

Supplemental information

**Systemic IL-15, IFN- γ , and IP-10/CXCL10 signature
associated with effective immune response
to SARS-CoV-2 in BNT162b2 mRNA vaccine recipients**

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Table S1. Relevant history of vaccine recipients with pre-existing CoV-2 immunity, Related to Figure 1.

	COVID Symptoms	COVID PCR test	COVID Ab test
Recipient 1	March, 2020	Not done	Not done
Recipient 2		Not done	Not done
Recipient 3	Fever, fatigue, headache	Positive (08/13/2020)	Positive (September, 2020)
Recipient 4	none		Positive (May, 2020)
Recipient 5	Flu-like symptoms (May 2020)		Positive (June, 2020; December, 2020)

Table S2. Cytokines and Chemokines tested, Related to Figures 2, 3, 4, and 5.

Analytes with changes (n=19)	CRP (C-Reactive Protein)
	Eotaxin (CCL11)
	IFN- γ
	IP-10 (CXCL10)
	IL-1Ra
	IL-3
	IL-6
	IL-7
	IL-8
	IL-12/IL-23p40
	IL-15
	IL-16
	MCP-1 (CCL2)
	MDC (CCL22)
	MIP-1 α (CCL3)
	MIP-1 β (CCL4)
	SAA (serum amyloid A)
	TNF- α
	VEGF-A
Analytes with minimal or no change (n=8)	Eotaxin-3
	ICAM-1
	IL-17C
	IL-17B
	MCP-4
	TARC
	TSLP
	VCAM-1
Analytes below detection threshold (n=14)	IL-1 α
	IL-1 β
	IL-2
	IL-4
	IL-5
	IL-9
	IL-10
	IL-12p70
	IL-13
	IL-17A
	IL-17A/F
	IL-17D
	GM-CSF
	TNF- β

Table S3. Adverse effects elicited by mRNA vaccination, Related to Figures 2, 3, 4, and 5.

Adverse effects	Vaccination 1 (40 vaccinees, %)	Vaccination 2 (50 vaccinees, %)
injection site pain	32 (80%)	38 (76%)
fatigue	4 (10%)	9 (18%)
headache	2 (5%)	7 (14%)
myalgia		9 (18%)
fever, shivers		9 (18%)
diarrhea	1 (2.5%)	
axillar pain	1 (2.5%)	
dizziness	1 (2.5%)	2 (4%)

Table S4. Correlations of anti-Spike antibodies at day 36 and cytokines log2 fold changes upon 2nd vaccination (d23-d22), Related to Figure 6.

	Spike-RBD Antibody	
	Spearman r correlation coefficient	<i>p</i> value*
MIP-1α (CCL3)	0.432	0.001
IL-1Ra	0.334	0.013
MCP-1 (CCL2)	0.241	0.074
MIP-1β (CCL4)	0.322	0.015
CRP (C-Reactive Protein)	0.167	0.219
SAA (serum amyloid A)	0.271	0.043
IP-10 (CXCL10)	0.145	0.285
IL-6	0.21	0.121
TNF- α	0.103	0.451
IFN-γ	0.433	0.001
IL-15	0.389	0.003
IL-3	-0.145	0.29
IL-7	0.24	0.075
IL-8	0.114	0.402
Eotaxin (CCL11)	0.120	0.377
MDC (CCL22)	0.394	0.003
IL-12/IL-23p40	0.353	0.008
IL-16	0.248	0.066
VEGF-A	0.303	0.023

* These univariate correlations were determined using a cut-off for a Spearman correlation coefficient corresponding to *p* value <0.05 (non-adjusted for multiple comparisons).

