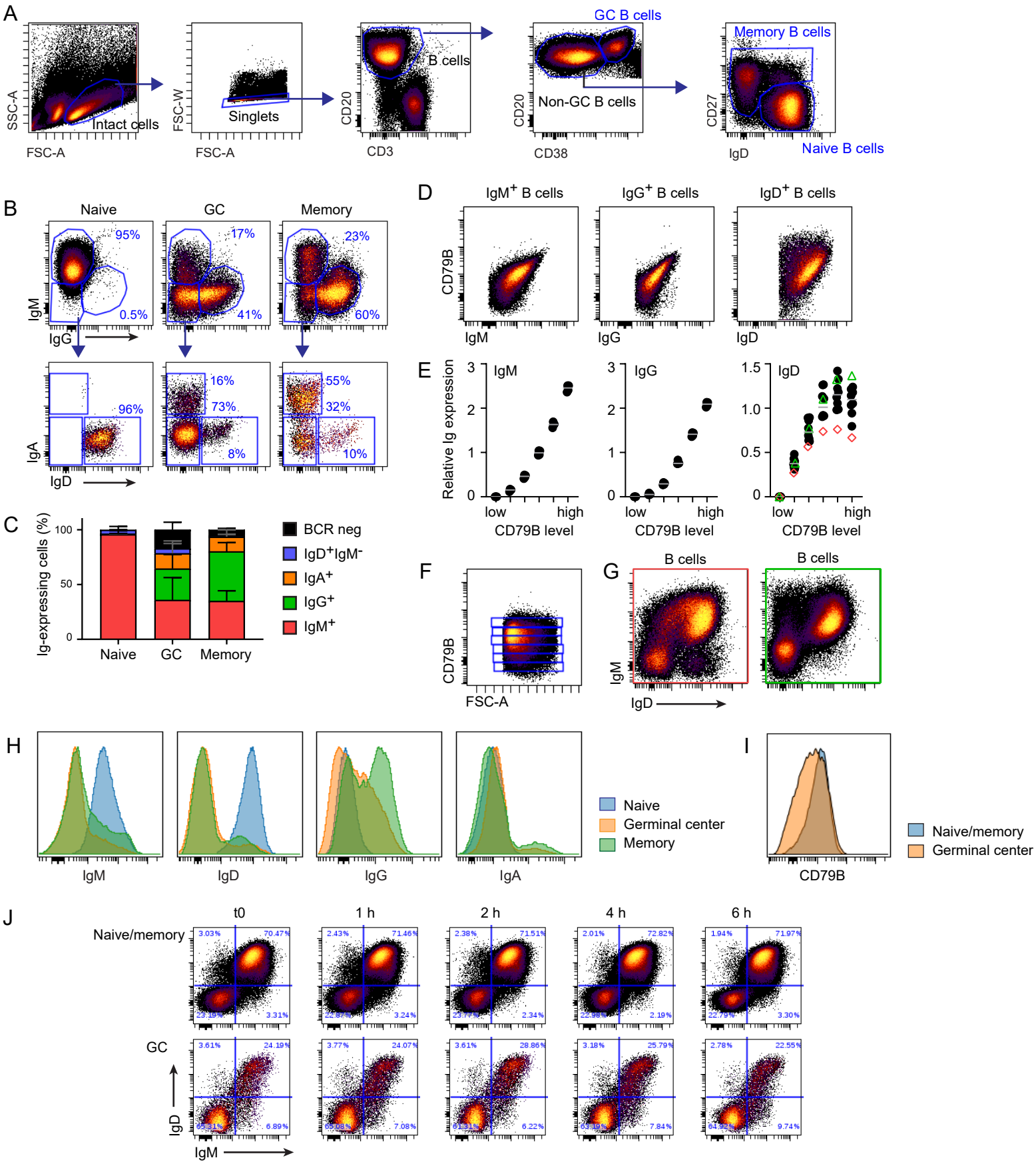
