RNA extraction and gene expression analysis

RNA was extracted from lymph node and lungs using Trizol and after DNAse digestion cleaned up using RNeasy minikit (Qiagen). One microgram of RNA was reverse transcribed using RT^2 First Strand Kit and ran on Th17 and autoimmunity plates (SABiosciences). Data were interpreted by using SABiosciences data analysis tool and Statminer.

Table S1. Analysis of leukocyte populations in blood of IL-22R1 tg mice

Parameters	Results	Normal Range	Remarks
WBC [a]	**13.12**	1.8-10.7	Leukocytosis
Neutrophils	**7.24**	0.1-2.4	Neutrophilia
Lymphocytes	3.94	0.9-9.3	Normal
Monocytes	**0.88**	0.0-0.4	Monocytosis
Eosinophils	0.25	0.0-0.2	Eosinophilia
Basophils	0.25	0.0-0.2	Basophilia

[a]Values are expressed as 10^3 cells/ul.

Table S2. Analysis of leukocyte populations in blood of IL-22R1 tg bone marrow recepients

animal	NE	LY	MO	EO	BA
wt > wt	26.84± 1.20	66.19± 0.19	5.37± 1.72	1.12± 1.22	0.48± 0.75
tg > wt	54.36± 3.87	32.23± 5.39	12.37± 7.19	1.02± 0.45	0.03± 0.02

Figure S1. **Gene expression profile of inflammatory genes in lymph node.** (a) Heat map comparison of gene expression between wt > wt and tg > wt animals (b) heat map showing correlation across biological groups (c) Volcano plot showing changes in gene expression, the green and red dots above the blue line represent fold change in gene expression which are statistically significant. Fold change of genes over (d) and under (e) expressed which are statistically significant. The data represented are biological triplicates from each group.

Figure S2. Thymic involution and changes in T-cell profiles in thymus and lymph nodes in IL-22R1 tg mice (a) Thymocyte profile was analyzed after gating on CD4 and CD8 cells. (b) Percentages are shown for DN ($CD4^- CD8^-$), DP ($CD4^+CD8^+$), CD4 SP and CD8 SP cells. (c) The DN population was further distinguished based on the $CD25^+$ and $CD44^+$ to distinguish between DN1, DN2, DN3 and DN4. (d) Percentages are shown for DN1-4 cells. (e) Lymph node T-cell profile was analyzed after gating on CD4 and CD8 cells. (f) Percentages are shown for CD4 SP and CD8 SP cells. Representative data from one experiment with three animals per group which is shown as mean ± SEM. * $p<0.05$, ** $p<0.01$, *** $p<0.001$.

