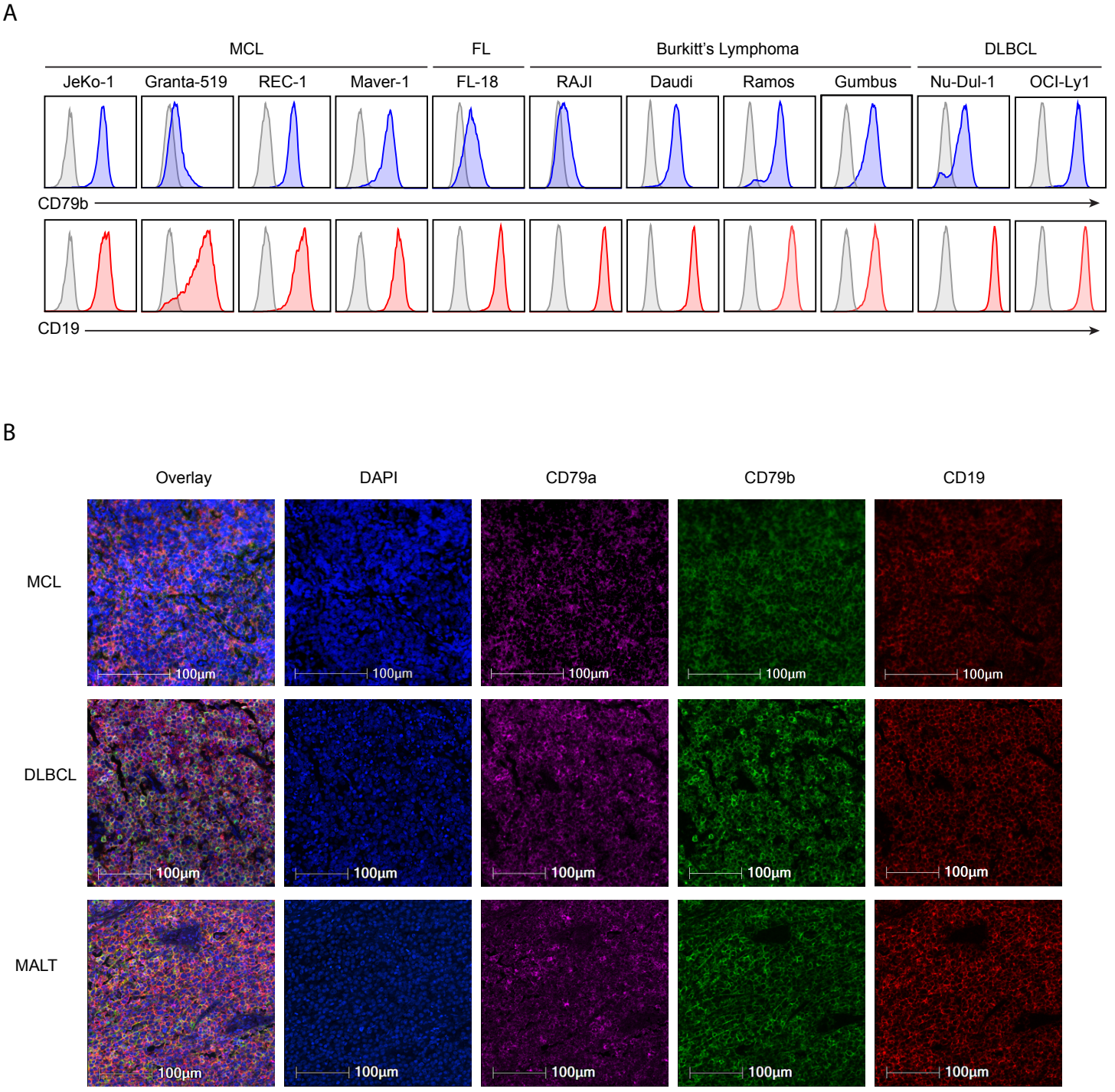
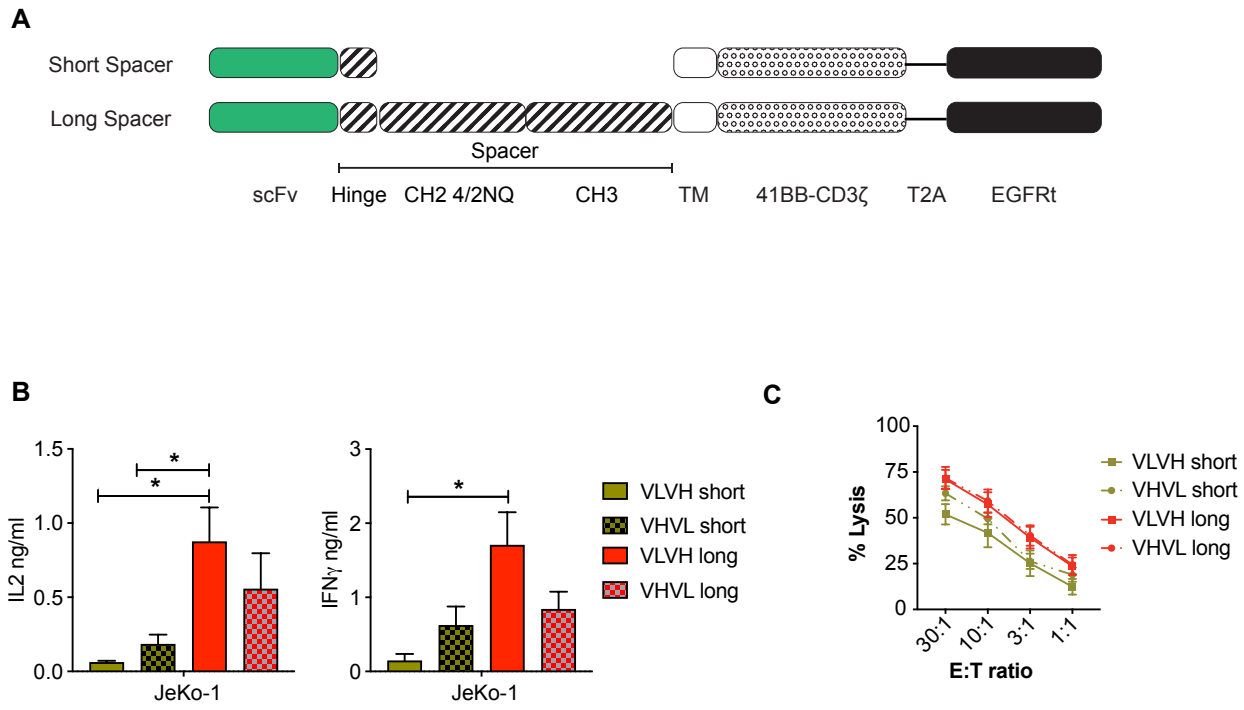
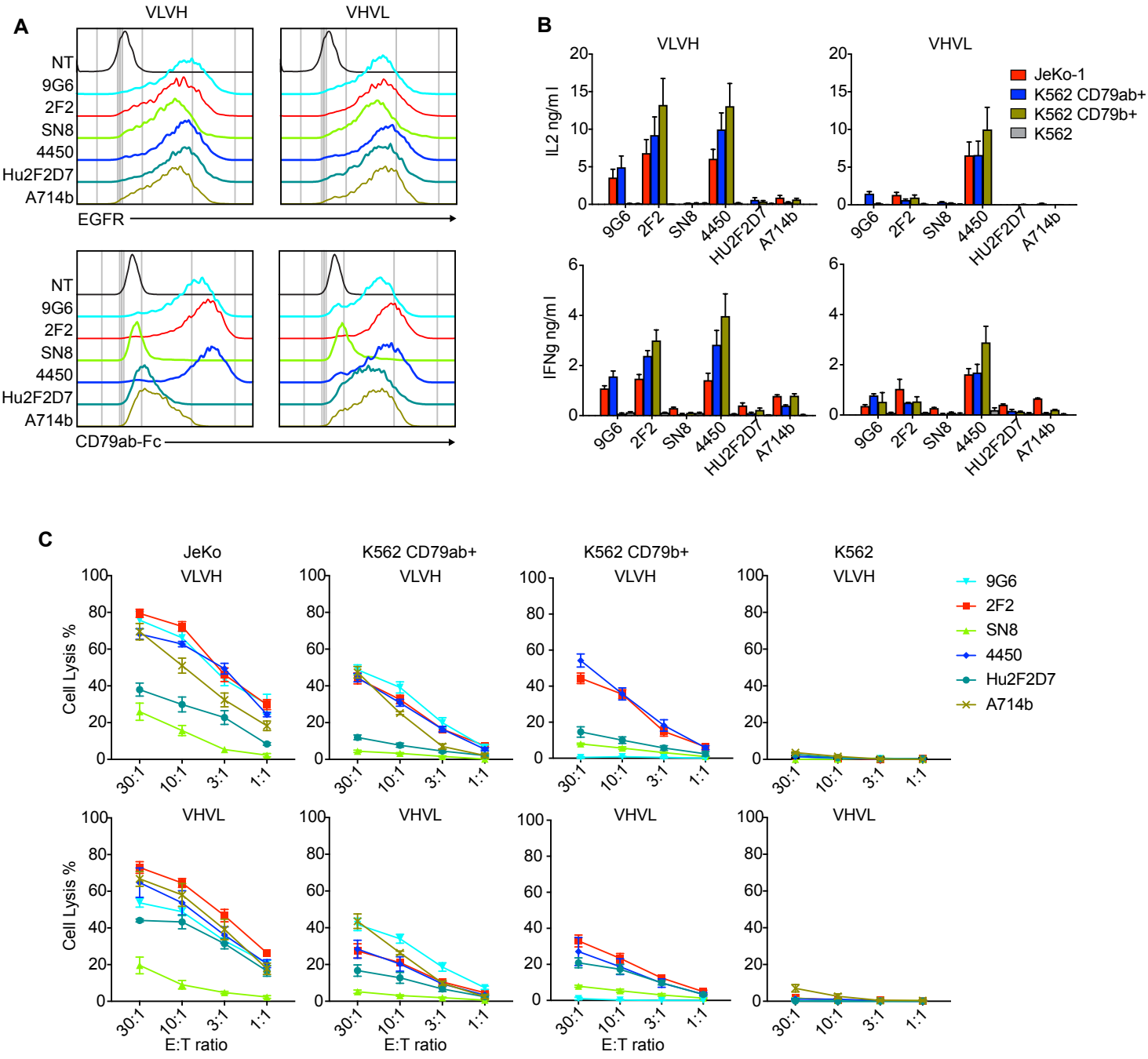


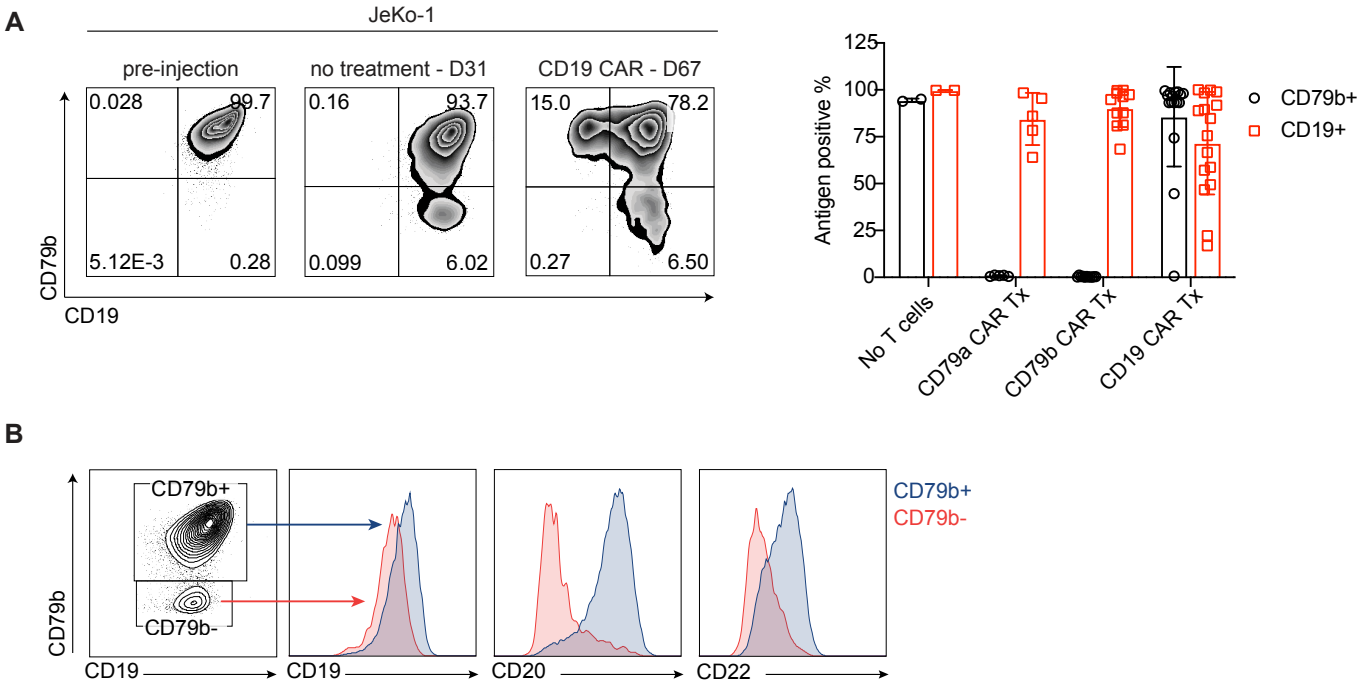
Supplemental Figure 1. CD79ab and CD19 expression on tumor cell lines and primary specimens. A. Flow cytometric evaluation of CD79b and CD19 expression on the indicated tumor cell lines. MCL= mantle cell lymphoma, FL= follicular lymphoma, Burkitt's = Burkitt's lymphoma, DLBCL = Diffuse Large B-cell Lymphoma and MALT = lymphoma of the mucosa-associated lymphoid tissue. B. Representative fluorescent images of IHC staining of CD79a, Cd79b, and CD19 on lymphoma subtypes.



