

TABLES

For each modified lysine, the mean of the fold change in CLL samples treated either with vehicle (DMSO) or with 0.25 μ M MLN4924 with respect to untreated healthy donors samples, is shown.

Table 1. Modification of proteins related to the NEDDylation pathway in CLL.

Protein	Mean DMSO CLL vs Control	Mean MLN4924 CLL vs Control	Site	Peptide
CUL1	4.0	-2.0	410	FINNNAVTK*MAQSSSK
CUL3	3.4	-16.5	292	NGK*TEDLGCMYK
CUL5	8.2	-4.8	724	TQEAIQIMK*M#R
NAE1	-2.0	-27.3	338	GTIPDMIADSGK*YIK
NAE1	-2.8	-18.9	12	LLKEQK*YDR
UBA3	6.5	1.9	409	SPAITATLEGK*NR
UBE2M	2.0	-2.4	92	VGQGYPHDPPK*VK
UBE2M	2.6	-1.7	72	LVICPDEGFYK*SGK
DCUN1D1	-0.4	-5.2	143	AQIPK*MEQELKEPGR
DCUN1D1	-1.9	-3.3	63	K*KLEQLYNR
DDB1	14.0	2.1	1121	MQEVVANLQYDDGSGMK*R
COPS7B	14.9	0.3	221	TLK*ATASSSAQEMEQLAER
NEDD8	1.8	-12.5	54	QMNDEK*TAADYK
NEDD8	2.0	-8.2	6	VK*TLTGKEIDIEPTDKVER
NEDD8	2.5	-4.2	22	TLTGKEIDIEPTDK*VER
NEDD8	1.7	-4.0	48	LIYSGK*QMNDEK
NEDD8	-1.5	-5.4	11	VK*TLTGK

Table 2. Modification of proteins related to the ubiquitination machinery in CLL.

Protein	Mean DMSO CLL vs Control	Mean MLN4924 CLL vs Control	Site	Peptide	Involvement in pathways relevant in CLL
RBCK1	-5.3	-14.4	174	GPLEPGPPK*PGVPQEPGR	p53, NF-kB
MIB1	20.1	11.4	895	AAVLFQPCGHMCACENCANLM K*K	Notch, NF-kB
MIB1	20.1	11.4	896	AAVLFQPCGHMCACENCANLM KK*	
PCNP	27.3	18.8	82	K*ASAIK	MAPK, PI3K/AKT/mTOR
PCNP	10.0	3.7	167	NIK*SHLGNVHDQDN	
RNF185	-4.7	-12.4	105	EK*TPPRPQGQRPEPENR	Wnt
ZNF313	19.9	13.9	126	ATIK*DASLQPR	p21
XIAP	12.9	8.0	31	LK*TFANFSPGSPVSASTLAR	Apoptosis
MKRN1	4.0	-0.5	321	SAK*QFESK	Wnt, p53, p21
UBE2E1	17.7	13.1	43	NSK*LLSTSAK	Involved in AML
TRIM22	-6.0	-9.3	265	SESWTLK*KPK	PI3K/AKT/mTOR
TRAF2	-0.9	-4.6	176	APCCGADVK*AHHEVCPK	NF-kB and JNK
TRAF2	-1.5	-4.6	27	TLLGTK*LEAK	
TRAF2	-5.7	-8.6	119	GTLK*EYESCHEGR	
ITCH	2.8	-0.0	249	VSGNNSPSLSNGGFK*PSRPPR PSRPPPTPR	Role in CLL, Jun
cIAP2	0.0	-2.6	231	HFPK*CPFIENQLQDTSR	Role in CLL, NF-kB
USP22	11.0	6.9	166	K*ITSNCTIGLR	Potential oncogene
RBBP6	18.4	8.6	901	NIGSNYPEK*LSAR	p53
Cbl-b	6.4	4.0	881	RLPGENVK*TNR	BCR signaling
Cbl-b	27.4	17.1	64	LCQNP*KLQLK	
SKP1A	23.1	4.5	155	K*ENQWCEEK	Cell cycle
SKP1A	3.9	1.5	128	TVANMIK*GK	
USP7	4.2	-0.1	882	KLYYQQLK*MK	p53, Notch, NF-kB, Wnt
USP7	13.2	7.7	1096	YTYLEK*AIK	
UCHL5	4.8	-0.4	315	TLAEHQQLIPLVEK*AK	Wnt, TGFβ
USP48	5.6	2.7	551	LTVK*ALCK	NF-kB, DNA repair
ataxin-3	-22.4	-27.0	117	SFICNYK*EHWFTVR	DNA repair, cytoskeleton

Table 3. Modification of proteins related to the DNA repair machinery in CLL.

