Serial infection with SARS-CoV-2 Omicron BA.1 and BA.2 following three-dose COVID-19 vaccination

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ABSTRACT

SARS-CoV-2 Omicron infections are common among individuals who are vaccinated or have recovered from prior variant infection, but few reports have documented serial Omicron infections. We characterized SARS-CoV-2 humoral responses in a healthy young person who acquired laboratory-confirmed Omicron BA.1.15 ten weeks after a third dose of BNT162b2, and BA.2 thirteen weeks later. Responses were compared to those of 124 COVID-19 naive vaccinees. One month after the second and third vaccine doses, the participant's wild-type and BA.1-specific IgG, ACE2 competition and virus neutralization activities were average for a COVID-19 naive triple-vaccinated individual. BA.1 infection boosted the participant's responses to the cohort ≥95th percentile, but even this strong "hybrid" immunity failed to protect against BA.2. Moreover, reinfection increased BA.1 and BA.2-specific responses only modestly. Results illustrate the risk of Omicron infection in fully vaccinated individuals and highlight the importance of personal and public health measures as vaccine-induced immune responses wane.

INTRODUCTION

SARS-CoV-2 infections, predominantly fueled by the Omicron (B.1.1.529) variant, are increasingly common among individuals who are vaccinated and/or have recovered from prior infections (1-3). Globally, the highly transmissible and immune evasive Omicron variant has rapidly overtaken the previously dominant Delta variant (3-7), and the original Omicron BA.1 strain is being outcompeted by newer Omicron sub-lineages BA.2, BA.3, BA.4 and BA.5 (8, 9). In British Columbia (BC), Canada, Omicron BA.1 had overtaken Delta by December 2021 and BA.2 had largely outcompeted BA.1 by March 2022 (10, 11).

COVID-19 vaccine coverage in BC is relatively high, with 93%, 90% and 57% of individuals aged 12 years or older having received one, two and three COVID-19 immunizations, respectively (12). Persons at elevated risk of severe COVID-19 are also eligible for fourth doses (13). Despite this, the province experienced fifth and sixth waves of COVID-19, dominated by BA.1 and BA.2, respectively, as public health measures were gradually relaxed (10, 11). Indeed, it is estimated that between December 2021 and March 2022, nearly half of British Columbians experienced a SARS-CoV-2 infection, likely due to Omicron (14, 15).

While several reports have examined post-vaccination Omicron infections, or Omicron reinfections following exposure to prior variants (16-23), we are aware of only one study that assessed repeat Omicron infection incidence through viral genomic surveillance (24). No studies appear to have investigated the vaccine- and infection-induced immune responses after serial Omicron infections. Here, we longitudinally characterize SARS-CoV-2 humoral responses in a healthy young person who experienced serial BA.1 and BA.2 Omicron infections following

three-dose COVID-19 mRNA vaccination. Responses were compared to those of 124 COVID-19-naive vaccinees over the same period. Taken together with existing literature, our results suggest that vaccination provides limited protection against infection and/or reinfection by Omicron variants.

METHODS

Observational COVID-19 vaccine cohort and SARS-CoV-2 infection monitoring. In December 2020, we established a prospective longitudinal study in Vancouver, Canada, to examine SARS-CoV-2 specific humoral immune responses following vaccination with BNT162b2 (Comirnaty; BioNTech/Pfizer) or mRNA-1273 (Spikevax; Moderna) in a cohort of 151 adults aged 24-98 years (described in (25, 26)). Serum and plasma were collected longitudinally up to 6 months following the third dose (Figure 1A). At each visit, serum was tested for the presence of SARS-CoV-2 anti-nucleocapsid (N) antibodies, which indicate seroconversion following infection, using the Elecsys Anti-SARS-CoV-2 assay on a Cobas e601 module analyzer (Roche Diagnostics). In addition to the case participant, immune measures from a comparison group of 124 additional cohort participants who remained anti-N seronegative up until at least one month post-third vaccine dose are included for context.

Ethics approval. All participants provided written informed consent. This study was approved by the University of British Columbia/Providence Health Care and Simon Fraser University Research Ethics Boards (protocol H20-03906).

SARS-CoV-2 diagnostics and lineage confirmation. Diagnostic samples from the case participant's two SARS-CoV-2 infections were tested at the St. Paul's Hospital Virology Laboratory using the cobas® SARS-CoV-2 Test which targets conserved regions within the Orf1a/b and E genes (Roche Diagnostics) followed by screening using a real-time reverse transcription (RT)-PCR based algorithm for SARS-CoV-2 lineage classification that is frequently updated to detect emerging variants (27, 28). Following this, the diagnostic samples were subjected to full-genome SARS-CoV-2 sequencing in two independent laboratories: the BC Centre for Disease Control, the provincial laboratory that performs all SARS-CoV-2 sequencing for epidemiological surveillance, and the BC Centre for Excellence in HIV/AIDS. Both laboratories use the Illumina platform. The SARS-CoV-2 full genome sequences for the participant's BA.1.15 and subsequent BA.2 infections have been submitted to GISAID (Accession ID EPI_ISL_12767799 and EPI_ISL_12662303, respectively).

