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Long-term effects of homologous and heterologous SARS-CoV-2 vaccination on humoral and cellular immune responses

Moritz M. Hollstein[1], Lennart Münsterkötter[1], Michael Schön[1], Armin Bergmann[1], Thea M. Husar[1], Anna Abratis[1], Abass Eidizadeh[1], Sascha Dierks[1], Meike Schaffrinski[1], Karolin Zachmann[1], Anne Schmitz[2], Jason S. Holsapple[2], Hedwig Stanisz-Bogeski[1], Julie Schanz[1], Andreas Fischer[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: Humoral and cellular immune responses to SARS-CoV-2 vaccines wane with time. In the COV-ADAPT cohort, we recently studied both immunological components and their interdependencies following different vaccine combinations before (T1) and up to three months after second immunization (T2). This follow-up investigated the stability of long-term immune responses and aimed to identify predictive markers. **Methods:** We assessed humoral (anti-spike-RBD-IgG, neutralization capacity, avidity) and cellular (spike-induced T-cell interferon-γ release) immune responses three-seven months after secondary vaccination (T3) in blood samples of 318 healthcare workers with previous homologous ChAdOx1 nCoV-19 (ChAdOx1), homologous BNT162b2 or heterologous ChAdOx1/BNT162b2 vaccinations. **Results:** At T3, homologous ChAdOx1 vaccination resulted in significantly lower anti-spike-RBD-IgG (152±151 BAU/ml) as compared to heterologous ChAdOx1/BNT162b2 (388±300 BAU/ml) and homologous BNT162b2 (435±327 BAU/ml). In all groups, anti-spike-RBD-IgG (T3) exceeded antibody levels before second vaccination (T1). T-cell interferon-γ release following heterologous ChAdOx1/BNT162b2 vaccination was significantly higher at T3 (1062±2083 mIU/ml) vs. T1 (680±1691 mIU/ml), yet did not differ significantly between the three groups at T3. Associations between humoral and cellular responses were found at T3 (all groups combined). Additionally, the early cellular response (at T1) was significantly associated with late (T3) humoral (ChAdOx1/BNT162b2, BNT162b2/BNT162b2) and cellular responses (all groups). In contrast to T2, neutralization capacity at T3 was significantly higher for ChAdOx1/BNT162b2 and BNT162b2/BNT162b2 vs. ChAdOx1/ChAdOx1. **Conclusions:** We identified (i) long-term interdependencies between the humoral and the cellular immune system, (ii) observed distinct waning dynamics following different vaccination regimes, and (iii) uncovered early T-cell responses as a useful predictor of long-term immune responses.

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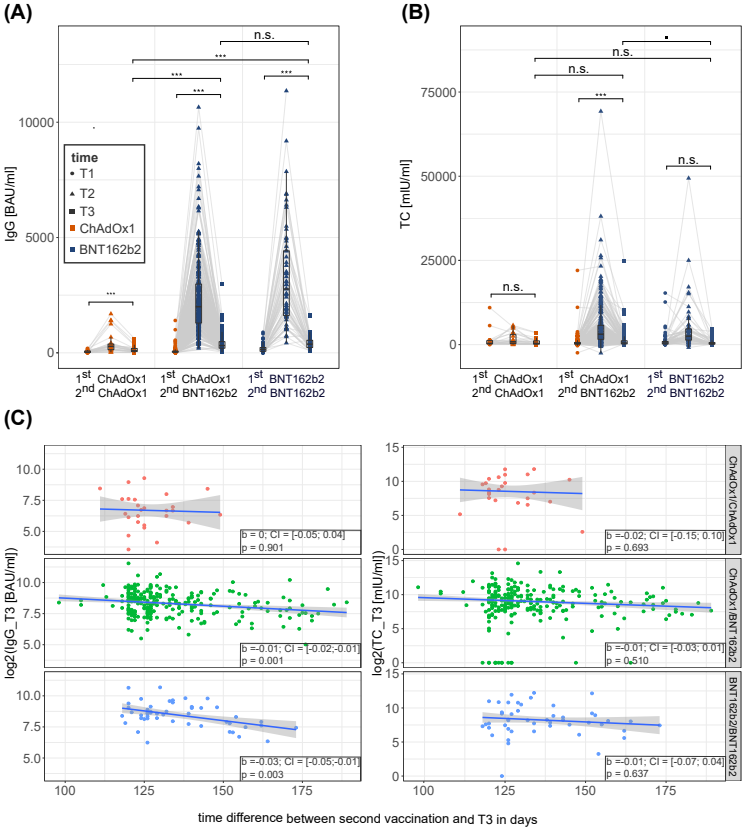
Figure 1_Hollstein et al.



