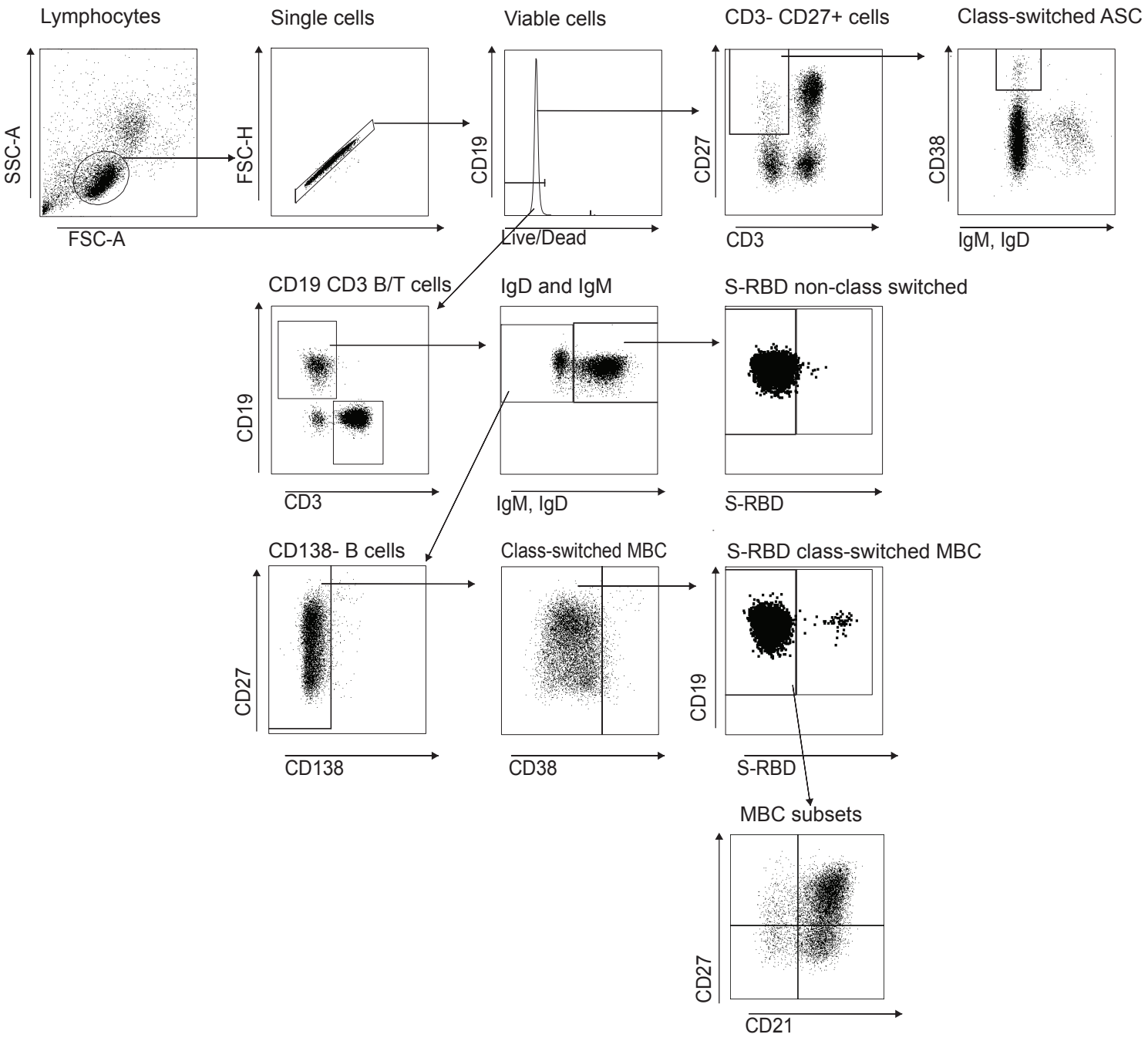
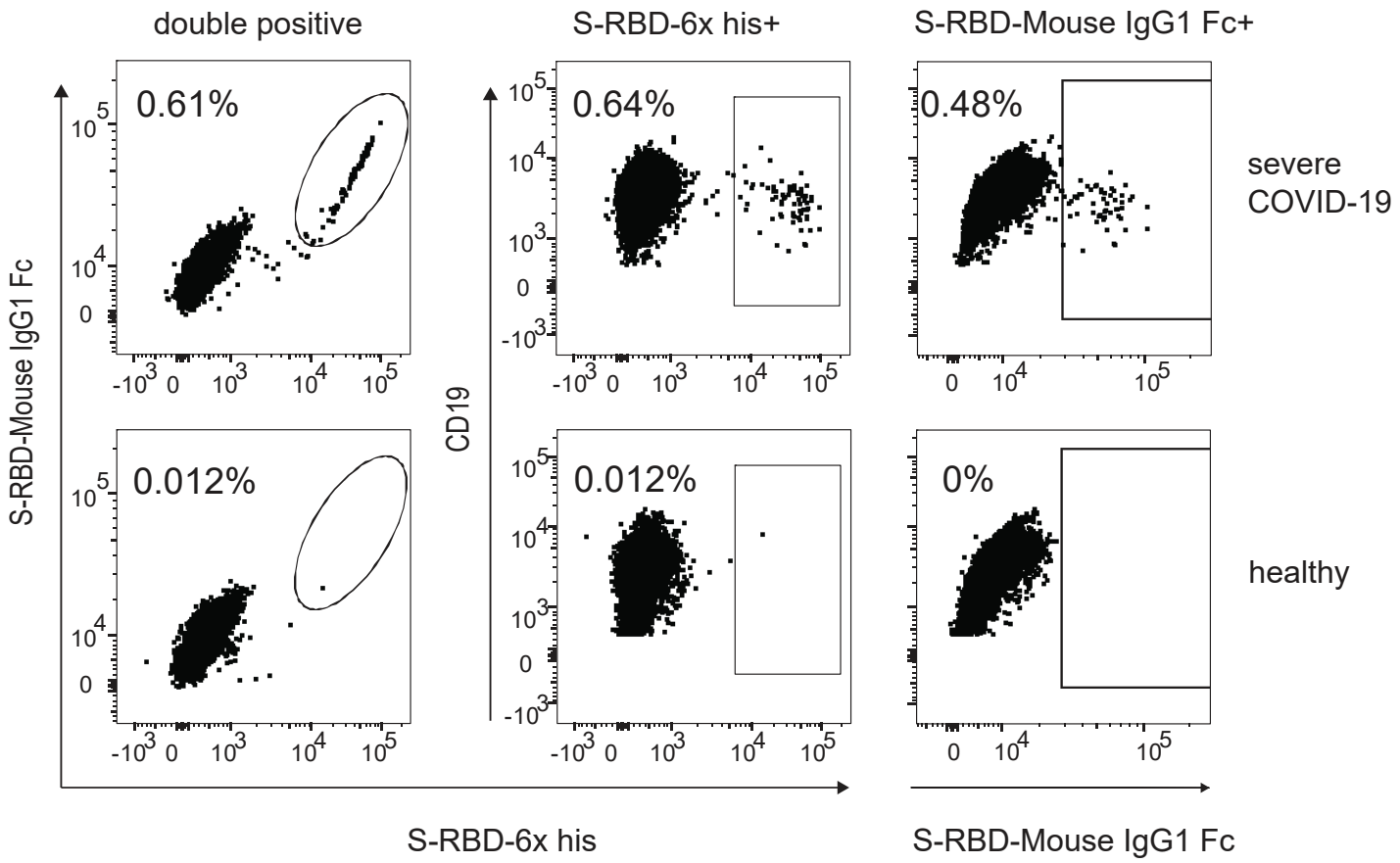
Supplemental Table 1. Antibodies used

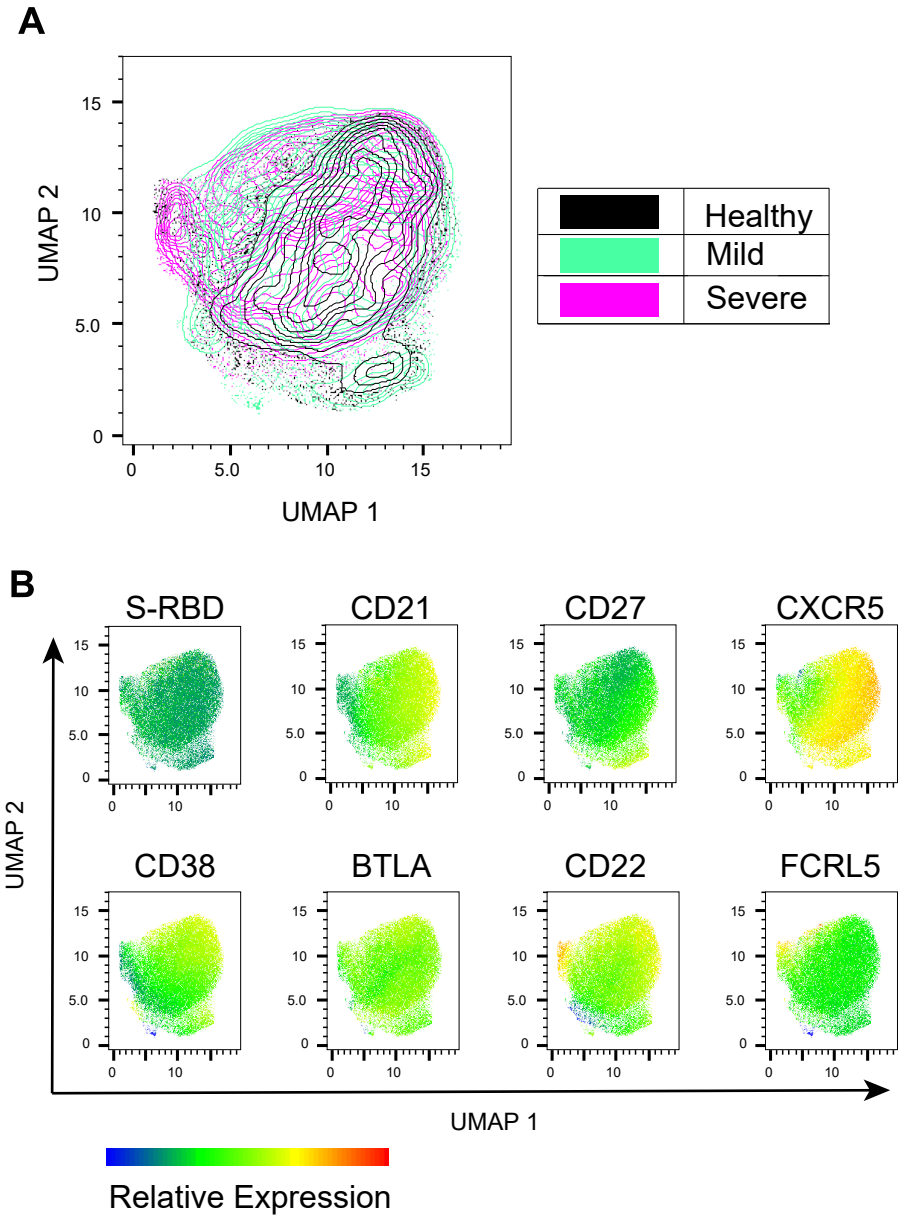
Target	Fluorophore	Clone	Cat #	Vendor
IgM	BB515	G20-127	564622	BD Biosciences
IgD	BB515	IA6-2	565243	BD Biosciences
CD19	APC-R700	HIB19	564977	BD Biosciences
CD3	APC-H7	SK7	560176	BD Biosciences
CD138	BV711	MI15	563184	BD Biosciences
CD21	PE-CF594	B-LY4	563474	BD Biosciences
CD27	BV786	L128	563327	BD Biosciences
CD38	BB700	HIT2	566445	BD Biosciences
BTLA (CD272)	BV421	J168-540	564802	BD Biosciences