Binding antibody assays. We quantified anti-Spike Receptor Binding Domain (RBD) binding IgG concentrations in serum using the V-plex SARS-CoV-2 (IgG) Panel 22 ELISA kit (Meso Scale Diagnostics), which features wild-type and Omicron BA.1 RBD antigens. For a subset of participants, Anti-Spike binding IgG concentrations in serum were also quantified using the V-plex SARS-CoV-2 (IgG) Panel 25 ELISA kit (Meso Scale Diagnostics), which features full-length S antigens from wild-type, Omicron BA.1 and Omicron BA.2. At the time of analysis, no panel featuring Omicron BA.2 RBD was offered by the manufacturer. Both assays were performed on a Meso QuickPlex SQ120 instrument, with sera diluted 1:10000. Results are reported in arbitrary Units/mL.

123 ***ACE2 competition assays.*** We assessed the ability of serum antibodies to block the wild-type
124 and Omicron BA.1 RBD-ACE2 receptor interaction by competition ELISA (Panel 22 V-plex
125 SARS-CoV-2 [ACE2]; Meso Scale Diagnostics). For a subset of participants, we also assessed
126 the ability of serum antibodies to block the wild-type, BA.1 and BA.2 Spike-ACE2 receptor
127 interaction using the same methods (Panel 25 V-plex SARS-CoV-2 [ACE2]). Both assays were
128 performed on a Meso QuickPlex SQ120 instrument, with sera diluted 1:40. Results are reported
129 as % ACE2 displacement.
130
131 ***Live virus neutralization assays.*** Neutralizing activity in plasma was examined in live SARS-
132 CoV-2 assays using a wild-type isolate (USA-WA1/2020; BEI Resources) and a local Omicron
133 BA.1 isolate (GISAID Accession # EPI_ISL_9805779) on VeroE6-TMPRSS2 (JCRB-1819)
134 target cells. Viral stock was adjusted to 50 TCID50/200 µl in Dulbecco's Modified Eagle
135 Medium in the presence of serial 2-fold plasma dilutions (from 1/20 to 1/2560), incubated at 4°C
136 for 1 hour and added to target cells in 96-well plates in triplicate. Cultures were maintained at
137 37°C with 5% CO2 and the appearance of viral cytopathic effect (CPE) was recorded three days
138 post-infection. Neutralizing activity is reported as the reciprocal of the highest plasma dilution
139 able to prevent CPE in all triplicate wells. Samples exhibiting partial or no neutralization at 1/20
140 dilution were defined as below the limit of quantification (BLOQ).
141
142 ***Statistical analysis.*** Data visualization and statistical analysis was conducted in Prism v9.2.0
143 (GraphPad).
144
145

RESULTS

Case participant SARS-CoV-2 vaccination and infection timeline.

The participant was a frontline health care worker in their early 30s with no chronic health conditions. They received three doses of mRNA vaccine (all BNT162b2; 30mcg) in late December 2020, early February 2021 and late October 2021 (Figure 1A). All blood samples collected up to one month following the third immunization were anti-N seronegative.

In early January 2022, ten weeks after the third immunization, the participant experienced moderate symptoms including sore throat, fatigue, congestion, body aches, severe headaches, loss of taste and smell, coughing, shortness of breath and nausea. Symptoms, primarily cough, intensified in the second week after diagnosis requiring corticosteroid therapy. By the third week, symptoms had subsided except for shortness of breath and fatigue, with minimal improvement from short- and long-acting bronchodilating agents. A saline gargle collected in early January 2022 tested positive on the cobas® SARS-CoV-2 Test with a cycle threshold (Ct) value of 21 for both Orf1a/b and E gene targets. Real-time RT-PCR-based molecular screening identified the infection as Omicron BA.1, with subsequent full-genome viral sequencing confirming the specific lineage as BA.1.15.

In early April 2022, 13 weeks following the BA.1 infection (and 23 weeks following the third immunization) the participant experienced a different, more mild symptom profile compared to their first infection, consisting of a sore throat, fever, body aches, headaches, and diarrhea. No change in sense of taste or smell was noted. The participant noted persisting weakness, fatigue and mental fog, as well as severe long-term, treatment-resistant shortness of breath triggered by

mild activities or exercises. A nasopharyngeal swab collected in early April 2022 tested positive on the cobas® SARS-CoV-2 Test with Ct values of 24 (Orf1a/b) and 23 (E). This second infection was identified as BA.2 by molecular screening and confirmed by full-genome viral sequencing.

