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## Supplemental information

# Deep immunological imprinting due to the ancestral spike in the current bivalent COVID-19 vaccine

**Qian Wang, Yicheng Guo, Anthony R. Tam, Riccardo Valdez, Aubree Gordon, Lihong Liu, and David D. Ho**

**SUPPLEMENTAL INFORMATION TITLES AND LEGENDS**

**Table S1. Demographics of clinical cohorts. See also Figure 1.**

| Sample ID | Vaccine type and infected strain | Days post-vaccination or *infection | Confirmed COVID-19 | Age | Gender |
|---|---|---|---|---|---|
| *4-dose monovalent* | | | | | |
| UM-65 | BNT162b2/BNT162b2/BNT162b2/BNT162b2 | 24 | No | 52 | Female |
| UM-66 | BNT162b2/BNT162b2/BNT162b2/BNT162b2 | 20 | No | 57 | Female |
| UM-67 | BNT162b2/BNT162b2/BNT162b2/BNT162b2 | 20 | No | 61 | Female |
| UM-68 | mRNA-1273/mRNA-1273/mRNA-1273/mRNA-1273 | 22 | No | 48 | Female |
| UM-69 | BNT162b2/BNT162b2/BNT162b2/BNT162b2 | 23 | No | 50 | Female |
| UM-70 | BNT162b2/BNT162b2/BNT162b2/BNT162b2 | 22 | No | 50 | Female |
| UM-71 | BNT162b2/BNT162b2/BNT162b2/BNT162b2 | 20 | No | 58 | Female |
| UM-72 | BNT162b2/BNT162b2/BNT162b2/BNT162b2 | 26 | No | 56 | Female |
| UM-73 | BNT162b2/BNT162b2/BNT162b2/BNT162b2 | 29 | No | 63 | Female |
| UM-74 | BNT162b2/BNT162b2/BNT162b2/BNT162b2 | 25 | No | 58 | Female |
| UM-75 | BNT162b2/BNT162b2/BNT162b2/BNT162b2 | 21 | No | 62 | Male |
| UM-76 | BNT162b2/BNT162b2/BNT162b2/BNT162b2 | 26 | No | 54 | Female |
| UM-77 | BNT162b2/BNT162b2/BNT162b2/BNT162b2 | 23 | No | 53 | Male |
| UM-78 | BNT162b2/BNT162b2/BNT162b2/BNT162b2 | 21 | No | 55 | Female |
| UM-79 | BNT162b2/BNT162b2/BNT162b2/BNT162b2 | 23 | No | 59 | Female |
| UM-80 | BNT162b2/BNT162b2/BNT162b2/BNT162b2 | 21 | No | 49 | Female |
| UM-81 | BNT162b2/BNT162b2/BNT162b2/BNT162b2 | 27 | No | 57 | Female |
| UM-82 | BNT162b2/BNT162b2/BNT162b2/BNT162b2 | 27 | No | 55 | Female |
| Q97 | BNT162b2/BNT162b2/BNT162b2/BNT162b2 | 36 | No | 53 | Female |
| *3-dose monovalent + bivalent* | | | | | |
| UM-36 | BNT162b2/BNT162b2/BNT162b2/Moderna Bivalent | 24 | No | 38 | Female |
| UM-37 | BNT162b2/BNT162b2/BNT162b2/Moderna Bivalent | 27 | No | 42 | Female |
| UM-39 | mRNA-1273//mRNA-1273/mRNA-1273/Moderna Bivalent | 24 | No | 36 | Male |
| UM-40 | BNT162b2/BNT162b2/BNT162b2/Pfizer Bivalent | 25 | No | 37 | Female |
| UM-43 | BNT162b2/BNT162b2/BNT162b2/Pfizer Bivalent | 25 | No | 49 | Female |
| UM-44 | BNT162b2/BNT162b2/BNT162b2/Moderna Bivalent | 25 | No | 37 | Female |
| UM-47 | BNT162b2/BNT162b2/BNT162b2/Pfizer Bivalent | 26 | No | 45 | Male |
| UM-48 | BNT162b2/BNT162b2/mRNA-1273/Moderna Bivalent | 26 | No | 43 | Female |
| UM-51 | mRNA-1273/mRNA-1273/mRNA-1273/Moderna Bivalent | 29 | No | 32 | Female |
| UM-52 | BNT162b2/BNT162b2/BNT162b2/Pfizer Bivalent | 23 | No | 43 | Female |
| UM-53 | BNT162b2/BNT162b2/BNT162b2/Pfizer Bivalent | 26 | No | 43 | Female |
| UM-54 | BNT162b2/BNT162b2/mRNA-1273/Moderna Bivalent | 29 | No | 38 | Female |
| UM-55 | BNT162b2/BNT162b2/BNT162b2/Moderna Bivalent | 28 | No | 38 | Female |
| UM-56 | BNT162b2/BNT162b2/mRNA-1273/Moderna Bivalent | 27 | No | 36 | Female |
| UM-60 | BNT162b2/BNT162b2/BNT162b2/Moderna Bivalent | 30 | No | 24 | Female |
| Q101 | mRNA-1273/mRNA-1273/mRNA-1273/Moderna Bivalent | 30 | No | 32 | Female |
| Q102 | BNT162b2/BNT162b2/mRNA-1273/Moderna Bivalent | 23 | No | 39 | Male |
| Q103 | BNT162b2/BNT162b2/BNT162b2/Pfizer Bivalent | 30 | No | 26 | Female |
| Q104 | mRNA-1273/mRNA-1273/mRNA-1273/Pfizer Bivalent | 30 | No | 27 | Female |
| Q105 | BNT162b2/BNT162b2/BNT162b2/Pfizer Bivalent | 23 | No | 23 | Male |
| *BA.5 breakthrough* | | | | | |
| Q71 | mRNA-1273/mRNA-1273/BNT162b2/BA.5.2.1 | *29 | Yes | 29 | Female |
| Q77 | BNT162b2/BNT162b2/BNT162b2/BA.5 | *22 | Yes | 61 | Female |
| Q79 | mRNA-1273/mRNA-1273/mRNA-1273/BA.5 | *15 | Yes | 28 | Female |

