

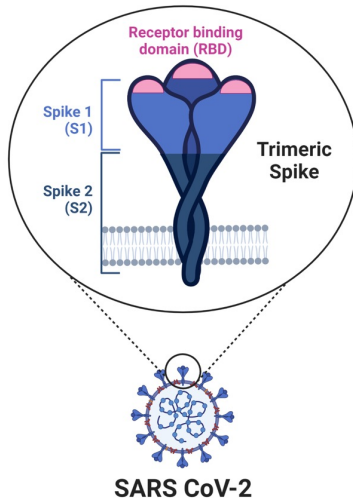
# Supp Figures

(15 Supp Figures  
+ 3 Supp Tables)

**A Summary of pre-pandemic controls and vaccinated cohorts**

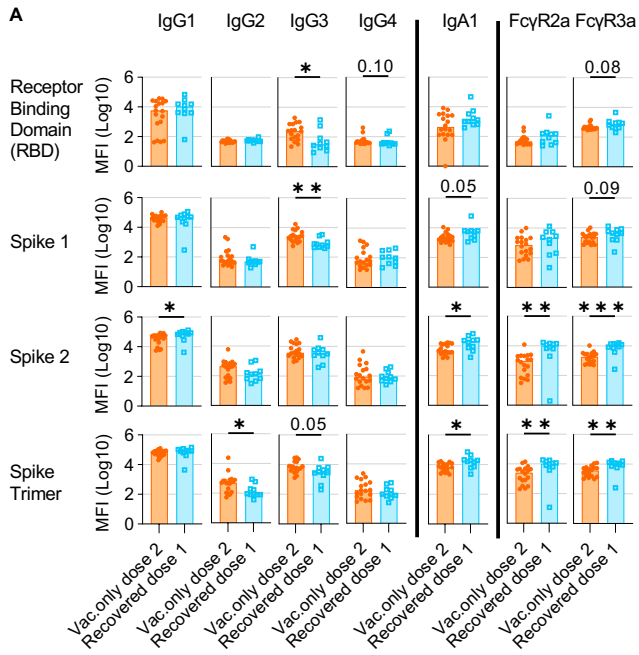
| Variables                                                                            | Pre-pandemic Controls | Comirnaty / BNT162b2 (Pfizer-BioNtech) vaccinees |                                                      | ChAdOx1 nCoV-19 (AstraZeneca) vaccinees |
|--------------------------------------------------------------------------------------|-----------------------|--------------------------------------------------|------------------------------------------------------|-----------------------------------------|
|                                                                                      | Pre-pandemic (n=20)   | Vaccinated only (n=20)                           | COVID-19 Recovered (Convalescent, vaccinated) (n=10) | Vaccinated only (n=17)                  |
| Age, mean (range), years                                                             | 30.5 (21 – 60)        | 34.6 (26 – 58)                                   | 49.5 (24 – 65)                                       | 46.5 (23 – 69)                          |
| Gender                                                                               |                       |                                                  |                                                      |                                         |
| Female (%)                                                                           | 16 (80.0%)            | 13 (65.0%)                                       | 6 (60.0%)                                            | 10 (58.8)                               |
| Male (%)                                                                             | 4 (20.0%)             | 7 (35.0%)                                        | 4 (40.0%)                                            | 7 (41.2)                                |
| Time from symptom onset till sample collection, mean (range), days                   |                       |                                                  | 478.1 (412 – 534)                                    |                                         |
| Vaccination                                                                          |                       |                                                  |                                                      |                                         |
| Time after 1 <sup>st</sup> shot till sample collection, mean (range), days           |                       | 9.1 (6 – 12)                                     | 12.5 (7 – 18)                                        | 13.4 (7 – 22)                           |
| Time between 1 <sup>st</sup> and 2 <sup>nd</sup> shot, mean (range), days            |                       | 24.0 (21 – 33)                                   | 28.0 (21 – 48)                                       | 83 (70 – 92)                            |
| Time after 2 <sup>nd</sup> shot till sample collection, mean (range), days           |                       | 14.1 (12 – 22)                                   | 20.1 (10 – 34)                                       | 13.4 (7 – 22)                           |
| Time between 2 <sup>nd</sup> shot and 5 months sample collection, mean (range), days |                       | 218.8 (188 – 226)                                |                                                      | 149.6 (101 – 184)                       |
| Time after 3 <sup>rd</sup> shot till sample collection, mean (range), days           |                       | 12.4 (10 – 15)                                   |                                                      | 20.1 (10 – 31)                          |

**B Schematic of SARS-CoV-2 spike protein**



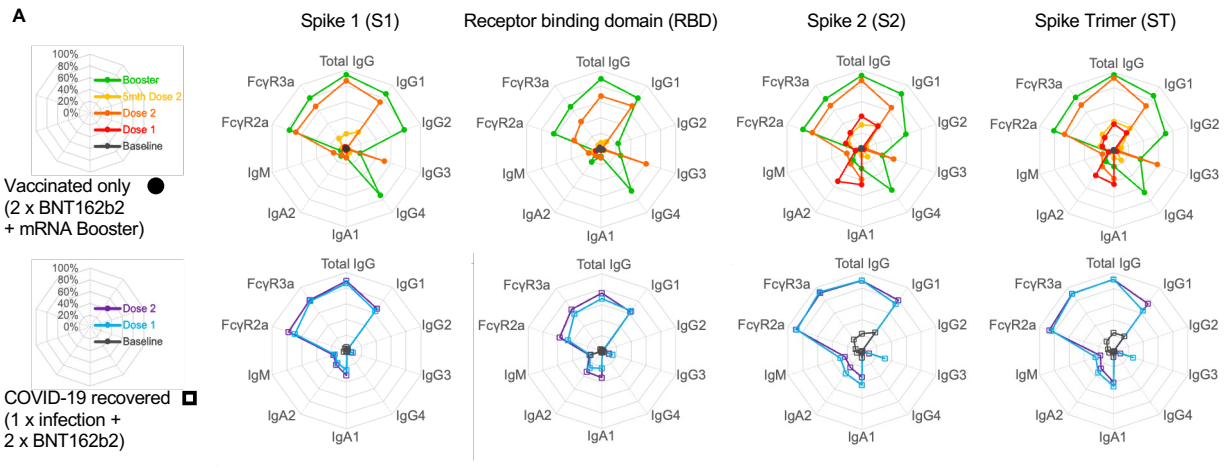
**Supplementary Figure 1: Cohort Information and Spike schematic.** Details of the pre-pandemic controls, vaccinated only vaccinees and COVID-19 recovered vaccinees included in the study (A). Schematic of the SARS-CoV-2 Spike protein describing the four different types of Spike proteins used in the multiplex assays (B).

Saliva antibody comparisons after two antigen exposures

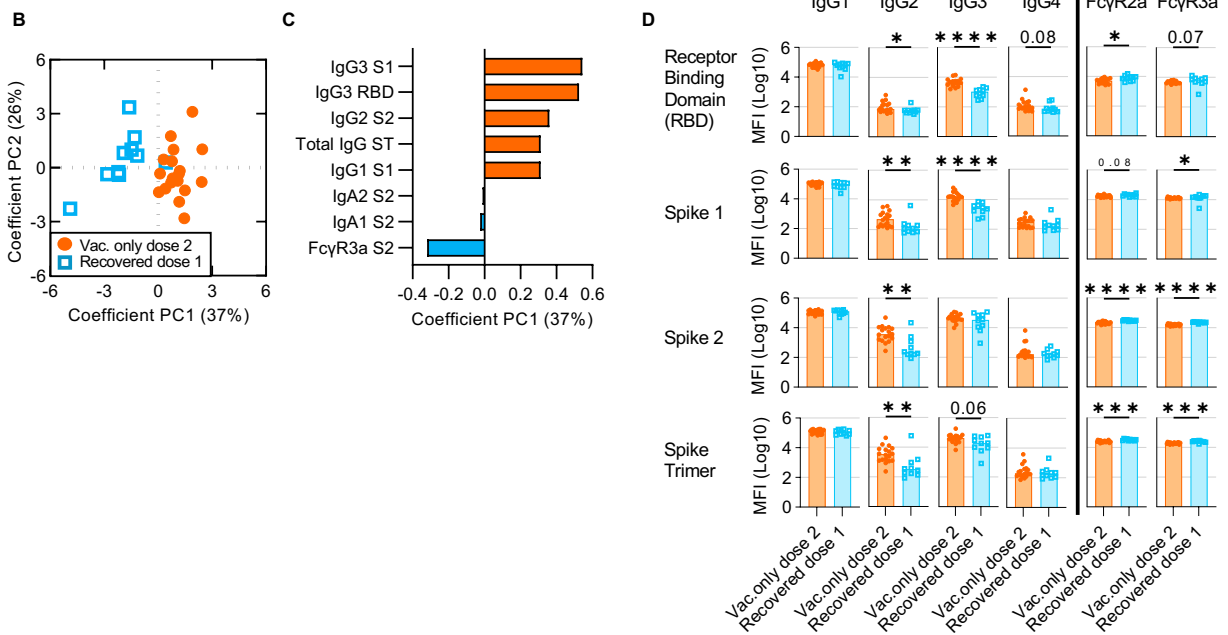


**Supplementary Figure 2: Comparisons of mucosal antibody responses between vaccinated only and COVID-19 recovered vaccinees after two antigen exposures.** Bar graphs describe the key differences in ancestral SARS-CoV-2 Spike-specific salivary (**A**) antibody responses between vaccinated only ( $n = 18$ ) and COVID-19 recovered cohorts ( $n = 10$ ) after two antigens exposures. Statistical significance was calculated using the two-tailed Mann-Whitney  $U$  test. Where significant or trending significance,  $P$ -values were reported ( $*P \leq 0.05$ ;  $**P \leq 0.01$ ;  $***P \leq 0.001$ ;  $****P \leq 0.0001$ ).

Plasma antibody signatures following BNT162b2 vaccination

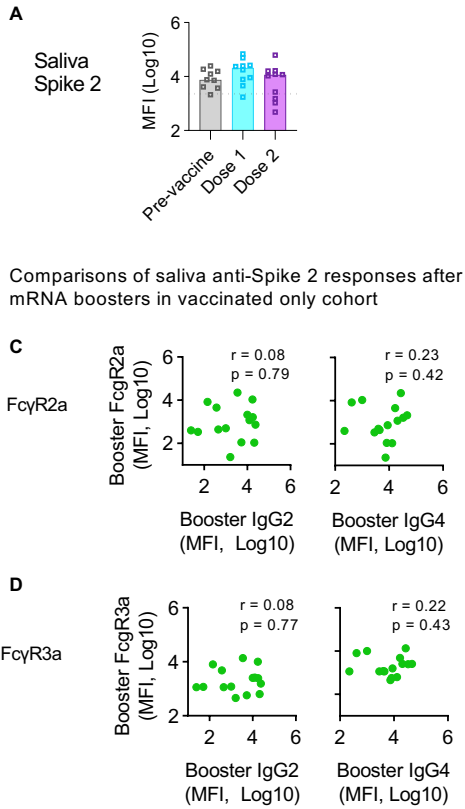


Plasma antibody comparisons after two antigen exposures

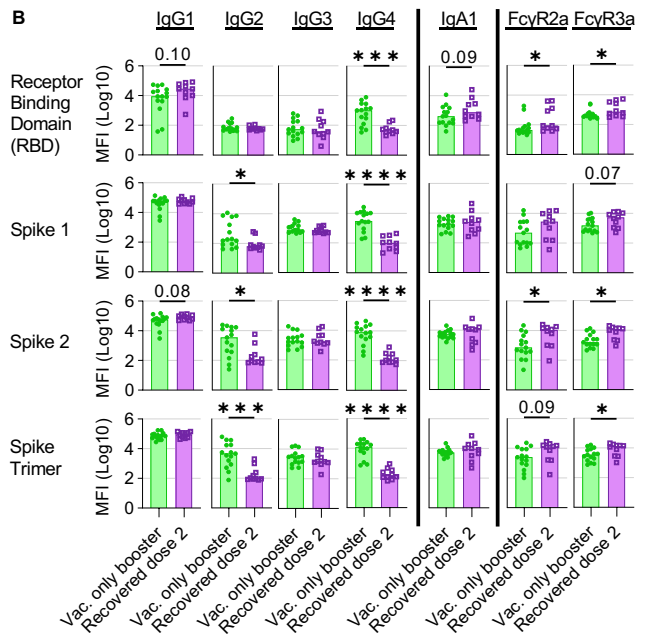


**Supplementary Figure 3: Plasma antibodies from vaccinated only vaccinees show rises in IgG2 and IgG3 responses after two antigen exposures.** Plasma antibody isotype and subclass responses from both cohorts against the various SARS-CoV-2 Spike antigens were compiled into respective radar plots (A). The individual median antibody isotype/subclass response for each Spike antigen was transformed into percentages using the antigen-specific MFI from the 98<sup>th</sup> percentile for that detector (98<sup>th</sup> percentile was chosen to minimize the impact of outliers on the data transformation). PCA of all 40 antibody features for vaccinated only (closed circles) ( $n = 18$ ) and COVID-19 recovered (open squares) ( $n = 10$ ) individuals after two antigen exposures (B). Loading plots and bar graphs describe the key differences between both cohorts after two (C and D) antigens exposure. Statistical significance was calculated using the two-tailed Mann-Whitney  $U$  test and where significant or trending significance,  $P$ -values were reported (\* $P \leq 0.05$ ; \*\* $P \leq 0.01$ ; \*\*\* $P \leq 0.001$ ; \*\*\*\* $P \leq 0.0001$ ).

