PRIOR SARS-COV-2 INFECTION PROTECTS AGAINST SYMPTOMATIC COMMON COLD CORONAVIRUSES

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David J Bean [1], Janet Monroe [2], Alex Olson [2], Janice Weinberg [3], Manish Sagar [1,2]

[1] Department of Microbiology, Boston University Chobanian & Avedisian School of Medicine, Boston, MA, USA, [2] Department of Medicine, Boston University Chobanian & Avedisian School of Medicine, Boston, MA, USA, [3] Department of Biostatistics, Boston University School of Public Health, Boston, MA, USA

Background

- In the past twenty years, highly pathogenic coronaviruses have emerged in the human population (SARS-CoV-1, MERS-CoV, SARS-CoV-2).
- Efforts to create a pan-CoV vaccine are imperative as we prepare for future novel coronavirus outbreaks.
- Both natural infection and vaccination methods provide substantial protection against severe COVID-19 and immediate reinfection.
- Yet, little is known how this immunity against SARS-CoV-2 protects against heterologous coronaviruses, including common cold coronaviruses (ccCoV) and future emerging CoVs.
- **We examined incidence of and immune differences against related but different ccCoV as a proxy for response against a future emerging CoV among those with SARS-CoV-2 infection, COVID-19 vaccination, or neither type of SARS-CoV-2 exposure.**

Methods

Patient Recruitment and Sample Collection from BMC

Dec 2019 – Oct 2021

SARS-CoV-2 infection (n=493), COVID-19 vaccination (n=1,568), or neither exposure (n=2,874).

Dec 2020 – Oct 2021

Signs of a respiratory infection. Underwent a comprehensive respiratory pathogen test at BMC

Tested positive for an endemic human coronavirus (229E, HKU1, NL63, OC43)

Tested positive for a different respiratory pathogen (rhinovirus, enterovirus, etc.)

Analyzed incidence of respiratory infections dependent on the time since SARS-CoV-2 exposure (infection, vaccination, or neither) (**Figure 1**)

Dec 2020 – Oct 2021

Blood was collected from a subset of patients without a symptomatic respiratory infection

SARS-CoV-2 infection (n=21), COVID-19 vaccination (n=20), or neither exposure (n=81).

Levels of T cell activation was measured in the presence of various CoV peptide pools (**Figure 2**).

Plasma was tested for the ability to neutralize CoV spike pseudovirus (**Figure 3**)

Results

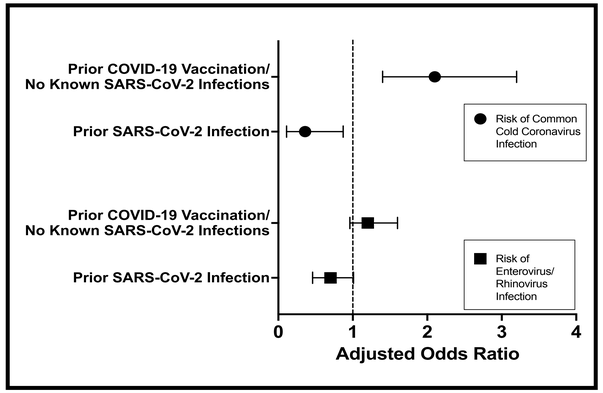


Figure 1. Risk of respiratory infections after SARS-CoV-2 infection or COVID-19 vaccination. The incidence of common cold coronavirus (circles) and enterovirus/ rhinovirus (squares) infections were measured after either a SARS-CoV-2 infection or a COVID-19 vaccination. The odds ratio of infection was calculated in comparison to the incidence of infection of individuals without a prior SARS-CoV-2 infection or a COVID-19 vaccination. The odds ratio was adjusted to account for differences in age, gender, and pre-existing co-morbidities. The error bars represent the 95% confidence interval.

