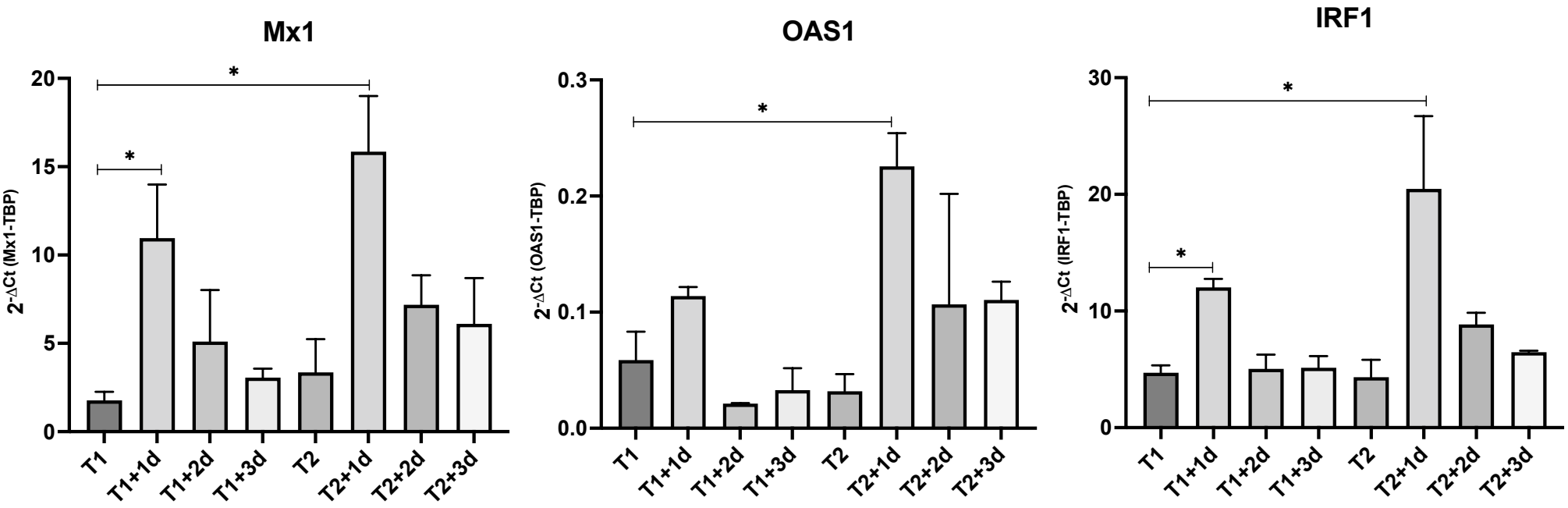
