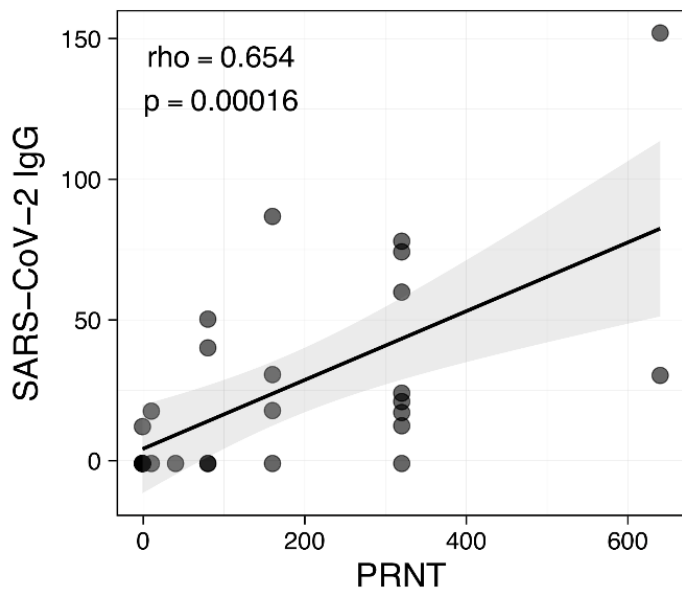


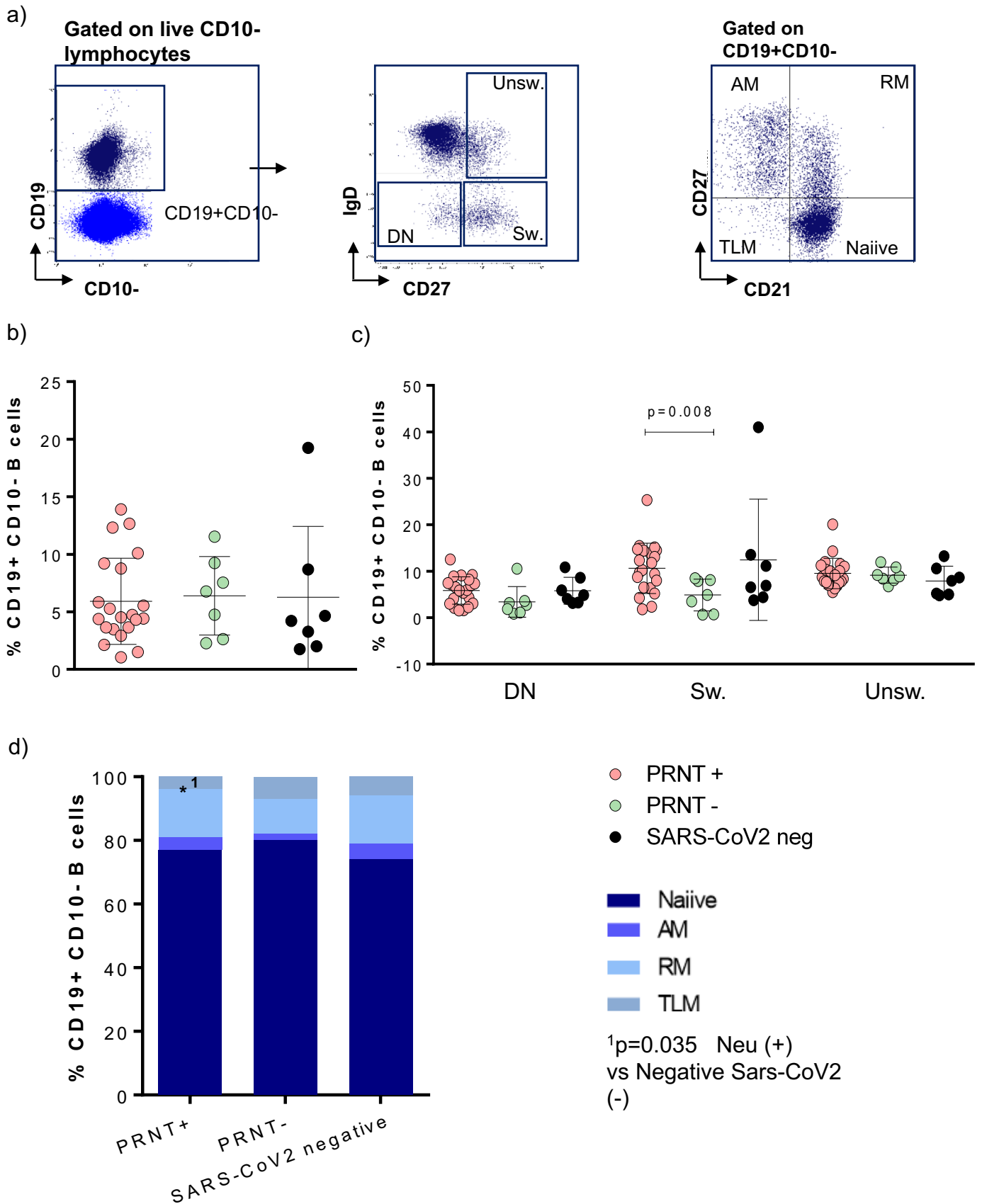
Supplemental information

**Virological and immunological features
of SARS-CoV-2-infected children
who develop neutralizing antibodies**

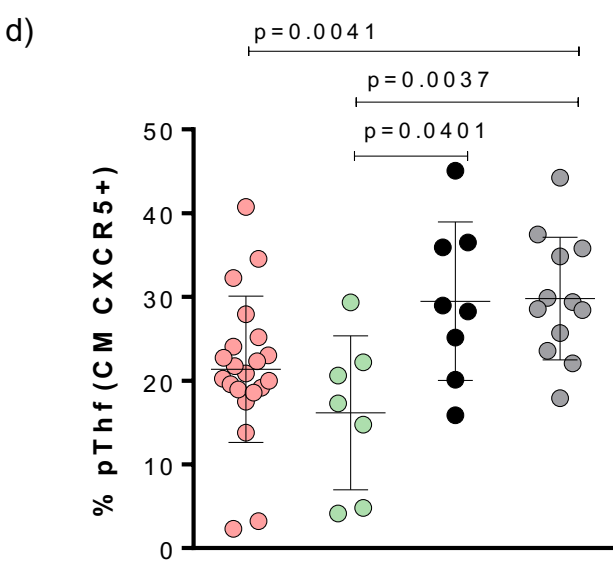
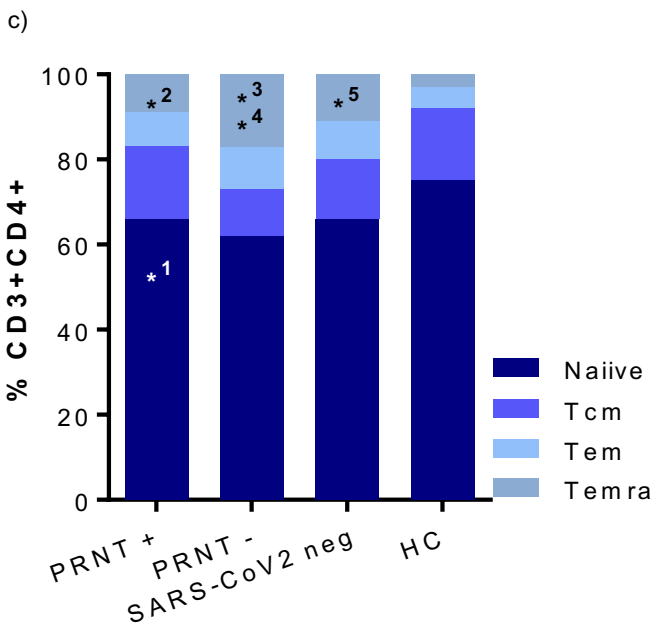
