

Supplementary materials

Supplemental Tables 1 to 3, Multivariable linear mixed model for treatment group, age and BMI and **Supplemental Table 5**, percentage of samples seroconverted and passing median confidence thresholds are attached separately as excel files.

Supplemental Table 4: BAU/mL conversions

Nucleocapsid - Plasma

Dilution (d)		160		2,560		
Volume equivalent (µl)		0.0625		0.00391		
Relative Ratio (RR)	log ₂ (RR)	log ₂ (BAU/ml)	BAU/ml	log ₂ (BAU/ml)	BAU/ml	
2	1.0	8.38	333.98	12.38	5,343.76	Upper limit of linear range
1	0.0	6.98	126.34	10.98	2,021.37	
0.5	-1.0	5.58	47.79	9.58	764.62	
0.396	-1.3	5.16	34.46	9.16	571.19	Positivity threshold 160-fold dilution (0.0625 µl/well)
0.25	-2.0	4.18	18.08	8.17	289.23	
0.125	-3.0	2.77	6.84	6.77	109.41	
0.0625	-4.0	1.37	2.59	5.37	41.38	Lower limit of linear range
$\log_2(\text{BAU/mL @ sample dilution } d) = (\log_2(\text{RR}) - 0.243) / 0.713 + \log_2(d)$ With standard volume equivalents of .0625 µl and .00391 µl, range is 3 to 5344 BAU/ml, with positivity threshold of 34 BAU/ml						

RBD - Plasma

Dilution (d)		160		2,560		
Volume equivalent (µl)		0.0625		0.00391		
Relative Ratio (RR)	log ₂ (RR)	log ₂ (BAU/ml)	BAU/ml	log ₂ (BAU/ml)	BAU/ml	
1	0.0	8.12	278.37	12.12	4,453.99	Upper limit of linear range
0.5	-1.0	6.82	112.63	10.82	1,802.02	
0.25	-2.0	5.51	45.57	9.51	729.07	

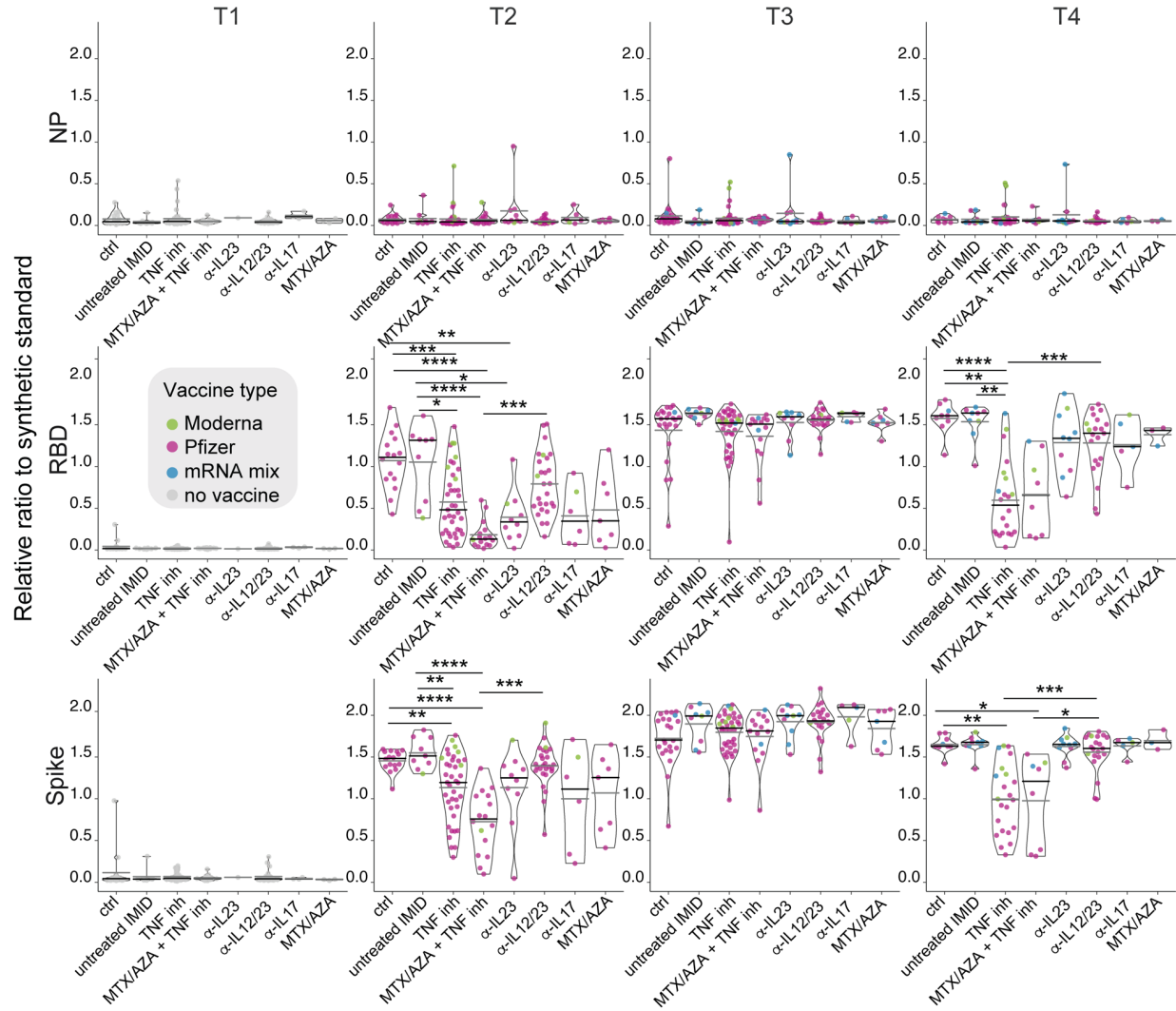
0.186	-2.4	4.95	30.97	8.95	495.58	Positivity threshold 160-fold dilution (0.0625 µl/well)
0.125	-3.0	4.20	18.44	8.20	294.97	
0.0625	-4.0	2.90	7.46	6.90	119.34	
0.03125	-5.0	1.59	3.02	5.59	48.28	Lower limit of linear range

