Figure S1

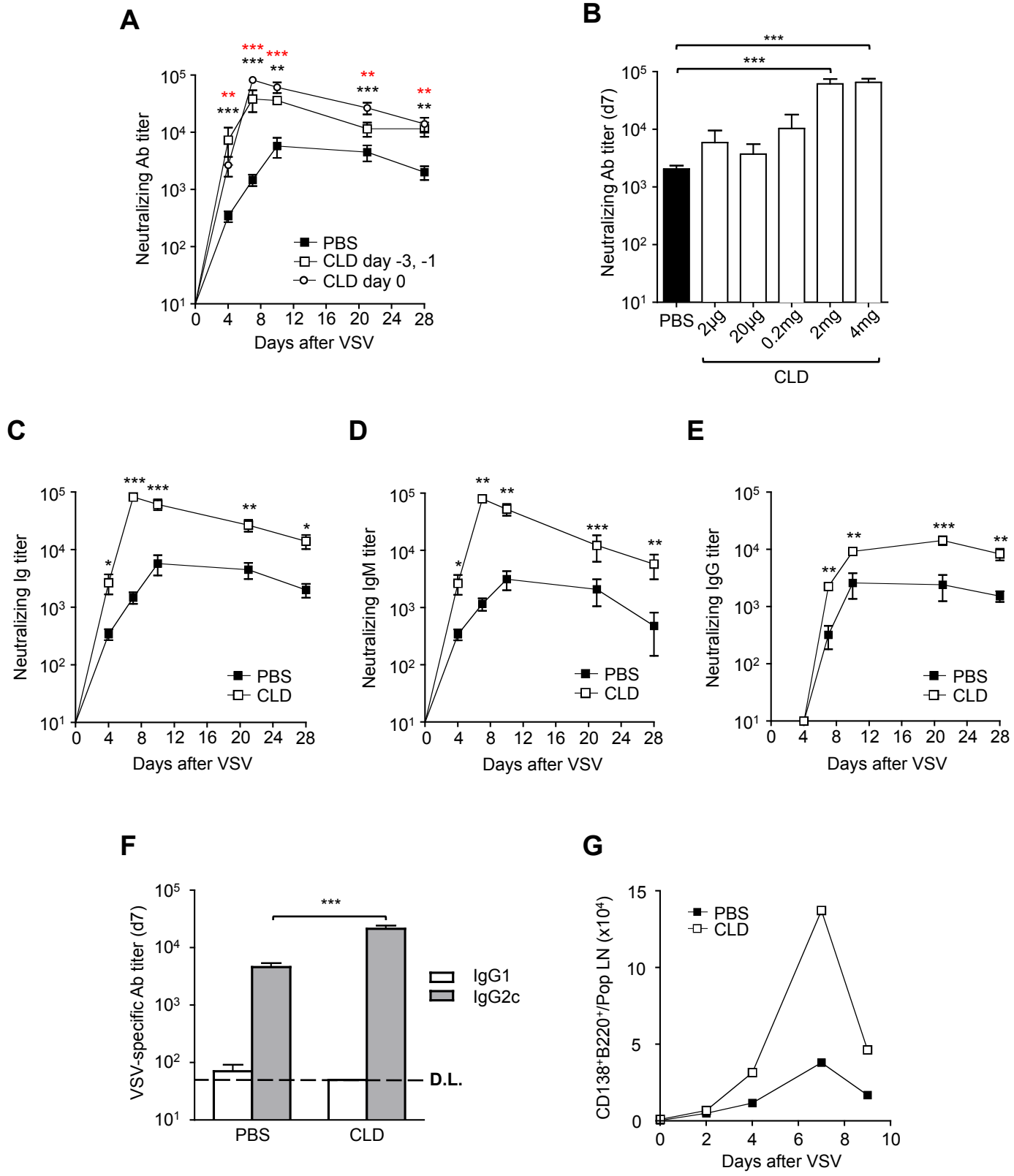

A
Neutralizing Ab titer
Days after VSV
PBS
CLD day -3, -1
CLD day 0
B
Neutralizing Ab titer (d7)
PBS
2µg
20µg
0.2mg
2mg
4mg
CLD
C
Neutralizing Ig titer
Days after VSV
PBS
CLD
D
Neutralizing IgM titer
Days after VSV
PBS
CLD
E
Neutralizing IgG titer
Days after VSV
PBS
CLD
F
VSV-specific Ab titer (d7)
IgG1
IgG2c
D.L.
PBS
CLD
G
CD138+B220+/Pop LN (x10^4)
Days after VSV
PBS
CLD