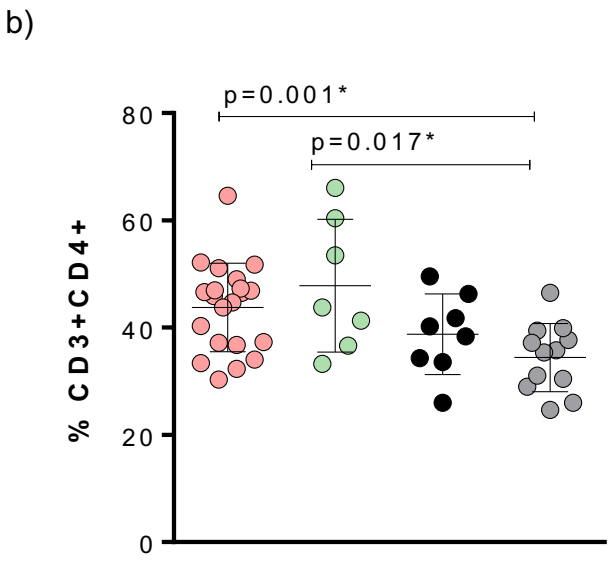
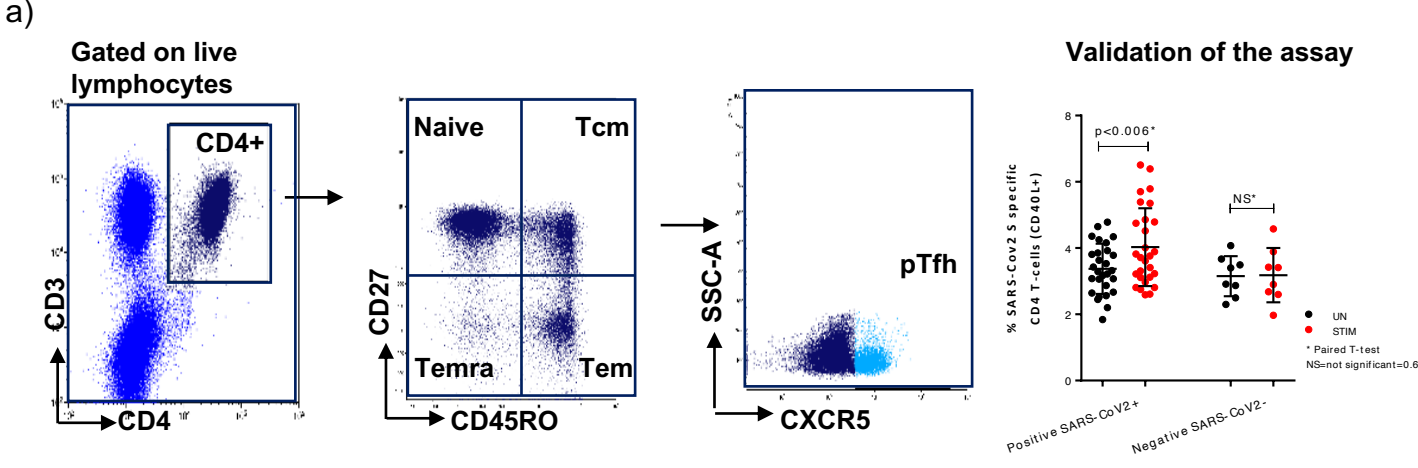
Nicola Cotugno, Alessandra Ruggiero, Francesco Bonfante, Maria Raffaella Petrara, Sonia Zicari, Giuseppe Rubens Pascucci, Paola Zangari, Maria Antonietta De Ioris, Veronica Santilli, E.C. Manno, Donato Amodio, Alessio Bortolami, Matteo Pagliari, Carlo Concato, Giulia Linardos, Andrea Campana, Daniele Donà, Carlo Giaquinto, The CACTUS Study Team, Petter Brodin, Paolo Rossi, Anita De Rossi, and Paolo Palma



Supplementary Figure 1 (Related to Figure 1) SARS-CoV-2 IgG associates with neutralization activity (PRNT). N=28