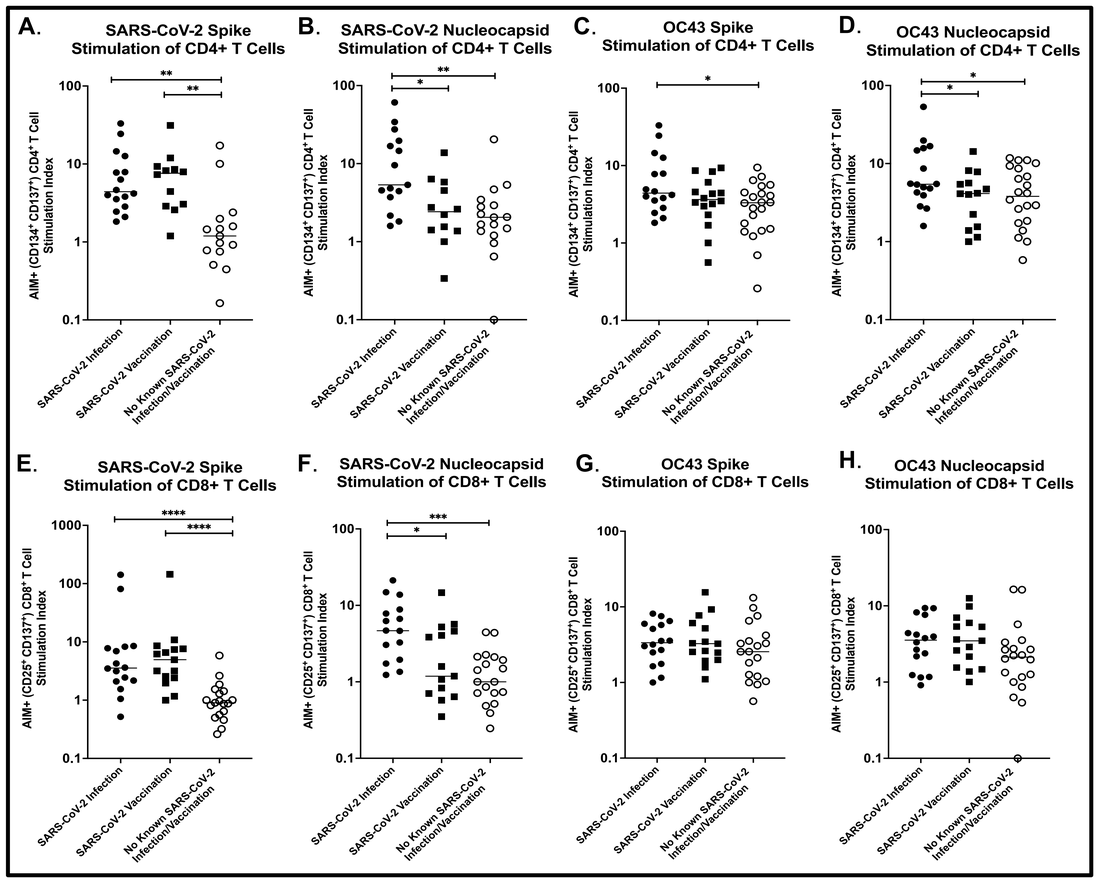


Figure 2. T cell activation after CoV peptide stimulation. The percent of activated CD4+ (CD134+, CD137+) and CD8+ (CD25+ CD137+) T cells were measured after stimulation with viral protein derived peptide pools: SARS-CoV-2 spike (A, E), SARS-CoV-2 nucleocapsid (B, F), OC43 spike (C, G), OC43 nucleocapsid (D, H). The stimulation index was calculated from the ratio of virus specific T cell response to the negative control T cell response. Univariate comparisons between groups were done by Mann-Whitney *U* tests. *, **, ***, **** denotes p≤0.05, p≤0.01, p≤0.001, and p≤0.0001 respectively.

Results

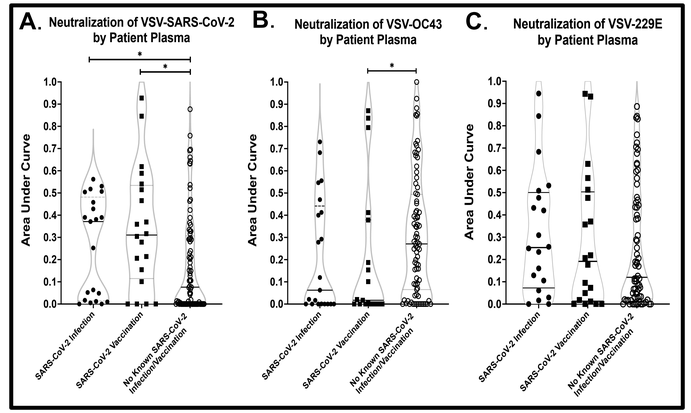


Figure 3. Neutralization of CoV spike pseudotyped virus by patient plasma. A series of dilutions of patient plasma was tested for the ability to neutralize various VSV-CoV-spike pseudoviruses: VSV-SARS-CoV-2-spike (A), VSV-OC43-spike (B), and VSV-229E-spike (C). Neutralization curves were created from the dilution series and area under the curve (AUC) was calculated. Univariate comparisons between groups were done by Mann-Whitney *U* tests. * denotes p≤0.05.

Conclusions

- A previous SARS-CoV-2 natural infection was associated with a lower risk of a subsequent ccCoV infection compared to individuals with or without a COVID-19 vaccination.
- CD4+ T cell responses against CoV nucleocapsids were elevated in individuals with a previous SARS-CoV-2 infection.
- CD4+ and CD8+ T cell responses against CoV spikes were similar between individuals with either a prior SARS-CoV-2 infection or COVID-19 vaccination.
- CD8+ T cell responses to OC43 spike and nucleocapsid were similar between individuals with either a prior SARS-CoV-2 infection or COVID-19 vaccination.
- Neutralization of pseudoviruses expressing CoV spikes was similar between individuals with either a prior SARS-CoV-2 infection or COVID-19 vaccination.
- Addition of non-spike CoV antigens to future vaccines could improve pan-CoV vaccine efforts.

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