Figure S2

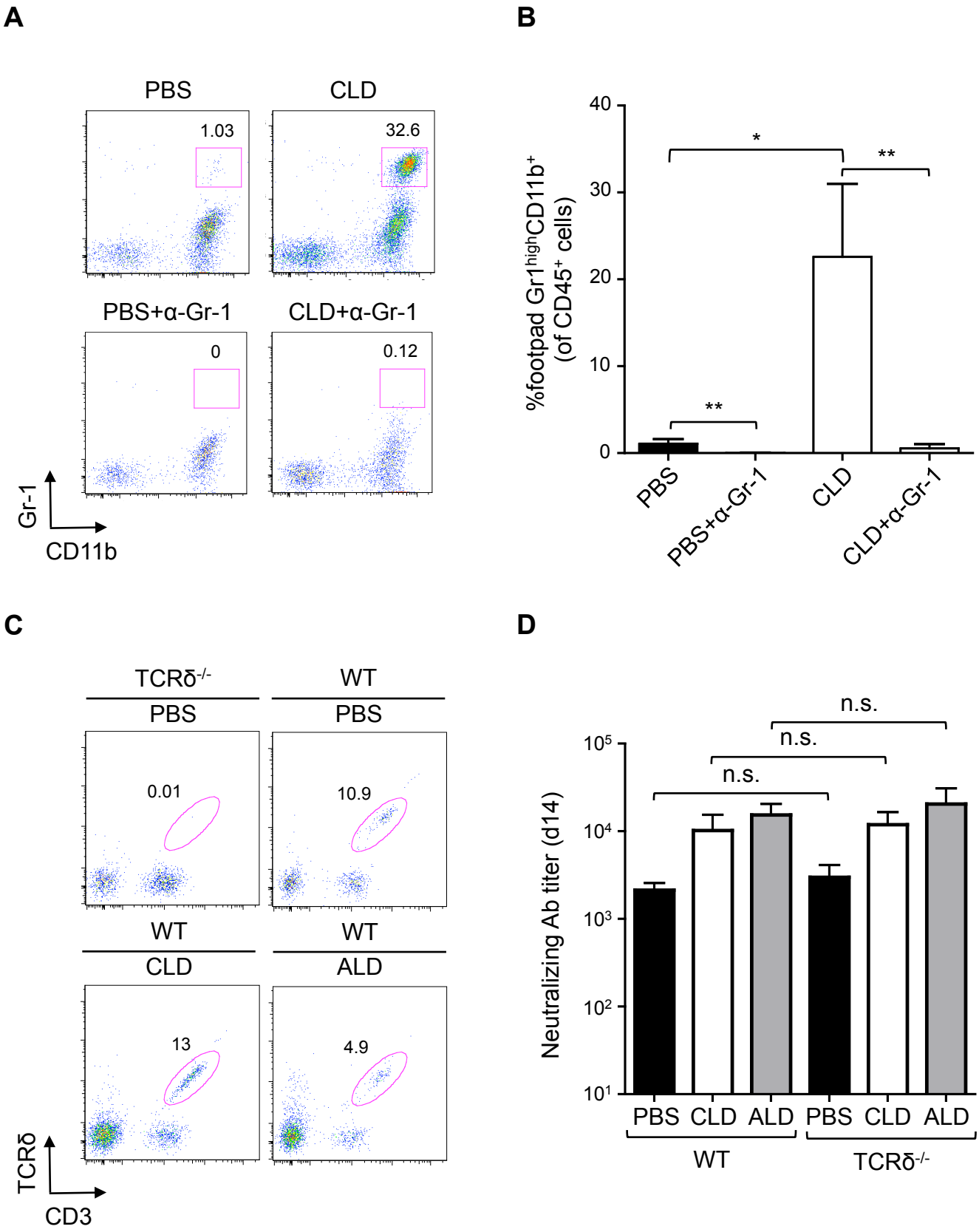

A
PBS
CLD
1.03
32.6
PBS+α-Gr-1
CLD+α-Gr-1
0
0.12
Gr-1
CD11b
B
%footpad Gr1highCD11b+ (of CD45+ cells)
40
30
20
10
0
*
**
**
PBS
PBS+α-Gr-1
CLD
CLD+α-Gr-1
C
TCRδ-/-
WT
PBS
PBS
0.01
10.9
WT
WT
CLD
ALD
13
4.9
TCRδ
CD3
D
Neutralizing Ab titer (d14)
10^5
10^4
10^3
10^2
10^1
n.s.
n.s.
n.s.
PBS CLD ALD PBS CLD ALD
WT
TCRδ-/-

Figure S3

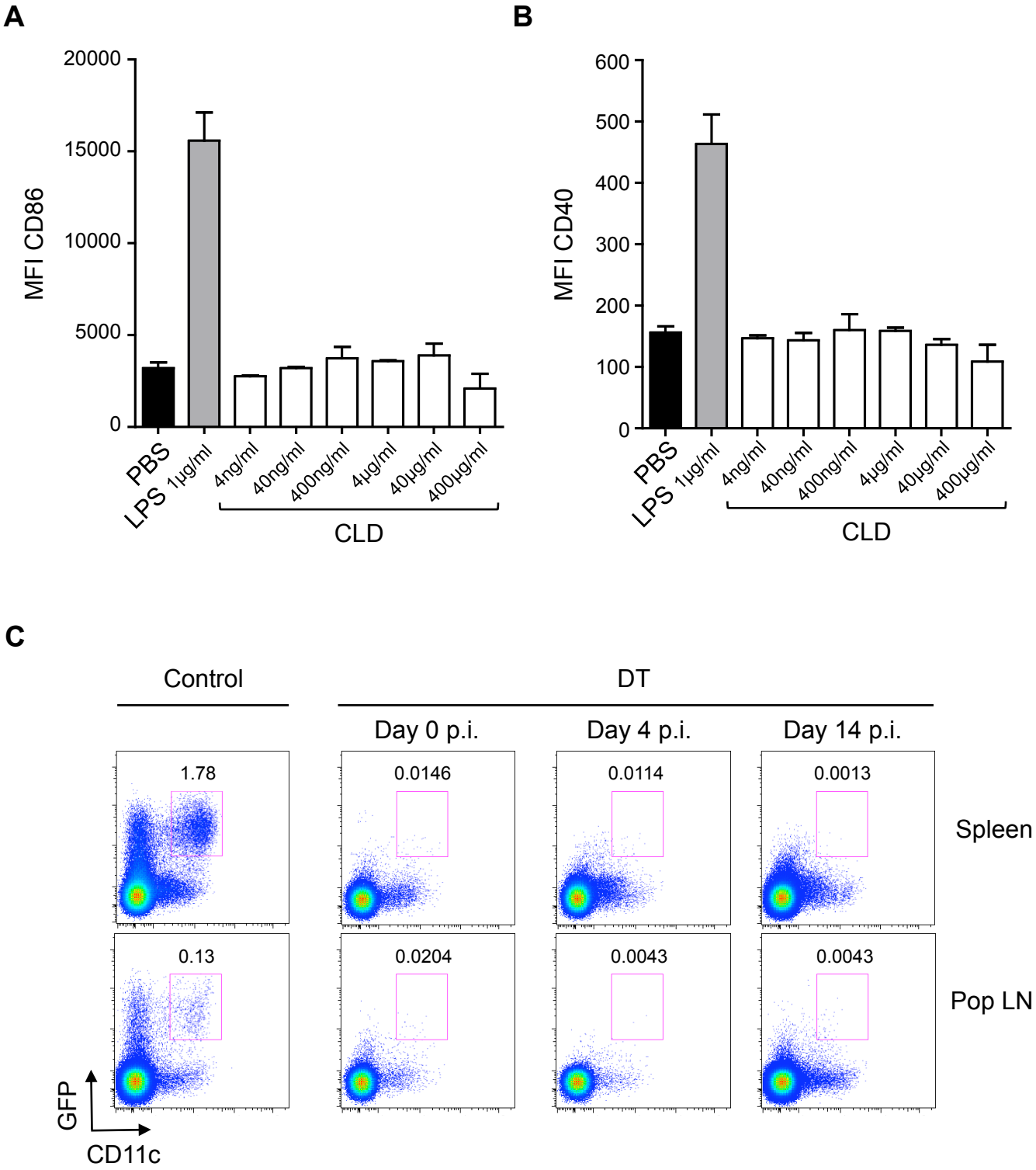

A
MFI CD86
20000
15000
10000
5000
0
PBS
LPS 1µg/ml
4ng/ml
40ng/ml
400ng/ml
4µg/ml
40µg/ml
400µg/ml
CLD
B
MFI CD40
600
500
400
300
200
100
0
PBS
LPS 1µg/ml
4ng/ml
40ng/ml
400ng/ml
4µg/ml
40µg/ml
400µg/ml
CLD
C
Control
DT
Day 0 p.i.
Day 4 p.i.
Day 14 p.i.
1.78
0.0146
0.0114
0.0013
Spleen
0.13
0.0204
0.0043
0.0043
Pop LN
GFP
CD11c