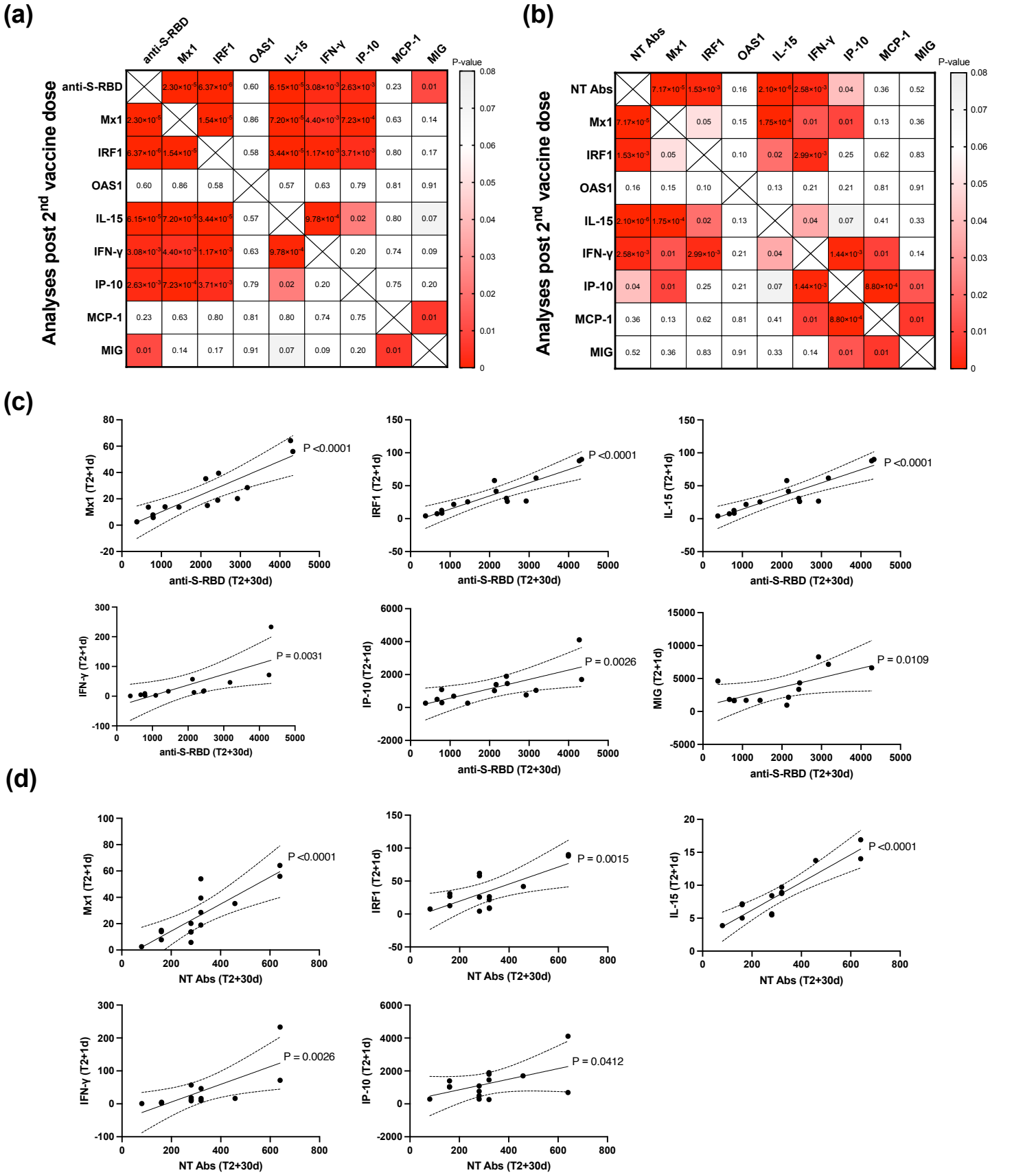
