Humoral and cellular immune responses in fully vaccinated individuals with or without SARS-CoV-2 breakthrough infection: results from the CoV-ADAPT cohort

Moritz Schnelle[1], Moritz M. Hollstein[1], Sascha Dierks[1], Michael P. Schön[1], Armin Bergmann[1], Anna Abratis[1], Abass Eidizadeh[1], Sarah Kaltenbach[1], Julie Schanz[1], Uwe Groß[1], Andreas Leha[1], Andreas E. Zautner[1], Andreas Fischer[1], and Luise Erpenbeck[1]

[1]Universitatsmedizin Gottingen

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Abstract

Despite recent advances in prophylactic vaccination, SARS-CoV-2 infections continue to cause significant morbidity. A better understanding of immune response differences between vaccinated individuals with and without later SARS-CoV-2 breakthrough infection is urgently needed. CoV-ADAPT is a prospective long-term study comparing humoral (anti-spike-RBD-IgG, neutralization capacity, avidity) and cellular (spike-induced T-cell interferon-γ release) immune responses in individuals vaccinated against SARS-CoV-2 at four different time points (three before and one after third vaccination). In this cohort study, 62 fully vaccinated individuals presented with SARS-CoV-2 breakthrough infections vs 151 without infection 3-7 months following third vaccination. Breakthrough infections significantly increased anti-spike-RBD-IgG ($p<0.01$), but not spike-directed T-cell interferon-γ release (TC), antibody neutralization capacity or avidity. Anti-spike-RBD-IgG and antibody avidity decreased with age ($p<0.01$) and females showed higher anti-spike-RBD-IgG ($p<0.01$), and a tendency towards higher antibody avidity ($p=0.051$). The association between humoral and cellular immune responses previously reported at various time points was lost in subjects after breakthrough infections ($p=0.807$). Finally, a machine-learning approach based on our large immunological data set (a total of 49 variables) from different time points was unable to predict breakthrough infections (AUC: 0.55). In conclusion, distinct differences in humoral vs cellular immune responses in fully vaccinated individuals with or without breakthrough infection could be demonstrated. Breakthrough infections predominantly drive the humoral response without boosting the cellular component. Breakthrough infections could not be predicted based on immunological data, which indicates a superior role of environmental factors (e.g. virus exposure) in individualized risk assessment.

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Figure 1_Hollstein et al.

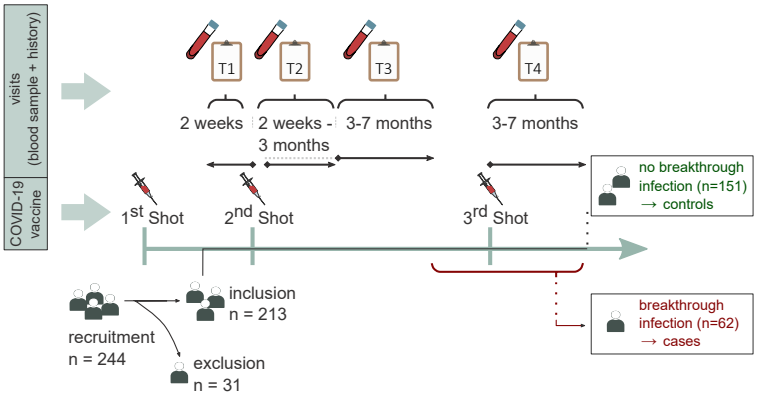

Figure 2_Hollstein et al.

