

Supplementary Table 1: Immunophenotyping panels. Each of the flow cytometry samples were split into three tubes. Information about antibodies used and their tube distribution is listed below.

Tube	Antibody	Fluorochrome	Clone	Art.nr	Producer
T regulatory cells	CD3	FITC	SK7	345763	BD Biosciences
	CD4	PerCP-Cy5.5	SK3	332772	BD Biosciences
	CD25	PE	2A3	341011	BD Biosciences
	CD45RO	APC-H7	UCHL1	561137	BD Biosciences
	CD127	BV421	HIL-7R-M21	562437	BD Biosciences
	HLA-DR	HZV500	G46-6	561225	BD Biosciences
	HLA-G	APC	MEM-G/9	A15708	Life Technologies
	CCR4 (CD194)	PE-Cy7	L291H4	359410	NordicBioSite
Other T cells	CD3	FITC	SK7	345763	BD Biosciences
	CD4	PerCP-Cy5.5	SK3	332772	BD Biosciences
	CXCR3 (CD183)	PE	G025H7	353705	NordicBioSite
	CD45RA	APC-H7	HI100	560674	BD Biosciences
	CCR7	V450	150503	560864	BD Biosciences
	CCR6	BV510	11A9	563241	BD Biosciences
	CXCR5	APC	J252D4	356907	NodicBioSite
	CCR4 (CD194)	PE-Cy7	L291H4	359410	NordicBioSite
B subpopulations	IgD	FITC	Polyclonal	F0189	Agilent/Dako
	CD5	PerCP-Cy5.5	L17F12	341109	BD Biosciences
	CD24	PE	ML5	560991	BD Pharmigen
	CD38	APC-H7	HB7	656646	BD Biosciences
	CD20	eFluor450	2H7	48-0209-42	AH Diagnostics
	CD27	BV510	O323	302835	NodicBioSite
	IgM	APC	G20-127	551062	BD Pharmigen
	CD19	PE-Cy7	J3-119	IM3628	Nerliens Meszanky

Supplementary Table 2: Differentially expressed genes. All differentially expressed genes, both in the original analysis and post adjustment, with their respective cluster, p-value and log fold change. Found in separate Excel sheet.

Supplementary Table 3a: Summary of differentially expressed genes. Number of up- and downregulated differentiated expressed genes before and after cell adjustment*.

Contrast	Upregulated		Downregulated	
	Original	adjusted	Original	adjusted
SPRAvsHealthy	2	4	5	13
SNRAvsHealthy	0	0	1	1
SLEvsHealthy	760	285	1938	234
SPRAvsSNRA	0	0	3	4
SPRAvsSLE	940	37	390	140
SNRAvsSLE	273	28	361	118
Time1_SPRAvsHealth	0	0	0	1
Time3_SPRAvsHealth	0	3	0	5
Time1_SLEvsHealthy	164	46	96	68
Time2_SLEvsHealthy	42	20	6	3
Time3_SLEvsHealthy	162	2	84	1
Time4_SLEvsHealthy	2115	14	3987	12
Time5_SLEvsHealthy	662	17	2543	4
Time0_SPRAvsSNRA	139	189	55	30
Time1_SPRAvsSLE	27	2	66	6
Time2_SPRAvsSLE	8	0	62	0
Time3_SPRAvsSLE	13	0	163	0
Time4_SPRAvsSLE	2263	15	586	13
Time5_SPRAvsSLE	689	3	152	29
Time6_SPRAvsSLE	7	0	2	1
Time0_SNRAvsSLE	0	0	0	1
Time1_SNRAvsSLE	0	0	40	0
Time2_SNRAvsSLE	11	0	31	0
Time3_SNRAvsSLE	0	0	0	4
Time4_SNRAvsSLE	5	1	0	4

* The up- and downregulated genes have a p value < 0.05 and a fold change (\log_2) above or below zero respectively. GroupTimes without up- or downregulated genes are removed for readability.

Supplementary Table 3b: Expanded summary of differentially expressed genes. Number of up- and downregulated differentiated expressed genes. Both in the original analysis and per cell type adjusted for.