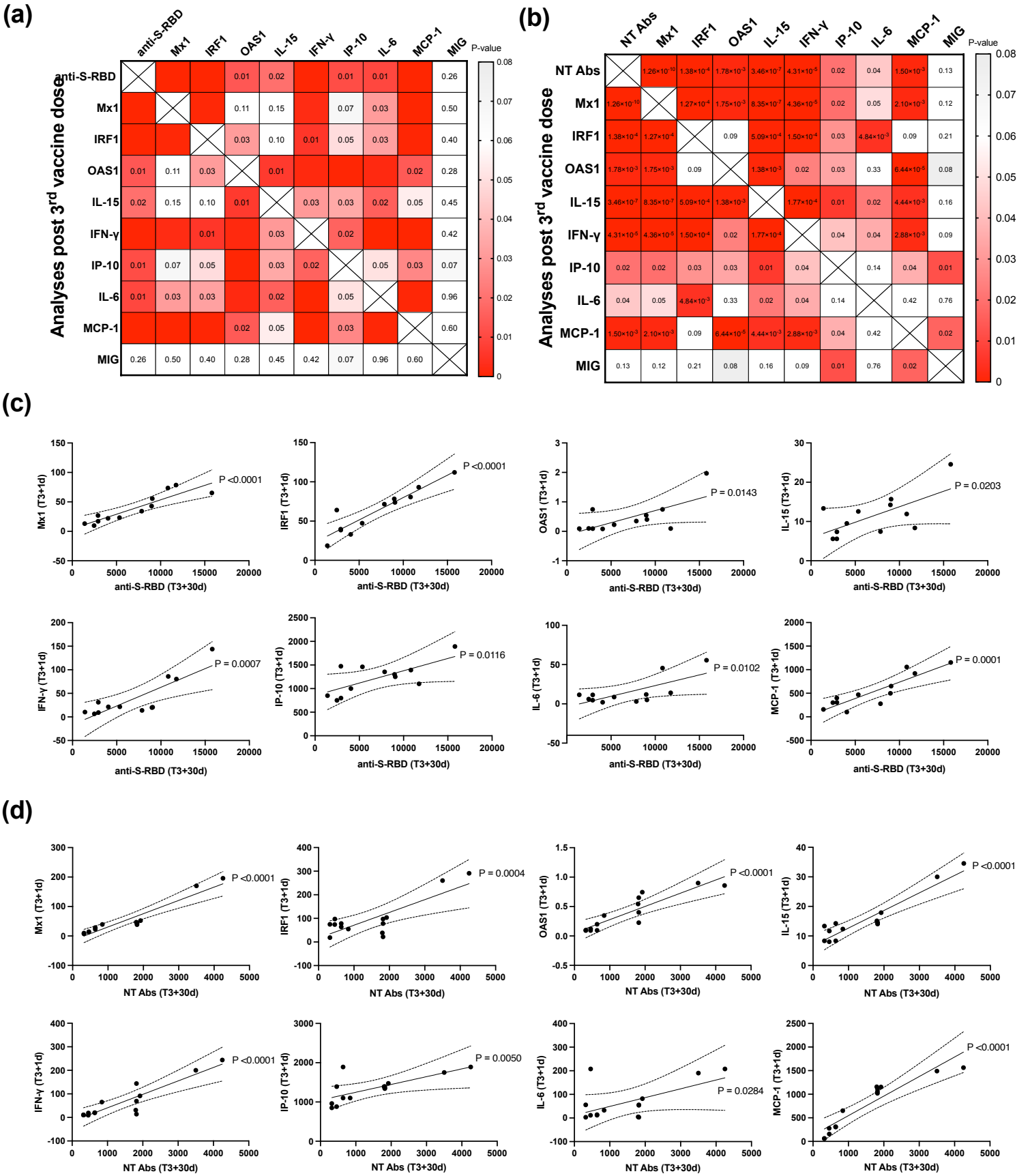


