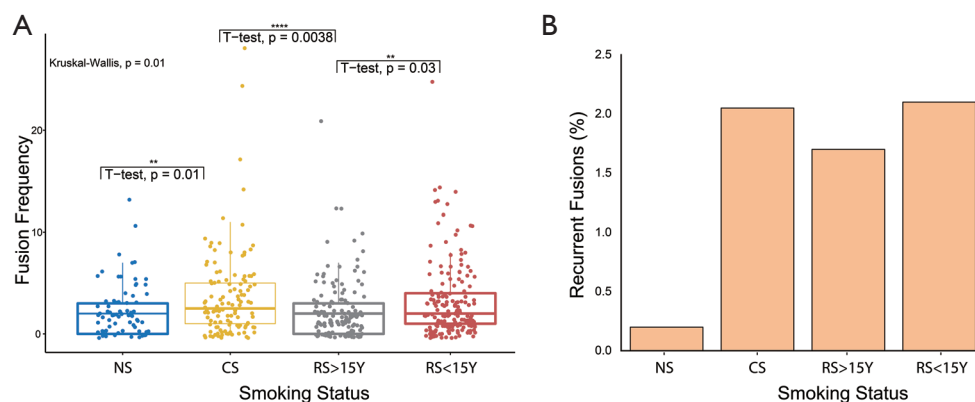


Figure S1 (A) Fusion frequencies identified across different LUAD smoking groups. (B) Percentage of recurrent fusions identified across different LUAD groups. CS, Current Smokers; NS, Nonsmokers, RF>15Ys, Reformed smokers for more than 15Ys; RF<15Ys, Reformed smokers for less than 15Ys.

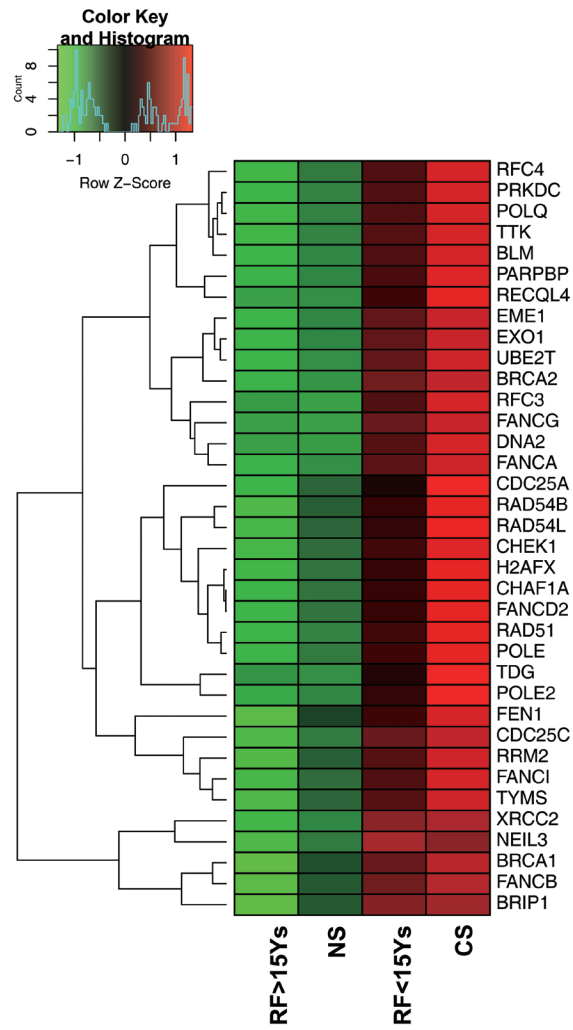


Figure S5 Genes in the DDR pathway differentially expressed across the different groups in LUAD. CS, Current Smokers; NS, Nonsmokers; RF>15Ys, Reformed smokers for more than 15Ys; RF<15Ys, Reformed smokers for less than 15Ys.

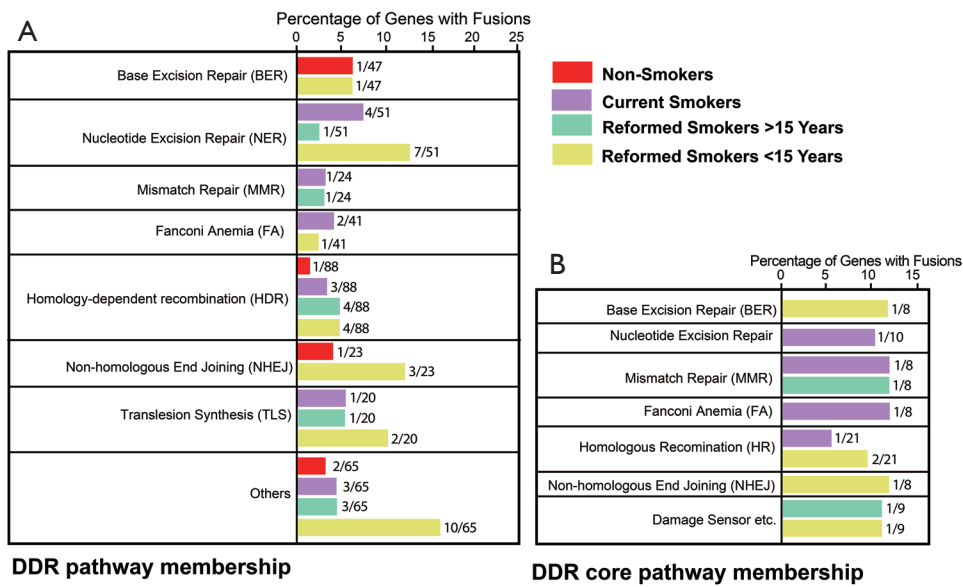


Figure S6 Percentage of genes in the DDR pathway that participated in fusions among different smoking groups in LUAD.

