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Supplemental information

Reduced antibody activity against SARS-CoV-2 B.1.617.2 delta virus in serum of mRNA-vaccinated individuals receiving tumor necrosis factor-α inhibitors

Rita E. Chen, Matthew J. Gorman, Daniel Y. Zhu, Juan Manuel Carreño, Dansu Yuan, Laura A. VanBlargan, Samantha Burdess, Douglas A. Lauffenburger, Wooseob Kim, Jackson S. Turner, Lindsay Droit, Scott A. Handley, Salim Chahin, Parakkal Deepak, Jane A. O'Halloran, Michael A. Paley, Rachel M. Presti, Gregory F. Wu, Florian Krammer, Galit Alter, Ali H. Ellebedy, Alfred H.J. Kim, and Michael S. Diamond

SUPPLEMENTAL FIGURE AND TABLE TITLES

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Table S1. Deep sequencing of Viral RNA Stocks, Related to Figures 2, 4, and 5.

Table S2. Immunocompetent (IC) volunteers and chronic inflammatory disease (CID) patient demographic characteristics, Related to Figures 1-5.

Table S3. Regression analysis of effects on serum neutralization titers against B.1.617.2 infection, Related to Figures 4 and S4.

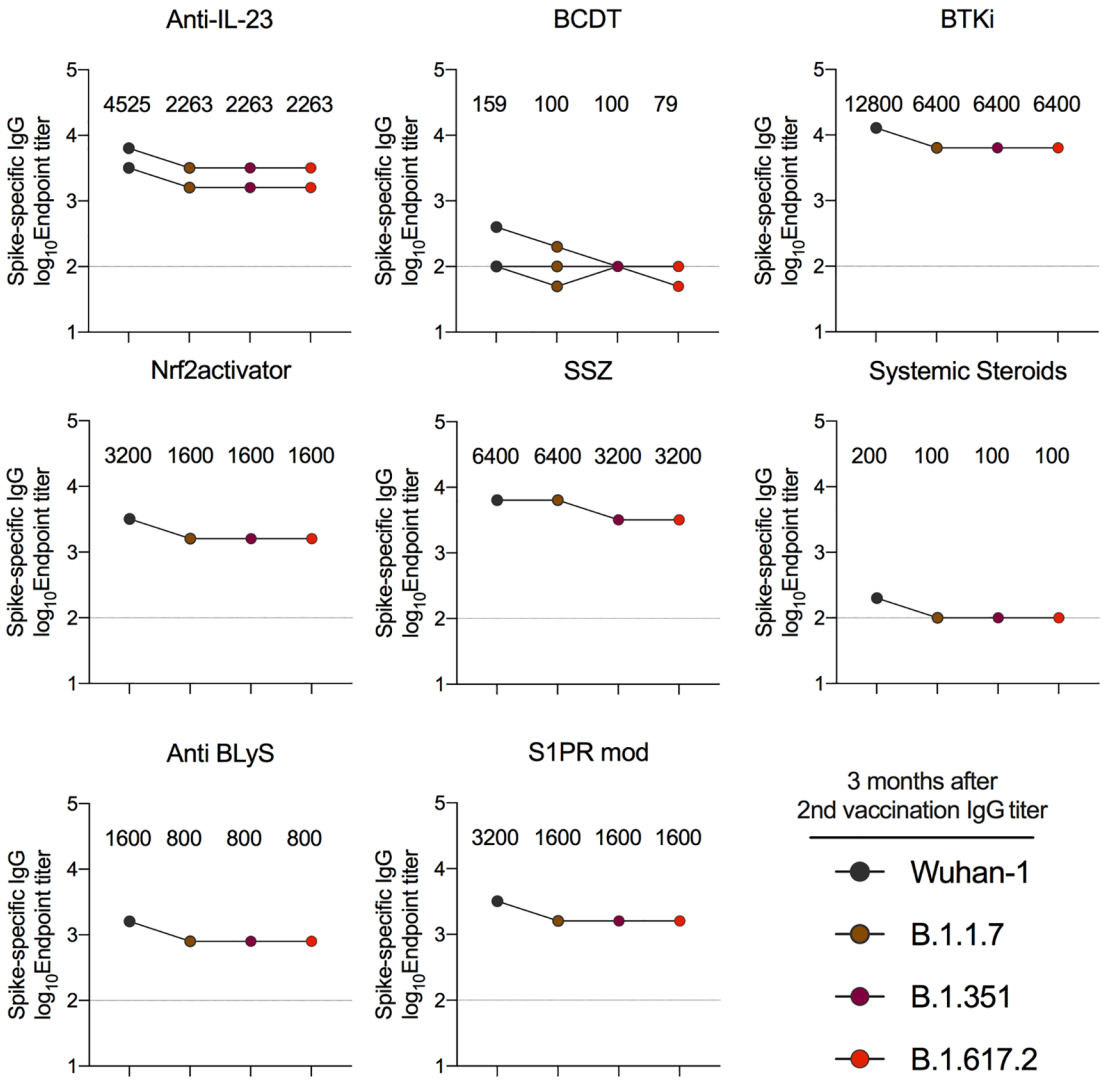


Figure S1. Serum IgG titers against SARS-CoV-2 variant spike proteins at three months after second vaccination, small n, Related to Figure 1. Paired analyses of spike-specific endpoint IgG serum titers measured by ELISA from humans at three months after second vaccination with BNT162b2 mRNA vaccine. Individuals were grouped by immunosuppressive drug class: anti-IL-23 inhibitors, B cell depletion therapy (BCDT), Bruton's tyrosine kinase inhibitor (BTKi), nuclear factor erythroid-2-related factor 2 (Nrf2) activator, sulfasalazine (SSZ), systemic steroid, anti-B lymphocyte stimulator (anti-BLyS), and sphingosine 1-phosphate receptor modulator (S1PR mod). GMT values are shown on graph. Dotted line represents limit of detection of the assay.