Figure S4

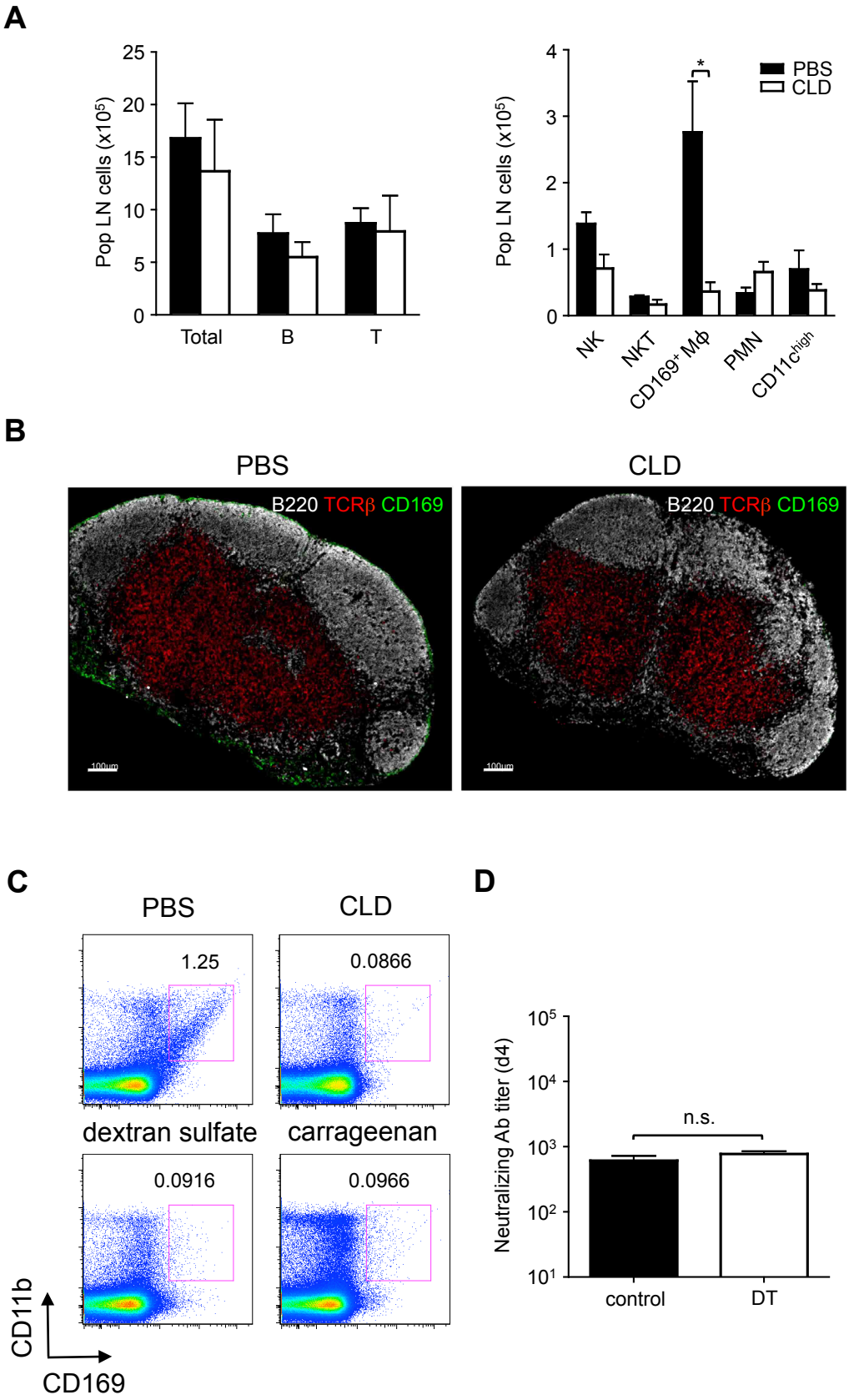

A
Pop LN cells (x10^5)
25
20
15
10
5
0
Total
B
T
Pop LN cells (x10^5)
4
3
2
1
0
*
PBS
CLD
NK
NKT
CD169+ Mφ
PMN
CD11c^high
B
PBS
CLD
B220 TCRβ CD169
B220 TCRβ CD169
100μm
100μm
C
PBS
CLD
1.25
0.0866
dextran sulfate
carrageenan
0.0916
0.0966
CD11b
CD169
D
Neutralizing Ab titer (d4)
10^5
10^4
10^3
10^2
10^1
n.s.
control
DT