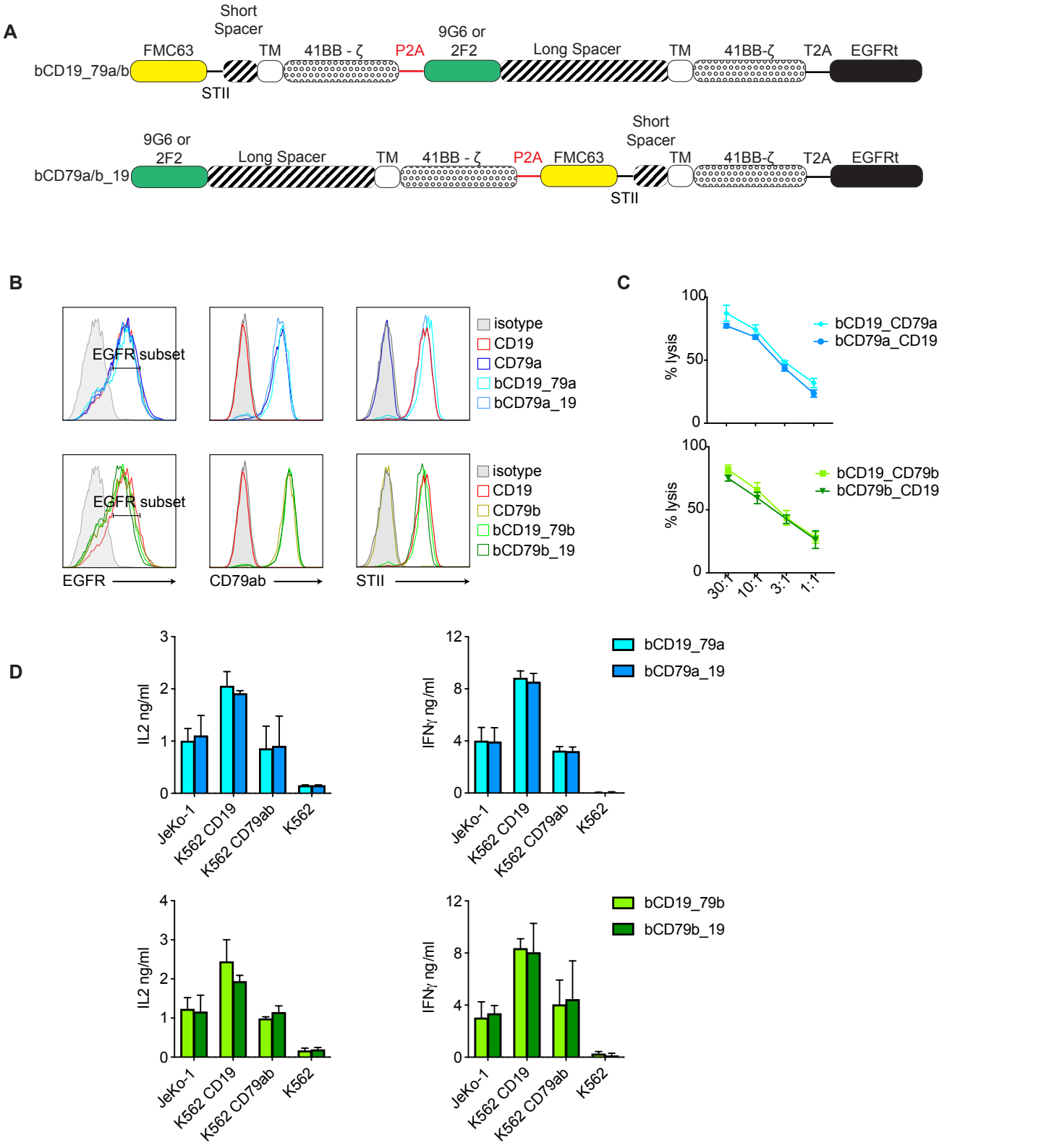
Supplemental Figure 2. CD79b CAR designed with a long spacer is functionally more active than with a short spacer. A. Schematic of CAR constructs with long or short spacers. B. IL-2 and IFNγ production by CAR-T cells measured by ELISA after co-culture with JeKo-1 tumor cells. Data shown are from three independent experiments performed with different donors. C. Lysis of 51Cr labeled JeKo-1 tumor cells by CAR-T cells prepared from two different donors. VLVH indicates the variable light domain was encoded in the N-terminal position relative to the variable heavy domain and vice versa for VHVL. *P <0.5 were calculated with one-way ANOVA Tukey's multiple comparisons test. All error bars are S.E.M.



