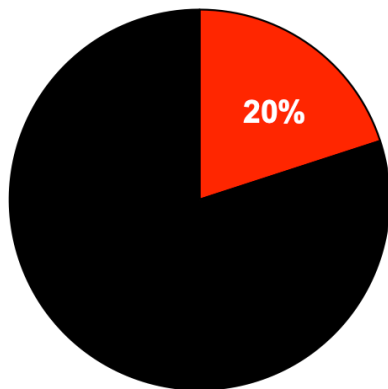


## Supplementary Figures

Table S1. Demographic and clinical description of the cohort

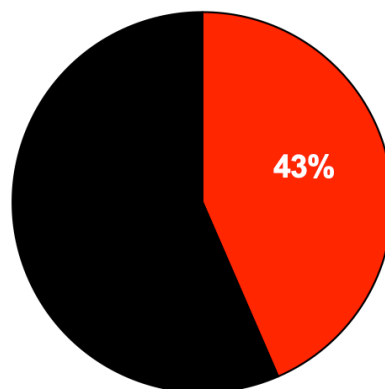
| Study ID | Age | Gender | PCR positive test | First positive PCR | Days admitted after COVID test | Incidental admission | Days between PCR test and plasma collection | Vaccinated | Vaccine type | Date of vaccination | Virus name (GISAID) | GISAID accession number        | WGS coverage  | Pangolin lineage | Nextstrain clade | HIV status | Severity COVID | Neutralization responder or non-responder |
|----------|-----|--------|-------------------|--------------------|--------------------------------|----------------------|---|------------|--------------|---------------------|---------------------|--------------------------------|---------------|------------------|------------------|------------|----------------|---|
| Cov191   | 55  | Female | 12/05/2022        | Confirmed          | 0                              | -                    | 4   | No         | -            | -                   | N44167              | EPI_ISL_13830452               | 99.16%        | BA.4             | 22A (Omicron)    | Negative   | Moderate       | Responder                                 |
| Cov192   | 20  | Female | 09/05/2022        | Yes                | 1                              | -                    | 2   | No         | -            | -                   | Not sequenced       | Not sequenced                  | Not sequenced | Not sequenced    | Not sequenced    | Negative   | Mild           | Responder                                 |
| Cov193   | 19  | Male   | 12/05/2022        | Confirmed          | 0                              | -                    | 4   | Yes        | BNT162b2     | Unknown             | N44168              | EPI_ISL_13830451               | 98.25%        | BA.4             | 22A (Omicron)    | Negative   | Mild           | Responder                                 |
| Cov194   | 26  | Male   | 11/05/2022        | Confirmed          | 1                              | -                    | 5   | No         | -            | -                   | N44169              | EPI_ISL_13830450               | 99.56%        | BA.4             | 22A (Omicron)    | Negative   | Mild           | Responder                                 |
| Cov197   | 69  | Female | 09/05/2020        | Confirmed          | 2                              | -                    | 2   | No         | -            | -                   | Not sequenced       | Not sequenced                  | Not sequenced | Not sequenced    | Not sequenced    | Negative   | Mild           | Responder                                 |
| Cov199   | 47  | Female | 09/05/2022        | Yes                | 1                              | -                    | 3   | Yes        | BNT162b2     | Unknown             | Not sequenced       | Not sequenced                  | Not sequenced | Not sequenced    | Not sequenced    | Negative   | Moderate       | Responder                                 |
| Cov201   | 62  | Female | 30/05/2022        | No                 | 0                              | -                    | 1   | Yes        | Ad26.CoV.2S  | Jan-22              | N45794              | Low coverage sample_run_220614 | 7.1%          | Unassigned       | Unassigned       | Negative   | Mild           | Responder                                 |
| Cov202   | 50  | Male   | 14/05/2022        | Yes                | -2                             | -                    | 3   | No         | -            | -                   | N44171              | EPI_ISL_19189988               | 61.91%        | Unassigned       | Unassigned       | Negative   | Mild           | Responder                                 |
| Cov203   | 57  | Male   | 08/05/2022        | Confirmed          | 8                              | -                    | 9   | No         | -            | -                   | N44172              | EPI_ISL_19189987               | 11.53%        | Unassigned       | Unassigned       | Negative   | Moderate       | Responder                                 |
| Cov204   | 67  | Female | 16/05/2022        | Confirmed          | 0                              | -                    | 1   | Yes        | BNT162b2     | Nov-21              | N44173              | EPI_ISL_13830449               | 99.64%        | BA.4             | 22A (Omicron)    | Negative   | Mild           | Responder                                 |
