Interdependencies of cellular and humoral immune responses in heterologous and homologous SARS-CoV-2 vaccination

Moritz M. Hollstein¹, Lennart Münsterkötter¹, Michael Schön¹, Armin Bergmann¹, Thea M. Husar¹, Anna Abratis¹, Abass Eidizadeh¹, Meike Schaffrinski¹, Karolin Zachmann¹, Anne Schmitz², Jason S. Holsapple², Hedwig Stanisz-Bogeski¹, Julie Schanz¹, Uwe Groß¹, Andreas Leha¹, Andreas E. Zautner¹, Moritz Schnelle¹, and Luise Erpenbeck¹

¹Universitätsmedizin Göttingen
²Universitätsklinikum Münster

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Abstract

Background: Homologous and heterologous SARS-CoV-2 vaccinations yield different spike protein-directed humoral and cellular immune responses. This study aimed to explore their currently unknown interdependencies. Methods: COV-ADAPT is a prospective, observational cohort study of 417 healthcare workers who received vaccination with homologous ChAdOx1 nCoV-19, homologous BNT162b2 or with heterologous ChAdOx1 nCoV-19/BNT162b2. We assessed humoral (anti-spike-RBD-IgG, neutralizing antibodies, avidity) and cellular (spike-induced T cell interferon-γ release) immune responses in blood samples up to 2 weeks before (T1) and 2 to 12 weeks following secondary immunization (T2). Results: Initial vaccination with ChAdOx1 nCoV-19 resulted in lower anti-spike-RBD-IgG compared to BNT162b2 (70±114 vs. 226±279 BAU/ml, p<0.01) at T1. Booster vaccination with BNT162b2 proved superior to ChAdOx1 nCoV-19 at T2 (anti-spike-RBD-IgG: ChAdOx1 nCoV-19/BNT162b2 2387±1627 and homologous BNT162b2 3202±2184 vs. homologous ChAdOx1 nCoV-19 413±461 BAU/ml, both p<0.001; spike-induced T cell interferon-γ release: ChAdOx1 nCoV-19/BNT162b2 5069±6733 and homologous BNT162b2 4880±7570 vs. homologous ChAdOx1 nCoV-19 1152±2243 mIU/ml, both p<0.001). No significant differences were detected between BNT162b2-boostered groups at T2. For ChAdOx1 nCoV-19, no booster effect on T cell activation could be observed. We found associations between anti-spike-RBD-IgG levels (ChAdOx1 nCoV-19/BNT162b2 and homologous BNT162b2) and T cell responses (homologous ChAdOx1 nCoV-19 and ChAdOx1 nCoV-19/BNT162b2) from T1 to T2. All regimes yielded neutralizing antibodies and increased antibody avidity at T2. Conclusions: Interdependencies between humoral and cellular immune responses differ between common SARS-CoV-2 vaccination regimes. T cell activation is unlikely to compensate for poor humoral responses.

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Figure 1

Subjects recruited $n=417$

Excluded: $n=19$

ChAdOx1 prime $n=326$

BNT162b2 prime $n=72$

First blood draw (T1)

2 weeks to 3 months

ChAdOx1 boost $n=27$

BNT162b2 boost $n=287$

mRNA-1273 boost $n=2$

BNT162b2 boost $n=68$

Second blood draw (T2)

Figure 2

A

B

C

log10[lgG$_{12}$ [BAU/mL]]

0.0 2.5 5.0 7.5 10.0

0.0 2.5 5.0 7.5 10.0 12.5

0.0 3.0 6.0 9.0

ChAdOx1/ChAdOx1

ChAdOx1/BNT162b2

BNT162b2/BNT162b2

b = -0.42; CI = [-0.50, 0.10]; p < 0.001

b = -0.38; CI = [-0.31, 0.45]; p < 0.001

b = 0.11; CI = [0.01, 0.21]; p < 0.05
Figure 3

A

B

C

Figure 4

A

B

C

D

E
Figure 5

A

B

NI

RAI

1st ChAdOx1
2nd ChAdOx1
1st ChAdOx1
2nd BNT162b2
1st BNT162b2
2nd BNT162b2

1st ChAdOx1
2nd ChAdOx1
1st ChAdOx1
2nd BNT162b2
1st BNT162b2
2nd BNT162b2

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