Figure S5

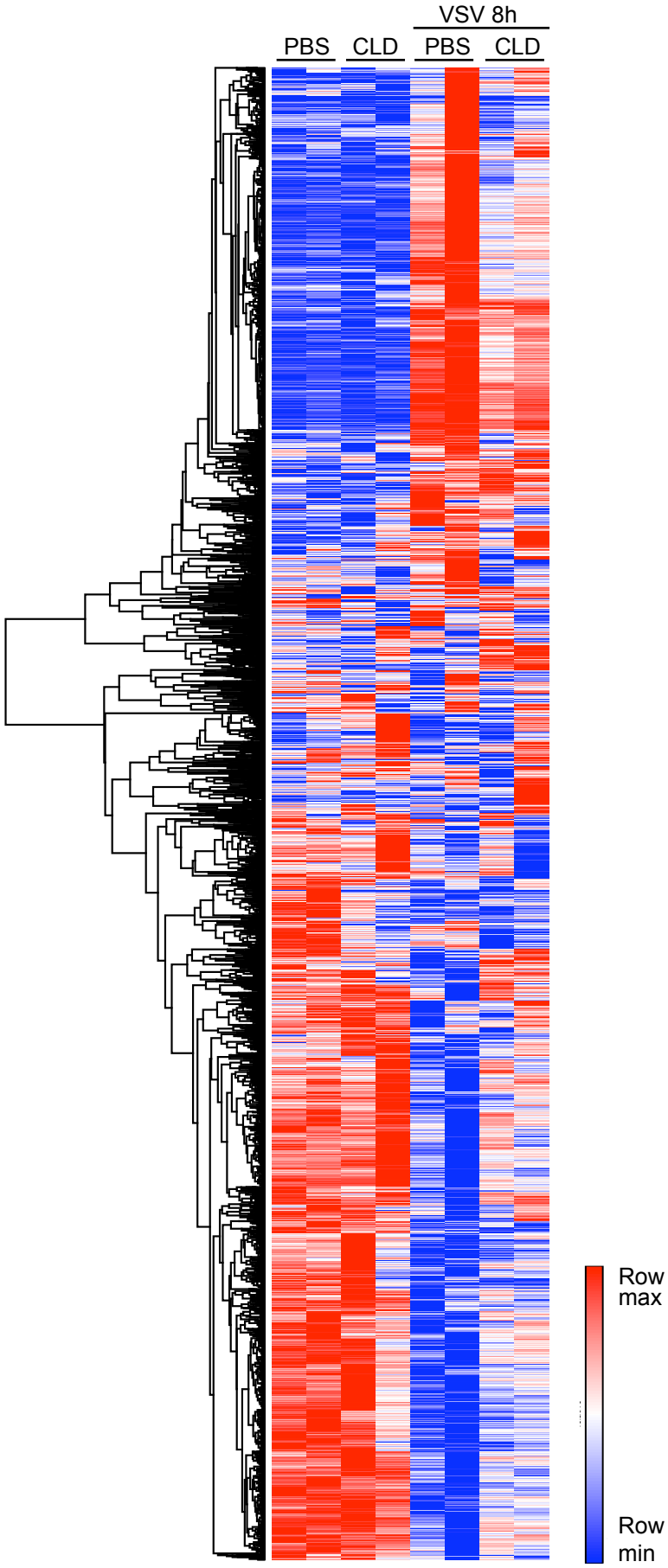


Figure S6

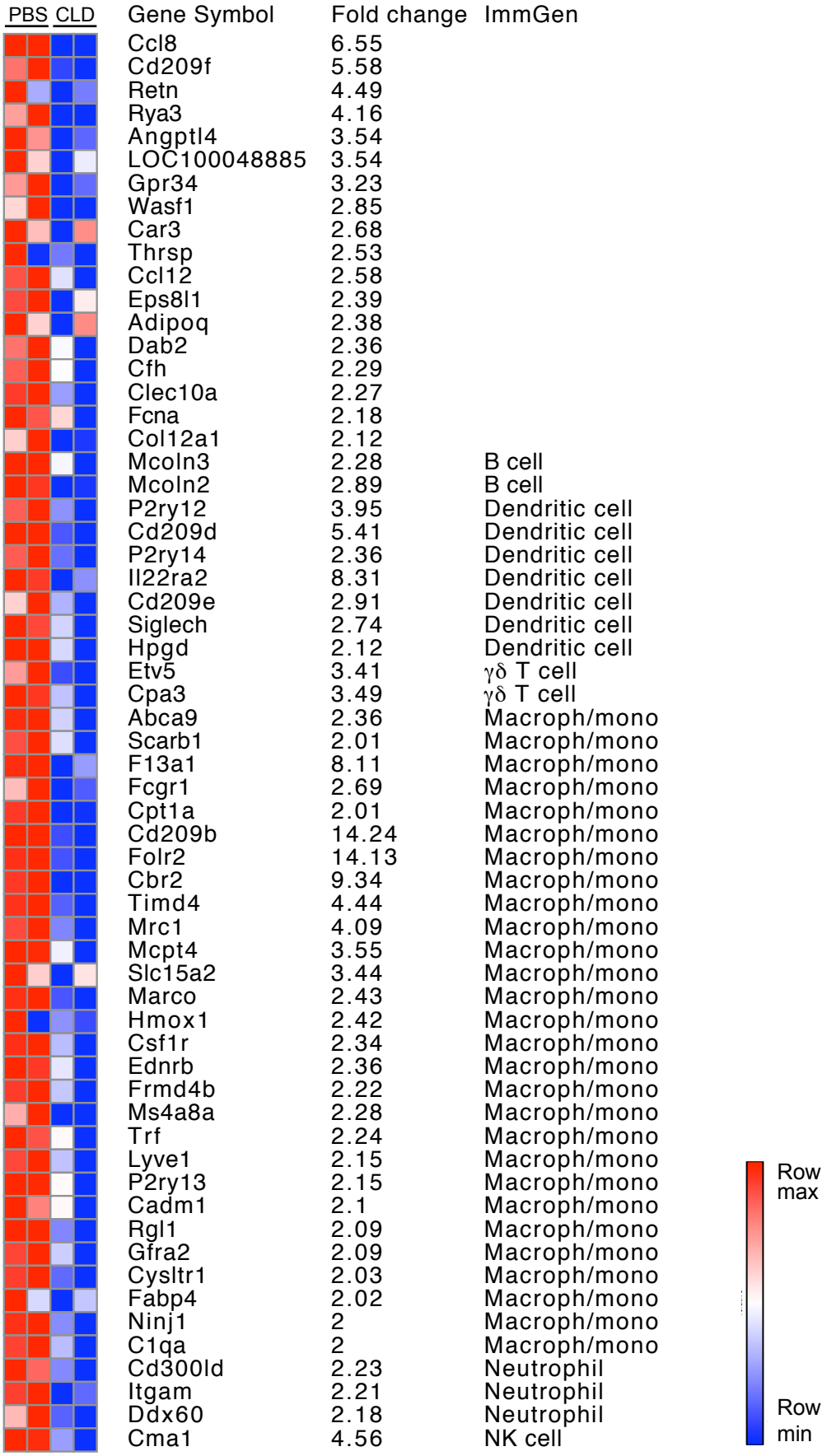

PBS CLD
Gene Symbol
Fold change
ImmGen
Ccl8 6.55
Cd209f 5.58
Retn 4.49
Rya3 4.16
Angptl4 3.54
LOC100048885 3.54
Gpr34 3.23
Wasf1 2.85
Car3 2.68
Thrsp 2.53
Ccl12 2.58
Eps8l1 2.39
Adipoq 2.38
Dab2 2.36
Cfh 2.29
Clec10a 2.27
Fcna 2.18
Col12a1 2.12
Mcoln3 2.28 B cell
Mcoln2 2.89 B cell
P2ry12 3.95 Dendritic cell
Cd209d 5.41 Dendritic cell
P2ry14 2.36 Dendritic cell
Il22ra2 8.31 Dendritic cell
Cd209e 2.91 Dendritic cell
Siglech 2.74 Dendritic cell
Hpgd 2.12 Dendritic cell
Etv5 3.41 γδ T cell
Cpa3 3.49 γδ T cell
Abca9 2.36 Macroph/mono
Scarb1 2.01 Macroph/mono
F13a1 8.11 Macroph/mono
Fcgr1 2.69 Macroph/mono
Cpt1a 2.01 Macroph/mono
Cd209b 14.24 Macroph/mono
Folr2 14.13 Macroph/mono
Cbr2 9.34 Macroph/mono
Timd4 4.44 Macroph/mono
Mrc1 4.09 Macroph/mono
Mcpt4 3.55 Macroph/mono
Slc15a2 3.44 Macroph/mono
Marco 2.43 Macroph/mono
Hmox1 2.42 Macroph/mono
Csf1r 2.34 Macroph/mono
Ednrb 2.36 Macroph/mono
Frmd4b 2.22 Macroph/mono
Ms4a8a 2.28 Macroph/mono
Trf 2.24 Macroph/mono
Lyve1 2.15 Macroph/mono
P2ry13 2.15 Macroph/mono
Cadm1 2.1 Macroph/mono
Rgl1 2.09 Macroph/mono
Gfra2 2.09 Macroph/mono
Cysltr1 2.03 Macroph/mono
Fabp4 2.02 Macroph/mono
Ninj1 2 Macroph/mono
C1qa 2 Macroph/mono
Cd300ld 2.23 Neutrophil
Itgam 2.21 Neutrophil
Ddx60 2.18 Neutrophil
Cma1 4.56 NK cell
Row max
Row min