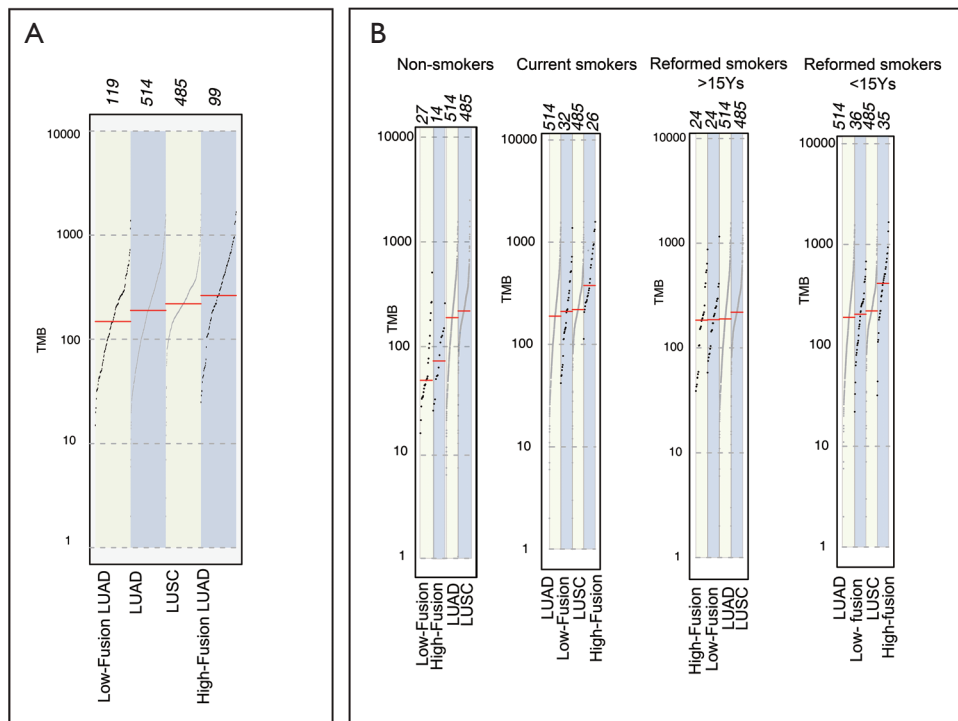


Figure S7 Tumor mutation burden across LUAD and LUSC (A). Tumor mutation burden across different smoking groups in LUAD is shown in B.

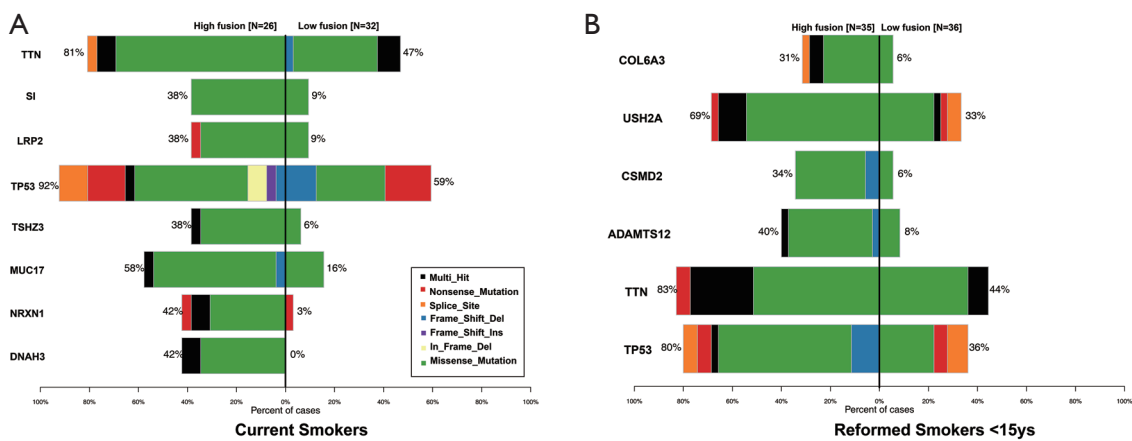


Figure S8 Comparison of mutations across LUAD samples with high or low fusions in Current Smokers (A) and Reformed Smokers <15ys. The percentage of mutated samples in each group is represented along with the type of mutations.

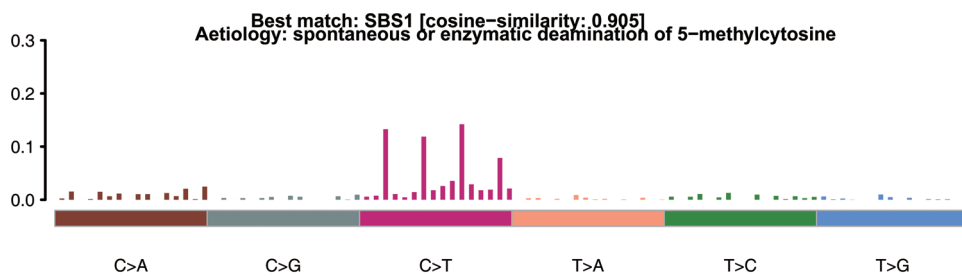


Figure S9 Mutational signatures identified in LUAD samples with high fusions.