Salivary IgA in COVID-19 recovered individuals following BNT162b2 vaccination

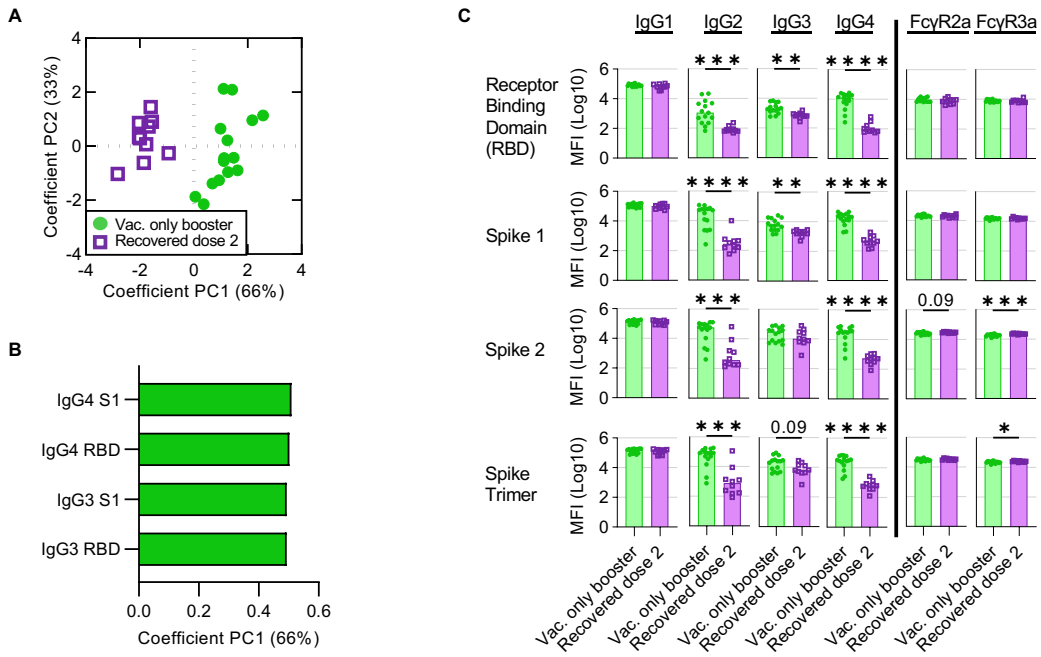


Saliva antibody comparisons after three antigen exposures

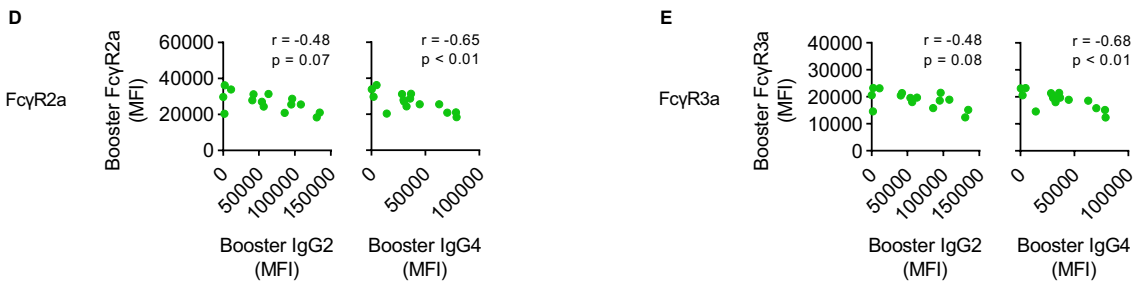


**Supplementary Figure 4: Salivary antibody responses after three antigen exposures.** Bar graphs illustrate the changes in anti-Spike 2 IgA responses in saliva of COVID-19 recovered individuals ( $n = 10$ ) after their first and second mRNA vaccination (**A**). Statistical significance was calculated using Friedman's test followed by Dunn's test for multiple comparisons. Bar graphs also describe the key differences in ancestral SARS-CoV-2 Spike-specific salivary antibody responses between vaccinated only ( $n = 15$ ) and COVID-19 recovered cohorts ( $n = 10$ ) after three antigen exposures (**B**). Statistical significance was calculated using the two-tailed Mann-Whitney  $U$  test. Where significant or trending significance,  $P$ -values were reported ( $*P \leq 0.05$ ;  $**P \leq 0.01$ ;  $***P \leq 0.001$ ;  $****P \leq 0.0001$ ). Spearman correlations describe salivary IgG2 and IgG4 responses against FcγR2a (**D**) and FcγR3a (**E**) engagement in the vaccinated only cohort ( $n = 20$ ) after three mRNA vaccines.

Plasma antibody comparisons after three antigen exposures

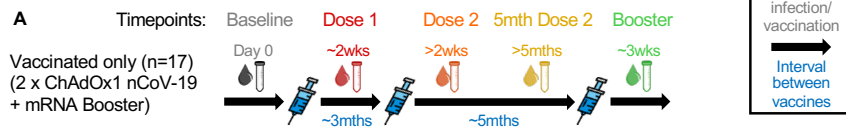


Comparisons of plasma anti-Spike 2 responses after mRNA boosters in vaccinated only cohort

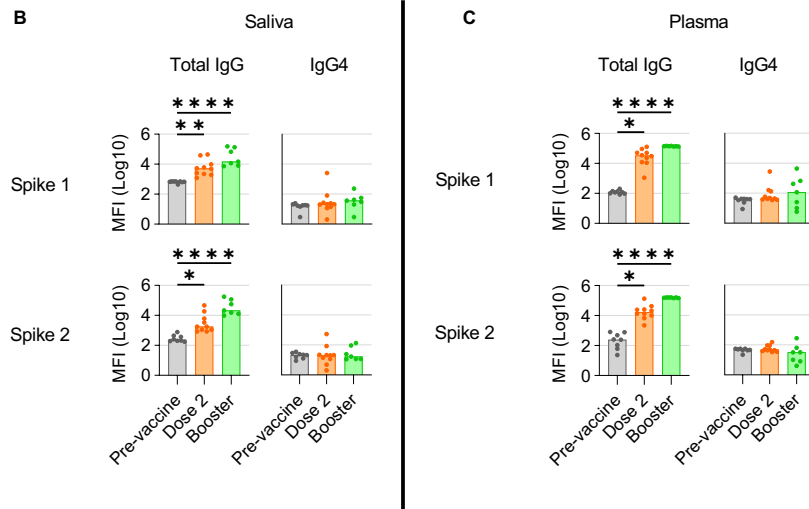


**Supplementary Figure 5: Plasma antibodies from vaccinated only vaccinees show strong IgG2 and IgG4 responses after receiving third COVID-19 mRNA vaccine.** PCA of all 40 antibody features for vaccinated only (closed circles) ( $n = 15$ ) and COVID-19 recovered (open squares) ( $n = 10$ ) individuals after three (A) antigen exposures. Loading plots and bar graphs describe the key differences between both cohorts after three antigen exposures (B and C). Statistical significance was calculated using the two-tailed Mann-Whitney  $U$  test and where significant or trending significance,  $P$ -values were reported ( $*P \leq 0.05$ ;  $**P \leq 0.01$ ;  $***P \leq 0.001$ ;  $****P \leq 0.0001$ ). Spearman correlations describe plasma IgG2 and IgG4 responses against FcγR2a (D) and FcγR3a (E) engagement in the vaccinated only cohort ( $n = 15$ ) after three mRNA vaccines.

ChAdOx1 nCoV-19 vaccinated cohort timepoints

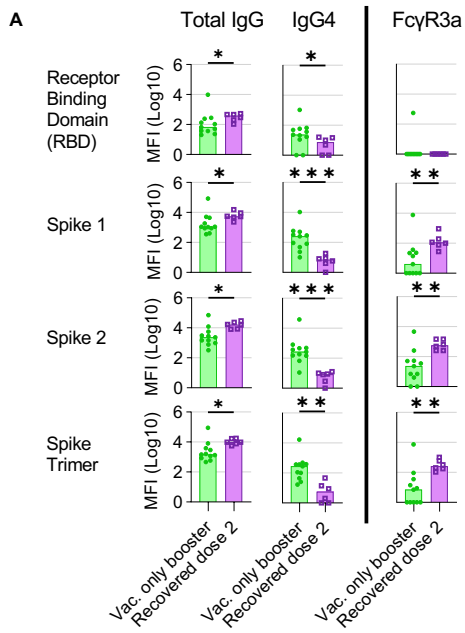


Saliva and plasma antibody signatures following ChAdOx1 nCoV-19 vaccination

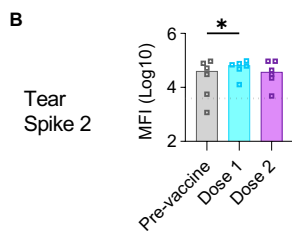


**Supplementary Figure 6: No changes in salivary or plasma IgG4 responses after repeated adenoviral vector COVID-19 vaccination.** Paired saliva and plasma samples were collected pre- and post-vaccination from vaccinated only vaccinees at the indicated time-points (A). Bar graphs illustrate the changes in total IgG and IgG4 responses against Spike 1 and Spike 2 respectively in saliva (B) and plasma (C) of vaccinated only vaccinees ( $n = 17$ ) after their second ChAdOx1 nCoV-19 vaccine (orange) or mRNA booster (green). Statistical significance was calculated using Friedman's test followed by Dunn's test for multiple comparisons. Where significant or trending significance,  $P$ -values were reported ( $*P \leq 0.05$ ;  $**P \leq 0.01$ ;  $***P \leq 0.001$ ;  $****P \leq 0.0001$ ).

Tear antibody comparisons after three antigen exposure



Tear IgA in COVID-19 recovered individuals following BNT162b2 vaccination

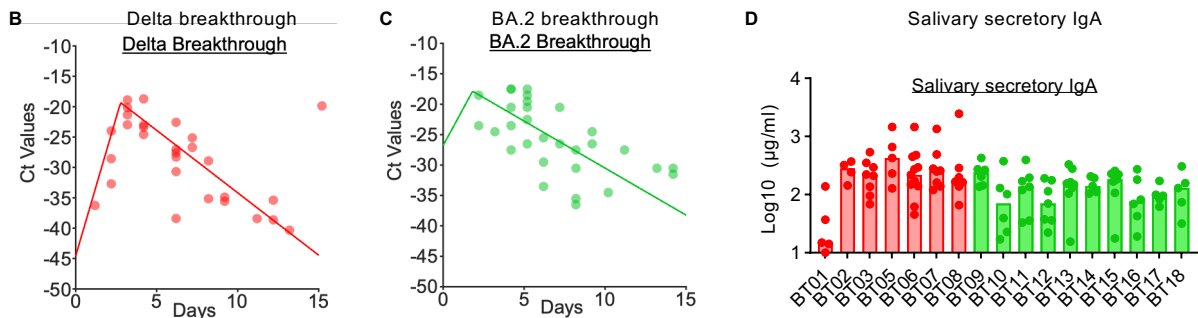


**Supplementary Figure 7: Tear antibody responses following COVID-19 vaccination corroborate with salivary responses.** Bar graphs describing key features in ancestral SARS-CoV-2 Spike-specific tear antibody responses between vaccinated only ( $n = 11$ ) and COVID-19 recovered cohorts ( $n = 6$ ) after three antigens exposures (**A**). Statistical significance was calculated using the two-tailed Mann-Whitney  $U$  test. Bar graphs also illustrate the changes in anti-Spike 2 IgA responses in tear fluid (**B**) of COVID-19 recovered individuals ( $n = 6$ ) after their first and second mRNA vaccination. Statistical significance was calculated using Friedman's test followed by Dunn's test for multiple comparisons. Where significant or trending significance,  $P$ -values were reported (\* $P \leq 0.05$ ; \*\* $P \leq 0.01$ ; \*\*\* $P \leq 0.001$ ; \*\*\*\* $P \leq 0.0001$ ).