Supplementary figure 1: Kinetic study of type I and II Interferon gene signature in healthy vaccine recipients.
Freshly isolated peripheral blood mononuclear cells (PBMC) were collected from healthy subjects (n=4) immediately before (T1) and 1, 2 or 3 days after the 1st BNT162b2 vaccine dose (T1+1d, T1+2d and T1+3d respectively), as well as 1,2 and 3 days after the 2nd vaccine dose (T2+1d, T2+2d and T2+3d respectively). Relative expression of the interferon-stimulated genes Mx1, OAS1, IRF1 was measured by quantitative real time PCR analysis and normalized to the housekeeping gene TBP level by using the equation $2^{-\Delta Ct}$ in cDNA derived from total RNA isolated from PBMC. Star scale *P*-values were as follows: * ≤0.05.



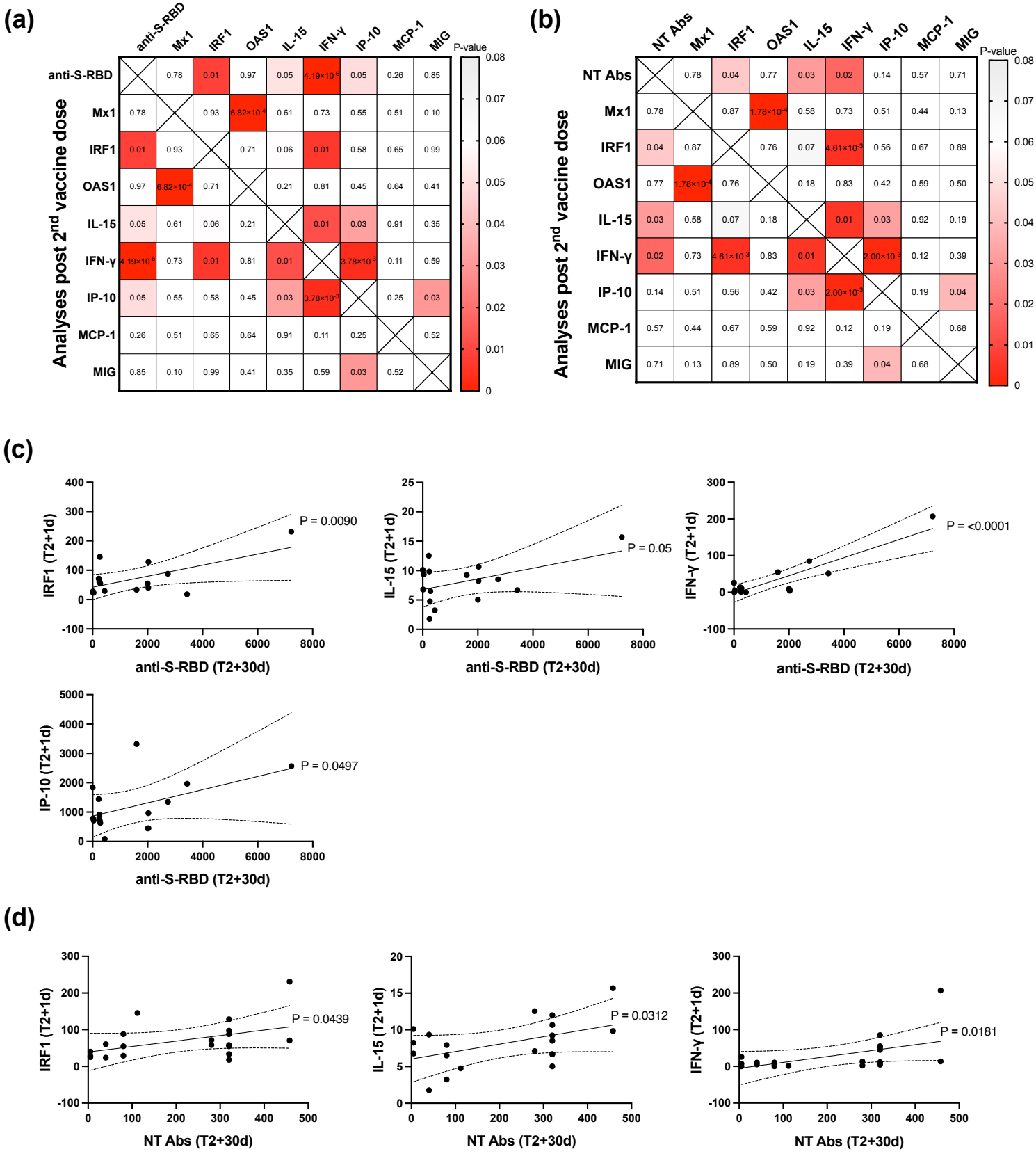
Supplementary figure 2: Correlation of vaccine-specific antibody production with early innate signature in healthy recipients after 2nd dose.

