

Supplemental Table S1. Genes included in the next generation sequencing panel used in the study.

ABI1	CASP8	ECT2L	FSTL3	KLF4	NF1	PRRX1	STAT3
ABL1	CBFA2T3	EGFR	FUBP1	KLHL6	NF2	PSIP1	STAT4
ABL2	CBFB	EIF4A2	FUS	KLK2	NFE2L2	PTCH1	STAT5B
ACKR3	CBL	ELF4	GAS7	KMT2A	NFIB	PTEN	STIL
ACSL3	CBLB	ELK4	GATA1	KMT2C	NFKB2	PTPN11	STK11
ACSL6	CBLC	ELL	GATA2	KMT2D	NFKBIA	PTPRC	SUFU
ADGRA2	CCDC6	ELN	GATA3	KNL1	NIN	RABEP1	SUZ12
AFDN	CCNB1IP1	EML4	GID4	KRAS	NKX2-1	RAC1	SYK
AFF1	CCND1	EMSY	GMPS	KTN1	NONO	RAD21	TAF15
AFF3	CCND2	EP300	GNA11	LASP1	NOTCH1	RAD50	TAL1
AFF4	CCND3	EPHA3	GNA13	LCK	NOTCH2	RAD51	TAL2
AKAP9	CCNE1	EPHA5	GNAQ	LCP1	NPM1	RAD51B	TBL1XR1
AKT1	CD274	EPHB1	GNAS	LGR5	NR4A3	RAF1	TCEA1
AKT2	CD74	EPS15	GOLGA5	LHFPL6	NRAS	RALGDS	TCF12
AKT3	CD79A	ERBB2	GOPC	LIFR	NSD1	RANBP17	TCF3
ALDH2	CD79B	ERBB3	GPC3	LMO1	NSD2	RAP1GDS1	TCF7L2
ALK	CDC73	ERBB4	GPHN	LMO2	NSD3	RARA	TC11A
AMER1	CDH1	ERC1	GRIN2A	LPP	NT5C2	RB1	TERT
APC	CDH11	ERCC1	GSK3B	LRIG3	NTRK1	RBM15	TET1
AR	CDK12	ERCC2	H3F3A	LRP1B	NTRK2	RECQL4	TET2
ARAF	CDK4	ERCC3	H3F3B	LYL1	NTRK3	REL	TFE3
ARFRP1	CDK6	ERCC4	HERPUD1	MAF	NUMA1	RET	TFEB
ARHGAP26	CDK8	ERCC5	HEY1	MAFB	NUP214	RHOH	TFG
ARHGEF12	CDKN1B	ERG	HGF	MALT1	NUP93	RICTOR	TFPT
ARID1A	CDKN2A	ESR1	HIP1	MAML2	NUP98	RM12	TFRC
ARID2	CDKN2B	ETV1	HIST1H3B	MAP2K1	NUTM1	RNF213	TGFBR2
ARNT	CDKN2C	ETV4	HIST1H4I	MAP2K2	NUTM2B	RNF43	THRFP3
ASPSCR1	CDX2	ETV5	HLF	MAP2K4	OLIG2	ROS1	TLX1
ASXL1	CEBPA	ETV6	HMGA1	MAP3K1	OMD	RPL10	TLX3
ATF1	CHCHD7	EWSR1	HMGA2	MAX	P2RY8	RPL22	TMPRSS2
ATIC	CHEK1	EXT1	HMG2N2P46	MCL1	PAFAH1B2	RPL5	TNFAIP3
ATM	CHEK2	EXT2	HNF1A	MDM2	PAK3	RPN1	TNFRSF14
ATP1A1	CHIC2	EZH2	HNRNPA2B1	MDM4	PALB2	RPTOR	TNFRSF17
ATP2B3	CHN1	EZR	HOOK3	MDS2	PATZ1	RUNX1	TOP1
ATR	CIC	FAM46C	HOXA11	MECOM	PAX3	RUNX1T1	TP53
ATRX	CIITA	FANCA	HOXA13	MED12	PAX5	SBDS	TPM3
AURKA	CLP1	FANCC	HOXA9	MEF2B	PAX7	SDC4	TPM4
AURKB	CLTC	FANCD2	HOXC11	MEN1	PAX8	SDHAF2	TPR
AXIN1	CLTCL1	FANCE	HOXC13	MET	PBRM1	SDHB	TRAF7
AXL	CNBP	FANCF	HOXD11	MITF	PBX1	SDHC	TRIM26
BAP1	CNOT3	FANCG	HOXD13	MRTFA	PCM1	SDHD	TRIM27
BARD1	CNTRL	FANCL	HRAS	MLF1	PCSK7	SEPT5	TRIM33
BCL10	COL1A1	FAS	HSP90AA1	MLH1	PDCD1	SEPTIN6	TRIP11
BCL11A	COPB1	FBXO11	HSP90AB1	MLL1	PDCD1LG2	SEPTIN9	TRRAP
BCL11B	COX6C	FBXW7	IDH1	MLL10	PDE4DIP	SET	TSC1
BCL2	CREB1	FCRL4	IDH2	MLL11	PDGFB	SETBP1	TSC2
BCL2L11	CREB3L1	FEV	IGF1R	MLL13	PDGFRA	SETD2	TSHR
BCL2L2	CREB3L2	FGF10	IKBKE	MLL16	PDGFRB	SF3B1	TTL
BCL3	CREBBP	FGF14	IKZF1	MN1	PDK1	SFPQ	U2AF1
BCL6	CRKL	FGF19	IL2	MNX1	PER1	SH2B3	UBR5
BCL7A	CRLF2	FGF23	IL21R	MPL	PHF6	SH3GL1	USP6
BCL9	CRTC1	FGF3	IL6ST	MRE11	PHOX2B	SLC34A2	VEGFA
BCOR	CRTC3	FGF4	IL7R	MSH2	PICALM	SLC45A3	VEGFB
BCORL1	CSF1R	FGF6	INHBA	MSH6	PIK3CA	SMAD2	VHL
BCR	CSF3R	FGFR1	IRF4	MSI2	PIK3CG	SMAD4	VT11A
BIRC3	CTCF	FGFR10P	IRS2	MSN	PIK3R1	SMARCA4	WAS
BLM	CTLA4	FGFR2	ITK	MTCP1	PIK3R2	SMARCB1	WDCP
BMPR1A	CTNNA1	FGFR3	JAK1	MTOR	PIM1	SMARCE1	WIF1
BRAF	CTNNB1	FGFR4	JAK2	MUC1	PLAG1	SMO	FKBP1
BRCA1	CYLD	FH	JAK3	MUTYH	PML	SNX29	WRN
BRCA2	CYP2D6	FHIT	JAZF1	MYB	PMS1	SOCS1	WT1
BRD3	DAXX	FIP1L1	JUN	MYC	PMS2	SOX10	WWTR1
BRD4	DDB2	FLCN	KAT6A	MYCL	POLE	SOX2	XPA
BRIP1	DDIT3	FLI1	KAT6B	MYCN	POT1	SPECC1	XPC
BTG1	DDR2	FLT1	KCNJ5	MYD88	POU2AF1	SPEN	XPO1
BTK	DDX10	FLT3	KDM5A	MYH11	POU5F1	SPOP	YWHAE
BUB1B	DDX5	FLT4	KDM5C	MYH9	PPARG	SRC	ZBTB16
C15orf65	DDX6	FBNP1	KDM6A	NACA	PPP2R1A	SRGAP3	ZMYM2
CACNA1D	DEK	FOXA1	KDR	NBN	PRCC	SRSF2	ZNF217
CALR	DICER1	FOXL2	KDSR	NCKIPSD	PRDM1	SRSF3	ZNF331
CAMTA1	DNM2	FOXO1	KEAP1	NCOA1	PRDM16	SS18	ZNF384
CANT1	DNMT3A	FOXO3	KIAA1549	NCOA2	PRF1	SS18L1	ZNF521
CARD11	DOT1L	FOXO4	KIF5B	NCOA4	PRKAR1A	SSX1	ZNF703
CARS	EBF1	FOXP1	KIT	NDRG1	PRKDC	STAG2	ZRSR2

Supplemental Table S2. Mutations in 26 cases of DLBCL/HGBL with CNS or systemic/non-CNS relapse. COSMIC identifiers according to COSMIC release V91, 7th April 2020 (<https://cancer.sanger.ac.uk/cosmic/>)