Figure S7

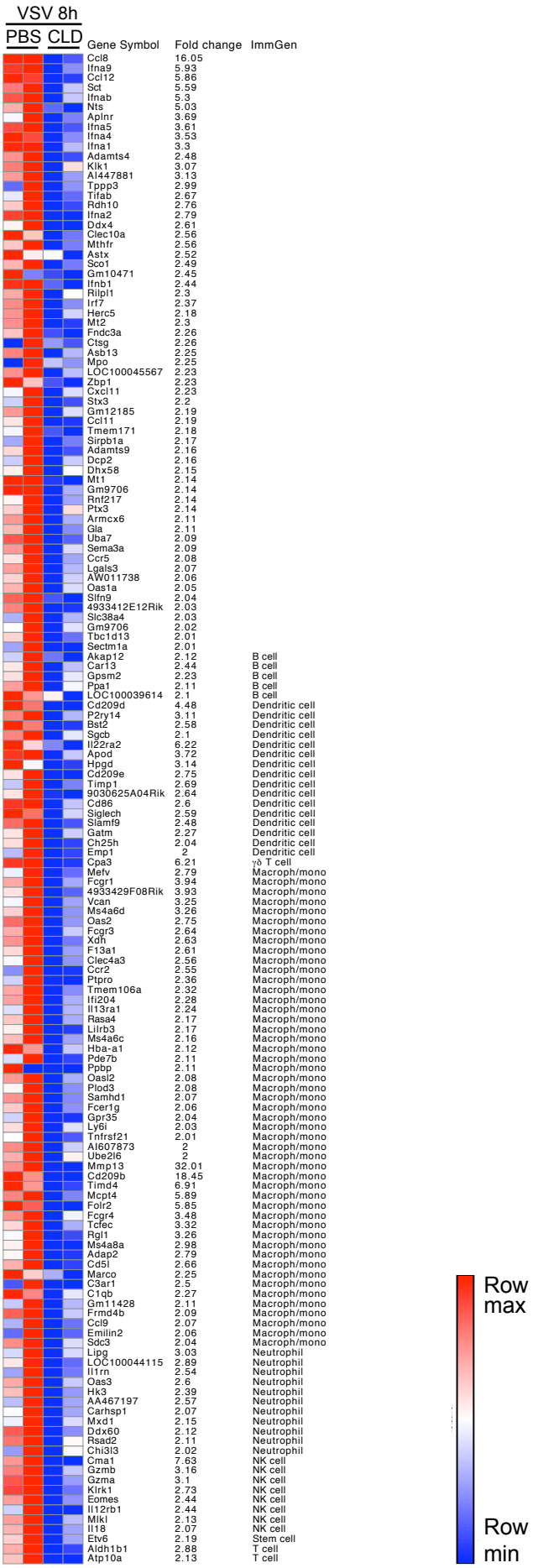

VSV 8h
PBS CLD
Gene Symbol Fold change ImmGen
Ccl8 16.05
Ifna9 5.93
Ccl12 5.86
Sct 5.59
Ifnab 5.3
Nts 5.03
Aplnr 3.69
Ifna5 3.61
Ifna4 3.53
Ifna1 3.3
Adamts4 2.48
Klk1 3.07
AI447881 3.13
Tppp3 2.99
Tifab 2.67
Rdh10 2.76
Ifna2 2.79
Ddx4 2.61
Clec10a 2.56
Mthfr 2.56
Astx 2.52
Sco1 2.49
Gm10471 2.45
Ifnb1 2.44
Rilpl1 2.3
Irf7 2.37
Herc5 2.18
Mt2 2.3
Fndc3a 2.26
Ctsg 2.26
Asb13 2.25
Mpo 2.25
LOC100045567 2.23
Zbp1 2.23
Cxcl11 2.23
Stx3 2.2
Gm12185 2.19
Ccl11 2.19
Tmem171 2.18
Sirpb1a 2.17
Adamts9 2.16
Dcp2 2.16
Dhx58 2.15
Mt1 2.14
Gm9706 2.14
Rnf217 2.14
Ptx3 2.14
Armcx6 2.11
Gla 2.11
Uba7 2.09
Sema3a 2.09
Ccr5 2.08
Lgals3 2.07
AW011738 2.06
Oas1a 2.05
Slfn9 2.04
4933412E12Rik 2.03
Slc38a4 2.03
Gm9706 2.02
Tbc1d13 2.01
Sectm1a 2.01
Akap12 2.12 B cell
Car13 2.44 B cell
Gpsm2 2.23 B cell
Ppa1 2.11 B cell
LOC100039614 2.1 B cell
Cd209d 4.48 Dendritic cell
P2ry14 3.11 Dendritic cell
Bst2 2.58 Dendritic cell
Sgcb 2.1 Dendritic cell
Il22ra2 6.22 Dendritic cell
Apod 3.72 Dendritic cell
Hpgd 3.14 Dendritic cell
Cd209e 2.75 Dendritic cell
Timp1 2.69 Dendritic cell
9030625A04Rik 2.64 Dendritic cell
Cd86 2.6 Dendritic cell
Siglech 2.59 Dendritic cell
Slamf9 2.48 Dendritic cell
Gatm 2.27 Dendritic cell
Ch25h 2.04 Dendritic cell
Emp1 2 Dendritic cell
Cpa3 6.21 γδ T cell
Mefv 2.79 Macroph/mono
Fcgr1 3.94 Macroph/mono
4933429F08Rik 3.93 Macroph/mono
Vcan 3.25 Macroph/mono
Ms4a6d 3.26 Macroph/mono
Oas2 2.75 Macroph/mono
Fcgr3 2.64 Macroph/mono
Xdh 2.63 Macroph/mono
F13a1 2.61 Macroph/mono
Clec4a3 2.56 Macroph/mono
Ccr2 2.55 Macroph/mono
Ptpro 2.36 Macroph/mono
Tmem106a 2.32 Macroph/mono
Ifi204 2.28 Macroph/mono
Il13ra1 2.24 Macroph/mono
Rasa4 2.17 Macroph/mono
Lilrb3 2.17 Macroph/mono
Ms4a6c 2.16 Macroph/mono
Hba-a1 2.12 Macroph/mono
Pde7b 2.11 Macroph/mono
Ppbp 2.11 Macroph/mono
Oasl2 2.08 Macroph/mono
Plod3 2.08 Macroph/mono
Samhd1 2.07 Macroph/mono
Fcer1g 2.06 Macroph/mono
Gpr35 2.04 Macroph/mono
Ly6i 2.03 Macroph/mono
Tnfrsf21 2.01 Macroph/mono
AI607873 2 Macroph/mono
Ube2l6 2 Macroph/mono
Mmp13 32.01 Macroph/mono
Cd209b 18.45 Macroph/mono
Timd4 6.91 Macroph/mono
Mcpt4 5.89 Macroph/mono
Folr2 5.85 Macroph/mono
Fcgr4 3.48 Macroph/mono
Tcfec 3.32 Macroph/mono
Rgl1 3.26 Macroph/mono
Ms4a8a 2.98 Macroph/mono
Adap2 2.79 Macroph/mono
Cd5l 2.66 Macroph/mono
Marco 2.25 Macroph/mono
C3ar1 2.5 Macroph/mono
C1qb 2.27 Macroph/mono
Gm11428 2.11 Macroph/mono
Frmd4b 2.09 Macroph/mono
Ccl9 2.07 Macroph/mono
Emilin2 2.06 Macroph/mono
Sdc3 2.04 Macroph/mono
Lipg 3.03 Neutrophil
LOC100044115 2.89 Neutrophil
Il1rn 2.54 Neutrophil
Oas3 2.6 Neutrophil
Hk3 2.39 Neutrophil
AA467197 2.57 Neutrophil
Carhsp1 2.07 Neutrophil
Mxd1 2.15 Neutrophil
Ddx60 2.12 Neutrophil
Rsad2 2.11 Neutrophil
Chi3l3 2.02 Neutrophil
Cma1 7.63 NK cell
Gzmb 3.16 NK cell
Gzma 3.1 NK cell
Klrk1 2.73 NK cell
Eomes 2.44 NK cell
Il12rb1 2.44 NK cell
Mlkl 2.13 NK cell
Il18 2.07 NK cell
Etv6 2.19 Stem cell
Aldh1b1 2.88 T cell
Atp10a 2.13 T cell
Row max
Row min