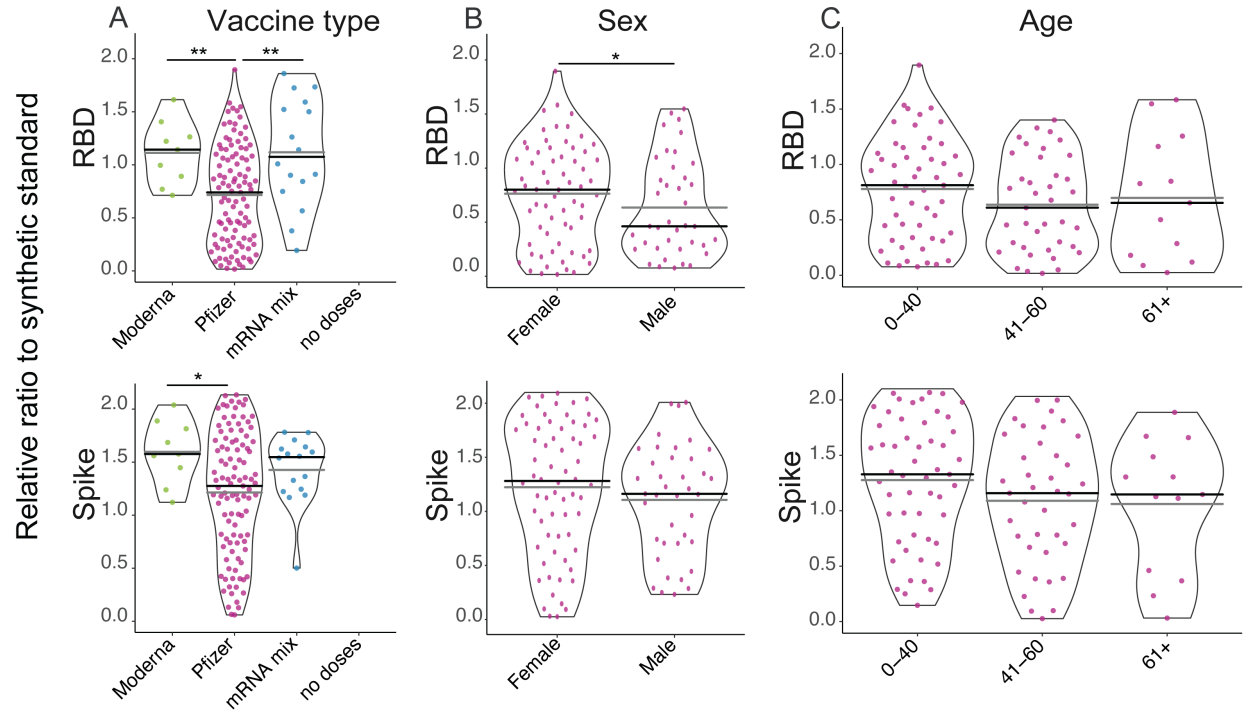
$\log_2(\text{BAU/ml @ sample dilution d}) = (\log_2(\text{RR}) + 0.612)/0.766 + \log_2(d)$.
 With standard volume equivalents of .0625 µl and .00391 µl, range is 2 to 4,454 BAU/ml, with positivity threshold of 31 BAU/ml