Summary of breakthrough cohorts

| Variables                                                                    | Delta breakthroughs | Omicron BA.2 breakthroughs |
|------------------------------------------------------------------------------|---------------------|----------------------------|
|                                                                              | (n=8)               | (n=10)                     |
| Age, mean (range), years                                                     | 34.6 (19 – 58)      | 54.3 (40 – 66)             |
| Gender                                                                       |                     |                            |
| Female (%)                                                                   | 5 (62.5%)           | 5 (50.0%)                  |
| Male (%)                                                                     | 3 (37.5%)           | 5 (50.0%)                  |
| Vaccination doses prior to breakthrough infection (%)                        | 2 (100.0%)          | 3 (100.0%)                 |
| Time from last vaccination till breakthrough infection, mean (range), months | 3.3 (0.3 – 5.3)     | 3.2 (1.6 – 5.3)            |

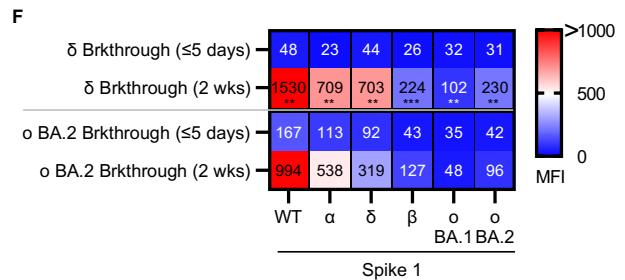
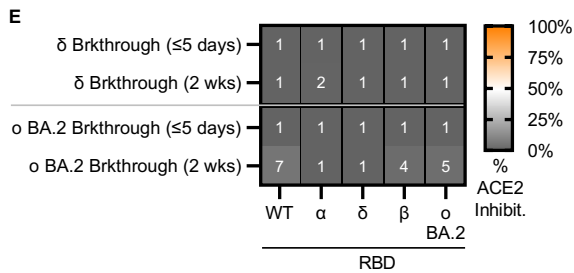
Breakthrough infections, viral load kinetics



Saliva SARS-CoV-2 VoC antibody signatures following breakthrough infections

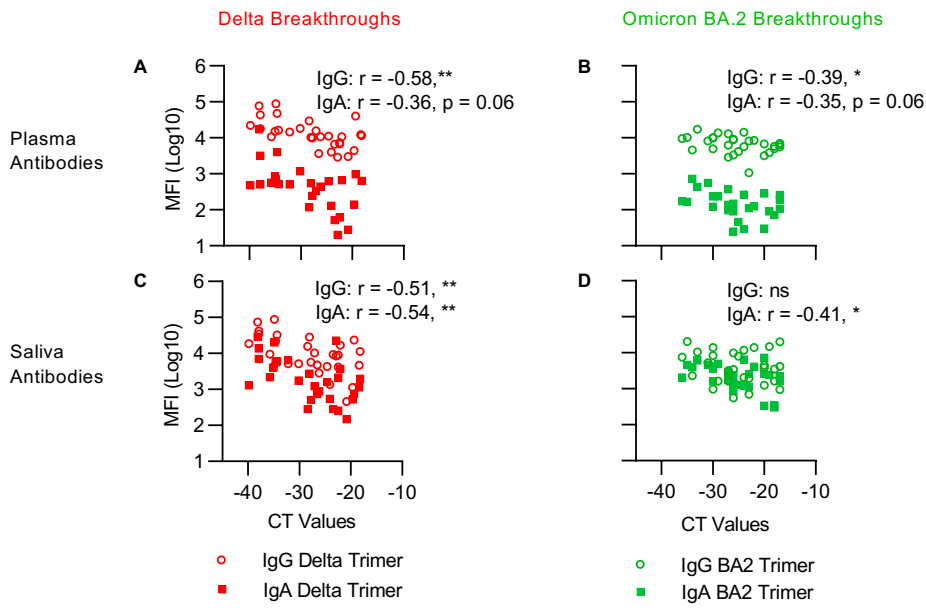
% ACE2 Inhibition (≤5 days vs 2 weeks post-onset)

FcγR3a Responses (≤5 days vs 2 weeks post-onset)



**Supplementary Figure 8: Viral load kinetics of breakthrough infections and influence of pre-existing vaccine-induced immunity on elicited antibody responses.** Details of vaccination status and samples collected for the COVID-19 breakthrough infection cohorts post symptom onset (A). Modelled kinetic curves describe the viral load (Ct value) post-symptom onset as determined by nasal swab samples collected during the Delta ( $n = 8$ ) (B) (Red) and Omicron BA.2 ( $n = 10$ ) (C) (Green) COVID-19 breakthrough waves. Bar graphs show the secretory IgA present in serially collected saliva samples from COVID-19 breakthrough individuals (D). Heat maps compare the salivary inhibition of RBD-ACE2 interactions against the ancestral wildtype (WT) SARS-CoV-2 or the VoCs ( $\alpha$ , Alpha;  $\delta$ , Delta;  $\beta$ , Beta; o BA.1, Omicron BA.1; o BA.2, Omicron BA.2) between the start and clearance of Delta ( $n = 8$ ) and Omicron BA.2 ( $n = 10$ ) COVID-19 breakthrough infections (E). Heat maps also describe the salivary antibody responses capable of Fc $\gamma$ R3a engagement that are elicited early and 2 weeks post-symptom onset of Delta ( $n = 8$ ) and Omicron BA.2 ( $n = 10$ ) COVID-19 breakthrough infections (F). Significant differences between both timepoints were calculated using Friedman's test followed by Dunn's test for multiple comparisons. Where significant or trending significance,  $P$ -values were reported ( $*P \leq 0.05$ ;  $**P \leq 0.01$ ;  $***P \leq 0.001$ ;  $****P \leq 0.0001$ ).

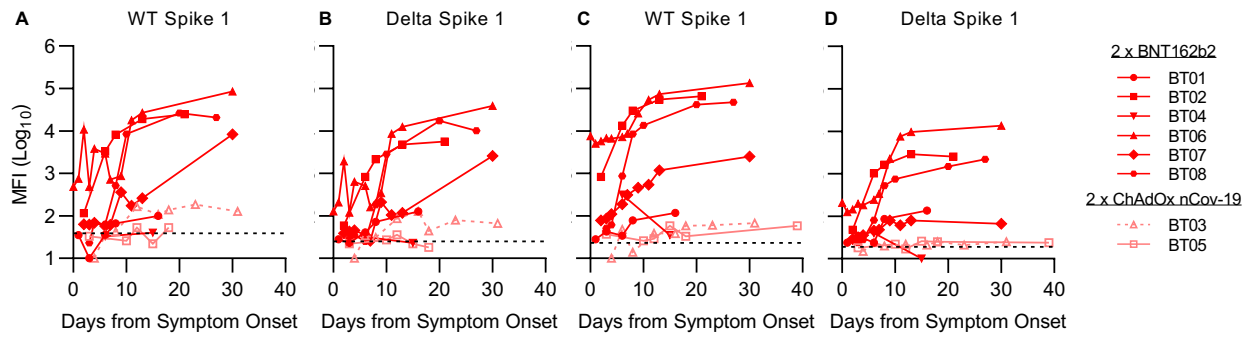
Breakthrough infections, comparison of antibody responses vs viral load



**Supplementary Figure 9: Correlations of antibody responses and viral load post-breakthrough infections.** Spearman correlation of plasma (**A and B**) and saliva (**C and D**) IgG (open circles) and IgA (closed squares) responses against viral load (Ct value) in the Delta ( $n = 8$ ) (**A and C**) (Red) and Omicron BA.2 ( $n = 10$ ) (**B and D**) (Green) COVID-19 breakthrough waves. Where significant or trending significance,  $P$ -values were reported ( $*P \leq 0.05$ ;  $**P \leq 0.01$ ;  $***P \leq 0.001$ ;  $****P \leq 0.0001$ ).

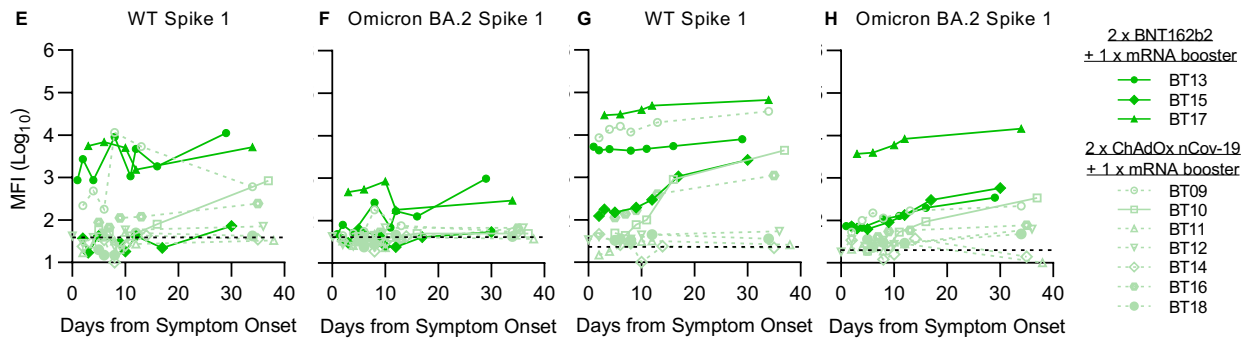
Saliva IgG4 responses to Delta breakthroughs

Plasma IgG4 responses to Delta breakthroughs



Saliva IgG4 responses to Omicron BA.2 breakthroughs

Plasma IgG4 responses to Omicron Ba.2 breakthroughs

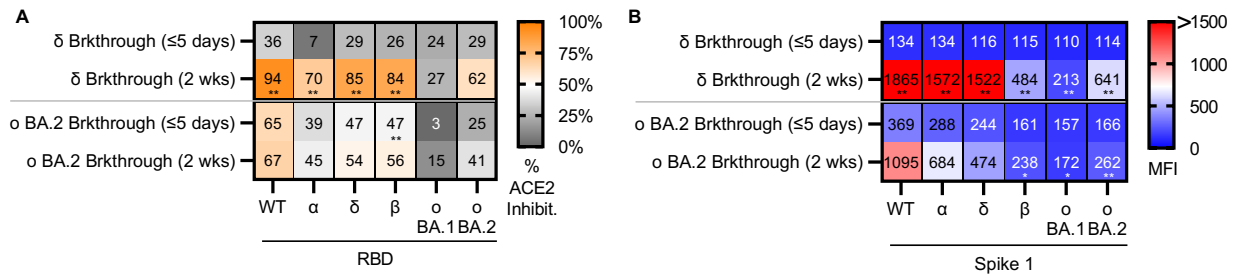


**Supplementary figure 10: IgG4 anti-Spike 1 responses following breakthrough infection.** Line graphs describe the salivary (A, B, E and F) and plasma (C, D, G and H) IgG4 responses post symptom onset against ancestral wildtype (WT) SARS-CoV-2 (A, C, E and G), Delta (B and D) or Omicron BA.2 Spike 1 (F and H) respectively after Delta ( $n = 8$ ) (A-D) and Omicron BA.2 ( $n = 10$ ) (E-H) breakthrough infections. Solid lines depict individuals who received multiple mRNA vaccines (2 x BNT162b2; 2 x BNT162b2 + 1 x mRNA booster), while dotted lines depict individuals who did not receive mRNA vaccines (2 x ChAdOx nCov-19) or only received a single mRNA booster (2 x ChAdOx nCov-19 + 1 x mRNA booster).