Figure S8

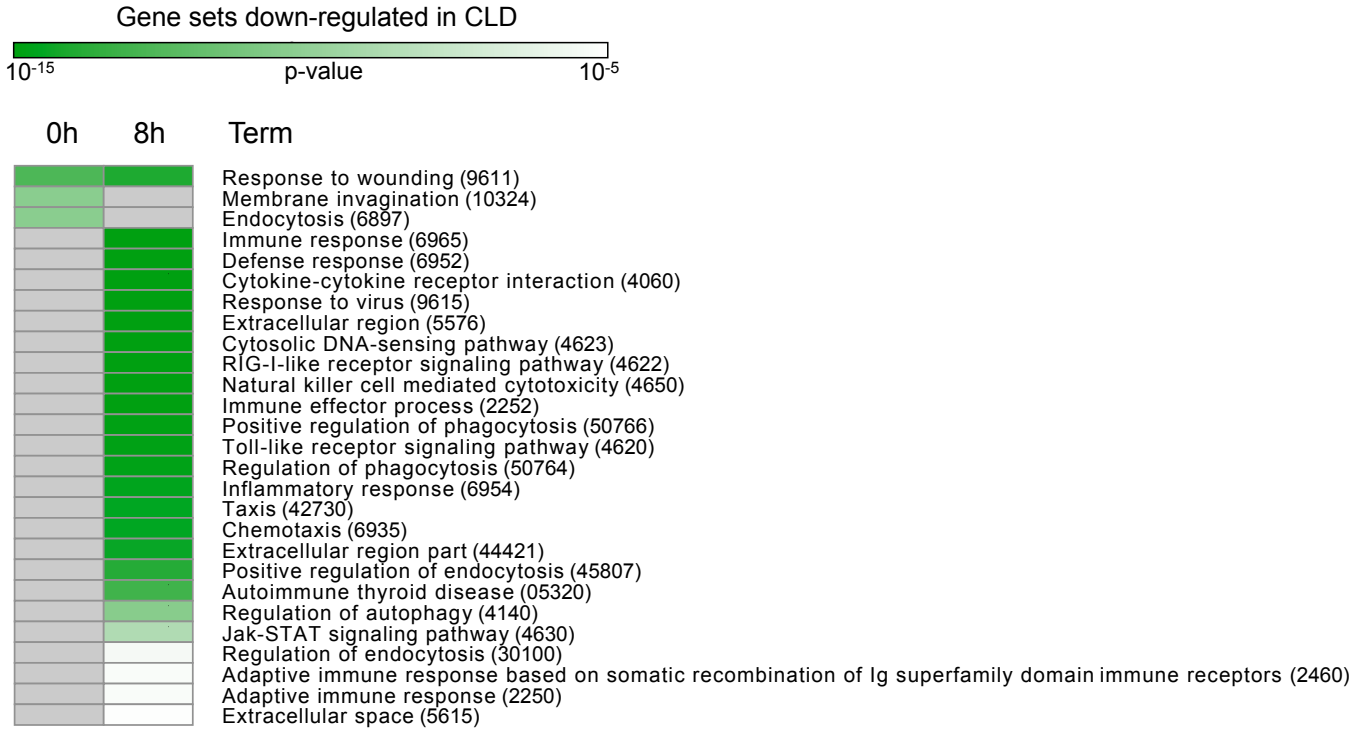
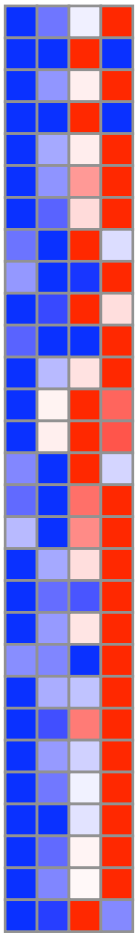

Gene sets down-regulated in CLD
10-15
p-value
10-5
0h
8h
Term
Response to wounding (9611)
Membrane invagination (10324)
Endocytosis (6897)
Immune response (6965)
Defense response (6952)
Cytokine-cytokine receptor interaction (4060)
Response to virus (9615)
Extracellular region (5576)
Cytosolic DNA-sensing pathway (4623)
RIG-I-like receptor signaling pathway (4622)
Natural killer cell mediated cytotoxicity (4650)
Immune effector process (2252)
Positive regulation of phagocytosis (50766)
Toll-like receptor signaling pathway (4620)
Regulation of phagocytosis (50764)
Inflammatory response (6954)
Taxis (42730)
Chemotaxis (6935)
Extracellular region part (44421)
Positive regulation of endocytosis (45807)
Autoimmune thyroid disease (05320)
Regulation of autophagy (4140)
Jak-STAT signaling pathway (4630)
Regulation of endocytosis (30100)
Adaptive immune response based on somatic recombination of Ig superfamily domain immune receptors (2460)
Adaptive immune response (2250)
Extracellular space (5615)

Figure S9



Gene Symbol	Fold change	ImmGen
Fpr2	2.38	
Slc4a1	2.44	
Camp	3.03	
Ahsp	3.45	
Ltf	4	
Rrm2	2.13	B cell
Ccnb1	2.08	B cell
Hbb-b1	3.45	B cell
Igh-6	2.08	B cell
Igkv14-111	2.27	B cell
Ighg1	2.56	B cell
Ngp	2.78	B cell
Igh-3	5.56	B cell
Ighg	6.25	B cell
Hba-a1	2.78	Macroph/mono
Ppbp	3.57	Macroph/mono
Slpi	2.33	Neutrophil
S100a8	2	Neutrophil
Stfa2l1	2.04	Neutrophil
S100a9	2.04	Neutrophil
Slfn4	2.17	Neutrophil
Trem3	2.22	Neutrophil
Mmp9	3.23	Neutrophil
1100001G20Rik	3.13	Neutrophil
Ifitm6	3.57	Neutrophil
Cd177	3.57	Neutrophil
Lcn2	3.85	Neutrophil
Mmp8	5	Neutrophil
Car2	3.13	Stem cell

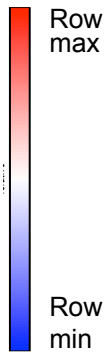
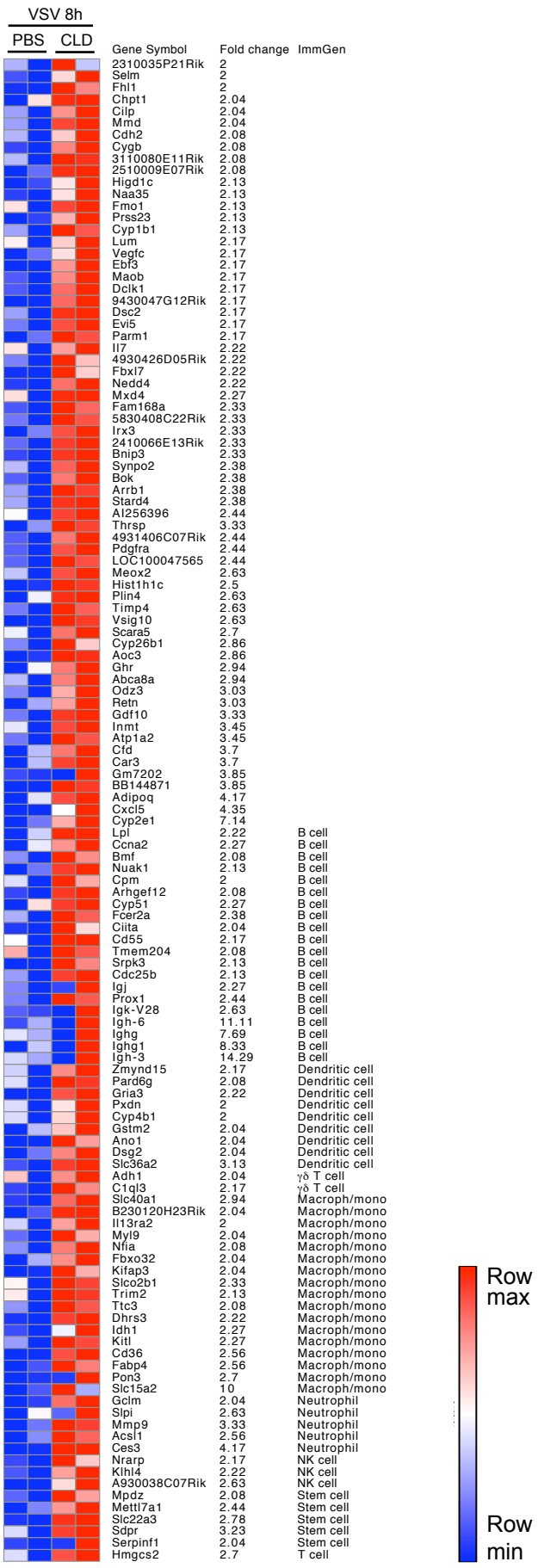


