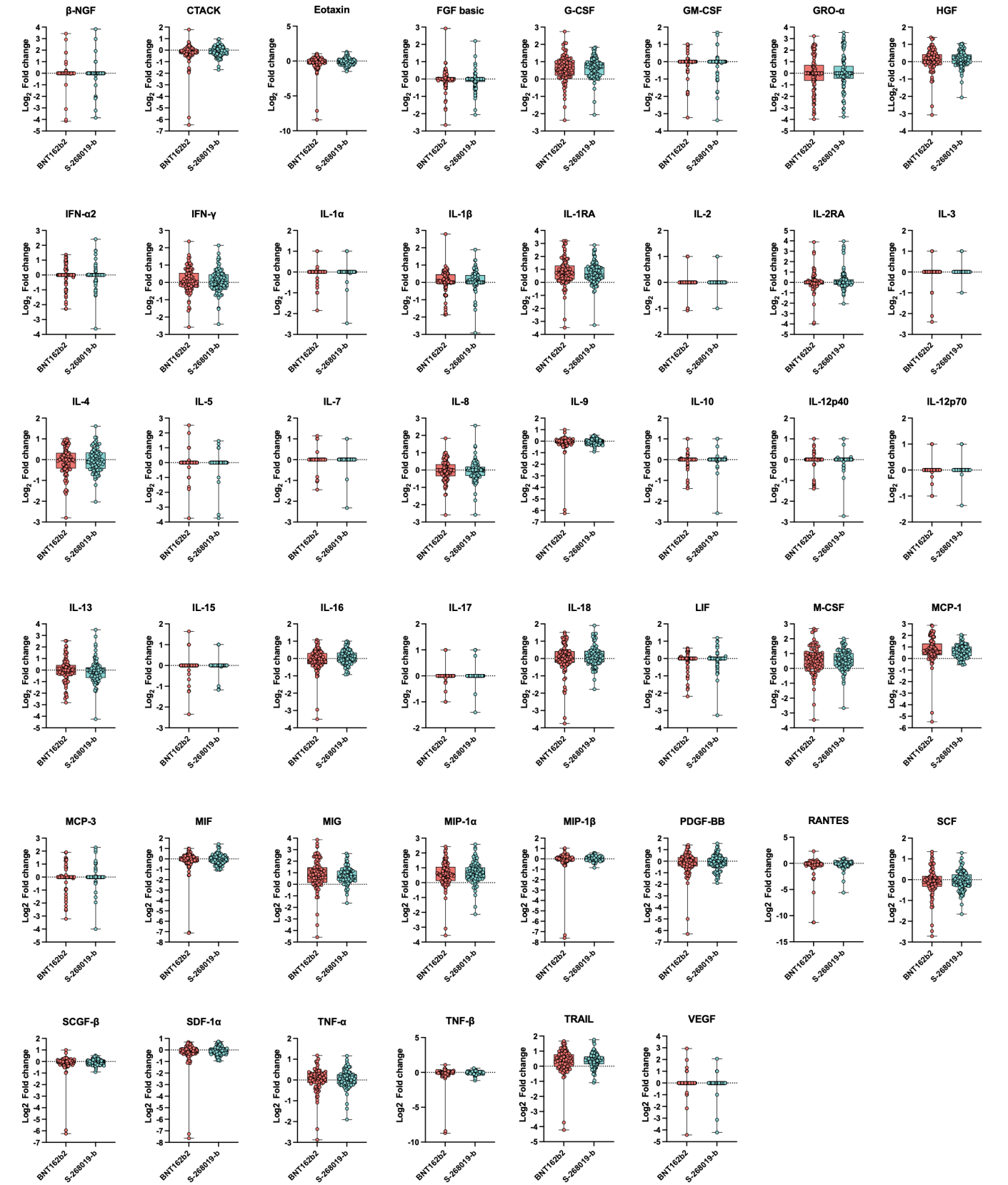
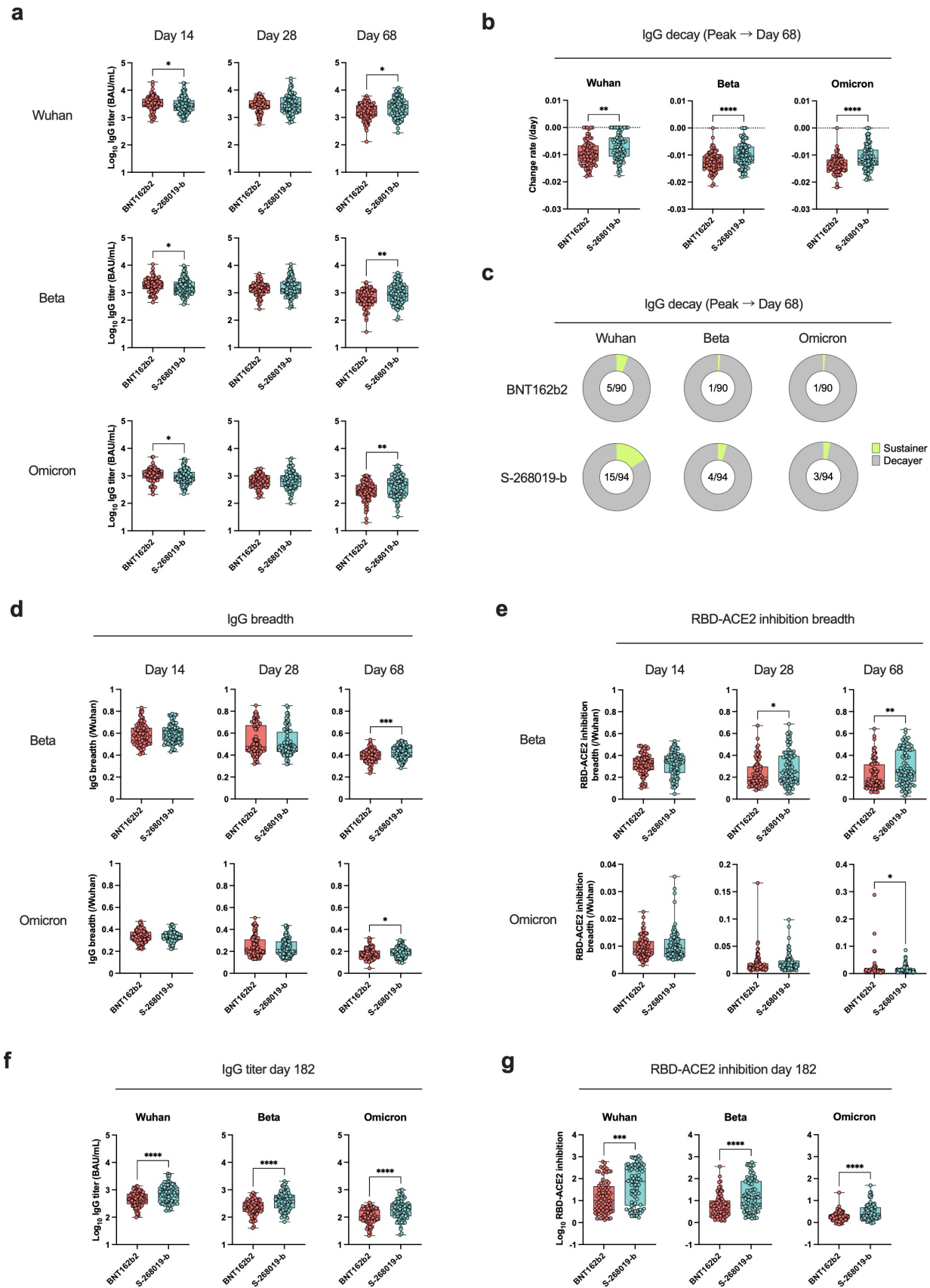