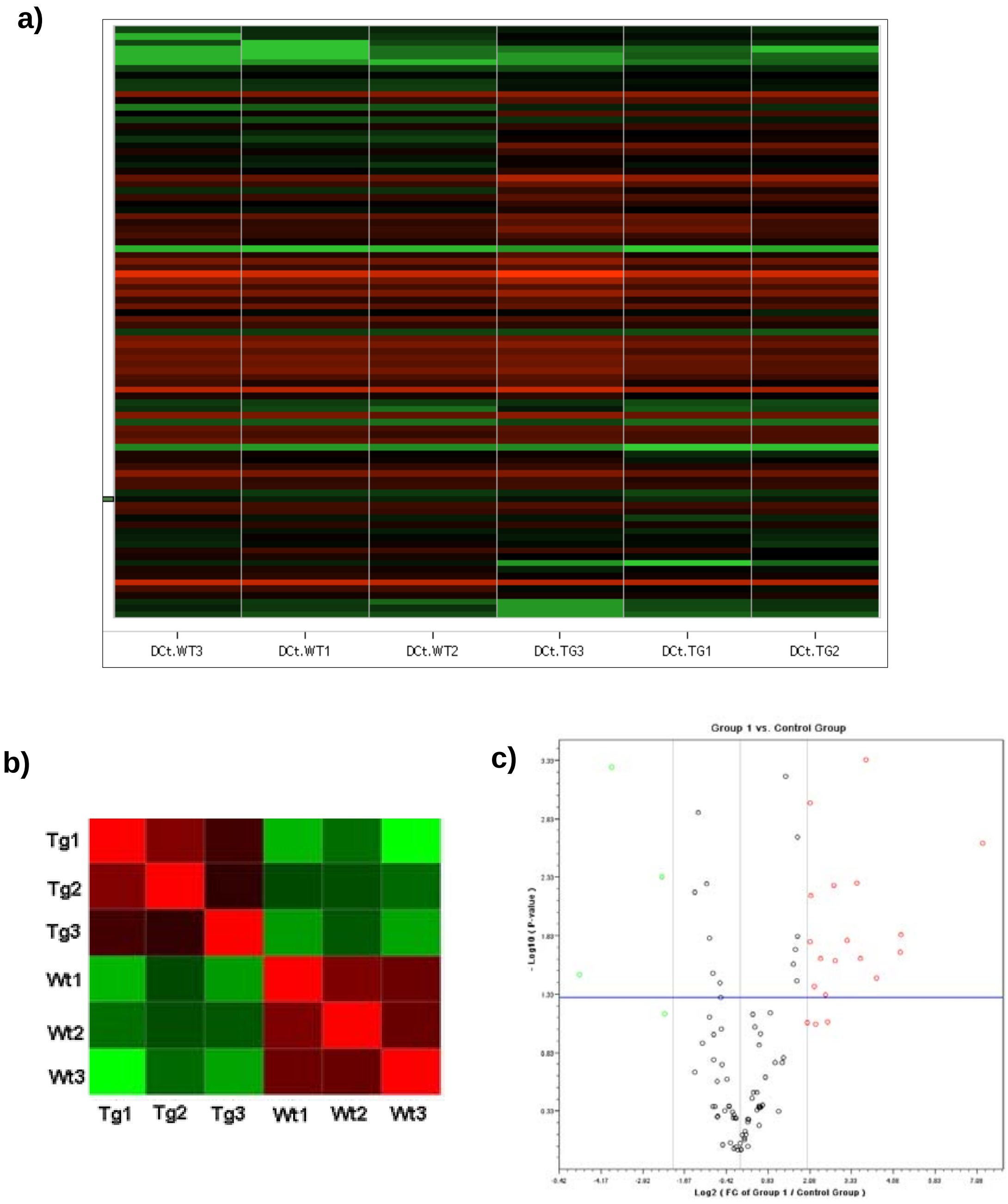
Figure S3. The graph shows percentage of neutrophils ($FSC^{hi}F4/80^{lo}$) in blood measured by flow cytometry during weeks 4, 5 and 6 in wt > wt and tg > wt animals.

Figure S4. Gene expression profile of inflammatory genes in lungs. (a) Heat map comparison of gene expression between wt > wt and tg > wt animals. Fold change of genes over (b) and under (c) expressed.

Figure S5. Patient who had elevated IL-22 in serum 3 months post EPOCH treatment was assayed for IL-22 for 6, 9 and 12 months post treatment.

Figure S6. Cytokine levels in DLBCL patients. (a) Cytometric bead array to assay the concentrations of IFN-γ, IL-17A, IL-8, IL-22, IL-6 and TNF-α in of DLBCL serum patients pre treatment. (b) Comparison of IL-17A and IL-22 of ALCL and DLBCL pre-treatment serum samples.

Figure S1



d) Genes over expressed

Gene	Fold Change	p-value
IFN-8	153.0437	0.002381
Cxcl2	27.8563	0.014374
Csf3	27.4398	0.020321
IL-12rb2	16.8791	0.034073
IL-22	13.6608	0.000457
Mmp13	12.0989	0.023027
IL-1b	11.1876	0.005196
Cebpb	9.166	0.01608
IL-6	7.1331	0.024045
Mmp3	6.9768	0.005411
IL-12rb1	6.0929	0.080281
IL-27	5.8784	0.04742
Cxcl1	5.3284	0.02297
Ccl7	4.7715	0.083585
Csf2	4.6741	0.039799
Clec7a	4.3206	0.006697
Socs3	4.2612	0.016467
IL-10	4.2343	0.001079
Ccl2	4.0474	0.081941

e) Genes under expressed

Gene	Fold Change	p-value
IL-4	-28.1052	0.031564
Ccl22	-14.3724	0.000531
Cd40lg	-5.0414	0.004595
IL-17rb	-4.7655	0.067818