Contrast	Upregulated						Downregulated					
	Original	SC-M2	SC-T2	SC-T4	SC-B1	SC-M1	Original	SC-M2	SC-T2	SC-T4	SC-B1	SC-M1
SPRAvsHealthy	2	2	2	2	2	4	5	4	13	13	12	13
SNRAvsHealthy	0	0	0	0	0	0	1	1	1	1	1	1
SLEvsHealthy	760	267	240	220	360	285	1938	798	331	194	330	234
SPRAvsSNRA	0	0	0	0	0	0	3	3	4	4	4	4
SPRAvsSLE	940	79	29	17	44	37	390	50	73	77	189	140
SNRAvsSLE	273	23	33	25	51	28	361	66	105	120	185	118
Time1_SPRAvsHealthy	0	0	0	0	0	0	0	0	0	0	1	1
Time3_SPRAvsHealthy	0	2	0	0	1	3	0	0	0	0	1	5
Time1_SLEvsHealthy	164	54	82	80	156	46	96	21	73	63	145	68
Time2_SLEvsHealthy	42	4	5	5	18	20	6	1	1	1	3	3
Time3_SLEvsHealthy	162	2	2	2	3	2	84	1	1	1	2	1
Time4_SLEvsHealthy	2115	1476	7	0	2	14	3987	2885	28	5	8	12
Time5_SLEvsHealthy	662	170	24	13	13	17	2543	900	19	3	3	4
Time0_SPRAvsSNRA	139	195	396	380	82	189	55	72	175	128	12	30
Time1_SPRAvsSLE	27	1	4	2	4	2	66	8	23	17	27	6
Time2_SPRAvsSLE	8	0	0	0	0	0	62	0	0	0	3	0
Time3_SPRAvsSLE	13	0	0	0	5	0	163	0	4	4	15	0
Time4_SPRAvsSLE	2263	121	2	1	5	15	586	20	2	2	2	13
Time5_SPRAvsSLE	689	51	0	0	2	3	152	10	3	2	15	29
Time6_SPRAvsSLE	7	0	0	0	0	0	2	0	0	0	0	1
Time0_SNRAvsSLE	0	0	0	0	0	0	0	0	0	0	1	1
Time1_SNRAvsSLE	0	0	0	0	0	0	40	0	0	0	0	0
Time2_SNRAvsSLE	11	0	0	0	0	0	31	0	0	0	0	0
Time3_SNRAvsSLE	0	0	0	0	0	0	0	0	0	0	0	4
Time4_SNRAvsSLE	5	0	1	0	0	1	0	0	0	2	2	4
Time5_SNRAvsSLE	15	1	2	0	0	0	22	0	0	0	0	0

Supplementary Table 4: Gene ontology enrichment. Results both from the original and adjusted analysis. Found in separate Excel sheet.

Supplementary Table 5a: Genes in the 28 gene Interferon signature (IFN 28). List of genes used to calculate the IFN28 score and their corresponding clusters in our material. This score was calculated from 27 genes as one of the genes in the original list was not found to be significantly expressed in our material (Benjamini-Hochberg adjusted p-value > 0.05).

Gene	ENSG	Cluster	Adjusted Cluster
CXCL10	ENSG00000169245	G11	NA
IFIT2	ENSG00000119922	G11	AdjG2
LAMP3	ENSG00000078081	G11	NA
OASL	ENSG00000135114	G11	AdjG2
IFIT1	ENSG00000185745	G11	AdjG2
SIGLEC1	ENSG00000088827	G11	AdjG2
IFIT3	ENSG00000119917	G11	AdjG2
GBP1	ENSG00000117228	G11	NA
HERC5	ENSG00000138646	G11	AdjG2
IFI6	ENSG00000126709	G11	AdjG2
MX1	ENSG00000157601	G11	AdjG2
IFIT5	ENSG00000152778	G11	AdjG2
SPATS2L	ENSG00000196141	G13	AdjG2
RSAD2	ENSG00000134321	G11	AdjG2
EPST11	ENSG00000133106	G11	AdjG2
OAS1	ENSG00000089127	G11	AdjG2
IFI27	ENSG00000165949	G13	AdjG2
OAS3	ENSG00000111331	G11	AdjG2
RTP4	ENSG00000136514	G11	AdjG2
HERC6	ENSG00000138642	G11	AdjG2
OAS2	ENSG00000111335	G11	AdjG2
ISG15	ENSG00000187608	G11	AdjG2
IFI44L	ENSG00000137959	G11	AdjG2
IFI44	ENSG00000137965	G11	AdjG2
DDX60	ENSG00000137628	G11	AdjG2
USP18	ENSG00000184979	G11	AdjG2
LY6E	ENSG00000160932	G11	AdjG2

Supplementary Table 5b: Genes used in the M1.2 Module interferon score. List of genes used to calculate the Interferon score of submodule M1.2 and their corresponding clusters in our material.