Spike - Plasma

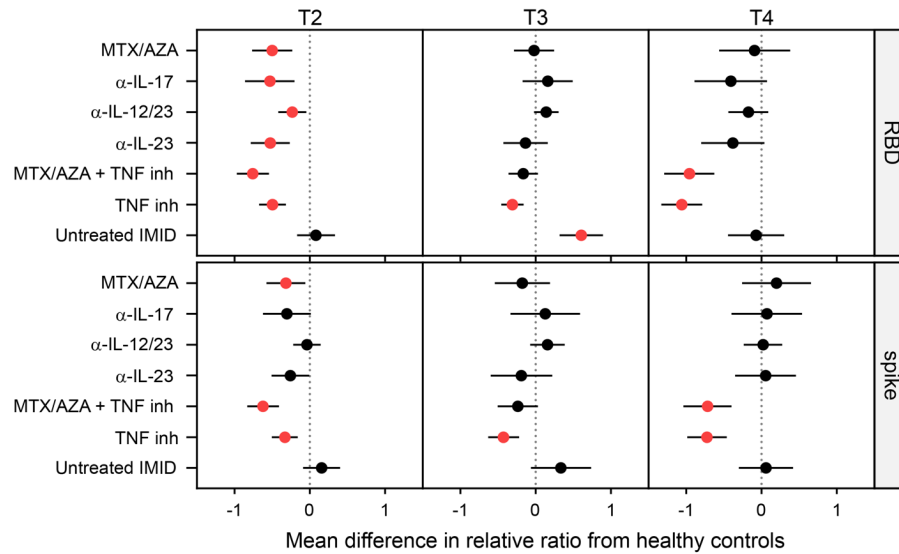
Dilution (fold)		160		2,560		
Volume equivalent (µl added per well)		0.0625		0.00391		
Relative Ratio (RR)	$\log_2(\text{RR})$	$\log_2(\text{BAU/ml})$	BAU/ml	$\log_2(\text{BAU/ml})$	BAU/ml	
1	0.0	6.55	93.80	10.55	1,500.80	Upper limit of linear range
0.5	-1.0	5.28	38.75	9.28	619.95	
0.25	-2.0	4.00	16.01	8.00	256.09	
0.19	-2.4	3.50	11.28	7.50	180.45	Positivity threshold at 160-fold dilution (0.0625 µl/well)
0.125	-3.0	2.72	6.61	6.72	105.78	
0.0625	-4.0	1.45	2.73	5.45	43.70	
0.03125	-5.0	0.17	1.13	4.17	18.05	Lower limit of linear range

$\log_2(\text{BAU/ml @ dilution d}) = (\log_2(\text{RR}) - 0.604)/0.784 + \log_2(d)$
 With standard volume equivalents of .0625 µl and .00391 µl, range is 1 to 1,501 BAU/ml, with positivity threshold of 11 BAU/ml