Figure S10


VSV 8h
PBS
CLD
Gene Symbol
Fold change
ImmGen
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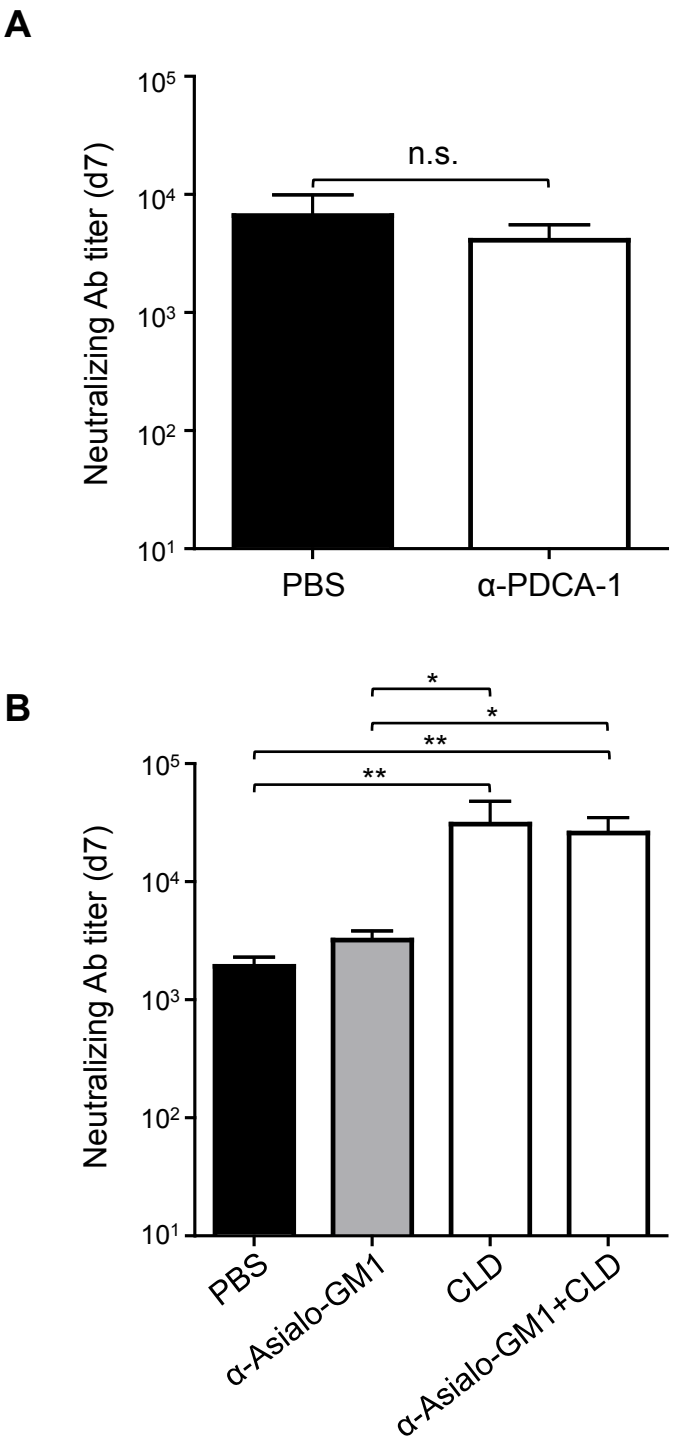
Selm 2
Fhl1 2
Chpt1 2.04
Cilp 2.04
Mmd 2.04
Cdh2 2.08
Cygb 2.08
3110080E11Rik 2.08
2510009E07Rik 2.08
Higd1c 2.13
Naa35 2.13
Fmo1 2.13
Prss23 2.13
Cyp1b1 2.13
Lum 2.17
Vegfc 2.17
Ebf3 2.17
Maob 2.17
Dclk1 2.17
9430047G12Rik 2.17
Dsc2 2.17
Evi5 2.17
Parm1 2.17
Il7 2.22
4930426D05Rik 2.22
Fbxl7 2.22
Nedd4 2.22
Mxd4 2.27
Fam168a 2.33
5830408C22Rik 2.33
Irx3 2.33
2410066E13Rik 2.33
Bnip3 2.33
Synpo2 2.38
Bok 2.38
Arrb1 2.38
Stard4 2.38
AI256396 2.44
Thrsp 3.33
4931406C07Rik 2.44
Pdgfra 2.44
LOC100047565 2.44
Meox2 2.63
Hist1h1c 2.5
Plin4 2.63
Timp4 2.63
Vsig10 2.63
Scara5 2.7
Cyp26b1 2.86
Aoc3 2.86
Ghr 2.94
Abca8a 2.94
Odz3 3.03
Retn 3.03
Gdf10 3.33
Inmt 3.45
Atp1a2 3.45
Cfd 3.7
Car3 3.7
Gm7202 3.85
BB144871 3.85
Adipoq 4.17
Cxcl5 4.35
Cyp2e1 7.14
Lpl 2.22 B cell
Ccna2 2.27 B cell
Bmf 2.08 B cell
Nuak1 2.13 B cell
Cpm 2 B cell
Arhgef12 2.08 B cell
Cyp51 2.27 B cell
Fcer2a 2.38 B cell
Ciita 2.04 B cell
Cd55 2.17 B cell
Tmem204 2.08 B cell
Srpk3 2.13 B cell
Cdc25b 2.13 B cell
Igj 2.27 B cell
Prox1 2.44 B cell
Igk-V28 2.63 B cell
Igh-6 11.11 B cell
Ighg 7.69 B cell
Ighg1 8.33 B cell
Igh-3 14.29 B cell
Zmynd15 2.17 Dendritic cell
Pard6g 2.08 Dendritic cell
Gria3 2.22 Dendritic cell
Pxdn 2 Dendritic cell
Cyp4b1 2 Dendritic cell
Gstm2 2.04 Dendritic cell
Ano1 2.04 Dendritic cell
Dsg2 2.04 Dendritic cell
Slc36a2 3.13 Dendritic cell
Adh1 2.04 γδ T cell
C1ql3 2.17 γδ T cell
Slc40a1 2.94 Macroph/mono
B230120H23Rik 2.04 Macroph/mono
Il13ra2 2 Macroph/mono
Myl9 2.04 Macroph/mono
Nfia 2.08 Macroph/mono
Fbxo32 2.04 Macroph/mono
Kifap3 2.04 Macroph/mono
Slco2b1 2.33 Macroph/mono
Trim2 2.13 Macroph/mono
Ttc3 2.08 Macroph/mono
Dhrs3 2.22 Macroph/mono
Idh1 2.27 Macroph/mono
Kitl 2.27 Macroph/mono
Cd36 2.56 Macroph/mono
Fabp4 2.56 Macroph/mono
Pon3 2.7 Macroph/mono
Slc15a2 10 Macroph/mono
Gclm 2.04 Neutrophil
Slpi 2.63 Neutrophil
Mmp9 3.33 Neutrophil
Acsl1 2.56 Neutrophil
Ces3 4.17 Neutrophil
Nrarp 2.17 NK cell
Klhl4 2.22 NK cell
A930038C07Rik 2.63 NK cell
Mpdz 2.08 Stem cell
Mettl7a1 2.44 Stem cell
Slc22a3 2.78 Stem cell
Sdpr 3.23 Stem cell
Serpinf1 2.04 Stem cell
Hmgcs2 2.7 T cell
Row max
Row min