Module	Gene	ENSG	Cluster	Adjusted Cluster
M1.2	LY6E	ENSG00000160932	G11	AdjG2
M1.2	IFIT1	ENSG00000185745	G11	AdjG2
M1.2	OAS1	ENSG00000089127	G11	AdjG2
M1.2	IFIT1	ENSG00000185745	G11	AdjG2
M1.2	IFIT3	ENSG00000119917	G11	AdjG2
M1.2	OAS3	ENSG00000111331	G11	AdjG2
M1.2	IFIT3	ENSG00000119917	G11	AdjG2
M1.2	OAS1	ENSG00000089127	G11	AdjG2
M1.2	OASL	ENSG00000135114	G11	AdjG2
M1.2	ISG15	ENSG00000187608	G11	AdjG2
M1.2	HERC5	ENSG00000138646	G11	AdjG2
M1.2	OAS1	ENSG00000089127	G11	AdjG2
M1.2	MX1	ENSG00000157601	G11	AdjG2
M1.2	BATF2	ENSG00000168062	G11	NA
M1.2	LAMP3	ENSG00000078081	G11	NA
M1.2	IFI44L	ENSG00000137959	G11	AdjG2
M1.2	XAF1	ENSG00000132530	G11	AdjG2
M1.2	OASL	ENSG00000135114	G11	AdjG2
M1.2	IFI44	ENSG00000137965	G11	AdjG2
M1.2	OAS2	ENSG00000111335	G11	AdjG2
M1.2	TRIM6	ENSG00000121236	G13	AdjG2
M1.2	HES4	ENSG00000188290	G11	AdjG2
M1.2	OTOF	ENSG00000115155	G11	AdjG2
M1.2	IFITM3	ENSG00000142089	G13	NA
M1.2	IFIT3	ENSG00000119917	G11	AdjG2
M1.2	CXCL10	ENSG00000169245	G11	NA
M1.2	EPST1	ENSG00000133106	G11	AdjG2
M1.2	SERPING1	ENSG00000149131	G11	AdjG2
M1.2	OAS2	ENSG00000111335	G11	AdjG2
M1.2	RSAD2	ENSG00000134321	G11	AdjG2
M1.2	RTP4	ENSG00000136514	G11	AdjG2

Supplementary Table 5c: Genes used in the M3.4 Module interferon score. List of genes used to calculate the Interferon score of submodule M3.4 and their corresponding clusters in our material.

Module	Gene	ENSG	Cluster	Adjusted Cluster
M3.4	IFIH1	ENSG00000115267	G11	AdjG2
M3.4	IRF7	ENSG00000185507	G11	AdjG2
M3.4	PARP14	ENSG00000173193	G11	NA
M3.4	IFIT2	ENSG00000119922	G11	AdjG2
M3.4	IFI35	ENSG00000068079	G11	NA
M3.4	SAMD9L	ENSG00000177409	G11	AdjG2
M3.4	STAT1	ENSG00000115415	G11	NA
M3.4	OAS2	ENSG00000111335	G11	AdjG2
M3.4	IFIT5	ENSG00000152778	G11	AdjG2
M3.4	ATF3	ENSG00000162772	G11	NA
M3.4	HERC6	ENSG00000138642	G11	AdjG2
M3.4	IFITM1	ENSG00000185885	G11	NA
M3.4	EIF2AK2	ENSG00000055332	G13	AdjG2
M3.4	AIM2	ENSG00000163568	G13	NA
M3.4	MOV10	ENSG00000155363	G11	NA
M3.4	ZBP1	ENSG00000124256	G11	AdjG2
M3.4	WARS	ENSG00000140105	G11	NA
M3.4	LAP3	ENSG00000002549	G11	NA
M3.4	TNFSF10	ENSG00000121858	G13	NA
M3.4	GBP1	ENSG00000117228	G11	NA
M3.4	STAT1	ENSG00000115415	G11	NA
M3.4	FBXO6	ENSG00000116663	G13	NA
M3.4	PARP10	ENSG00000178685	G11	NA
M3.4	OAS2	ENSG00000111335	G11	AdjG2
M3.4	TRIM22	ENSG00000132274	G11	AdjG2
M3.4	PARP10	ENSG00000178685	G11	NA
M3.4	ZNF684	ENSG00000117010	G11	NA
M3.4	GALM	ENSG00000143891	G11	NA
M3.4	DHX58	ENSG00000108771	G11	AdjG2
M3.4	CEACAM1	ENSG00000079385	G13	NA
M3.4	UBE2L6	ENSG00000156587	G11	NA
M3.4	PML	ENSG00000140464	G11	NA
M3.4	CEACAM1	ENSG00000079385	G13	NA
M3.4	APOL6	ENSG00000221963	G11	NA
M3.4	LGALS3BP	ENSG00000108679	G11	AdjG2
M3.4	SCO2	ENSG00000284194	G11	NA
M3.4	DDX58	ENSG00000107201	G11	AdjG2
M3.4	UBE2L6	ENSG00000156587	G11	NA
M3.4	PML	ENSG00000140464	G11	NA
M3.4	TNFAIP6	ENSG00000123610	G13	NA
M3.4	MT2A	ENSG00000125148	G11	NA
M3.4	GBP6	ENSG00000183347	G11	NA
M3.4	STAT2	ENSG00000170581	G11	NA
M3.4	STAT1	ENSG00000115415	G11	NA
M3.4	PARP12	ENSG00000059378	G11	AdjG2
M3.4	PLSCR1	ENSG00000188313	G13	AdjG2
M3.4	PARP9	ENSG00000138496	G13	AdjG2
M3.4	GBP4	ENSG00000162654	G11	NA