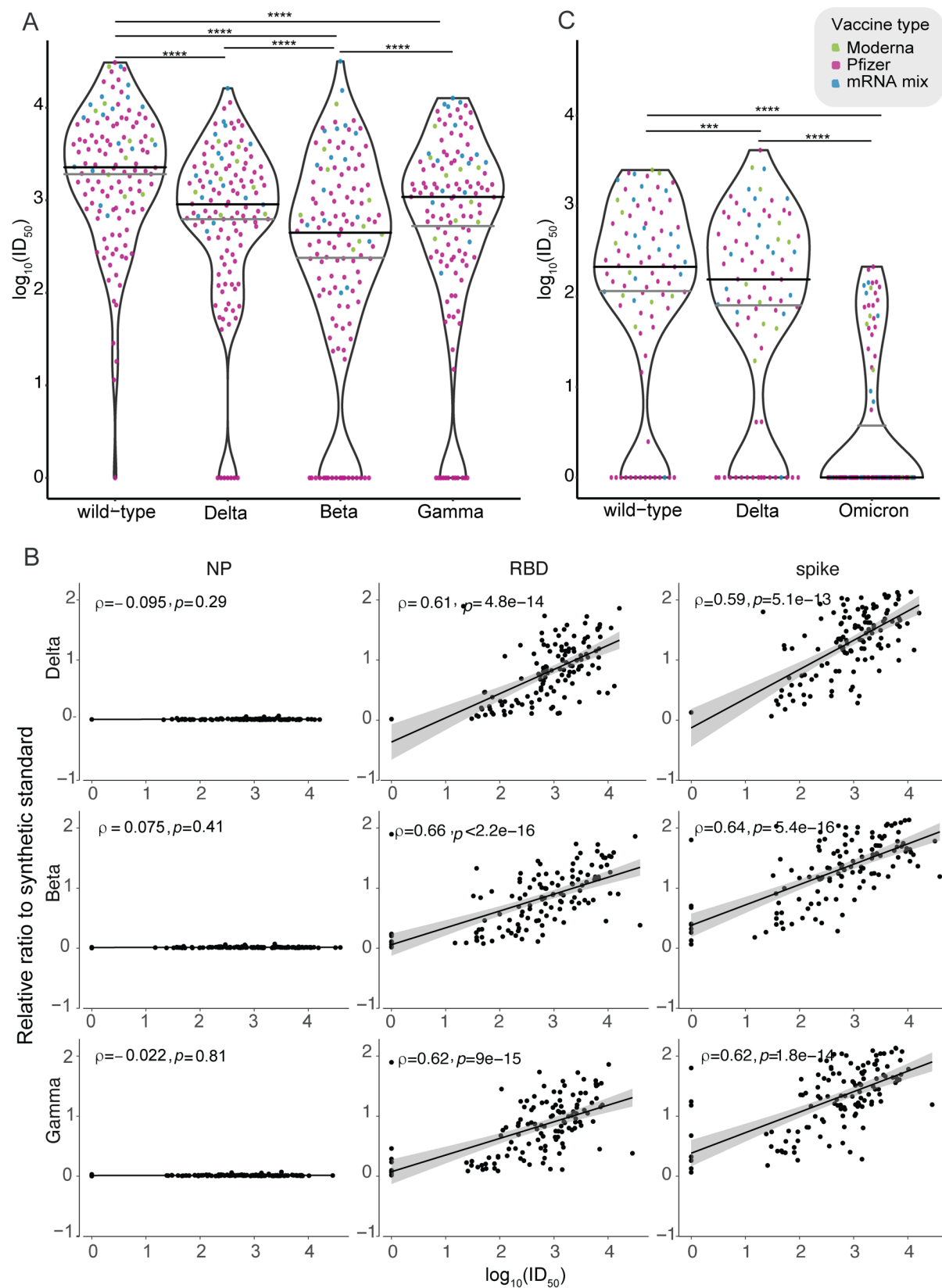




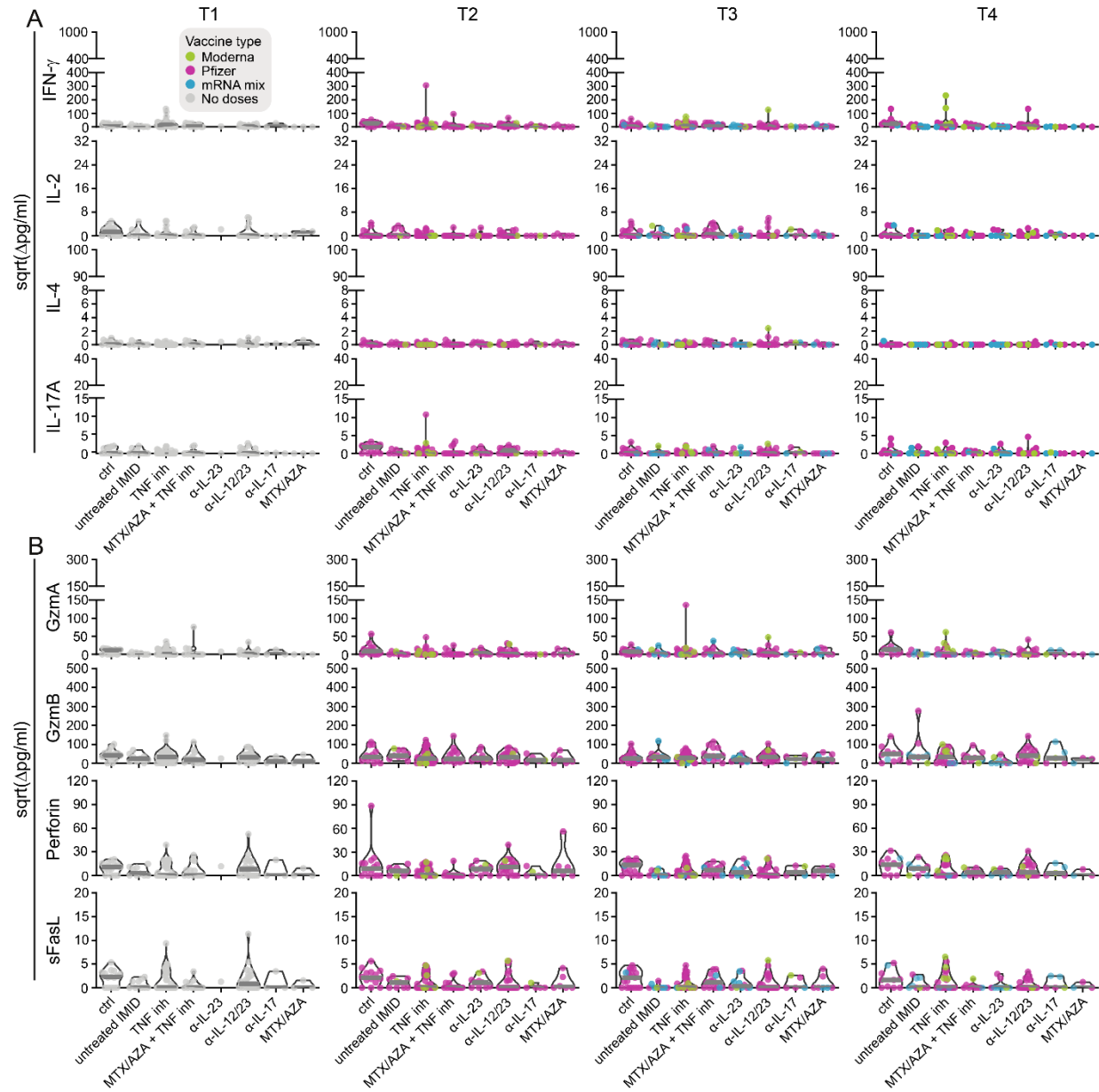
Supplemental Figure 2. Effect of vaccine type, sex and age on antibody responses. Levels of anti-RBD and anti-spike IgG stratified by (A) vaccine type, (B) sex and (C) age using 0.0039 μ l of sample at T3 (see figure 1A). Black lines indicate the median and gray lines signify the mean ratio value for each violin. Statistical analysis for A was for the entire cohort, B and C for BNT162b/BNT162b group only. Unpaired comparisons were made by nonparametric Mann-Whitney test or Dunn's multiple comparisons test. $*p \leq 0.05$, $**p \leq 0.01$.



