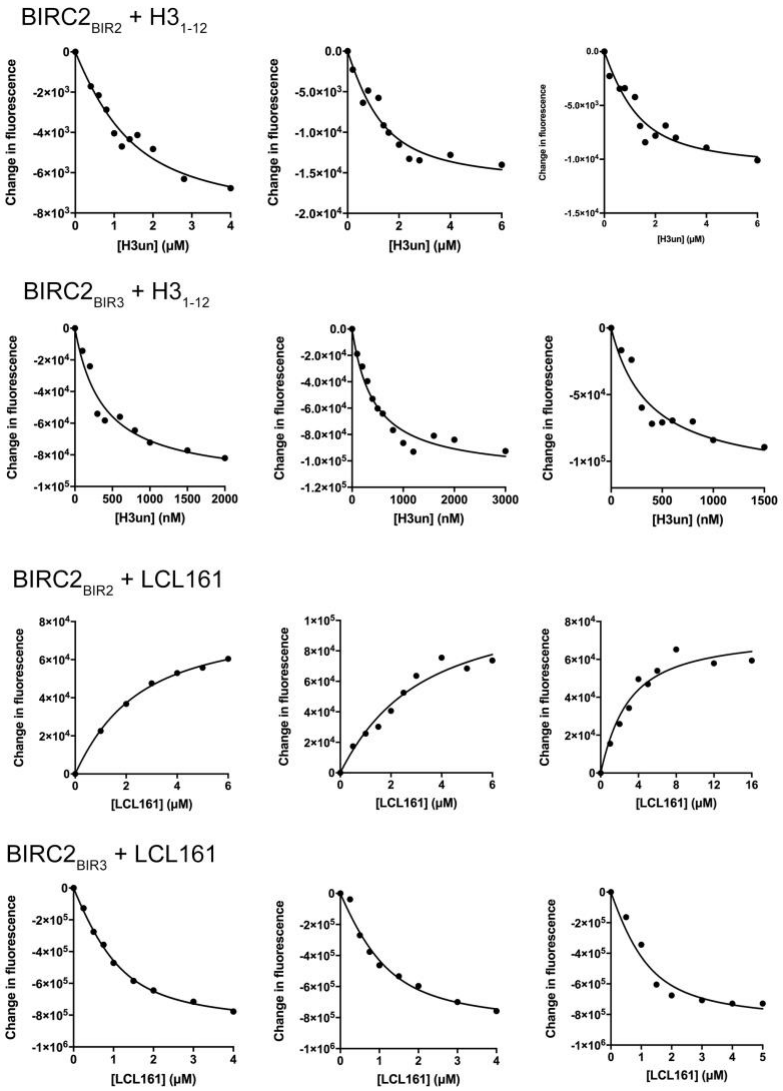
Table of contents

a



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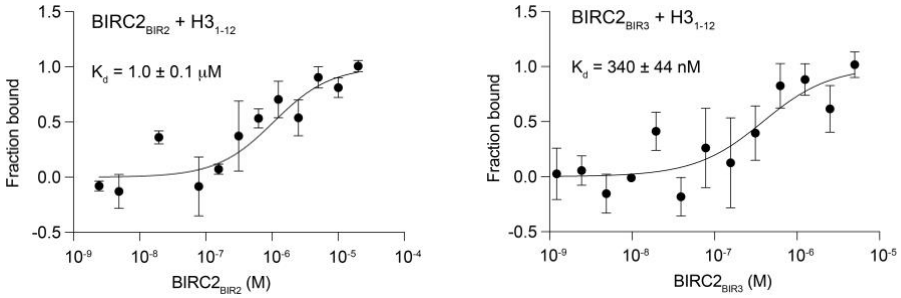
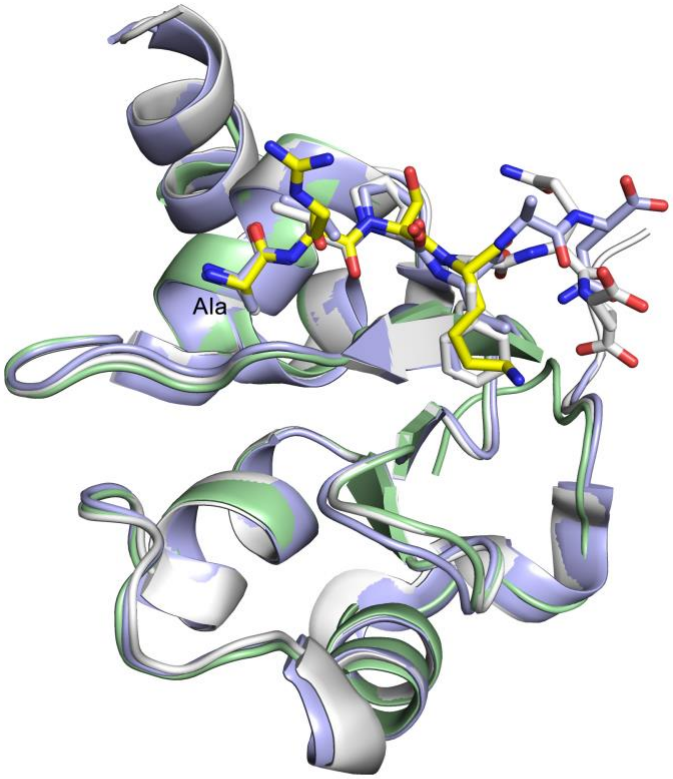
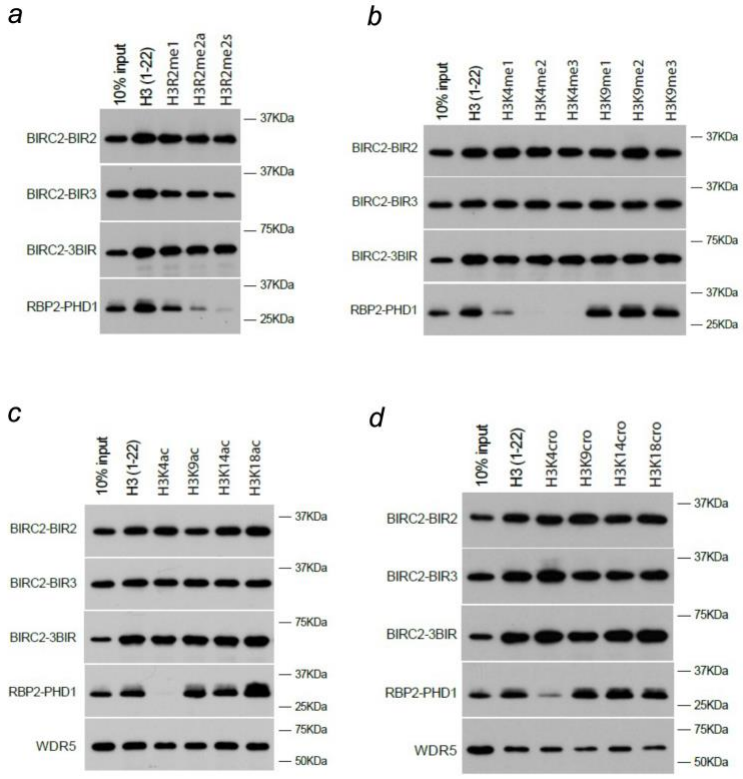


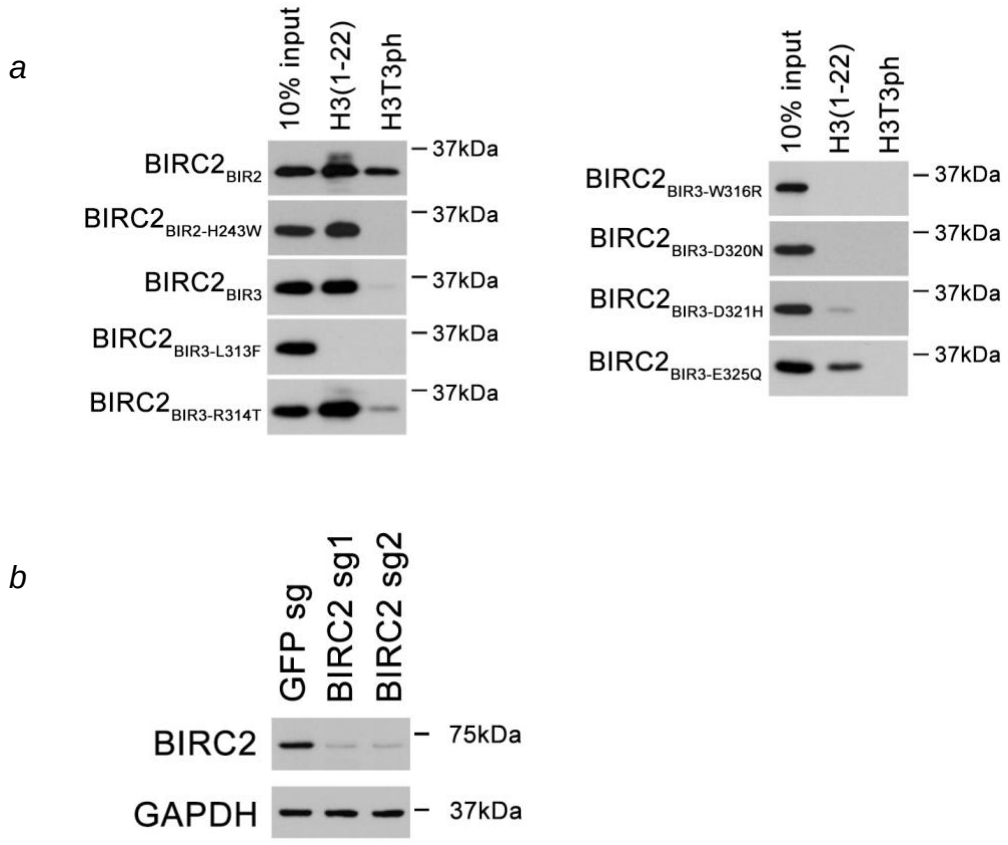
Supplementary Figure 1. (a) Binding curves used to