| Sample ID | Vaccine type and infected strain | Days post-vaccination or *infection | Confirmed COVID-19 | Age | Gender |
|---|---|---|---|---|---|
| Q80 | mRNA-1273/mRNA-1273/mRNA-1273/BA.5 | *21 | Yes | 24 | Female |
| Q81 | BNT162b2/BNT162b2/BNT162b2/BA.5 | *75 | Yes | 35 | Female |
| Q82 | BNT162b2/BNT162b2/mRNA-1273/BA.5 | *63 | Yes | 46 | Female |
| Q83 | BNT162b2/BNT162b2/BNT162b2/BA.5 | *28 | Yes | 55 | Male |
| Q84 | BNT162b2/BNT162b2/BNT162b2/BA.5 | *17 | Yes | 57 | Female |
| UM-85 | BNT162b2/BNT162b2/BNT162b2/BA.5 | *29 | Yes | 44 | Female |
| UM-86 | BNT162b2/BNT162b2/mRNA-1273/BA.5 | *29 | Yes | 36 | Female |
| UM-87 | BNT162b2/BNT162b2/BNT162b2/BNT162b2/BA.5 | *31 | Yes | 54 | Female |
| UM-88 | BNT162b2/BNT162b2/BNT162b2/BNT162b2/BA.5 | *28 | Yes | 69 | Male |
| UM-89 | BNT162b2/BNT162b2/BNT162b2/BNT162b2/BA.5 | *42 | Yes | 44 | Male |
| UM-90 | BNT162b2/BNT162b2/BNT162b2/BNT162b2/BA.5 | *28 | Yes | 41 | Female |
| UM-91 | BNT162b2/BNT162b2/BNT162b2/BNT162b2/BA.5 | *28 | Yes | 44 | Female |
| UM-92 | BNT162b2/BNT162b2/BNT162b2/BNT162b2/BA.5 | *31 | Yes | 29 | Female |
| UM-93 | BNT162b2/BNT162b2/BNT162b2/BNT162b2/BA.5 | *29 | Yes | 48 | Female |
| UM-96 | BNT162b2/BNT162b2/BNT162b2/BNT162b2/BA.5 | *33 | Yes | 58 | Female |
| Q106 | mRNA-1273/mRNA-1273/mRNA-1273/mRNA-1273/BA.5 | *18 | Yes | 32 | Female |
| *BQ breakthrough* | | | | | |
| BQ-1 | BNT162b2/BNT162b2/BNT162b2/BNT162b2/mRNA-1273/BQ | *33 | Yes | 53 | Female |
| BQ-2 | BNT162b2/BNT162b2/BNT162b2/mRNA-1273/BQ | *30 | Yes | 32 | Female |
| BQ-3 | BNT162b2/BNT162b2/BNT162b2/mRNA-1273/BQ | *21 | Yes | 35 | Female |
| BQ-4 | BNT162b2/BNT162b2/mRNA-1273/BQ | *39 | Yes | 52 | Female |
| BQ-5 | BNT162b2/BNT162b2/BNT162b2/BNT162b2/mRNA-1273/BQ | *22 | Yes | 62 | Female |
| BQ-6 | BNT162b2/BNT162b2/mRNA-1273/BQ | *34 | Yes | 29 | Female |
| BQ-7 | BNT162b2/BNT162b2/BQ | *44 | Yes | 35 | Female |
| BQ-8 | mRNA-1273/mRNA-1273/mRNA-1273/mRNA-1273/BQ | *59 | Yes | 33 | Female |
| BQ-9 | BNT162b2/BNT162b2/BNT162b2/BNT162b2/BQ | *44 | Yes | 45 | Female |
| BQ-10 | JNJ-78436735/JNJ-78436735/BNT162b2/BNT162b2/BQ | *32 | Yes | 47 | Female |
| BQ-11 | BNT162b2/BNT162b2/BNT162b2/BQ | *36 | Yes | 36 | Female |
| BQ-12 | BNT162b2/BNT162b2/BNT162b2/BNT162b2/BNT162b2/BQ | *77 | Yes | 59 | Female |
| BQ-13 | BNT162b2/BNT162b2/BNT162b2/BNT162b2/BQ | *25 | Yes | 39 | Female |
| BQ-14 | BNT162b2/BNT162b2/BNT162b2/BNT162b2/BQ | *67 | Yes | 43 | Female |