CD22	PE-Cy7	HIB22	563941	BD Biosciences
FCRL5 (CD307e)	PE	509F6	566734	BD Biosciences
CXCR5 (CD185)	BV480	RF8B2	566142	BD Biosciences
6x-His Tag mAb	Alexa Fluor 647	HIS.H8	MA1-21315-A647	ThermoFisher
Fixable Yellow Dead	BV480	Viablity Dye	L34968	ThermoFisher
IgG1 Kpa ItCl	BB700	X40	566404	BD Biosciences
IgG1 Kpa ItCl	BV711	X40	563044	BD Biosciences
IgG1 Kpa ItCl	BV421	X40	562438	BD Biosciences
IgG1 Kpa ItCl	PE-Cy7	MOPC-21	557872	BD Biosciences
IgG2a Kpa ItCl	PE	G155-178	554648	BD Biosciences
anti-mouse IgG1 Antibody	PE	RMG1-1	406608	BioLegend
Rat/Ham Ig Kpa Comp Bead			552845	BD Biosciences
Ms Ig Kpa Comp Bead Set			552843	BD Biosciences
Hu Fc Block Pure Fc1.3216			564220	BD Biosciences
ArC Amine Comp			A10346	ThermoFisher



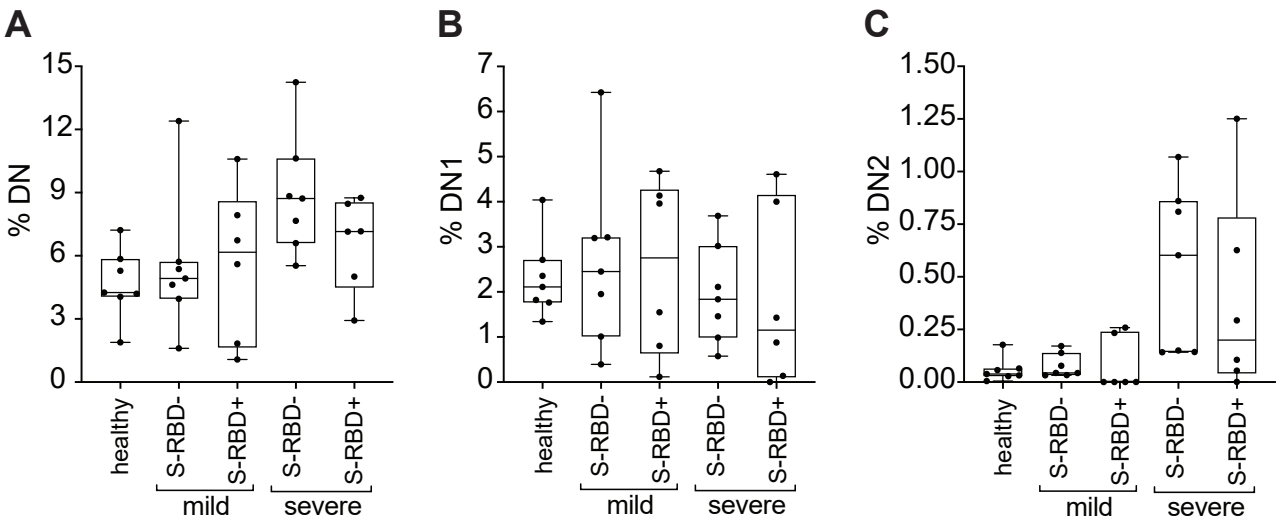
Supplemental Figure 1. Gating schematic. All antibodies used are listed in supplemental table 1. Fluorescence minus one (FMO) and isotype controls were used as guide to differentiate positive and negative populations. For S-RBD specific B cells, healthy participants were used as controls to set the gate for positive cells. All cells were run on an LSRII flow cytometer and analyzed using FlowJo



Supplemental Figure 2. Confirmation of specificity of S-RBD staining. Class switched MBC (CD3-, CD19+, IgM-, IgD-, CD38+/- (excluding ++), CD138-) from a "healthy" (COVID-19 negative) and a "severe" (COVID-19+, hospitalized) participant were stained with 6XHis-S-RBD-6x and Mouse-Fc-S-RBD simultaneously (first column), or with each S-RBD protein individually (second and third columns). Frequency of S-RBD+ cells was similar using double staining (0.61%) or 6XHis-S-RBD alone (0.64%).