Sample	Type of recurrence	Gene	DNA change	Protein change	Variant type	COSMIC ID
ID_10	CNS	<i>ADGRA2</i>	c.2476A>G	p.I826V	Missense	
ID_10	CNS	<i>BCL2</i>	c.23G>A	p.G8E	Missense	COSV61377264
ID_10	CNS	<i>BCL2</i>	c.23G>A	p.G8E	Missense	COSV61377264
ID_10	CNS	<i>CBL</i>	c.2216C>T	p.S739F	Missense	COSV50634108
ID_10	CNS	<i>CCND3</i>	c.869T>G	p.I290R	Missense	COSV57828165
ID_10	CNS	<i>CREBBP</i>	c.3718T>G	p.C1240G	Missense	
ID_10	CNS	<i>IL6ST</i>	c.1301C>G	p.P434R	Missense	COSV61140205
ID_10	CNS	<i>MTOR</i>	c.4329+1G>A		Splicing site	
ID_10	CNS	<i>MYC</i>	c.230_231delinsGT	p.S77C	Missense	
ID_10	CNS	<i>RAF1</i>	c.122G>A	p.R41Q	Missense	
ID_10	CNS	<i>TENT5C</i>	c.112C>T	p.R38*	Nonsense	COSV65616704
ID_10	CNS	<i>TNFRSF14</i>	c.500dupC	p.T169fs	Frameshift indel	
ID_28	CNS	<i>ARID1A</i>	c.4805G>A	p.S1602N	Missense	
ID_28	CNS	<i>ARID2</i>	c.3694A>G	p.T1232A	Missense	
ID_28	CNS	<i>ARID2</i>	c.4268T>C	p.L1423S	Missense	
ID_28	CNS	<i>BCL9</i>	c.1808G>A	p.R603Q	Missense	COSV52342408
ID_28	CNS	<i>BTG1</i>	c.138_139delinsCT	p.E46D	Missense	COSV55460075
ID_28	CNS	<i>BTG1</i>	c.251C>T	p.A84V	Missense	
ID_28	CNS	<i>BTG1</i>	c.49G>A	p.A17T	Missense	
ID_28	CNS	<i>BTG1</i>	c.413C>T	p.T138I	Missense	COSV104372376
ID_28	CNS	<i>BTG1</i>	c.20_29dup10	p.M11fs	Frameshift indel	
ID_28	CNS	<i>CAMTA1</i>	c.1681A>T	p.T561S	Missense	
ID_28	CNS	<i>COL1A1</i>	c.1882G>A	p.A628T	Missense	COSV56811045
ID_28	CNS	<i>EP300</i>	c.1771A>G	p.I591V	Missense	
ID_28	CNS	<i>ETV6</i>	c.33+1delG		Splicing site	
ID_28	CNS	<i>ETV6</i>	c.33+1G>A		Splicing site	
ID_28	CNS	<i>FOXO1</i>	c.445C>T	p.P149S	Missense	COSV101092219
ID_28	CNS	<i>IRF4</i>	c.59G>A	p.G20D	Missense	COSV66706041
ID_28	CNS	<i>IRF4</i>	c.191G>A	p.R64H	Missense	COSV66705585
ID_28	CNS	<i>IRF4</i>	c.208C>G	p.L70V	Missense	COSV66704349
ID_28	CNS	<i>IRF4</i>	c.53G>A	p.S18N	Missense	COSV66705195
ID_28	CNS	<i>IRF4</i>	c.70C>T	p.L24F	Missense	COSV66705084
ID_28	CNS	<i>MCL1</i>	c.464G>A	p.S155N	Missense	
ID_28	CNS	<i>MCL1</i>	c.469G>A	p.D157N	Missense	
ID_28	CNS	<i>MLL1</i>	c.1127C>T	p.P376L	Missense	
ID_28	CNS	<i>NCKIPSD</i>	c.482A>G	p.Y161C	Missense	
ID_28	CNS	<i>NKX2-1</i>	c.566C>T	p.P189L	Missense	COSV61388583
ID_28	CNS	<i>PDE4DIP</i>	c.5038A>C	p.T1680P	Missense	
ID_28	CNS	<i>PIM1</i>	c.550C>T	p.L184F	Missense	COSV65164505
ID_28	CNS	<i>PIM1</i>	c.97C>T	p.P33S	Missense	COSV65166500
ID_28	CNS	<i>PIM1</i>	c.149G>A	p.G50D	Missense	COSV65166199
ID_28	CNS	<i>PIM1</i>	c.4C>T	p.L2F	Missense	COSV65164509
ID_28	CNS	<i>PIM1</i>	c.403G>A	p.E135K	Missense	COSV65164498
ID_28	CNS	<i>PIM1</i>	c.149G>T	p.G50V	Missense	
ID_28	CNS	<i>PIM1</i>	c.83G>A	p.G28D	Missense	COSV65164472
ID_28	CNS	<i>PIM1</i>	c.208G>A	p.E70K	Missense	COSV65164585
ID_28	CNS	<i>PRDM1</i>	c.799_800delTA	p.Y267fs	Frameshift indel	
ID_28	CNS	<i>PTCH1</i>	c.2558A>G	p.Q853R	Missense	
ID_28	CNS	<i>RPL22</i>	c.12+1G>A		Splicing site	COSV52377262
ID_28	CNS	<i>TCL1A</i>	c.154C>T	p.R52C	Missense	COSV68085859
ID_29	CNS	<i>AXIN1</i>	c.299G>A	p.S100N	Missense	
ID_29	CNS	<i>BLM</i>	c.3044C>T	p.T1015I	Missense	COSV61926480
ID_29	CNS	<i>IDH2</i>	c.608G>A	p.G203D	Missense	
ID_29	CNS	<i>MSH2</i>	c.1327C>A	p.L443I	Missense	
ID_29	CNS	<i>NUP214</i>	c.1291C>T	p.P431S	Missense	COSV99053497
ID_29	CNS	<i>RNF43</i>	c.235G>A	p.E79K	Missense	
ID_29	CNS	<i>TPR223</i>	c.1140G>A	p.W380*	Nonsense	
ID_3	CNS	<i>FANCD2</i>	c.2945C>T	p.P982L	Missense	
ID_3	CNS	<i>FANCF</i>	c.91G>A	p.V31M	Missense	
ID_3	CNS	<i>HOXD11</i>	c.446C>G	p.A149G	Missense	
ID_3	CNS	<i>LRIG3</i>	c.302G>A	p.R101Q	Missense	COSV57865811
ID_3	CNS	<i>NF1</i>	c.8395G>A	p.V2799I	Missense	
ID_3	CNS	<i>RANBP17</i>	c.1670G>A	p.R557H	Missense	
ID_3	CNS	<i>SDHB</i>	c.576_578delinsCAC	p.S193T	Missense	
ID_3	CNS	<i>TRIM26</i>	c.562A>G	p.I188V	Missense	

