

Supplementary Table S3. Patient Characteristics: clinical and pathologic features of patients who received CX-5461 therapy. N/A = sample unavailable for sequencing. No mutations were identified in *ATR*, *CHEK2*, *BRCA1*, *BRCA2* or *MYC*; no significant copy number variations were identified in *MYC* or *MDM2*. All sequenced genes listed in Supplementary Table 4; complete sequence variant/copy number variation (CNV) data in Supplementary Table 5.

Patient ID	Dose (mg/m ²)	Sex	Disease Type	Total Cycles	Best Confirmed Response	Mutational Status	
						<i>TP53</i>	<i>ATM</i>
PMC-01	25	Male	Multiple Myeloma	6	Stable Disease	N/A	N/A
PMC-03	25	Female	Multiple Myeloma	4	Stable Disease	Wildtype	Val2424Gly
PMC-04	25	Female	Diffuse Large B Cell Lymphoma	1	Progressive Disease	Lys291*	Wildtype
PMC-05	50	Female	Cutaneous T Cell Lymphoma (Mycosis Fungoides)	2	Clinical and Metabolic Response (in one disease site)	Wildtype	Wildtype
PMC-06	50	Female	Hodgkin's Lymphoma	1	Progressive Disease	N/A	N/A
PMC-07	50	Male	Chronic Lymphocytic Leukemia (Richter's Transformation)	1	Progressive Disease	Arg248Trp	Wildtype
PMC-08	50	Female	Diffuse Large B Cell Lymphoma	16	Stable Disease	Leu93Cysfs*30	Wildtype
PMC-09	100	Male	Multiple Myeloma	1	Progressive Disease	Cys238Tyr	Wildtype
PMC-10	100	Male	T-cell Prolymphocytic Leukemia	1	Progressive Disease	Wildtype	Arg1204*
PMC-11	100	Female	Diffuse Large B Cell Lymphoma	2	Progressive Disease	Arg248Gln	Wildtype
PMC-12	100	Male	Hodgkin's Lymphoma	2	Progressive Disease	Wildtype	Wildtype
PMC-13	170	Female	Multiple Myeloma	2	Progressive Disease	Wildtype	Wildtype
PMC-14	170	Male	Multiple Myeloma	4	Stable Disease	Wildtype	Wildtype
PMC-15	170	Female	Diffuse Large B Cell Lymphoma	4	Stable Disease	Wildtype	Wildtype
PMC-16	250	Female	Multiple Myeloma	1	Progressive Disease	N/A	N/A
PMC-17	250	Male	Anaplastic Large Cell lymphoma	18	Partial Response	Wildtype	Wildtype

Supplementary Table S4. List of genes assessed for sequence variants by hybridisation-based next generation sequencing

AKT1	GNAS
ASXL1	KDM2B
ATM	KDM6A
ATR	KMT2D
ATRX	MAP2K1
BCL2	MAP3K14
BCL6	MAX
BCOR	MED12
BRAF	MGA
BRCA1	MTOR
BRCA2	MYC
BRD2	NF1
BRD3	NPM1
BRD4	NRAS
BRIP1	PALB2
CCND1	PIK3CA
CCND2	PIK3CD
CDKN1B	PIK3R1
CDKN2A	PIM1
CDKN2C	PIM2
CEBPA	PTEN
CHD2	RAD51C
CHD4	RAF1
CHEK2	RB1
DNMT3A	RPL11
ERCC4	RPL15
EZH2	RPL26
FANCA	RPL35A
FANCB	RPL5
FANCC	RPS10
FANCD2	RPS14
FANCE	RPS15
FANCF	RPS17
FANCG	RPS19
FANCI	RPS24
FANCL	RPS26
FANCM	RPS29
FBXW7	RPS7
FOXO1	TP53
FUBP1	

Supplementary Table S5: Sequence and copy number (CN) variants detected by hybridisation-based next generation sequencing in 13 patients

