Functional humoral responses to SARS-CoV-2 Omicron sublineages in hematopoietic stem cell transplant (HSCT) recipients and healthy controls.

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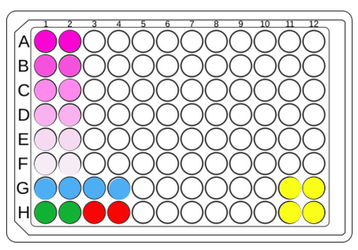
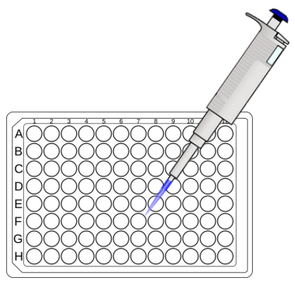
Introduction

Covid-19 was one of the most detrimental pandemics the human population has experienced, and it is still ongoing. Millions of deaths and long-term illnesses have been caused by the virus (SARS-CoV-2). Although various vaccines have been developed and distributed worldwide, the virus has continuously mutated and continued to survive, making it essential to maintain herd immunity. The answer scientists are seeking is whether the vaccines administered to billions of people are effective and if they provide long-term immunity. Hundreds of volunteers came forward and donated blood samples pre-vaccination and post-vaccination at multiple time points. This act allowed the Clinical Infection Research Group and other institutes to analyse how effective the vaccine was throughout its course. We studied the antibody content of the patient samples and their defences when combined with CHO cells; they were reinfected with different sublineages of SARS-CoV-2 pseudotyped lentiviruses. Each sample was compared to millions of other samples, in which we could begin to understand the vaccine's effectiveness at all time points for each dose.

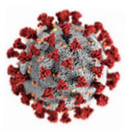
Methods

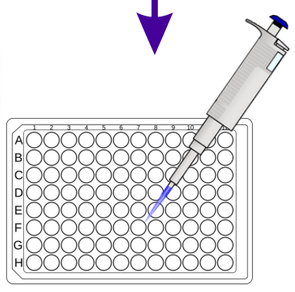


Do a serial dilution for all serum samples and positive and negative controls (started with 1;20 dilution)

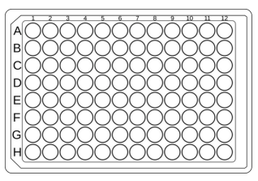


Add all serum samples to each well

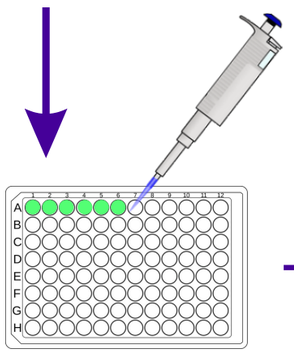




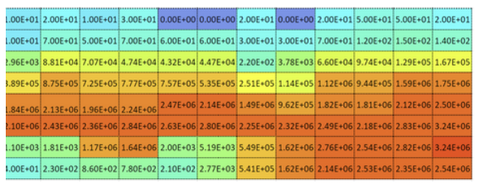
Add pseudovirus to all wells accept cell control wells



After 1 hour of incubation in a 37°C incubator, add culture CHO cells to all wells, and incubate for 24 hours.



Add Glo Bright Luciferase to all wells and observe using a Glo Max microplate reader