ID_3	CNS	<i>UBR5</i>	c.4268C>T	p.A1423V	Missense	
ID_3	CNS	<i>WIF1</i>	c.487A>G	p.T163A	Missense	
ID_30	CNS	<i>ACSL6</i>	c.1430G>T	p.C477F	Missense	
ID_30	CNS	<i>ATM</i>	c.1051G>A	p.D351N	Missense	
ID_30	CNS	<i>CBFA2T3</i>	c.1304C>T	p.A435V	Missense	
ID_30	CNS	<i>CD79B</i>	c.467C>G	p.T156R	Missense	
ID_30	CNS	<i>CD79B</i>	c.596T>A	p.L199Q	Missense	
ID_30	CNS	<i>EGFR</i>	c.286G>A	p.V96M	Missense	
ID_30	CNS	<i>GAS7</i>	c.1301A>G	p.D434G	Missense	COSV60443218
ID_30	CNS	<i>KDM6A</i>	c.1751C>T	p.T584M	Missense	COSV104429198
ID_30	CNS	<i>LRIG3</i>	c.613T>A	p.S205T	Missense	
ID_30	CNS	<i>LRP1B</i>	c.2803G>A	p.G935R	Missense	COSV67205521
ID_30	CNS	<i>MYD88</i>	c.728G>A	p.S243N	Missense	
ID_30	CNS	<i>NUP93</i>	c.2350-2A>G		Splicing site	
ID_30	CNS	<i>PBRM1</i>	c.4655A>G	p.H1552R	Missense	
ID_30	CNS	<i>TLX1</i>	c.160G>A	p.A54T	Missense	COSV100930063
ID_30	CNS	<i>TRRAP</i>	c.6889G>A	p.E2297K	Missense	
ID_31	CNS	<i>CD79B</i>	c.587A>C	p.Y196S	Missense	
ID_31	CNS	<i>CD79B</i>	c.560A>G	p.K187R	Missense	
ID_31	CNS	<i>CDH11</i>	c.877A>G	p.K293E	Missense	
ID_31	CNS	<i>CDH11</i>	c.853dupG	p.E285fs	Frameshift indel	
ID_31	CNS	<i>EPHA5</i>	c.2145A>C	p.E715D	Missense	
ID_31	CNS	<i>HOXC13</i>	c.451G>A	p.D151N	Missense	
ID_31	CNS	<i>MYD88</i>	c.794T>C	p.L265P	Missense	COSV57169334
ID_31	CNS	<i>NCOA2</i>	c.610G>A	p.V204I	Missense	
ID_31	CNS	<i>NOTCH1</i>	c.5629C>T	p.R1877C	Missense	COSV53052835
ID_31	CNS	<i>PAX3</i>	c.541G>A	p.E181K	Missense	COSV51338660
ID_31	CNS	<i>PAX7</i>	c.1423G>A	p.A475T	Missense	
ID_31	CNS	<i>PIM1</i>	c.237G>C	p.E79D	Missense	COSV65164484
ID_31	CNS	<i>PIM1</i>	c.58C>G	p.L20V	Missense	COSV65165051
ID_31	CNS	<i>PIM1</i>	c.237G>C	p.E79D	Missense	COSV65164484
ID_31	CNS	<i>PRDM1</i>	c.1617_1619delinsTG	p.S542fs	Frameshift indel	
ID_31	CNS	<i>PTPRC</i>	c.3373T>C	p.W1125R	Missense	COSV61418349
ID_31	CNS	<i>RUNX1</i>	c.210G>C	p.K70N	Missense	
ID_31	CNS	<i>TBL1XR1</i>	c.1321C>T	p.H441Y	Missense	
ID_32	CNS	<i>AXL</i>	c.2356A>C	p.S786R	Missense	
ID_32	CNS	<i>CEBPA</i>	c.724G>A	p.G242S	Missense	COSV57196802
ID_32	CNS	<i>DDX5</i>	c.440_441+2delCTGT		Splicing site	
ID_32	CNS	<i>FHIT</i>	c.137G>A	p.R46H	Missense	COSV59284122
ID_32	CNS	<i>KIAA1549</i>	c.5798A>C	p.E1933A	Missense	
ID_32	CNS	<i>MAFB</i>	c.273C>G	p.N91K	Missense	
ID_32	CNS	<i>MET</i>	c.820T>A	p.F274I	Missense	
ID_32	CNS	<i>MKL1</i>	c.2149C>T	p.P717S	Missense	
ID_32	CNS	<i>PICALM</i>	c.1394A>G	p.H465R	Missense	
ID_32	CNS	<i>TET2</i>	c.3035C>T	p.P1012L	Missense	
ID_32	CNS	<i>TP53</i>	c.681dupT	p.D228fs	Frameshift indel	
ID_33	CNS	<i>CARD11</i>	c.377G>A	p.G126D	Missense	COSV62717294
ID_33	CNS	<i>CARD11</i>	c.1010G>A	p.R337Q	Missense	COSV67796739
ID_33	CNS	<i>CBLB</i>	c.2713C>T	p.P905S	Missense	COSV51426495
ID_33	CNS	<i>ETV6</i>	c.17C>T	p.A6V	Missense	COSV67153958
ID_33	CNS	<i>ETV6</i>	c.33+1G>A		Splicing site	COSV67148243
ID_33	CNS	<i>MAML2</i>	c.982A>G	p.N328D	Missense	
ID_33	CNS	<i>MUC1</i>	c.747+1G>A		Splicing site	
ID_33	CNS	<i>MYD88</i>	c.794T>C	p.L265P	Missense	COSV57169334
ID_33	CNS	<i>PIM1</i>	c.427C>G	p.L143V	Missense	COSV65165620
ID_33	CNS	<i>PIM1</i>	c.403G>A	p.E135K	Missense	COSV65164498
ID_33	CNS	<i>RICTOR</i>	c.5003C>T	p.P1668L	Missense	COSV57117235
ID_33	CNS	<i>RNF213</i>	c.8512G>A	p.V2838I	Missense	
ID_33	CNS	<i>SBDS</i>	c.695G>T	p.G232V	Missense	
ID_33	CNS	<i>TBL1XR1</i>	c.1322A>G	p.H441R	Missense	
ID_33	CNS	<i>XPO1</i>	c.1786C>T	p.R596C	Missense	
ID_4	CNS	<i>BCL11A</i>	c.353G>A	p.R118K	Missense	COSV59627391
ID_4	CNS	<i>BCL2</i>	c.314C>T	p.S105F	Missense	
ID_4	CNS	<i>BTG1</i>	c.142C>A	p.L48M	Missense	
ID_4	CNS	<i>CD79B</i>	c.586T>C	p.Y196H	Missense	
ID_4	CNS	<i>DDIT3</i>	c.470G>A	p.R157Q	Missense	
ID_4	CNS	<i>DOT1L</i>	c.3527A>G	p.N1176S	Missense	COSV67113692
ID_4	CNS	<i>ERCC4</i>	c.1370A>G	p.D457G	Missense	
ID_4	CNS	<i>ETV6</i>	c.17C>T	p.A6V	Missense	COSV67153958
ID_4	CNS	<i>FCRL4</i>	c.1168G>A	p.A390T	Missense	COSV54859347
ID_4	CNS	<i>FOXO1</i>	c.1069T>G	p.S357A	Missense	
ID_4	CNS	<i>FUBP1</i>	c.2_3delinsAC	p.M1N	Missense	
ID_4	CNS	<i>IL7R</i>	c.419G>A	p.R140Q	Missense	COSV100286272

ID_4	CNS	<i>KLHL6</i>	c.185T>C	p.L62P	Missense	
ID_4	CNS	<i>KMT2D</i>	c.16442G>A	p.C5481Y	Missense	
ID_4	CNS	<i>MN1</i>	c.1569_1571dupACA	p.Q524dup	Inframe indel	
ID_4	CNS	<i>MYD88</i>	c.794T>C	p.L265P	Missense	COSV57169334
ID_4	CNS	<i>NFE2L2</i>	c.750T>A	p.F250L	Missense	
ID_4	CNS	<i>PIM1</i>	c.159C>G	p.Y53*	Nonsense	COSV100998570
ID_4	CNS	<i>PIM1</i>	c.64G>A	p.A22T	Missense	
ID_4	CNS	<i>PIM1</i>	c.757G>A	p.V253I	Missense	COSV65166535
ID_4	CNS	<i>PIM1</i>	c.413C>T	p.A138V	Missense	COSV65164653
ID_4	CNS	<i>RNF213</i>	c.12895G>A	p.G4299S	Missense	COSV60405281
ID_4	CNS	<i>RUNX1</i>	c.1126C>T	p.R376C	Missense	COSV99038633
ID_4	CNS	<i>SPEN</i>	c.3095A>G	p.E1032G	Missense	
ID_4	CNS	<i>TERT</i>	c.838G>A	p.E280K	Missense	COSV57204773
ID_4	CNS	<i>TRIP11</i>	c.217A>G	p.K73E	Missense	
ID_4	CNS	<i>USP6</i>	c.4045G>A	p.E1349K	Missense	
ID_5	CNS	<i>AFF4</i>	c.1579G>A	p.A527T	Missense	
ID_5	CNS	<i>ALK</i>	c.628G>A	p.A210T	Missense	
ID_5	CNS	<i>ATM</i>	c.4709T>C	p.V1570A	Missense	
ID_5	CNS	<i>BRAF</i>	c.1782T>G	p.D594E	Missense	COSV56284149
ID_5	CNS	<i>BRAF</i>	c.1782T>G	p.D594E	Inframe indel	COSV56284149
ID_5	CNS	<i>BTG1</i>	c.109_114delCTGCAG		Inframe indel	
ID_5	CNS	<i>CALR</i>	c.366G>T	p.M122I	Missense	
ID_5	CNS	<i>CCND3</i>	c.403C>G	p.R135G	Missense	
ID_5	CNS	<i>CD79B</i>	c.586T>C	p.Y196H	Missense	
ID_5	CNS	<i>CDH11</i>	c.28G>A	p.A10T	Missense	COSV51770897
ID_5	CNS	<i>EP300</i>	c.4232C>T	p.T1411I	Missense	
ID_5	CNS	<i>FLT4</i>	c.475C>G	p.L159V	Missense	
ID_5	CNS	<i>KDR</i>	c.1253A>T	p.Y418F	Missense	
ID_5	CNS	<i>KLHL6</i>	c.56G>C	p.S19T	Missense	
ID_5	CNS	<i>KLHL6</i>	c.71_74delTGGC	p.L24fs	Frameshift indel	
ID_5	CNS	<i>KLK2</i>	c.500G>A	p.R167H	Missense	COSV57568443
ID_5	CNS	<i>KMT2A</i>	c.968A>C	p.E323A	Missense	
ID_5	CNS	<i>MYC</i>	c.169C>T	p.P57S	Missense	COSV104388023
ID_5	CNS	<i>MYD88</i>	c.794T>C	p.L265P	Missense	COSV57169334
ID_5	CNS	<i>PIM1</i>	c.327G>A	p.W109*	Nonsense	COSV65164598
ID_5	CNS	<i>PIM1</i>	c.290G>A	p.S97N	Missense	COSV65164769
ID_5	CNS	<i>PIM1</i>	c.189+1G>A		Splicing site	COSV65165653
ID_5	CNS	<i>PIM1</i>	c.373C>G	p.P125A	Missense	COSV65165013
ID_5	CNS	<i>PIM1</i>	c.286G>A	p.V96M	Missense	COSV65164628
ID_5	CNS	<i>PIM1</i>	c.403G>A	p.E135K	Missense	COSV65164498
ID_5	CNS	<i>PIM1</i>	c.83G>A	p.G28D	Missense	COSV65164472
ID_5	CNS	<i>PIM1</i>	c.88G>A	p.E30K	Missense	COSV65166054
ID_5	CNS	<i>PRKDC</i>	c.4883A>T	p.K1628M	Missense	
ID_5	CNS	<i>ROS1</i>	c.1144T>C	p.Y382H	Missense	COSV63863083
ID_5	CNS	<i>ROS1</i>	c.2092G>A	p.E698K	Missense	
ID_5	CNS	<i>SLC45A3</i>	c.886G>A	p.V296M	Missense	
ID_5	CNS	<i>SOCS1</i>	c.529C>G	p.L177V	Missense	COSV59658959
ID_5	CNS	<i>ZNF703</i>	c.1531_1542del12		Inframe indel	
ID_6	CNS	<i>ABL1</i>	c.1624A>G	p.R542G	Missense	
ID_6	CNS	<i>ARHGAP26</i>	c.2095G>A	p.V699I	Missense	COSV50824137
ID_6	CNS	<i>BCL2</i>	c.174T>A	p.H58Q	Missense	COSV61372226
ID_6	CNS	<i>BCL7A</i>	c.92+1G>A		Splicing site	COSV55850485
ID_6	CNS	<i>BCL7A</i>	c.92+1G>T		Splicing site	
ID_6	CNS	<i>CCNB1IP1</i>	c.772_773insT	p.P258fs	Frameshift indel	
ID_6	CNS	<i>CCNB1IP1</i>	c.242G>A	p.R81Q	Missense	COSV100738559
ID_6	CNS	<i>CDK12</i>	c.1876A>G	p.T626A	Missense	COSV71000603
ID_6	CNS	<i>EP300</i>	c.757T>C	p.Y253H	Missense	
ID_6	CNS	<i>ERBB3</i>	c.2406C>G	p.H802Q	Missense	
ID_6	CNS	<i>EZH2</i>	c.1936T>A	p.Y646N	Missense	COSV57445823
ID_6	CNS	<i>FCRL4</i>	c.263G>A	p.R88Q	Missense	COSV54861298
ID_6	CNS	<i>FOXO1</i>	c.62G>T	p.R21L	Missense	COSV104427937
ID_6	CNS	<i>GNA13</i>	c.200A>G	p.Q67R	Missense	
ID_6	CNS	<i>HNRNPA2B1</i>	c.264+2T>A		Splicing site	
ID_6	CNS	<i>KMT2D</i>	c.15143G>A	p.R5048H	Missense	COSV56418956
ID_6	CNS	<i>MLLT1</i>	c.632G>A	p.S211N	Missense	
ID_6	CNS	<i>MYC</i>	c.774G>T	p.E258D	Missense	
ID_6	CNS	<i>MYC</i>	c.458T>G	p.F153C	Missense	COSV52375241
ID_6	CNS	<i>MYC</i>	c.550A>T	p.S184C	Missense	COSV99422123
ID_6	CNS	<i>MYC</i>	c.464C>T	p.A155V	Missense	
ID_6	CNS	<i>MYC</i>	c.761T>C	p.V254A	Missense	
ID_6	CNS	<i>MYC</i>	c.799T>G	p.S267A	Missense	
ID_6	CNS	<i>PIM1</i>	c.248G>A	p.G83D	Missense	COSV65164544
ID_6	CNS	<i>POLE</i>	c.1973A>C	p.K658T	Missense	