(a, b) Correlation matrices between anti-SARS-CoV-2 Spike-receptor binding domain Immunoglobulin G (anti-S-RBD, expressed as BAU ml^{-1}) **(a)** or neutralizing antibodies against wild-type Wuhan SARS-CoV-2 variant (NT Abs, expressed as IC50) **(b)**, measured 30 days post 2nd vaccine dose (T2+30d), and correspondent early vaccine-induced signature, measured 1 day post 2nd vaccine dose (T2+1d), were constructed. Correlations were obtained by deriving a Pearson r correlation coefficient and here the probabilistic adjusted *P*-value associated to each correlation is shown. Significant correlations (with *P*-values ≤0.05) are indicated by shades of red color. **(c, d)** Single correlation curves between anti-S-RBD **(c)** or NT Abs **(d)** and specific early immune factors with significant linear regression (with *P*-values ≤0.05) are reported. 99% confidence bands of the best fit-line are also shown for each slope.



Supplementary figure 3: Correlation of vaccine-specific antibody production with early innate signature in healthy recipients after 3rd dose.

(a, b) Correlation matrices between anti-SARS-CoV-2 Spike-receptor binding domain Immunoglobulin G (anti-S-RBD, expressed as BAU ml^{-1}) **(a)** or neutralizing antibodies against wild-type Wuhan SARS-CoV-2 variant (NT Abs, expressed as IC50) **(b)**, measured 30 days post 3rd vaccine dose (T2+30d), and correspondent early vaccine-induced signature, measured 1 day post 3rd vaccine dose (T2+1d), were constructed. Correlations were obtained by deriving a Pearson r correlation coefficient and here the probabilistic adjusted *P*-value associated to each correlation is shown. Significant correlations (with *P*-values ≤0.05) are indicated by shades of red color. **(c, d)** Single correlation curves between anti-S-RBD **(c)** or NT Abs **(d)** and specific early immune factors with significant linear regression (with *P*-values ≤0.05) are reported. 99% confidence bands of the best fit-line are also shown for each slope.



Supplementary figure 4: Correlation of vaccine-specific antibody production with early innate signature in people with Multiple Sclerosis after 2nd dose.

(a, b) Correlation matrices between anti-SARS-CoV-2 Spike-receptor binding domain Immunoglobulin G (anti-S-RBD, expressed as BAU ml^{-1}) **(a)** or neutralizing antibodies against wild-type Wuhan SARS-CoV-2 variant (NT Abs, expressed as IC50) **(b)**, measured 30 days post 2nd vaccine dose (T2+30d), and correspondent early vaccine-induced signature, measured 1 day post 2nd vaccine dose (T2+1d), were constructed. Correlations were obtained by deriving a Pearson r correlation coefficient and here the probabilistic adjusted *P*-value associated to each correlation is shown. Significant correlations (with *P*-values ≤0.05) are indicated by shades of red color. **(c, d)** Single correlation curves between anti-S-RBD **(c)** or NT Abs **(d)** and specific early immune factors with significant linear regression (with *P*-values ≤0.05) are reported. 99% confidence bands of the best fit-line are also shown for each slope.

Supplementary table 1: Serum level of inflammatory factors, cytokines and chemokines in healthy vaccine recipients

	sCD40L	EGF	Eotaxin	FGF-2	FLT-3L	Fractalkine	G-CSF	GRO-alpha	MCP-3	M-CSF	MDC	MIP-1alpha	MIP-1beta	PDGF-AA	PDGF-AB/BB	VEGF-A
Mean (T1)	11332,31	191,95	99,72	50,74	34,58	165,91	44,16	18,81	23,74	76,26	721,25	312,49	278,82	5388,83	26258,60	304,87
Mean (T1+1d)	11734,50	190,55	94,89	54,92	31,12	175,21	51,02	19,40	23,99	43,15	711,16	203,35	66,15	5609,07	20584,82	286,65
Mean (T2+2d)	9646,22	199,65	88,83	50,44	33,88	151,99	46,60	17,84	21,42	103,27	644,64	168,89	103,34	4627,27	19217,73	269,21
SD (T1)	7057,55	200,55	36,54	52,73	30,78	137,52	42,35	18,54	29,48	66,72	200,85	859,61	950,58	1474,16	24631,66	213,96
SD (T1+1d)	7978,59	179,79	45,07	52,71	28,31	168,37	45,31	13,48	29,48	19,12	220,00	358,09	88,61	1814,71	3376,69	146,60
SD (T2+2d)	6722,86	183,54	41,31	57,89	32,46	80,14	33,82	12,48	20,64	22,90	222,38	345,52	109,81	1284,49	3623,50	192,84
paired Student's *t*-test (T1 vs T1+1d)	0,76	0,95	0,52	0,43	0,40	0,45	0,36	0,92	0,94	0,20	0,84	0,20	0,38	0,44	0,33	0,52
paired Student's *t*-test (T1 vs T2+1d)	0,32	0,92	0,27	0,52	0,71	0,57	0,56	0,84	0,47	0,20	0,08	0,68	0,46	0,02	0,20	0,22
paired Student's *t*-test (T1+1d vs T2+1d)	0,34	0,84	0,66	0,82	0,43	0,49	0,94	0,87	0,52	0,02	0,23	0,93	0,21	0,02	0,10	0,64

