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

Moritz M. Hollstein[1], Lennart Münsterkötter[1], Michael Schön[1], Armin Bergmann[1], Thea M. Husar[1], Anna Abratis[1], Abass Eidizadeh[1], Meike Schaffrinski[1], Karolin Zachmann[1], Anne Schmitz[2], Jason S. Holsapple[2], Hedwig Stanisz-Bogeski[1], Julie Schanz[1], Uwe Groß[1], Andreas Leha[1], Andreas E. Zautner[1], Moritz Schnelle[1], and Luise Erpenbeck[1]

[1]Universitatsmedizin Gottingen
[2]Universitatsklinikum Munster

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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-$\gamma$ 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$\pm$114 vs. 226$\pm$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$\pm$1627 and homologous BNT162b2 3202$\pm$2184 vs. homologous ChAdOx1 nCoV-19 413$\pm$461 BAU/ml, both $p<0.001$; spike-induced T cell interferon-$\gamma$ release: ChAdOx1 nCoV-19/BNT162b2 5069$\pm$6733 and homologous BNT162b2 4880$\pm$7570 vs. homologous ChAdOx1 nCoV-19 1152$\pm$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. Additionally, anti-spike-RBD-IgG and T cell response were linked at both time points (all groups combined). 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**

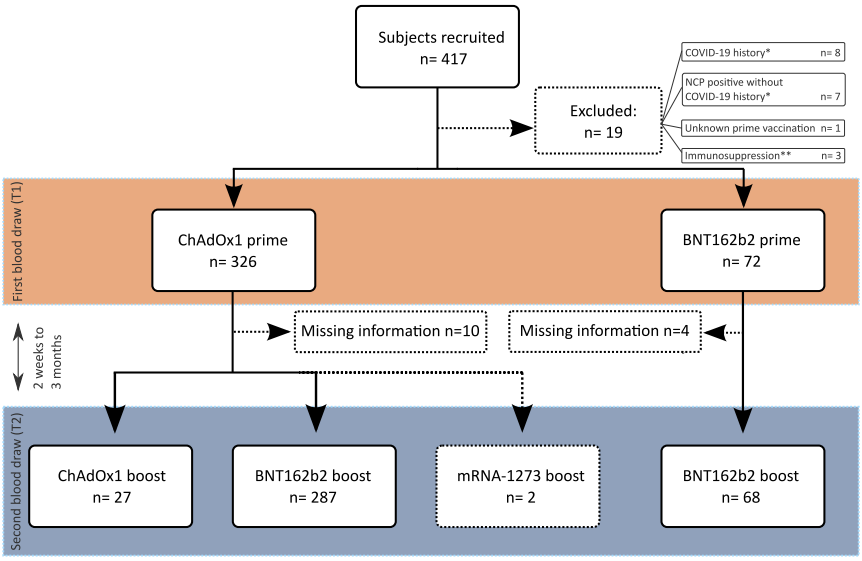
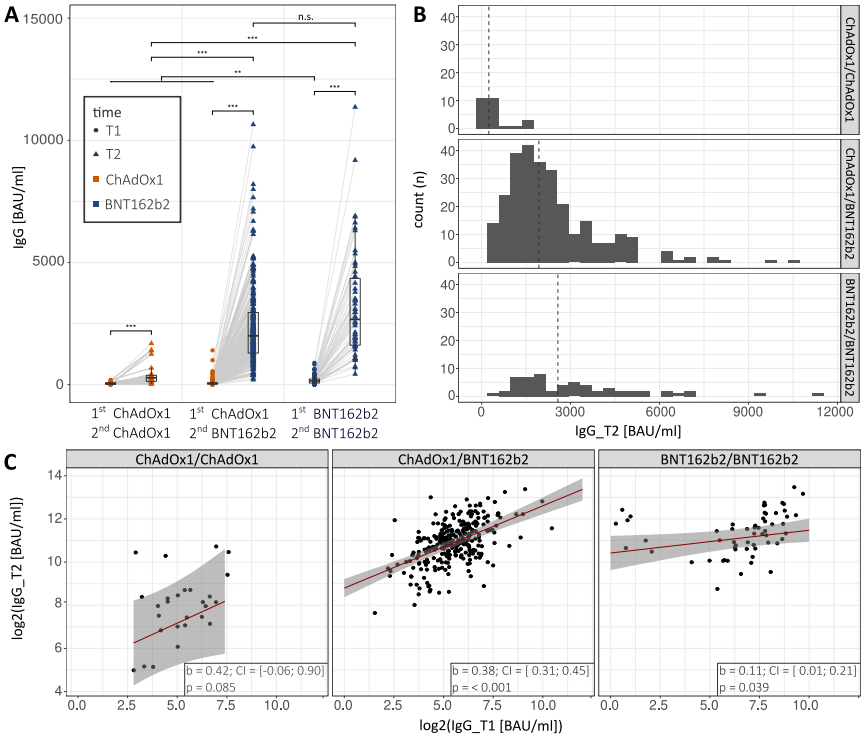



