SUPPLEMENTARY MATERIAL

Recurrent SARS-CoV-2 infection is linked to the TLR7 rs179008 variant and related to diminished baseline T-Cell immunity

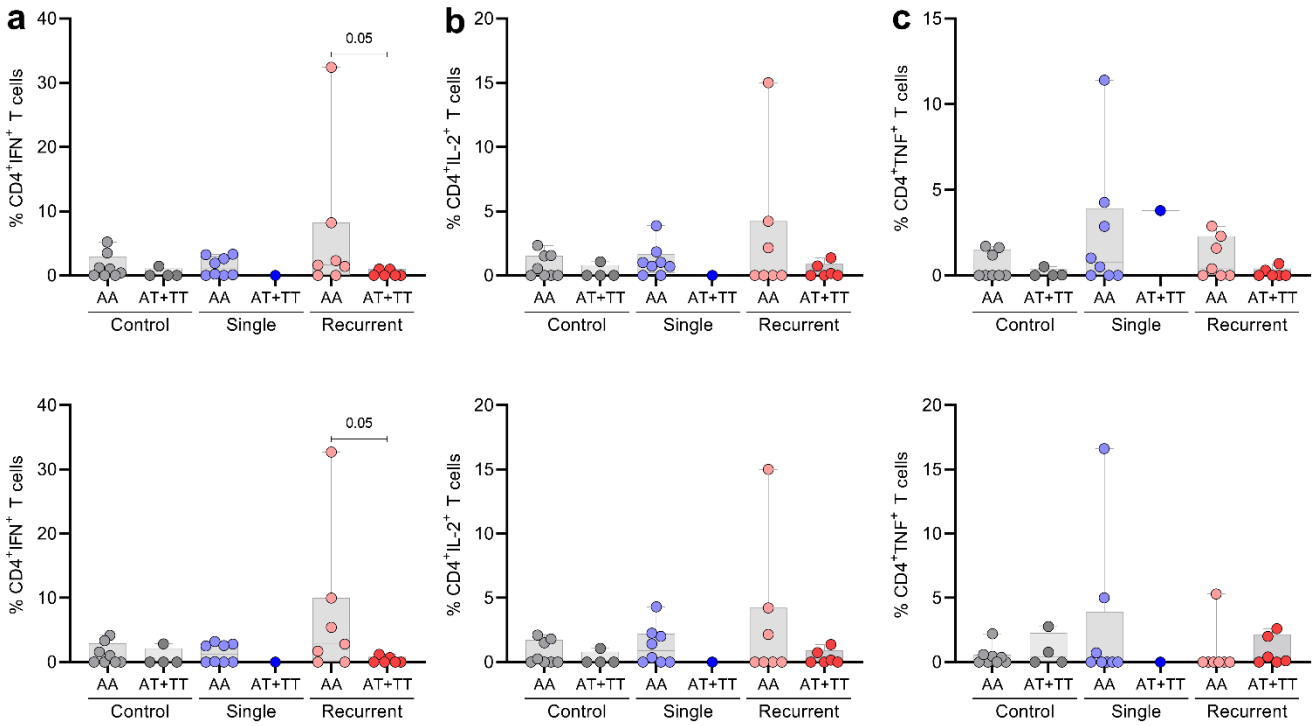
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Supplementary Table S1. Genotype frequencies of ACE2, CXCL8, MICB, and CXCL10 SNPs and its association with recurrent COVID-19.