| Cov205   | 39  | Female | 17/05/2022        | Confirmed          | 0                              | -                    | 0   | Yes        | BNT162b2     | Nov-21              | N44174              | EPI_ISL_19189988               | 2.85%         | Unassigned       | Unassigned       | Negative   | Mild           | Responder                                 |
| Cov208   | 48  | Female | 16/05/2022        | Yes                | 0                              | -                    | 2   | No         | -            | -                   | N44177              | EPI_ISL_19189989               | 26.38%        | Unassigned       | Unassigned       | Negative   | Mild           | Responder                                 |
| Cov211   | 20  | Female | 16/05/2022        | Confirmed          | 0                              | -                    | 0   | No         | -            | -                   | N44179              | EPI_ISL_13830448               | 99.21%        | BA.4             | 22A (Omicron)    | Negative   | Moderate       | Responder                                 |
| Cov215   | 27  | Female | 17/05/2022        | Confirmed          | -1                             | -                    | 3   | No         | -            | -                   | N44183              | EPI_ISL_13830442               | 72.81%        | Unassigned       | Unassigned       | Negative   | Mild           | Responder                                 |
| Cov221   | 81  | Female | 24/05/2022        | Yes                | 0                              | -                    | 1   | No         | -            | -                   | N45800              | EPI_ISL_13830437               | 98.65%        | BA.5             | 22B (Omicron)    | Negative   | Severe         | Responder                                 |
| Cov222   | 52  | Female | 24/05/2022        | Confirmed          | 1                              | -                    | 1   | Yes        | BNT162b2     | 24-Aug-21           | N45801              | Low coverage sample_run_220614 | 3.55%         | Unassigned       | Unassigned       | Negative   | Mild           | Responder                                 |
| Cov223   | 45  | Female | 26/05/2022        | Yes                | 2                              | -                    | 1   | Yes        | BNT162b2     | Unknown             | N45802              | Low coverage sample_run_220614 | 2.44%         | Unassigned       | Unassigned       | Negative   | Mild           | Responder                                 |
| Cov225   | 74  | Male   | 29/05/2022        | Confirmed          | 4                              | -                    | 2   | Yes        | -            | -                   | N45804              | Low coverage sample_run_220614 | 51.32%        | Unassigned       | Unassigned       | Negative   | Moderate       | Responder                                 |
| Cov226   | 79  | Female | 30/05/2022        | Confirmed          | 1                              | -                    | 1   | Yes        | BNT162b2     | Unknown             | N45805              | Low coverage sample_run_220614 | 4.53%         | Unassigned       | Unassigned       | Negative   | Moderate       | Responder                                 |
| Cov227   | 49  | Male   | 30/05/2022        | No                 | 0                              | -                    | 1   | Yes        | Ad26.CoV.2S  | Apr-21              | N45806              | Low coverage sample_run_220614 | 53.24%        | Unassigned       | Unassigned       | Negative   | Severe         | Responder                                 |
| Cov228   | 80  | Male   | 26/05/2022        | Confirmed          | 2                              | -                    | 5   | No         | -            | -                   | N45807              | Low coverage sample_run_220614 | 51.74%        | Unassigned       | Unassigned       | Negative   | Moderate       | Responder                                 |
| Cov229   | 31  | Male   | 29/05/2022        | Confirmed          | 1                              | -                    | 2   | No         | -            | -                   | N45808              | Low coverage sample_run_220614 | 54.37%        | Unassigned       | Unassigned       | Negative   | Mild           | Responder                                 |
