

Supplementary Table 1: Fluorochrome-labelled antibodies used for flowcytometric analysis

	Antibodies	Clones
Surface staining panel	Brilliant Violet 421 TM anti-human CD4	OKT4
	Brilliant Violet 510 TM anti-human CD14	63D3
	Brilliant Violet 605 TM anti-human CD127	A019D5
	Brilliant Violet 711 TM anti-human CD28	CD28.2
	FITC anti-human CD197 (CCR7)	G043H7
	PerCP/Cyanine5.5 anti-human CD8	SK1
	PE anti-human CD25	BC96
	PE/Cyanine7 anti-human CD196 (CCR6)	G034E3
	APC anti-human CD183 (CXCR3)	G025H
	Alexa Fluor® 700 anti-human CD45RA	HI100
	APC/Cyanine7 anti-human CD185 (CXCR5)	J252D4
	Intracellular staining panel	Brilliant Violet 421 TM anti-human IL-17A
Brilliant Violet 510 TM anti-human CD14		63D3
Brilliant Violet 605 TM anti-human TNF- α		MAb11
Brilliant Violet 711 TM anti-human IL-2		MQ1-17H12
FITC anti-human CD4		SK3
PerCP/Cyanine5.5 anti-human IL-4		MP4-25D2
PE anti-human IL-21		3A3-N2
PE/Cyanine7 anti-human IFN- γ		B27
APC anti-human CD154		24-31
Alexa Fluor® 700 anti-human CD45RA		HI100
APC/Cyanine7 anti-human CD185 (CXCR5)		J252D4

All antibodies were purchased from BioLegend

Supplementary Table 2: Background variables associated with antigen-specific CD4+ T cells (%CD154+)

(n=431)	Univariate analysis		Multivariate analysis		
	ρ score	p values	β	t values	p values
Clinical variables					
Age	0.1023	0.0337	0.05	0.95	0.3433
Medication					
TNF- α inhibitors use		0.0171	0.05	0.96	0.3391
user (n=86)	(1.07)				
non-user (n=345)	(1.24)				
Th2-type (%)	0.1292	0.0072	0.12	2.33	0.0204
Th17-type (%)	-0.0820	0.0891	-0.02	-0.31	0.7585
Tfh-type (%)	-0.0840	0.0814	-0.01	-0.18	0.8543
Treg-type (%)	0.1221	0.0112	0.09	1.82	0.0698

Supplementary Table 3: Background variables associated with antigen-specific TNF- α production (%CD154+ TNF- α +) (n=431)

(n=431)	Univariate analysis		Multivariate analysis		
	ρ score	p values	β	t values	p values
Clinical variables					
None					
Medication					
MTX user		0.0763	0.07	1.46	0.1438
user (n=329)	(9.13)				
non-user (n=102)	(10.43)				
Immunological variables					
Th1-type (%)	0.1194	0.0131	0.05	0.73	0.4647
Th2-type (%)	-0.1073	0.0259	-0.01	-1.55	0.1230
Tfh-type (%)	-0.0868	0.0717	-0.09	-1.70	0.0893
Treg-type (%)	0.1116	0.0205	0.06	1.13	0.2588

Supplementary Table 4: Background variables associated with antigen-specific IL-2 production (%CD154+ IL-2+)

(n=431)	Univariate analysis		Multivariate analysis		
	ρ score	p values	β	t values	p values
Clinical variables					
Age	-0.2646	<0.0001	-0.22	-4.38	<0.0001
Disease duration	-0.0939	0.0515	0.05	0.91	0.3638
Stage (I/II/III/IV)	6.83/7.07 5.34/5.75	0.0296	-0.09	-1.51	0.1324
History of surgery		0.0249	0.02	0.47	0.6418
Yes (n=71)	(5.29)				
No (n=360)	(6.60)				
ESR	-0.1087	0.0240	-0.04	-0.83	0.4074
Medication					
JAK inhibitors use		0.0064	0.09	1.86	0.0642
user (n=13)	(3.30)				
non-user (n=418)	(6.48)				
Immunological variables					
Th1-type (%)	0.1877	<0.0001	0.15	2.57	0.0105
Th2-type (%)	-0.2061	<0.0001	-0.04	-0.73	0.4640
Treg-type (%)	0.1800	0.0002	0.09	1.87	0.0617

