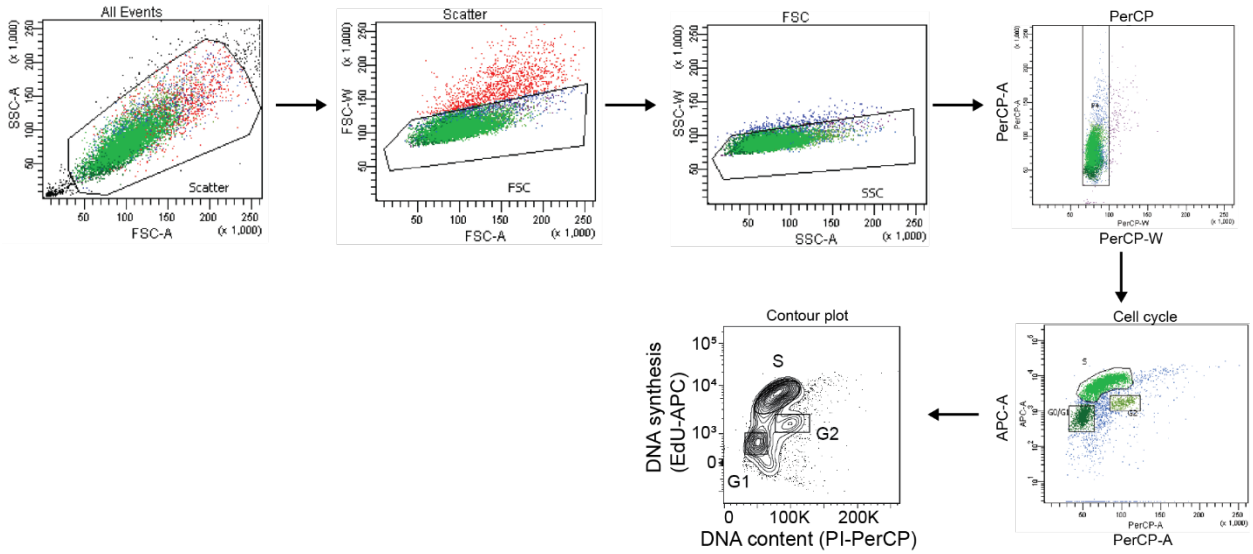

Supplementary Figure 1. Flow cytometry gating strategy for cell cycle analysis, corresponding to Extended Data Figure 1b. RBE cells were gated based on SSC-A/FSC-A/FSC-W/SSC-W/PerCP-W/PerCP-A before analyzing cell populations at each cell cycle stage. The scatter plot was then converted to the contour plot for formatting.

Supplementary Table 13. Small molecule screening data

Category	Parameter	Description
Assay	Type of assay	CellTiter-Glo Luminescent Cell Viability Assay
	Target	None
	Primary measurement	ATP content
	Key reagents	CellTiter-Glo (Promega) reagent quantifies cellular ATP levels as a proxy for viability
	Assay protocol	Details in Supplementary Table 11
	Additional comments	None
Library	Library size	7,988 compounds
	Library composition	Mechanism Interrogation Plate (MIPE) comprised of 1,912 compounds, the NCATS Pharmacologically Active Chemical Toolbox (NPACT) comprised of 5,099 compounds, and a kinase inhibitor library comprised of 977 compounds.
	Source	NCATS
	Additional comments	None
Screen	Format	Quantitative high-throughput screen (qHTS)
	Concentration(s) tested	92.1 μM, 18.4 μM, 3.68 μM, 0.73 μM, 0.15 μM, 0.03 μM and 0.006 μM
	Plate controls	Positive control (2 mM Bortezomib) and neutral control (DMSO only wells)
	Reagent/ compound dispensing system	Reagent: dispenser (Aspect Automation, St. Paul, MN) Compounds: pintool (Kalypsys, San Diego, CA)
	Detection instrument and software	ViewLux microplate imager (PerkinElmer, Waltham, MA)
	Assay validation/QC	QC by S:B ratio, Z'-factor and CV%
	Correction factors	None
	Normalization	Data was normalized relative to positive control (2 mM Bortezomib, 0% activity, full inhibition) and DMSO only wells (basal, 100% activity).
	Additional comments	Data normalization and curve fitting were performed using in-house informatics tools.
Post-HTS analysis	Hit criteria	High confidence cytotoxic compounds were defined as those that yielded a curve class of -1.1, -1.2, -2.1, -2.2, a maximum response of >50% and an IC_{50} of < 10 μM
	Hit rate	1.9%
	Additional assay(s)	CellTiter-Glo assay for hit confirmation
	Confirmation of hit purity and structure	Hit was resynthesized in-house and the structure was determined by 1H NMR
	Additional comments	None