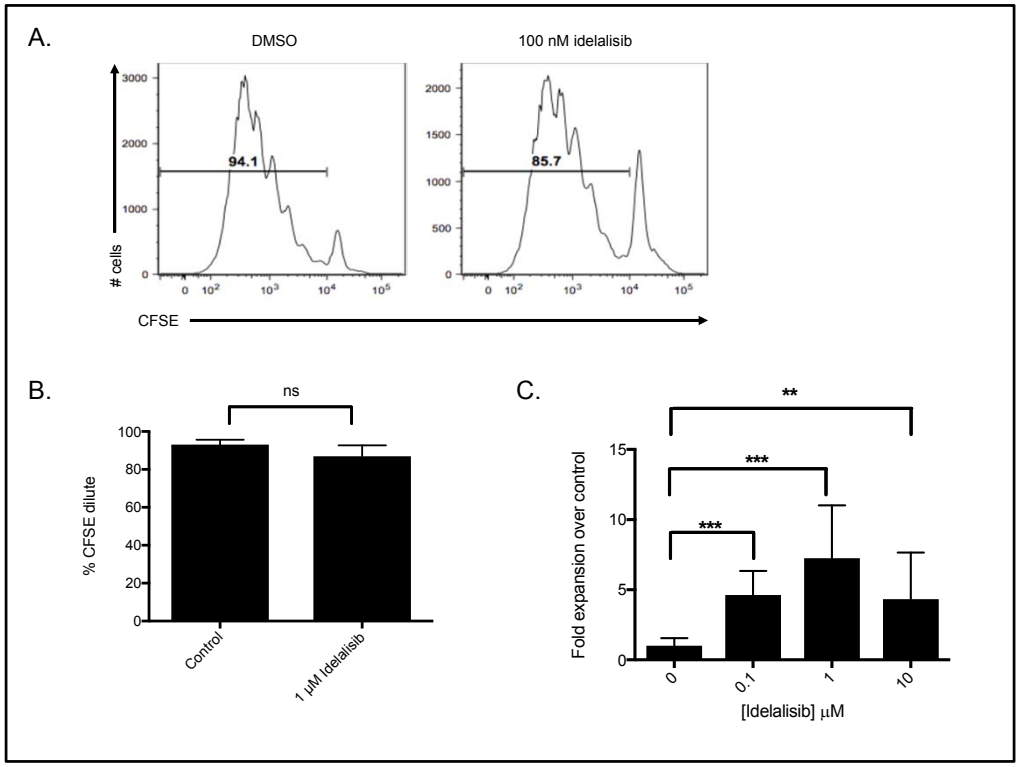
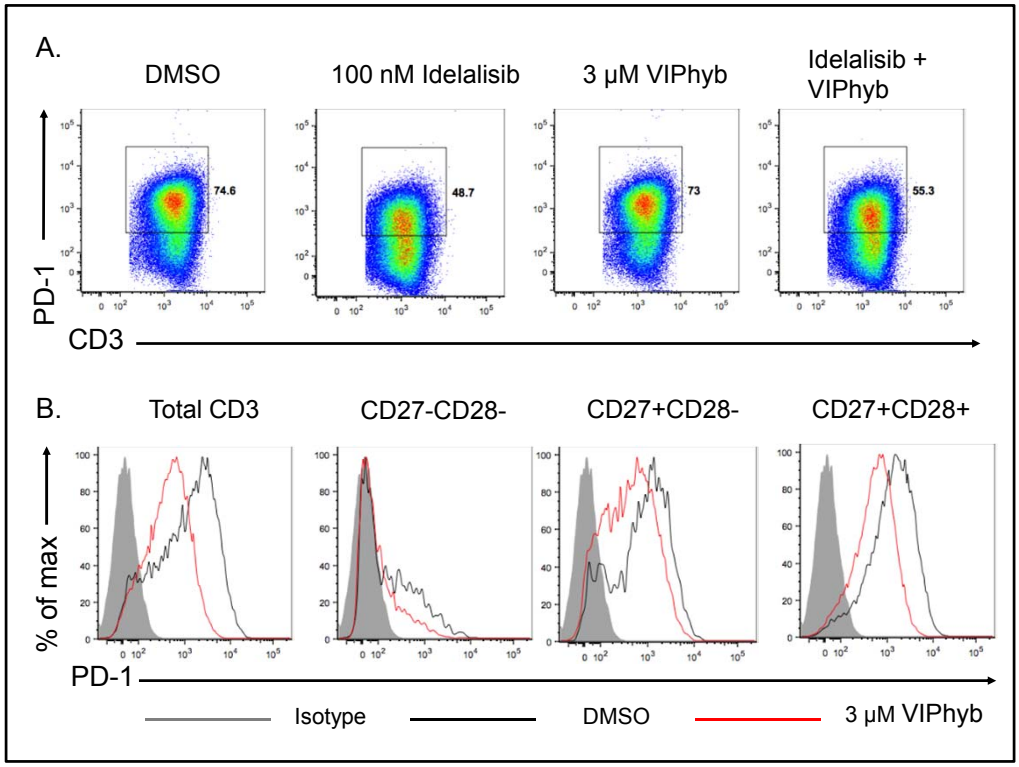
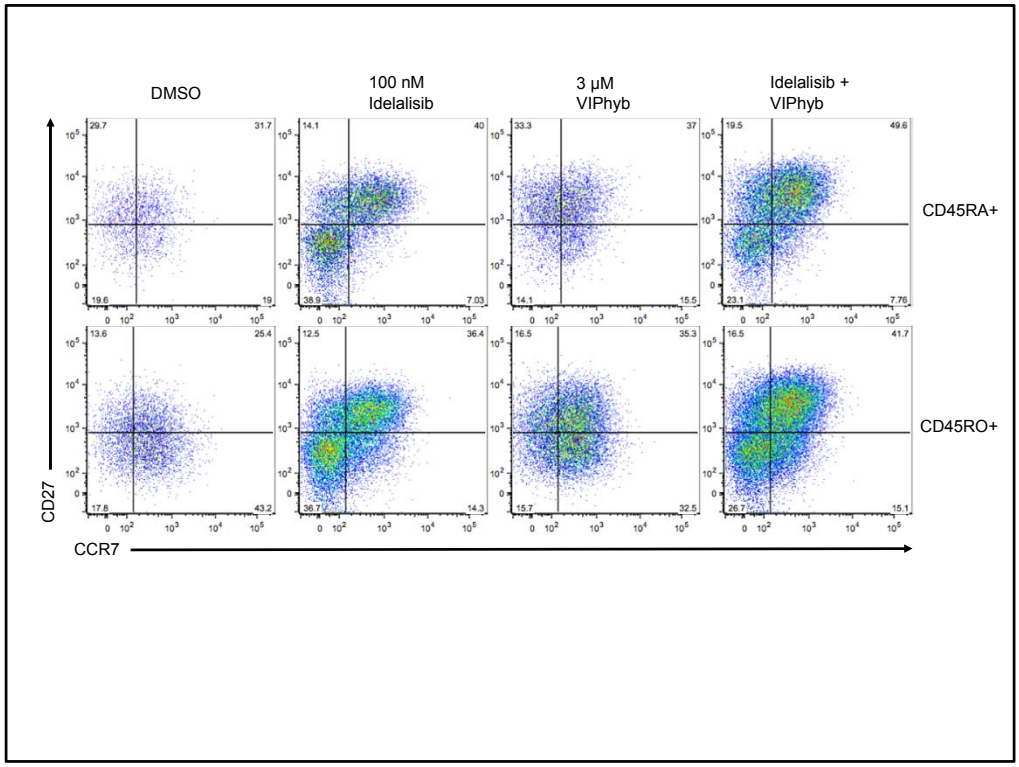


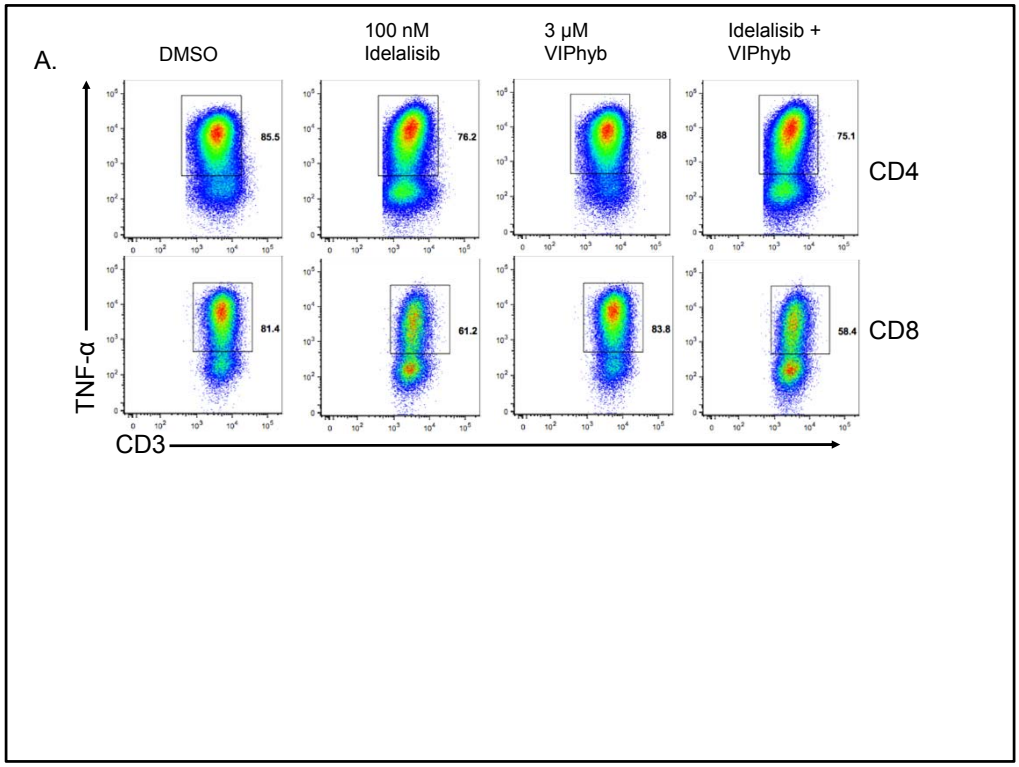
Supplementary Figure 1: Expansion in the presence of idelalisib and VIPhyb does not significantly inhibit T cell proliferation but does affect yield. CFSE-labeled or luciferase+ murine T cells were stimulated with anti-CD3/CD28 beads +/- Idelalisib and/or VIPhyb for 3 days followed by flow cytometry analysis or bioluminescent imaging. (A) Representative histograms