ID_6	CNS	<i>SPEN</i>	c.4936A>T	p.T1646S	Missense	
ID_6	CNS	<i>TNFRSF14</i>	c.552-2A>C		Splicing site	COSV63188463
ID_6	CNS	<i>TP53</i>	c.533A>C	p.H178P	Missense	COSV52689182
ID_6	CNS	<i>TRIM33</i>	c.1486C>G	p.P496A	Missense	
ID_6	CNS	<i>UBR5</i>	c.1415G>A	p.R472Q	Missense	COSV99642843
ID_6	CNS	<i>ZNF521</i>	c.1301A>G	p.E434G	Missense	
ID_6	CNS	<i>ZNF521</i>	c.1576T>G	p.S526A	Missense	COSV64123874
ID_7	CNS	<i>ARID2</i>	c.3145G>A	p.V1049I	Missense	
ID_7	CNS	<i>BCL2</i>	c.260G>A	p.S87N	Missense	COSV61379900
ID_7	CNS	<i>BUB1B</i>	c.805A>G	p.N269D	Missense	
ID_7	CNS	<i>CBLB</i>	c.2729C>T	p.P910L	Missense	
ID_7	CNS	<i>CREBBP</i>	c.1996G>T	p.E666*	Nonsense	
ID_7	CNS	<i>EP300</i>	c.5054T>G	p.V1685G	Missense	
ID_7	CNS	<i>ERCC5</i>	c.1195G>A	p.E399K	Missense	COSV63245088
ID_7	CNS	<i>EZH2</i>	c.1937A>C	p.Y646S	Missense	COSV57446054
ID_7	CNS	<i>GNA13</i>	c.100delA	p.I34fs	Frameshift indel	
ID_7	CNS	<i>GNA13</i>	c.571C>A	p.P191T	Missense	
ID_7	CNS	<i>GNA13</i>	c.201G>C	p.Q67H	Missense	COSV71474738
ID_7	CNS	<i>IGF1R</i>	c.1097G>A	p.R366Q	Missense	COSV51271636
ID_7	CNS	<i>KMT2D</i>	c.7609_7612delACTT	p.T2537fs	Frameshift indel	
ID_7	CNS	<i>KTN1</i>	c.52A>G	p.I18V	Missense	
ID_7	CNS	<i>LASP1</i>	c.590G>A	p.R197H	Missense	
ID_7	CNS	<i>MKL1</i>	c.25G>A	p.A9T	Missense	
ID_7	CNS	<i>NUMA1</i>	c.2563_2565dupAAG	p.K855dup	Inframe indel	
ID_7	CNS	<i>PTPRC</i>	c.2579C>G	p.T860R	Missense	
ID_7	CNS	<i>XPA</i>	c.700G>T	p.V234L	Missense	
ID_8	CNS	<i>ATP2B3</i>	c.1631A>G	p.E544G	Missense	
ID_8	CNS	<i>EP300</i>	c.1207T>A	p.W403R	Missense	COSV54346271
ID_8	CNS	<i>EP300</i>	c.1218T>A	p.C406*	Nonsense	
ID_8	CNS	<i>HOXD13</i>	c.491T>C	p.V164A	Missense	
ID_8	CNS	<i>MYC</i>	c.218C>T	p.T73I	Missense	COSV52367994
ID_8	CNS	<i>MYC</i>	c.223C>A	p.P75T	Missense	COSV52375216
ID_8	CNS	<i>MYC</i>	c.19G>A	p.V7M	Missense	COSV52367188
ID_8	CNS	<i>MYC</i>	c.218C>T	p.T73I	Missense	COSV52367994
ID_8	CNS	<i>MYC</i>	c.218C>T	p.T73I	Missense	COSV52367994
ID_8	CNS	<i>PDE4DIP</i>	c.3676C>T	p.R1226C	Missense	COSV57711551
ID_8	CNS	<i>RUNX1</i>	c.155T>A	p.M52K	Missense	COSV55868681
ID_8	CNS	<i>TP53</i>	c.724T>A	p.C242S	Missense	COSV52677021
ID_8	CNS	<i>TP53</i>	c.724T>A	p.C242S	Missense	COSV52677021
ID_8	CNS	<i>TP53</i>	c.724T>A	p.C242S	Missense	COSV52677021
ID_11	Systemic	<i>AKAP9</i>	c.10672A>G	p.I3558V	Missense	COSV62352026
ID_11	Systemic	<i>BCL11B</i>	c.1229C>T	p.P410L	Missense	COSV61733191
ID_11	Systemic	<i>BCL7A</i>	c.89A>G	p.K30R	Missense	
ID_11	Systemic	<i>CD74</i>	c.125+2T>A		Splicing site	
ID_11	Systemic	<i>EZH2</i>	c.1936T>A	p.Y646N	Missense	COSV57445823
ID_11	Systemic	<i>KLHL6</i>	c.286T>G	p.Y96D	Missense	
ID_11	Systemic	<i>LRP1B</i>	c.13769T>C	p.I4590T	Missense	
ID_11	Systemic	<i>MLLT10</i>	c.698A>G	p.K233R	Missense	
ID_11	Systemic	<i>P2RY8</i>	c.890C>T	p.S297F	Missense	
ID_11	Systemic	<i>PSIP1</i>	c.768A>C	p.E256D	Missense	
ID_11	Systemic	<i>PTEN</i>	c.510T>A	p.S170R	Missense	COSV64295950
ID_11	Systemic	<i>PTEN</i>	c.510T>A	p.S170R	Missense	COSV100909234
ID_11	Systemic	<i>TNFRSF14</i>	c.415C>T	p.R139C	Missense	COSV100859035
ID_12	Systemic	<i>AKAP9</i>	c.6386T>G	p.L2129W	Missense	
ID_12	Systemic	<i>ALK</i>	c.2557A>G	p.T853A	Missense	
ID_12	Systemic	<i>ASXL1</i>	c.1268A>G	p.N423S	Missense	
ID_12	Systemic	<i>CD79B</i>	c.587A>G	p.Y196C	Missense	
ID_12	Systemic	<i>ELL</i>	c.704C>T	p.T235M	Missense	COSV53213296
ID_12	Systemic	<i>EMSY</i>	c.3331C>T	p.R1111C	Missense	COSV58259784
ID_12	Systemic	<i>ESR1</i>	c.1301G>A	p.R434Q	Missense	COSV52791763
ID_12	Systemic	<i>ETV1</i>	c.731G>T	p.S244I	Missense	
ID_12	Systemic	<i>ETV6</i>	c.1153-1_1165del14		Splicing site	
ID_12	Systemic	<i>KEAP1</i>	c.706G>A	p.D236N	Missense	COSV50260398
ID_12	Systemic	<i>KMT2D</i>	c.3326_3336del11	p.A1109fs	Frameshift indel	
ID_12	Systemic	<i>KMT2D</i>	c.14341G>T	p.E4781*	Nonsense	
ID_12	Systemic	<i>MSH2</i>	c.1489A>G	p.I497V	Missense	
ID_12	Systemic	<i>MYD88</i>	c.794T>C	p.L265P	Missense	COSV57169334
ID_12	Systemic	<i>NFKBIA</i>	c.506C>T	p.T169I	Missense	
ID_12	Systemic	<i>PCM1</i>	c.3346T>C	p.F1116L	Missense	
ID_12	Systemic	<i>POLE</i>	c.1282G>A	p.A428T	Missense	COSV57679901
ID_12	Systemic	<i>RBM15</i>	c.1825G>A	p.E609K	Missense	COSV63923357
ID_12	Systemic	<i>RPTOR</i>	c.2734G>A	p.A912T	Missense	
ID_12	Systemic	<i>SETBP1</i>	c.1483T>A	p.S495T	Missense	