Supplementary Table 5d: Genes used in the M5.12 Module interferon score. List of genes used to calculate the Interferon score of submodule M5.12 and their corresponding clusters in our material.

Module	Gene	ENSG	Cluster	Adjusted Cluster
M5.12	RBCK1	ENSG00000125826	G11	NA
M5.12	TRAFD1	ENSG00000135148	G11	AdjG2
M5.12	TRIM21	ENSG00000132109	G11	AdjG2
M5.12	CHMP5	ENSG00000086065	G13	NA
M5.12	TAP2	ENSG00000204267	G11	NA
M5.12	SP110	ENSG00000135899	G11	NA
M5.12	GADD45B	ENSG00000099860	G13	NA
M5.12	IFI16	ENSG00000163565	G11	NA
M5.12	TAP1	ENSG00000168394	G11	NA
M5.12	ZNF1	ENSG00000124201	G11	NA
M5.12	PHF11	ENSG00000136147	G11	AdjG2
M5.12	ACTA2	ENSG00000107796	G14	NA
M5.12	SP140	ENSG00000079263	G11	NA
M5.12	ABCA1	ENSG00000165029	G7	AdjG2
M5.12	ZC3HAV1	ENSG00000105939	G11	NA
M5.12	HSH2D	ENSG00000196684	G11	AdjG2
M5.12	GBP2	ENSG00000162645	G11	NA
M5.12	TRIM5	ENSG00000132256	G11	AdjG2
M5.12	RHBDF2	ENSG00000129667	G13	NA
M5.12	TMEM140	ENSG00000146859	G11	AdjG2
M5.12	ADAR	ENSG00000160710	G11	AdjG2
M5.12	BTN3A1	ENSG00000026950	G9	NA
M5.12	PARP10	ENSG00000178685	G11	NA
M5.12	LGALS9	ENSG00000168961	G11	AdjG2
M5.12	NBN	ENSG00000104320	G13	NA
M5.12	SAMD9	ENSG00000205413	G10	NA
M5.12	SRBD1	ENSG00000068784	G11	NA
M5.12	NCOA7	ENSG00000111912	G0	NA
M5.12	DRAP1	ENSG00000175550	G11	NA
M5.12	UNC93B1	ENSG00000110057	G11	AdjG2
M5.12	SP100	ENSG00000067066	G11	AdjG2
M5.12	NTNG2	ENSG00000196358	G13	AdjG2
M5.12	DHRS9	ENSG00000073737	G11	AdjG2
M5.12	TDRD7	ENSG00000196116	G11	NA
M5.12	TRIM5	ENSG00000132256	G11	AdjG2
M5.12	REC8	ENSG00000100918	G11	NA
M5.12	ISG20	ENSG00000172183	G11	NA
M5.12	DYNLT1	ENSG00000146425	G13	NA
M5.12	LHFPL2	ENSG00000145685	G11	AdjG2
M5.12	TRIM56	ENSG00000169871	G12	NA
M5.12	SP140	ENSG00000079263	G11	NA
M5.12	TRIM25	ENSG00000121060	G13	NA
M5.12	TRIM38	ENSG00000112343	G11	NA
M5.12	ETV7	ENSG00000010030	G11	NA
M5.12	PSMB9	ENSG00000240065	G11	NA
M5.12	BST2	ENSG00000130303	G11	AdjG2
M5.12	CASP1	ENSG00000137752	G13	NA
M5.12	NMI	ENSG00000123609	G13	NA

Supplementary Table 6: scRNA-seq clusters. An overview of the number of cells per cluster, both per timepoint and disease. Cell type and timepoint dominating each cluster is shown by odds ratio. Significant odds ratios are shown in bold.

