

Supplementary Tables and Figures

Table S1. List of primers for assessment of gene expression using real time qPCR.

Gene Name	Primer Sequence	Amplicon Size (bp)
CXCL10	F: AAGGAATCTTTCTGCTTTGG R: ACCTTCCTGTATGTGTTTGG	184
RELA	F: TAGAAGAGCAGCGTGGGGA R: AGAGTTTCGGTTCACCTCGGC	176
CCL2	F: CAGCCAGATGCAATCAATGCC R: TGGAATCCTGAACCCACTTCT	190
CCR4	F: GAAAGTATCCCCAAGCCTTGC R: AAGGGAGGGAAAACACGAAGA	214
IBTK	F: AAGTCTGGTAAGACCAATTCTGTG R: CGGTTTGACTTTCGCCTCAAT	156
ITGB7	F: GTGGAAACTAAAGCCCAGAGAG R: CCGAGATCCCAAGCCGTAG	122
CKLF	F: TATCACTGGATTTGAAGTCACCG R: GCCAACACAGATACGATGAGC	153
PECAM-1	F: CCCAGCCCAGGATTTCTTAT R: ACCGCAGGATCATTGAGTT	163
CXCL16	F: CCCGCCATCGGTTCAAGTTC R: CCCCAGTAAGCATGTCCAC	181
TLR3	F: GTCCCAAGCCTTCAACGACT R: GTTTGCGTGTTCAGAGCC	216
BTK	F: GCTCAAAAACGTAATCCGGTACA R: GTCTTCCGGTGAGAACTCCC	171
ICAM1	F: GGTAGCAGCCGAGTCATAA R: GATAGGTTCAAGGAGGCGTG	149
TLR10	F: GATTACTCTGGGACGACCTTTT R: GTCAAGATAAGCCTTACCACCAA	108
IL1B	F: AGCTACGAATCTCCGACCAC R: CGTTATCCCATGTGTCGAAGAA	186
IL12RB2	F: AGGACGAGACACCCACTTATAC R: ATTGACAGCAGTAACCTTGGC	172
CXCR6	F: ATGTGTTCTGGTGAACCTA R: GGCCTTAACCACTACAATGA	203
CXCR2	F: GACAAATCTCCACCTTCAGA R: ATGAAACAACCTTGACGATG	224
CXCR1	F: TGGGGACTGTCTATGAATCTGT R: GCAACACCATCCGCCATTTT	127
CD56	F: TGTCCGATTCATAGTCTGTCC R: CTCACAGCGATAAGTGCCCTC	82

Table S2. Summary of Clinical Data of Recruited Healthy Controls and RA Patients

WBC: White blood cells, RBC: red blood cells, HCT: Hematocrit, MCV: mean corpuscular volume, MCH: mean corpuscular hemoglobin, MCHC: mean corpuscular hemoglobin concentration, RDW: red blood cell distribution width, MPV: mean platelet volume, PDW: platelet distribution width, HbA1c: Hemoglobin A1c, GFR: Glomerular filtration rate, HDL: high-density lipoprotein, LDL: low-density lipoprotein, TSH: Thyroid-stimulating hormone, TPO: Thyroid peroxidase, CRP: C-reactive protein, BSA: Body Surface Area, BMI: Body Mass Index, RF: Rheumatoid Factor