**Figure 2**



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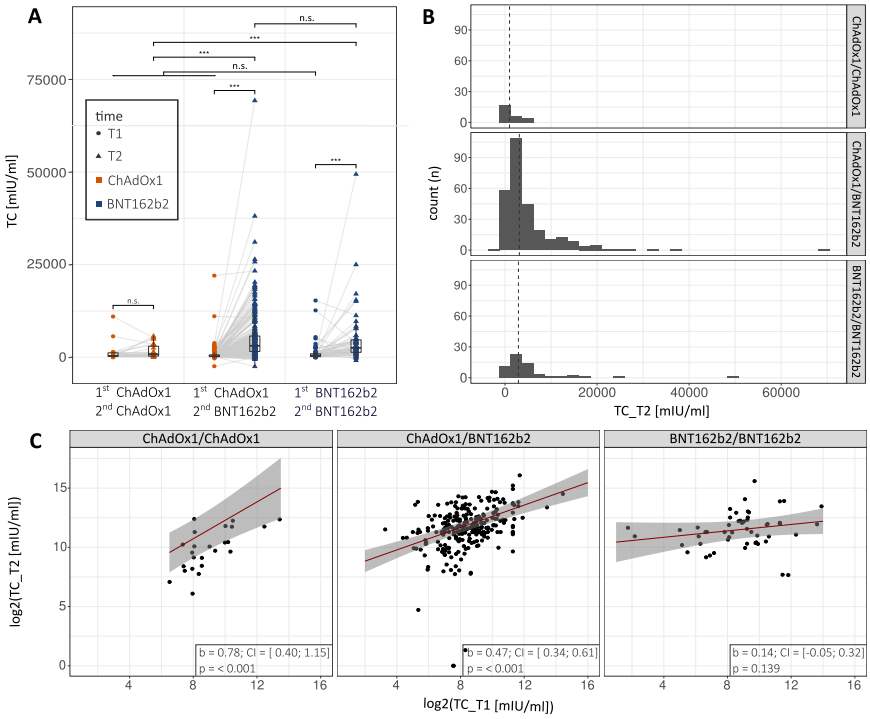


**Figure 4**

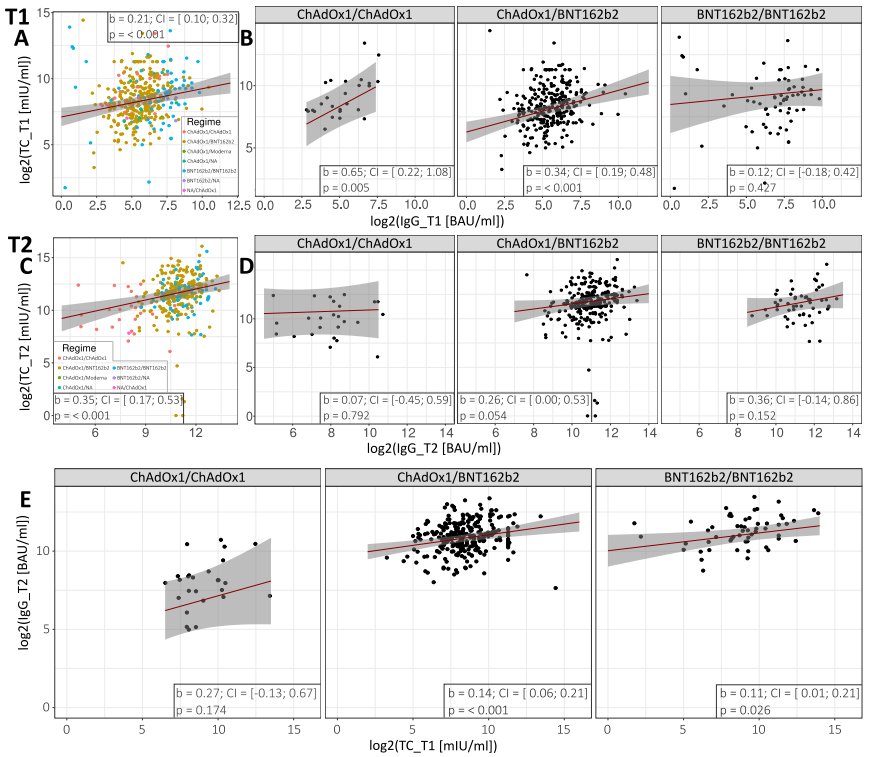

**Figure 5**