Cluster	CellType	Number of cells				Odds ratio			
		RA		SLE		RAvsSLE		TP3 vs TP4	
		TP3	TP4	TP3	TP4	TP3	TP4	RA	SLE
SC-T1	Naive T-helper, high metabolic activity	2137	2862	77	209	5.35	4.10	0.12	-1.12
SC-T2	Naive T-helper	46	54	743	780	-4.37	-4.32	0.27	0.32
SC-T3	IFN induced T	159	224	866	973	-2.82	-2.61	0.00	0.21
SC-T4	Memory T-helper	604	1096	271	473	1.10	1.03	-0.42	-0.49
SC-T5	Memory T	153	265	205	303	-0.58	-0.51	-0.31	-0.23
SC-T6	MAIT	246	335	96	204	1.26	0.44	0.05	-0.76
SC-T7	Gamma/delta T	114	226	34	133	1.63	0.49	-0.50	-1.65
SC-T8	Memory T-cytotoxic	318	640	216	824	0.44	-0.73	-0.55	-1.73
SC-NK1	NK-cells	194	341	220	319	-0.33	-0.20	-0.33	-0.20
SC-NK2	CD16neg/CD56bright NK	37	43	44	64	-0.39	-0.87	0.28	-0.20
SC-M1	Classical monocytes	756	817	217	392	1.81	0.84	0.44	-0.54
SC-M2	IFN induced monocytes	60	25	1119	706	-4.71	-5.28	1.77	1.20
SC-M3	Non-classical monocytes	61	74	195	182	-1.86	-1.62	0.22	0.46
SC-B1	Memory B	326	423	31	42	0.14	0.20	0.13	0.19
SC-B2	Naive B	146	199	11	10	-1.12	-0.81	0.05	0.36
SC-DC1	Myeloid dendritic	23	43	271	304	-0.57	-0.26	-0.41	-0.10
SC-DC2	Plasmacytoid dendritic	10	5	279	280	-0.28	-1.29	1.50	0.48
SC-PC1	Plasma cells	6	13	17	88	-1.64	-3.07	-0.62	-2.04
ART	Artefact (RBC/GRAN)	85	45	66	30	-	-	-	-
Sum		5481	7730	4978	6316				
Total		24505							

Supplementary Table 7: Flow cytometry results for B-and T-cell subpopulations. T-helper cells and B- cells subpopulations are given as percentages of CD4+ T-cells and B-cells, respectively.

Flow cytometry tube	Cell type	RA		SLE	
		TP3	TP4	TP3	TP4
T-helper cells (Subpopulation of CD4+ T-cells)	Naive	55.0	56.1	67.5	53.7
	Th1	31.4	28.4	20.9	30.3
	Th2	2.31	0.73	0.70	0.59
	Th17	11.3	14.7	10.9	15.4
	T reg	6.4	6.2	7.4	8.2
	Central memory	34.8	33.6	28.0	36.6
	Effector memory RA	1.2	1.3	0.4	0.7
	Effector memory	9.3	10.1	5.8	10.8
Th1/Th2-ratio		14	39	30	51
B-cells subpopulations	Plasma cells	0.6	0.8	2.4	10.7
	Transitional	1.3	4.9	3.2	6.7
	Naive	77.9	72.6	69.8	65.8
	Unswitched memory	10.3	10.3	8.7	5.7
	Switched memory	9.9	11.4	15.9	11.0

Supplementary Table 8: Significant cell type estimation differences. Tukey's range test was used to find significant fluctuation differences over time and between groups. p-values were calculated from the averaged level estimations.