Parameters	Healthy Controls			Rheumatoid Arthritis Patients		
	Range	Mean \pm SD	Mean \pm SEM	Range	Mean \pm SD	Mean \pm SEM
Age	23-70	45.81 \pm 10.07	45.81 \pm 2.517	27-89	53.76 \pm 14.83	53.76 \pm 3.597
WBC	2.61-7.84	5.449 \pm 1.4	5.449 \pm 0.35	3.87-13.86	6.901 \pm 2.343	6.901 \pm 0.5684
RBC	4.02-5.42	4.639 \pm 0.487	4.639 \pm 0.1218	3.45-5.58	4.664 \pm 0.5589	4.664 \pm 0.1356
Hemoglobin	11.3-13.6	12.68 \pm 0.7123	12.68 \pm 0.1781	10.4-16.4	12.95 \pm 1.341	12.95 \pm 0.3253
HCT	33.9-41.4	37.77 \pm 1.755	37.77 \pm 0.4388	32.6-49.1	38.92 \pm 4.027	38.92 \pm 0.9767
MCV	67.6-95.7	82.06 \pm 7.722	82.06 \pm 1.931	73.1-101.5	83.88 \pm 6.773	83.88 \pm 1.643
MCH	21.8-32.3	27.62 \pm 3.306	27.62 \pm 0.8265	23.4-34.2	27.95 \pm 2.666	27.95 \pm 0.6467
MCHC	30.9-36.4	33.58 \pm 1.392	33.58 \pm 0.3481	31.2-35.8	33.29 \pm 1.134	33.29 \pm 0.275
RDW	12-19.9	13.74 \pm 1.945	13.74 \pm 0.4862	12.5-20	14.73 \pm 1.697	14.73 \pm 0.4116
Platelet	189-363	279.9 \pm 49.36	279.9 \pm 12.34	191-450	300.5 \pm 74.45	300.5 \pm 18.06
MPV	6.4-10.9	8.338 \pm 1.079	8.338 \pm 0.2699	6.7-13.5	8.376 \pm 1.717	8.376 \pm 0.4164
% Neutrophils	32-67.8	51.52 \pm 8.479	51.52 \pm 2.12	26-88.5	55.5 \pm 15.45	55.5 \pm 3.746
% Lymphocytes	25-53	37.62 \pm 7.579	37.62 \pm 1.895	9.7-54.6	32.85 \pm 11.91	32.85 \pm 2.889
% Monocytes	3.4-10.1	5.969 \pm 1.872	5.969 \pm 0.4679	1.8-12.2	6.029 \pm 2.531	6.029 \pm 0.6138
% Eosinophils	0.8-6.1	2.925 \pm 1.575	2.925 \pm 0.3938	0.1-11.6	3.413 \pm 2.8	3.413 \pm 0.7
% Basophils	0.1-1.1	0.5313 \pm 0.2983	0.5313 \pm 0.07456	0.1-1.5	0.5875 \pm 0.3757	0.5875 \pm 0.0939
Absolute Neutrophils	1.23-4.15	2.84 \pm 0.9821	2.84 \pm 0.2455	1.43-11.04	3.964 \pm 2.448	3.964 \pm 0.612
Absolute Lymphocytes	1.11-2.8	2.012 \pm 0.5409	2.012 \pm 0.1352	0.76-3.79	2.143 \pm 0.7916	2.143 \pm 0.1979
Absolute Monocytes	0.16-0.69	0.3288 \pm 0.151	0.3288 \pm 0.03775	0.14-0.6	0.3763 \pm 0.1256	0.3763 \pm 0.0314
Absolute Eosinophils	0.04-0.4	0.1525 \pm 0.1075	0.1525 \pm 0.02687	0.08-0.79	0.2386 \pm 0.1835	0.2386 \pm 0.0491