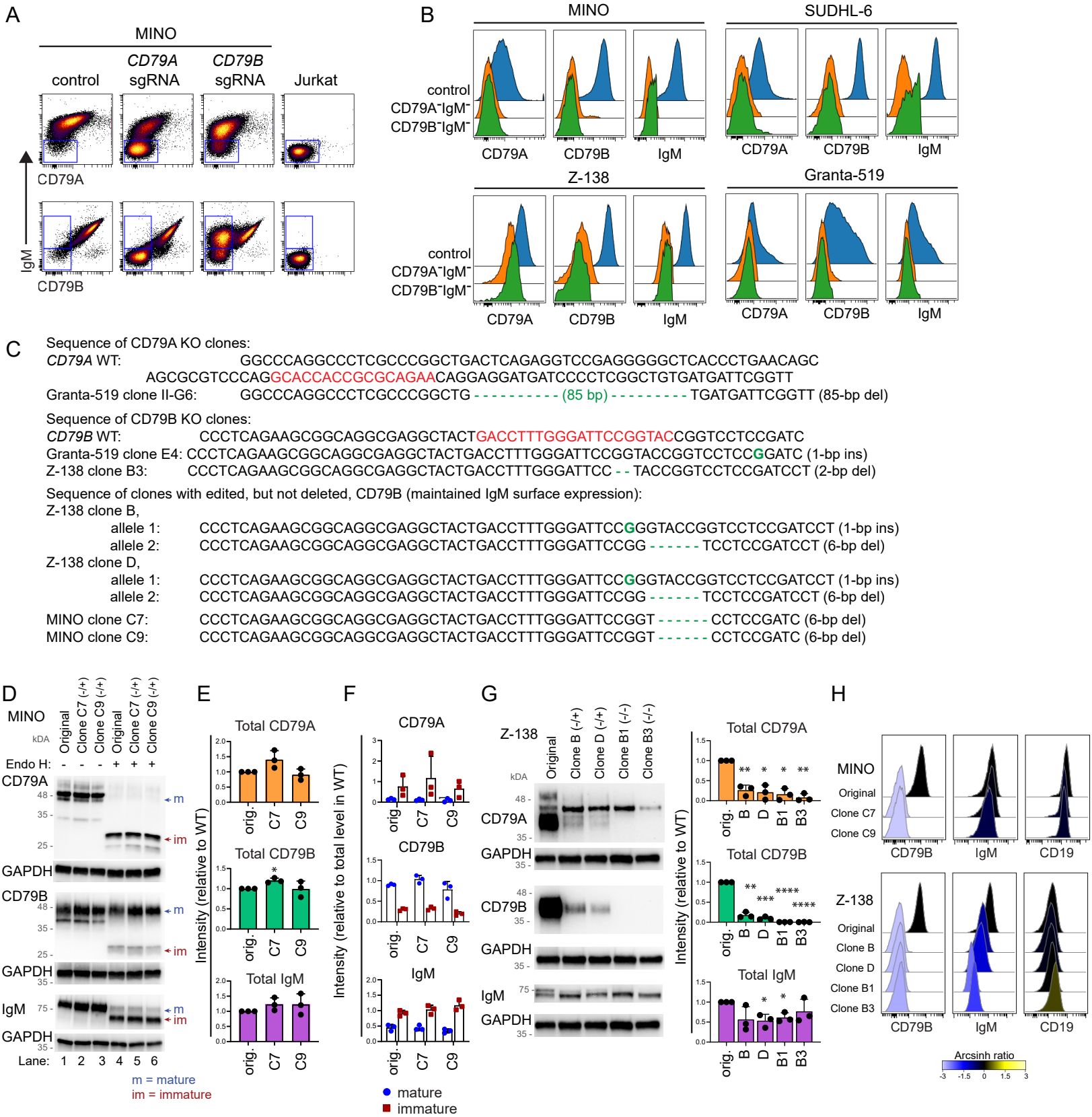