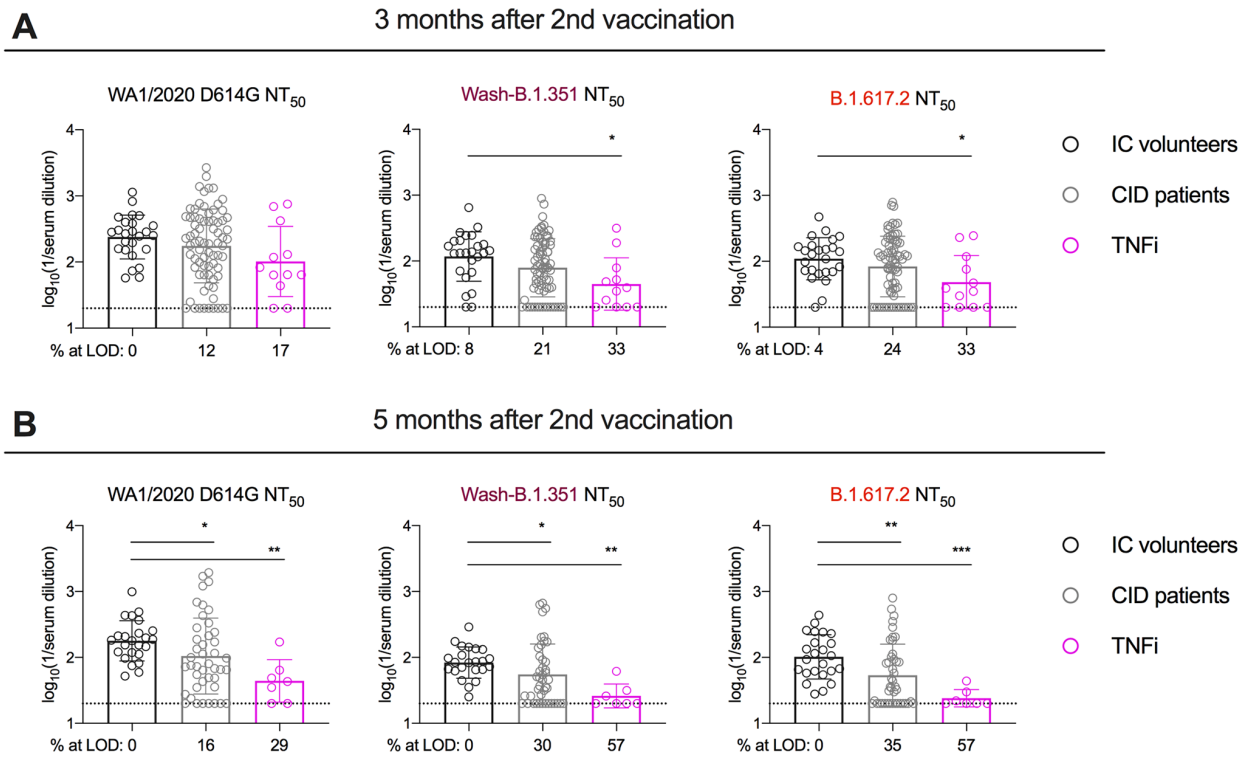


Figure S2. Serum neutralization titers against SARS-CoV-2 variant viruses at three and five months after second vaccination of immunocompetent volunteers, CID patients, and TNFi recipients, Related to Figures 2 and 4. Neutralization (NT_{50}) titers in serum measured by FRNT from humans at (**A**) three months or (**B**) five months after second vaccination with BNT162b2 mRNA vaccine. Individuals were grouped as immunocompetent (IC) volunteers, CID patients, or TNFi recipients for neutralization against indicated SARS-CoV-2 viruses (one way ANOVA with Dunn's post-test; * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$). Beneath each graph is the percentage of data points in a group that were at the limit of detection (dotted line, 1/20 dilution).