Supplementary Figure 1



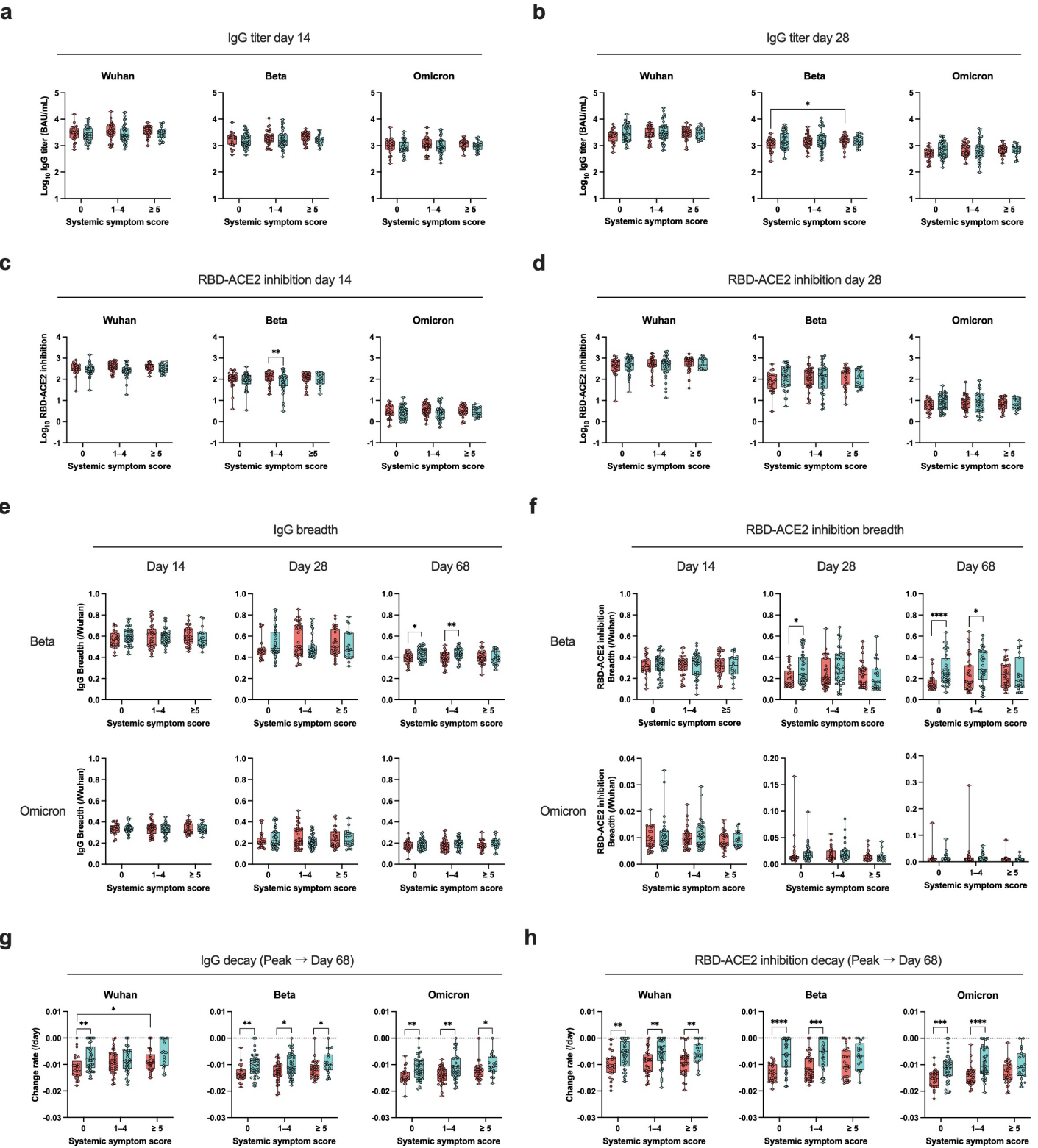
Supplementary Figure 1 | Plasma cytokine/chemokine dynamics following the third vaccination.
Fold change (day 1 concentration/day 0 concentration) of the plasma cytokines/chemokines after the third vaccination. The box and whisker plots indicate the quartile minimum, maximum, and quartile points. Each dot represents data from individuals. Statistical analyses were performed using the Mann-Whitney test. Data were pooled from 3 independent experiments (BNT162b2, n = 90; S-268019-b, n = 94).

Supplementary Figure 2



Supplementary Figure 2 | Durability of plasma antibody responses following the third vaccination .
a IgG titers for the variants on days 14, 28, and 68. **b** Decay rate of the IgG titers from the peak to day 68 after the third vaccination to the variant RBDs. **c** Ratios of the IgG titer sustainers and decayers. The breadth of the IgG titers (**d**) and relative RBD-ACE2 inhibition (**e**) to the variant RBDs on days 14, 28, and 68. **f** IgG titers for the variants on day 182. **g** Relative RBD-ACE2 inhibition to the variants on day 182. The box and whisker plots indicate quartile minimum, maximum, and quartile points (**a**, **b**, and **d-g**). Each dot represents data from individuals (**a**, **b**, and **d-g**). Statistical analyses were performed using a Mann-Whitney test (**a**, **b**, and **d-g**; * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, and **** $P < 0.0001$). Data were pooled from ≥ 2 independent experiments [(**a**, **b**, **d**, and **e**) BNT162b2, $n = 90$; S-268019-b, $n = 94$; (**f** and **g**) BNT162b2, $n = 80$; S-268019-b, $n = 81$].

