

Supplementary Table S1. Serum cytokines lower limits of quantitation.

Analyte	Lower LoQ (pg/mL)
BAFF	3.38
CXCL13	11
IL-17 A/F	6.10
IL-18	12
IL-21	9.69
IL-22	20
PD-L2	49
TNF-R2	1.17

Lower limits of quantitation (LoQ) are showed in pg/mL.

Supplementary Table S2. Antibody combinations.

	FITC	PE	ECD	PC5.5	PC7	APC	APC-AF750	PaB	KrO
Samples analyzed from April 2014 to December 2015*									
Tube 1	CD45RA	CD197 (CCR7)		CD38	CD8	CD4	CD3	HLA-DR	CD45
Tube 2		CD25			CD127	CD4	CD3		
Tube 3		CD183 (CXCR3)			CD196 (CCR6)	CD4	CD3		
Tube 4	IgD	IgM		CD19	CD27	CD38	CD20	CD5	CD45
Tube 5	CD14	CD56		CD33	CD16		CD3		CD45
Samples analyzed from January 2016 to September 2017*									
Tube 1	CD45RA	CD197 (CCR7)	CD3	CD38	CD8	CD4		HLA-DR	CD45
Tube 2		CD25	CD3		CD127	CD4			
Tube 3		CD183 (CXCR3)	CD3		CD196 (CCR6)	CD4			
Tube 4	IgD	IgM	CD20		CD27	CD38	CD19	CD5	CD45
Tube 5	CD14	CD56	CD3	CD33	CD16				CD45

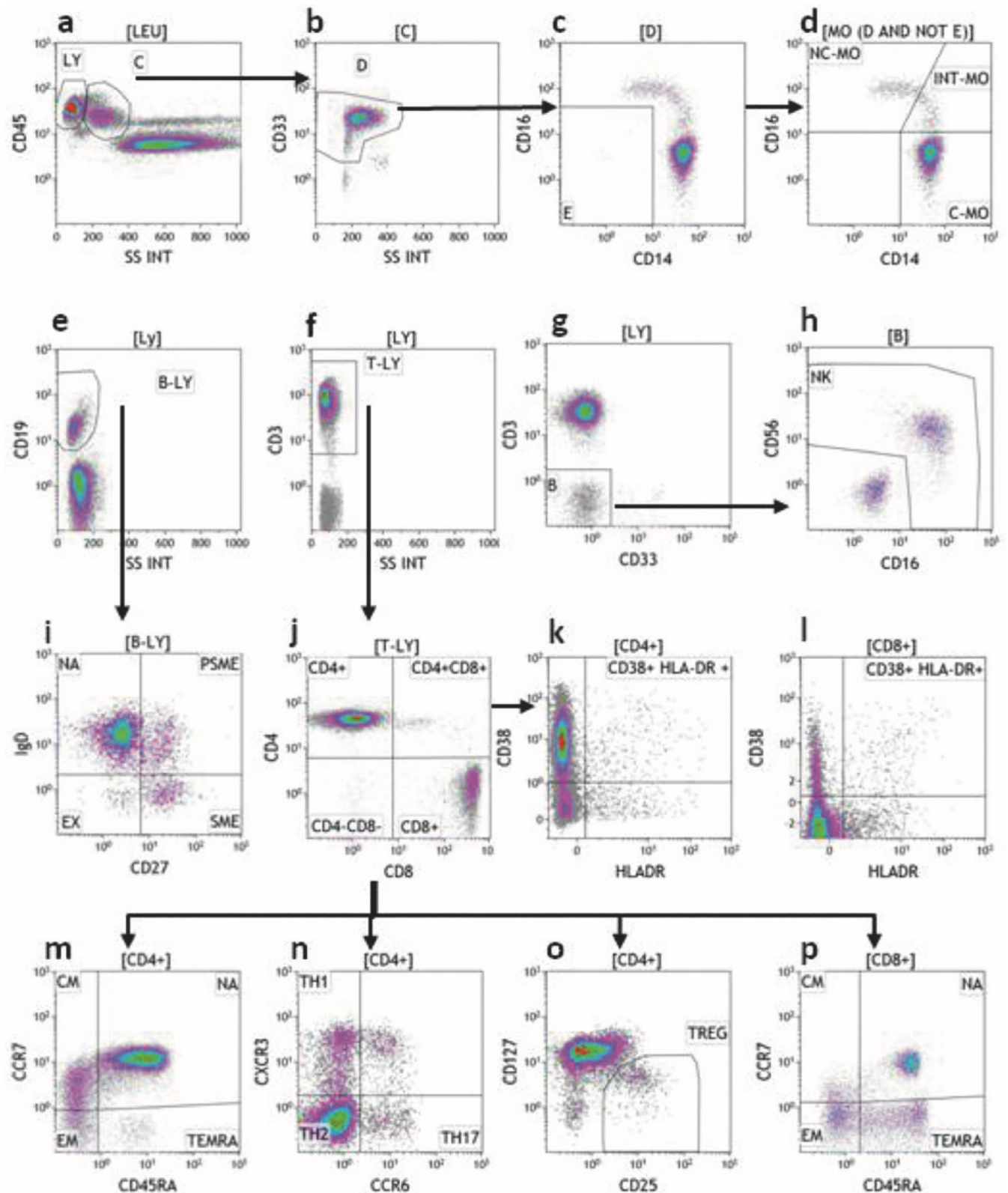
FITC: fluorescein isothiocyanate; PE: phycoerythrin; ECD: Texas red-Phycoerythrin; PC5.5: Phycoerythrin-Cyanin 5.5; PC7: Phycoerythrin-Cyanin 7; APC: Allophycocyanin; APC-AF750: APC-Alexa Fluor 750; PaB: Pacific Blue; KrO: Krome Orange

*Due to commercial reasons, there were minor differences in the panel used before and after January 2016.