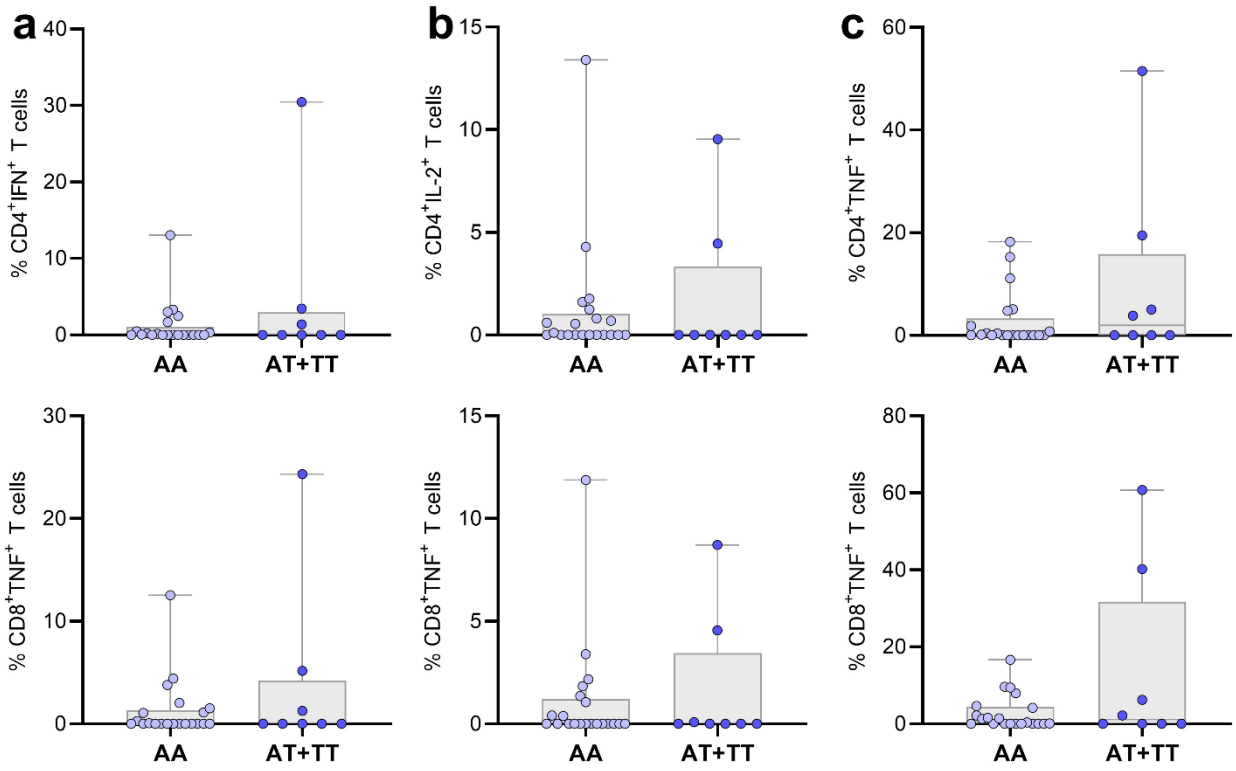
Model	Genotype	Control n (%)	Case n (%)	OR	Lower CI	Upper CI	p-value	AIC
ACE2 rs2074192								
Codominant	C/C	10 (38.5)	5 (25)	1.0				
	C/T	12 (46.2)	12 (60)	2.00	0.52	7.63	0.589	67.9
	T/T	4 (15.4)	3 (15)	1.50	0.24	9.46		
Dominant	C/C	10 (38.5)	5 (25)	1.0			0.3746	66.2
	C/T-T/T	16 (61.5)	15 (75)	1.79	0.49	6.55		
Recessive	C/C-C/T	22 (84.6)	17 (85)	1.0			0.971	67.0
	T/T	4 (15.4)	3 (15)	0.97	0.19	4.93		
Overdominant	C/C-T/T	14 (53.8)	8 (40)	1.0			0.350	66.1
	C/T	4 (46.2)	12 (60)	1.75	0.54	5.70		
CXCL8 rs4073								
Codominant	A/A	10 (38.5)	6 (30)	1.0				
	A/T	10 (38.5)	11 (55)	1.83	0.49	6.90	0.523	67.7
	T/T	6 (23.1)	3 (15)	0.83	0.15	4.64		
Dominant	A/A	10 (38.5)	6 (30)	1.0				
	A/T-T/T	16 (61.5)	14 (70)	1.46	0.42	5.04	0.589	66.6
Recessive	A/A-A/T	20 (76.9)	17 (85)	1.0			0.489	66.5
	T/T	6 (23.1)	3 (15)	0.59	0.13	2.71		
Overdominant	A/A-T/T	16 (61.5)	9 (45)	1.0			0.263	65.7
	A/T	10 (38.5)	11 (55)	1.96	0.60	6.39		
MICB rs3132468								
Codominant	T/T	18 (69.2)	14 (70)	1.0				
	C/T	6 (23.1)	4 (20)	0.86	0.20	3.64	0.942	68.9
	C/C	2 (7.7)	2 (10)	1.29	0.24	10.30		
Dominant	T/T	18 (69.2)	14 (70)	1.0			0.955	67.0
	T/C-C/C	8 (30.8)	6 (30)	0.96	0.27	3.43		
Recessive	T/T-C/T	24 (92.3)	18 (90)	1.0			0.783	66.9
	C/C	2 (7.7)	2 (10)	1.33	0.17	10.39		
Overdominant	T/T-C/C	20 (76.9)	16 (80)	1.0			0.801	66.9
	C/T	6 (23.1)	4 (20)	0.83	0.20	3.47		
MICB rs3131639								
Codominant	G/G	19 (73.1)	15 (75)	1.0				
	A/G	5 (19.2)	4 (20)	1.01	0.23	4.45	0.933	68.8