Supplemental Figure 1.

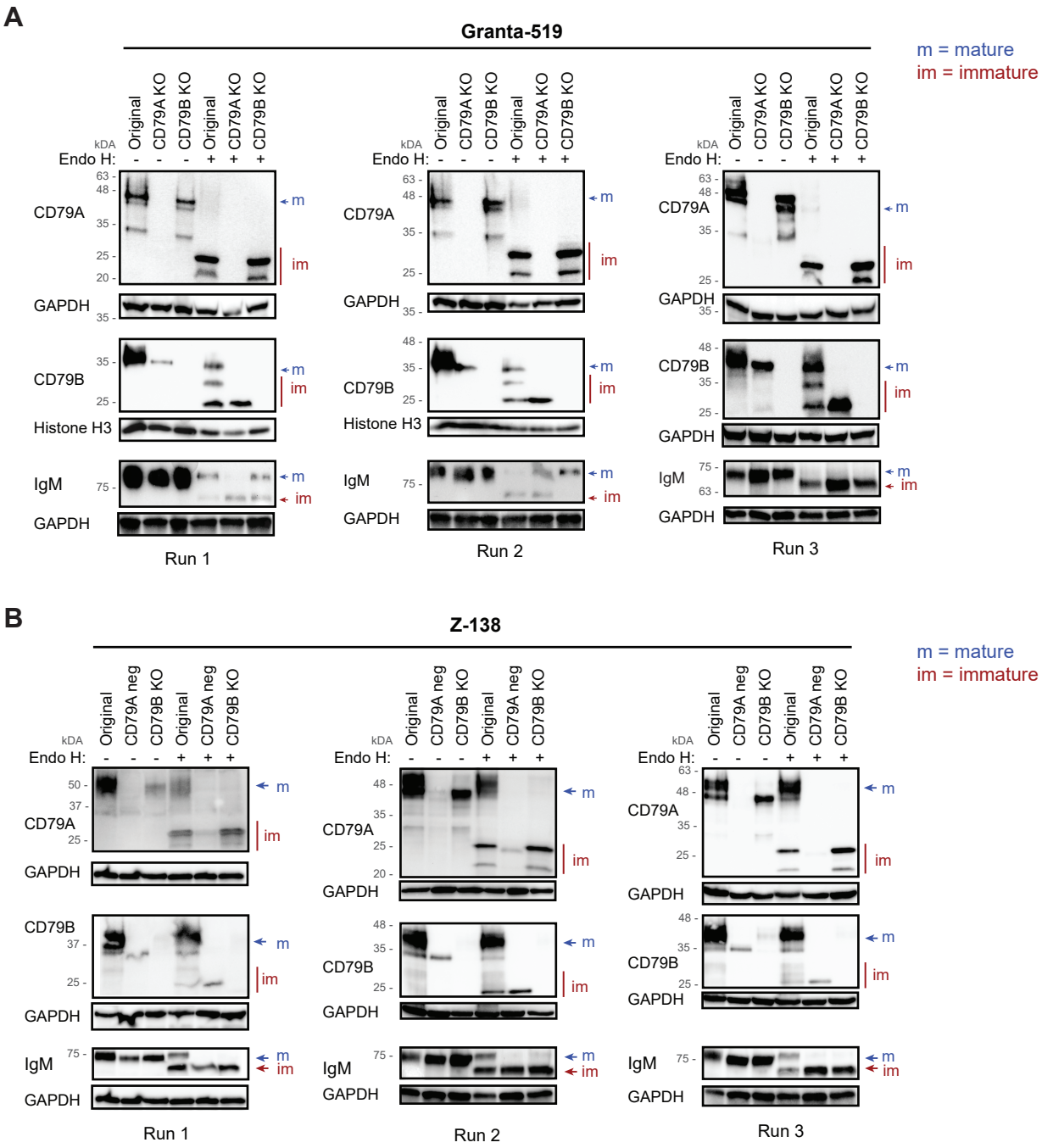
A-I: Related to Figure 1. **A.** Gating strategy for naive, memory and germinal center (GC) B cells. **B-C:** Percentage of IgM^+, IgD^+, IgG^+ and IgA^+ were measured in B cell subsets. One representative tonsil (B) and mean ± SD (C) of ten tonsils is shown. **D.** Relationship between CD79B and IgM, IgG or IgD in populations of IgM^+, IgG^+ and IgD^+ B cells. **E-F.** B cells were gated based on six levels of CD79B and plotted against level of IgM, IgG or IgD expression in IgM^+, IgG^+ and IgD^+ B cells, respectively. **G.** CD79B and IgD did not show a linear relationship as some tonsils had a large population of $IgD^{low}IgM^{high}$ B cells. In these cells, the CD79B brought to the surface by IgM will not correlate with IgD expression. **H-I.** Overlaid histograms display the range of Ig expression in B-cell subsets. Although the percentage of positive cells for the different isotypes differs between the subsets, maximum expression level is similar.