Supplementary Figure 3

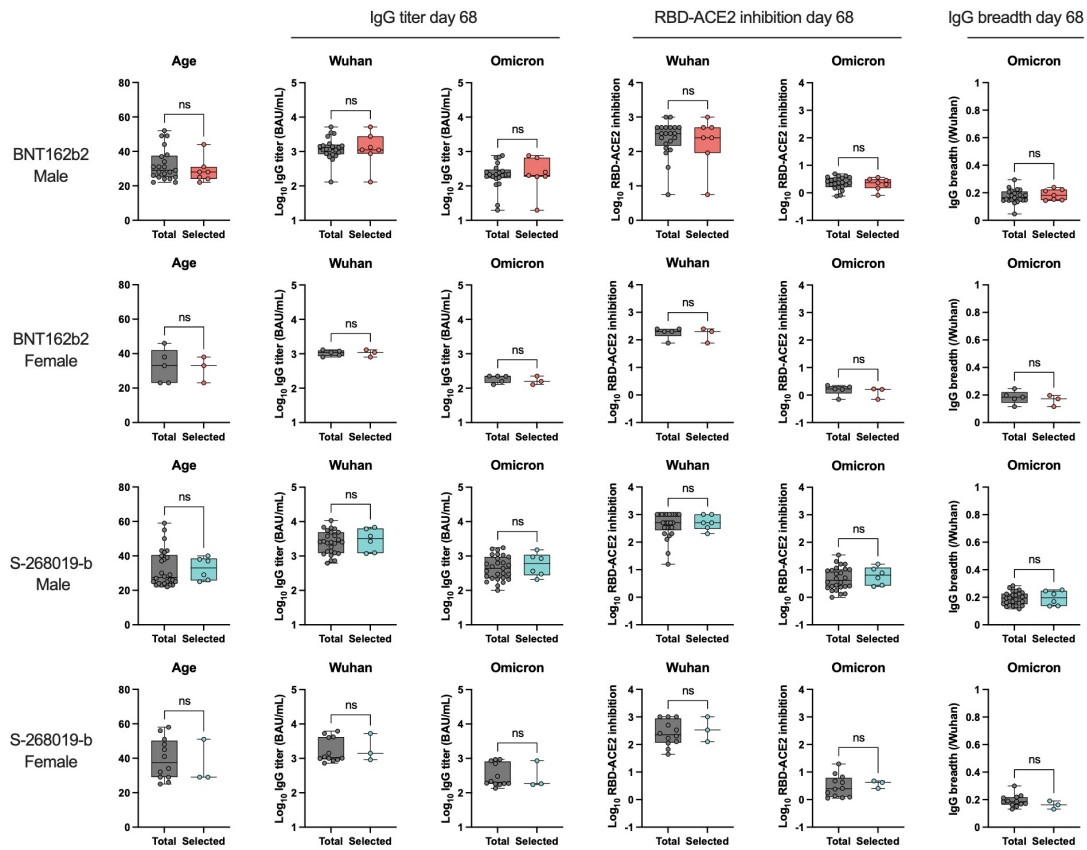


Supplementary Figure 3 | Comparative analyses of the variant reactivity and durability of antibody stratified by the systemic symptom scores, Related to Figure 3.