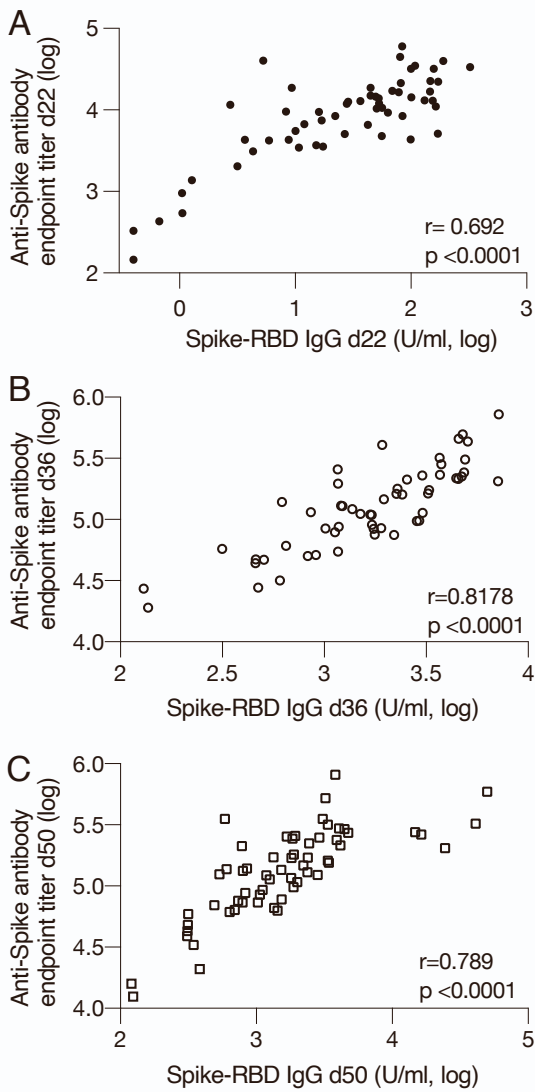


Figure S1. Correlations of Spike and Spike-RBD antibodies, Related to Figure 1.

Correlations of antibodies against full length trimeric Spike (ELISA, endpoint titer in log) and Spike-RBD (ROCHE, log) at day 22 (A), day 36 (B) and day 50 (C). Spearman r and p values are given (GraphPad Prism).

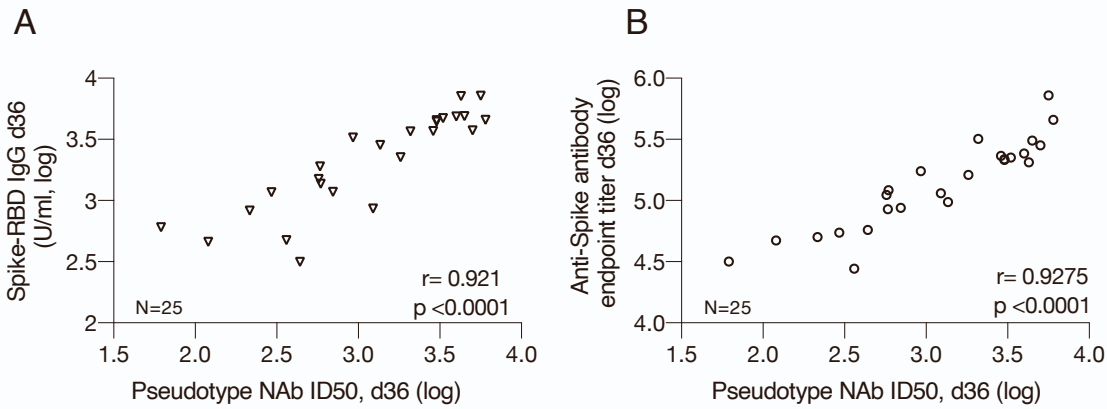


Figure S2. Correlation of binding and neutralizing antibodies, Related to Figure 1.

NAb assays were performed in using a HIV-1_{NL}ΔEnv-NanoLuc derived pseudotype neutralization assay in HEK-ACE2 cells using Wuhan-Hu-1 Spike. using sera from a subset of naïve vaccinees (day 36) selected to cover a range of low to high responses. Correlations of (A) Spike-RBD (ROCHE, log) and (B) antibodies against full length trimeric Spike (ELISA, endpoint titer in log) and pseudotype NAb measured at day 36 (samples from Figure 1). Spearman r and p values are given (GraphPad Prism).