Plasma SARS-CoV-2 VoC antibody signatures following breakthrough infections

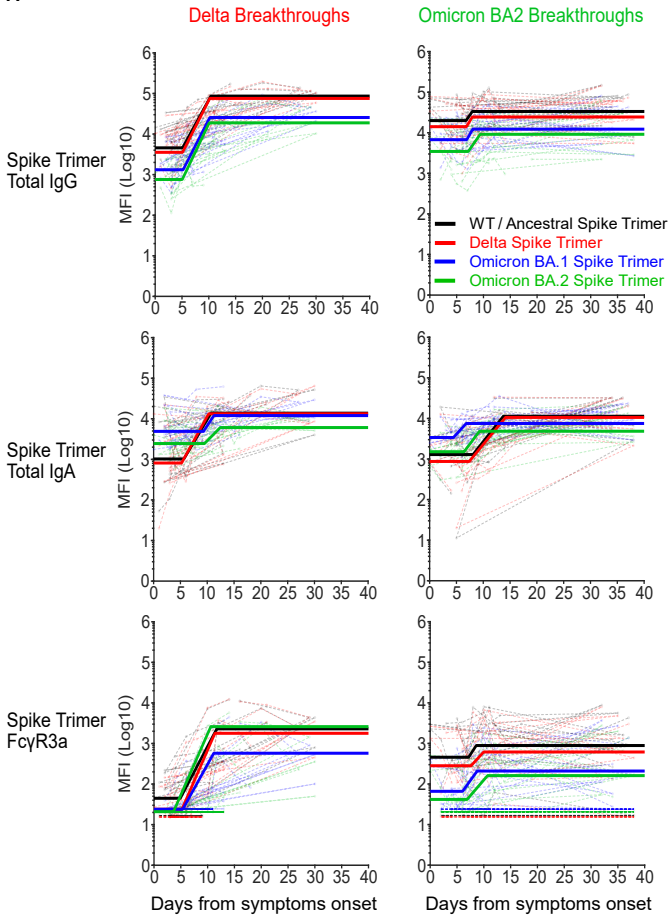
% ACE2 Inhibition (≤5 days vs 2 weeks)

FcγR3a Responses (≤5 days vs 2 weeks)

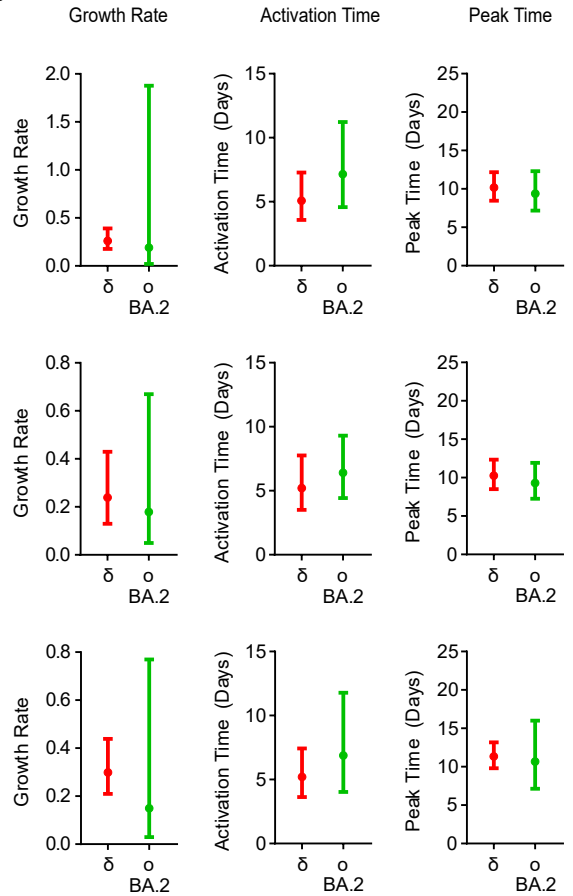


**Supplementary Figure 11: Plasma antibody signatures following breakthrough infections.** Heat maps compare the plasma inhibition of RBD-ACE2 interactions against the ancestral wildtype (WT) SARS-CoV-2 or the VoCs (α, Alpha; δ, Delta; β, Beta; o BA.1, Omicron BA.1; o BA.2, Omicron BA.2) between the start and clearance of Delta ( $n = 8$ ) and Omicron BA.2 ( $n = 10$ ) COVID-19 breakthrough infections (**A**). Heat maps also describe the plasma antibody responses capable of FcγR3a engagement that are elicited early and 2 weeks post-symptom onset of Delta ( $n = 8$ ) and Omicron BA.2 ( $n = 10$ ) COVID-19 breakthrough infections (**B**). Significant differences between both timepoints were calculated using Friedman's test followed by Dunn's test for multiple comparisons. Where significant or trending significance,  $P$ -values were reported ( $*P \leq 0.05$ ;  $**P \leq 0.01$ ;  $***P \leq 0.001$ ;  $****P \leq 0.0001$ ).

A

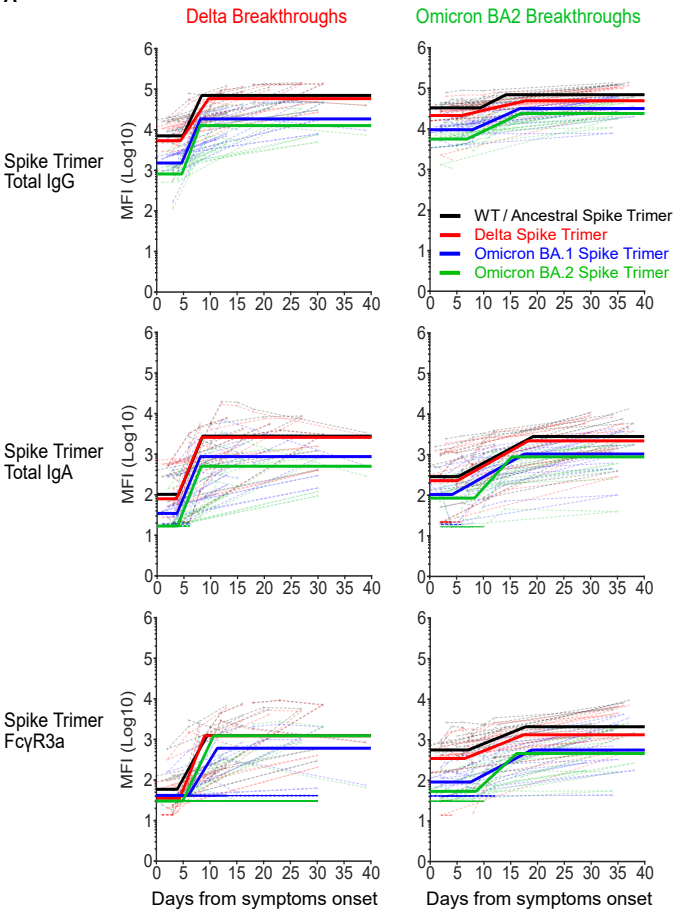


B

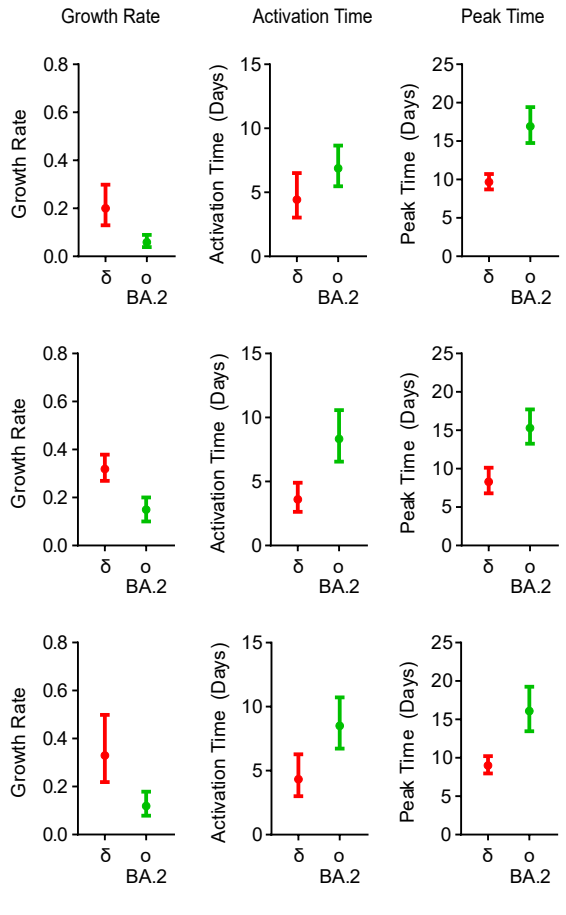


**Supplementary Figure 12: Pre-existing vaccine-induced immunity modulate salivary antibody kinetics against Spike trimer during COVID-19 breakthrough infections.** Modelled kinetic curves (WT: black; Delta: red; Omicron BA.1: blue; Omicron BA.2: green) describe the ancestral wildtype and variant-specific Spike Trimer antibody responses from serially collected saliva samples during Delta ( $n = 8$ ) or Omicron BA.2 ( $n = 10$ ) breakthrough infection for up to 40 days post-symptom onset (A). Connected dotted lines indicate serial samples from the same individual. Lines with open circles at the bottom of each graph reflect samples that were excluded from the model for being below the threshold of detection (2 S.D. background readings). Dot plots displaying 95% confidence intervals beside each row of kinetic curves list the calculated growth rate, time to activation and time to peak of variant-specific salivary responses (Delta: red; Omicron BA.2: green) by their respective breakthrough cohorts (eg: Delta variant responses during the Delta breakthroughs) (B).