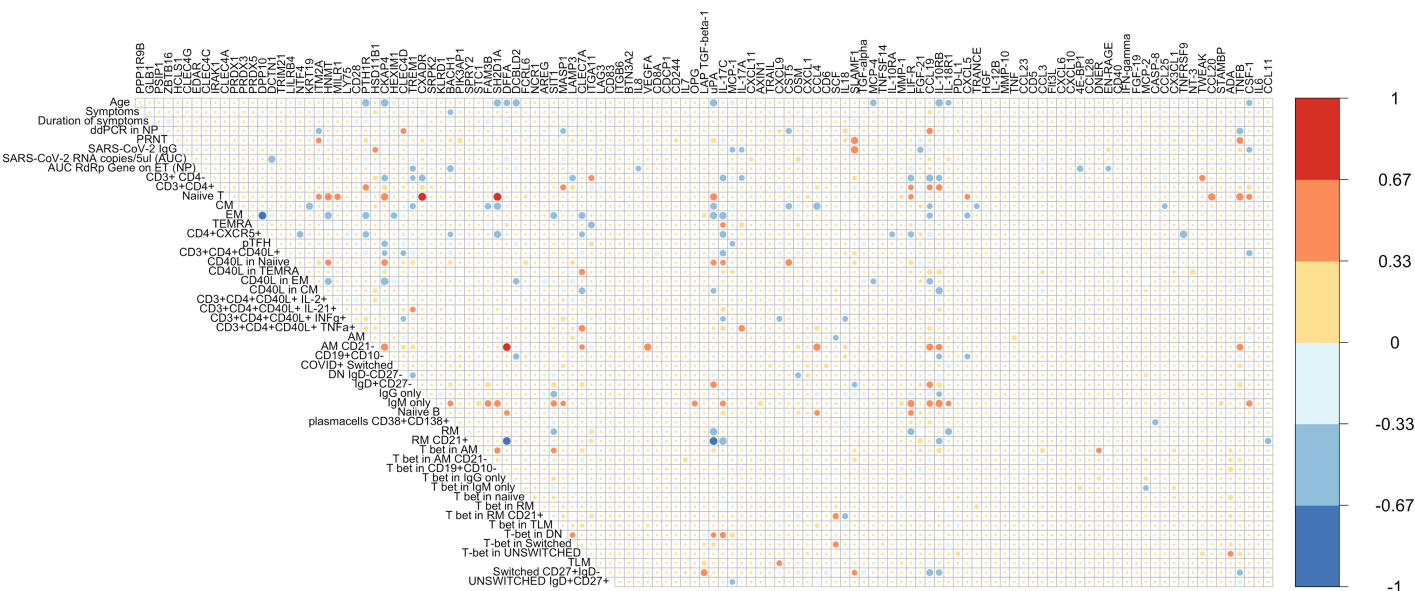
Supplementary Figure 2 (Related to Figure 2) B cells phenotype. Gating strategy for B-cells phenotype is shown in panel a. B cell populations were analyzed in PRNT (+, light purple solid circle), PRNT (-, light green solid circle) and SARS-CoV-2 neg (black solid circle) using non-parametric Mann Whitney test b), c), d). Unsw.: unswitched CD27+IgD+ B cells; Sw.: switched CD27+IgD- B cells AM=activated memory; RM= resting memory; TLM= tissue like memory. Light purple solid circle= PRNT+; light green solid circle = PRNT-; black solid circle = SARS-CoV-2 negative (neg). N=28



¹p=0.05 Neu (+) vs Healthy
²p= 0.008 Neu (+) vs Healthy
³p=0.047 Neu (+) vs Neu (-)
⁴p=0.008 Neu (-) vs Healthy
⁵p=0.024 Neu (-) vs SARS-COV-2 neg

