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Title

SARS-CoV-2 vaccination protects against infection-induced autoantibody formation
2302309

Permalink

<https://escholarship.org/uc/item/38v337v2>

Journal

The Journal of Immunology, 215(Supplement_1)

ISSN

0022-1767

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Publication Date

2026-08-01

DOI

10.1093/jimmun/vkag141.1243

Peer reviewed

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Abstract citation ID: vkag141.1243
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Abstract

Introduction SARS-CoV-2 infection is known to induce autoantibodies across a wide range of targets, including immune modulatory proteins and pro-thrombotic factors. It is not known if vaccination with SARS-CoV-2 mRNA vaccines would induce a similar autoantibody profile, or whether

prior vaccination would protect recipients from autoantibody production upon SARS-CoV-2 infection.

Methods Our group followed a cohort of over 65,000 blood donors across repeat donations in the COVID-19 era. We identified SARS-CoV-2 naïve donors who were infected without prior vaccination (n = 150) or were vaccinated then became infected (n = 100). We tested samples from the naïve time point and 6–10 weeks after infection (2 paired samples) or naïve then vaccination then infection (three samples) using a T7 bacteriophage array displaying 731,724 peptides (49 amino acids each) spanning the human proteome. Data were partitioned into five random groups and peptide comparisons between groups were performed using ranksum, with 80% used for training and 20% used for testing iteratively.

Results Autoantibodies targeting 15 peptides were induced with a z-score >2 after SARS-CoV-2 infection of unvaccinated naïve donors (p < 1x10⁻⁵). Of these infection-induced autoantibodies, 1 was induced after mRNA vaccination, as well as 2 distinct vaccine induced autoantibodies. In donors who were infected after prior vaccination, autoantibody responses were blunted, targeting 7 of 15 peptides.

Conclusion In contrast to SARS-CoV-2 infection of immunologically naïve individuals, SARS-CoV-2 mRNA vaccination induces only a limited autoantibody repertoire. Furthermore, prior vaccination protects against development of approximately half the autoantibodies induced by SARS-CoV-2 infection in this study. These data confirm the induction of autoantibodies following infection and underline both the safety of mRNA vaccines in terms of autoantibody induction, as well as potential protective effects of vaccination from COVID-19 associated autoimmunity.

Funding Source NIH

Topic Categories Viral Immunology (VIR)

Keywords: Animals — Human, Infections — Viral, Molecules — Autoantibodies.