**A**

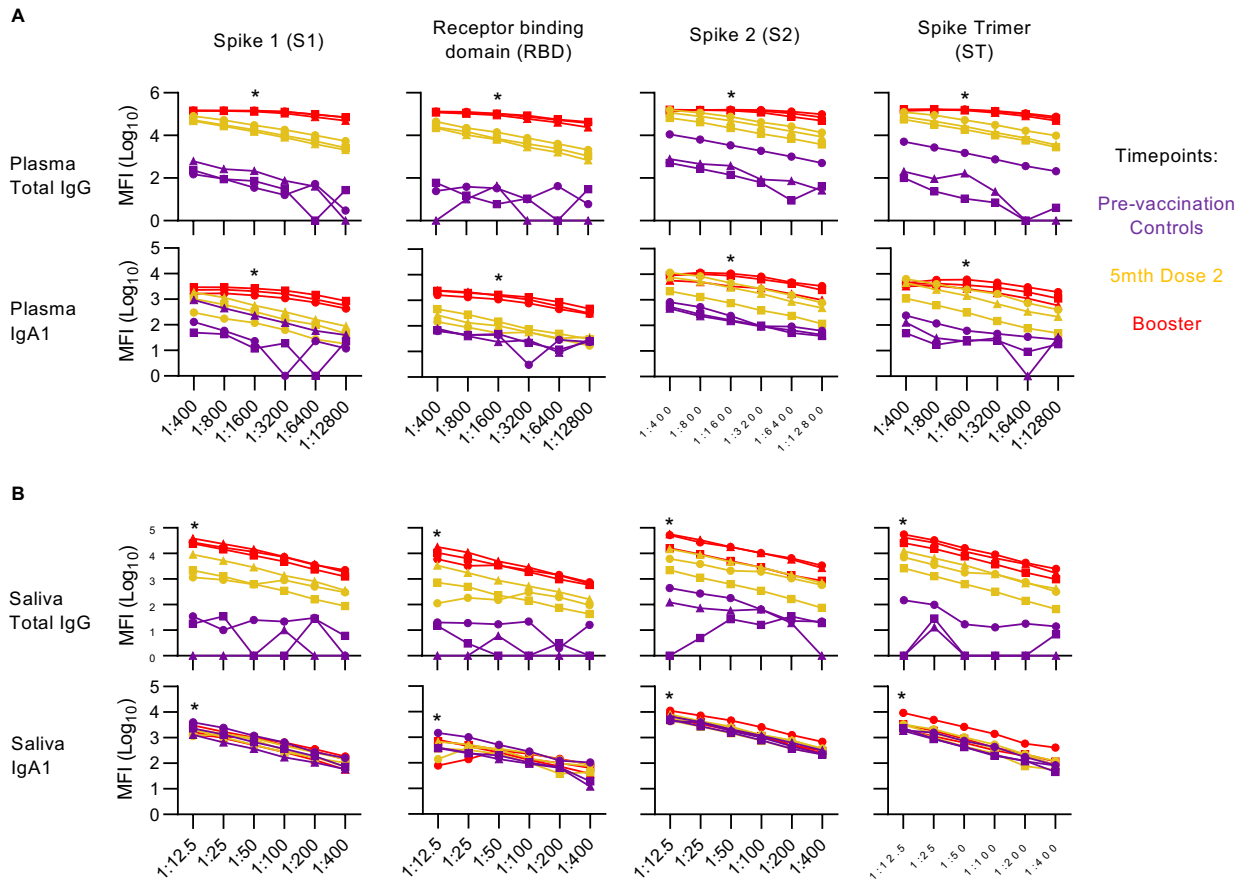


**B**

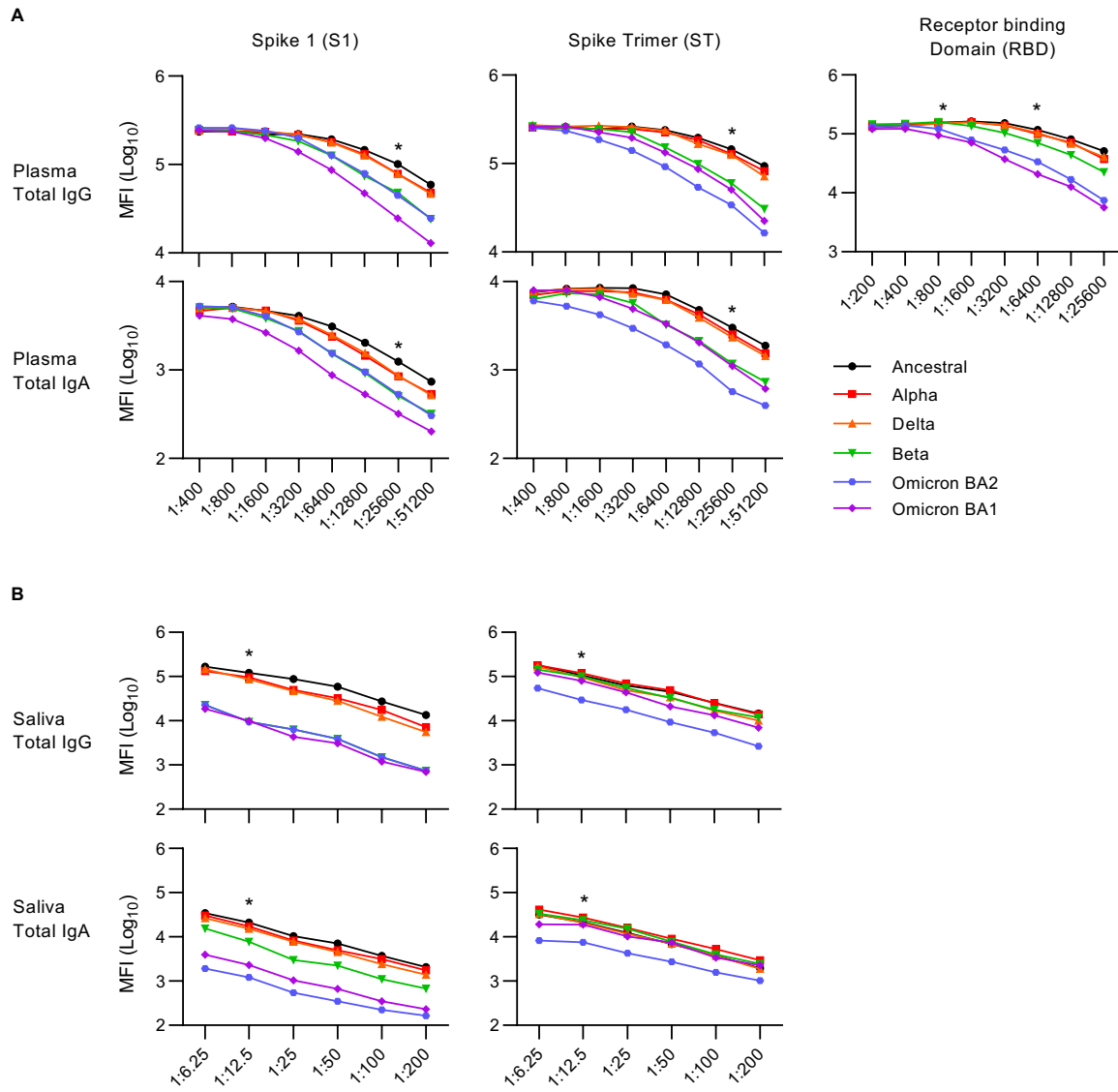


**Supplementary Figure 13: Plasma antibody responses show delayed kinetics during Omicron BA.2 breakthrough infections.**

Modelled kinetic curves (WT: black; Delta: red; Omicron BA.1: blue; Omicron BA.2: green) describe the ancestral wildtype and variant-specific Spike Trimer antibody responses from serially collected plasma samples during Delta ( $n = 8$ ) or Omicron BA.2 ( $n = 10$ ) breakthrough infection for up to 40 days post-symptom onset (A). Connected dotted lines indicate serial samples from the same individual. Lines with open circles at the bottom of each graph reflect samples that were excluded from the model for being below the threshold of detection (2 S.D. background readings). Dot plots displaying 95% confidence intervals beside each row of kinetic curves list the calculated growth rate, time to activation and time to peak of variant-specific plasma responses (Delta: red; Omicron BA.2: green) by their respective breakthrough cohorts (eg: Delta variant responses during the Delta breakthroughs) (B).



**Supplementary Figure 14: Titration curves for SARS-CoV-2 ancestral Spike coupled arrays.** Titration curves depict the plasma (A) and salivary (B) total IgG and IgA responses against ancestral wildtype (WT) Spike antigens using samples from three vaccinated individuals at the respective timepoints. Asterisks define the respective dilutions chosen for the multiplex assays.



**Supplementary Figure 15: Titration curves for SARS-CoV-2 variant Spike coupled arrays.** Titration curves depict the plasma (**A**) and salivary (**B**) total IgG and IgA responses against ancestral wildtype (WT) Spike and the VoC Spikes using pooled plasma from COVID-19 boosted individuals and the saliva sample from a boosted individual who seroconverted strongly during their Delta breakthrough infection. Asterisks define the respective dilutions chosen for the multiplex assays.

Supplementary Table 1: Cohort information for COVID-19 vaccinees (V) and uninfected, unvaccinated controls (P)

| Donor: | Gender: | Age:         | Time from previous COVID-19 (days): | 1st vaccine dose: | Timepoint post 1st dose (days): | Time between 1st and 2nd dose: | 2nd vaccine dose: | Timepoint post 2nd dose (days): | Extended timepoint post 2nd dose (days) | 3rd vaccine dose: | Timepoint post 3rd dose (days): |
|--------|---------|--------------|-------------------------------------|-------------------|---------------------------------|--------------------------------|-------------------|---------------------------------|-----------------------------------------|-------------------|---------------------------------|
| V01    | F       | In their 50s | n.d.                                | BNT162b2          | n.d.                            | 22                             | BNT162b2          | 12                              | 224                                     | BNT162b2          | 11                              |
| V02    | M       | In their 30s | n.d.                                | BNT162b2          | 11                              | 23                             | BNT162b2          | 13                              | 225                                     | mRNA-1273         | 11                              |
| V03    | F       | In their 20s | n.d.                                | BNT162b2          | 10                              | 22                             | BNT162b2          | 13                              | n.d.                                    | n.d.              | n.d.                            |
| V04    | F       | In their 20s | n.d.                                | BNT162b2          | 9                               | 21                             | BNT162b2          | 13                              | 225                                     | BNT162b2          | 14                              |
| V05    | M       | In their 30s | n.d.                                | BNT162b2          | n.d.                            | 27                             | BNT162b2          | 14                              | 219                                     | BNT162b2          | 11                              |
| V06    | F       | In their 30s | n.d.                                | BNT162b2          | 9                               | 28                             | BNT162b2          | 13                              | n.d.                                    | n.d.              | n.d.                            |
| V07    | F       | In their 30s | n.d.                                | BNT162b2          | 8                               | 21                             | BNT162b2          | 12                              | 224                                     | BNT162b2          | 13                              |
| V08    | F       | In their 30s | n.d.                                | BNT162b2          | n.d.                            | 29                             | BNT162b2          | 13                              | 217                                     | BNT162b2          | 15                              |
| V09    | F       | In their 20s | n.d.                                | BNT162b2          | 10                              | 24                             | BNT162b2          | 18                              | 223                                     | BNT162b2          | 10                              |
| V10    | F       | In their 20s | n.d.                                | BNT162b2          | n.d.                            | 33                             | BNT162b2          | 14                              | 213                                     | BNT162b2          | 14                              |
| V11    | M       | In their 30s | n.d.                                | BNT162b2          | 10                              | 22                             | BNT162b2          | 13                              | 225                                     | BNT162b2          | 10                              |
| V12    | F       | In their 30s | n.d.                                | BNT162b2          | 10                              | 22                             | BNT162b2          | 13                              | 225                                     | BNT162b2          | 13                              |
| V13    | M       | In their 30s | n.d.                                | BNT162b2          | 6                               | 23                             | BNT162b2          | 15                              | n.d.                                    | n.d.              | n.d.                            |
| V14    | F       | In their 30s | n.d.                                | BNT162b2          | 6                               | 23                             | BNT162b2          | 15                              | 220                                     | BNT162b2          | 14                              |
| V15    | M       | In their 30s | n.d.                                | BNT162b2          | n.d.                            | 21                             | BNT162b2          | 13                              | 225                                     | BNT162b2          | 13                              |
| V16    | F       | In their 50s | n.d.                                | BNT162b2          | 7                               | 21                             | BNT162b2          | 13                              | 225                                     | mRNA-1273         | 11                              |
| V17    | M       | In their 30s | n.d.                                | BNT162b2          | 10                              | 21                             | BNT162b2          | 14                              | 226                                     | BNT162b2          | 13                              |
| V18    | M       | In their 40s | n.d.                                | BNT162b2          | 12                              | 33                             | BNT162b2          | 22                              | n.d.                                    | n.d.              | n.d.                            |
| V19    | F       | In their 30s | n.d.                                | BNT162b2          | n.d.                            | 23                             | BNT162b2          | n.d.                            | 197                                     | BNT162b2          | 15                              |
| V20    | F       | In their 30s | n.d.                                | BNT162b2          | n.d.                            | 21                             | BNT162b2          | n.d.                            | 188                                     | BNT162b2          | 10                              |
| V21    | F       | In their 20s | n.d.                                | ChAdOx nCoV-19    | 15                              | 85                             | ChAdOx nCoV-19    | 14                              | 168                                     | mRNA-1273         | 14                              |
| V22    | F       | In their 50s | n.d.                                | ChAdOx nCoV-19    | 13                              | 85                             | ChAdOx nCoV-19    | 12                              | n.d.                                    | n.d.              | n.d.                            |
| V23    | M       | In their 50s | n.d.                                | ChAdOx nCoV-19    | 13                              | 80                             | ChAdOx nCoV-19    | 17                              | n.d.                                    | n.d.              | n.d.                            |
| V24    | F       | In their 60s | n.d.                                | ChAdOx nCoV-19    | 22                              | 84                             | ChAdOx nCoV-19    | 14                              | n.d.                                    | n.d.              | n.d.                            |
| V25    | M       | In their 60s | n.d.                                | ChAdOx nCoV-19    | 14                              | 70                             | ChAdOx nCoV-19    | 7                               | n.d.                                    | n.d.              | n.d.                            |





Supplementary Table 2. Cohort of SARS-CoV-2 breakthrough infections

| Donor: | Age:           | Gender: | Vaccination History:                | Time from last vaccination till breakthrough infection (months): | Timepoints post onset for plasma / saliva samples (bold: incl. nasal swabs): | Breakthrough VoC |
|--------|----------------|---------|-------------------------------------|------------------------------------------------------------------|------------------------------------------------------------------------------|------------------|
| BT01   | In their 50s   | F       | 2 x BNT162b2                        | 5.3                                                              | <b>1, 3, 6, 8, 16</b>                                                        | Delta            |
| BT02   | In their 30s   | M       | 2 x BNT162b2                        | 4.3                                                              | <b>2, 6, 8, 13, 21</b>                                                       | Delta            |
| BT03   | In their 50s   | F       | 2 x ChAdOx nCoV-19                  | 3                                                                | <b>4, 6, 8, 12, 16, 18, 23, 31</b>                                           | Delta            |
| BT04   | In their teens | F       | 2 x BNT162b2                        | 0.3                                                              | <b>6, 15</b>                                                                 | Delta            |
| BT05   | In their 20s   | M       | 2 x ChAdOx nCoV-19                  | 1                                                                | 3, 10, <b>12, 15, 18, 39</b>                                                 | Delta            |
| BT06   | In their 30s   | F       | 2 x BNT162b2                        | 4.6                                                              | 0, <b>1, 2, 3, 4, 6, 7, 9, 11, 13, 30</b>                                    | Delta            |
| BT07   | In their 30s   | F       | 2 x BNT162b2                        | 3.6                                                              | <b>2, 3, 4, 6, 7, 9, 11, 13, 30</b>                                          | Delta            |
| BT08   | In their 20s   | M       | 2 x BNT162b2                        | 4.3                                                              | <b>3, 4, 6, 8, 10, 20, 27</b>                                                | Delta            |
| BT09   | In their 50s   | F       | 2 x ChAdOx nCoV-19<br>1 x mRNA-1273 | 4.3                                                              | <b>2, 4, 6, 8, 13, 34</b>                                                    | Omicron BA.2     |
| BT10   | In their 50s   | M       | 2 x ChAdOx nCoV-19<br>1 x mRNA-1273 | 4                                                                | <b>5, 7, 9, 11, 16, 37</b>                                                   | Omicron BA.2     |
| BT11   | In their 50s   | F       | 2 x ChAdOx nCoV-19<br>1 x mRNA-1273 | 5.3                                                              | <b>2, 4, 8, 10, 12, 38</b>                                                   | Omicron BA.2     |
| BT12   | In their 60s   | M       | 2 x ChAdOx nCoV-19<br>1 x mRNA-1273 | 2.6                                                              | 0, <b>2, 6, 8, 10, 36</b>                                                    | Omicron BA.2     |
| BT13   | In their 40s   | F       | 3 x BNT162b2                        | 4                                                                | <b>1, 2, 4, 8, 11, 16, 29</b>                                                | Omicron BA.2     |
| BT14   | In their 50s   | F       | 2 x ChAdOx nCoV-19<br>1 x mRNA-1273 | 2                                                                | <b>2, 6, 8, 10, 14, 35</b>                                                   | Omicron BA.2     |
| BT15   | In their 40s   | M       | 3 x BNT162b2                        | 1.6                                                              | <b>2, 3, 5, 9, 12, 17, 30</b>                                                | Omicron BA.2     |
| BT16   | In their 60s   | M       | 2 x ChAdOx nCoV-19<br>1 x mRNA-1273 | 3.3                                                              | <b>5, 7, 9, 13, 35</b>                                                       | Omicron BA.2     |
| BT17   | In their 40s   | F       | 2 x BNT162b2<br>1 x mRNA-1273       | 3                                                                | <b>3, 6, 10, 12, 34</b>                                                      | Omicron BA.2     |
| BT18   | In their 60s   | M       | 2 x ChAdOx nCoV-19<br>1 x BNT162b2  | 1.6                                                              | <b>5, 6, 8, 12, 34</b>                                                       | Omicron BA.2     |