Figure S2

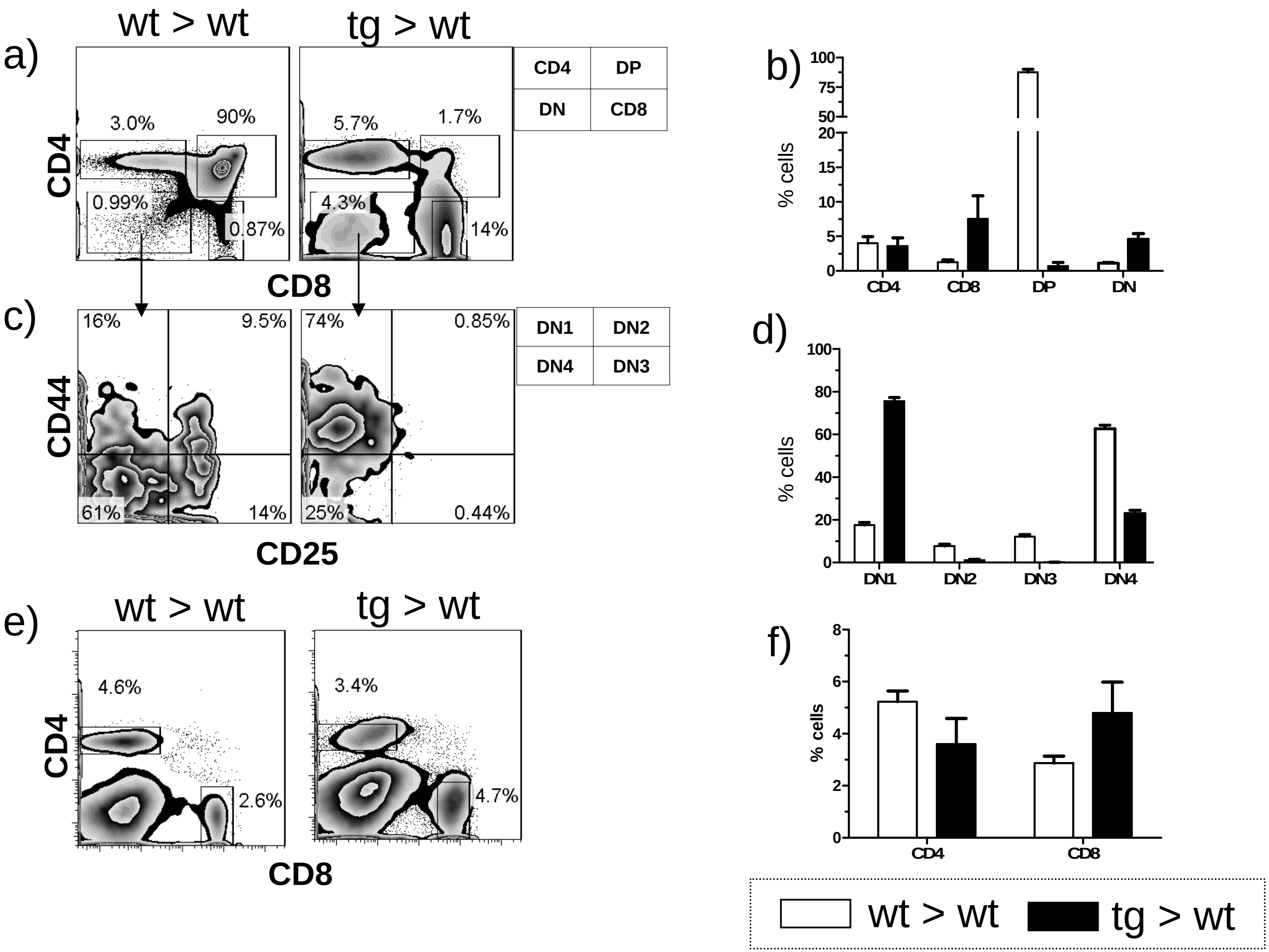

a)
wt > wt
tg > wt
3.0%
90%
0.99%
0.87%
5.7%
1.7%
4.3%
14%
CD4
CD8
CD4 DP
DN CD8
b)
100
75
50
20
15
10
5
0
% cells
CD4
CD8
DP
DN
c)
16%
9.5%
61%
14%
74%
0.85%
25%
0.44%
CD44
CD25
DN1 DN2
DN4 DN3
d)
100
80
60
40
20
0
% cells
DN1
DN2
DN3
DN4
e)
wt > wt
tg > wt
4.6%
2.6%
3.4%
4.7%
CD4
CD8
f)
8
6
4
2
0
% cells
CD4
CD8
wt > wt
tg > wt