Absolute			0.02375 ±			
Basophils	0.01-0.05	0.02375 ± 0.0115		0.01-0.11	0.036 ± 0.02586	0.036 ± 0.00668
PDW	9.4-66.9	41.39 ± 19.86	41.39 ± 4.965	9.7-69.4	40.19 ± 17.5	40.19 ± 4.376
Erythrocyte						
Sedimentation	6-50	20.69 ± 14	20.69 ± 3.884	6-80	33.76 ± 21.84	33.76 ± 5.298
Rate (ESR)						
Sodium	131-143	139.1 ± 3.125	139.1 ± 0.8351	132-143	138.5 ± 3.184	138.5 ± 0.7723
Creatinine	43-91	59.5 ± 12.68	59.5 ± 3.17	31-111	62.59 ± 20.34	62.59 ± 4.933
Uric acid	4.6-350	241.3 ± 81.8	241.3 ± 21.86	145-508	275.5 ± 88.64	275.5 ± 22.89
Fasting						
Glucose	4.9-6	5.375 ± 0.3732	5.375 ± 0.1319	6-8.5	6.9 ± 1.389	6.9 ± 0.8021
Glucose	4-7.8	5.558 ± 1.039	5.558 ± 0.3134	5-29.1	8.121 ± 6.164	8.121 ± 1.647
HbA1c	4.8-6	5.414 ± 0.414	5.414 ± 0.1565	4.9-10.4	6.615 ± 1.521	6.615 ± 0.4218
Urea level	2.3-8	4.231 ± 1.894	4.231 ± 0.5253	2.7-9.1	4.724 ± 1.796	4.724 ± 0.4356
GFR	55-119	101.4 ± 21.51	101.4 ± 7.604	39-186.1	98.88 ± 31.22	98.88 ± 7.805
Total protein	70-92	78.69 ± 6.183	78.69 ± 1.715	68-85	75.94 ± 4.582	75.94 ± 1.146
Albumin	33.1-45	38.86 ± 3.821	38.86 ± 1.06	29.2-38.9	34.16 ± 3.208	34.16 ± 0.802
Total Bilirubin	6.6-18.4	9.731 ± 3.216	9.731 ± 0.8919	4.2-14.9	8.606 ± 3.568	8.606 ± 0.8921
Ferritin	10-162	67.88 ± 51.2	67.88 ± 18.1	9-66	27.9 ± 18.26	27.9 ± 5.774
Iron	8.4-20.3	14.24 ± 4.837	14.24 ± 1.71	2.9-27.7	13.24 ± 8.423	13.24 ± 2.664
Transferrin	211-339	254 ± 46.83	254 ± 19.12	216-336	257.2 ± 41.47	257.2 ± 13.11
Cholesterol	3.46-7.82	5.344 ± 1.198	5.344 ± 0.3094	4-7.2	5.013 ± 0.9165	5.013 ± 0.2366
Triglycerides	0.57-2	1.069 ± 0.4152	1.069 ± 0.1072	0.43-3.82	1.508 ± 0.9503	1.508 ± 0.2454
HDL	0.9-1.87	1.424 ± 0.2761	1.424 ± 0.07129	0.95-2.11	1.399 ± 0.3633	1.399 ± 0.09379
LDL	1.74-5.83	3.539 ± 1.179	3.539 ± 0.3045	0.26-3.64	2.655 ± 0.8625	2.655 ± 0.2227
Vitamin D	30.47- 100.8	55.01 ± 19.55	55.01 ± 5.047	17.82-130.7	56.3 ± 32.03	56.3 ± 8.884
Complement 3	97-196	137.7 ± 34.07	137.7 ± 13.91	85-202	153.7 ± 42.81	153.7 ± 17.48
Complement 4	11-36	26 ± 8.408	26 ± 3.432	19.9-44.2	31.83 ± 9.008	31.83 ± 3.677
T4 free	11.95- 17.46	15.31 ± 1.887	15.31 ± 0.4871	7.67-25.64	15.63 ± 4.008	15.63 ± 1.002
T3 free	3.59-4.93	4.304 ± 0.5167	4.304 ± 0.1722	3.17-5.25	4.259 ± 0.6329	4.259 ± 0.2002
TSH	0.66-3.29	1.581 ± 0.7203	1.581 ± 0.1801	0.16-10.51	2.56 ± 2.774	2.56 ± 0.6728
TPO Antibody	6.6-1300	192.8 ± 406.3	192.8 ± 128.5	6.4-316.9	97.59 ± 114.8	97.59 ± 38.28

Thryoglobulin Antibody	10-261.3	62.21 ± 85.43	62.21 ± 27.02	12-1900	306.5 ± 555.4	306.5 ± 167.5
Thryglobulin	1.74-164	35.63 ± 58.04	35.63 ± 21.94	0.3-405.4	70.27 ± 164.2	70.27 ± 67.04
CRP	0-15.4	2.846 ± 4.119	2.846 ± 1.142	0.1-94.8	13.83 ± 23.07	13.83 ± 5.595
Height	149-169	157.1 ± 6.26	157.1 ± 1.565	142-168	154.8 ± 5.747	154.8 ± 1.394
Weight	43-86	69.09 ± 12.16	69.09 ± 3.041	47.8-112	76.29 ± 16.41	76.29 ± 3.981
BSA	1.34-1.99	1.729 ± 0.1674	1.729 ± 0.04184	1.44-2.2	1.802 ± 0.1962	1.802 ± 0.04758
BMI	19-36	28.19 ± 5.18	28.19 ± 1.295	20-47	31.87 ± 7.454	31.87 ± 1.808
Systolic Blood Pressure	98-148	122.1 ± 15.15	122.1 ± 3.786	114-166	134.6 ± 15.64	134.6 ± 3.792
Diastolic Blood Pressure	52-84	69.69 ± 8.987	69.69 ± 2.247	50-94	78.18 ± 9.697	78.18 ± 2.352
RF	-	-	-	0.01-400 (65% Positive)	98.45 ± 140.2	98.45 ± 42.26