determine K_d values for the interactions of $BIRC2_{BIR3}$ and $BIRC2_{BIR2}$ with H3 peptide and LCL161 by tryptophan fluorescence. (b) Binding curves used to determine K_d values for the interactions of $BIRC2_{BIR3}$ and $BIRC2_{BIR2}$ with fluorescently labeled H3 peptide by MST. Error bars are SEM from average for each protein concentration. K_d values were averaged over three independent experiments, and error was calculated as the standard deviation between the runs. Related to Figure 1.



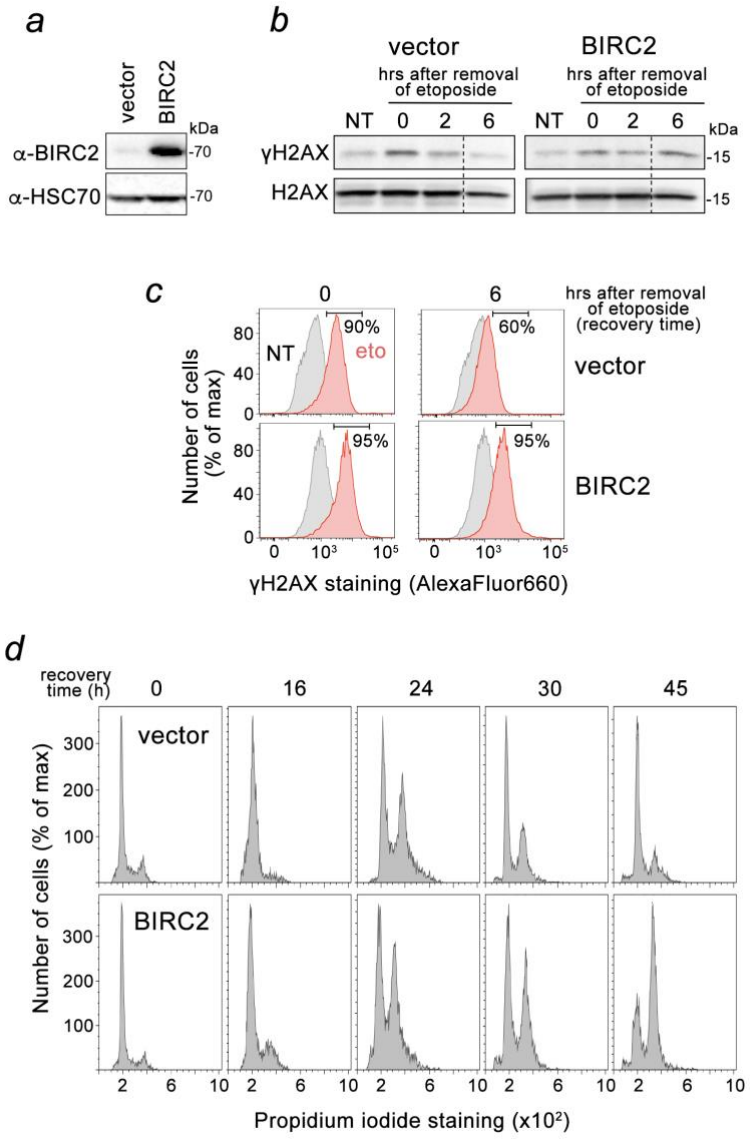
Supplementary Figure 2. Structural overlay of $BIRC2_{BIR3}$ bound to the H3 peptide (yellow), caspase-9 (grey) and Smac (light blue). Related to Figure 1.