ID_12	Systemic	<i>STIL</i>	c.2225G>A	p.R742H	Missense	
ID_12	Systemic	<i>SYK</i>	c.353G>A	p.G118E	Missense	
ID_12	Systemic	<i>TRIP11</i>	c.217A>G	p.K73E	Missense	
ID_12	Systemic	<i>TSC2</i>	c.5116C>T	p.R1706C	Missense	
ID_12	Systemic	<i>USP6</i>	c.1826T>G	p.I609R	Missense	
ID_12	Systemic	<i>WRN</i>	c.2937T>G	p.I979M	Missense	
ID_12	Systemic	<i>WT1</i>	c.571G>A	p.G191S	Missense	
ID_13	Systemic	<i>EPHB1</i>	c.?	p.I250V	Missense	
ID_13	Systemic	<i>KAT6A</i>	c.?	p.A1504T	Missense	
ID_13	Systemic	<i>KMT2D</i>	c.?	p.G2623E	Missense	
ID_13	Systemic	<i>MAP3K6</i>	c.3373_3375del	p.K1125del	Inframe indel	COSV58872709
ID_13	Systemic	<i>PRDM1</i>	c.291+1G>C		Splicing site	
ID_13	Systemic	<i>SPOP</i>	c.224G>T	p.G75V	Missense	COSV61654912
ID_13	Systemic	<i>TAF1</i>	c.?	p.R1181C	Missense	
ID_13	Systemic	<i>TCL1A</i>	c.113C>G	p.T38S	Missense	COSV68085683
ID_15	Systemic	<i>AXIN1</i>	c.1666C>A	p.R556S	Missense	COSV99250091
ID_15	Systemic	<i>BCL2</i>	c.20C>T	p.T7I	Missense	COSV61373565
ID_15	Systemic	<i>BLM</i>	c.559A>C	p.K187Q	Missense	
ID_15	Systemic	<i>BRCA2</i>	c.4685A>C	p.Q1562P	Missense	
ID_15	Systemic	<i>CACNA1D</i>	c.5264C>T	p.S1755L	Missense	COSV55437928
ID_15	Systemic	<i>CBFA2T3</i>	c.799C>G	p.Q267E	Missense	
ID_15	Systemic	<i>CBFA2T3</i>	c.469A>G	p.T157A	Missense	
ID_15	Systemic	<i>CHEK2</i>	c.538C>T	p.R180C	Missense	COSV60418120
ID_15	Systemic	<i>CREBBP</i>	c.4507T>A	p.Y1503N	Missense	COSV52115152
ID_15	Systemic	<i>MITF</i>	c.776G>A	p.R259Q	Missense	
ID_15	Systemic	<i>MSH2</i>	c.1690A>G	p.T564A	Missense	COSV99254905
ID_15	Systemic	<i>PRKDC</i>	c.1337T>A	p.F446Y	Missense	
ID_15	Systemic	<i>RALGDS</i>	c.2116G>A	p.A706T	Missense	
ID_15	Systemic	<i>SMARCB1</i>	c.1148C>G	p.P383R	Missense	
ID_15	Systemic	<i>TFPT</i>	c.635C>T	p.P212L	Missense	
ID_15	Systemic	<i>TP53</i>	c.658T>C	p.Y220H	Missense	COSV52760651
ID_16	Systemic	<i>ARHGAP26</i>	c.2008A>G	p.T670A	Missense	
ID_16	Systemic	<i>BCOR</i>	c.4274A>G	p.N1425S	Missense	
ID_16	Systemic	<i>BCOR</i>	c.409G>A	p.V137I	Missense	COSV60702169
ID_16	Systemic	<i>BTG1</i>	c.443G>A	p.S148N	Missense	
ID_16	Systemic	<i>CD79B</i>	c.550-1G>A		Splicing site	
ID_16	Systemic	<i>COPB1</i>	c.2682C>G	p.N894K	Missense	
ID_16	Systemic	<i>ETV6</i>	c.33+1G>A		Splicing site	COSV67148243
ID_16	Systemic	<i>GOLGA5</i>	c.979A>G	p.S327G	Missense	
ID_16	Systemic	<i>HSP90AA1</i>	c.1199_1204delAGAAGA		Inframe indel	
ID_16	Systemic	<i>KMT2D</i>	c.7078C>G	p.P2360A	Missense	
ID_16	Systemic	<i>LPP</i>	c.208C>A	p.P70T	Missense	
ID_16	Systemic	<i>LRP1B</i>	c.9554A>G	p.N3185S	Missense	
ID_16	Systemic	<i>LRP1B</i>	c.10405G>A	p.A3469T	Missense	
ID_17	Systemic	<i>ATM</i>	c.5975A>C	p.K1992T	Missense	COSV53768482
ID_17	Systemic	<i>BARD1</i>	c.1694G>A	p.R565H	Missense	COSV99640229
ID_17	Systemic	<i>CACNA1D</i>	c.3421A>G	p.I1141V	Missense	
ID_17	Systemic	<i>CCND3</i>	c.875T>A	p.L292Q	Missense	
ID_17	Systemic	<i>CD74</i>	c.211delC	p.L71fs	Frameshift indel	
ID_17	Systemic	<i>CREBBP</i>	c.4444T>A	p.Y1482N	Missense	COSV52124105
ID_17	Systemic	<i>CREBBP</i>	c.3698+2T>A		Splicing site	
ID_17	Systemic	<i>FAS</i>	c.652-1G>A		Splicing site	COSV58240493
ID_17	Systemic	<i>HOXC11</i>	c.610_612delGAG		Inframe indel	
ID_17	Systemic	<i>NUP93</i>	c.1671G>C	p.E557D	Missense	
ID_17	Systemic	<i>PCSK7</i>	c.1321C>T	p.R441W	Missense	COSV58007222
ID_17	Systemic	<i>PCSK7</i>	c.2072G>T	p.R691M	Missense	
ID_17	Systemic	<i>POU2AF1</i>	c.16+2T>G		Splicing site	
ID_17	Systemic	<i>PRKDC</i>	c.871G>A	p.V291M	Missense	COSV58052890
ID_17	Systemic	<i>PTPN11</i>	c.925A>G	p.I309V	Missense	COSV100692935
ID_17	Systemic	<i>RANBP17</i>	c.1471C>T	p.R491C	Missense	
ID_17	Systemic	<i>SEPTIN6</i>	c.1108C>T	p.R370C	Missense	COSV59714035
ID_17	Systemic	<i>STAT4</i>	c.128G>A	p.W43*	Nonsense	
ID_17	Systemic	<i>TRAF7</i>	c.64_75del12		Inframe indel	
ID_18	Systemic	<i>AFF3</i>	c.637A>C	p.N213H	Missense	
ID_18	Systemic	<i>AKAP9</i>	c.11310delA	p.V3771fs	Frameshift indel	
ID_18	Systemic	<i>ALK</i>	c.1625C>A	p.P542Q	Missense	COSV66588105
ID_18	Systemic	<i>APC</i>	c.596C>T	p.A199V	Missense	COSV57335627
ID_18	Systemic	<i>ARHGEF12</i>	c.3707T>A	p.I1236N	Missense	
ID_18	Systemic	<i>BAP1</i>	c.638G>A	p.R213H	Missense	COSV56235828
ID_18	Systemic	<i>CACNA1D</i>	c.5438G>C	p.R1813P	Missense	
ID_18	Systemic	<i>CARD11</i>	c.1201G>A	p.D401N	Missense	COSV67796605
ID_18	Systemic	<i>CCDC6</i>	c.847+1G>A		Splicing site	
ID_18	Systemic	<i>CNTRL</i>	c.5707C>T	p.R1903*	Nonsense	

