Table S1. Patient clinical features

Age at diagnosis [median (IQR [a])]		60 (range 52 – 67) years		n = 285
Men & women		193 (68%) men		n = 285
		92 (32%) women		
VA & Duke patients		79 (28%) VA		n = 285
		206 (72%) Duke		
Race		27 Black (10%)		n = 271[b]
		244 Caucasian (90%)		
Rai stage:	0	161 (57%)		n = 281
	1	73 (26%)		
	2	25 (9%)		
	3	7 (2%)		
	4	15 (5%)		
Treatment history:	untreated	145 (51%)		n = 285
	treated	140 (49%)		
CD38 expression		220 negative (78%)		n = 281
		61 positive (22%)		
Zap70 expression		126 negative (49%)		n = 259
		133 positive (51%)		
IGVH mutation status		114 unmutated (44%)		n = 261
		147 mutated (56%)		
Cytogenetics		Normal	41 (18.5%)	n = 222
		13q del[c]	129 (58.1%)	
		13q del only	89 (40.1%)	
		Trisomy 12[c]	38 (17.1%)	
		Trisomy 12 only	30 (13.5%)	
		17p del[c]	31 (14.0%)	
		17p del only	9 (4.1%)	
		11q del[c]	33 (14.9%)	
		11q del only	8 (3.6%)	
		2 abn.	41 (18.5%)	
		3 or more abn.	4 (1.8%)	
Length of follow-up (median, IQR)		6.0 (3.2 – 9.8) years		n = 285
Treated during the course of disease		140 (49%)		n = 285
Died		66 (23%)		n = 285

[a] Interquartile range (25th to 75th percentile)

[b] Not all analyses were performed on samples from each patient

[c] denotes patients with this abnormality and these patients may have multiple abnormalities

Table S2. Cytotoxicity of COG compounds for CLL cells

Compound	Sequence	CLL ED50 (μM)	Normal ED50 (μM)
COG056 (reverse 133)	LLRKRLKRLHSALRVRL	12.9 ± 4.6	>20
COG133	LRVRLASHLRKLRKRLL	4.4 ± 1.5	>20
COG1410	AS(Aib)LRKL(Aib)KRLL*	5.7 ± 3.0	>20
COG112	RQIKIWFQNRRMKWKK-C-LRVRLASHLRKLRKRLL	1.4 ± 0.7	>20
COG445 (disulfide linked COG112)	RQIKIWFQNRRMKWKK-C-LRVRLASHLRKLRKRLL | RQIKIWFQNRRMKWKK-C-LRVRLASHLRKLRKRLL	0.11 ± 0.08	>10
COG449 (BMOE* linked COG112)	RQIKIWFQNRRMKWKK-C-LRVRLASHLRKLRKRLL <bmoe> RQIKIWFQNRRMKWKK-C-LRVRLASHLRKLRKRLL	0.10 ± 0.01	> 10

* Aib = aminoisobutyric acid
** BMOE = bismaleimidoethane

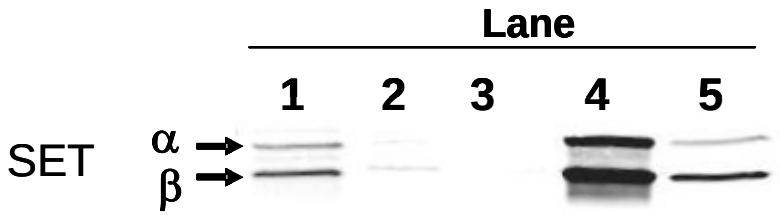

Figure S1. COG peptides binds to both SET isoforms from primary human CLL cells. A lysate CLL cells from a patient was prepared and mixed with or without biotin-COG112 or biotin-COG133. Complexes bound to Neutravidin-Agarose (NA) beads were then detected by Western blotting. Lane 1 contains 20 μg of cell lysate as a loading control. Lanes 2-5 contain extract from 300 μg of lysate incubated with either buffer (lane 2), 10 μM biotin (lane 3), 10 μM Biotin-labeled COG133 (lane 4) or 10 μM Biotin-labeled COG112 (lane 5). Lysates were incubated with biotin reagents for 1 hr before addition of NA beads and then incubated for an additional hour. After rigorous washing, the beads were boiled in SDS PAGE buffer, separated by PAGE and blotted to nitrocellulose. SET appears as bands at ~39 (β) and 41 kDa (α) that bound to the biotin-labeled COG112/133 (lanes 4 &5), but not in buffer alone (lane 2) or biotin only lanes (lane 3).