	IL-1alpha	IL-1beta	IL-1RA	IL-2	IL-4	IL-5	IL-7	IL-9	IL-10	IL-12p40	IL-12p70	IL-13	IL-17A	IL-17E / IL-25	IL-17F	IL-18	IL-22	IL-27	TGF-alpha	TNF-beta
Mean (T1)	94,08	169,12	14,3	2,70	2,50	13,00	24,70	39,87	14,65	41,89	20,33	59,71	29,83	614,41	45,50	20,28	104,10	1355,80	9,76	13,67
Mean (T1+1d)	37,76	20,06	4,42	1,46	3,18	13,76	23,86	38,09	15,37	34,90	22,66	62,35	14,07	619,29	43,21	21,18	146,27	1462,40	9,74	18,67
Mean (T2+2d)	35,94	125,39	10,6	2,71	1,59	9,13	29,20	36,38	17,80	40,95	6,89	43,68	34,05	634,05	43,97	23,73	84,04	2327,56	11,02	9,84
SD (T1)	81,05	414,66	28,4	3,06	3,49	16,84	81,87	35,10	23,77	78,87	26,58	69,27	46,36	790,64	78,50	11,28	36,73	861,88	17,59	18,87
SD (T1+1d)	18,17	17,84	3,74	1,61	5,02	20,38	79,80	34,98	19,65	50,93	38,29	78,39	20,76	645,16	60,15	11,35	55,45	745,07	14,89	30,36
SD (T2+2d)	29,21	278,53	14,0	2,78	2,12	9,36	101,1	34,61	14,59	65,73	5,97	41,97	40,86	879,79	67,58	23,77	5,19	153,59	16,11	7,82
paired Student's *t*-test (T1 vs T1+1d)	0,31	0,46	0,60	0,54	0,18	0,54	0,52	0,25	0,78	0,39	0,40	0,45	0,37	0,90	0,37	0,69	0,54	0,39	0,99	0,27
paired Student's *t*-test (T1 vs T2+1d)	0,48	0,52	0,92	0,83	0,41	0,34	0,38	0,78	0,90	0,81	0,29	0,44	0,68	0,60	0,83	0,45	0,89	0,0026	0,30	0,43
paired Student's *t*-test (T1+1d vs T2+1d)	0,34	0,84	0,66	0,82	0,43	0,49	0,94	0,87	0,52	0,02	0,23	0,93	0,21	0,02	0,10	0,64	0,9	0,01	0,46	0,37

T1: baseline pre-Pfizer-BionTech BNT162b2 anti-COVID-19 vaccine, T1+1d: 1 day after 1st vaccine dose, T2+1d: 1 day after 2nd vaccine dose; SD: standard deviation.
Indicated in red color the statistically significant *P*-values (≤ 0.05) as calculated by the paired Student's *t*-test.

Supplementary table 2: Demographic and therapy-related information of vaccinated people with Multiple Sclerosis

CODE	SEX	Age	Therapy
MS-V-1	F	29	IFN-beta (Peg)
MS-V-2	M	45	DMF
MS-V-3	F	44	Ocrelizumab
MS-V-4	F	29	IFN-beta (1-a)
MS-V-5	F	21	Fingolimod
MS-V-6	F	46	IFN-beta (1-a)
MS-V-7	M	41	Fingolimod
MS-V-8	M	39	DMF
MS-V-9	F	36	Fingolimod
MS-V-10	M	39	natalizumab
MS-V-11	F	45	IFN-beta (1-a)
MS-V-12	M	46	DMF
MS-V-13	F	37	Fingolimod
MS-V-14	F	41	IFN-beta (1-a)
MS-V-15	M	41	IFN-beta (1-b)
MS-V-16	F	31	natalizumab
MS-V-17	M	49	no therapy
MS-V-18	M	39	natalizumab
MS-V-19	F	26	Ocrelizumab
MS-V-20	F	41	no therapy
MS-V-21	F	29	Ocrelizumab
MS-V-22	F	40	no therapy

MS-V: people with Multiple Sclerosis vaccinated with anti-COVID-19 BNT162b2 vaccine; M: male; F: female