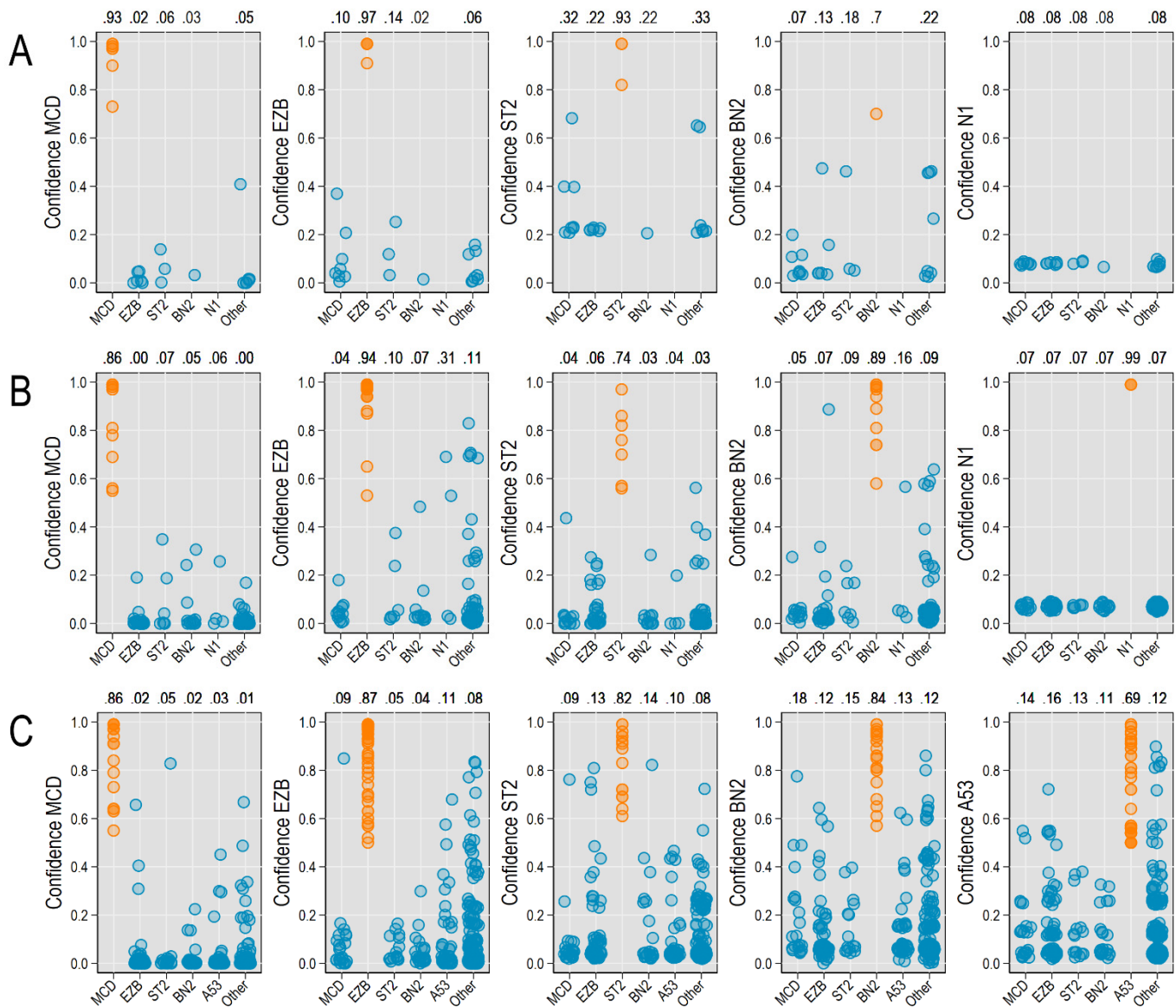
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ID_18	Systemic	<i>ERBB2</i>	c.1807G>A	p.G603S	Missense	
ID_18	Systemic	<i>ERCC5</i>	c.3122T>C	p.M1041T	Missense	COSV63244391
ID_18	Systemic	<i>ETV6</i>	c.18_33del16	p.Q7fs	Frameshift indel	
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ID_18	Systemic	<i>FCRL4</i>	c.52+1G>A		Splicing site	
ID_18	Systemic	<i>FGF6</i>	c.362C>G	p.S121C	Missense	
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ID_18	Systemic	<i>FHIT</i>	c.125G>A	p.R42Q	Missense	
ID_18	Systemic	<i>FOXA1</i>	c.575C>T	p.T192M	Missense	COSV51644184
ID_18	Systemic	<i>HMGA2</i>	c.86G>A	p.R29H	Missense	COSV100666657
ID_18	Systemic	<i>IDH2</i>	c.734C>T	p.P245L	Missense	
ID_18	Systemic	<i>IRS2</i>	c.3148G>A	p.V1050I	Missense	
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ID_18	Systemic	<i>MAFB</i>	c.7G>A	p.A3T	Missense	
ID_18	Systemic	<i>MAP3K1</i>	c.3070A>C	p.K1024Q	Missense	
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ID_18	Systemic	<i>NCKIPSD</i>	c.298C>T	p.R100W	Missense	
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ID_18	Systemic	<i>PDK1</i>	c.145T>C	p.Y49H	Missense	
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ID_18	Systemic	<i>PLAG1</i>	c.688C>T	p.R230*	Nonsense	COSV100387966
ID_18	Systemic	<i>PMS2</i>	c.475G>A	p.V159M	Missense	COSV99763777
ID_18	Systemic	<i>PRDM16</i>	c.1091G>A	p.R364Q	Missense	
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ID_18	Systemic	<i>TP53</i>	c.743G>A	p.R248Q	Missense	COSV52661580
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ID_19	Systemic	<i>MLL2</i>	c.1945C>T	p.P649S	Missense	
ID_19	Systemic	<i>MYD88</i>	c.794T>C	p.L265P	Missense	COSV57169334
ID_19	Systemic	<i>NIN</i>	c.4648T>G	p.S1550A	Missense	
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ID_19	Systemic	<i>PIM1</i>	c.241C>T	p.P81S	Missense	COSV65164906
ID_19	Systemic	<i>SETD2</i>	c.4376G>A	p.R1459Q	Missense	
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ID_19	Systemic	<i>SOCS1</i>	c.47C>T	p.A16V	Missense	
ID_19	Systemic	<i>SRGAP3</i>	c.2663G>A	p.R888Q	Missense	COSV64538081
ID_19	Systemic	<i>TBL1XR1</i>	c.971_973delCTT		Inframe indel	
ID_19	Systemic	<i>TCF3</i>	c.424G>A	p.G142S	Missense	
ID_19	Systemic	<i>TCL1A</i>	c.325G>T	p.E109*	Nonsense	
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ID_19	Systemic	<i>TRAF7</i>	c.476-2A>G		Splicing site	
ID_19	Systemic	<i>XPC</i>	c.1599G>C	p.E533D	Missense	
ID_21	Systemic	<i>ADGRA2</i>	c.2396G>A	p.R799H	Missense	COSV55102467
ID_21	Systemic	<i>ATM</i>	c.6670A>G	p.M2224V	Missense	
ID_21	Systemic	<i>BCL7A</i>	c.92+1G>C		Splicing site	COSV55846678
ID_21	Systemic	<i>CACNA1D</i>	c.6031C>T	p.R2011W	Missense	
ID_21	Systemic	<i>CDKN1B</i>	c.232G>A	p.E78K	Missense	COSV57431456
ID_21	Systemic	<i>CNTRL</i>	c.5782C>G	p.Q1928E	Missense	