Cluster	Dominating cell type	p-value				significant in
		Group	Time	GroupTime	SPRA vs SNRA	
T- and NK-cells						
SC-T1	Naive T-helper, high cell turnover	0.02	0.00	0.08	0.65	Group and Time
SC-T2	Naive T-helper	0.00	0.00	0.55	0.08	Group and Time
SC-T3	IFN-induced T, T-reg	0.00	0.16	0.24	1.00	Group
SC-T4	Memory T-helper	0.00	0.00	0.20	0.84	Group and Time
SC-T5	Memory T (helper and cytotoxic)	0.12	0.00	0.44	0.59	Time
SC-T6	MAIT-cells	NA	NA	NA	NA	
SC-T7	Gamma/delta T-cells	0.00	0.00	0.09	0.04	Group, Time and SPRA vs SNRA
SC-T8	Memory T-cytotoxic	0.25	0.00	0.93	0.31	Time
SC-NK1	CD16 positive NK-cells	0.82	0.22	0.76	0.84	
SC-NK2	CD16neg/CD56bright NK-cells	0.20	0.20	0.49	1.00	
Myeloid cells						
SC-M1	Classical monocytes	0.00	0.00	0.18	0.99	Group and Time
SC-M2	IFN induced monocytes	0.00	0.00	0.79	0.87	Group and Time
SC-M3	Non-classical monocytes	0.00	0.21	0.42	0.86	Group
SC-DC1	Myeloid dendritic cells	1.00	0.00	0.24	1.00	Time
SC-DC2	Plasmacytoid dendritic cells	NA	NA	NA	NA	
B-cells						
SC-B1	Memory B-cells	0.91	0.00	0.83	0.96	Time
SC-B2	Naive B-cells, CD69 positive	NA	NA	NA	NA	
SC-PC1	Plasma cells	0.00	0.02	0.57	0.99	Group and Time

Supplementary Table 9: All cell type estimation results, given as percentages of cells pr sample. Found in separate Excel sheet.

Supplementary Table 10: Overview of gene distribution between clusters pre and post cell adjustment. Genes in G0 and AdjG0 are outliers. Unique genes are found to be differentially expressed either pre or post adjustment.

	AdjG0	AdjG1	AdjG2	AdjG3	AdjG4	AdjG5	AdjG6	Unique	Total
G0	7	4	3	1	3	3	11	164	196
G1		5						65	70
G2		23						66	89
G3	2							135	137
G4		25						27	52
G5	1	236				2	10	4128	4377
G6		19						42	61
G7	1		4		64	51	1	85	206
G8						5	5	60	70
G9	1		3			1	40	52	97
G10	1		12	1				33	47
G11	2		125		3	4	2	151	287
G12	1		1					55	57
G13			25	10	39			437	511
G14		2			1			1611	1614
Unique	17	13	35	45	23	22	28	0	183
Total	33	327	208	57	133	88	97	7111	8054

Supplementary Table 11: Contrasts. Differential gene expression was found using both overall and timepoint comparisons. These were incorporated into the analysis as contrasts created by `makeContrasts()`.

Contrast	Overall comparisons	Individual timepoint comparison
SPRA vs Healthy	$SPRAvsHealthy = SPRA_ALL - HEALTHY_ALL$	Time1_SPRAvsHealthy=SPRA_1-HEALTHY_1, Time2_SPRAvsHealthy=SPRA_2-HEALTHY_2, Time3_SPRAvsHealthy=SPRA_3-HEALTHY_3, Time4_SPRAvsHealthy=SPRA_4-HEALTHY_4, Time5_SPRAvsHealthy=SPRA_5-HEALTHY_5
SNRA vs Healthy	$SNRAvsHealthy = SNRA_ALL - HEALTHY_ALL$	Time1_SNRAvsHealthy=SNRA_1-HEALTHY_1, Time2_SNRAvsHealthy=SNRA_2-HEALTHY_2, Time3_SNRAvsHealthy=SNRA_3-HEALTHY_3, Time4_SNRAvsHealthy=SNRA_4-HEALTHY_4, Time5_SNRAvsHealthy=SNRA_5-HEALTHY_5
SLE vs Healthy	$SLEvsHealthy = SLE_ALL - HEALTHY_ALL$	Time1_SLEvsHealthy=SLE_1-HEALTHY_1, Time2_SLEvsHealthy=SLE_2-HEALTHY_2, Time3_SLEvsHealthy=SLE_3-HEALTHY_3, Time4_SLEvsHealthy=SLE_4-HEALTHY_4, Time5_SLEvsHealthy=SLE_5-HEALTHY_5
SPRA vs SNRA	$SPRAvsSNRA = SPRA_ALL - SNRA_ALL$	Time0_SPRAvsSNRA=SPRA_0-SNRA_0, Time1_SPRAvsSNRA=SPRA_1-SNRA_1, Time2_SPRAvsSNRA=SPRA_2-SNRA_2, Time3_SPRAvsSNRA=SPRA_3-SNRA_3, Time4_SPRAvsSNRA=SPRA_4-SNRA_4, Time5_SPRAvsSNRA=SPRA_5-SNRA_5, Time6_SPRAvsSNRA=SPRA_6-SNRA_6
SPRA vs SLE	$SPRAvsSLE = SPRA_ALL - SLE_ALL$	Time0_SPRAvsSLE=SPRA_0-SLE_0, Time1_SPRAvsSLE=SPRA_1-SLE_1, Time2_SPRAvsSLE=SPRA_2-SLE_2, Time3_SPRAvsSLE=SPRA_3-SLE_3, Time4_SPRAvsSLE=SPRA_4-SLE_4, Time5_SPRAvsSLE=SPRA_5-SLE_5, Time6_SPRAvsSLE=SPRA_6-SLE_6
SNRA vs SLE	$SNRAvsSLE = SNRA_ALL - SLE_ALL$	Time0_SNRAvsSLE=SNRA_0-SLE_0, Time1_SNRAvsSLE=SNRA_1-SLE_1, Time2_SNRAvsSLE=SNRA_2-SLE_2, Time3_SNRAvsSLE=SNRA_3-SLE_3, Time4_SNRAvsSLE=SNRA_4-SLE_4, Time5_SNRAvsSLE=SNRA_5-SLE_5, Time6_SNRAvsSLE=SNRA_6-SLE_6