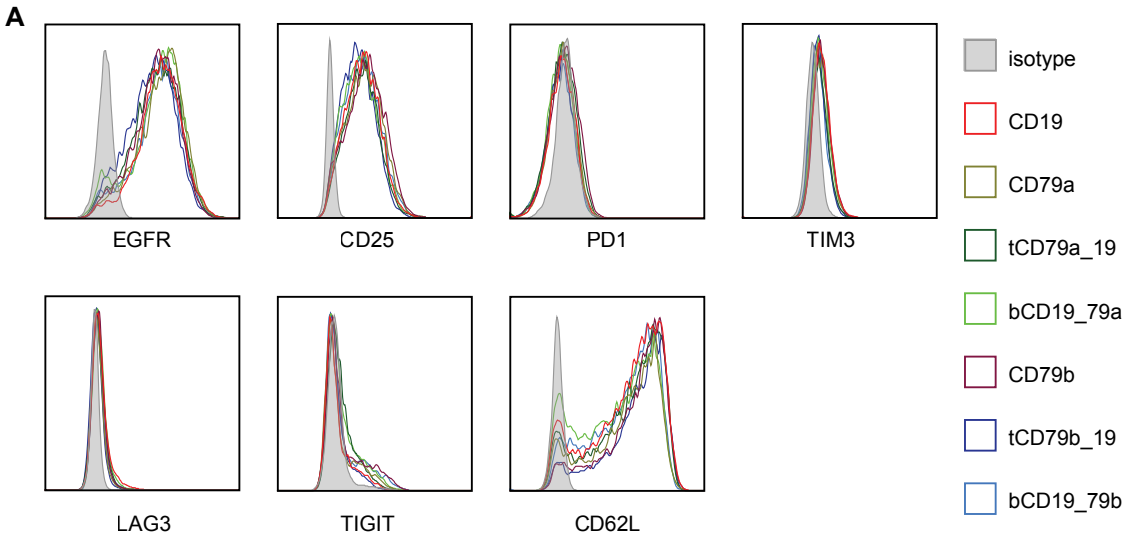
Supplemental Figure 3. 2F2 and 9G6 scFvs cloned in the VLVH orientation provide potent CD79b or CD79a CARs, respectively. A. EGFRt (transduction marker) expression (top panels) and binding of CD79ab-Fc (bottom panels) by CD8+ CAR-T cells assayed by flow cytometry. Data is representative of results from three donors. Left and right panels showing staining of T cells expressing CARs in the VHVL or VLVH orientation, respectively. B. Lysis of 51Cr labelled tumor cells by CD79a or CD79b CAR-T cells at various effector to tumor ratios. Data are means +/- S.E.M of two independent experiments. C. IL2 (top) and IFNγ (bottom) production by CAR T cells cultured with tumor cells expressing CD79a and/or CD79b measured by ELISA. Data are means +/- S.E.M of three independent experiments.