Protein	Mean DMSO CLL vs Control	Mean MLN4924 CLL vs Control	Site	Peptide
DDB2	13.4	1.6	151	DKPTFIK*GIGAGGSITGLK
H2AX	19.5	10.6	128	KTSATVGPK*APSGGKK
Ku80	7.7	1.4	195	LGGHGPSFPLK*GITEQQK
Ku80	7.6	2.0	660	FNNFLK*ALQEK
XPC	2.1	-3.0	508	KDPSLPAASSSSSSSK*R
XPC	9.0	5.2	785	K*LDIDCVQAI
Ku70	9.0	5.6	114	NIYVLQELDNPQAK*R
MORF4L1	10.6	6.5	127	ANQEYAEQK*MR
MORF4L1	9.1	5.5	111	YVDTNLQK*QR
MORF4L1	8.3	5.4	117	ELQK*ANQEYAEQK
MORF4L1	9.5	6.6	143	TSQLQK*NVEVK
RAD23B	2.6	-0.0	151	QEKPAEK*PAETPVATSPTATDSTSGDSSR

Table 4. Modification of histones and DNA binding proteins in CLL.

Protein	Mean DMSO CLL vs Control	Mean MLN4924 CLL vs Control	Site	Peptide
H1B	911.8	516.9	49	ATGPPVSELITK*AVAASK
H1B	8.6	1.1	194	SPAKPK*AVKPK
H1B	11.7	5.6	37	K*ATGPPVSELITK
H1B	3.4	-0.5	17	SETAPAETATPAPVEK*SPAK
H1C	-90.8	-398.1	17	AAPPAEK*APVK
H1C	58.7	28.8	160	K*PAAATVTK
H1C	21.9	8.2	21	PAAPAAAPPAEKAPVK*K
H1C	17.5	9.3	159	KAK*KPAAATV
H1C	12.2	6.3	201	AAKPK*VVKPK
H1C	724.4	415.1	46	KASGPPVSELITK*AVAASK
H1C	17.6	14.8	63	SGVSLAALK*K
H1C	60.4	32.4	90	SLVSK*GTLVQTK
H1C	-6.4	-10.3	63	SLAALK*K
H1C	8.5	5.8	97	GTLVQTK*GTGASGSFK
H1D	7.3	4.2	35	RK*ASGPPVSELI
H1E	10.8	3.0	17	SETAPAAPAAPAPAEK*TPVK
H1X	3.8	0.3	19	TTAEGMAK*K
H1X	1.9	-0.8	23	KVTK*AGGSAALSPSK
H2AE	13.4	9.5	119	VTIAQGGVLPNIQAVLLPK*KTESHHKT
H2AE	1.8	-1.5	100	LLGK*VTIAQGGVLPNIQAV
H2AFY	569.1	537.5	123	GK*LEAIITPPPAK
H2AFY	65.0	36.1	167	QGEVSK*AASADSTTEGTPADGFTVLSTK
H2AFY	1.0	-3.7	332	QTAAQLILK*AI
H2AFY	11.3	6.9	323	NGFPK*QTAAQLILK
H2AFY	-12.7	-16.1	117	ASGGVLPNIHPELLAKK*
H2AFY	2.9	-0.2	295	TVK*NCLALADDDK
H2AFY	10.2	7.6	189	AASADSTTEGTPADGFTVLSTK*SLFLGQK
H2B	9.8	4.0	117	HAVSEGTK*AVTKYTSSK
H2B	4.6	1.6	117	HAVSEGTK*AVTK
H2B	15.4	7.7	6	PEPSK*SAPAPK
H2B1D	16.0	7.3	6	PEPTK*SAPAPK
H2B1D	12.1	4.8	21	KAVTK*AQK
H2B1L	11.4	5.9	6	PELAK*SAPAPK
H2B1M	45.0	23.2	6	PEPVK*SAPVPK

H2B2F	5.5	2.9	6	PDPAK*SAPAPK
H2B2F	11.3	8.3	21	AVTK*VQK
H3	20.4	11.4	19	K*QLATK*AAR
H3	13.1	4.2	24	KQLATK*AAR
H3F3A	4.0	-0.6	37	PSTGGVK*KPHR
H3F3A	3.5	-0.2	28	K*SAPSTGGVK
HIST1H2AE	292.8	142.6	119	QGGVLPNIQAVLLPK*K*
HIST1H2AE	20.0	14.2	120	VTIAQGGVLPNIQAVLLPK*K*TESH
HIST3H3	1.2	-4.4	37	SAPATGGVK*KPHR
HIST3H3	4.5	-1.0	28	K*SAPATGGVK
HIST3H3	9.4	0.5	37	TGGVK*KPHR
HMG2	12.3	6.0	31	LSAK*PAPPKPEPKPK
HMG2	9.4	4.0	36	LSAKPAPPK*PEPKPK
HMG2	9.4	4.0	40	LSAKPAPPKPEPK*PK
HMG2	8.8	4.5	31	LSAK*PAPPKPEPK
HMG2	29.8	6.9	16	AK*VKDEPQR
HMG4	21.1	14.9	31	LSAK*PAPPKPEPR
NUCKS	17.3	14.3	175	LK*ATVTPSPVK
ZNF638	13.9	11.4	951	K*AAESMVK

Table 5. Modification of proteins of the cytoskeleton in CLL.