Table S3. Significant correlation analyses between DEGs in NK cells and clinical parameters of healthy controls and RA patients

Gene Name	Clinical Parameter	P value	r value
CD56	WBC	0.0179	-0.4098
	Absolute Lymphocytes	0.0391	-0.3665
PECAM-1	CRP	0.0167	0.4337
ITGB7	WBC	0.0435	-0.3536
IBTK	WBC	0.0138	-0.4245
TLR10	Percent Lymphocytes	0.0355	-0.3673
IL12RB2	Absolute Lymphocytes	0.0118	-0.4399
	ESR	0.0368	-0.3828
CXCR1	Percent Lymphocytes	0.0050	-0.4770
	Absolute Lymphocytes	0.0038	-0.4974
CXCR2	Percent Lymphocytes	0.0158	-0.4168
	Absolute Lymphocytes	0.0013	-0.5427
CXCR6	Percent Lymphocytes	0.0218	-0.3981
	Absolute Lymphocytes	0.0272	-0.3904
CCL2	ESR	0.0221	-0.4162
	CRP	0.0135	-0.4459
CCR4	Percent Lymphocytes	0.0417	-0.3565

Table S4. Pathways shared by the 11 significant selected genes in Reactome Pathways Option of STRING.

Description	Observed gene count	Background gene count	False discovery rate	Matching proteins in your network (IDs)	Matching proteins in your network (labels)
Immune System	8	1925	4.60E-05	ENSP00000225831,E NSP00000263341,ENS P00000267082,ENSP00 000308925,ENSP00000 384273,ENSP00000457 421,ENSP00000480132, ENSP00000483570	BTK,CCL2,IL1B,ITG B7,NCAM1,PECAM1, RELA,TLR10
Diseases associated with the TLR signaling cascade	3	24	4.60E-05	ENSP00000308925,E NSP00000384273,ENS P00000483570	BTK,RELA,TLR10
CLEC7A/inflammasome pathway	2	6	0.00024	ENSP00000263341,E NSP00000384273	IL1B,RELA
Interleukin-1 processing	2	7	0.00025	ENSP00000263341,E NSP00000384273	IL1B,RELA
Toll-like Receptor Cascades	3	151	0.0015	ENSP00000308925,E NSP00000384273,ENS P00000483570	BTK,RELA,TLR10
Innate Immune System	5	1012	0.0023	ENSP00000263341,E NSP00000308925,ENS P00000384273,ENSP00 000457421,ENSP00000 483570	BTK,IL1B,PECAM1, RELA,TLR10
Cytokine Signaling in Immune system	4	654	0.0046	ENSP00000225831,E NSP00000263341,ENS P00000384273,ENSP00 000480132	CCL2,IL1B,NCAM1, RELA
Chemokine receptors bind chemokines	2	48	0.0046	ENSP00000293778,E NSP00000332659	CCR4,CXCL16
Interleukin-10 signaling	2	45	0.0046	ENSP00000225831,E NSP00000263341	CCL2,IL1B
Extracellular matrix organization	3	298	0.0059	ENSP00000267082,E NSP00000457421,ENS P00000480132	ITGB7,NCAM1,PEC AM1
MyD88:MAL(TIRAP) cascade	2	94	0.01	ENSP00000384273,E NSP00000483570	BTK,RELA