	A/A	2 (7.7)	1 (5)	0.63	0.05	7.67		
Dominant	G/G	19 (38.5)	15 (75)	1.0			0.882	67.0
	A/G-A/A	7 (61.5)	5 (25)	0.90	0.24	3.43		
Recessive	G/G-A/G	24 (92.3)	19 (95)	1.0			0.710	66.8
	A/A	2 (7.7)	1 (5)	0.63	0.05	7.50		
Overdominant	G/G-T/T	21 (80.8)	16 (80)	1.0			0.948	67.0
	A/G	5(19.2)	4 (20)	1.05	0.24	4.55		
CXCL10 rs4508917								
Codominant	A/A	10 (38.5)	5 (35)	1.0				
	A/G	12 (46.2)	11 (55)	1.31	0.37	4.64	0.790	68.5
	G/G	4 (15.4)	2 (10)	0.71	0.10	5.04		
Dominant	A/A	10 (38.5)	7 (35)	1.0			0.809	66.9
	A/G-G/G	16 (61.5)	13 (65)	1.16	0.35	3.90		
Recessive	A/A-A/G	22 (84.6)	18 (90)	1.0			0.586	66.7
	G/G	4 (15.4)	2 (10)	0.61	0.10	3.73		
Overdominant	A/A-G/G	14 (53.8)	9 (45)	1.0			0.551	66.6
	A/G	4 (46.2)	11 (55)	1.43	0.44	4.60		

n, number of individuals; CI, confidence interval; AIC, Aikake information criterion. Case group: all individuals of the Recurrent group. Control group: individuals from Single COVID-19 and Control groups. The association was analyzed through a univariate logistic regression analysis using "SNPassoc" package in R Studio.



Supplementary Figure S1. Evaluation of T-cell responses by SNP genotype (a–c). PBMCs were stimulated for 18 hours and analyzed by flow cytometry for IFN-γ, IL-2, and TNF-α production. Comparisons are shown by rs179008 genotype (AA vs. AT+TT) within each study group (Control, Single, and Recurrent COVID-19). Each symbol represents an individual patient; bars denote the minimum, maximum, and median values. Statistical significance was assessed using the Mann–Whitney test.



Supplementary Figure S2. Effect of vaccination in the response of T-cell accordingly SNP genotype **(a–c)** PBMCs were analyzed by flow cytometry after 18 hours of stimulation. T cells were examined based on the production of the cytokines IFN-γ, IL-2, and TNF-α.
Comparisons were made according to the rs179008 genotype, including patients with a history of COVID-19 regardless of the number of episodes. Each dot represents a patient, while the bars indicate the minimum, maximum, and median values. Statistical comparisons were performed using the Mann-Whitney test.