Supplementary Table S3. Antibodies, clones and sources.

Antibody	Clone	Label	Source
CD45RA	2H4LDH11LDB9	FITC	Beckman Coulter
IgD	IA6-2	FITC	Beckman Coulter
CD14	RMO52	FITC	Beckman Coulter
CD197 (CCR7)	G043H7	PE	Beckman Coulter
CD25	B1.49.9	PE	Beckman Coulter
CD183 (CXCR3)	1C6/CXCR3	PE	Becton Dickinson
IgM	SA-DA4	PE	Beckman Coulter
CD56	N901 (NKH-1)	PE	Beckman Coulter
CD3	UCHT1	ECD	Beckman Coulter
CD20	B9E9	ECD	Beckman Coulter
CD38	LS198-4-3	PC5.5	Beckman Coulter
CD19	J3-119	PC5.5	Beckman Coulter
CD33	D3HL60.251	PC5.5	Beckman Coulter
CD8	B9.11	PC7	Beckman Coulter
CD127 (IL-7R α)	R34.34	PC7	Beckman Coulter
CD196 (CCR6)	11A9	PC7	Becton Dickinson
CD27	JA4CD27	PC7	Beckman Coulter
CD16	3G8	PC7	Beckman Coulter
CD4	13B8.2	APC	Beckman Coulter
CD38	LS198-4-3	APC	Beckman Coulter
CD3	UCHT1	APC-AF750	Beckman Coulter
CD20	B9E9	APC-AF750	Beckman Coulter
CD19	J3-119	APC-AF750	Beckman Coulter
HLA-DR	Immu-357	PaB	Beckman Coulter
CD5	BL1a	PaB	Beckman Coulter
CD45	J.33	KrO	Beckman Coulter

FITC: Fluorescein Isothiocyanate; PE: Phycoerythrin; ECD: Texas red-Phycoerythrin; PC5.5: Phycoerythrin-Cyanin 5.5; PC7: Phycoerythrin-Cyanin 7; APC: Allophycocyanin; APC-AF750: APC-Alexa Fluor 750; PB: Pacific Blue; KrO: Krome Orange.



Supplementary Fig. S1. Representative gating strategy used in the identification of lymphocyte populations.

Lymphocytes (LY) and monocytes are selected based on their side scatter (SS) properties and CD45 expression (a); Monocyte gate (MO) is refined with CD33, CD14 and CD16 expression pattern (b,c); classical monocytes (C-MO), non-classical monocytes (NC-MO), intermediate monocytes (INT-MO) (d); B-lymphocytes (CD19+) (B-LY) (e) are plotted on a IgD vs. CD27 plot for subpopulations analysis (i); T CD4+ and T CD8+ lymphocytes are selected in a CD4 vs. CD8 plot gated previously on CD3+ lymphocytes (f, j); NK cells are selected as lymphocytes CD3-, CD33-, CD56+ AND/OR CD16+ (g,h); We defined T cell activation as the co-expression of HLA-DR and CD38 on T-CD4 and T-CD8 lymphocytes (k,l); T CD4 and CD8 subsets are analyzed on m, n, o and p plots; NA (Naïve); CM (central memory); EM (effector memory); TEMRA (effector memory re-expressing CD45RA); TREG (T-regulatory); SME (switched memory); NSME (non-switched memory); EX (exhausted).

Supplementary Table S4. Serum cytokines concentrations in patients with Sjögren's syndrome, patients with *Sicca* syndrome and healthy volunteers.

	Sjögren's syndrome <i>N</i> = 66	<i>Sicca</i> syndrome <i>N</i> = 25	Healthy volunteers <i>N</i> = 23	<i>Global P value</i>	<i>Sicca vs. HV P value</i>
BAFF	1844.7 (1020.0)	1485.6 (691.1)	1641.8 (450.6)	0.0026	0.1494
CXCL13	594.8 (678.5)	243.1 (156.7)	459.8 (494.7)	0.0001	0.0804
IL-17 A/F	14.30 (35.13)	8.58 (11.45)	3.81 (4.11)	0.5995	0.8111
IL-18	10.94 (15.73)	15.76 (17.54)	10.53 (11.37)	0.3237	0.9941
IL-21	231.89 (853.66)	31.01 (82.02)	73.54 (234.16)	0.0049	0.9973
IL-22	86.52 (75.13)	66.40 (42.09)	63.82 (34.67)	0.6110	0.9996
PD-L2	2113.90 (1280.00)	2588.92 (1486.68)	3120.34 (1456.94)	0.0133	0.5381
TNF-R2	257.20 (110.32)	262.19 (84.14)	291.26 (132.67)	0.5217	0.8723

Serum cytokines concentrations are expressed as mean (standard deviation) and values are showed in in pg/mL.

Supplementary Table S5. Poisson regression of ESSDAI and serum cytokines.

	Coefficient	OR	<i>p</i> -value
BAFF	.00019633	1.0001964	0.0017
CXCL13	.00016095	1.0001610	0.0641
IL-17 A/F	.00172916	1.0017307	0.3466
IL-18	.00966010	1.0097069	0.0167
IL-21	.00010085	1.0001009	0.1300
IL-22	.00191137	1.0019132	0.0397
PD-L2	.00005216	1.0000522	0.3703
TNF-R2	.00070467	1.0007049	0.2921