| Cov196   | 70  | Female | 10/05/2022        | Yes                | 1                              | Yes                  | 2   | No         | -            | -                   | Not sequenced       | Not sequenced                  | Not sequenced | Not sequenced    | Not sequenced    | Negative   | Moderate       | Non-responder                             |
| Cov198   | 66  | Female | 11/05/2022        | Yes                | -2                             | Yes                  | 2   | No         | -            | -                   | Not sequenced       | Not sequenced                  | Not sequenced | Not sequenced    | Not sequenced    | Negative   | Moderate       | Non-responder                             |
| Cov206   | 79  | Female | 16/05/2022        | Yes                | Asymptomatic                   | Yes                  | 1   | No         | -            | -                   | N44175              | EPI_ISL_13830448               | 99.57%        | BA.4             | 22A (Omicron)    | Negative   | Severe         | Non-responder                             |
| Cov207   | 70  | Male   | 16/05/2022        | Yes                | 0                              | No                   | 2   | No         | -            | -                   | N44176              | Low coverage sample_run_220614 | 99.31%        | BA.4             | 22A (Omicron)    | Negative   | Moderate       | Non-responder                             |
| Cov209   | 61  | Female | 21/05/2022        | Confirmed          | Asymptomatic                   | Yes                  | 3   | No         | -            | -                   | N45795              | EPI_ISL_13830440               | 98.17%        | BA.4             | 22A (Omicron)    | Negative   | Mild           | Non-responder                             |
| Cov210   | 41  | Male   | 16/05/2022        | Confirmed          | 0                              | Yes                  | 2   | No         | -            | -                   | N44178              | EPI_ISL_13830447               | 99.42%        | BA.4             | 22A (Omicron)    | Negative   | Mild           | Non-responder                             |
| Cov213   | 32  | Female | 17/05/2022        | Yes                | 0                              | Yes                  | 2   | No         | -            | -                   | N44181              | EPI_ISL_13830444               | 99.43%        | BA.4             | 22A (Omicron)    | Negative   | Mild           | Non-responder                             |
| Cov216   | 79  | Male   | 18/05/2022        | Confirmed          | 2                              | No                   | 5   | Yes        | BNT162b2     | Aug-21              | N45796              | EPI_ISL_13830439               | 99.38%        | BA.4             | 22A (Omicron)    | Negative   | Severe         | Non-responder                             |
| Cov218   | 41  | Male   | 22/05/2022        | Confirmed          | Asymptomatic                   | Yes                  | 2   | No         | -            | -                   | N45797              | Low coverage sample_run_220614 | 3.17%         | Unassigned       | Unassigned       | Negative   | Mild           | Non-responder                             |
| Cov220   | 79  | Female | 25/05/2022        | Confirmed          | 2                              | Yes                  | 1   | No         | -            | -                   | N45799              | EPI_ISL_13830438               | 98.37%        | BA.5             | 22B (Omicron)    | Negative   | Mild           | Non-responder                             |
| Cov224   | 85  | Male   | 29/05/2022        | Confirmed          | 0                              | Yes                  | 2   | Yes        | BNT162b2     | Did not complete    | N45803              | Low coverage sample_run_220614 | 60.93%        | Unassigned       | Unassigned       | Negative   | Mild           | Non-responder                             |
| Cov230   | 62  | Male   | 27/05/2022        | Confirmed          | 0                              | Yes                  | 4   | No         | -            | -                   | N45809              | Low coverage sample_run_220614 | 60.36%        | Unassigned       | Unassigned       | Negative   | Mild           | Non-responder                             |