Supplementary Table 3: Parameters and confidence intervals for modelled kinetic curves of COVID-19 breakthrough cohorts

## Delta breakthrough cohort (Plasma)

| Sample: Plasma<br>Detector: Pan IgG | WT Spike 1      |          |           | Delta Spike 1      |          |           | BA1 Spike 1      |          |          | BA2 Spike 1      |          |          |
|-------------------------------------|-----------------|----------|-----------|--------------------|----------|-----------|------------------|----------|----------|------------------|----------|----------|
|                                     | Lower CI        | Mean     | Upper CI  | Lower CI           | Mean     | Upper CI  | Lower CI         | Mean     | Upper CI | Lower CI         | Mean     | Upper CI |
| Initial MFI:                        | 2452.00         | 4570.88  | 8520.79   | 1450.37            | 2691.53  | 4994.82   | 147.64           | 416.87   | 1177.06  | 474.68           | 977.24   | 2011.87  |
| Growth rate:                        | 0.18            | 0.26     | 0.37      | 0.24               | 0.32     | 0.43      | 0.35             | 0.49     | 0.68     | 0.35             | 0.46     | 0.60     |
| Activation time (days):             | 3.25            | 4.31     | 5.70      | 3.37               | 4.26     | 5.39      | 3.72             | 4.48     | 5.40     | 3.67             | 4.44     | 5.37     |
| Peak time (days):                   | 7.35            | 8.58     | 10.03     | 7.08               | 8.17     | 9.42      | 6.40             | 7.39     | 8.54     | 6.46             | 7.39     | 8.45     |
| Maximum MFI:                        | 60022.75        | 80786.00 | 108731.74 | 40682.38           | 58140.08 | 83089.26  | 7549.81          | 12057.31 | 19255.94 | 15847.52         | 25655.55 | 41533.76 |
| Sample: Plasma<br>Detector: Pan IgG | WT Spike Trimer |          |           | Delta Spike Trimer |          |           | BA1 Spike Trimer |          |          | BA2 Spike Trimer |          |          |
|                                     | Lower CI        | Mean     | Upper CI  | Lower CI           | Mean     | Upper CI  | Lower CI         | Mean     | Upper CI | Lower CI         | Mean     | Upper CI |
| Initial MFI:                        | 3533.13         | 7079.46  | 14185.35  | 2340.78            | 5370.32  | 12320.83  | 731.88           | 1513.56  | 3130.11  | 426.30           | 812.83   | 1549.82  |
| Growth rate:                        | 0.22            | 0.28     | 0.37      | 0.13               | 0.20     | 0.30      | 0.24             | 0.31     | 0.41     | 0.27             | 0.35     | 0.47     |
| Activation time (days):             | 3.79            | 4.90     | 6.34      | 3.03               | 4.44     | 6.50      | 3.69             | 4.66     | 5.90     | 3.79             | 4.71     | 5.86     |
| Peak time (days):                   | 7.27            | 8.41     | 9.74      | 8.74               | 9.68     | 10.72     | 7.05             | 8.17     | 9.46     | 7.04             | 8.08     | 9.28     |
| Maximum MFI:                        | 63778.05        | 87397.54 | 119764.24 | 52597.18           | 75669.39 | 108862.42 | 19256.18         | 29932.47 | 46528.08 | 11581.74         | 19694.09 | 33488.68 |
| Sample: Plasma<br>Detector: IgA     | WT Spike 1      |          |           | Delta Spike 1      |          |           | BA1 Spike 1      |          |          | BA2 Spike 1      |          |          |
|                                     | Lower CI        | Mean     | Upper CI  | Lower CI           | Mean     | Upper CI  | Lower CI         | Mean     | Upper CI | Lower CI         | Mean     | Upper CI |
| Initial MFI:                        | 29.96           | 50.12    | 83.84     | 11.71              | 19.95    | 33.98     | 10.47            | 10.47    | 10.47    | 14.45            | 14.45    | 14.45    |
| Growth rate:                        | 0.26            | 0.31     | 0.36      | 0.28               | 0.46     | 0.76      | 0.21             | 0.48     | 1.09     | 0.17             | 0.55     | 1.80     |
| Activation time (days):             | 2.69            | 4.06     | 6.12      | 3.08               | 4.18     | 5.66      | 3.77             | 4.85     | 6.25     | 2.60             | 3.82     | 5.61     |
| Peak time (days):                   | 7.50            | 8.94     | 10.65     | 6.51               | 7.69     | 9.09      | 6.44             | 7.32     | 8.31     | 5.69             | 7.17     | 9.04     |
| Maximum MFI:                        | 1139.05         | 3602.69  | 11394.95  | 731.38             | 2240.54  | 6863.79   | 59.48            | 202.24   | 687.63   | 144.51           | 506.60   | 1776.00  |
| Sample: Plasma<br>Detector: IgA     | WT Spike Trimer |          |           | Delta Spike Trimer |          |           | BA1 Spike Trimer |          |          | BA2 Spike Trimer |          |          |
|                                     | Lower CI        | Mean     | Upper CI  | Lower CI           | Mean     | Upper CI  | Lower CI         | Mean     | Upper CI | Lower CI         | Mean     | Upper CI |
| Initial MFI:                        | 40.39           | 102.33   | 259.27    | 27.75              | 79.43    | 227.34    | 17.38            | 34.67    | 69.16    | 16.98            | 16.98    | 16.98    |
| Growth rate:                        | 0.26            | 0.32     | 0.40      | 0.27               | 0.32     | 0.38      | 0.21             | 0.32     | 0.48     | 0.19             | 0.33     | 0.57     |
| Activation time (days):             | 2.97            | 4.01     | 5.43      | 2.63               | 3.60     | 4.91      | 2.52             | 3.71     | 5.44     | 2.51             | 3.78     | 5.70     |
| Peak time (days):                   | 7.08            | 8.50     | 10.21     | 6.83               | 8.33     | 10.15     | 6.93             | 8.08     | 9.44     | 7.06             | 8.25     | 9.64     |
| Maximum MFI:                        | 2715.44         | 6904.71  | 17557.04  | 2572.90            | 6526.89  | 16557.30  | 784.21           | 2646.87  | 8933.70  | 422.03           | 1412.80  | 4729.51  |
| Sample: Plasma<br>Detector: FcγR3a  | WT Spike 1      |          |           | Delta Spike 1      |          |           | BA1 Spike 1      |          |          | BA2 Spike 1      |          |          |
|                                     | Lower CI        | Mean     | Upper CI  | Lower CI           | Mean     | Upper CI  | Lower CI         | Mean     | Upper CI | Lower CI         | Mean     | Upper CI |
| Initial MFI:                        | 10.58           | 22.39    | 47.35     | 7.73               | 7.73     | 7.73      | 7.00             | 7.00     | 7.00     | 12.02            | 12.02    | 12.02    |
| Growth rate:                        | 0.29            | 0.41     | 0.58      | 0.39               | 0.63     | 1.02      | 0.29             | 0.71     | 1.74     | 0.32             | 0.72     | 1.59     |
| Activation time (days):             | 3.04            | 4.14     | 5.63      | 3.18               | 4.26     | 5.72      | 4.23             | 5.16     | 6.28     | 3.69             | 4.62     | 5.77     |
| Peak time (days):                   | 7.43            | 8.58     | 9.92      | 6.88               | 7.85     | 8.95      | 6.13             | 6.89     | 7.74     | 6.13             | 6.89     | 7.75     |
| Maximum MFI:                        | 1149.22         | 2440.14  | 5181.15   | 500.78             | 1307.45  | 3413.48   | 34.33            | 81.56    | 193.77   | 80.78            | 289.76   | 1039.33  |
| Sample: Plasma<br>Detector: FcγR3a  | WT Spike Trimer |          |           | Delta Spike Trimer |          |           | BA1 Spike Trimer |          |          | BA2 Spike Trimer |          |          |
|                                     | Lower CI        | Mean     | Upper CI  | Lower CI           | Mean     | Upper CI  | Lower CI         | Mean     | Upper CI | Lower CI         | Mean     | Upper CI |
| Initial MFI:                        | 19.93           | 58.88    | 173.94    | 15.26              | 35.48    | 82.51     | 41.69            | 41.69    | 41.69    | 30.20            | 30.20    | 30.20    |
| Growth rate:                        | 0.14            | 0.24     | 0.39      | 0.22               | 0.33     | 0.50      | 0.12             | 0.22     | 0.40     | 0.17             | 0.28     | 0.46     |
| Activation time (days):             | 3.06            | 3.90     | 4.97      | 3.01               | 4.35     | 6.29      | 4.99             | 5.99     | 7.19     | 4.11             | 4.90     | 5.85     |
| Peak time (days):                   | 7.97            | 9.49     | 11.29     | 7.96               | 9.03     | 10.23     | 9.77             | 11.36    | 13.21    | 9.28             | 10.70    | 12.34    |
| Maximum MFI:                        | 1280.79         | 2880.93  | 6480.22   | 889.36             | 2214.45  | 5513.83   | 206.32           | 569.38   | 1571.34  | 116.46           | 360.96   | 1118.75  |

Delta breakthrough cohort (Saliva)