HEALTHY_ALL: $1/5*(HEALTHY_1+HEALTHY_2+HEALTHY_3+HEALTHY_4+HEALTHY_5)$,

SPRA_ALL: $1/7*(SPRA_0+SPRA_1+SPRA_2+SPRA_3+SPRA_4+SPRA_5+SPRA_6)$

SNRA_ALL: $1/7*(SNRA_0+SNRA_1+SNRA_2+SNRA_3+SNRA_4+SNRA_5+SNRA_6)$,

SLE_ALL: $1/7*(SLE_0+SLE_1+SLE_2+SLE_3+SLE_4+SLE_5+SLE_6)$

Supplementary Table 12: SCS sample ID. Overview of IDs for whole blood bulk mRNA samples with corresponding plasma samples used for single cell sequencing.

Group	Timepoint	Sample ID		
RA	T3	S31		
		S60		
		S66		
		NA		
	T4	S30		
		S59		
		S65		
		S235		
		SLE	T3	S185
				S194
S200				
S240				
T4	S186			
	S195			
	S201			
	S241			

Supplementary Table 13a: Main cell type findings. Overview of main changes in cell types and cell type composition.

Findings	Whole blood mRNA	PBMC scRNA-seq	PBMC flow cytometry	Cell abundance estimation	Cell-adjusted whole blood mRNA
Cell type changes during pregnancy					
Increase	-	- IFN induced monocytes (SC-M2)	-	- Classical monocytes (SC-M1) - IFN induced monocytes (SC-M2) - Naïve T-helper (SC-T2)	- Neutrophil genes (<i>FOLR3, ANPEP, ST6GALNAC2, CYP27A1, MRV1, UBE2J1, GALNT14</i>) - Classical monocyte genes (<i>FOLR3, TMEM158/RIS1</i>)
Decrease	- Natural killer (NK)-cell receptors (<i>KLRC2, KLRC3, GNLY, KLRF1, FGFBP2</i>) - Gamma-delta T (gdT) cell receptors (<i>TRDC, TRDV2</i>) - Regulator T-cell (Treg) enriched receptors (<i>TRAV8-2, TRAV8-6</i>) - MAIT-enriched receptors (<i>TRAV1-2</i>)	- Memory T-helper (SC-T4) - gdT (SC-T7) - Memory T-cytotoxic (SC-T8)	- Th1/Th2-ratio	- Naïve T-helper, high metabolic activity (SC-T1) - Memory T-helper (SC-T4) - Memory T (SC-T5) - gdT (SC-T7) - Memory T-cytotoxic (SC-T8) - Myeloid dendritic (SC-DC1) - Memory B (SC-B1) - Plasma cells (SC-PC1)	- Basophil, Eosinophil genes (<i>NKX3-1, HDC, CLC</i>) - Genes in innate cytotoxic cells (NK, gdT, MAIT receptors) - Genes in B-cells, plasma cells (31 IGL-, IGH-chain genes)
Cell type changes in SLE					
Increase	- Neutrophil genes (<i>ABCA1, APOBR, GRN, PRKCD</i>)	- Naïve T-helper (SC-T2) - IFN induced T (SC-T3) - Memory T (SC-T5) - IFN induced monocytes (SC-M2) - Non-classical monocytes (SC-M3) - Naïve B (SC-B2) - Plasma cells (SC-PC1)	- Plasma cells	- IFN induced T (SC-T3) - IFN induced monocytes (SC-M2) - Non-classical monocytes (SC-M3) - Plasma cells (SC-PC1)	- Monocyte genes (e.g. <i>RRAS, ZFAND5, STXBP2</i>) - Plasma cell genes (e.g. <i>CISD2, TCF3</i>) - Dendritic cell genes (e.g. <i>IL18, ST6GALNAC4</i>)
Decrease	- MAIT genes (<i>SLC4A10, CFH, IL23R, RORC, ADAM12, ADAM23</i>)	- Naïve T-helper, high metabolic activity (SC-T1) - Memory T-helper (SC-T4) - MAIT (SC-T6) - gdT (SC-T7) - Classical monocytes (SC-M1)	-	- Naïve T-helper, high metabolic activity (SC-T1) - Naïve T-helper (SC-T2) - Memory T-helper (SC-T4) - gdT (SC-T7) - Classical monocytes (SC-M1)	- Naïve T-helper genes (<i>FHIT, THEM4</i>)
Cell type changes in RA					
Increase					- Monocyte genes (<i>CYBRD1, NAAA</i>)
Decrease	- T cell genes (<i>SLC4A10, SNHG16, NKX3-1, RPS26, HLA-H</i>)	-	-	- SNRA, postpartum: Naïve T-helper, high metabolic activity (SC-T1)	- MAIT genes (<i>GZMK, NCR3, SLC4A10</i>)