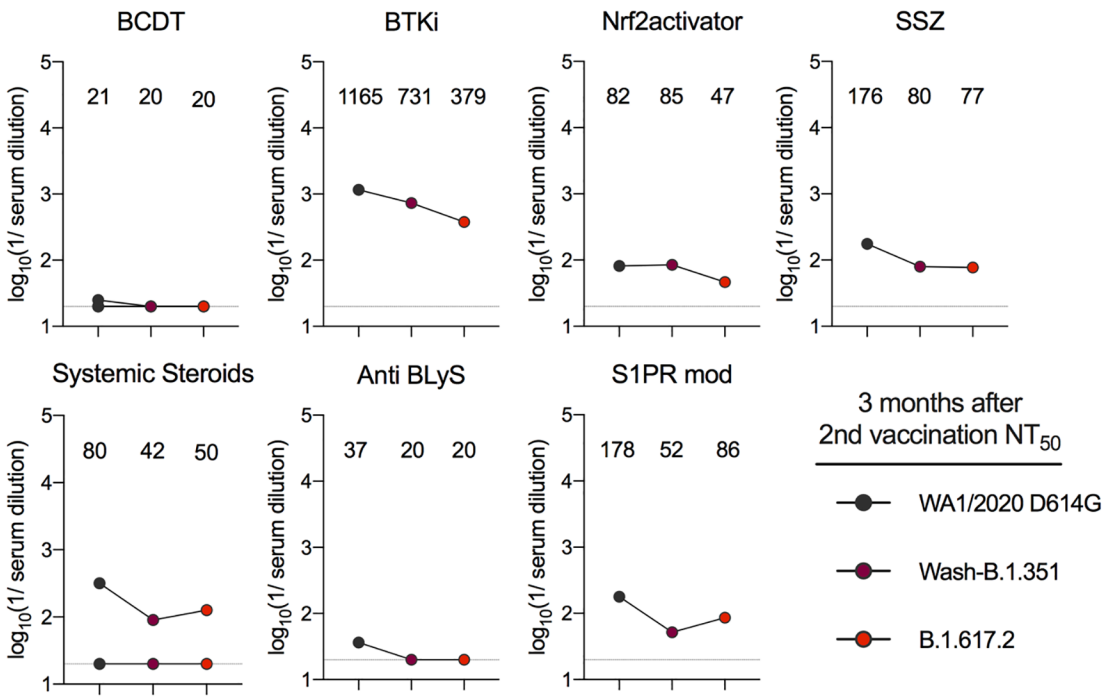
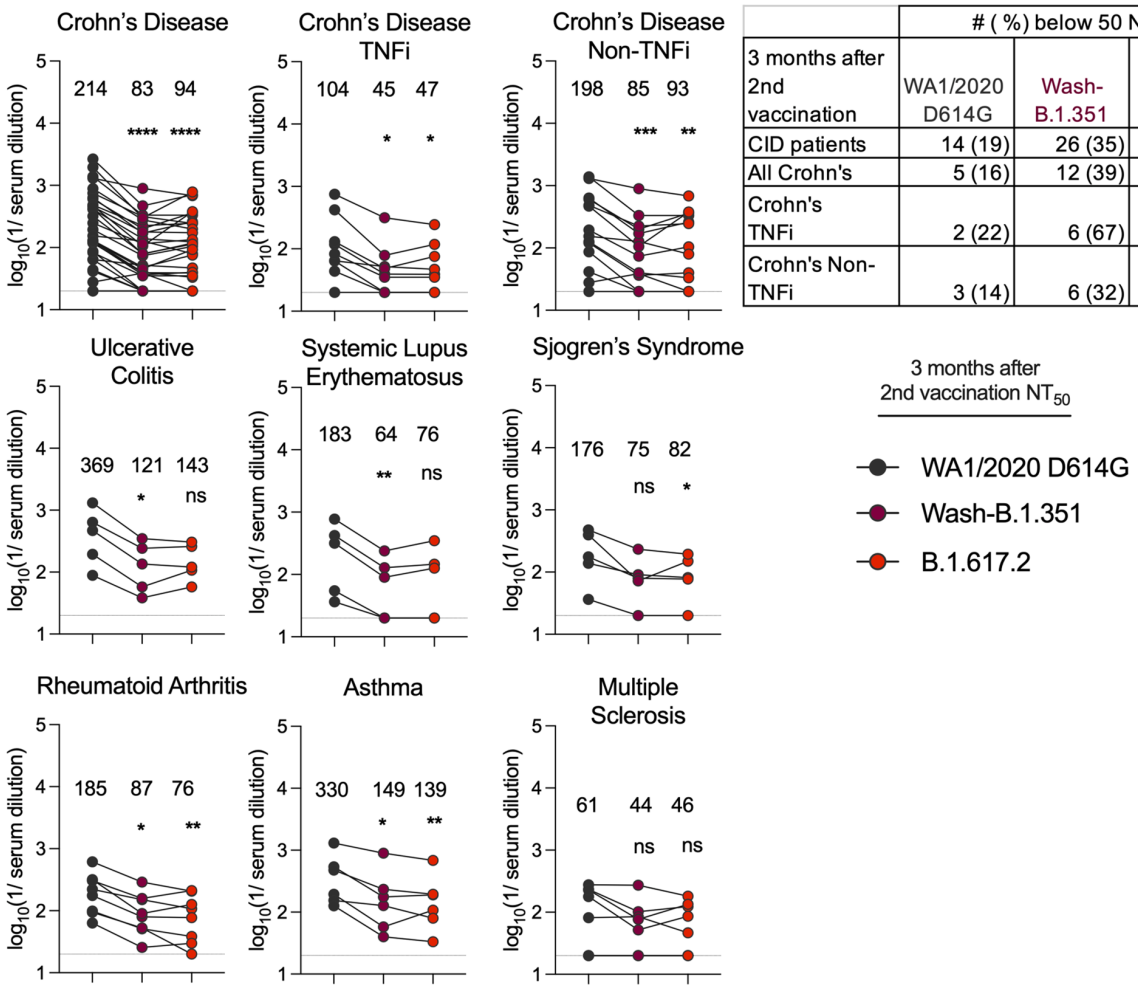


Figure S3. Serum neutralization titers against SARS-CoV-2 variant viruses at three months after second vaccination, small n, Related to Figure 2. Paired analyses of neutralization (NT_{50}) titers in serum measured by FRNT from humans at three months after second vaccination with BNT162b2 mRNA vaccine. Individuals were grouped by immunosuppressive drug class: B cell depletion therapy (BCDT), Bruton's tyrosine kinase inhibitor (BTKi), nuclear factor erythroid-2-related factor 2 (Nrf2) activator, sulfasalazine (SSZ), systemic steroid, anti-B lymphocyte stimulator (anti-BLyS), and sphingosine 1-phosphate receptor modulator (S1PR mod). GMT values are shown on graph. Dotted line represents limit of detection of the assay.