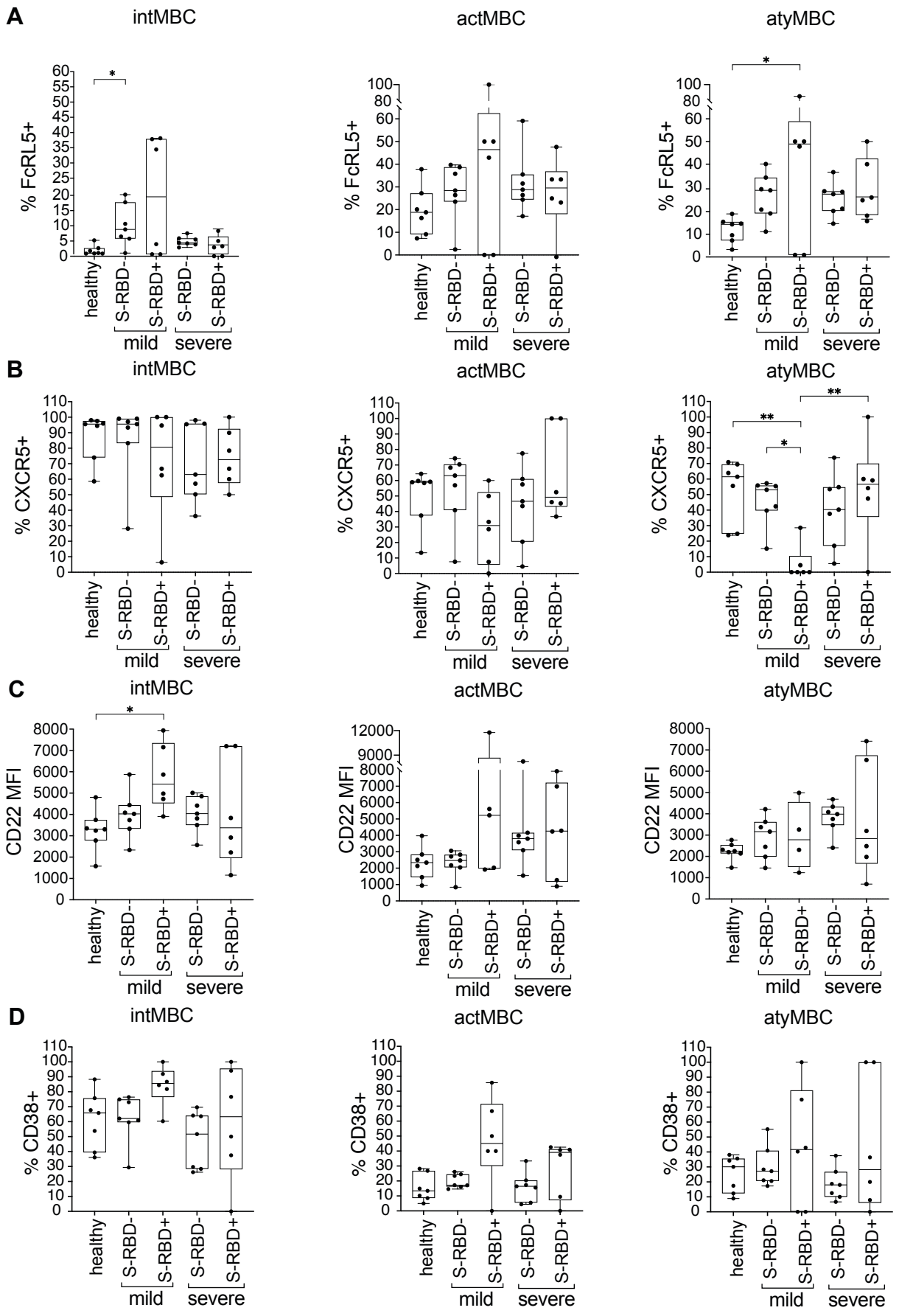


Supplemental Figure 3. UMAP projection of class switched MBC and heatmap statistic of surface receptors. (A) Concatenated class switched MBC from healthy, mild, and severe subjects projected as a UMAP of CD21, CD27, CD38, FcRL5, CD22, CXCR5, and BTLA expression. Unlike Figure 3, S-RBD binding was not included as a variable in the generation of this UMAP. All S-RBD+ MBC were included in the analysis, and S-RBD- MBC were downsampled to 3000 cells per participant. **(B)** Cell surface markers multigraph color mapping of the UMAP projection showing S-RBD, CD21, CD27, CD38, FcRL5, CD22, CXCR5, and BTLA expression. Lowest expression is indicated by blue and highest expression by red

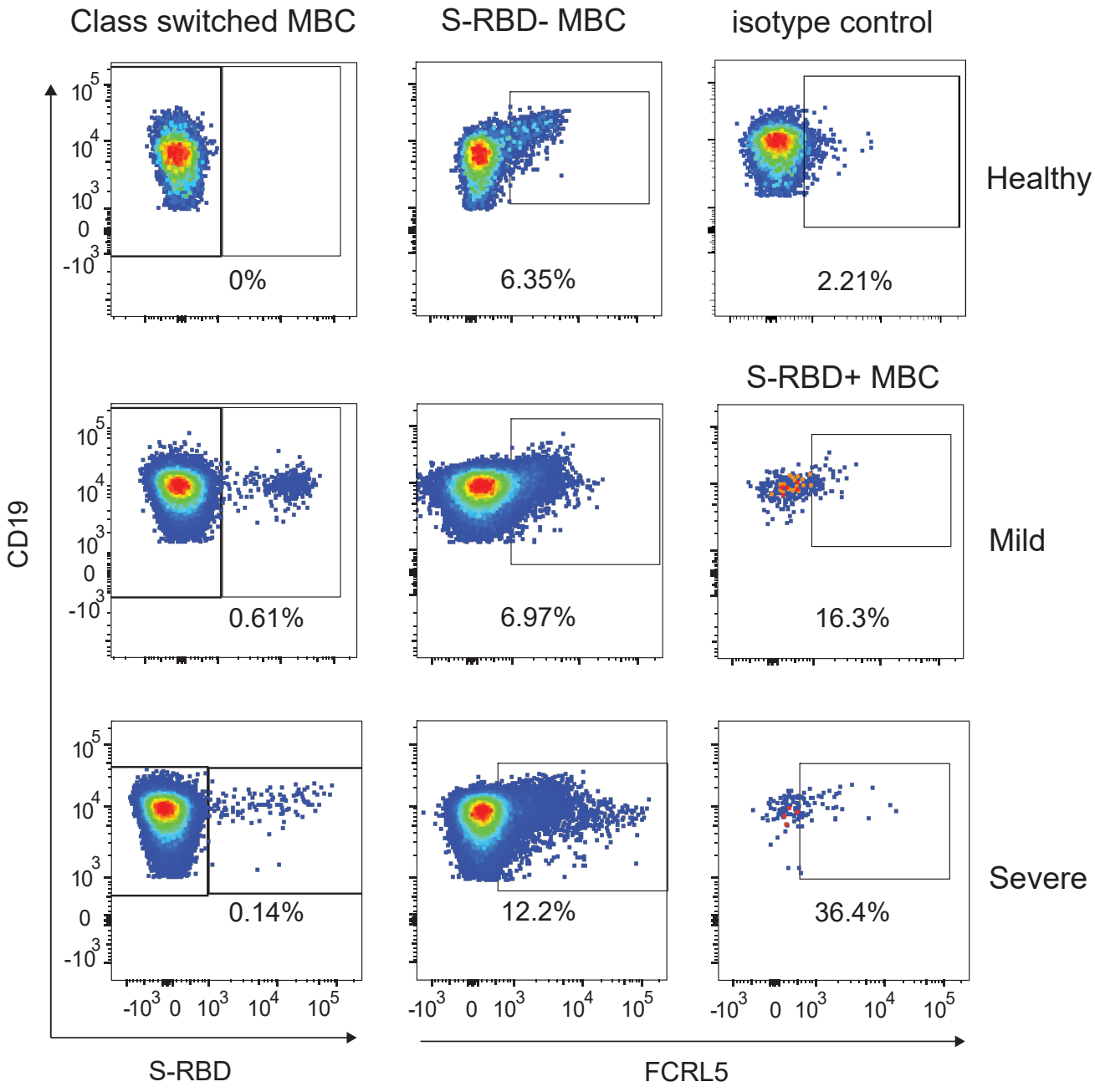


Supplemental Figure 4. Frequency of class-switched double negative (DN) cells in S-RBD nonspecific (S-RBD-) or S-RBD specific (S-RBD+) B cells from healthy, mild, or severe participants. A) Class-switched DN B cells are defined as CD3-, CD19+, IgD-, CD27-, IgM-, CD138-, CD38+/- (excluding ++) **B)** Class-switched DN1 B