J. Related to Fig. 2. Single cell suspensions from human tonsils were thawed and stained with anti-IgM $F(ab')_2$ before culturing. Cells were fixed after 0-6 hours to check the stability of the IgM-FITC signal. After 6 hours, cells from all time points were stained with anti-IgD antibodies in addition to lineage markers.



Supplemetal Figure 2.

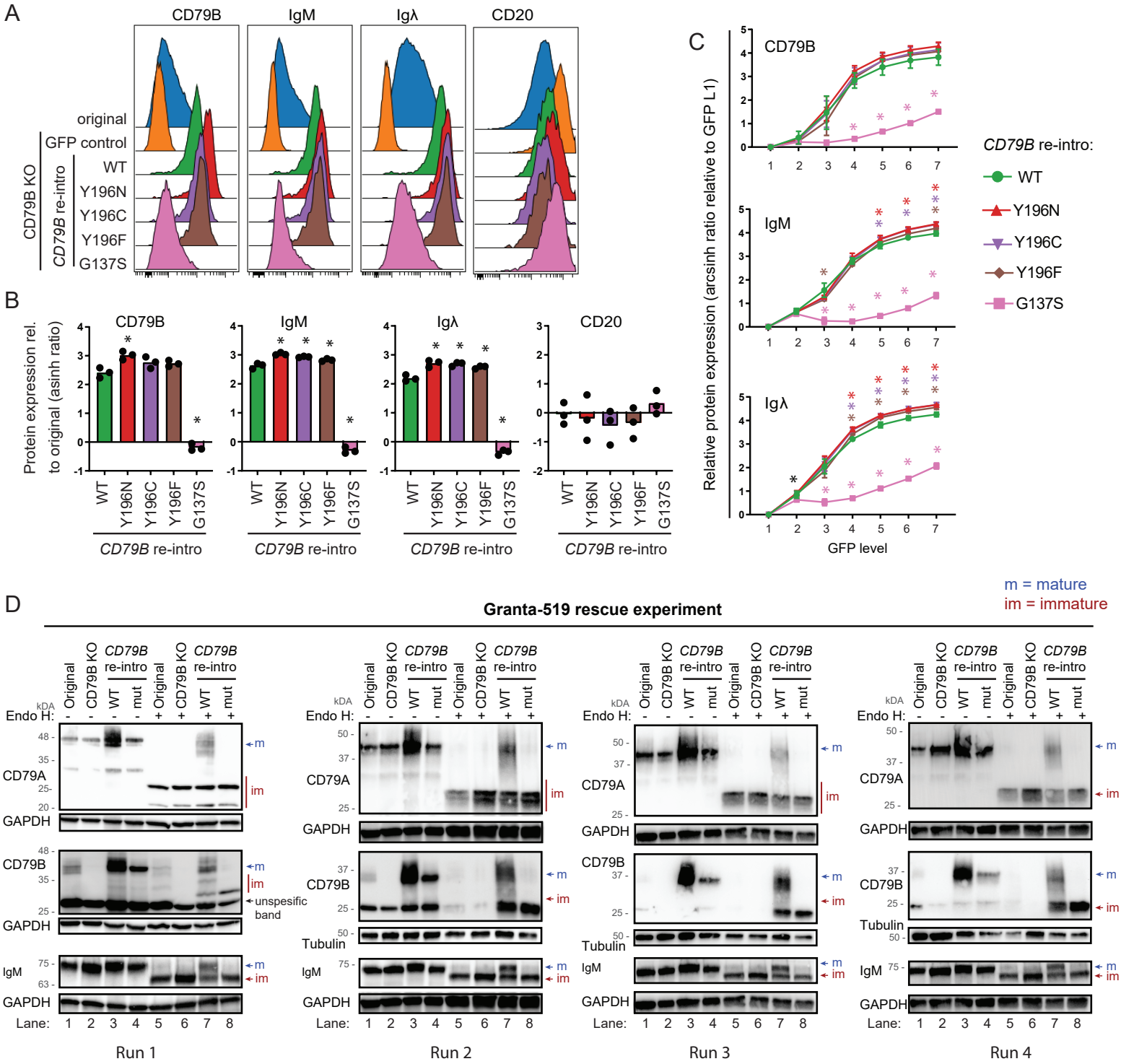
A-C: Related to Figure 3. **A.** *CD79A*-edited and *CD79B*-edited MINO cells are compared to Jurkat cell which are negative for CD79A, CD79B and IgM. After *CD79B*-editing, two surface CD79B$^-$ populations appeared whereas only one new population appeared after *CD79A*-editing. **B.** The CD79A$^-$IgM$^-$ and the CD79B$^-$IgM$^-$ populations from transduced cells of each cell line compared to the original cell lines. **C.** The sequence of CD79A and CD79B KO clones of Granta-519 and Z-138, and clones of MINO and Z-138 where *CD79B* was edited but not deleted. Red indicates the sgRNA binding sites and green indicates deletion (del) or insertion (ins). **D-F.** Protein lysates from original MINO cells and clone C7 and C9 were left untreated or treated with Endo-H for 1 hour before western blot analysis. One representative out of three experiments (D). The intensity of the bands in lane 1-3 (total protein level; E) and the mature and immature fraction (lane 4-6; F) of CD79A, CD79B and IgM were quantified and plotted relative to total protein expression in original cells (lane 1). Mean ± SD (n = 3). *in E indicates significance after one sample t-test comparing sample means of clone C7 and C9 to 1. In F, ANOVA test of mature fraction in CD79A negative and CD79B KO against original was performed. **G.