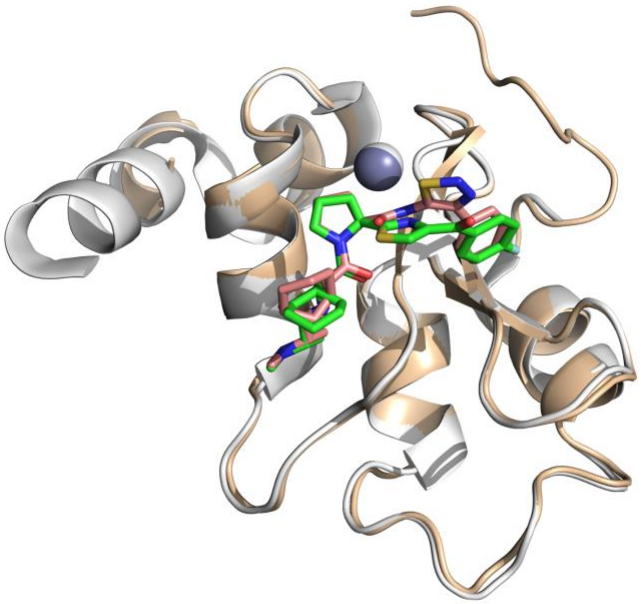
Supplementary Figure 3. Western blot analysis of pull-downs of the GST-tagged BIR domains of BIRC2 with the indicated histone peptides. RBP2-PHD, control. The experiments were performed independently two times and show similar results. Related to Figure 2.