Supplementary Table 13b: Main cell type findings. Overview of main changes in pathways and gene expression.

Findings	Whole blood mRNA	Cell-adjusted whole blood mRNA
Pathway changes during pregnancy		
Increased	<ul style="list-style-type: none"> - Olfactory signalling - G-protein coupled receptor (GPCR) signalling - Regulation of NK cell mediated immunity 	<ul style="list-style-type: none"> - Neutrophil degranulation - GPCR signalling
Decreased	<ul style="list-style-type: none"> - Humoral immunity 	<ul style="list-style-type: none"> - Translation pathways - Heme scavenging - Classical antibody-mediated complement activation
Pathway changes in SLE		
Increased:	<ul style="list-style-type: none"> - Interferon (IFN) signalling - Platelet activation, signalling, and aggregation 	<ul style="list-style-type: none"> - IFN signalling - Platelet activation, signalling, and aggregation - Transcriptional regulation of granulopoiesis - Cell cycle
Decreased	-	<ul style="list-style-type: none"> - Translation pathways
Notable gene expression changes during pregnancy		
Increase	<ul style="list-style-type: none"> - Regulators of placentation (increased tolerance, reduced inflammation, angiogenesis, vascular remodelling) (IDO, IL10, FLT1) - Long non-coding RNAs - Toll-like receptors (<i>TLR1,2,4,5,6,8</i>) - B-cell activating factor (<i>BAFF/TNFSF13B</i>) 	<ul style="list-style-type: none"> - Steroid and lipid metabolism (<i>CYP27A1</i>) - ER-stress (<i>MRV1, UBE2J1</i>) - Galactosylation (<i>GALNT14</i>)
Decrease	<ul style="list-style-type: none"> - Regulators of placentation (<i>IL5RA, PTGDR2, NKX3-1, SOCS5</i>) - Immunoglobulins (<i>IGH</i>, 6 genes; <i>IGL</i>, 14 genes; <i>IGK</i>, 8 genes) 	<ul style="list-style-type: none"> - Immunoglobulins (31 <i>IGL</i> and <i>IGH</i> genes)
Notable gene expression changes in SLE		
Increase	<ul style="list-style-type: none"> - Interferon (IFN) signalling (e.g., <i>SIGLEC1, IFI44, IFI44L, USP18, RSAD2, ISG15</i>) - Lipid and steroid hormone metabolism (<i>ABCA1, APOBR</i>) - Inflammation or endoplasmic reticulum stress (<i>GRN, PRKCD</i>) 	<ul style="list-style-type: none"> - Interferon (IFN) signalling
Decrease	<ul style="list-style-type: none"> - Metalloproteases (<i>ADAM12, ADAM23</i>) 	-
Notable gene expression changes in RA		
Increase	-	<ul style="list-style-type: none"> - Distinct in RA (<i>LRRC8B, NAAA</i>) - Possible immune regulator (<i>TFAFA2</i>)
Decrease	-	<ul style="list-style-type: none"> - Distinct in RA (<i>NBPF26, DEF6, CNR1</i>) - Placental development (<i>NKX3-1, SNHG16, NRCAM</i>) - Dysregulation linked to autoimmunity (<i>DEF6</i>)