SWITCH-ON study: Immune profiling of monovalent XBB.1.5 booster vaccine responses

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Introduction

The evolution of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and the emergence of Omicron subvariants have challenged vaccine efficacy. To overcome this, an mRNA-based monovalent XBB.1.5 spike (S) vaccine was administered to the public in late 2023. In this study, we evaluated the immunogenicity of the monovalent XSBB.1.5 vaccine by assessing (cross-)reactivity of virus-specific T-cells and neutralizing antibodies. We employed the interferon gamma release assay (IGRA) to generate extensive T-cell profiles from HCW up to 6 months after booster vaccination (n=166). Small volumes of whole blood were stimulated with overlapping peptide pools from 20 different coronaviruses, including: 14 SARS-CoV-2 variants; four seasonal coronaviruses (i.e., OC43, HKU1, NL63, and 229E); and two zoonotic coronaviruses (SARS-CoV and MERS-CoV). By combining T-cell and neutralizing antibody profiles we can better identify COVID-19 immunity gaps on a population level, and inform future vaccine design as well as guide public health strategies.

Study design

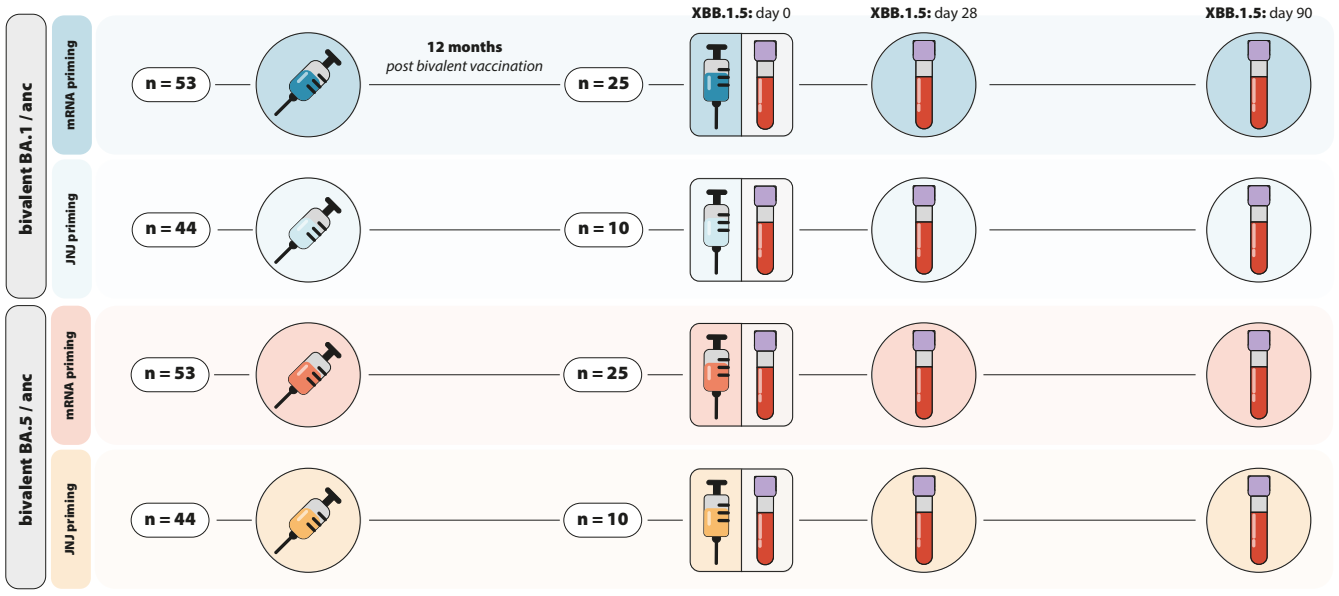

Fig.1. SWITCH-ON monovalent XBB.1.5 booster sub-study design.
HCW vaccinated with either the bivalent BA.1/ancestral or BA.5/ancestral vaccine were boosted with the monovalent XBB.1.5 vaccine 12 months after bivalent vaccination. Blood samples were collected at baseline (day 0), 28, and 90 days after monovalent XBB.1.5 booster vaccination.