Patient ID	Gene	HGVSp	HGVSc	HGVSp	Variant Allele Frequency	CN MDM2	CN MYC
PMC-04	TP53	chr17:g.7577067T>A	NM_000546.5:c.871A>T	NP_000537.3:p.(Lys291*)	79.3	2.11	2.67
	BCL2	chr18:g.60985311C>T	NM_000633.2:c.585+4G>A		59.1		
		chr18:g.60985307G>A	NM_000633.2:c.585+8C>T		18.8		
		chr18:g.60985739C>T	NM_000633.2:c.161G>A	NP_000624.2:p.(Gly54Glu)	43.3		
		chr18:g.60985849C>A	NM_000633.2:c.51G>T	NP_000624.2:p.(Lys17Asn)	36.4		
		chr18:g.60985881T>C	NM_000633.2:c.19A>G	NP_000624.2:p.(Thr7Ala)	31.6		
		chr18:g.60985896C>T	NM_000633.2:c.4G>A	NP_000624.2:p.(Ala2Thr)	29.6		
		chr18:g.60986407T>C	NM_000633.2:c.-287A>G	NP_000624.2:p.(=)	26.9		
KMT2D	chr12:g.49427851T>C	NM_003482.3:c.10739A>G	NP_003473.3:p.(Gln3580Arg)	42.3			
PMC-05	MTOR	chr1:g.11270908T>C	NM_004958.3:c.3617A>G	NP_004949.1:p.(His1206Arg)	34.3	1.86	2.32
PMC-07	TP53	chr17:g.7577539G>A	NM_000546.5:c.742C>T	NP_000537.3:p.(Arg248Trp)	13.3	2.08	2.03
	RB1	chr13:g.48921974dup	NM_000321.2:c.514dup	NP_000312.2:p.(Ile172Asnfs*13)	15.9		
PMC-11	TP53	chr17:g.7577538C>T	NM_000546.5:c.743G>A	NP_000537.3:p.(Arg248Gln)	83.3	2.03	1.96
	KMT2D	chr12:g.49437701G>A	NM_003482.3:c.5269C>T	NP_003473.3:p.(Arg1757*)	92.1		
PMC-12	FBXW7	chr4:g.153332756C>T	NM_033632.3:c.200G>A	NP_361014.1:p.(Gly67Glu)	47.9	1.97	1.96
PMC-15	BCL6	chr3:g.187442766C>T	NM_001706.4:c.1940G>A	NP_001697.2:p.(Ser647Asn)	10.9	2.56	1.99
PMC-03	ATM	chr11:g.108199929T>G	NM_000051.3:c.7271T>G	NP_000042.3:p.(Val2424Gly)	32.0	1.84	1.97
PMC-08	TP53	chr17:g.7579410del	NM_000546.5:c.277del	NP_000537.3:p.(Leu93Cysfs*30)	51.6	1.63	2.05
	BCL2	chr18:g.60985319C>T	NM_000633.2:c.581G>A	NP_000624.2:p.(Gly194Asp)	12.4		
	KMT2D	chr12:g.49432597G>A	NM_003482.3:c.8542C>T	NP_003473.3:p.(Gln2848*)	40.1		
		chr12:g.49443617G>A	NM_003482.3:c.3754C>T	NP_003473.3:p.(Arg1252*)	36.6		
PMC-09	BRAF	chr7:g.140453145A>C	NM_004333.4:c.1790T>G	NP_004324.2:p.(Leu597Arg)	41.1	1.96	1.98
	PIM1	chr6:g.37139054T>A	NM_002648.3:c.394T>A	NP_002639.1:p.(Phe132Ile)	46.1		
	TP53	chr17:g.7577568C>T	NM_000546.5:c.713G>A	NP_000537.3:p.(Cys238Tyr)	8.0		
PMC-10	ATM	chr11:g.108153470A>T	NM_000051.3:c.3610A>T	NP_000042.3:p.(Arg1204*)	24.5	2.46	2.01
PMC-13	NO MUTATIONS DETECTED					2.00	2.01
PMC-14	NO MUTATIONS DETECTED					2.00	2.07
PMC-17	NO MUTATIONS DETECTED					1.99	2.02

Supplementary Table S6. List of biotin-conjugated antibodies used for the negative selection of malignant cells via Magnetic-Activated Cell Sorting (MACS)

Antibody	Company	Catalogue	Clone, Species
CD3- Biotin	Miltenyi Biotec	130-093-377	OKT3, Mouse IgG2a
CD16 - Biotin	BD Biosciences	555405	3G8, Mouse IgG1
CD19 - Biotin	BD Biosciences	555411	HIB19, Mouse IgG1 κ
CD36 - Biotin	Miltenyi Biotec	130-095-478	AC106, Mouse IgG2a κ
CD56 - Biotin	BD Biosciences	555515	B159, Mouse IgG1 κ
CD123 - Biotin	BD Biosciences	554528	7G3, Mouse IgG2a κ
CD235a - Biotin	Abcam	ab93548	HIR2, Mouse IgG2b
CD14 - Biotin	Abcam	ab21889	MEM-18, Mouse IgG1

Supplementary Table S7. List of primary and secondary antibodies used for western blotting

Primary Incubation						
Antibody	Host	Size kDa	Clone	Company	Catalogue	Dilution
p53	Mouse	53	DO-1	Santa Cruz	sc-126	1:200
p21 Waf1/Cip1	Rabbit	21	12D1	Cell Signalling	#2947	1:1000
β -Actin	Mouse	42	C4	MP Biologicals	691002	1:10,000
Secondary Incubation						
Antibody	Company	Catalogue	Dilution			
Goat α -rabbit, HRP-conjugated	Bio-Rad	170-6515	1:2000			
Goat α -mouse, HRP-conjugated	Bio-Rad	172-1011	1:2000			