**Table S2. Summary of clinical cohorts. See also Figure 1.**

| Characteristic | 4-dose Monovalent (N=19) | 3-dose monovalent + bivalent (N=20) | BA.5 Breakthrough (N=19) | BQ Breakthrough (N=14) |
|---|---|---|---|---|
| **Sex - No. (%)** | | | | |
| Female | 17 (89.5%) | 16 (80.0%) | 16 (84.2%) | 14 (100%) |
| Male | 2 (10.5%) | 4 (20.0%) | 3 (15.8%) | 0 (0%) |
| **Mean Age (range)-year** | 55.3 (48 - 63) | 36.4 (23 - 49) | 43.9 (24 - 69) | 42.9 (29 - 62) |
| **Days post-vaccination or *infection** | 24.0 | 26.5 | *31.4 | *40.2 |

*For the BA.5 breakthrough cohort, days are measured between last dose of vaccine and documented breakthrough infection.

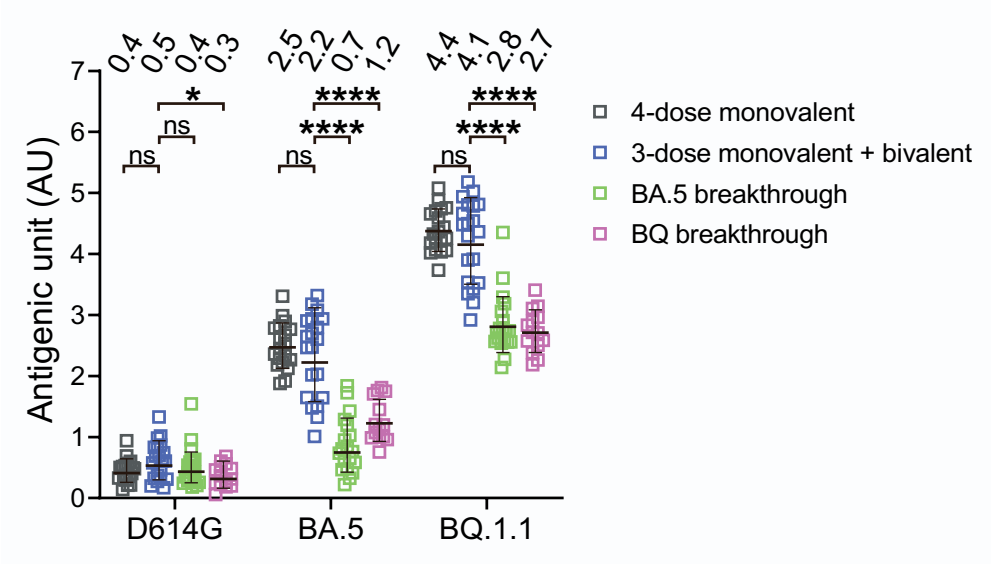


**Figure S1. Antigenic units from D614G, BA.5, and BQ.1.1 to the serum samples in the "4-dose monovalent", "3-dose monovalent + bivalent", "BA.5 breakthrough" and "BQ breakthrough" cohorts.** Data were generated based on the neutralization data from Figure 1. One AU corresponds to a two-fold serum dilution of the neutralization titer. Mann-Whitney test was used to compare the results for the "3-dose monovalent + bivalent cohort". ns, not significant; *$p < 0.05$; ****$p < 0.0001$. **See also Figure 2.**