initiated on plasma membrane					
Integrin cell surface interactions	2	83	0.01	ENSP00000267082,E NSP00000457421	ITGB7,PECAM1
Signaling by Interleukins	3	439	0.01	ENSP00000225831,E NSP00000263341,ENS P00000384273	CCL2,IL1B,RELA
Interleukin-4 and Interleukin-13 signaling	2	106	0.01	ENSP00000225831,E NSP00000263341	CCL2,IL1B
Interleukin-1 signaling	2	98	0.01	ENSP00000263341,E NSP00000384273	IL1B,RELA
MyD88 cascade initiated on plasma membrane	2	84	0.01	ENSP00000308925,E NSP00000384273	RELA,TLR10
Signaling by the B Cell Receptor (BCR)	2	107	0.01	ENSP00000384273,E NSP00000483570	BTK,RELA
Fc epsilon receptor (FCERI) signaling	2	126	0.0108	ENSP00000384273,E NSP00000483570	BTK,RELA
Adaptive Immune System	3	733	0.0279	ENSP00000267082,E NSP00000384273,ENS P00000483570	BTK,ITGB7,RELA
Signal Transduction	5	2605	0.0373	ENSP00000293778,E NSP00000332659,ENS P00000384273,ENSP00 000480132,ENSP00000 483570	BTK,CCR4,CXCL16, NCAM1,RELA

Figure S1. Flow chart summarizing the in-silico approach used in the study in order to obtain the DEGs of NK cells in

RA.

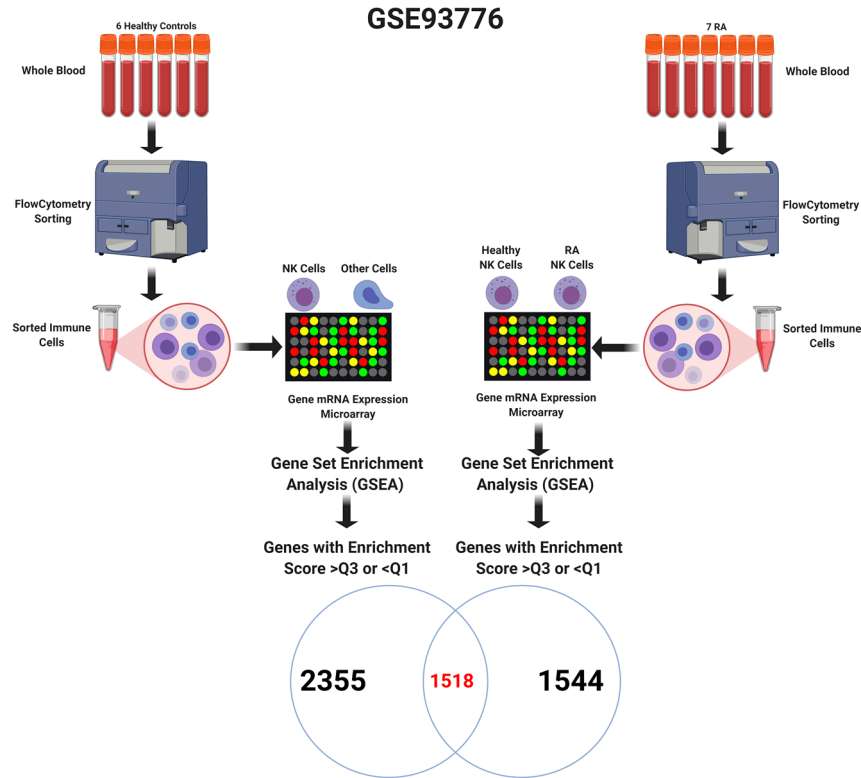


Figure S2. Spearman correlation matrix between each of the DEGs in comparison to the rest of the genes in NK cells of RA patients and healthy controls.