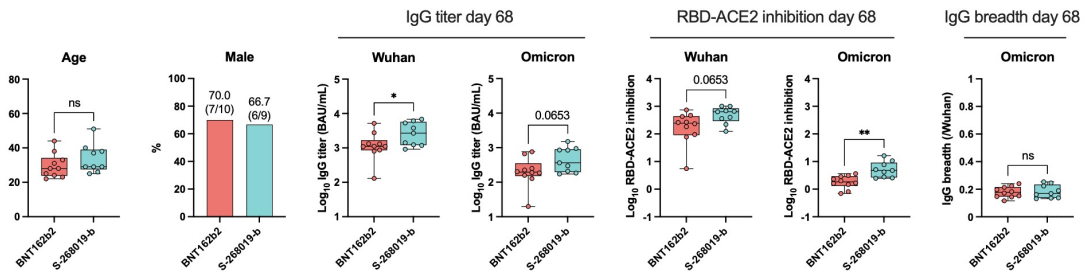
IgG titers for the variant RBDs on days 14 (a) and 28 (b). Relative RBD-ACE2 inhibition for the variant RBDs on days 14 (c) and 28 (d). Breadth of the IgG titer (e) and relative RBD-ACE2 inhibition (f) for the variants on days 14, 28, and 68. Decay rate of the IgG titer (g) and relative RBD-ACE2 inhibition (h) to the variants from the peak to day 68 after the third vaccination. The box and whisker plots indicate quartile minimum, maximum, and quartile points. Each dot represents data from individuals. Statistical analyses were performed using the Kruskal-Wallis test followed by Dunn's post hoc test (comparison among the groups stratified by systemic symptom severity scores within the same vaccine group) and Mann-Whitney test (comparison between BNT162b2 and S-268019-b groups within the same systemic symptom severity) (* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, and **** $P < 0.0001$). Data were pooled from ≥ 2 independent experiments [BNT162b2: $n = 25$ (score 0), $n = 35$ (score 1–4), and $n = 30$ (score ≥ 5); S-268019-b: $n = 38$ (score 0), $n = 37$ (score 1–4), and $n = 19$ (score ≥ 5)].