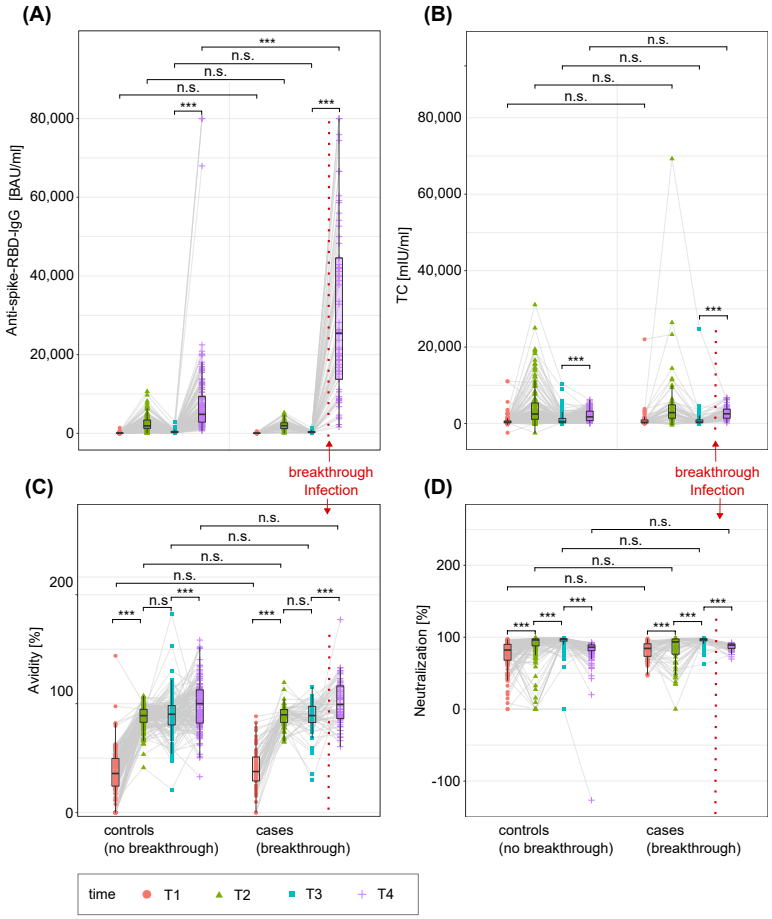

Figure 3_Hollstein et al.

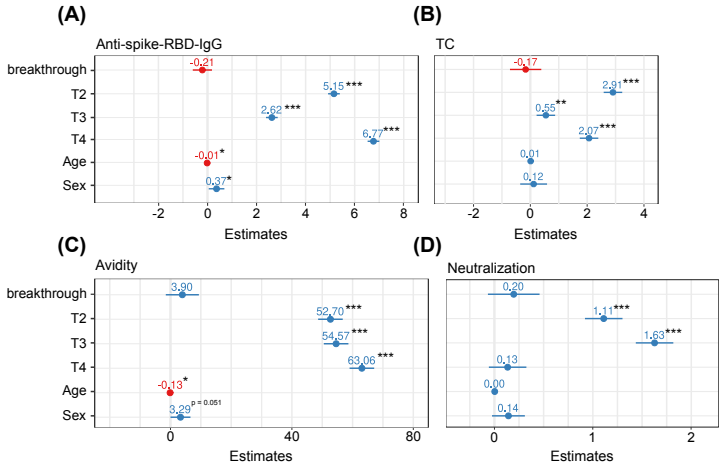

Figure 4_Hollstein et al.

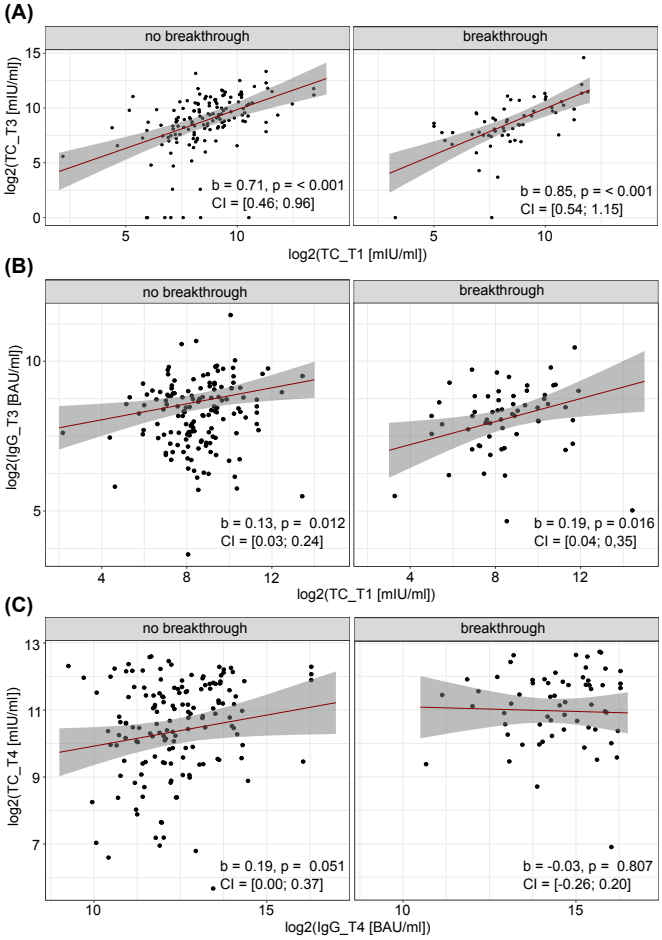

Figure 5_Hollstein et al.