Lower B Cell Responses Rather Than Circulating Antibody Titres Are Associated With SARS-CoV-2 Infection Post Third Dose COVID-19 Vaccination

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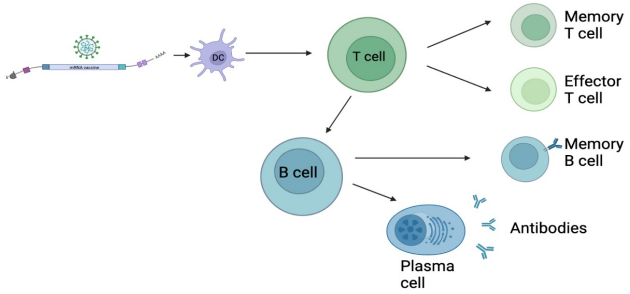
BACKGROUND

- Which components of the immune response to SARS-CoV-2 vaccination best protect against subsequent infection remains unclear.
- We explored:

1. SARS-CoV-2 specific antibody and B cell responses pre and post 3rd dose vaccine.
2. Their relationship to incident SARS-CoV-2 infection.



METHODS

- This is an analysis within the All Ireland Infectious Diseases (AIID) cohort study.
- Subjects in two centres provided samples before and 14 days post 3rd dose vaccine with Pfizer-BioNTech 162b2.
- At 18-22 weeks post vaccine, subjects self-reported incident COVID-19 infection.
- Electrochemiluminescence assays quantified antibodies to SARS-CoV-2 spike subunit 1 (S1), subunit 2 (S2) and receptor-binding domain (RBD) in plasma.
- In a subset of subjects, we assessed SARS-CoV-2 specific plasma cell and memory B cell responses from peripheral blood mononuclear cells. Stimulated plasma and memory B cells were seeded on plates coated with RBD or full Spike antigen and antigen specific responses measured by ELISpot.
- We compared between group differences by Wilcoxon signed rank or Mann–Whitney U tests. Data are median [IQR] unless specified.

RESULTS

- 47 of the 133 subjects (35.3%) reported incident COVID-19 infection post 3rd vaccine, demographics are in table 1.
- Antibody titres, plasma cell and memory B-cell responses all increased significantly at day 14 post 3rd vaccine (Table 1 & 2, all $p<0.001$).
- Day 14 antibody titres did not differ in those with and without incident infection (table 1).

Table 1: Characteristics of the Study Population (Antibody Titres)

		Incident COVID-19 Infection	
		Yes (n= 47)	No (n=86)
Age (years)		41 (33-47.5)	43.4 (32-51)
Female sex (n (%))		33 (70%)	73 (85%)
Previous (pre booster) COVID-19 infection (n (%))		7 (15%)	14 (16%)
Months since previous infection		10 (8.5-17)	10 (8.5-16.75)
Initial vaccinations Pfizer-BioNTech BNT162b2 (n (%)) AstraZeneca ChAdOx1 nCoV-19(n(%))		38 (81%) 9 (19%)	6 (73%) 2 (27%)
Days since 2nd vaccine		283 (245-286)	281.5 (185-285.75)
Anti RBD antibody titre (IU/mL)	Pre	194 (97-438)	229 (109-384)
	d14	7332 (4404-11017)	8310 (5004-11944)
Anti S1 antibody titre (IU/mL)	Pre	378 (194-869)	442 (201-683)
	d14	16011 (8405-22427)	16305 (10203-22799)
Anti S2 antibody titre (IU/mL)	Pre	30 (15-118)	23 (12-61)
	d14	470 (345-773)	612 (335-948)

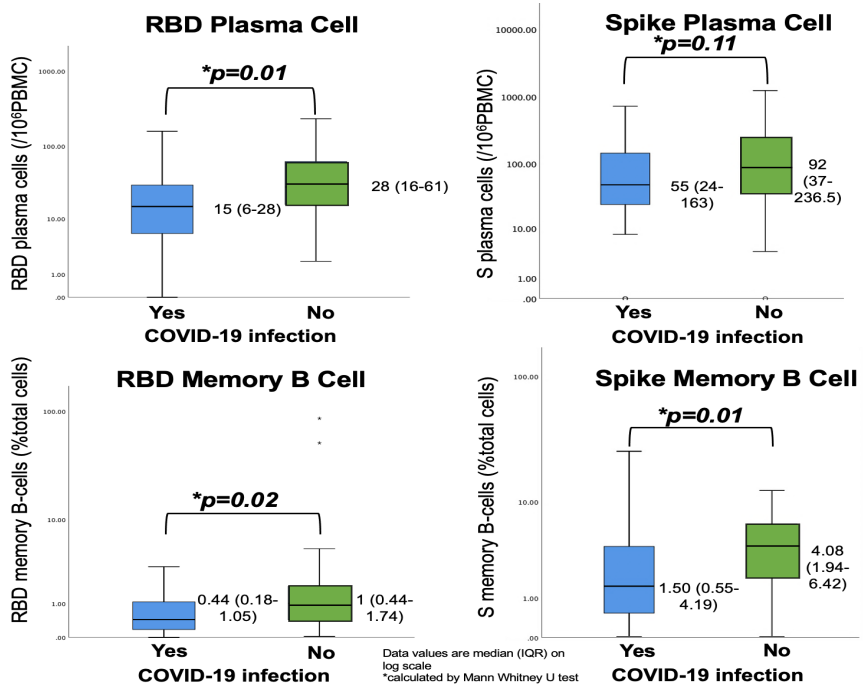
Table 2: B cell responses

		Incident COVID-19 Infection	
		Yes (n= 32)	No (n=44)
RBD plasma cells (cells/10^6PBMC)	Pre	11 (4-16.5)	11 (4-22)
	d14	15 (6-28)	28 (16-61)
RBD memory B cells (% total cells)	Pre	0.05 (0.02-0.15)	0.14 (0.06-0.27)
	d14	0.44 (0.18-1.05)	1 (0.44-1.74)
Spike plasma cells (cells/10^6PBMC)	Pre	11 (5.5-20.5)	14 (6-26)
	d14	55 (24-163)	92 (37-236.5)
Spike memory B cells (% total cells)	Pre	0.11 (0.04-0.31)	0.25 (0.1-0.56)
	d14	1.50 (0.55-4.19)	4.08 (1.94-6.42)

RESULTS

- Lower day 14 RBD plasma cells and lower RBD and full spike memory B cell responses were observed in those with incident COVID-19 infection (all $p<0.05$) (Figure 1).
- Similar results were observed with pre third dose RBD and full spike memory B-cell responses (both $p<0.05$) (table 2).

Figure 1: Day 14 B Cell Responses and Incident COVID-19 Infection



CONCLUSION

- Lower day 14 B cell responses, but not antibody titres were associated with incident COVID-19 infection suggesting B cell responses better predict protection against COVID-19 infection.

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