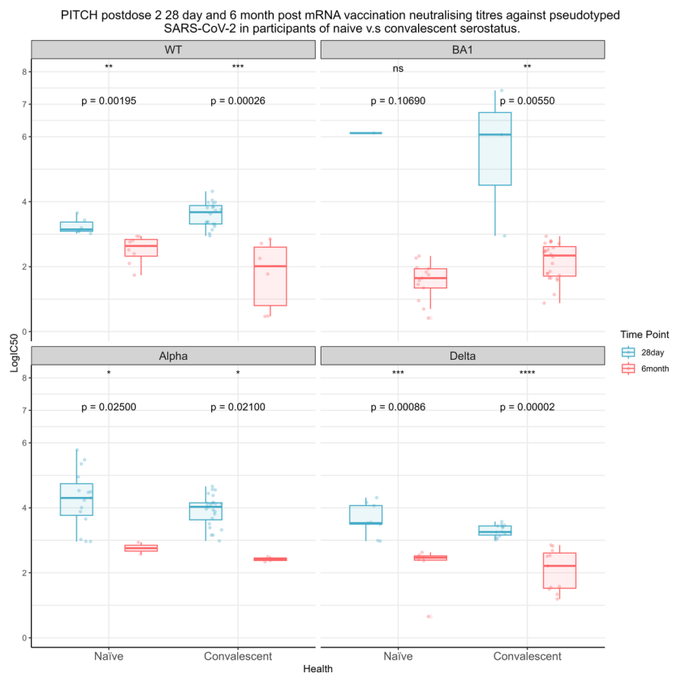


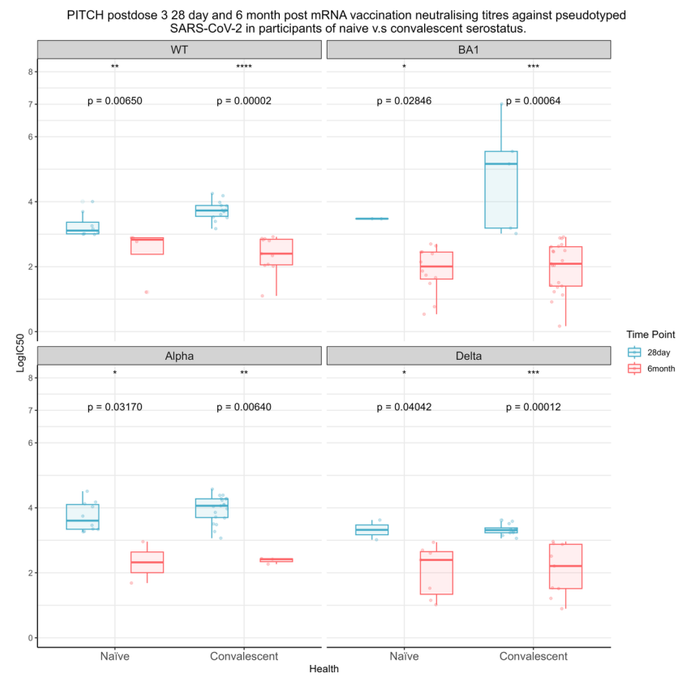
1.00E+01	2.00E+01	1.00E+01	3.00E+01	0.00E+00	0.00E+00	2.00E+01	0.00E+00	2.00E+01	5.00E+01	5.00E+01	2.00E+01
1.00E+01	7.00E+01	5.00E+01	7.00E+01	6.00E+01	6.00E+01	3.00E+01	3.00E+01	7.00E+01	1.20E+02	1.50E+02	1.40E+02
1.96E+03	8.81E+04	7.07E+04	4.74E+04	4.32E+04	4.47E+04	2.20E+02	3.78E+03	6.60E+04	9.74E+04	1.29E+05	1.67E+05
1.89E+05	8.75E+05	7.25E+05	7.77E+05	7.57E+05	5.35E+05	2.51E+05	1.14E+05	1.12E+06	9.44E+05	1.59E+06	1.75E+06
1.84E+06	2.13E+06	1.96E+06	2.24E+06	2.47E+06	2.14E+06	1.49E+06	9.62E+05	1.82E+06	1.81E+06	2.12E+06	2.50E+06
1.10E+06	2.43E+06	2.36E+06	2.84E+06	2.63E+06	2.80E+06	2.25E+06	2.32E+06	2.49E+06	2.18E+06	2.83E+06	3.24E+06
1.10E+03	1.81E+03	1.17E+06	1.64E+06	2.00E+03	5.19E+03	5.49E+05	1.62E+06	2.76E+06	2.54E+06	2.82E+06	3.24E+06
1.00E+01	2.30E+02	8.60E+02	7.80E+02	2.10E+02	2.77E+03	5.41E+05	1.62E+06	2.14E+06	2.53E+06	2.35E+06	2.54E+06

Results as shown will appear on the reader, files can be exported to an excel file for data analysis

Results + Discussion

Figure 1 - Post-dose-2 graph v.s post-dose-3 graph - graphs produced on RStudio representing the Log IC50 for each time point - 28 day and 6 month post vaccination, both naive and convalescent serum samples, for each pseudovirus.
P-values on the graph are a comparison of naive convalescent serum values in each time period.





The hypothesis is that the immune cells are more responsive to SARS-CoV-2 after a shorter period has passed post-vaccination.
A Wilcoxon test was undertaken using RStudio. All results, except post-dose-2 - BA1 - naive data, was proven to have a significant difference in the two-time points - 28 day and 6 month post vaccination. This is represented by P-values on the graph being lower than 0.01. These statistics enable the rejection of a null-hypothesis for the majority.
In all cases it is visually clear that 28-day post-vaccination data has a higher LogIC50 than 6 month post-vaccination, suggesting that the serum samples at 28-day post-vaccination can neutralise all pseudoviruses at a greater ability.
This lines up with the idea that memory cells have a 'limited' lifespan after some time without reinfection (this may be by natural infection or vaccination), and the immune system cannot respond to pathogens- such as SARS-CoV-2, as effectively.
The assumption can be made that the vaccination has short-term effectiveness against SARS-CoV-2.

Conclusion

If I were able to further this experiment, I would repeat the experiment for post-dose-2 - BA1 - naive serum. This would enable the understanding of whether the experimental method caused the non-significant data, or whether it was the pseudovirus tested against those samples.

Additionally, I would test the IC50 of serum samples for baseline and post-dose-1 vaccination-matched serum samples. This would enable the comparison of the T-cell response from baseline (before vaccination) to post-dose-1, post-dose 2, and post-dose 3. The effectiveness of 'booster' vaccinations and yearly doses could analysed, and whether a significant immune response occurs.

The relationship between the health of an individual and the immune response to SARS-CoV-2 could also be further analysed.
As presented in the data above, there is evidence to suggest that the immune response in naive v.s convalescent serum samples is significant, but testing this on a larger scale for all post-vaccination time-point would confirm the matter.