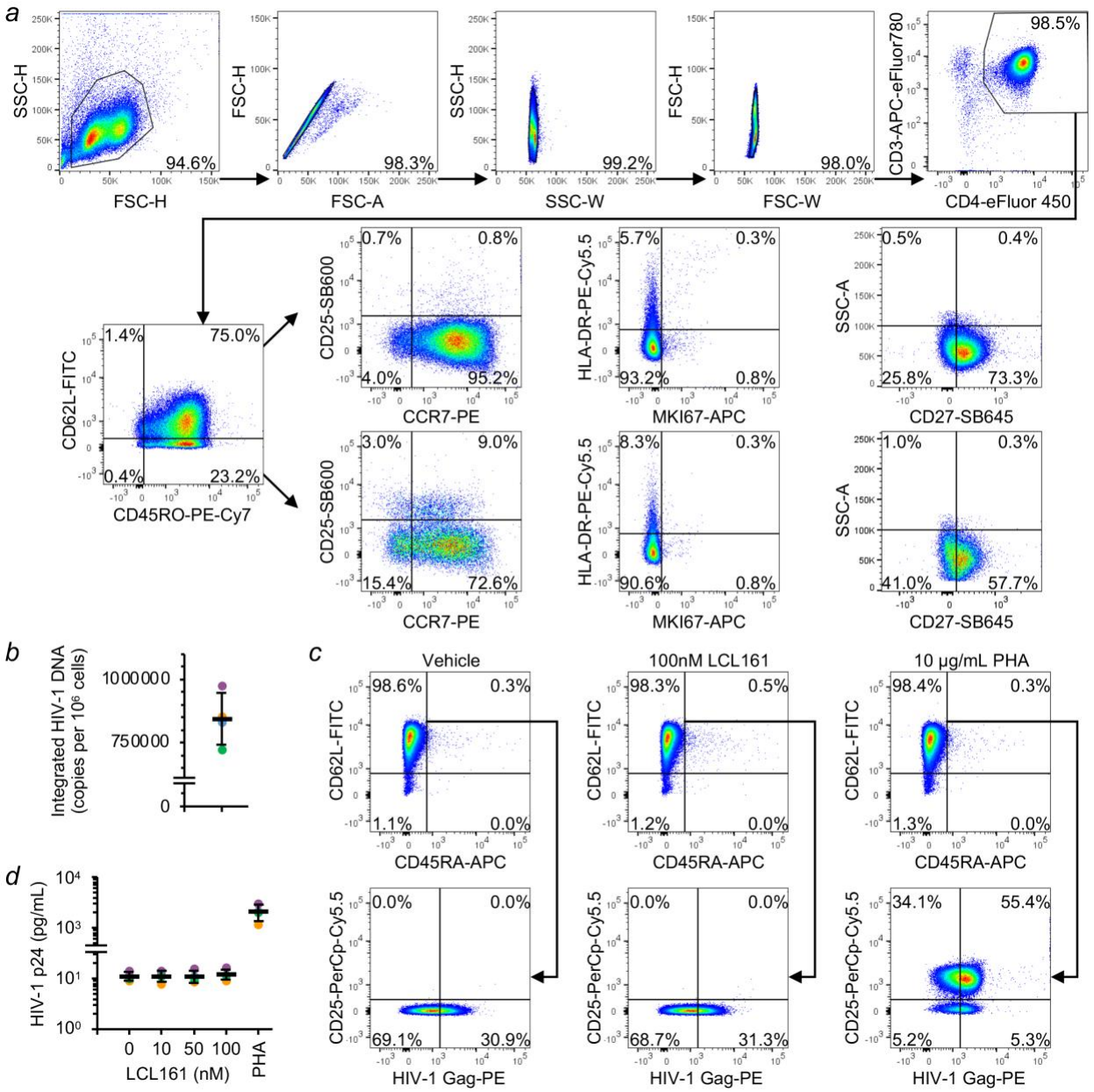
Supplementary Figure 4. (a) Peptide pull-down assays using cancer-relevant mutants of the GST-tagged BIRC2 BIR domains and the indicated histone peptides. The experiments were performed independently two times and show similar results. (b) Western blot of MCF7 cells treated with BIRC2 sgRNAs or the control GFP sgRNA. GAPDH is shown as a loading control. The experiment was performed independently three times and shows similar results. Related to Figures 2 and 3.