Humoral immune responses

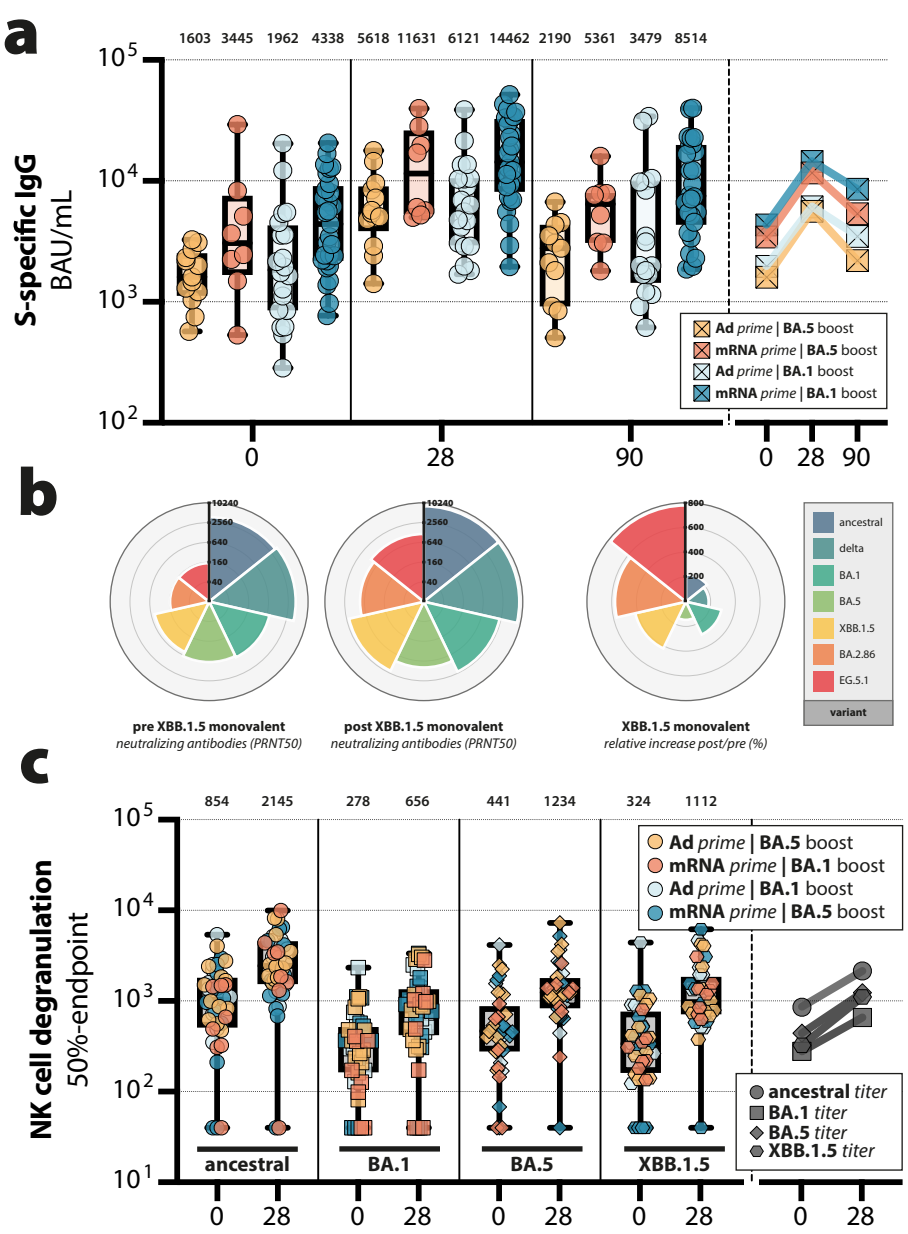

Fig.2. Broadening of functional antibody levels following monovalent XBB.1.5 booster.
(A) S1-specific binding antibody levels (IgG) are consistently higher in mRNA primed individuals. **(B)** Monovalent booster vaccination increases the breadth of the neutralizing antibody response and **(C)** ADCC-inducing antibody levels to circulating Omicron variants are increased following booster vaccination.