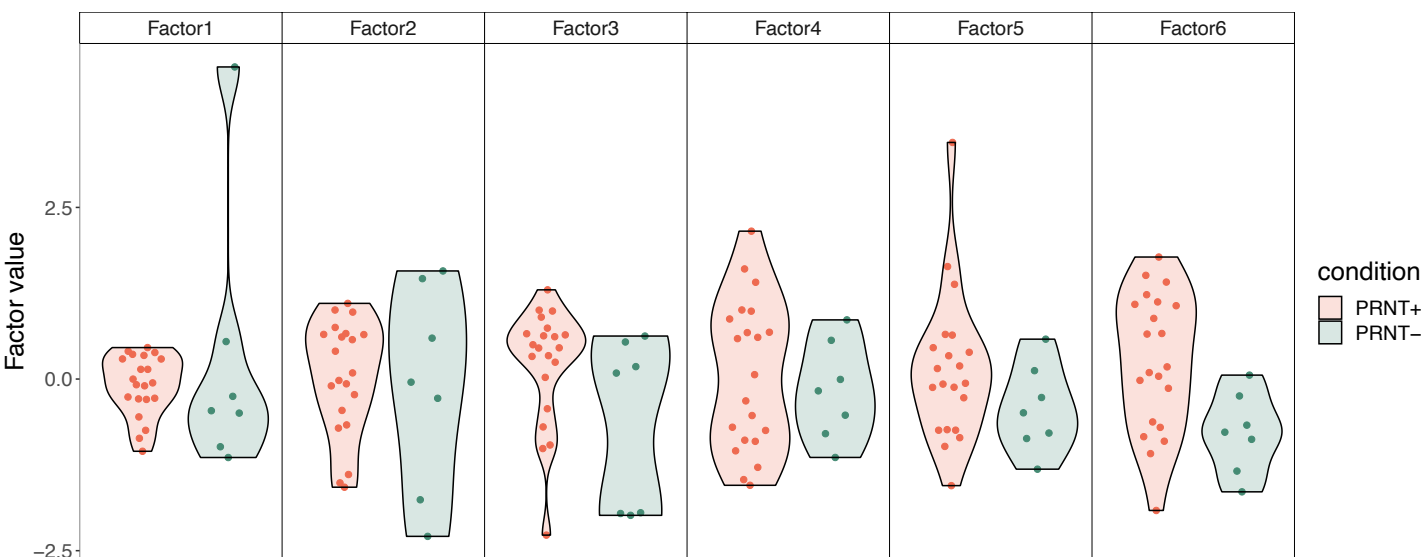
● PRNT+
 ● PRNT-
 ● SARS-CoV-2 neg
 ● HC

Supplementary Figure 3 (Related to Figure 3) CD4 T-cells phenotype. Gating strategy for T-cells phenotype is shown in panel a. Assay validation is shown in b. T-cell populations were analyzed in PRNT (+, light purple solid circle), PRNT (-, light green solid circle) and SARS-CoV-2 neg (black solid circle) using non-parametric Mann Whitney test c-e. Tcm= central memory; Tem=effector memory; Temra= terminally differentiated effector memory. UN=unstimulated, STIM= SARS-CoV-2 stimulated T-cells. N=28