Longitudinal humoral responses to wild-type and Omicron BA.1 variants

We began by investigating the magnitude of the participant's humoral immune responses following immunization, in context of a control group of 124 COVID-naïve individuals who were vaccinated during the same period. The comparison group was 74% female with a median age of 57 (Interquartile Range [IQR] 38-76) years. We quantified antibody responses to wild-type and Omicron BA.1 strains in the participant and the comparison group at one month after the second and third vaccine doses, as these time points should capture peak responses post-vaccination (Figures 1B-D).

One month post-second dose, the participant's wild-type and BA.1-specific RBD IgG concentrations were 4.90 and 4.26 $\log_{10}$ U/mL respectively, which were equivalent to the 53rd and 50th percentile values of the comparator cohort (Figure 1B). One month post-third dose, their wild-type and BA.1-specific RBD IgG concentrations had increased to 5.08 and 4.63 $\log_{10}$ U/mL respectively, equivalent to the 36th and 60th percentile values of the cohort. Similarly, one month post-second dose, their ability to disrupt the interaction between the ACE2 receptor and the wild-type and BA.1 RBDs were 97% (57th percentile) and 42% (55th percentile) respectively (Figure 1C). At one month post-third dose, their wild-type- and BA.1-specific RBD-ACE2 displacement activities had increased to 99% (74th percentile) and 76% (73rd percentile) respectively. Finally,

at one month post-second dose, the participant's plasma neutralized wild-type and BA.1 SARS-CoV-2 at reciprocal dilutions of 320 and 20, which were equivalent to the 97th and 76th percentile values of the cohort. At one month post-third dose, their wild-type and BA.1 neutralization titers were 320 (78th percentile) and 40 (59th percentile) respectively. These results indicate that the participant's overall vaccine responses were typical of the cohort, but nevertheless insufficient to prevent infection by BA.1 approximately six weeks later.

Seventeen days after testing positive with BA.1 (which coincided with a three-month post-third-dose study visit), the participant's wild-type and BA.1-specific responses were boosted substantially, reaching the cohort 95th percentile for most measures at this time when immune responses had begun to decline in the comparator cohort (Figures 1B-1D). Their wild-type RBD IgG concentration increased to 5.71 $\log_{10}$ U/mL, while their BA.1-specific RBD IgG concentration increased to 5.11 $\log_{10}$ U/mL (Figure 1B). For context, these values would have placed the participant in the 95th and 93rd percentile of "peak" cohort values, measured at one month post-third vaccine dose. Similarly, their wild-type-specific RBD-ACE2 competition activity remained high at 99.9%, while their BA.1-specific RBD-ACE2 competition activity increased to 96.3%. For context, these values were equivalent to the 99th percentiles of peak cohort values one month after three vaccine doses (Figure 1C). Their wild-type and BA.1-specific neutralization values held at 320 and 40, respectively, equivalent to the 78th and 59th percentiles of peak cohort values (Figure 1D). These results indicate that BA.1 infection substantially boosted the participant’s humoral response, however this was insufficient to prevent reinfection by BA.2 approximately 10 weeks later.

Sixteen days after testing positive with BA.2 (which coincided with a six-month post-third-dose study visit), the participant's wild-type-specific responses remained steady or declined slightly (*e.g.* RBD IgG) from prior measurements. Nevertheless, most values remained at the cohort 100th percentile at this time point, which is unsurprising given that vaccine-induced responses had declined substantially over this time in the COVID-19 naive comparison group.

By contrast, the BA.2 reinfection had mixed effects on BA.1 responses. While the BA.1-specific RBD IgG concentration rose substantially to 5.58 $\log_{10}$ U/mL (whereas the cohort median at this time point was nearly 2 $\log_{10}$ lower), no change was seen for BA.1-specific RBD-ACE2 competition, and BA.1 neutralization increased only modestly. The more pronounced impact of BA.2 reinfection was to extend the duration of BA.1-specific responses in the participant, who maintained an RBD-ACE2 competition activity of 95.7% (cohort median 29% at this time point) and a neutralization activity of 80 (cohort median BLOQ at this time point). Nevertheless, despite BA.1 infection and BA.2 reinfection, the participant's virus neutralization activity against BA.1 at this time point, which represented the highest activity measured during the study, remained 4-fold lower compared to that against the wild-type strain one month following their third vaccine dose (Figure 1D), suggesting that the participant may remain at risk of additional Omicron infection.