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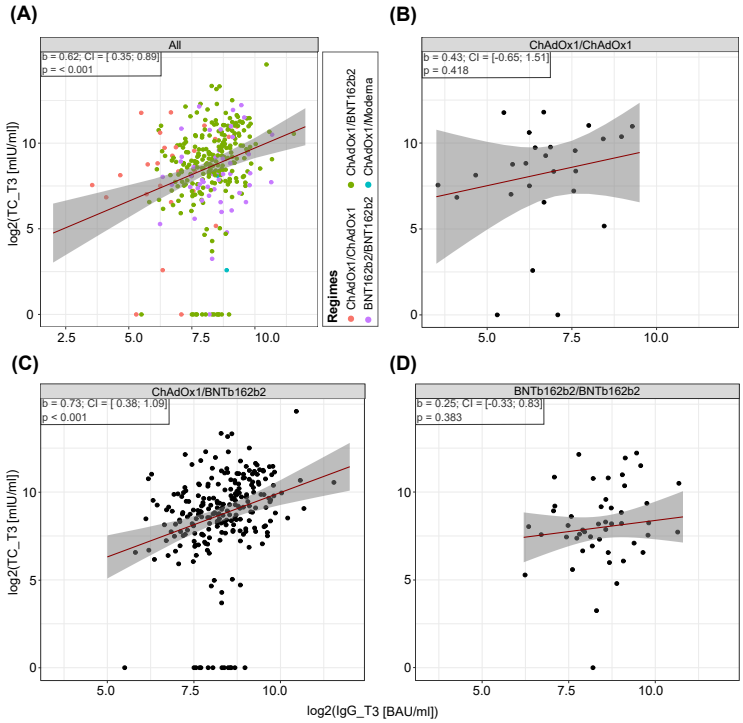

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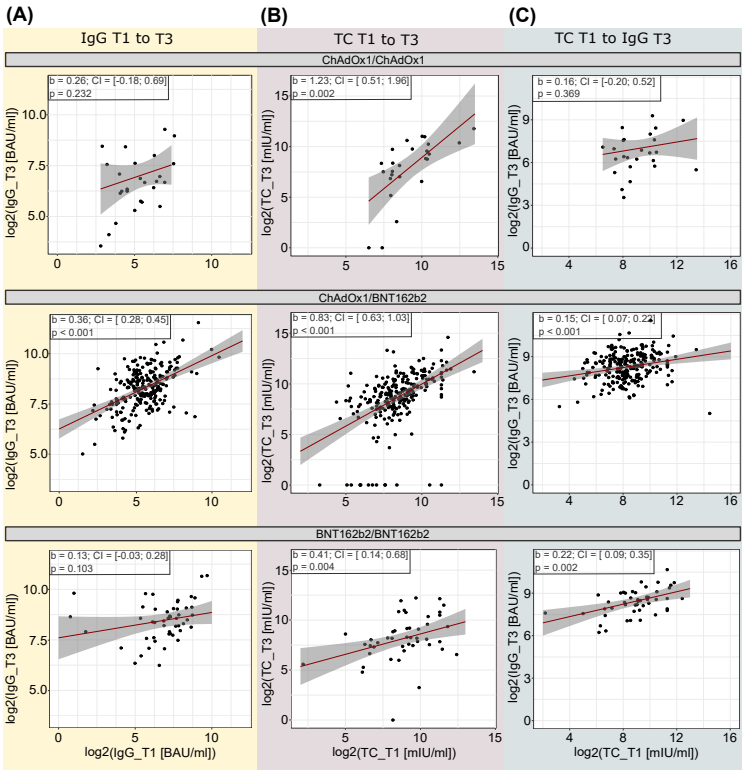

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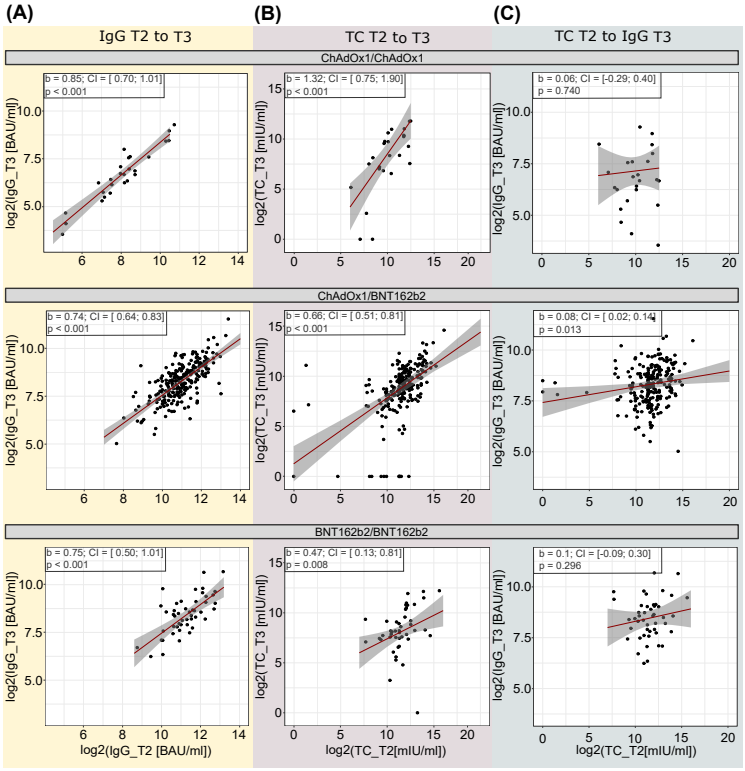

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Figure 5_Hollstein et al.