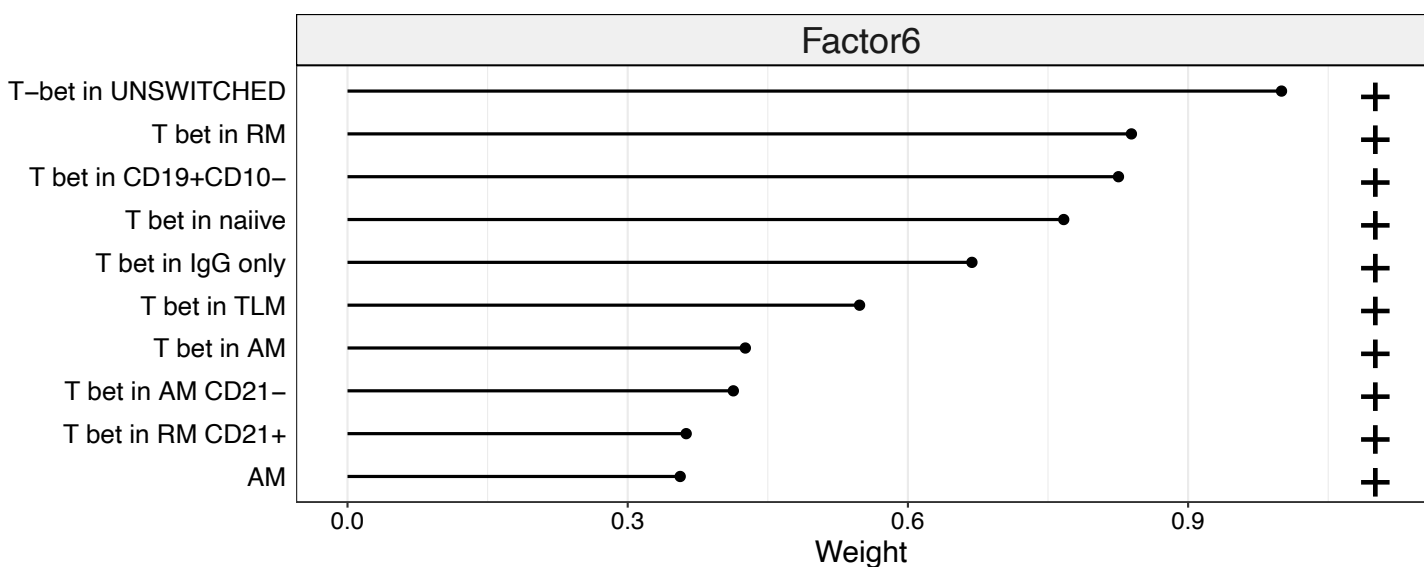


Supplementary Figure 4 (Related to Figure 5) Full set of correlation between Ag-specific B and T cells, humoral responses, viral data and proteomics. Only significant correlations are shown in the heatmap. N=28

a)



b)



Supplementary Figure 5 (Related Figure 5) MOFA analysis. a) Factors values distribution in PRNT- and PRNT+. b) B cells population contributing to the variance of factor 6. N=28

Table S1 (Related to Table 1). Table of different Symptoms at admission of the PRNT +, PRN- and SARS-CoV-2 negative patients.

Symptoms	PRNT+ (n=37)	PRNT- (n=23)^a	SARS-CoV-2 neg (n=11)
Respiratory, n/tot (%)	11/37 (30%)	6/23 (26%)	7/11
Gastrointestinal, n/tot (%)	8/37 (22%)	5/23 (22%)	4/11 (36%)
Convulsion, n/tot (%)	4/37 (11%)	3/23 (13%)	1/11 (9%)
Migraine, n/tot (%)	11/37 (30%)	5/23 (22%)	1/11 (9%)
Fever > 37.5, n/tot (%)	16/37 (43%)	8/23 (35%)	11/11 (100%)
Skin rash, n/tot (%)	1/37 (2%)	1/23 (4%)	2/11 (18%)
Conjunctivitis, n/tot (%)	3/37 (8%)	1/23 (4%)	2/11 (18%)
Joint pain, n/tot (%)	4/37 (11%)	2/23 (9%)	1/11 (9%)
Prescriptions/Treatments			
Azithromycin, n/tot (%)	8/37 (22%)	2/23 (8%)	0/8 ^b (0%)
Plaquenil, n/tot (%)	8/37 (22%)	4/23 (17%)	n.a.
Corticosteroids, n/tot (%)	7/37 ^b (19%)	1/23 (4%)	1/8 ^b (13%)
Anakirna, n/tot (%)	1/37 (2%)	0/23 (0%)	n.a.

^aFor 6 samples detailed symptoms history was not available; ^binformation not available for all the individuals of the group. na=not available.

Table S2 (Related to Table 1). Clinical and etiological diagnosis of SARS-CoV-2 neg.

Case	Age	Gender	Clinical diagnosis	Etiological diagnosis
1	5,3	F	Bronchitis	n.a.
2	3,5	F	Pneumonia	Parainfluenza and rhinovirus
3	8,0	M	Pneumonia	Mycoplasma pneumoniae
4	2,1	F	Pharyngitis	n.a.
5	4,9	F	pharyngitis	n.a.
6	5,5	M	mononucleosis	EBV
7	0,3	F	Bronchitis	n.a.
8	4,4	M	Gastroenteritis and Pharyngitis	HHV6
9	16,6	M	Pneumonia	EBV
10	5,6	F	Fever	HHV6
11	16,0	M	Pneumonia	Chlamydiae Pneumoniae