Figure S3

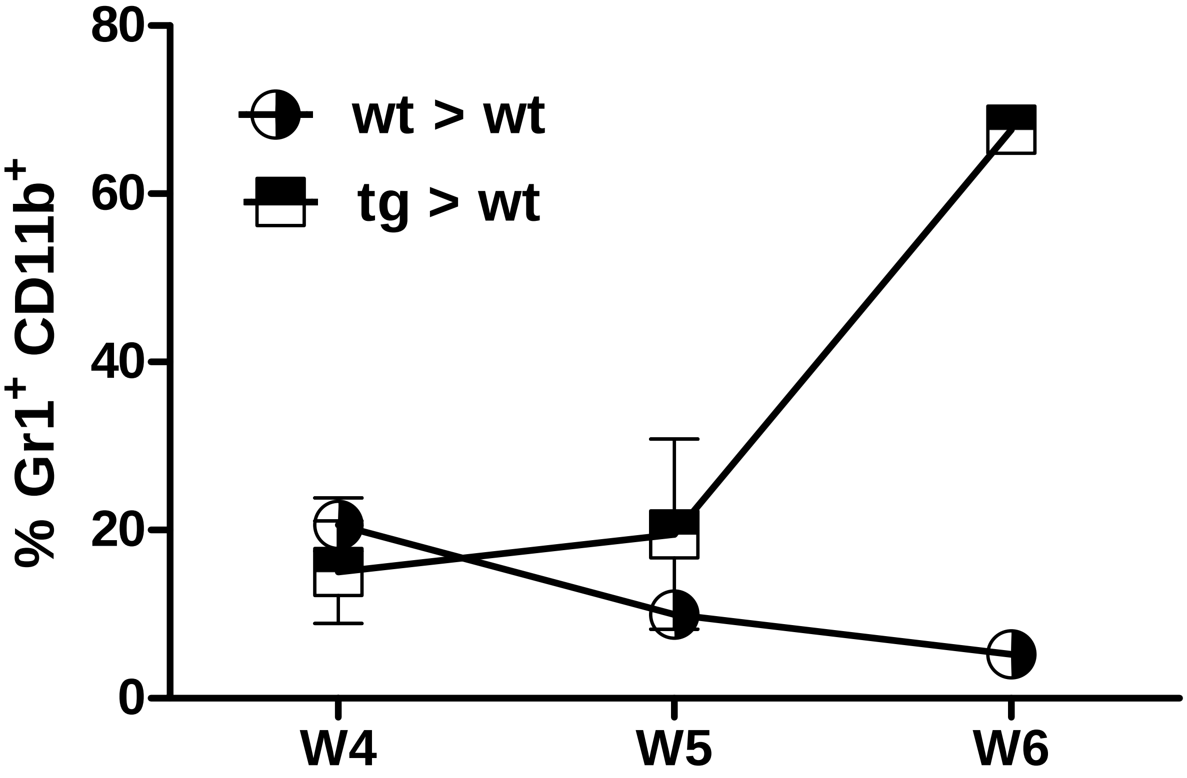
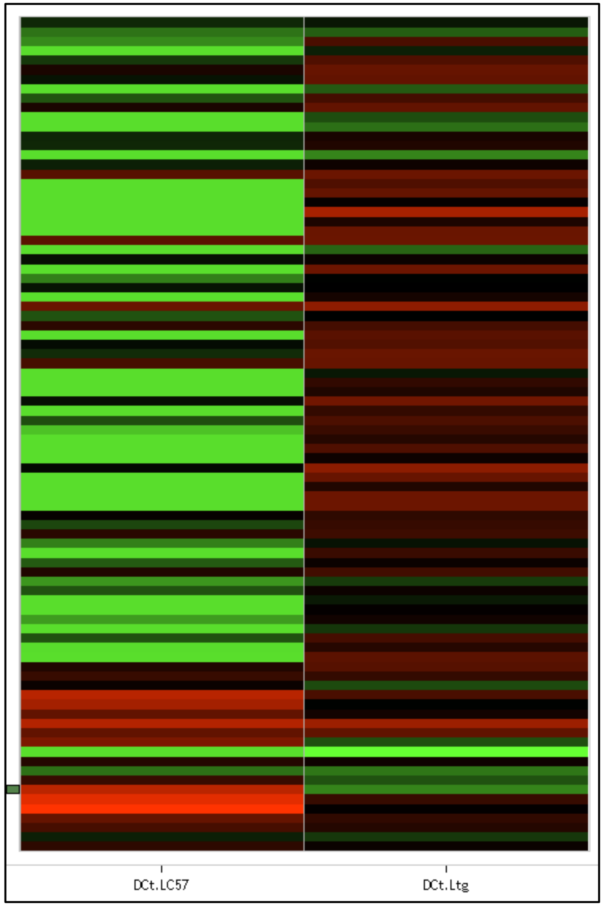