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ID_21	Systemic	<i>DOT1L</i>	c.1148C>G	p.A383G	Missense	
ID_21	Systemic	<i>FANCA</i>	c.2936C>T	p.A979V	Missense	
ID_21	Systemic	<i>FBXW7</i>	c.2020C>T	p.R674W	Missense	COSV55906908
ID_21	Systemic	<i>FGFR4</i>	c.2274_2282delinsAT	p.G759fs	Frameshift indel	
ID_21	Systemic	<i>FOXA1</i>	c.448C>T	p.R150C	Missense	
ID_21	Systemic	<i>HSP90AA1</i>	c.1202_1204delAGA		Inframe indel	
ID_21	Systemic	<i>IL6ST</i>	c.721A>G	p.K241E	Missense	
ID_21	Systemic	<i>MCL1</i>	c.603G>C	p.R201S	Missense	
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ID_21	Systemic	<i>NFKB2</i>	c.602G>A	p.S201N	Missense	
ID_21	Systemic	<i>NFKB2</i>	c.760C>A	p.Q254K	Missense	
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ID_21	Systemic	<i>NOTCH2</i>	c.6160A>T	p.M2054L	Missense	
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ID_21	Systemic	<i>PIM1</i>	c.4C>T	p.L2F	Missense	COSV65164509
ID_21	Systemic	<i>PIM1</i>	c.277C>G	p.L93V	Missense	
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ID_21	Systemic	<i>PIM1</i>	c.396_416del21		Inframe indel	
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ID_21	Systemic	<i>RECQL4</i>	c.2662C>T	p.Q888*	Nonsense	
ID_21	Systemic	<i>RICTOR</i>	c.821+2T>A		Splicing site	
ID_21	Systemic	<i>SOCS1</i>	c.448C>G	p.L150V	Missense	COSV59660658
ID_21	Systemic	<i>SOCS1</i>	c.592C>G	p.P198A	Missense	
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ID_21	Systemic	<i>TCL1A</i>	c.113C>G	p.T38S	Missense	COSV68085683
ID_21	Systemic	<i>TCL1A</i>	c.93G>C	p.Q31H	Missense	
ID_21	Systemic	<i>TCL1A</i>	c.91C>T	p.Q31*	Nonsense	
ID_21	Systemic	<i>TET2</i>	c.2249_2252delTAAA	p.I750fs	Frameshift indel	
ID_21	Systemic	<i>TOP1</i>	c.33+1G>A		Splicing site	COSV63692924
ID_22	Systemic	<i>ABL2</i>	c.3189A>C	p.K1063N	Missense	
ID_22	Systemic	<i>AFDN</i>	c.4092_4100del9		Inframe indel	
ID_22	Systemic	<i>BCL2L2</i>	c.17C>T	p.S6L	Missense	
ID_22	Systemic	<i>BTG1</i>	c.38G>A	p.G13D	Missense	
ID_22	Systemic	<i>BTG1</i>	c.250G>A	p.A84T	Missense	COSV55459984
ID_22	Systemic	<i>BTG1</i>	c.133C>G	p.Q45E	Missense	
ID_22	Systemic	<i>CDK12</i>	c.1469A>G	p.H490R	Missense	
ID_22	Systemic	<i>CIITA</i>	c.4C>T	p.R2C	Missense	COSV60853917
ID_22	Systemic	<i>EBF1</i>	c.1045G>A	p.E349K	Missense	COSV58168973
ID_22	Systemic	<i>ERBB2</i>	c.2228G>A	p.G743E	Missense	
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ID_22	Systemic	<i>ITK</i>	c.775G>T	p.E259*	Nonsense	
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ID_22	Systemic	<i>KNL1</i>	c.2893A>T	p.M965L	Missense	
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ID_22	Systemic	<i>PRDM16</i>	c.2747C>T	p.A916V	Missense	
ID_22	Systemic	<i>RECQL4</i>	c.1472G>A	p.R491Q	Missense	
ID_22	Systemic	<i>RPTOR</i>	c.404C>T	p.T135M	Missense	
ID_22	Systemic	<i>SOCS1</i>	c.37G>A	p.V13I	Missense	
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ID_22	Systemic	<i>SOCS1</i>	c.310C>G	p.R104G	Missense	
ID_22	Systemic	<i>SOCS1</i>	c.401G>C	p.R134P	Missense	
ID_22	Systemic	<i>SOCS1</i>	c.258_279delinsC		Inframe indel	
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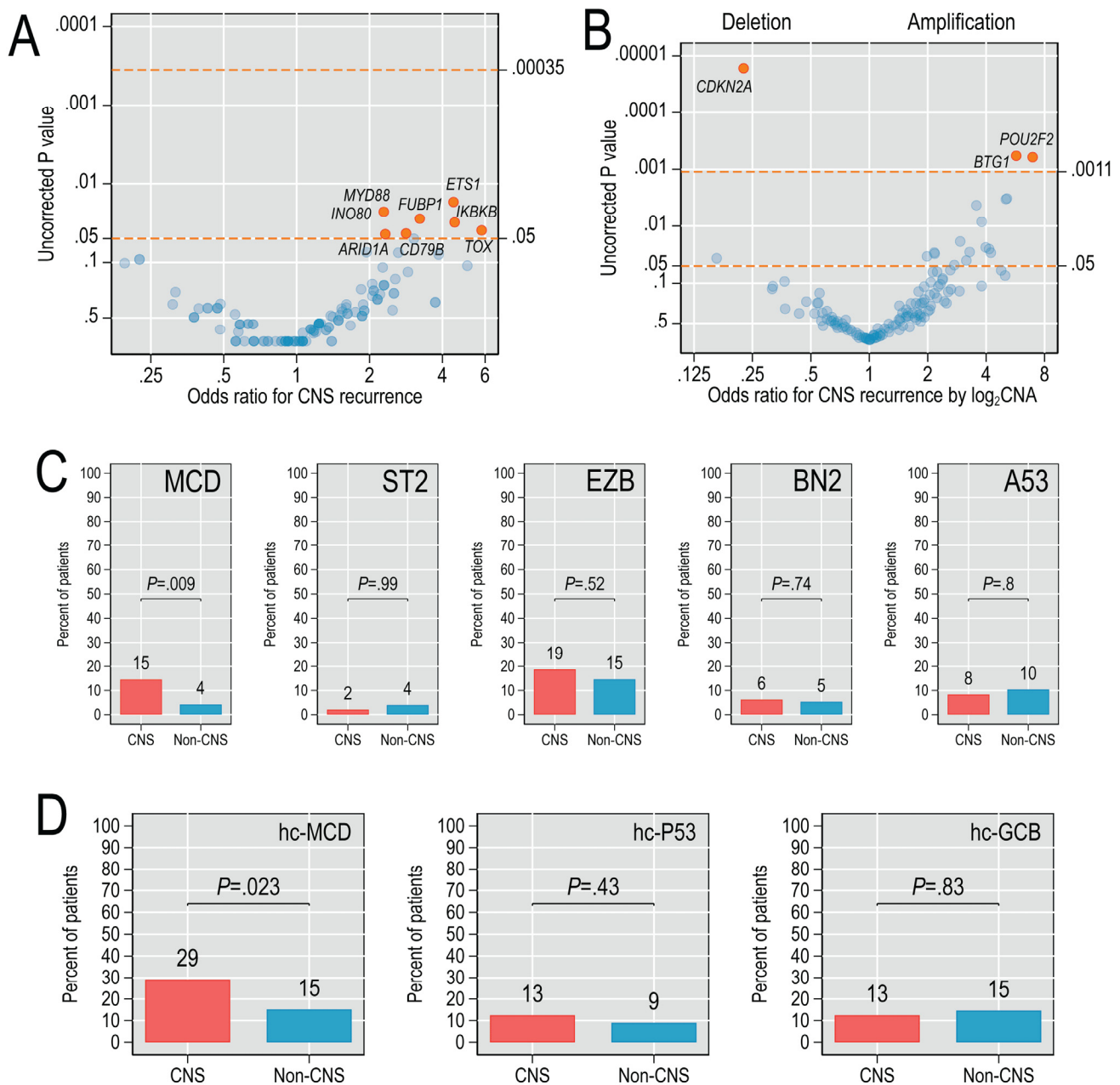
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ID_22	Systemic	<i>TRIP11</i>	c.4050A>C	p.E1350D	Missense	
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ID_22	Systemic	<i>XPO1</i>	c.1711G>A	p.E571K	Missense	COSV68944533
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ID_23	Systemic	<i>BCL10</i>	c.622C>T	p.Q208*	Nonsense	
ID_23	Systemic	<i>ERBB3</i>	c.1540C>A	p.P514T	Missense	
ID_23	Systemic	<i>ERBB3</i>	c.1541C>T	p.P514L	Missense	
ID_23	Systemic	<i>ERBB3</i>	c.1543G>A	p.G515S	Missense	
ID_23	Systemic	<i>ERCC5</i>	c.1789G>C	p.V597L	Missense	
ID_23	Systemic	<i>ETV5</i>	c.455C>A	p.P152Q	Missense	
ID_23	Systemic	<i>KDM5C</i>	c.3778G>T	p.A1260S	Missense	
ID_23	Systemic	<i>KMT2A</i>	c.9391C>T	p.L3131F	Missense	
ID_23	Systemic	<i>MED12</i>	c.91C>G	p.Q31E	Missense	COSV61332231
ID_23	Systemic	<i>PRCC</i>	c.1022A>G	p.D341G	Missense	
ID_23	Systemic	<i>PRKDC</i>	c.9292A>G	p.R3098G	Missense	
ID_23	Systemic	<i>RNF213</i>	c.12401T>C	p.I4134T	Missense	
ID_23	Systemic	<i>RPN1</i>	c.430A>G	p.T144A	Missense	COSV56189057
ID_23	Systemic	<i>TET2</i>	c.5353A>T	p.K1785*	Nonsense	COSV99480660
ID_23	Systemic	<i>TP53</i>	c.818G>A	p.R273H	Missense	COSV52660980
ID_25	Systemic	<i>APC</i>	c.8389A>G	p.S2797G	Missense	
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ID_25	Systemic	<i>CD79B</i>	c.587A>C	p.Y196S	Missense	
ID_25	Systemic	<i>CHEK1</i>	c.545_549delGAGAA	p.R182fs	Frameshift indel	
ID_25	Systemic	<i>CIITA</i>	c.3149+2T>C		Splicing site	
ID_25	Systemic	<i>CYP2D6</i>	c.19G>A	p.V7M	Missense	COSV99053720
ID_25	Systemic	<i>ETV6</i>	c.33+1G>C		Splicing site	
ID_25	Systemic	<i>EZR</i>	c.1445G>A	p.S482N	Missense	
ID_25	Systemic	<i>MYD88</i>	c.794T>C	p.L265P	Missense	COSV57169334
ID_25	Systemic	<i>MYH9</i>	c.139_141delAAG		Inframe indel	
ID_25	Systemic	<i>PIM1</i>	c.83G>A	p.G28D	Missense	COSV65164472
ID_25	Systemic	<i>PIM1</i>	c.111G>C	p.Q37H	Missense	COSV65165508
ID_25	Systemic	<i>PIM1</i>	c.117G>C	p.Q39H	Missense	
ID_25	Systemic	<i>PIM1</i>	c.28G>A	p.A10T	Missense	COSV65166493
ID_25	Systemic	<i>PIM1</i>	c.376_410del35	p.V126fs	Frameshift indel	
ID_25	Systemic	<i>SRGAP3</i>	c.2734C>T	p.R912W	Missense	COSV64532576
ID_35	Systemic	<i>ADGRA2</i>	c.?	p.D1313V	Missense	
ID_35	Systemic	<i>BCL2</i>	c.?	p.R6K	Missense	
ID_35	Systemic	<i>BTLA</i>	c.?	p.K93*	Nonsense	
ID_35	Systemic	<i>CREBBP</i>	c.4424C>T	p.P1475L	Missense	COSV52119252
ID_35	Systemic	<i>EZH2</i>	c.1936T>C	p.Y646H	Missense	COSV57445793
ID_35	Systemic	<i>FGFR3</i>	c.2334delC	p.779fs	Frameshift indel	
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ID_35	Systemic	<i>KMT2D</i>	c.829C>T	p.Q277*	Nonsense	
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ID_35	Systemic	<i>SDHA</i>	c.?	p.G206E	Missense	
ID_35	Systemic	<i>SPOP</i>	c.?	p.T25A	Missense	
ID_35	Systemic	<i>TNFRSF14</i>	c.?	p.E46G	Missense	