Longitudinal humoral responses to Omicron BA.2

We next characterized BA.2-specific Spike IgG and ACE2 competition activities in a subset of participants (79% Female, median age 59 years) beginning one month following the third vaccine dose (Figure 2). As these analyses focus on whole Spike (rather than RBD antigen), the

corresponding wild-type and BA.1-specific responses are also shown for context (Figure 2). We additionally confirmed the (strong) correlations between wild-type- and BA.1-specific RBD and Spike responses in these individuals (all $p<0.0001$; Figure S1). At one month post-third vaccine dose, the participant displayed wild-type, BA.1 and BA.2-specific Spike IgG concentrations of 5.81, 5.18 and 5.46 $\log_{10}$ U/mL respectively (Figure 2A), and ACE2 competition activities of 99.4%, 50.6% and 64.3% respectively (Figure 2B). Their wild-type and BA.2-specific Spike IgG concentrations were broadly average (54th and 68th percentiles respectively), as were their and Spike-ACE2 competition activities (46th and 54th percentiles respectively), though their values for BA.1-specific IgG and BA.1 Spike-ACE2 competition were slightly lower than average (37th and 39th percentiles respectively).

Following BA.1 infection, the participant's wild-type, BA.1 and BA.2-specific Spike IgG concentrations increased modestly, to 5.82, 5.22 and 5.48 log10 U/mL respectively (Figure 2A). Though the magnitude of these increases was not as pronounced as those observed for their wild-type- and BA.1-specific RBD IgG concentrations (shown in Figure 1B), these values nevertheless placed them at or above the cohort 85th percentile at this time point, when immune responses had begun to decline in the broader cohort. For context, these values would place the participant in the 57th, 39th, and 68th percentile of peak cohort values measured at one month post-third vaccine dose. Similar to the ACE2 competition activities measured using RBD antigens (shown in Figure 1C), the participant's wild-type Spike-ACE2 competition activities remained high at 99.7%, while BA.1 and BA.2 Spike-ACE2 activities rose substantially to 87.9% and 89.3% respectively (Figure 2B); values that represented the 71st, 75th, and 79th percentiles of peak cohort values at one month post-third vaccine dose.

Following BA.2 infection, the participant's wild-type Spike IgG concentration declined slightly to 5.77 $\log_{10}$ U/mL, whereas their BA.1 and BA.2-specific values increased slightly to 5.25 and 5.56 $\log_{10}$ U/mL respectively (Figure 2A). These trends were consistent with their wild-type- and BA.1-specific RBD IgG concentrations (shown in Figure 1B), though of a smaller magnitude. Similar to the ACE2 competition activities measured using RBD antigens (shown in Figure 1C), the participant's wild-type Spike-ACE2 competition activity remained high (99.5%) after BA.2 infection. BA.1 and BA.2 Spike-ACE2 activities increased, though only marginally, to 88.6% and 90% respectively (Figure 2B).

Together, these results confirm that the participant's humoral responses to wild-type and Omicron variants were broadly average one month post-third vaccine dose. Moreover, while BA.1 infection boosted Omicron-specific immune responses (highlighted by an increase in BA.1 and BA.2 Spike-ACE2 competition activities), BA.2 reinfection did not substantially augment these activities further but rather extended the duration of these responses.

DISCUSSION

This study provides detailed humoral characterization in a laboratory-confirmed case of serial infection by SARS-CoV-2 Omicron subvariants BA.1 and BA.2 in an otherwise healthy adult who had received three doses of COVID-19 mRNA vaccine. While data on repeat Omicron infections remain very limited, a recent study from Denmark identified 47 cases of BA.2 reinfection that occurred between 20 and 60 days following BA.1 infection (24). The authors concluded that such events were rare (<0.1% of cases during the brief window of analysis) and more likely to occur among unvaccinated individuals, but further evaluation of the data indicates

a majority of reinfection cases were due to BA.2 following BA.1. Moreover, given that the present case participant was one of only 151 enrolees of an observational COVID-19 vaccine study (25, 26), our results suggest that the risk of serial infection with Omicron subvariants may be greater than current assumptions based on low reinfection rates. We note however that the participant's status as a frontline healthcare worker may have resulted in an increased risk of exposure and (re-)infection over the general population.