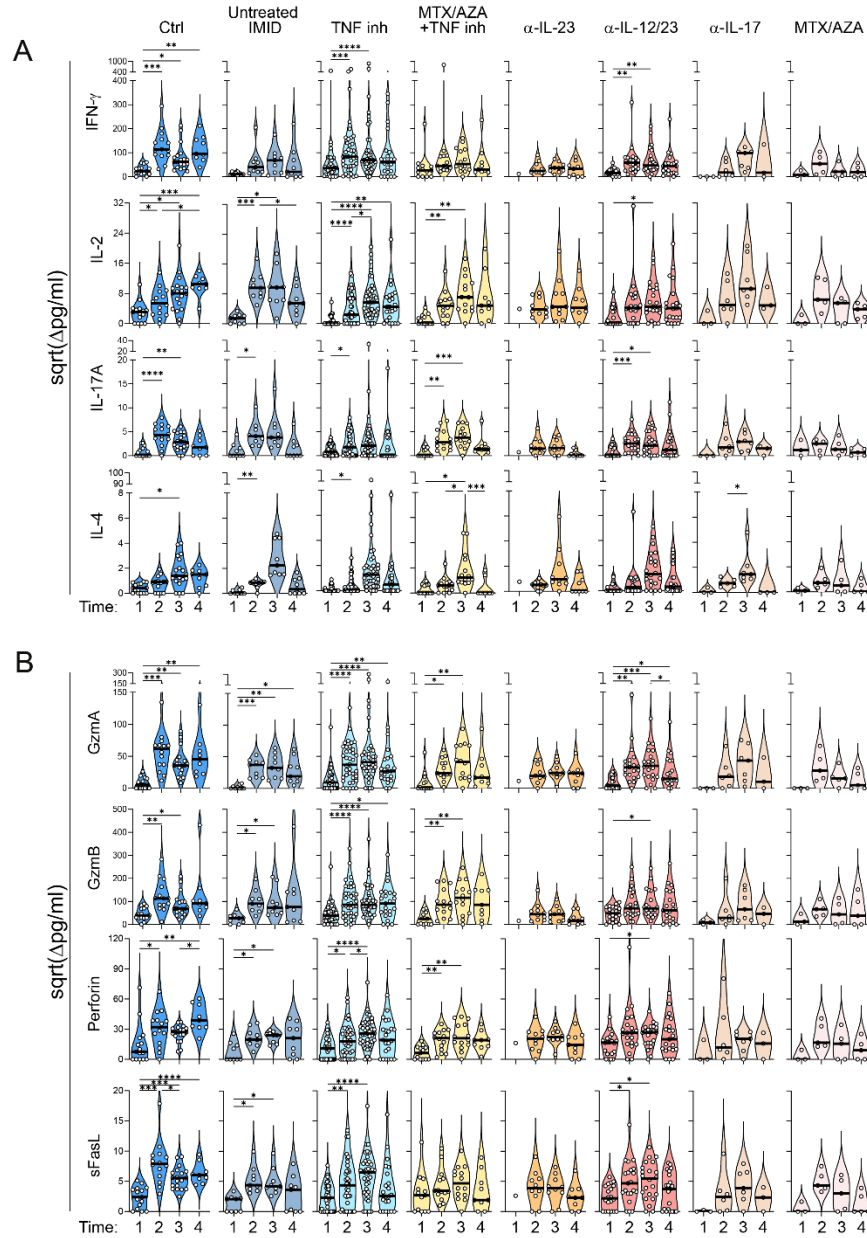
Supplemental Figure 3. Multivariate analysis of antibody responses controlling for age and sex in IMID patients relative to healthy controls. Timepoints are as defined in Figure 1A. The mean difference in relative ratio of RBD and spike from healthy controls at T2 and T4 were determined using 0.0625 µl of sample, and at T3 using 0.0039 µl of sample. Estimates that meet significance cut-off ($\alpha=0.05$) are colored red. Dotted black lines indicate the point of reference. Width of lines indicates 95% confidence interval. These analyses were restricted to the BNT162b/BNT162b cohort.



Supplemental Figure 4. Dynamics of neutralization response of the study groups across variants after second vaccine dose. (A) T3, n=135, (B) Correlation between the VOCs neutralization responses and IgG levels using the \log_{10} ID₅₀ values of the VOCs and the relative ratio values of the spike and RBD IgG levels at T3. Solid black line is the linear regression and gray shading indicates the 95% confidence interval. P-values and Spearman's rho coefficients are indicated in each graph for the entire cohort. (C) T4, n=86. Lentiviral particles used: wildtype, B.1.617.2 (Delta), B.1.351 (Beta), P.1 (Gamma), and B. 1.1.529 (Omicron). The vaccine type is shown as colored dots (see suppl. fig. S1). Black lines indicate median and gray lines denote mean ratio value for each violin. Pairwise comparisons were made by mixed-effects ANOVA with the Geisser-Greenhouse correction, *** $p \leq 0.001$, **** $p \leq 0.0001$.