Supplementary Figure 4

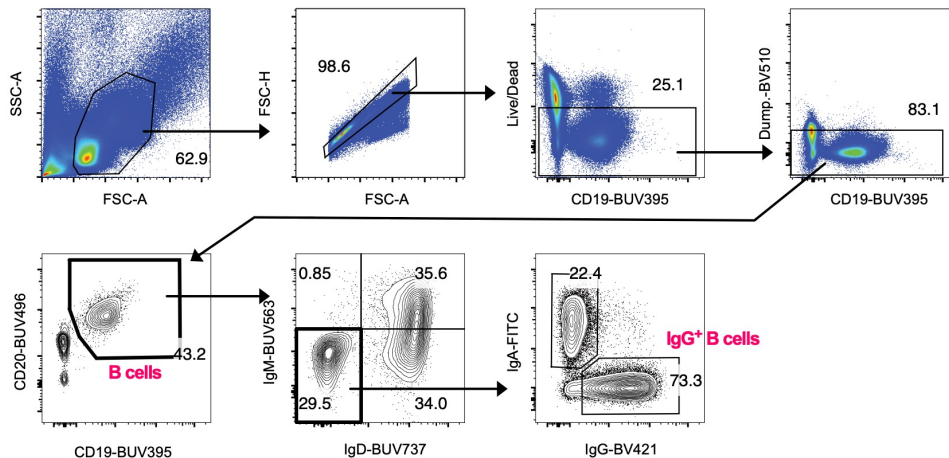
a



b



c

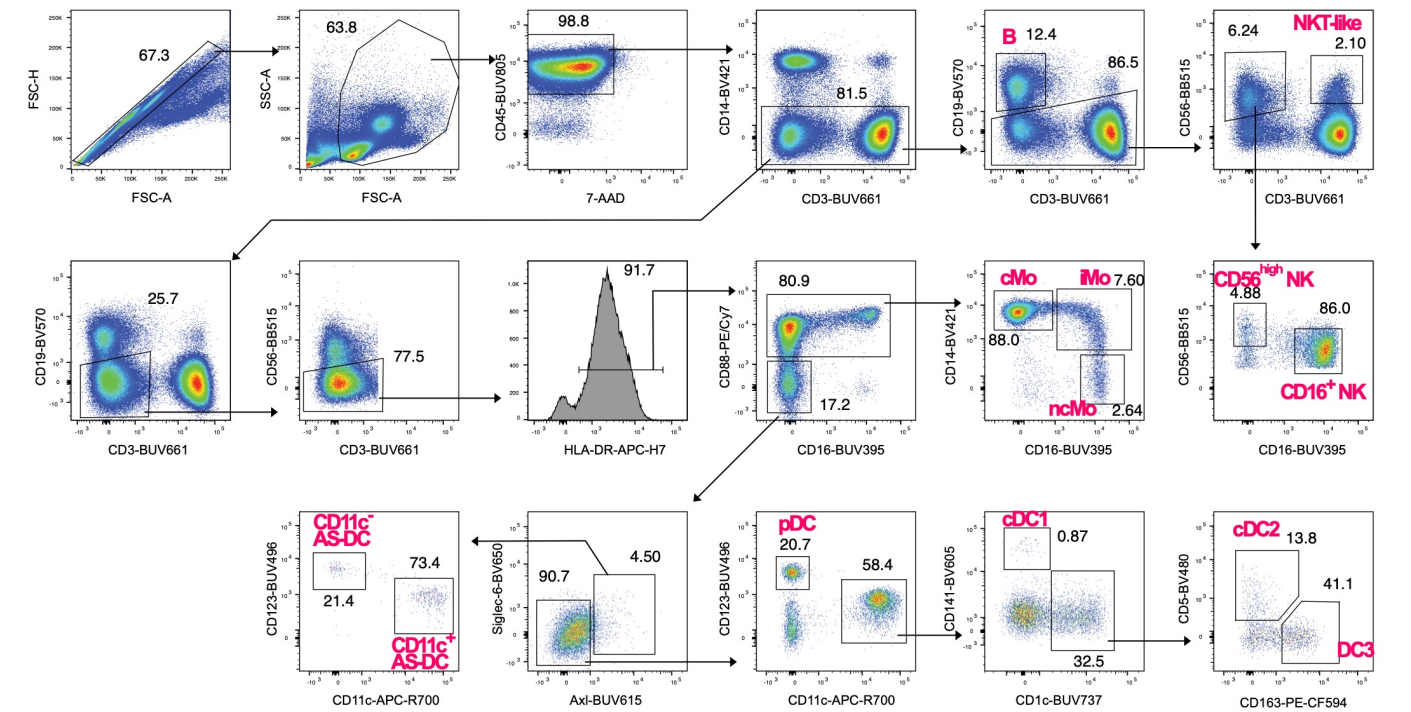


Supplementary Figure 4 | Demographic and antibody reactivities in the participants selected for the B_{mem} analysis.

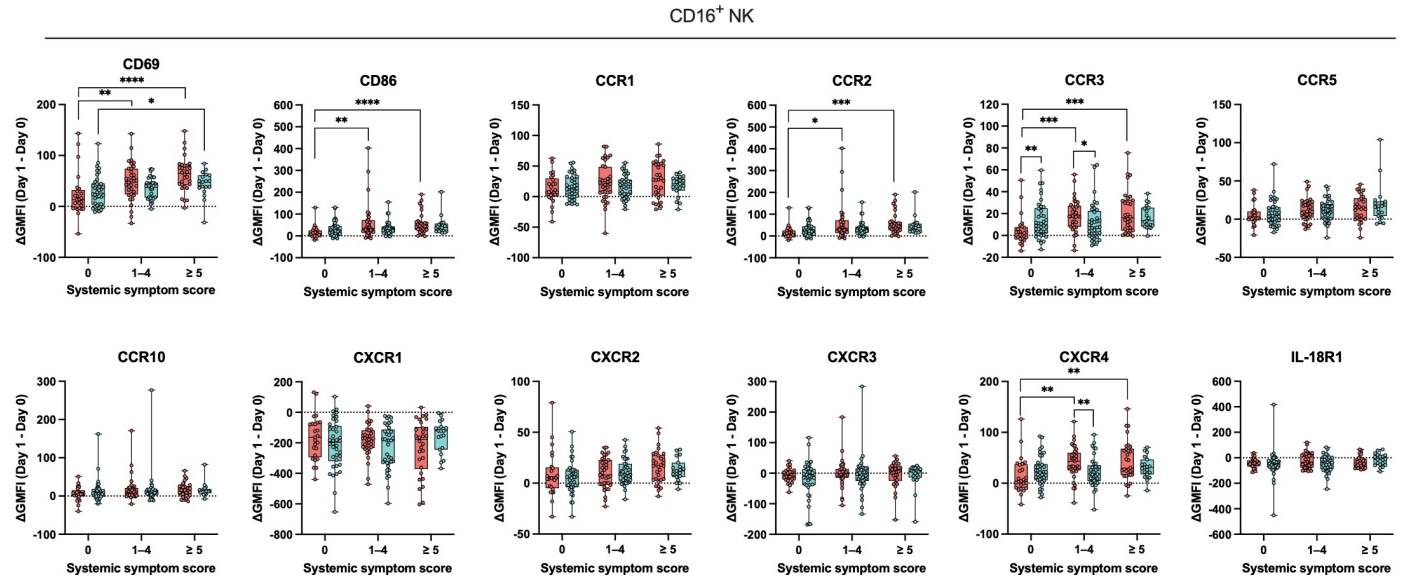
a Age, IgG titers, relative RBD-ACE2 inhibition, and breadth of IgG titers against the variants were compared between the total cohort (for each vaccine and gender group) and the selected samples for memory B cell subset analysis. **b** Age, frequency of male, IgG titers, relative RBD-ACE2 inhibition, and breadth of the IgG titers against the variants were compared between the BNT162b2 and S-268019-b groups selected for the memory B cell subset analysis. **c** Representative gating strategy for IgG⁺ B cells in peripheral blood. Dump: CD2, CD4, CD10, and CD14. The box and whisker plots indicate quartile minimum, maximum, and quartile points. Each dot represents data from individuals. Statistical analyses were performed using the Mann-Whitney test (**P* < 0.05 and ***P* < 0.01). Data were pooled from ≥ 2 independent experiments [**a** BNT162b2 Male: *n* = 21 (Total), *n* = 7 (Selected); BNT162b2 Female: *n* = 5 (Total), *n* = 3 (Selected); S-268019-b Male: *n* = 26 (Total), *n* = 6 (Selected); S-268019-b Female: *n* = 12 (Total), *n* = 3 (Selected); **b** BNT162b2: *n* = 10; S-268019-b, *n* = 9].