Acknowledging that our ability to generalize from a single case is limited, we note that initial vaccine-induced IgG, ACE2 competition and virus neutralization response magnitudes against wild-type and Omicron BA.1 in the participant were comparable to the median values observed in diverse controls who were vaccinated along the same timeline. The observation that average humoral responses to three-dose vaccination failed to protect against Omicron BA.1 infection is consistent with the extremely high rates of community transmission observed in many regions during the recent Omicron-driven pandemic waves. Given that third doses substantially boost humoral responses in individuals of all ages (29-32), the risk of Omicron infection is likely to be higher among individuals who have received fewer than three doses (18, 33) and is likely to increase with time following vaccination due to natural declines in antibody responses (26, 34-37). Additional studies are needed to assess these factors.

While it is perhaps unsurprising that COVID-19 vaccines based on ancestral SARS-CoV-2 sequences will not generate sterilizing immunity against Omicron strains that have evolved to evade host immune responses (4, 38-42), various lines of evidence suggest that "hybrid" immunity resulting from vaccination plus infection provides greater protection against SARS-

CoV-2 variants (5, 43), due in part to maturation of Spike-specific antibodies (44-46) and expansion of antiviral T cells (47-52). In light of this, we note that symptomatic BA.1 infection boosted vaccine-induced humoral responses against both BA.1 and BA.2 in our case participant, but the heightened response nevertheless failed to prevent subsequent symptomatic infection by BA.2. Moreover, even after vaccination plus two Omicron infections, the participant's ACE2 competition and virus neutralization responses against BA.1 (as well as ACE2 competition activity against BA.2) plateaued at levels substantially lower than those seen against the wild-type strain, suggesting that the participant will remain at risk of new Omicron infections. A limitation of our study is that it did not assess T cell responses, which can reduce disease severity but may have less impact on virus transmission (53, 54), and thus we may be underestimating the protection that results from infection and reinfection in this case. Indeed, the participant's symptoms following both infections were not severe enough to require hospitalization, demonstrating that vaccination was effective in its primary goal of preventing disease. Our results nevertheless illustrate the potentially limited ability of current vaccines to prevent recurrent infections and symptomatic disease caused by Omicron variants.

DATA AVAILABILITY STATEMENT

Sequences were submitted to GISAID. The raw data supporting the conclusions of this article will be made available by the authors upon reasonable request.

AUTHOR CONTRIBUTIONS

HRL and FM contributed equally as first authors. MGR, MAB and ZLB obtained project funding and contributed equally as senior authors. HRL, FM, MAB and ZLB designed the study. HRL,

FM, PKC, YS, FY, RK, SD, RW, GU, SE, LY, WD, DK, and LB contributed to specimen collection and data analysis. HRL, YS, VL, DH, MLD, JS, NM, JSGM, CJB, NP, MN, CFL, MGR, MAB, and ZLB supervised the research and contributed to project management. HRL, MAB and ZLB wrote the original manuscript draft. All authors reviewed and approved the submitted version of the manuscript.

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CONFLICT OF INTEREST

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

FIGURE LEGENDS

Figure 1. Case participant history and longitudinal humoral responses against wild-type and Omicron BA.1 SARS-CoV-2. Panel A: Case participant timeline. Immunizations and SARS-CoV-2 Omicron infection history are shown at the top. Longitudinal SARS-CoV-2 anti-N serology results are shown in small green (anti-N negative) or orange (anti-N positive) circles. Large black circles denote time points where additional humoral functions, shown in panels below, were measured. Panel B: Longitudinal anti-S-RBD IgG log10 concentrations in case participant (large circles) versus the comparison group of SARS-CoV-2-naive individuals (small circles) at various time points following two- and three-dose COVID-19 vaccination. Wild-type (WT) specific anti-S-RBD responses are shown in red; Omicron BA.1-specific ones are shown in blue. Matching solid lines connect the participant's longitudinal values, while dotted lines connect the median values for the comparison group. Approximate times of BA.1 and BA.2 infections are shown with arrows. Total Ns (including the case participant) are shown at the bottom of the plot. Later time points have smaller Ns because some control participants were censored due to post-vaccination SARS-CoV-2 infection or had not yet completed the visit. Panel C: same as previous, but for longitudinal ACE2% displacement function from wild-type (red) and BA.1 (blue) S-RBDs. Panel D: same as previous, but for longitudinal live virus neutralization function against wild-type (red) and BA.1 (blue) strains. ULOQ/LLOQ: upper/lower limit of quantification.

Figure 2. Longitudinal humoral responses against wild-type, BA.1 and BA.2 Spike antigens. Panel A: Anti-Spike IgG log10 concentrations in case participant (large circles) versus the subset of the comparison group of SARS-CoV-2-naive individuals (small circles) at one, three and six months following three-dose COVID-19 vaccination. Wild-type-specific (WT) anti-Spike responses are in red; BA.1-specific ones are in blue; BA.2-specific ones are in black. Matching solid lines connect the participant's longitudinal values; dotted lines connect the median values for the comparison group. Approximate times of BA.1 and BA.2 infections are shown with arrows. Total Ns (including the case participant) are shown at the bottom of the plot; the final time point has a smaller N because some control participants were censored due to post-vaccination SARS-CoV-2 infection or had not yet completed the visit. Panel B: same as previous, but for longitudinal ACE2% displacement function from wild-type (red), BA.1 (blue) and BA.2 (black) Spike protein.