cells are defined as CD3-, CD19+, IgD-, CD27-, IgM-, CD138-, CD38+ (excluding ++), CD21+, FCRL5-, CXCR5+. **C)** Class-switched DN2 B cells are defined as CD3-, CD19+, IgD-, CD27-, IgM-, CD138-, CD38-, CD21-, FCRL5+, CXCR5-. Horizontal lines indicate means, boxes are inter-quartile range, and whiskers are minimum to maximum. Normality of data was determined using Shapiro Wilk normality test, and comparisons were performed using one-way ANOVA for normally distributed data (**A, B**) or Kruskal-Wallis test for non-normally distributed data (**C**), with p values adjusted for multiple comparisons using the Benjamini, Krieger and Yekutieli method. No statistically significant comparisons were discovered.

Supplemental Figure 5



Supplemental Figure 5. Surface expression of FcRL5, CXCR5, CD22, and CD38 on S-RBD nonspecific (S-RBD-) or S-RBD specific (S-RBD+) class switched intMBC, actMBC, or atyMBC from healthy, mild, or severe participants. Expression is shown as either percent of cells positive or the mean fluorescent intensity (MFI). **(A)** FcRL5 **(B)** CXCR5 **(C)** CD22 **(D)** CD38. Horizontal lines indicate means, boxes are inter-quartile range, and whiskers are minimum to maximum. Normality of data was determined using Shapiro Wilk normality test, and comparisons were performed using one-way ANOVA for normally distributed data (**A, C, D**) or Kruskal-Wallis test for non-normally distributed data (**B**), with p values adjusted for multiple comparisons using the Benjamini, Krieger and Yekutieli method. Statistically significant comparisons are indicated (* P Ò0.05, ** P Ò0.01).



Supplemental Figure 6. Representative gating of FCRL5+ class switched MBC. The first column shows the gating strategy for S-RBD specific class switched MBC (CD3-, CD19+, IgM-, IgD-, CD38+/- (excluding ++), CD138-, S-RBD+). The top right panel shows a representative FCRL5 isotype control that was used in conjunction with a fluorescence minus one (FMO) sample to set the gate for FCRL5. The remaining panels represent FCRL5 staining as seen in S-RBD+ or S-RBD- cells from “healthy” (COVID-19 negative), “mild” (COVID-19+, ambulatory), and “severe” (COVID-19+, hospitalized) participants.