Protein	Mean DMSO CLL vs Control	Mean MLN4924 CLL vs Control	Site	Peptide
ACTA2	4.9	0.5	52	HQGVMVGMGQK*DSYVGDEAQSK*R
CAP1	-12.3	-15.2	126	GSK*LFNHLSAVSESI
Cofilin-1	-31.1	-34.3	112	FWAPESAPLK*SK
EPB41	7.4	2.4	366	ELEEK*VMELHK
EPB41	2.7	-0.4	361	LAPNQTK*ELEEK
Ezrin	22.7	9.3	357	LQDYEEK*TK
Ezrin	9.5	4.2	523	RITEAEK*NER
Ezrin	6.5	2.9	450	AK*EAQDDLK
Ezrin	7.9	4.1	35	QLFDQVVK*TIGLR
Ezrin	28.3	13.3	306	RKPDTIEVQQMK*AQAR
Ezrin	73.8	61.3	263	K*APDFVFYAPR
Ezrin	8.6	4.8	262	FVIKPIDK*K
Ezrin	13.0	9.0	3	PK*PINVR
Lamin B1	-6.5	-30.0	417	K*RVDVEESEASSSV
Lamin B1	1.7	-4.7	111	CK*AEHDQLLNLYAK
Lamin B1	1.6	-3.8	109	AKLQIELGK*CK
Lamin B2	0.0	-4.8	186	AQLAK*AEDGHAVAK
Lamin B2	5.9	1.3	123	LQIEIGK*LR
Lamin B2	2.9	-0.3	196	K*QLEKETLMR
Lamin B2	6.8	4.1	520	FTPK*YILR
Lamin B2	6.1	3.5	290	LDSAK*LSSDQNDK
profilin 1	194.6	154.0	108	TDK*TLVLLMGK
STMN1	30.2	16.9	128	DK*HIEEVR
TUBB1	-35.3	-55.9	324	MSTK*EVDQQLSVQTR
Vimentin	2.1	-3.0	168	RQVDQLTNDK*AR
Vinculin	7.8	4.4	219	NSK*NQGIEEALK

Table 6. Modification of proteins of the RNA splicing machinery in CLL.

Protein	Mean DMSO CLL vs Control	Mean MLN4924 CLL vs Control	Site	Peptide
SF3A1	8.6	1.1	102	HKVSEFK*EGK
SF3A1	16.8	10.4	419	ASKPLPPAPAPDEYLVSPITGEK*IPASK
SFRS3	12.3	7.2	23	VYVGNLGNNGNK*TELER
SFRS3	27.8	14.4	85	VRVELSNGEK*R
SFRS7	16.3	7.8	24	VYVGNLGTGAGK*GELER
SFRS7	13.0	5.7	70	GLDGK*VICGSR
SFRS15	11.7	1.5	1078	GK*EKPEVTDR
SF1	1.9	-1.9	227	NILK*QGIETPEDQNDLRK
SF2	4.9	2.1	174	K*LDNTK*FR

Table 7. Modification of proteins of the NF- κ B pathway in CLL.

Protein	Mean DMSO CLL vs Control	Mean MLN4924 CLL vs Control	Site	Peptide
IKK β	3.6	7.6	106	K*YLNQFENCCGLR
NEMO	3.6	5.4	344	LK*ASCQESAR
TANK	9.0	3.8	189	LNIPDTATETQCSVPIQCTDKTDK*QEALFK*PQAK
TANK	7.5	3.2	308	TTDK*TKPSNLVNTCIR
TANK	7.9	3.7	195	LNIPDTATETQCSVPIQCTDKTDKQEALFK*PQAK*DDINR
TRAF2	-0.9	-4.6	176	APCCGADV*AHHEVCPK
TRAF2	-1.5	-4.6	27	TLLGTK*LEAK
TRAF2	-5.7	-8.6	119	GTLK*EYESCHEGR
CD40	-36.2	-66.2	267	QEPQEINFDDLPGSNTAAPVQETLHGCQPVTQEDGK*ESR

Table 8. Modification of p53 and related proteins in CLL.

Protein	Mean DMSO CLL vs Control	Mean MLN4924 CLL vs Control	Site	Peptide
p53	13.7	7.5	120	LGFLHSGTAK*SVTCTYSPALNK
USP7	13.2	7.7	1096	YTYLEK*AIK
USP7	4.2	-0.1	882	KLYYQQLK*MK
TP53RK	0.4	5.1	40	FLSGLELVK*QGAEAR