Figure S1. Correlations between wild-type (WT) and BA.1-specific anti-S-RBD and anti-Spike humoral responses measured following three COVID-19 vaccine doses using Meso Scale Diagnostics V-plex panels 22 and 25. All participants who were evaluated for BA.2 responses (i.e. those shown in Figure 2) are included in this analysis. Symbols are coloured based on post-vaccination time point, though the Spearman's rho (ρ) and p-value reported are for the combined data.

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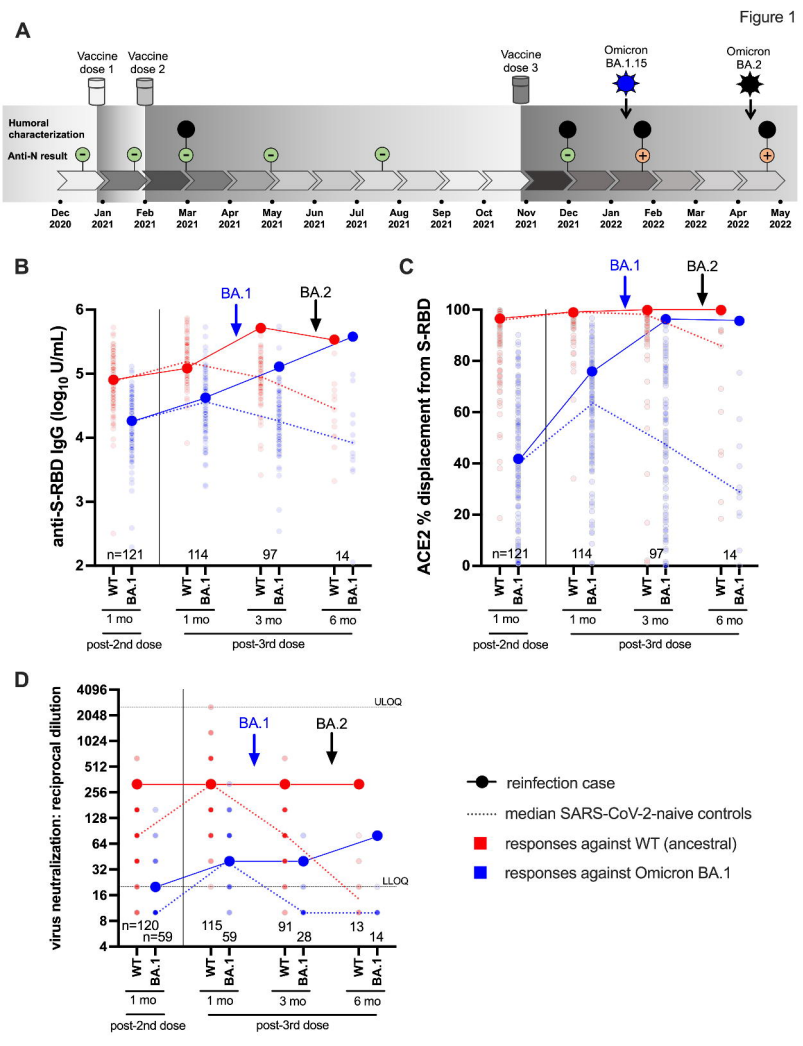
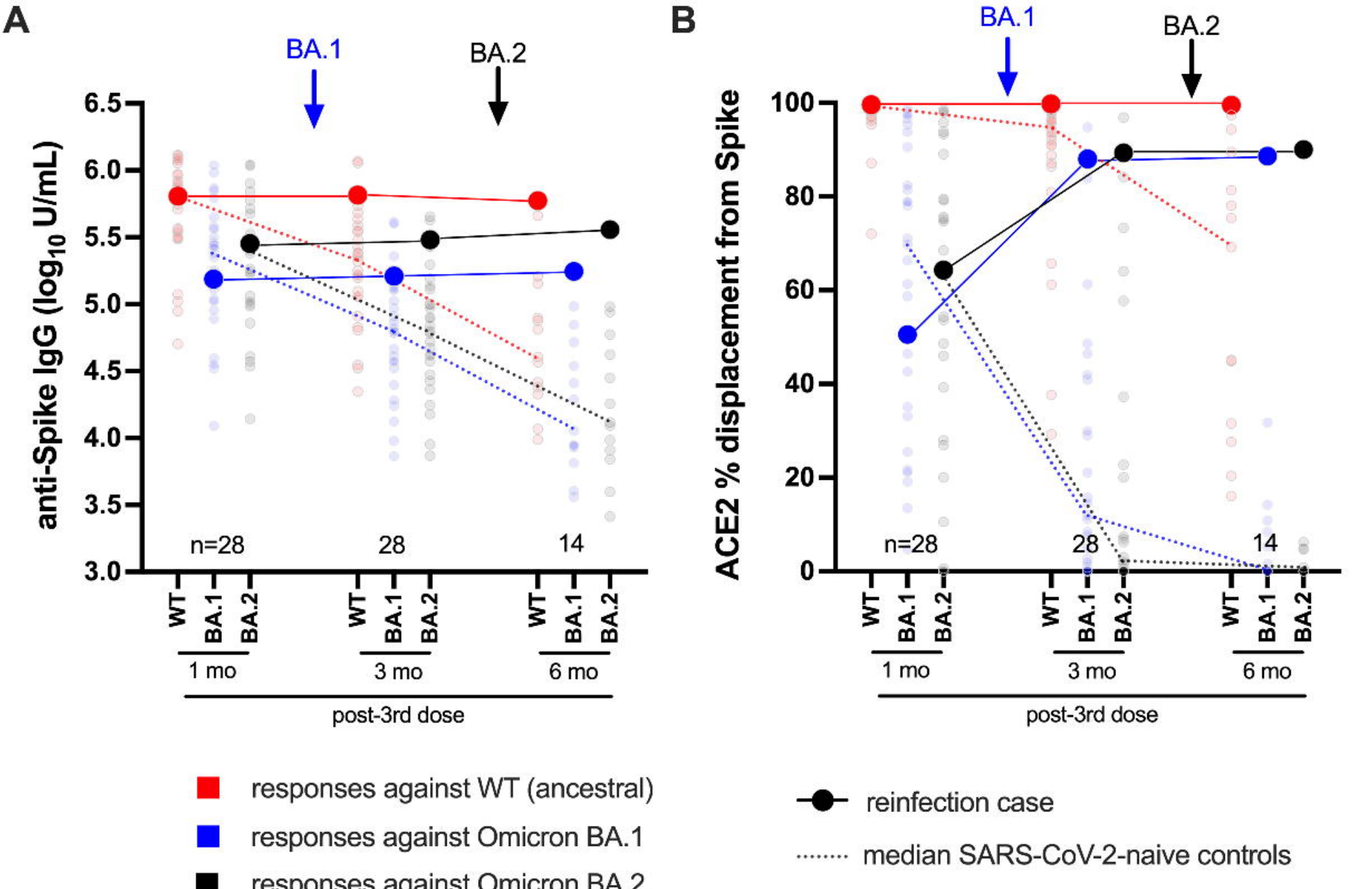
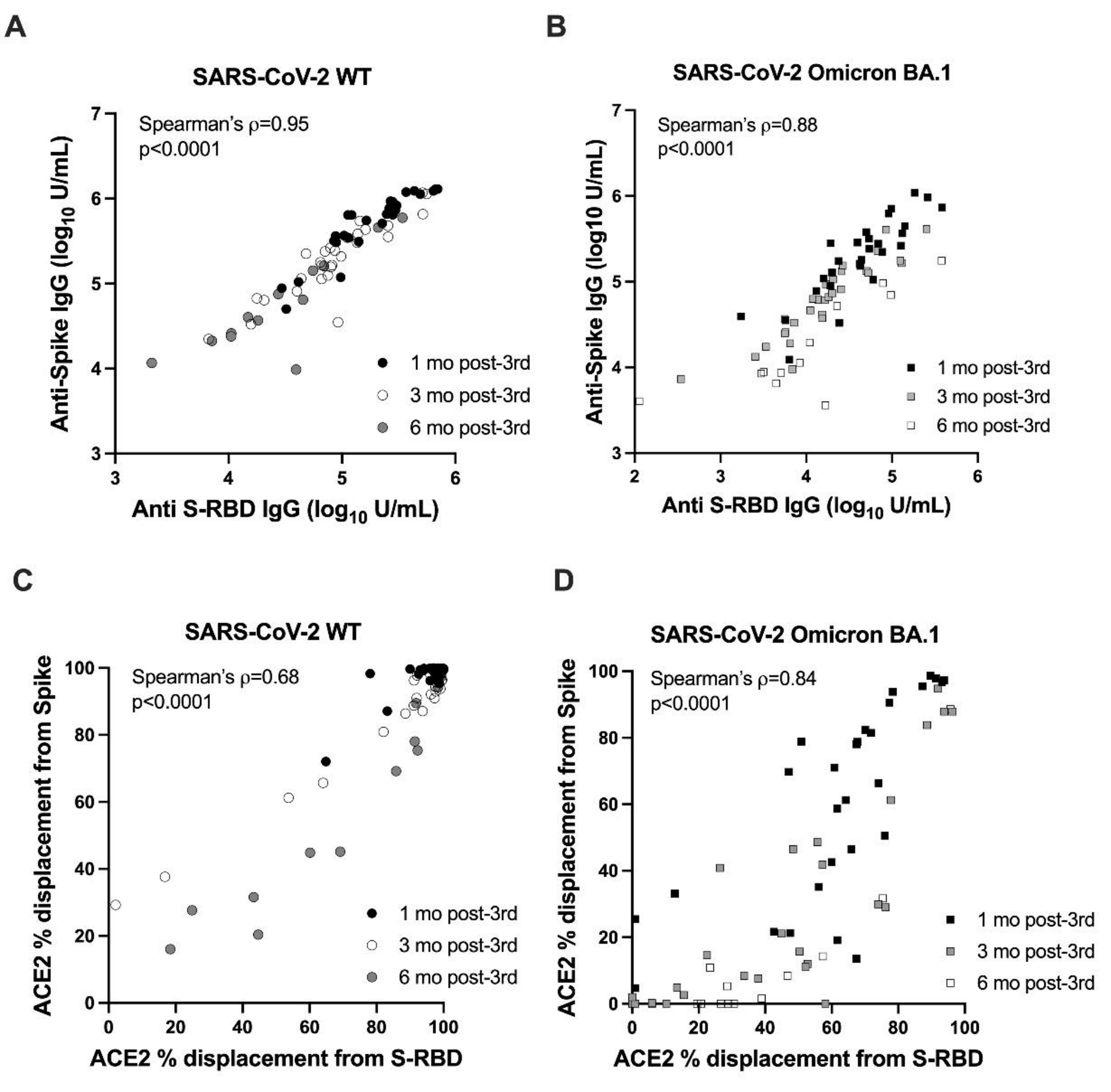
Figure 1