Cellular immune responses

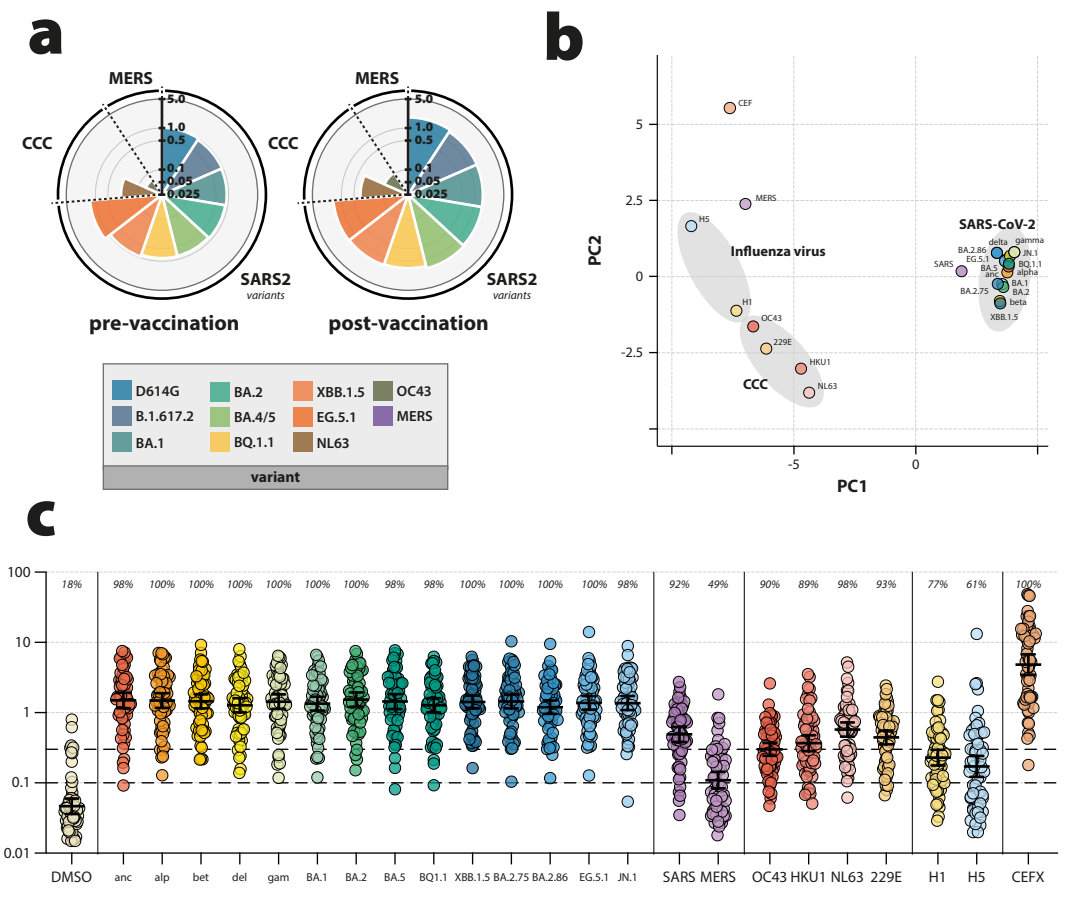

Fig.3. Induction of cross-reactive T-cell responses by monovalent booster.
(A) S-specific T-cell responses to ancestral an circulating variants increase following booster vaccination. **(B)** PCA illustrating the correlation matrix of S-specific T-cell responses, shows close antigenic relationship between SARS-CoV-2 variants. **(C)** The S-specific T-cell response remains cross-reactive to circulating variants up to 18 months after receiving last booster.

Conclusions

The monovalent XBB.1.5 booster vaccination **rapidly recalls** humoral and cellular immune responses, peaking at 28 days post-vaccination and gradually waning over three months. Booster vaccination **enhances cross-reactive** neutralizing and non-neutralizing responses but **does not induce de novo immune responses.** However, **T-cell responses remain cross-reactive** to circulating SARS-CoV-2 variants for months following the booster.


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