Supplementary Table 5: Background variables associated with antigen-specific IFN- γ production (%CD154+ IFN- γ +) (n=431)

(n=431)	Univariate analysis		Multivariate analysis		
	ρ score	p values	β	t values	p values
Clinical variables					
Age	-0.2835	<0.0001	-0.21	-4.30	<0.0001
ESR	-0.0921	0.0560	-0.02	-0.50	0.6191
Medication					
IL-6 inhibitors use		0.0989	-0.07	-1.44	0.1510
user (n=29)	(3.83)				
non-user (n=402)	(2.55)				
CTLA4-Ig use		0.0558	0.04	0.90	0.3678
user (n=5)	(0.96)				
non-user (n=426)	(2.87)				
Immunological variables					
RF positivity		0.0278	-0.09	-1.96	0.0503
positive (n=331)	(2.80)				
negative (n=100)	(2.07)				
Th1-type (%)	0.1860	0.0001	0.16	2.70	0.0072
Th2-type (%)	-0.2232	<0.0001	-0.02	-0.33	0.7432
Treg-type (%)	0.1254	0.0092	0.04	0.75	0.4519

Supplementary Table 6: Background variables associated with antigen-specific IL-4 production (%CD154+ IL-4+)

(n=431)	Univariate analysis		Multivariate analysis		
	ρ score	p values	β	t values	p values
Clinical variables					
Sex		0.0409	0.03	0.51	0.6133
Male (n=32)	(1.11)				
Female (n=399)	(1.07)				
CRP	0.1133	0.0186	0.09	1.69	0.0927
Medication					
PSL dose	-0.1094	0.0231	-0.13	-2.38	0.0177
PSL use		0.0212	0.14	2.61	0.0095
user (n=184)	(0.84)				
non-user (n=247)	(1.24)				
IL-6 inhibitors use		0.0034	0.11	1.90	0.0581
user (n=29)	(0.39)				
non-user (n=402)	(1.12)				
Immunological variables					
RF level	-0.1438	0.0099	-0.09	-1.66	0.0986

Supplementary Table 7: Background variables associated with antigen-specific IL-17A production (%CD154+ IL-17A+)

(n=431)	Univariate analysis		Multivariate analysis		
	ρ score	p values	β	t values	p values
Clinical variables					
CRP	0.1021	0.0341	0.03	0.61	0.5423
Medication					
IL-6 inhibitors use		0.0086	0.07	1.51	0.1316
user (n=29)	(1.00)				
non-user (n=402)	(1.53)				
Immunological variables					
Th2-type (%)	-0.1551	0.0012	-0.08	-1.69	0.0921
Th17-type (%)	0.1051	0.0291	0.07	1.33	0.1833

Supplementary Table 8: Background variables associated with antigen-specific IL-21 production (%CD154+ IL-21+)

(n=431)	Univariate analysis		Multivariate analysis		
	ρ score	p values	β	t values	p values
Clinical variables					
Disease duration	0.1322	0.0060	0.10	1.98	0.0486
History of surgery		0.0790	-0.03	-0.68	0.4977
Yes (n=71)	(0.54)				
No (n=360)	(0.38)				
Medication					
None					
Immunological variables					
Tfh-type (%)	0.0832	0.0843	0.02	0.45	0.6563

Supplementary Table 9: Statistics of antigen-specific cytokine production by CD4+ T cells in the three clusters of RA patients.

	Th1-dominant	All high	All low	p (ANOVA)
%CD154+ TNF- α +	14.73 \pm 6.82*	9.57 \pm 5.75*	5.67 \pm 5.75*	<0.05
%CD154+ IL-2+	9.87 \pm 5.81*	7.42 \pm 5.41*	3.62 \pm 2.54*	<0.05
%CD154+ IFN- γ +	3.85 \pm 3.65	4.16 \pm 2.95	1.32 \pm 1.04**	<0.05
%CD154+ IL-4+	0.77 \pm 1.67	3.04 \pm 2.84**	0.68 \pm 0.89	<0.05
%CD154+ IL-17A+	1.07 \pm 1.02	4.00 \pm 1.89**	1.03 \pm 1.03	<0.05
%CD154+ IL-21+	0.10 \pm 0.26	1.35 \pm 1.91**	0.33 \pm 0.62	<0.05

Tukey's HSD analysis

*Significant difference (p<0.05) was detected among all groups

**Significant difference (p<0.05) was detected with the rest