Unvaccinated BA.1-infected



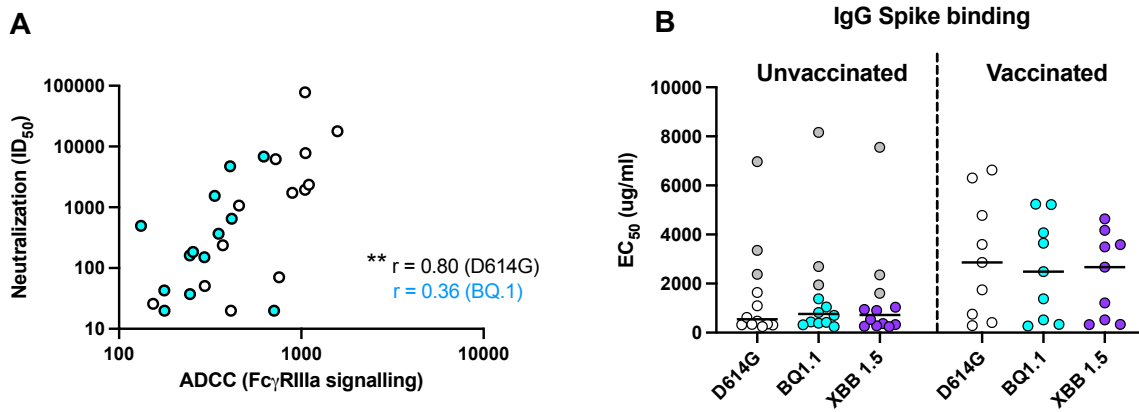
■ No neutralization  
■ BA.1 sensitive

Unvaccinated BA.4/5-infected



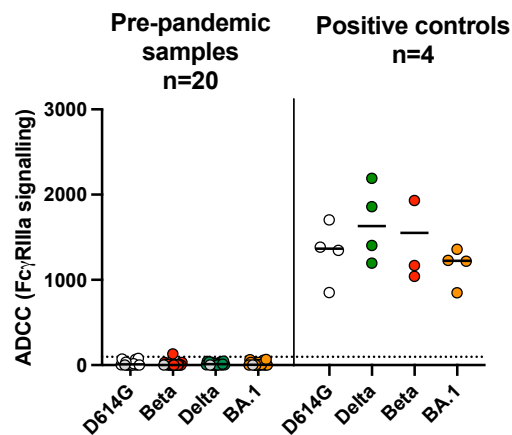
■ No neutralization  
■ BA.4 sensitive

Figure S1: Comparison of the proportion of neutralization non-responders, defined as those individuals with no detectable neutralization to spike-matched pseudoviruses in unvaccinated convalescent donors infected with BA.1 (n=25) or BA.4/5 (n=23). Red denotes lack of neutralization, and black denotes neutralization with an ID<sub>50</sub> of greater than 20, which is the limit of detection of the assay.



**Figure S2: Correlation between Fc $\gamma$ R11a signalling and neutralization activity of BA.4/5 elicited plasma antibodies**

(A) Spearman's correlations are shown against D614G (black) and BQ.1 (blue) with significance indicated as \*\* $p < 0.01$  where only samples showing detectable neutralization titers against BA.4 were included. (B) IgG spike binding EC<sub>50</sub> as determined by ELISA against D614G, BQ.1 and XBB.1.5 spike proteins across unvaccinated and vaccinated BA.4/5 individuals.



**Figure S3: Fc $\gamma$ R11a signalling of pre-pandemic samples and positive controls against several SARS-CoV-2 VOCs**

Twenty plasma samples collected prior to the SARS-CoV-2 pandemic and four positive controls were tested for ADCC potential as measured by Fc $\gamma$ R11a (CD16) cross-linking against D614G, Beta, Delta and Omicron BA.1. The dotted line represents the limit of detection of the assay, calculated on the highest mean of the tested VOCs plus 3 standard deviations of the mean.