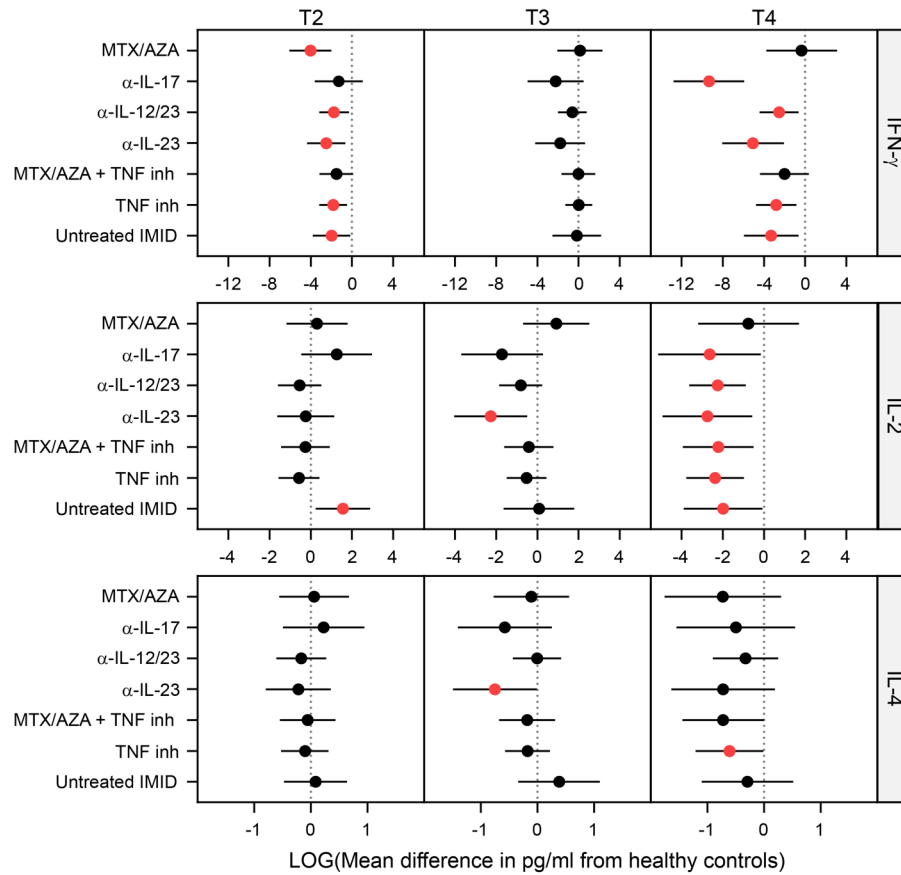


Supplemental Figure 5. Cellular immune responses in IMID patients to NP before or after first and second doses of mRNA vaccine. The release of cytokines and cytotoxic molecules in cell culture supernatants were analyzed by multiplex bead array following 48h stimulation with SARS-CoV-2 NP peptide pools. Violin plots show (A) release of cytokines IFN- γ , IL-2, IL-17A and IL-4 and (B) release of cytotoxic molecules GzmA, GzmB, perforin and sFasL at T1; n=100, T2; n=114, T3; n=123, and T4; n= 85, with T1 to T4 defined in Figure 1A. The grey line indicates the median. Values are reported in pg/ml after subtracting background signal from wells containing PBMCs cultured with DMSO alone, as indicated by “ Δ ”. Ctrl = Healthy controls, inh = inhibitor, MTX = methotrexate, AZA = azathioprine. Statistical analysis was restricted to BNT162b/BNT162b cohort.