** Protein lysates from original Z-138 cells and clone B, D, B1 and B3 were analyzed by western blot analysis. One representative out of three experiments. Mean ± SD (n = 3). *indicates significance after one sample t-test comparing sample means of clone B, D, B1 and B3 to 1. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, ****$p < 0.0001$. **H.** Original MINO cells compared to clone C7 and C9 and original Z-138 cells compared to clone B, D, B1 and B3 by flow cytometry.



Supplemental Figure 3. Showing the three replicates of western blots.

A. Related to Figure 5.

B. Related to Figure 6.



Supplemental Figure 4.
CD79B WT and the mutants *CD79B* Y196N, *CD79B* Y196C, *CD79B* Y196F and *CD79B* G137S were reintroduced into a Granta-519 CD79B KO cells by retroviral transduction.
A. Surface protein expression in GFP$^+$ cells and unmodified Granta-519 cells (original) was measured by flow cytometry.
B. Mean values of MFI relative to MFI in original Granta-519 cells. Data points represent separate experiments, $n = 3$.
* $p \leq 0.05$ in ANOVA and Dunnett's test against WT.
C. Protein expression (MFI) for 7 levels of GFP expression relative to GFP$^-$ cells. $n = 3$, mean ± SD, * $p \leq 0.05$ in ANOVA and Dunnett's test against WT (colored as in legend).
D. Related to Figure 7. Showing the three replicates of western blots.