Figure S4

a) Heatmap



b) Genes upregulated

Detector	Log10 RQ	Detector	Log10 RQ
CD3g	5.442065416	IL-12rb1	2.762808146
IFN-g	5.439988309	Ccl20	2.535891735
CD3d	5.43568358	IL-6ra	2.5104547
S1pr1	5.386766206	Stat6	2.483964061
IL-1b	5.15638795	Icam1	2.44913489
CD3e	5.128994221	Ccl2	2.435076789
Nfkb1	4.961079689	**IL-17f**	2.389591157
ICOS	4.960628144	Socs1	2.233627516
IL-18	4.598489059	IL-4	2.167611638
CD28	4.501075753	Ccl7	2.132361026
Traf6	4.469256882	IL-12rb2	2.041811203
Stat3	4.284304053	Nfatc2	2.040998422
Mmp9	4.248782513	IL-3	2.014869018
Cxcl2	4.198149268	CD8a	1.933109272
IL-10	4.178010361	IL-13	1.824377237
TNF	4.140742848	**IL-22**	1.810499754
Myd88	4.12310249	Ccl22	1.674163269
Csf2	4.020752292	Syk	1.565310823
IL-27	3.893296191	CD34	1.546044903
Tlr4	3.768790185	CSF3	1.489330852
IL-6	3.733690088	**IL-17a**	1.485146535
TGF-b1	3.488501156	**Cxcl1**	1.339718944
Ccl1	3.271759559	CD2	1.244111818
IL-21	3.237562552	CD247	1.189354461
IL-2	3.142617691	Clec7a	1.177855116
Tbx21	2.842611198	CD4	1.019874574

c) Genes downregulated

Detector	Log10 RQ
IL-17d	-5.239442
Rorc	-4.110941
IL-5	-3.346355
Tirap	-2.827891
Mmp13	-2.73123
IL-23a	-2.255663
Jak2	-1.817423
IL-17rb	-1.421178
Gata3	-1.295528