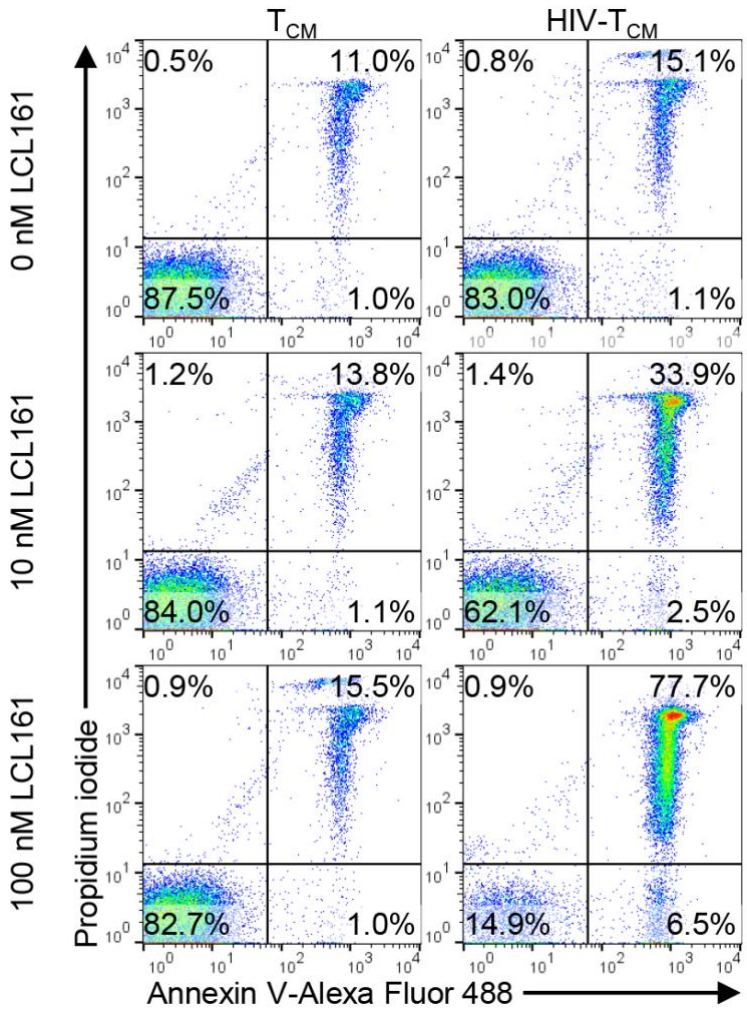
Supplementary Figure 5. HeLa cells transfected with either BIRC2-encoding or empty vector were untreated (NT) or treated with 1 μM etoposide (eto) for 3 h (0), then washed and incubated for 2 to 45 h in a drug-free medium. Western blot analysis of BIRC2 and the loading control HSC70 is shown in (a). Western blot analysis of γH2AX, a mark of DNA damage, in untreated cells (NT) or etoposide treated cells that were washed and incubated for additional 2 or 6 h in an etoposide-free medium is shown in (b). The experiments in (a) and (b) were performed independently three times and two times, respectively. Flow cytometry analysis of γH2AX in untreated cells (NT, grey histograms) or etoposide treated cells that were washed and incubated for additional 2 or 6 h in an etoposide-free medium (eto, red histograms) is shown in (c). The percentage of cells expressing γH2AX is indicated. (d) Flow cytometry analysis of the cell cycle in etoposide treated HeLa cells that were incubated for indicated time in an etoposide-free medium. DNA was stained with Propidium iodide. Related to Figure 3.



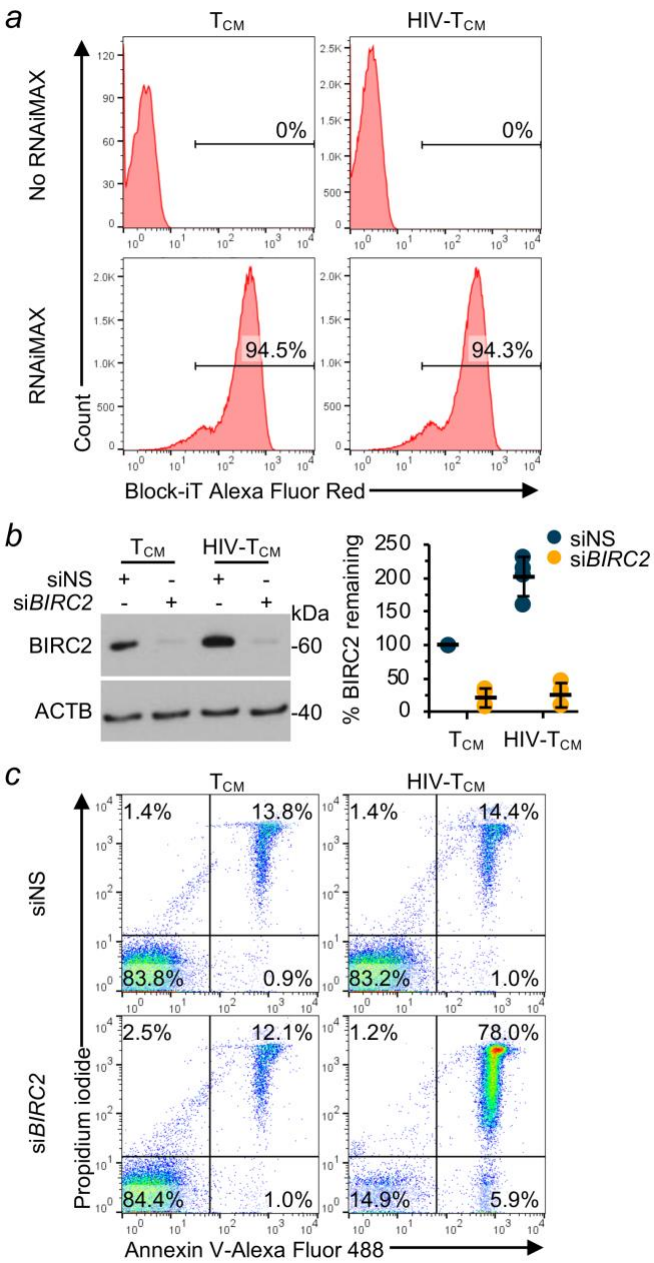
Supplementary Figure 6. Structural overlay of $BIRC2_{BIR3}$ in complex with LCL161 and GDC0152, PDB:3UW4. Related to Figure 4.



Supplementary Figure 7. (a) Flow cytometry pseudocolor plot profiles of CD4+ T cells using lineage (CCR7, CD27, CD45R0, CD62L), activation (CD25, HLA-DR) and proliferation (MKI67) markers to analyze cells at 30 d post memory CD4+ T cell isolation as described in the methods. Gating strategy was determined using FMO and INC controls. (b) DNA was extracted from HIV-T_{CM} and analyzed for integrated HIV-1 DNA using an Alu-LTR nested qPCR. *n* = 4 biologically independent replicates. Data are presented