A
Vaccine dose 1
Vaccine dose 2
Vaccine dose 3
Omicron BA.1.15
Omicron BA.2
Humoral characterization
Anti-N result
Dec 2020
Jan 2021
Feb 2021
Mar 2021
Apr 2021
May 2021
Jun 2021
Jul 2021
Aug 2021
Sep 2021
Oct 2021
Nov 2021
Dec 2021
Jan 2022
Feb 2022
Mar 2022
Apr 2022
May 2022
B
anti-S-RBD IgG (log10 U/mL)
BA.1
BA.2
n=121
114
97
14
WT
BA.1
1 mo
post-2nd dose
post-3rd dose
3 mo
6 mo
C
ACE2 % displacement from S-RBD
D
virus neutralization: reciprocal dilution
ULOQ
LLOQ
n=120
n=59
115
59
91
28
13
reinfection case
median SARS-CoV-2-naive controls
responses against WT (ancestral)
responses against Omicron BA.1


A
B
BA.1
BA.2
anti-Spike IgG (log10 U/mL)
ACE2 % displacement from Spike
n=28
28
14
WT
BA.1
BA.2
1 mo
3 mo
6 mo
post-3rd dose
responses against WT (ancestral)
responses against Omicron BA.1
responses against Omicron BA.2
reinfection case
median SARS-CoV-2-naive controls


A
SARS-CoV-2 WT
Spearman's ρ=0.95
p<0.0001
Anti-Spike IgG (log10 U/mL)
Anti S-RBD IgG (log10 U/mL)
1 mo post-3rd
3 mo post-3rd
6 mo post-3rd
B
SARS-CoV-2 Omicron BA.1
Spearman's ρ=0.88
p<0.0001
Anti-Spike IgG (log10 U/mL)
Anti S-RBD IgG (log10 U/mL)
1 mo post-3rd
3 mo post-3rd
6 mo post-3rd
C
SARS-CoV-2 WT
Spearman's ρ=0.68
p<0.0001
ACE2 % displacement from Spike
ACE2 % displacement from S-RBD
1 mo post-3rd
3 mo post-3rd
6 mo post-3rd
D
SARS-CoV-2 Omicron BA.1
Spearman's ρ=0.84
p<0.0001
ACE2 % displacement from Spike
ACE2 % displacement from S-RBD
1 mo post-3rd
3 mo post-3rd
6 mo post-3rd