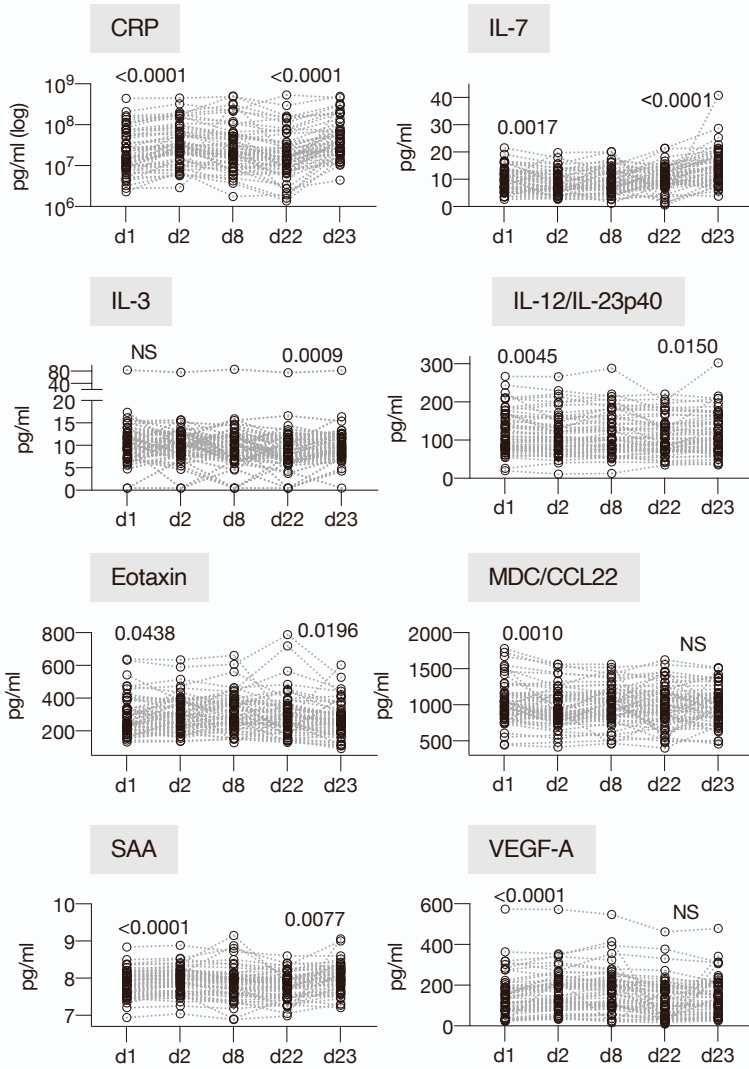


Figure S3. Additional serum cytokine/chemokine levels affected by COVID-19 vaccination, Related to Figure 2. Cytokine and chemokine levels were measured over time using the MSD assay as described in Figure 2 for the 58 COVID-19 naïve vaccine recipients. Serum levels of 8 of 19 analytes showing changes upon vaccination are plotted over time.

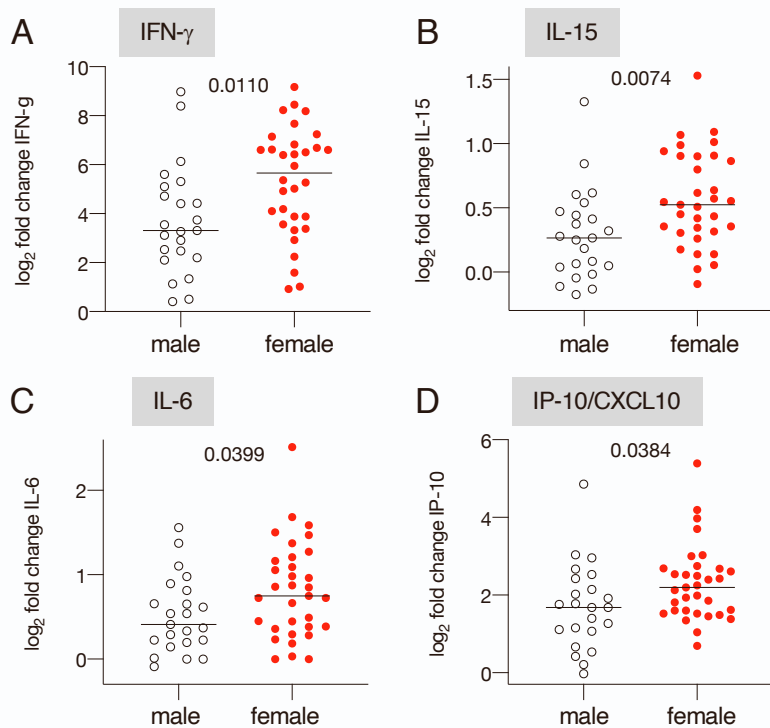


Figure S4. Differential levels of cytokine in male and female vaccine recipients upon COVID-19 vaccination, Related to Figure 3.

Comparison of log₂ fold changes after the 2nd vaccination (d23_d22) in serum of (A) IFN- γ , (B) IL-15, (C) IL-6 and (D) IP-10/CXCL10 which are significantly higher in female vaccine recipients (N=33) to male vaccine recipients (N=23) at one day after the 2nd vaccination (d23). P values are from unpaired non-parametric t test (Mann-Whitney).

Vaccination 1 (d2_d1)

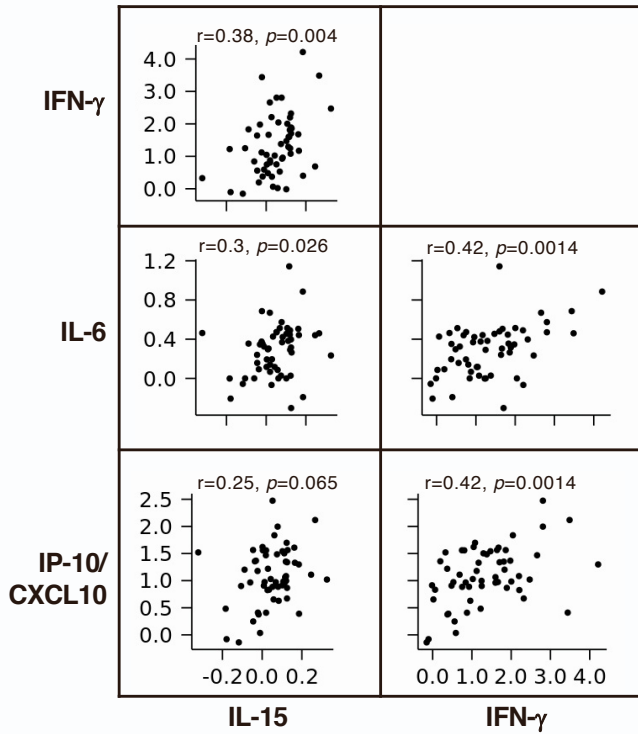


Figure S5. Serum cytokine associations after the 1st vaccination in antigen-naïve vaccine recipients, Related to Figure 5.