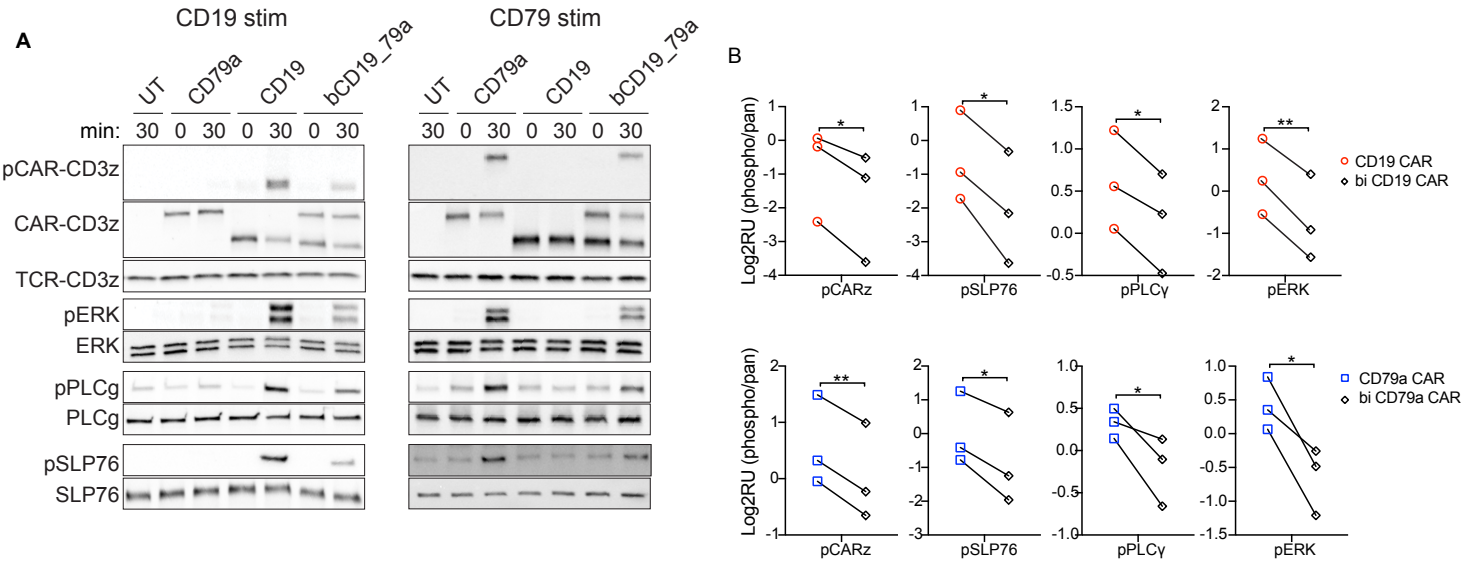
Supplemental Figure 4. CD79b loss on JeKo-1 tumor cells in vivo occurs in a minor fraction of tumor cells in untreated and CD19 CAR T cell treated mice and is associated with downregulation of other B cell markers. A. Left panels: Flow cytometry plots showing CD19 and CD79b staining of JeKo-1 cells from BM suspensions of mice that were untreated or treated with CD19 CAR-T cells. Day of euthanasia is shown above the plots. Right panel: Bar graphs are quantification of tumor cells that expressed CD79b or CD19 for mice that were untreated or treated with the indicated CAR T cells. Each data point represents samples from individual mice at the time of euthanasia. Data shown are collected from multiple experiments done with different doses of CAR T cells and are not solely from the survival experiment shown in Figure 2. B. Histograms showing CD19, CD20, and CD22 expression on CD79b positive and negative JeKo-1 cells isolated from BM of treated mice.



Supplemental Figure 5. The order of which the CARs are encoded within the bicistronic construct does not impact CAR expression or function. A. Schematics of bicistronic CAR constructs. B. CAR expression as measured by CD79ab-Fc binding and STII staining on EGFRt+ sorted cells. C. Lysis of JeKo-1 tumor cells measured by 51Cr release. D. CAR-T cell IL-2 and IFNγ production measured by ELISA after coculture of CAR-T cells with the indicated tumor cell lines. Data are means+/- S.E.M from two independent experiments.



Supplemental Figure 6. Tandem and bicistronic CAR-T cells have similar cell surface phenotype as monospecific CAR-T cells at the end of culture. Flow cytometric histograms of EGFRt+ sorted CAR-T cells on day 14 post transduction for the indicated cell surface molecules.



Supplemental Figure 7. Expression of CD79b and CD19 in JeKo-1 cells in which CD79b or CD19 were edited by CRISPR. Flow cytometric histograms of Cd79b and CD19 staining on Jeko-1, JeKo-1CD19- and JeKo-1CD79ab- cells.