| Sample: Saliva<br>Detector: Pan IgG | WT Spike 1      |          |           | Delta Spike 1      |          |           | BA1 Spike 1      |          |          | BA2 Spike 1      |          |          |
|-------------------------------------|-----------------|----------|-----------|--------------------|----------|-----------|------------------|----------|----------|------------------|----------|----------|
|                                     | Lower CI        | Mean     | Upper CI  | Lower CI           | Mean     | Upper CI  | Lower CI         | Mean     | Upper CI | Lower CI         | Mean     | Upper CI |
| Initial MFI:                        | 1456.26         | 2630.27  | 4750.73   | 757.74             | 1412.54  | 2633.18   | 83.96            | 208.93   | 519.90   | 196.01           | 398.11   | 808.57   |
| Growth rate:                        | 0.23            | 0.28     | 0.33      | 0.15               | 0.32     | 0.67      | 0.26             | 0.36     | 0.51     | 0.18             | 0.40     | 0.90     |
| Activation time (days):             | 3.24            | 4.81     | 7.14      | 3.21               | 4.81     | 7.20      | 2.03             | 4.18     | 8.61     | 2.03             | 4.39     | 9.51     |
| Peak time (days):                   | 8.61            | 10.07    | 11.79     | 6.98               | 9.87     | 13.97     | 7.72             | 9.12     | 10.77    | 7.36             | 8.94     | 10.85    |
| Maximum MFI:                        | 52419.76        | 82960.99 | 131296.40 | 34349.48           | 59621.86 | 103488.23 | 8189.38          | 15292.07 | 28554.98 | 15572.19         | 29617.63 | 56331.43 |
| Sample: Saliva<br>Detector: Pan IgG | WT Spike Trimer |          |           | Delta Spike Trimer |          |           | BA1 Spike Trimer |          |          | BA2 Spike Trimer |          |          |
|                                     | Lower CI        | Mean     | Upper CI  | Lower CI           | Mean     | Upper CI  | Lower CI         | Mean     | Upper CI | Lower CI         | Mean     | Upper CI |
| Initial MFI:                        | 2333.24         | 4570.88  | 8954.47   | 1778.77            | 3548.13  | 7077.50   | 791.63           | 1318.26  | 2195.23  | 453.48           | 758.58   | 1268.94  |
| Growth rate:                        | 0.16            | 0.24     | 0.37      | 0.18               | 0.26     | 0.39      | 0.18             | 0.26     | 0.38     | 0.22             | 0.28     | 0.35     |
| Activation time (days):             | 3.56            | 5.10     | 7.32      | 3.58               | 5.10     | 7.28      | 3.58             | 5.21     | 7.57     | 3.74             | 5.05     | 6.82     |
| Peak time (days):                   | 8.32            | 10.38    | 12.95     | 8.49               | 10.18    | 12.19     | 8.30             | 10.18    | 12.48    | 8.74             | 10.07    | 11.61    |
| Maximum MFI:                        | 59092.74        | 83926.20 | 119195.80 | 48672.35           | 72419.92 | 107754.08 | 19554.12         | 31559.85 | 50936.77 | 11795.82         | 21236.87 | 38234.29 |
| Sample: Saliva<br>Detector: IgA     | WT Spike 1      |          |           | Delta Spike 1      |          |           | BA1 Spike 1      |          |          | BA2 Spike 1      |          |          |
|                                     | Lower CI        | Mean     | Upper CI  | Lower CI           | Mean     | Upper CI  | Lower CI         | Mean     | Upper CI | Lower CI         | Mean     | Upper CI |
| Initial MFI:                        | 1277.50         | 2089.30  | 3416.96   | 586.81             | 870.96   | 1292.71   | 12.02            | 12.02    | 12.02    | 7.80             | 19.05    | 46.57    |
| Growth rate:                        | 0.18            | 0.32     | 0.56      | 0.13               | 0.28     | 0.60      | 0.21             | 0.32     | 0.49     | 0.20             | 0.35     | 0.62     |
| Activation time (days):             | 6.41            | 7.39     | 8.52      | 5.64               | 7.10     | 8.93      | 4.55             | 6.05     | 8.04     | 3.78             | 5.58     | 8.25     |
| Peak time (days):                   | 8.50            | 9.49     | 10.59     | 8.76               | 9.97     | 11.35     | 8.27             | 9.12     | 10.05    | 8.50             | 10.38    | 12.68    |
| Maximum MFI:                        | 12793.77        | 24412.07 | 46581.21  | 24012.78           | 37021.41 | 57077.32  | 5170.17          | 8866.42  | 15205.17 | 6382.85          | 11109.55 | 19336.50 |
| Sample: Saliva<br>Detector: IgA     | WT Spike Trimer |          |           | Delta Spike Trimer |          |           | BA1 Spike Trimer |          |          | BA2 Spike Trimer |          |          |
|                                     | Lower CI        | Mean     | Upper CI  | Lower CI           | Mean     | Upper CI  | Lower CI         | Mean     | Upper CI | Lower CI         | Mean     | Upper CI |
| Initial MFI:                        | 405.70          | 1023.29  | 2581.07   | 354.29             | 812.83   | 1864.83   | 2699.48          | 4897.79  | 8886.28  | 1587.32          | 2454.71  | 3796.09  |
| Growth rate:                        | 0.13            | 0.22     | 0.39      | 0.13               | 0.24     | 0.43      | 0.08             | 0.20     | 0.47     | 0.02             | 0.13     | 0.99     |
| Activation time (days):             | 3.77            | 5.64     | 8.43      | 3.50               | 5.21     | 7.75      | 7.86             | 9.30     | 11.00    | 6.89             | 9.49     | 13.06    |
| Peak time (days):                   | 9.03            | 10.70    | 12.67     | 8.54               | 10.28    | 12.37     | 9.55             | 11.25    | 13.24    | 8.96             | 12.43    | 17.24    |
| Maximum MFI:                        | 10434.39        | 26618.42 | 67904.31  | 44129.44           | 60879.45 | 83987.18  | 12923.19         | 22500.64 | 39176.01 | 6465.54          | 12044.92 | 22438.96 |
| Sample: Saliva<br>Detector: FcγR3a  | WT Spike 1      |          |           | Delta Spike 1      |          |           | BA1 Spike 1      |          |          | BA2 Spike 1      |          |          |
|                                     | Lower CI        | Mean     | Upper CI  | Lower CI           | Mean     | Upper CI  | Lower CI         | Mean     | Upper CI | Lower CI         | Mean     | Upper CI |
| Initial MFI:                        | 6.03            | 15.49    | 39.78     | 18.20              | 18.20    | 18.20     | 16.98            | 16.98    | 16.98    | 11.75            | 11.75    | 11.75    |
| Growth rate:                        | 0.26            | 0.39     | 0.60      | 0.22               | 0.35     | 0.54      | 0.12             | 0.23     | 0.47     | 0.27             | 0.40     | 0.59     |
| Activation time (days):             | 2.94            | 4.53     | 6.98      | 3.66               | 5.10     | 7.11      | 4.72             | 6.05     | 7.76     | 4.57             | 5.81     | 7.40     |
| Peak time (days):                   | 8.51            | 10.07    | 11.92     | 9.43               | 10.91    | 12.63     | 6.88             | 8.50     | 10.50    | 7.67             | 9.03     | 10.61    |
| Maximum MFI:                        | 1045.81         | 2594.15  | 6434.81   | 446.74             | 1508.93  | 5096.59   | 26.45            | 111.68   | 471.51   | 79.56            | 394.54   | 1956.52  |
| Sample: Saliva<br>Detector: FcγR3a  | WT Spike Trimer |          |           | Delta Spike Trimer |          |           | BA1 Spike Trimer |          |          | BA2 Spike Trimer |          |          |
|                                     | Lower CI        | Mean     | Upper CI  | Lower CI           | Mean     | Upper CI  | Lower CI         | Mean     | Upper CI | Lower CI         | Mean     | Upper CI |
| Initial MFI:                        | 18.53           | 44.67    | 107.70    | 11.60              | 23.99    | 49.61     | 23.99            | 23.99    | 23.99    | 20.89            | 20.89    | 20.89    |
| Growth rate:                        | 0.16            | 0.25     | 0.39      | 0.21               | 0.30     | 0.44      | 0.13             | 0.24     | 0.44     | 0.17             | 0.30     | 0.52     |
| Activation time (days):             | 3.11            | 4.90     | 7.73      | 3.64               | 5.21     | 7.44      | 3.72             | 5.37     | 7.74     | 2.15             | 3.63     | 6.13     |
| Peak time (days):                   | 9.80            | 11.70    | 13.97     | 9.80               | 11.36    | 13.17     | 9.12             | 11.13    | 13.60    | 8.62             | 10.59    | 13.01    |
| Maximum MFI:                        | 1705.03         | 3455.75  | 7004.10   | 1193.14            | 2761.96  | 6393.56   | 230.85           | 707.85   | 2170.46  | 146.19           | 490.87   | 1648.24  |

Omicron BA.2 breakthrough cohort (Plasma)

| Sample: Plasma<br>Detector: Pan IgG | WT Spike 1      |          |           | Delta Spike 1      |          |          | BA1 Spike 1      |          |          | BA2 Spike 1      |          |          |
|-------------------------------------|-----------------|----------|-----------|--------------------|----------|----------|------------------|----------|----------|------------------|----------|----------|
|                                     | Lower CI        | Mean     | Upper CI  | Lower CI           | Mean     | Upper CI | Lower CI         | Mean     | Upper CI | Lower CI         | Mean     | Upper CI |
| Initial MFI:                        | 13688.00        | 19952.62 | 29084.39  | 6957.29            | 11481.54 | 18947.85 | 921.38           | 1905.46  | 3940.58  | 2505.65          | 4365.16  | 7604.66  |
| Growth rate:                        | 0.04            | 0.06     | 0.08      | 0.05               | 0.07     | 0.10     | 0.14             | 0.29     | 0.58     | 0.05             | 0.07     | 0.11     |
| Activation time (days):             | 6.89            | 8.41     | 10.28     | 6.30               | 7.92     | 9.97     | 6.57             | 7.39     | 8.32     | 4.87             | 6.17     | 7.82     |
| Peak time (days):                   | 14.68           | 16.78    | 19.17     | 12.81              | 14.59    | 16.61    | 8.06             | 8.76     | 9.51     | 11.89            | 14.01    | 16.52    |
| Maximum MFI:                        | 43394.17        | 64444.81 | 95707.19  | 24012.78           | 37021.41 | 57077.32 | 3585.41          | 5948.38  | 9868.69  | 6382.85          | 11109.55 | 19336.50 |
| Sample: Plasma<br>Detector: Pan IgG | WT Spike Trimer |          |           | Delta Spike Trimer |          |          | BA1 Spike Trimer |          |          | BA2 Spike Trimer |          |          |
|                                     | Lower CI        | Mean     | Upper CI  | Lower CI           | Mean     | Upper CI | Lower CI         | Mean     | Upper CI | Lower CI         | Mean     | Upper CI |
| Initial MFI:                        | 23722.26        | 33113.11 | 46221.50  | 12495.68           | 21379.62 | 36579.69 | 6604.93          | 9549.93  | 13808.04 | 3712.62          | 5623.41  | 8517.65  |
| Growth rate:                        | 0.04            | 0.07     | 0.13      | 0.02               | 0.03     | 0.05     | 0.04             | 0.06     | 0.08     | 0.04             | 0.06     | 0.09     |
| Activation time (days):             | 7.81            | 9.39     | 11.30     | 4.49               | 5.87     | 7.68     | 6.46             | 7.92     | 9.72     | 5.49             | 6.89     | 8.65     |
| Peak time (days):                   | 12.57           | 14.15    | 15.94     | 14.84              | 17.81    | 21.38    | 14.57            | 16.78    | 19.32    | 14.78            | 16.95    | 19.43    |
| Maximum MFI:                        | 58368.56        | 79623.49 | 108618.41 | 44129.44           | 60879.45 | 83987.18 | 21860.87         | 34326.63 | 53900.75 | 17467.57         | 25411.93 | 36969.44 |
| Sample: Plasma<br>Detector: IgA     | WT Spike 1      |          |           | Delta Spike 1      |          |          | BA1 Spike 1      |          |          | BA2 Spike 1      |          |          |
|                                     | Lower CI        | Mean     | Upper CI  | Lower CI           | Mean     | Upper CI | Lower CI         | Mean     | Upper CI | Lower CI         | Mean     | Upper CI |
| Initial MFI:                        | 68.30           | 141.25   | 292.12    | 21.08              | 40.74    | 78.73    | 10.47            | 10.47    | 10.47    | 14.45            | 14.45    | 14.45    |
| Growth rate:                        | 0.07            | 0.10     | 0.16      | 0.07               | 0.12     | 0.20     | 0.11             | 0.35     | 1.08     | 0.08             | 0.12     | 0.18     |
| Activation time (days):             | 4.59            | 6.17     | 8.30      | 3.23               | 4.66     | 6.73     | 6.10             | 8.00     | 10.51    | 1.73             | 2.97     | 5.12     |
| Peak time (days):                   | 14.12           | 16.95    | 20.34     | 12.07              | 15.49    | 19.86    | 10.42            | 12.68    | 15.43    | 13.81            | 16.78    | 20.39    |
| Maximum MFI:                        | 1214.34         | 2706.92  | 6034.04   | 573.14             | 1200.10  | 2512.88  | 40.95            | 103.61   | 262.15   | 213.79           | 529.71   | 1312.47  |
| Sample: Plasma<br>Detector: IgA     | WT Spike Trimer |          |           | Delta Spike Trimer |          |          | BA1 Spike Trimer |          |          | BA2 Spike Trimer |          |          |
|                                     | Lower CI        | Mean     | Upper CI  | Lower CI           | Mean     | Upper CI | Lower CI         | Mean     | Upper CI | Lower CI         | Mean     | Upper CI |
| Initial MFI:                        | 165.55          | 288.40   | 502.44    | 137.57             | 229.09   | 381.49   | 56.43            | 104.71   | 194.32   | 49.52            | 85.11    | 146.29   |
| Growth rate:                        | 0.04            | 0.07     | 0.12      | 0.04               | 0.07     | 0.13     | 0.05             | 0.07     | 0.11     | 0.10             | 0.15     | 0.20     |
| Activation time (days):             | 3.88            | 5.31     | 7.27      | 3.65               | 5.16     | 7.28     | 2.59             | 4.22     | 6.88     | 6.55             | 8.33     | 10.60    |
| Peak time (days):                   | 14.93           | 19.30    | 24.95     | 14.17              | 18.36    | 23.78    | 14.27            | 17.64    | 21.79    | 13.25            | 15.33    | 17.74    |
| Maximum MFI:                        | 1876.28         | 4043.89  | 8715.69   | 1485.65            | 3058.28  | 6295.62  | 671.78           | 1487.06  | 3291.78  | 381.20           | 908.36   | 2164.53  |
| Sample: Plasma<br>Detector: FcγR3a  | WT Spike 1      |          |           | Delta Spike 1      |          |          | BA1 Spike 1      |          |          | BA2 Spike 1      |          |          |
|                                     | Lower CI        | Mean     | Upper CI  | Lower CI           | Mean     | Upper CI | Lower CI         | Mean     | Upper CI | Lower CI         | Mean     | Upper CI |
| Initial MFI:                        | 106.65          | 208.93   | 409.30    | 45.39              | 79.43    | 139.01   | 7.00             | 7.00     | 7.00     | 8.52             | 14.13    | 23.42    |
| Growth rate:                        | 0.04            | 0.07     | 0.11      | 0.04               | 0.06     | 0.09     | 0.05             | 0.11     | 0.27     | 0.06             | 0.09     | 0.14     |
| Activation time (days):             | 5.86            | 7.32     | 9.13      | 4.60               | 5.99     | 7.80     | 6.10             | 8.00     | 10.51    | 2.41             | 4.14     | 7.11     |
| Peak time (days):                   | 15.88           | 18.92    | 22.53     | 15.50              | 18.73    | 22.62    | 8.98             | 11.36    | 14.37    | 13.53            | 16.95    | 21.23    |
| Maximum MFI:                        | 728.37          | 1670.04  | 3829.10   | 258.17             | 629.14   | 1533.16  | 11.66            | 21.37    | 39.15    | 92.16            | 216.25   | 507.43   |
| Sample: Plasma<br>Detector: FcγR3a  | WT Spike Trimer |          |           | Delta Spike Trimer |          |          | BA1 Spike Trimer |          |          | BA2 Spike Trimer |          |          |
|                                     | Lower CI        | Mean     | Upper CI  | Lower CI           | Mean     | Upper CI | Lower CI         | Mean     | Upper CI | Lower CI         | Mean     | Upper CI |
| Initial MFI:                        | 283.19          | 562.34   | 1116.66   | 149.10             | 346.74   | 806.34   | 62.96            | 91.20    | 132.10   | 36.94            | 53.70    | 78.07    |
| Growth rate:                        | 0.03            | 0.05     | 0.09      | 0.03               | 0.05     | 0.09     | 0.04             | 0.07     | 0.11     | 0.08             | 0.12     | 0.18     |
| Activation time (days):             | 5.71            | 7.10     | 8.82      | 4.88               | 6.42     | 8.45     | 6.06             | 7.54     | 9.37     | 6.73             | 8.50     | 10.73    |
| Peak time (days):                   | 14.89           | 17.81    | 21.32     | 14.45              | 17.46    | 21.11    | 15.59            | 18.92    | 22.95    | 13.47            | 16.12    | 19.29    |
| Maximum MFI:                        | 1514.36         | 2750.59  | 4996.00   | 974.73             | 1835.16  | 3455.11  | 279.84           | 713.45   | 1818.96  | 190.99           | 446.85   | 1045.46  |