Correlations of log₂ fold changes of selected analytes after the 1st vaccination are shown. r and non-adjusted p value for the individual correlations are shown in the plots.

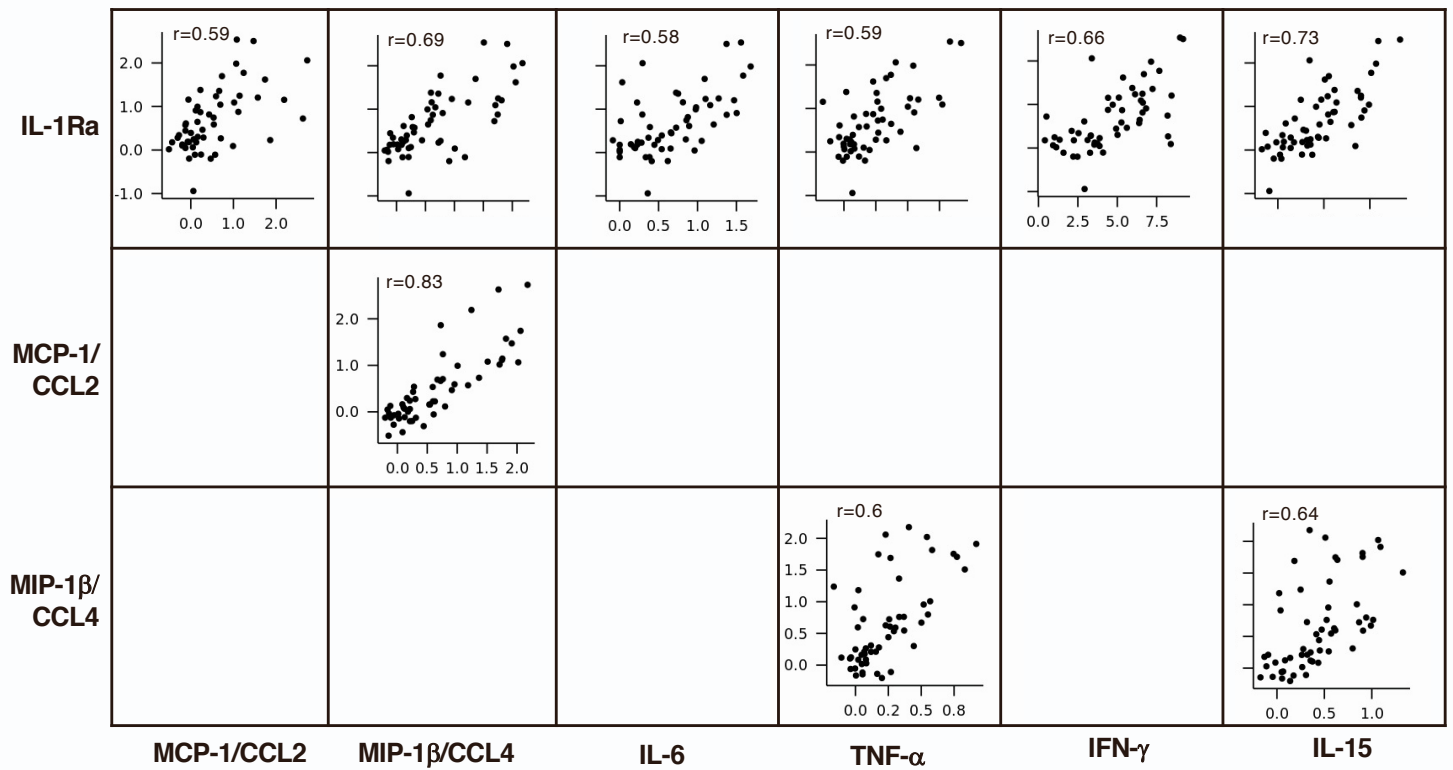


Figure S6. Coordinated vaccine response featuring inflammatory molecules and chemokines, Related to Figure 5.

Correlations of log₂ fold changes of selected analytes after the 2nd vaccination are shown derived from data depicted in heatmap in Figure 5A (grey box). r is shown in plots; all correlations are characterized by an adjusted $p < 0.05$.