Profiling antibody immunity to SARS-CoV-2 mRNA vaccination

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Introduction

COVID-19 mRNA vaccines induce ongoing SARS-COV-2 Spike-specific B cell affinity maturation which can be appreciated by simple serology using the Abu-Raya avidity method.

Objective

To measure the antibody maturation against SARS-CoV-2 and variants following each vaccine dose, and to determine the effect of dosing interval on antibody maturation.

Methods & Results

anti-Spike/RBD IgG fractional avidity assay

The proportions of 'very low' to 'very high' avidity of anti-SARS-CoV-2 (Spike and receptor-binding domain [RBD]) IgG in serum were determined using a titration of ammonium thiocyanate (0 – 2.0 M) on an MSD multiplex ECLIA (Figure 1).

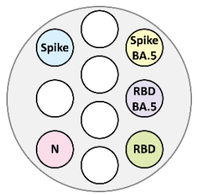


Figure 1. Multiplex MSD ECLIA.

Maturation cohort: Healthcare workers; COVID-19 uninfected confirmed by PCR and anti-N serology (n = 13).

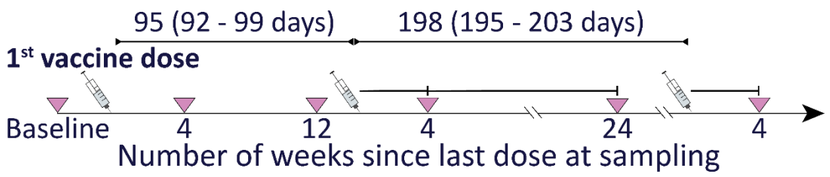
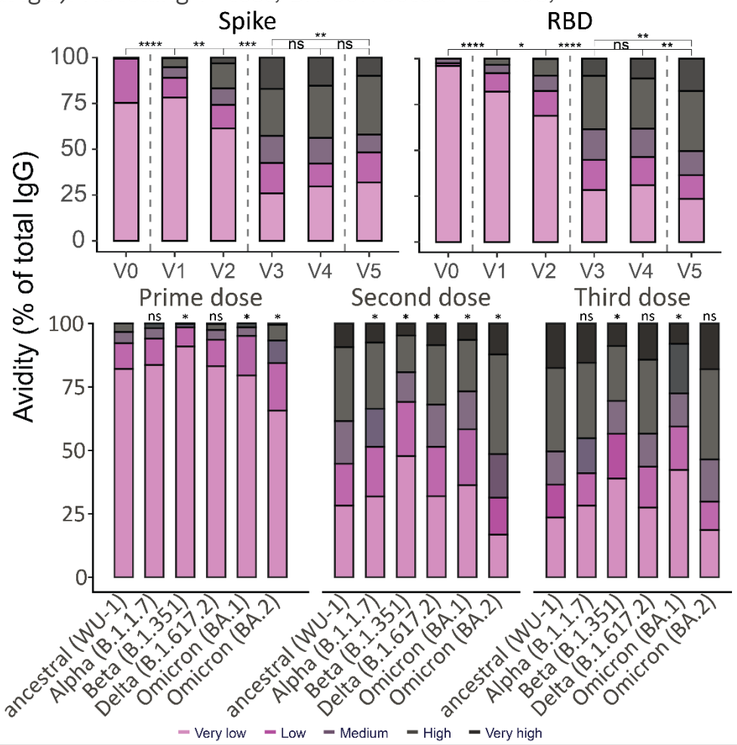


Figure 2. Maturation timelines.

Results

Figure 3. Anti-Spike/RBD and RBD variant avidity profiles (% of total IgG). Hotelling T^2 test; BH corrected $P \leq 0.05$, *.



Results (continued)

Short and mid interval: Paramedics; age, sex, comorbidity-matched; two (2) BNT162b2 mRNA vaccines with a short (n = 12) or mid (n = 14) 1st-2nd vaccine dosing interval.

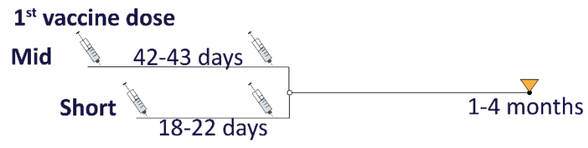
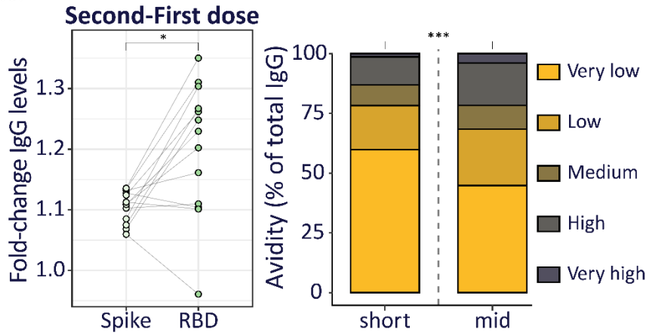


Figure 4. Short and mid interval.

Figure 5. Anti-Spike and RBD fold change post-second dose compared to first dose levels. Paired Wilcoxon rank sign test. Spike avidity profiles (% of total IgG) for short and mid vaccine intervals.



Conclusions

- IgG avidity continued to evolve after a prime dose up to 12 weeks which contributed to booster dose antibody function
- Requirement for at least a 2nd dose to generate potent RBD-directed antibodies with broad reactivity towards emerging variants in absence of exposure
- Avidity is greatly affected by vaccine intervals, where a difference of 20 days can dramatically enhance post-second dose antibody avidity

References

1. Robinson, W. H., Lanz, T. V., Brewer, R. C., *et al.* (2021). BNT162b2 vaccine induces divergent B cell responses to SARS-CoV-2 S1 and S2. *Nature Immunology 2021*, 1–7.
2. Abu Raya, B., Bamberger, E., Almog, M., *et al.* (2015). Immunization of pregnant women against pertussis: The effect of timing on antibody avidity. Vaccine, 33 (16), 1948–1952.

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