Supplementary Figure 5

a



b



Supplementary Figure 5. Flow cytometric analysis of the early immune cell dynamics.

a Gating strategy for identifying B cells, CD16⁺ NK cells, CD56^{high} NK cells, NKT-like cells, classical monocytes, intermediate monocytes, non-classical monocytes, cDC1s, cDC2s, DC3s, CD11c⁺ AS-DCs, CD11c⁻ AS-DCs, and pDCs. **b** Differences in the CD69, CD86, CCR1, CCR2, CCR3, CCR5, CCR10, CXCR1, CXCR2, CXCR3, CXCR4, and IL-18R1 expression levels on CD16⁺ NK cells between days 1 and 0. The box and whisker plots indicate quartile minimum, maximum, and quartile points. Each dot represents data from individuals (**b**). Statistical analyses were performed using the Kruskal-Wallis test followed by Dunn's post hoc test (comparison among the groups stratified by systemic symptom severity scores within the same vaccine group) and Mann-Whitney test (comparison between BNT162b2 and S-268019-b groups within the same systemic symptom severity) (**P* < 0.05, ***P* < 0.01, ****P* < 0.001, and *****P* < 0.0001). Data were pooled from 6 independent experiments [**b** BNT162b2: *n* = 25 (score 0), *n* = 35 (score 1–4), and *n* = 30 (score ≥ 5); S-268019-b: *n* = 38 (score 0), *n* = 37 (score 1–4), and *n* = 19 (score ≥ 5)].

Supplementary Table 1. Criteria of the symptom severity scores.

Systemic Symptom	Grade 1	Grade 2	Grade 3	Grade 4
Fever	38.0 – 38.4 °C	38.5 – 38.9 °C	39.0 – 40 °C	> 40 °C
Fatigue	No interference with activity	Some interference with activity	Prevents daily activity	ER visit or hospitalization
Headache	No interference with activity	Some interference with activity	Prevents daily activity	ER visit or hospitalization
Chills	No interference with activity	Some interference with activity	Prevents daily activity	ER visit or hospitalization
Vomiting	1 – 2 episodes / 24 h	> 2 episodes / 24 h	Requires intravenous hydration	ER visit or hospitalization
Diarrhea	2 – 3 loose stools / 24 h	4 – 5 loose stools / 24 h	6 or more loose stools / 24 h	ER visit or hospitalization
Muscle pain	No interference with activity	Some interference with activity	Prevents daily activity	ER visit or hospitalization
Joint pain	No interference with activity	Some interference with activity	Prevents daily activity	ER visit or hospitalization