Figure S5

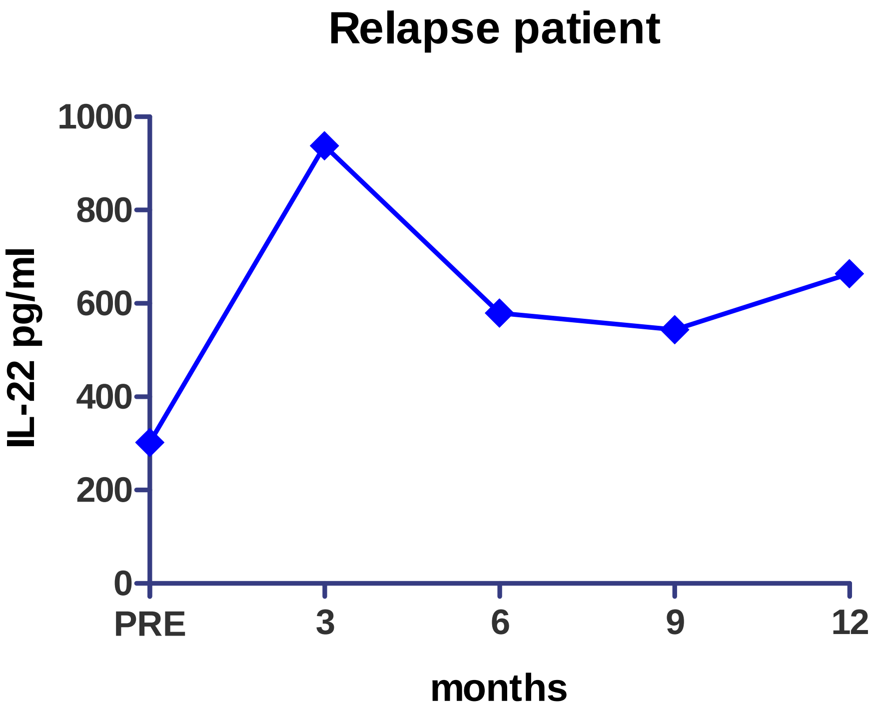
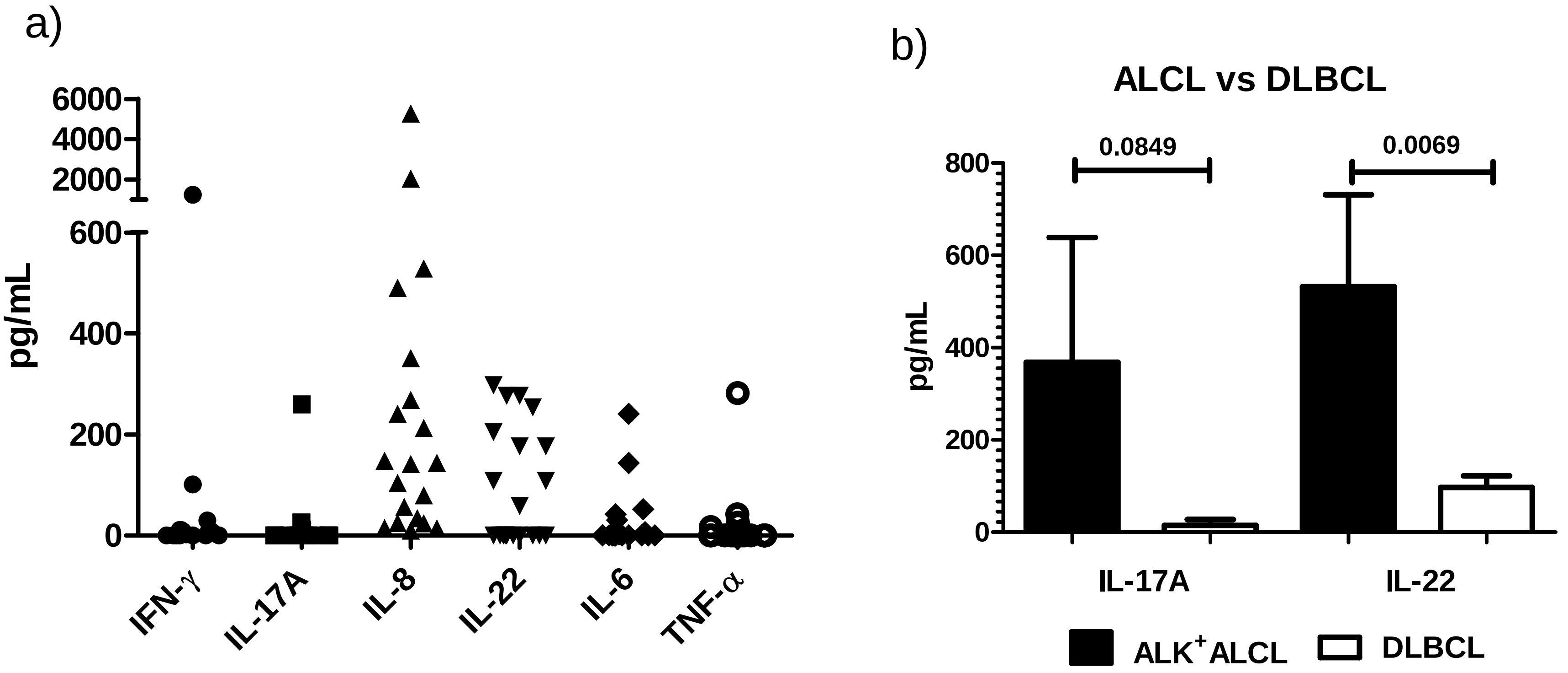

Relapse patient
1000
800
600
400
200
0
IL-22 pg/ml
PRE
3
6
9
12
months

Figure S6


a)
6000
4000
2000
600
400
200
0
pg/mL
IFN-γ
IL-17A
IL-8
IL-22
IL-6
TNF-α
b)
ALCL vs DLBCL
800
600
400
200
0
pg/mL
0.0849
0.0069
IL-17A
IL-22
ALK⁺ALCL
DLBCL