showing CFSE dilution of T cells stimulated in the presence or absence of idelalisib. (B) Quantification of the frequency of CFSE dilute T cells from 3 independent experiments. (C) Fold expansion of T cells relative to controls as assessed by bioluminescent imaging. **p<0.01, ***p<0.001



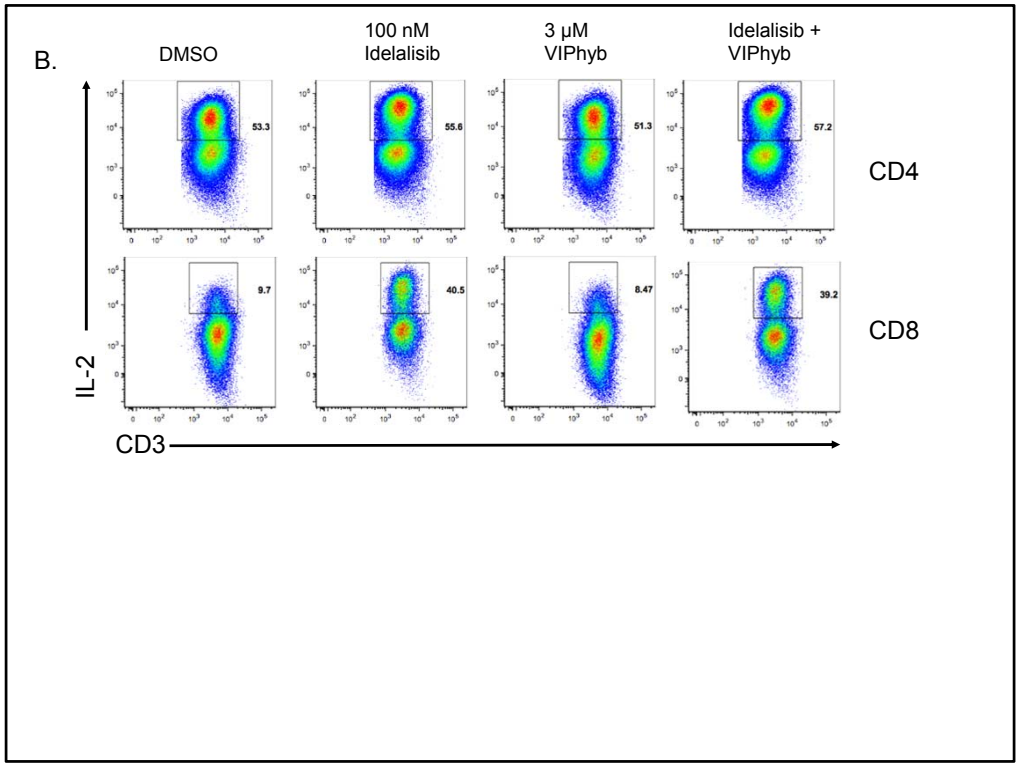
Supplementary Figure 2: Idelalisib and VIPhyb reduce PD-1 expression on DLBCL patient T cells stimulated with CD3/CD28 beads. DLBCL patient T cells were stimulated with anti-CD3/CD28 beads in the presence of IL-2 and then phenotyped by flow cytometry for the expression of PD-1. (A) PD-1 expression on DLBCL patient T cells on day 10 of expansion. (B) PD-1 expression on FACS-sorted T cell subsets that were stimulated for 4 days with CD3/CD28 beads in the presence or absence of VIPhyb.



Supplementary Figure 3: Idelalisib and VIPhyb preserve the naïve and central memory compartments in T cells stimulated with CD3/CD28 beads. DLBCL patient T cells were stimulated with anti-CD3/CD28 beads in the presence of IL-2 and then phenotyped by flow cytometry for the expression naïve and central memory markers. Cells are gated on viable CD3+ cells as well as on the subsets indicated on the right of the plots.



Supplementary Figure 4: Expansion of T cells in the presence of Idelalisib and VIPhyb reduces IFN-γ production by CD8 T cells but enhances IL-2 production. T cells from healthy controls (n=6) were expanded for 14 days using CD3/CD28 beads and IL-2. Cells were re-simulated with PMA and ionomycin on day 14 and stained for (A) TNF-α, (B) IL-2, and (C) IFN-γ.