Omicron BA.2 breakthrough cohort (Saliva)

| Sample: Saliva<br>Detector: Pan IgG | WT Spike 1      |          |            | Delta Spike 1      |          |          | BA1 Spike 1      |          |          | BA2 Spike 1      |          |          |
|-------------------------------------|-----------------|----------|------------|--------------------|----------|----------|------------------|----------|----------|------------------|----------|----------|
|                                     | Lower CI        | Mean     | Upper CI   | Lower CI           | Mean     | Upper CI | Lower CI         | Mean     | Upper CI | Lower CI         | Mean     | Upper CI |
| Initial MFI:                        | 6322.37         | 10964.78 | 19016.04   | 2778.69            | 5370.32  | 10379.11 | 543.75           | 1000.00  | 1839.08  | 1040.78          | 1905.46  | 3488.51  |
| Growth rate:                        | 0.01            | 0.27     | 6.03       | 0.00               | 0.27     | 17.04    | 0.00             | 0.27     | 454.14   | 0.02             | 0.25     | 2.78     |
| Activation time (days):             | 4.84            | 7.17     | 10.63      | 4.06               | 7.10     | 12.41    | 3.11             | 7.24     | 16.86    | 4.76             | 7.24     | 11.02    |
| Peak time (days):                   | 6.87            | 8.33     | 10.10      | 6.66               | 8.25     | 10.21    | 6.44             | 8.17     | 10.35    | 7.26             | 9.30     | 11.91    |
| Maximum MFI:                        | 26945.80        | 45975.98 | 78446.02   | 12113.07           | 24084.05 | 47885.57 | 2331.57          | 4606.06  | 9099.35  | 6490.79          | 12285.01 | 23251.65 |
| Sample: Saliva<br>Detector: Pan IgG | WT Spike Trimer |          |            | Delta Spike Trimer |          |          | BA1 Spike Trimer |          |          | BA2 Spike Trimer |          |          |
|                                     | Lower CI        | Mean     | Upper CI   | Lower CI           | Mean     | Upper CI | Lower CI         | Mean     | Upper CI | Lower CI         | Mean     | Upper CI |
| Initial MFI:                        | 12478.43        | 19952.62 | 31903.62   | 7999.08            | 14125.38 | 24943.65 | 4326.69          | 6760.83  | 10564.38 | 1963.54          | 3467.37  | 6122.94  |
| Growth rate:                        | 0.02            | 0.19     | 2.02       | 0.00               | 0.22     | 1071.06  | 0.03             | 0.23     | 1.65     | 0.02             | 0.19     | 1.88     |
| Activation time (days):             | 5.17            | 6.75     | 8.82       | 4.98               | 6.82     | 9.35     | 5.48             | 6.89     | 8.67     | 4.58             | 7.17     | 11.23    |
| Peak time (days):                   | 6.07            | 7.92     | 10.35      | 2.77               | 7.92     | 22.66    | 6.54             | 8.00     | 9.80     | 7.17             | 9.39     | 12.31    |
| Maximum MFI:                        | 39325.96        | 62988.29 | 100888.18  | 29573.63           | 50590.79 | 86544.28 | 17800.46         | 28637.84 | 46073.28 | 9207.57          | 17454.63 | 33088.45 |
| Sample: Saliva<br>Detector: IgA     | WT Spike 1      |          |            | Delta Spike 1      |          |          | BA1 Spike 1      |          |          | BA2 Spike 1      |          |          |
|                                     | Lower CI        | Mean     | Upper CI   | Lower CI           | Mean     | Upper CI | Lower CI         | Mean     | Upper CI | Lower CI         | Mean     | Upper CI |
| Initial MFI:                        | 1031.43         | 1905.46  | 3520.14    | 393.59             | 870.96   | 1927.35  | 12.02            | 12.02    | 12.02    | 1.31             | 5.42     | 22.46    |
| Growth rate:                        | 0.05            | 0.10     | 0.22       | 0.06               | 0.13     | 0.26     | 0.19             | 0.33     | 0.57     | 0.18             | 0.29     | 0.47     |
| Activation time (days):             | 6.70            | 8.85     | 11.69      | 6.51               | 8.33     | 10.66    | 8.79             | 11.47    | 14.98    | 3.49             | 5.37     | 8.26     |
| Peak time (days):                   | 11.50           | 14.01    | 17.08      | 10.28              | 12.55    | 15.33    | 12.29            | 15.33    | 19.13    | 10.95            | 13.20    | 15.90    |
| Maximum MFI:                        | 5968.77         | 12172.47 | 24824.05   | 2921.63            | 6310.56  | 13630.49 | 151.31           | 310.02   | 635.21   | 745.41           | 2012.94  | 5435.84  |
| Sample: Saliva<br>Detector: IgA     | WT Spike Trimer |          |            | Delta Spike Trimer |          |          | BA1 Spike Trimer |          |          | BA2 Spike Trimer |          |          |
|                                     | Lower CI        | Mean     | Upper CI   | Lower CI           | Mean     | Upper CI | Lower CI         | Mean     | Upper CI | Lower CI         | Mean     | Upper CI |
| Initial MFI:                        | 666.56          | 1288.25  | 2489.77    | 417.37             | 870.96   | 1817.52  | 2197.05          | 3388.44  | 5225.89  | 1019.76          | 1513.56  | 2246.47  |
| Growth rate:                        | 0.09            | 0.17     | 0.31       | 0.10               | 0.16     | 0.25     | 0.05             | 0.15     | 0.46     | 0.05             | 0.18     | 0.67     |
| Activation time (days):             | 6.06            | 8.08     | 10.78      | 5.63               | 7.39     | 9.70     | 2.88             | 4.44     | 6.83     | 4.43             | 6.42     | 9.32     |
| Peak time (days):                   | 11.60           | 13.74    | 16.26      | 11.75              | 14.15    | 17.05    | 4.90             | 6.82     | 9.50     | 7.25             | 9.30     | 11.93    |
| Maximum MFI:                        | 11746.97        | 18413.92 | 28864.67   | 10935.70           | 16786.36 | 25767.15 | 13049.94         | 17791.50 | 24255.84 | 7598.80          | 10574.82 | 14716.37 |
| Sample: Saliva<br>Detector: FcγR3a  | WT Spike 1      |          |            | Delta Spike 1      |          |          | BA1 Spike 1      |          |          | BA2 Spike 1      |          |          |
|                                     | Lower CI        | Mean     | Upper CI   | Lower CI           | Mean     | Upper CI | Lower CI         | Mean     | Upper CI | Lower CI         | Mean     | Upper CI |
| Initial MFI:                        | 81.46           | 177.83   | 388.22     | 20.32              | 50.12    | 123.59   | 16.98            | 16.98    | 16.98    | 10.23            | 10.23    | 10.23    |
| Growth rate:                        | 0.02            | 0.22     | 2.61       | 0.00               | 0.22     | 10.40    | 0.00             | 0.08     | 2.99     | 0.04             | 0.16     | 0.64     |
| Activation time (days):             | 5.28            | 8.00     | 12.13      | 3.43               | 7.24     | 15.28    | 3.68             | 6.62     | 11.92    | 1.66             | 4.35     | 11.36    |
| Peak time (days):                   | 7.00            | 10.07    | 14.51      | 5.97               | 9.30     | 14.48    | 5.07             | 8.50     | 14.26    | 5.69             | 9.49     | 15.82    |
| Maximum MFI:                        | 695.15          | 1797.52  | 4647.99    | 216.73             | 663.87   | 2033.50  | 26.12            | 46.70    | 83.51    | 64.77            | 215.22   | 715.20   |
| Sample: Saliva<br>Detector: FcγR3a  | WT Spike Trimer |          |            | Delta Spike Trimer |          |          | BA1 Spike Trimer |          |          | BA2 Spike Trimer |          |          |
|                                     | Lower CI        | Mean     | Upper CI   | Lower CI           | Mean     | Upper CI | Lower CI         | Mean     | Upper CI | Lower CI         | Mean     | Upper CI |
| Initial MFI:                        | 190.44          | 457.09   | 1097.08    | 113.26             | 281.84   | 701.33   | 31.80            | 66.07    | 137.25   | 18.33            | 41.69    | 94.78    |
| Growth rate:                        | 0.00            | 0.20     | 3305836.17 | 0.00               | 0.14     | 8.31     | 0.03             | 0.18     | 1.07     | 0.03             | 0.15     | 0.77     |
| Activation time (days):             | 0.99            | 7.17     | 51.91      | 4.16               | 7.61     | 13.95    | 3.91             | 6.05     | 9.37     | 4.03             | 6.89     | 11.79    |
| Peak time (days):                   | 2.78            | 8.58     | 26.55      | 5.11               | 9.97     | 19.46    | 5.55             | 8.76     | 13.83    | 7.14             | 10.70    | 16.02    |
| Maximum MFI:                        | 913.69          | 2515.28  | 6924.24    | 592.77             | 1823.82  | 5611.56  | 296.24           | 785.77   | 2084.23  | 180.93           | 535.25   | 1583.47  |

Supplementary Table 4: List of detection antibodies used.

| Antibody:                                | Clone:   | Company:         | Catalogue Number: |
|------------------------------------------|----------|------------------|-------------------|
| Mouse anti-human IgG1, biotinylated      | MTG1218  | Mabtech          | 3851-14-250       |
| Mouse anti-human IgG2, biotinylated      | HP6200   | Mabtech          | 3852-6-250        |
| Mouse anti-human IgG3, biotinylated      | MTG34    | Mabtech          | 3853-6-250        |
| Mouse anti-human IgG4, biotinylated      | MTG42    | Mabtech          | 3854-6-250        |
| Mouse anti-human total IgA, biotinylated | MT20     | Mabtech          | 3860-6-250        |
| Mouse anti-human IgM, biotinylated       | MT22     | Mabtech          | 3880-6-250        |
| Mouse anti-human total IgG, biotinylated | MT78/145 | Mabtech          | 3850-6-250        |
|                                          |          |                  |                   |
| Mouse anti-human total IgG-PE            | JDC-10   | Southern Biotech | 9040-09           |
| Mouse anti-human IgG1-PE                 | HP6001   | Southern Biotech | 9054-09           |
| Mouse anti-human IgG2-PE                 | HP6002   | Southern Biotech | 9070-09           |
| Mouse anti-human IgG3-PE                 | HP6050   | Southern Biotech | 9210-09           |
| Mouse anti-human IgG4-PE                 | HP6025   | Southern Biotech | 9200-09           |
| Mouse anti-human IgA1-PE                 | B3506B4  | Southern Biotech | 9130-09           |
| Mouse anti-human IgA2-PE                 | A9604D2  | Southern Biotech | 9140-09           |
| Mouse anti-human IgM                     | SA-DA4   | Southern Biotech | 9020-09           |