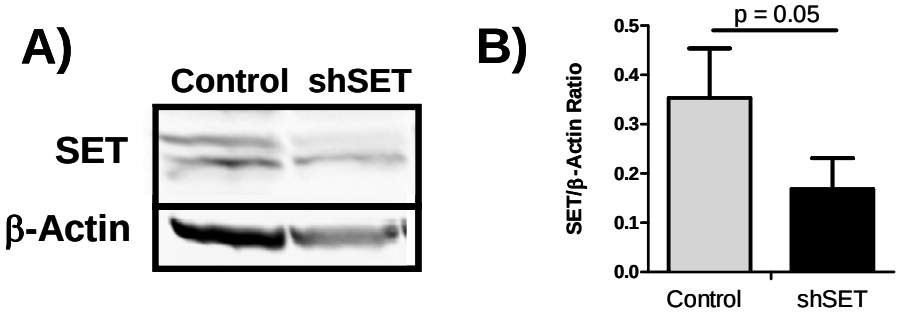

Figure S2. Silencing of SET inhibits SET protein expression in 32D:BCR/Abl cells. The cells used for PP2A phosphatase activity assays in **Fig. 3B** were assessed by immunoblot to quantify the level of knockdown of SET. (**A**) Western blots show that SET protein levels were reduced in the cells, and (**B**) quantitation of the SET levels show an approximate 50% reduction (n=3) relative to β-Actin loading controls (* = $p<0.05$ by T-test).

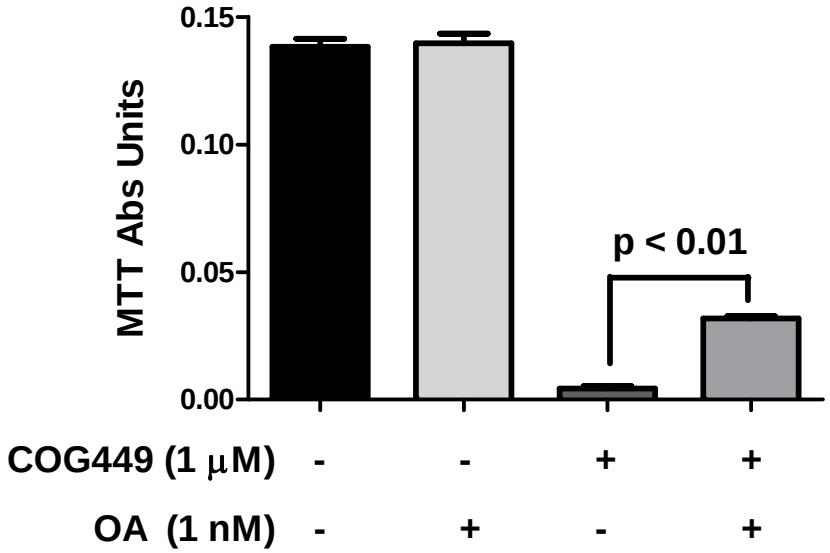

Figure S3. Cytotoxicity of COG449 can be modulated by a PP2A inhibitor in Ramos cells. Ramos cells were pretreated for 5 minutes with or without 1 nM OA before treatement with 1 μM COG449. After 24 hours, cytotoxicity was assessed using the MTT assay reagent to detect viable cells. Treatment with OA alone was not significantly cytotoxic while COG449 robustly inhibited growth. When COG449 treatment was preceded by OA treatment the cytotoxicity was significantly reduced indicating that PP2A plays a role in the cytotoxicity of COG449.

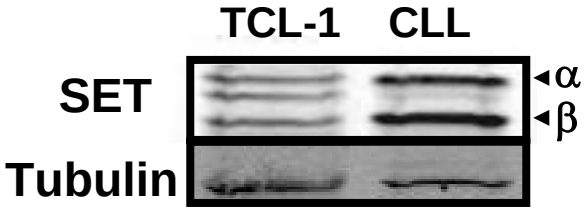

Figure S4. SET expression in TCL-1 mouse CD19+ cells. CLL-like CD5+ cells were purified from the spleen of a transgenic TCL-1 mouse with splenomegaly and a lysate was prepared from the purified mouse (left lane) and primary human CD5+/CD19+ CLL cells (right lane). Western blotting was performed to determine SET expression level in the mouse and human cells relative to a tubulin loading control.