Genes	CKLF	CXCL16	CD56	CCR4	PECAM-1	IBTK	ITGB7	CCL2	CXCL10	RELA	CXCR6	CXCR1	CXCR2	TLR3	ICAM	BTK	IL12RB2	TLR10	IL1B	IFNG
CKLF		0.055	0.026	-0.363	-0.217	0.319	0.105	0.153	-0.278	0.361	-0.258	-0.218	-0.170	-0.040	-0.157	0.461	0.149	-0.077	-0.142	0.390
CXCL16	0.055		0.147	0.016	0.480	0.028	0.076	-0.200	0.120	-0.056	0.100	0.165	0.120	0.266	0.070	0.611	0.211	0.266	0.158	0.136
CD56	0.026	0.147		0.685	0.507	0.567	0.623	0.245	0.691	0.286	0.737	0.755	0.650	0.538	0.619	0.133	0.365	0.581	0.223	-0.098
CCR4	-0.363	0.016	0.685		0.569	0.095	0.255	0.411	0.884	-0.189	0.904	0.899	0.783	0.596	0.771	-0.014	0.185	0.663	0.554	-0.304
PECAM-1	-0.217	0.480	0.507	0.569		-0.024	0.378	-0.048	0.501	-0.157	0.471	0.572	0.334	0.455	0.451	0.395	0.194	0.566	0.543	-0.162
IBTK	0.319	0.028	0.567	0.095	-0.024		0.484	0.111	0.249	0.677	0.250	0.229	0.276	0.228	0.209	0.087	0.398	0.262	-0.200	0.269
ITGB7	0.105	0.076	0.623	0.255	0.378	0.484		-0.195	0.256	0.452	0.257	0.367	0.080	0.295	0.311	0.121	0.285	0.334	0.212	0.246
CCL2	0.153	-0.200	0.245	0.411	-0.048	0.111	-0.195		0.371	-0.038	0.497	0.409	0.648	0.204	0.295	-0.046	0.214	0.239	0.081	-0.176
CXCL10	-0.278	0.120	0.691	0.884	0.501	0.249	0.256	0.371		-0.019	0.859	0.766	0.808	0.512	0.755	0.060	0.313	0.610	0.476	-0.388
RELA	0.361	-0.056	0.286	-0.189	-0.157	0.677	0.452	-0.038	-0.019		-0.130	-0.157	-0.075	0.021	-0.032	-0.022	0.338	-0.071	-0.332	0.222
CXCR6	-0.258	0.100	0.737	0.904	0.471	0.250	0.257	0.497	0.859	-0.130		0.901	0.904	0.699	0.822	0.037	0.366	0.770	0.475	-0.339
CXCR1	-0.218	0.165	0.755	0.899	0.572	0.229	0.367	0.409	0.766	-0.157	0.901		0.805	0.657	0.735	0.124	0.244	0.732	0.531	-0.156
CXCR2	-0.170	0.120	0.650	0.783	0.334	0.276	0.080	0.648	0.808	-0.075	0.904	0.805		0.613	0.743	0.078	0.408	0.652	0.363	-0.325
TLR3	-0.040	0.266	0.538	0.596	0.455	0.228	0.295	0.204	0.512	0.021	0.699	0.657	0.613		0.826	0.312	0.489	0.886	0.521	-0.095
ICAM	-0.157	0.070	0.619	0.771	0.451	0.209	0.311	0.295	0.755	-0.032	0.822	0.735	0.743	0.826		0.112	0.423	0.872	0.625	-0.324
BTK	0.461	0.611	0.133	-0.014	0.396	0.087	0.121	-0.046	0.060	-0.022	0.037	0.124	0.078	0.312	0.112		0.226	0.340	0.326	0.299
IL12RB2	0.149	0.211	0.365	0.185	0.194	0.398	0.285	0.214	0.313	0.338	0.366	0.244	0.408	0.489	0.423	0.226		0.599	0.093	-0.310
TLR10	-0.077	0.266	0.581	0.663	0.566	0.262	0.334	0.239	0.610	-0.071	0.770	0.732	0.652	0.886	0.872	0.340	0.599		0.550	-0.237
IL1B	-0.142	0.158	0.223	0.554	0.543	-0.200	0.212	0.081	0.476	-0.332	0.475	0.531	0.363	0.521	0.625	0.326	0.093	0.550		-0.196
IFNG	0.390	0.136	-0.098	-0.304	-0.162	0.269	0.246	-0.176	-0.388	0.222	-0.339	-0.156	-0.325	-0.095	-0.324	0.299	-0.310	-0.237	-0.196	