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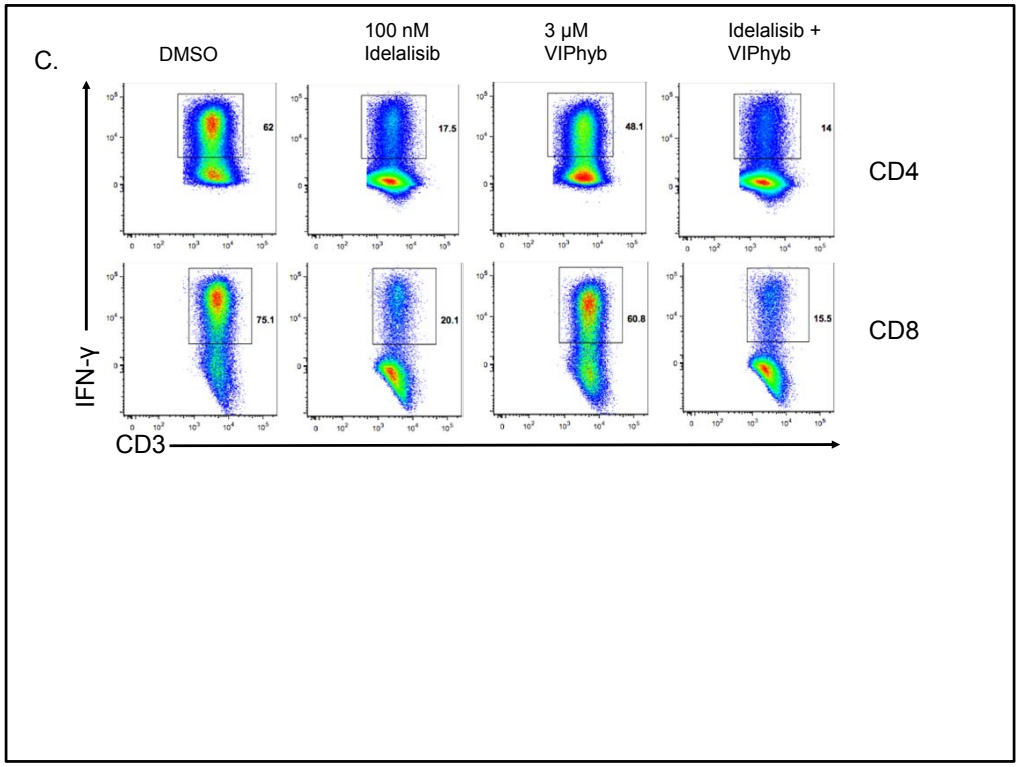

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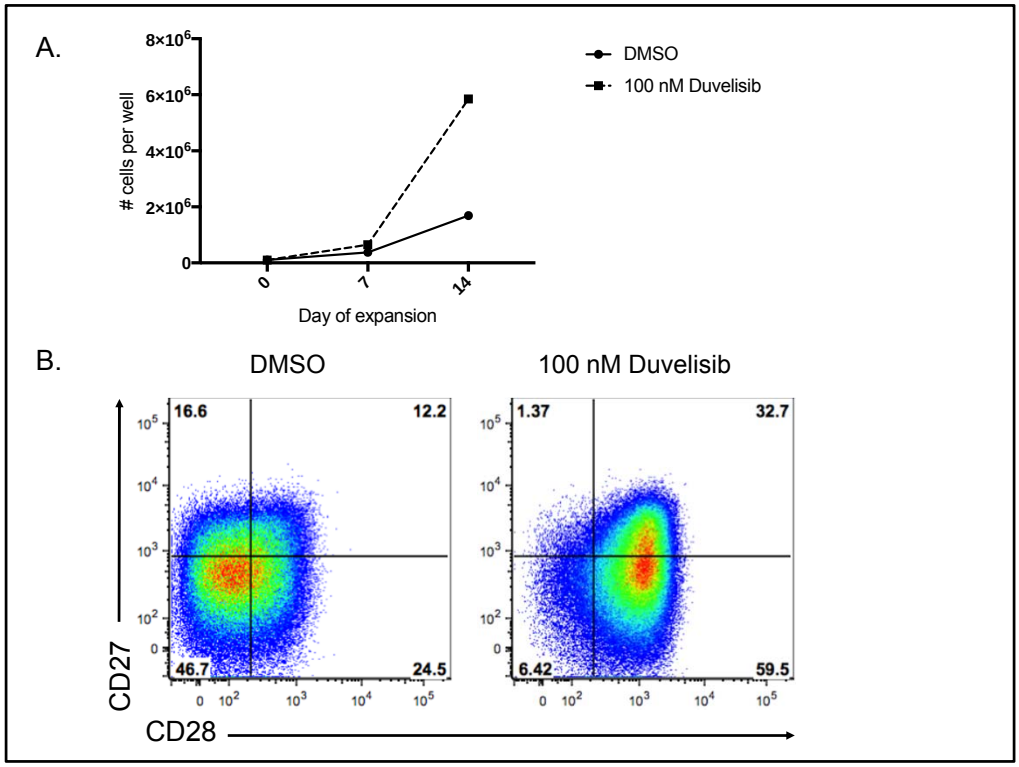
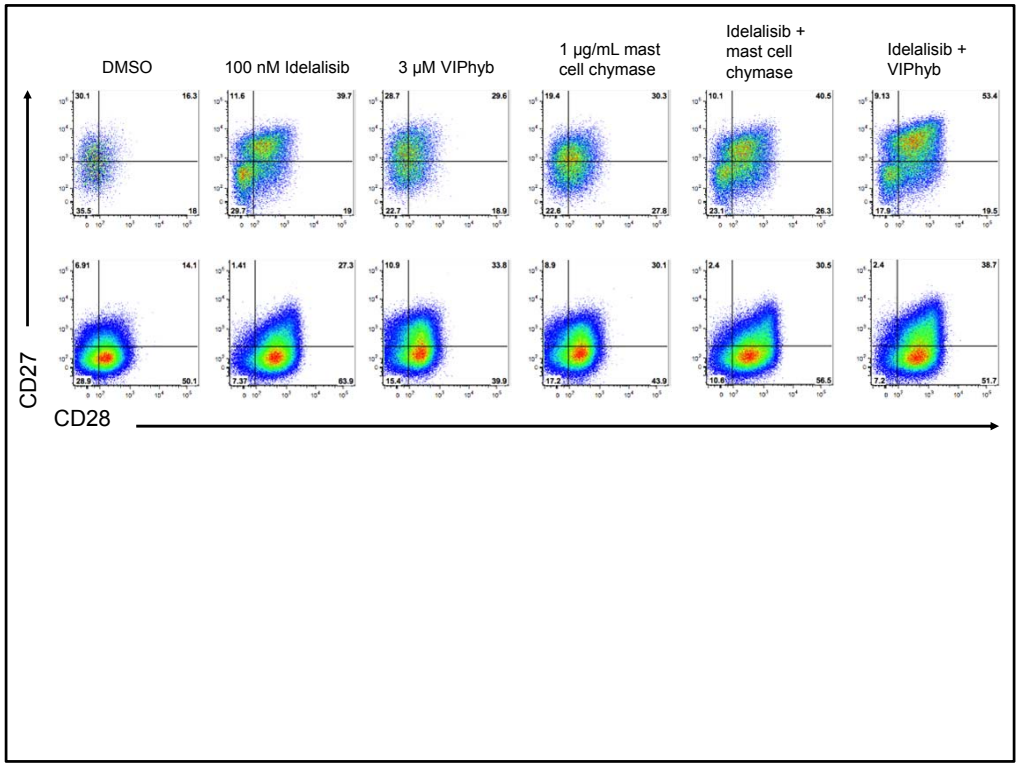


Supplementary Figure 5: The dual PI3K δ/γ inhibitor Duvelisib also increases DLBCL patient T cell yield and preserves expression of CD27 and CD28 at the end of the expansion period. DLBCL patient T cells were expanded for 14 days with CD3/CD28 beads in the presence or absence of Duvelisib. T cells were counted on days 7 and 14 and phenotyped by flow cytometry on day 14 to examine expression of the co-stimulatory molecules CD27 and CD28. (A) Expansion curve of DLBCL patient T cells. (B) Flow cytometry plots showing increased expression of CD27 and CD28 on DLBCL patient T cells expanded in the presence of Duvelisib.



Supplementary Figure 6: Antagonism of VIP signaling by either addition of VIPhyb or cleavage by mast cell chymase results in similar effects on DLBCL patient T cell phenotype at the end of expansion. DLBCL patient T cells were expanded for 10 days with CD3/CD28 beads in the presence or absence of Idelalisib, VIPhyb, and/or mast cell chymase. Cells were analyzed for expression of CD27 and CD28 at the end of the expansion period by flow cytometry. Flow cytometry plots of CD27 and CD28 expression are shown.