as means of biologically independent replicates with grand mean values +/- SD. (c) Viral reactivation was measured by flow cytometry after LCL161 or 10 µg/mL PHA treatment for 24 h. (d) HIV-1 p24 release was measured using a HIV-1 p24 ELISA after LCL161 or PHA treatment for 4 h. *n* = 4 biologically independent replicates. Data are presented as means of biologically independent replicates with grand mean values +/- SD. Related to Figure 6.



Supplementary Figure 8. T_{CM} and HIV-T_{CM} were treated with LCL161 for 4 h, harvested, stained with Alexa Fluor 488 conjugated annexin V and propidium iodide, and the frequency of annexin V and propidium iodide-positive labeling was recorded by flow cytometry and illustrated as a pseudocolor plot. Representative plots from a single donor are shown. *n* = 4. Related to Figure 6.



Supplementary Figure 9. T_{CM} and HIV-T_{CM} were transfected with RNAi for *BIRC2* (si*BIRC2*) or scrambled control (siNS) for 48 h. *n* = 4. (a) The transfection efficiency of Lipofectamine RNAiMAX in CD4+ T cells was assessed using BLOCK-iT Alexa Fluor Red fluorescent control. Cells were harvested 48 h post-transfection and analyzed by flow cytometry. A representative histogram is shown. (b) *Left*, representative western blots of BIRC2 with antibodies against BIRC2 and ACTB. *Right*, densitometric analysis of blots, n = 4 biologically independent replicates. Data are presented as means of biologically independent replicates with grand mean values +/- SD. (c) Cells were harvested, stained with Alexa Fluor 488 conjugated annexin V and propidium iodide, and the frequency of annexin V and propidium iodide-positive labeling was recorded by flow cytometry and illustrated as a pseudocolor plot. Representative plots from a single donor are shown. Related to Figure 6.