Supplemental Fig. S1. Performance characteristics of the LymphGen classifier¹ in 3 datasets: **(A)** the current study ($N=26$), **(B)** Dana-Farber Cancer Institute reference dataset;² **(C)** Reddy et al. validation dataset.³ Predictions for the second reference dataset (British Columbia Cancer Agency) were published and were not re-estimated.^{1,4} Note that the A53 subtype was not predicted directly in (A) and (B) as it is excluded from LymphGen prediction in the absence of full copy number alteration data; furthermore, the N1 subtype was not predicted in (C) as *NOTCH1* mutations were not recorded. Datasets for (B) and (C) were obtained from cBioPortal (<https://www.cbioportal.org/>).⁵

The probabilistic LymphGen algorithm (<https://lmpp.nih.gov/lymphgen/>) uses data on single nucleotide variants, insertions/deletions, *BCL2* and *BCL6* rearrangements, and copy number alterations (ideally obtained from a complete exome and copy number analysis) to generate prediction for 6 molecular subsets of DLBCL termed MCD (*MYD88*^{L265P}, *CD79B*), EZB (*EZH2*, *BCL2*), ST2 (*SGK1*, *TET2*), BN2 (*NOTCH2*, *BCL6* rearrangement), N1 (*NOTCH1*) and A53 (aneuploid, *TP53*).¹ Based on the number of genomic features present in the sample, the algorithm generates a “confidence” level for each subtype (between 0 and 1), and assigns the most likely subtype. The plots demonstrate distribution of confidence value for each subtype, according to subtype ultimately assigned (highlighted in orange). Mean values of the confidence levels in each category are listed above the plot.

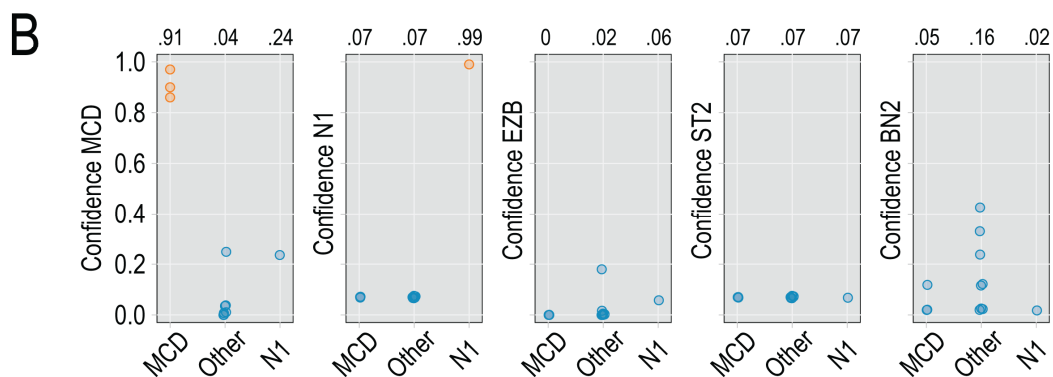
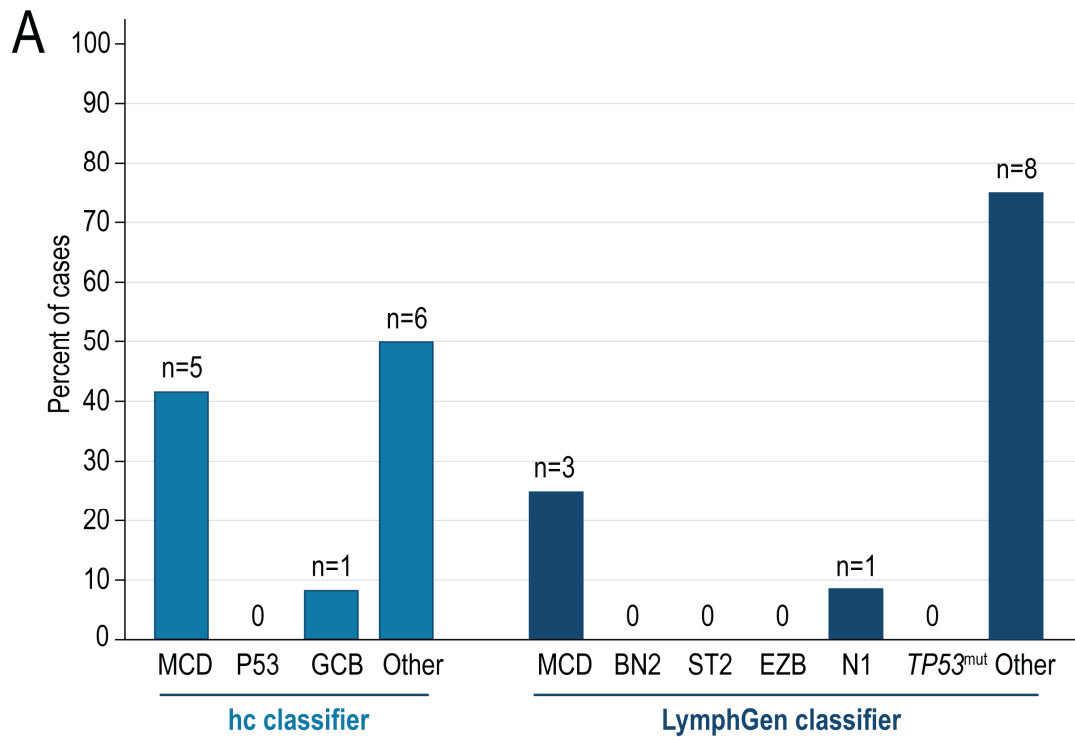


Supplemental Fig. S2. Analysis of the validation dataset from the study by Reddy et al.³ (data obtained from cBioPortal (<https://www.cbioportal.org/>)).⁵ A subset of samples from this study ($N=402$) had a designation of CNS recurrence or no CNS recurrence. We submitted mutation and copy number alteration (CNA) data for LymphGen prediction, and assigned the simplified hierarchical classifier (hc), as described in the main paper. **(A)** Smile plot showing association between mutations in specific single genes and the odds of CNS recurrence; genes with $P < .05$ are highlighted, but no gene retained statistical significance upon adjustment for false discovery rate (FDR) using Benjamini-Hochberg procedure;⁶ **(B)** smile plot showing association between \log_2 CNA values for specific genes (odds ratio $< .5$ generally correspond to deletions and > 2 amplifications) and the odds of CNS recurrence; *CDKN2A* deletion and *BTG1* or *POU2F2* gains were significantly associated with CNS recurrence even after FDR adjustment; **(C)** prevalence of specific LymphGen subtypes in the group with CNS and non-CNS recurrence; only the MCD subtype was significantly associated with CNS recurrence ($P = .009$); **(D)** prevalence of DLBCL subtypes defined by the hierarchical classifier (hc); the hc-MCD subtype was significantly associated with CNS recurrence ($P = .023$) and was assigned to 29% of tumors in the CNS recurrence group.



Supplemental Fig. S3. (A) Genomic subtypes of patients with CNS relapse in the phase 3 DLBCL GOYA trial.^{7,8} **(B)** Performance characteristics of the LymphGen classifier¹ in the GOYA dataset.

Among 1,418 enrolled patients, 38 experienced a CNS relapse, and 12 had available mutational profiles obtained by next-generation sequencing of 465 cancer-related genes (Foundation Medicine, Cambridge, MA). NGS data on non-CNS cases were not available. Among patients with CNS relapse, 61% had extranodal involvement, 47% had high CNS-IPI, and none had *MYC* rearrangement (and thus double-hit status), and only one had a *BCL6* rearrangement.⁷ Among the 12 patients with CNS relapse and available NGS data, 5 (42%) had *MYD88* mutations, and none had *TP53* a mutation. We used the publicly available gene list for FoundationOne Heme® test as input for the LymphGen algorithm.^{1,9}



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