	# (%) below 50 NT_{50}		
3 months after 2nd vaccination	WA1/2020 D614G	Wash-B.1.351	B.1.617.2
CID patients	14 (19)	26 (35)	27 (36)
All Crohn's	5 (16)	12 (39)	12 (39)
Crohn's TNFi	2 (22)	6 (67)	6 (67)
Crohn's Non-TNFi	3 (14)	6 (32)	6 (27)

Figure S4. Serum neutralization titers against SARS-CoV-2 variant viruses at three months after second vaccination by CID classification, Related to Figure 2. (***Left***) Paired analyses of neutralization (NT_{50}) titers in serum measured by FRNT from humans at three months after second vaccination with BNT162b2 mRNA vaccine. Individuals were grouped by CID diagnosis: Crohn's disease, ulcerative colitis, systemic lupus erythematosus, Sjogren's syndrome, rheumatoid arthritis, asthma, and multiple sclerosis. Crohn's disease patients were further divided by treatment with or without anti-TNF-α inhibitors. GMT values are shown on graph. Dotted line represents limit of detection of the assay. One way ANOVA with Dunn's post-test; * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; **** $p < 0.0001$. (***Right***) Table with number (or percentage) of patients with NT_{50} values below 1/50 for each group against WA1/2020 D614G, Wash-B.1.351, and B.1.617.2.

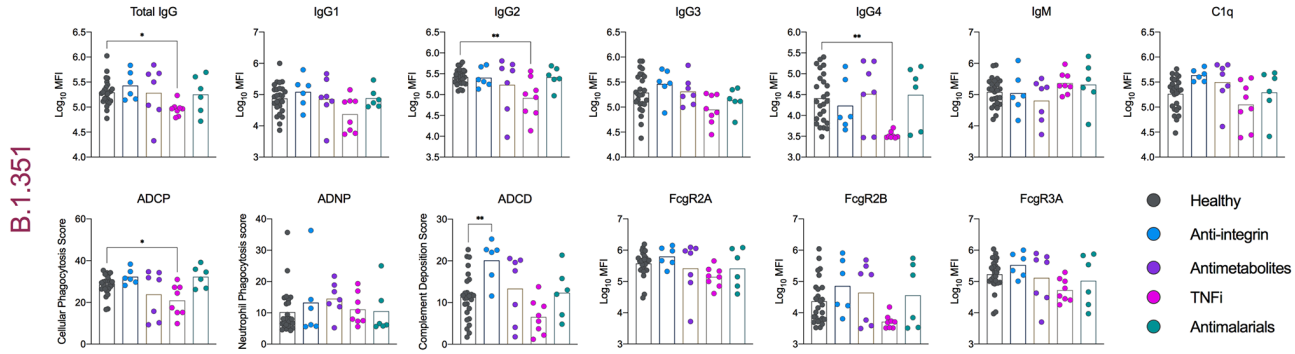


Figure S5. Effector functions against SARS-CoV-2 variant viruses at three months after second vaccination against B.1.351, Related to Figure 3. Serum from humans at three months after second vaccination with BNT162b2 mRNA vaccine were assayed for Total IgG, IgG subclasses (IgG1, IgG2, IgG3, IgG4, IgM), C1q binding, antibody-dependent cellular phagocytosis (ADCP), antibody-dependent neutrophil phagocytosis (ADNP), antibody-dependent complement deposition (ADCD), or FcγR (FcγR2A, FcγR2B, or FcγR3A) binding as measured by Luminex. Reponses were measured against B.1.351. Individuals were grouped as immunocompetent volunteers (n = 25) or subdivided by immunosuppressive drug class: TNFi (n = 8), antimetabolites (n = 7), antimalarials (n = 6), or anti-integrin inhibitors (n = 5). One-way ANOVA with Dunnett's post- test; * $p < 0.05$; ** $p < 0.01$.