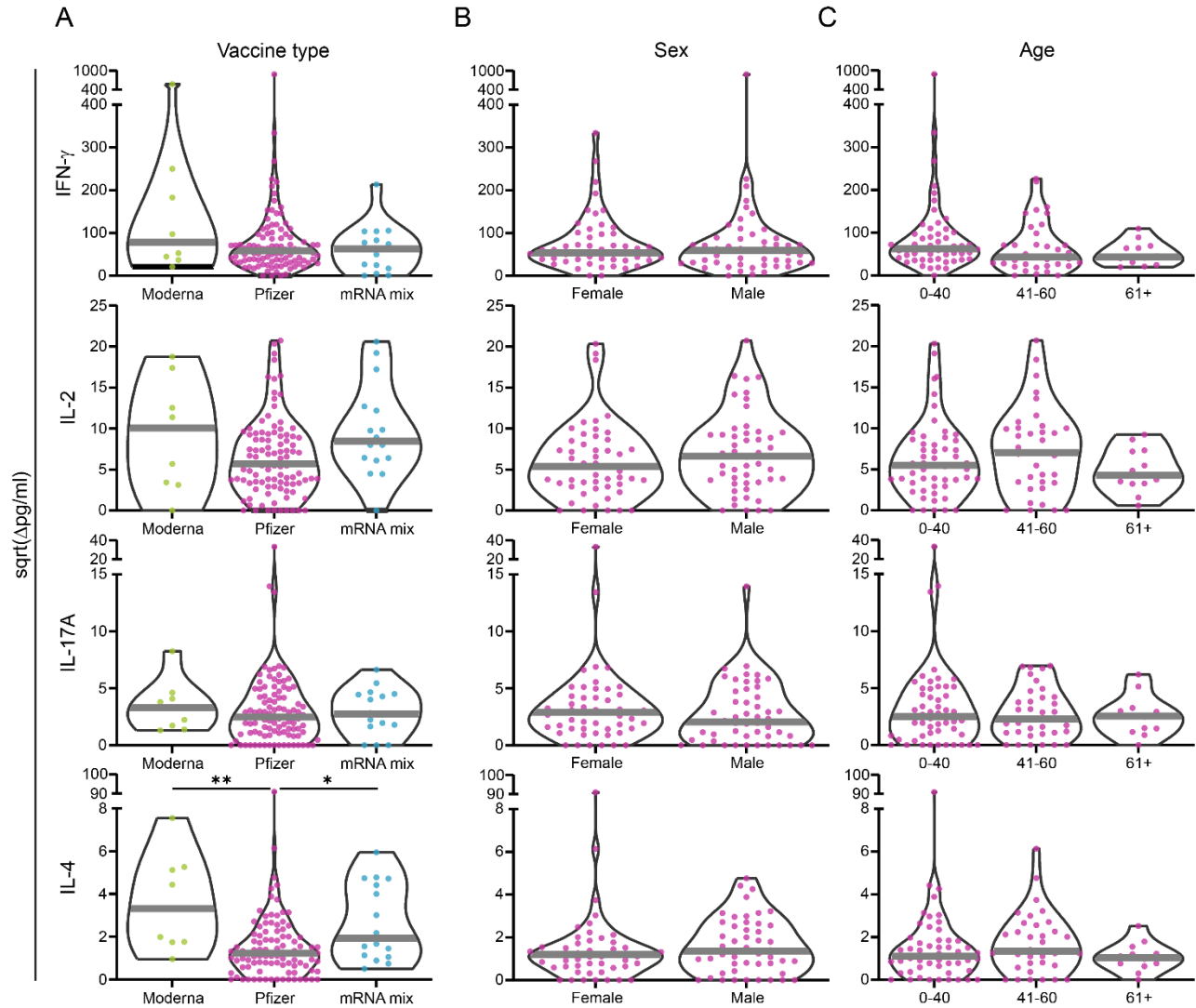


Supplemental Figure 6. Cytokine and cytotoxic responses in IMID patients to spike peptide pools over time.

The release of cytokines and cytotoxic molecules in cell culture supernatants was analyzed by multiplex bead array following 48h stimulation with SARS-CoV-2 S peptide pools. Violin plots show release of (A) cytokines IFN- γ , IL-2, IL-17A and IL-4 and (B) cytotoxic molecules GzmA, GzmB, Perforin and sFasL at timepoints T1-T4 (see Figure 1A) within each study group. The median value is indicated by the black line. Pairwise comparisons were made by mixed-effects ANOVA with the Geisser-Greenhouse correction. $*p \leq 0.05$, $**p \leq 0.01$, $***p \leq 0.001$, $****p \leq 0.0001$.



Supplemental Figure 7. Multivariate analysis of T cell cytokine responses in IMID patients relative to healthy controls.. Timepoints are as defined in Figure 1A. Estimates that meet significance cut-off ($\alpha=0.05$) are colored red. Dotted black lines indicate the point of reference. Width of lines indicates 95% confidence interval. These analyses were restricted to the BNT162b/BNT162b cohort.



Supplemental Figure 8. Effect of mRNA vaccine types on T cell cytokine responses to spike peptide pools in IMiD patients after two doses of the indicated vaccine type. Cytokine responses in the BNT162b (Pfizer) vaccinated population were further stratified by (A) vaccine type (B) sex and (C) age at T3 (see Figure 1A). Median value is indicated by the grey line. Unpaired comparisons were made by nonparametric Mann-Whitney test or Dunn's multiple comparisons test. * $p \leq 0.05$, ** $p \leq 0.01$.