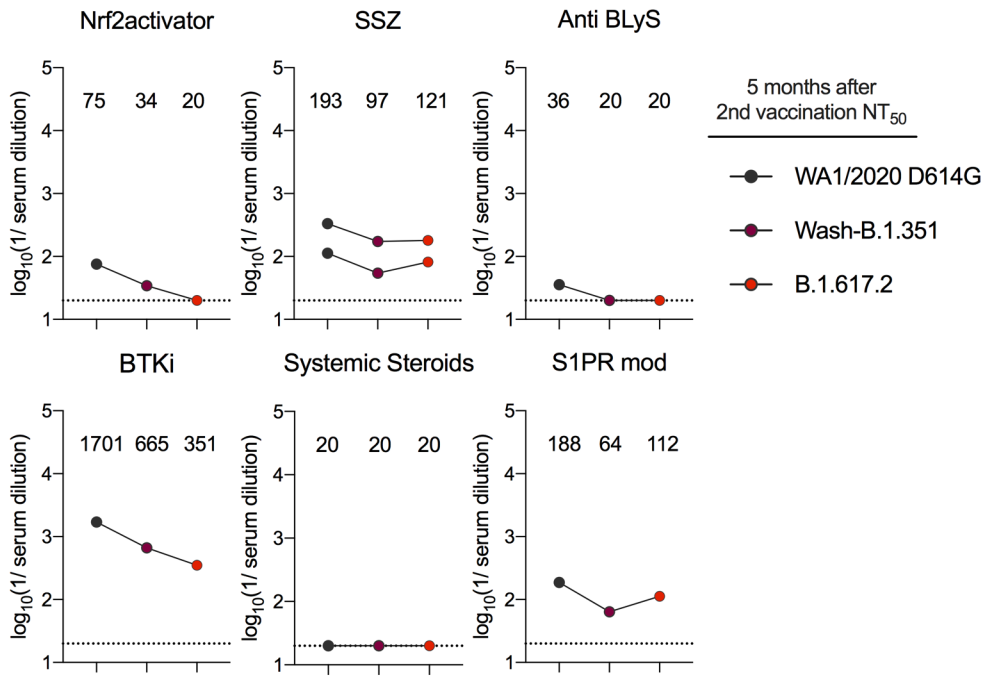


Figure S6. Serum neutralization titers of CID patients against SARS-CoV-2 variant viruses at five months after second vaccination, small n, Related to Figure 4. Paired analyses of neutralization (NT_{50}) titers in serum measured by FRNT from humans at five months after second vaccination with BNT162b2 mRNA vaccine. Individuals were grouped by immunosuppressive drug class: nuclear factor erythroid-2-related factor 2 (Nrf2) activator, sulfasalazine (SSZ), anti-B lymphocyte stimulator (anti-BLyS), Bruton's tyrosine kinase inhibitor (BTKi), systemic steroid, and sphingosine 1-phosphate receptor modulator (S1PR mod). GMT values are shown on graph. Dotted line represents limit of detection of the assay.

Table S2. Immunocompetent (IC) volunteers and chronic inflammatory disease (CID) patient demographic characteristics, Related to Figures 1-5.

	IC volunteers	CID patients	Crohn's patients	TNFi recipients
Variable	**Total N=25**	**Total N=77**	**Total N=31**	**Total N=14**
Age (median [range])	37 (27-55)	49 (22-82)	41 (24-64)	49 (25-68)
Sex N (%)				
Female	9 (36)	52 (68)	20 (65)	6 (43)
Male	16 (64)	24 (31)	11 (35)	8 (57)
N/A	0 (0)	1 (1)	0 (0)	0 (0)
Race N (%)				
White	18 (72)	69 (90)	29 (94)	13 (93)
Black	0 (0	5 (6)	0 (0)	0 (0)
Multiple Race	0 (0)	2 (3)	1 (3)	1 (7)
Asian	5 (20)	1 (1)	1 (3)	0 (0)
other	2 (8)	0 (0)	0 (0)	0 (0)

Table S3. Regression analysis of effects on serum neutralization titers against B.1.617.2 infection, Related to Fig 4 and S4.

	Log_{10} titer	**95% CI**	***p*-value**
TNFi	-0.3318	-0.6231 to -0.0406	0.026
Crohn's disease	-0.0592	-0.3229 to 0.2046	0.657

Multivariate tobit linear regression modeling was performed to examine the strength and independence of the association of TNFi and Crohn's disease with neutralization titers to B.1.617.2.