Figure S11


A
Neutralizing Ab titer (d7)
10^5
10^4
10^3
10^2
10^1
n.s.
PBS
α-PDCA-1
B
Neutralizing Ab titer (d7)
*
*
**
**
PBS
α-Asialo-GM1
CLD
α-Asialo-GM1+CLD

Supplementary Figure Titles and Legends.

Figure S1. *Bisphosphonates Increase Antibody Responses to Live and Inactive Viruses, Proteins, Haptens and Existing Commercial Vaccine Formulations, Related to Figure 1*. (**a**) VSV nAb titers in the serum of C57BL/6 mice that were footpad injected with CLD 3 days and 1 day (day -3, -1) or immediately (day 0) prior to VSV infection in the same footpad. *n* = 5 per group. Black asterisks, PBS versus CLD day -3, -1; red asterisks PBS versus CLD day 0; results are representative of 3 independent experiments. (**b**) VSV nAb titers 7 days p.i. in the serum of C57BL/6 mice that were footpad injected with PBS or with the indicated doses of CLD prior to VSV infection in the same footpad. *n* = 5 per group; results are representative of 2 independent experiments. (**c**) VSV nAb titers in the serum of C57BL/6 mice that were footpad injected with PBS or CLD prior to infection in the same footpad with VSV. *n* = 5 per group; results are representative of 3 independent experiments. (**d**) Neutralizing IgM titers in the serum of the same mice described in (a). (**e**) Neutralizing IgG titers of the same mice described in (a). (**f**) VSV-specific IgG1 and IgG2c titers 7 day p.i. in the serum of C57BL/6 mice that were footpad injected with PBS or CLD prior to VSV infection in the same footpad. *n* = 5 per group; results are representative of 2 independent experiments. (**g**) Total number of $CD138^+$ cells recovered from draining popliteal lymph nodes (Pop LN) that were pooled from 3 C57BL/6 mice footpad injected with PBS or CLD prior to VSV infection in the same footpad. Results are representative of 2 independent experiments.
***: $P < 0.001$; **: $P < 0.01$; *: $P < 0.05$; D.L.: detection limit.

Figure S2. *Neutrophils and $\gamma\delta$ T Cells Are Not Required for Bisphosphonate Adjuvant Activity, Related to Figure 2C,D*. Representative FACS plots (**a**) and quantification (**b**) of the number of $Gr\text{-}1^{high}CD11b^+$ cells present in digested footpads from the mice described in Fig. 2c. Numbers show the percentages of $CD45^+$ cells within each gate. *n* = 4 per group; results are representative of 2 independent experiments. (**c**) Representative FACS plots of digested footpads from PBS-injected $TCR\delta^{-/-}$ mice or PBS-, CLD- or alendronate (ALD)-injected C57BL/6 (WT) mice. Numbers show the percentages of $CD45^+$ cells within each gate. Results are representative of 2 independent experiments (*n* = 3 per experiment). (**d**) VSV nAb titers 14 days p.i. in the serum of C57BL/6 (WT) or $TCR\delta^{-/-}$ mice that were footpad injected with PBS, CLD or ALD prior to VSV infection in the same footpad. *n* = 5 per group; results are representative of 3 independent experiments.
**: $P < 0.01$; *: $P < 0.05$; n.s.: non statistically significant

Figure S3. *Bisphosphonate Adjuvant Activity Does Not Require Conventional Dendritic Cells (DC), Related to Figure 2E*. CD86 (**a**) or CD40 (**b**) expression on purified $CD11c^+$ DC that were cultured in the presence of 1 μg/ml LPS or with the indicated concentrations of CLD for 48 h prior to flow cytometry analysis. (**c**) Representative FACS plots of digested spleens or popliteal lymph nodes (Pop LN) from CD11c-GFP-DTR → C57BL/6 bone marrow chimeric mice that were left untreated (control) or injected with diphtheria toxin (DT). Numbers show the percentage of cells within each gate. Results are representative of 2 independent experiments (*n* = 3 per experiment).

Figure S4*. Lymph Node Macrophage Depletion per se Does Not Increase Humoral Immune Responses, Related to Figure 2F*. (**a**) Cellular subset frequency in popliteal lymph nodes (Pop LN) from C57BL/6 mice that were treated with PBS or CLD. n = 3 per group; results are representative of 3 independent experiments. (**b**) Representative confocal micrographs of Pop LN from C57BL/6 mice that were treated with PBS or CLD. Sections were stained with anti-B220 (grey), anti-TCRβ (red) and anti-CD169 (green) to identify B cells, T cells and macrophages, respectively. Scale bars represent 100 μm. Results are representative of 2 independent experiments (*n* = 3 per experiment). (**c**) Representative FACS plots of digested popliteal lymph nodes from C57BL/6 mice that were treated with PBS, CLD, dextran sulfate or carrageenan. Numbers show the percentage of cells within each gate. Results are representative of 2 independent experiments (*n* = 3 per experiment). (**d**) VSV nAb titers 4 days p.i. in the serum of CD11c-GFP-DTR mice that were left untreated (control) or were depleted of $CD169^+$ LN macrophages through a single footpad injection of diphtheria toxin (DT) 6 days prior to VSV infection. These mice were described in Supplementary Figure 3 from ref. (Iannacone et al., 2010).
*: $P < 0.05$; n.s.: non statistically significant

Figure S5. *mRNA Expression Profiles of Differentially Expressed Genes in Whole Lymph Node, Related to Figure 3A*. Shown are expression profiles for 4761 differentially expressed genes (rows) at 0 and 8 hours after VSV infection in mice treated with CLD or PBS as control (columns). Shown are genes with at least a 2-fold change in expression between treatments in both duplicate arrays (each column corresponds to a replicate). Values from multiple probe sets targeting the same gene were collapsed and gene-expression profiles were hierarchically clustered.

Figure S6. *mRNA Expression Profiles of Genes Decreased upon CLD Treatment in Whole Lymph Node Before Infection, Related to Fig. 3A*. Shown are expression profiles for 62 differentially expressed genes (rows) with at least a 2-fold decrease in expression in CLD-treated mice compared to controls

(PBS). The right-most column indicates the cell types in which each gene is specifically expressed based on the Immunological Genome (ImmGen) database.

Figure S7. *mRNA Expression Profiles of Genes Decreased upon CLD Treatment in Whole Lymph Node After Infection, Related to Figure 3A*. Shown are expression profiles for 155 differentially expressed genes (rows) with at least a 2-fold decrease in expression in CLD-treated mice compared to controls (PBS) at 8 hours after VSV infection. The right-most column indicates the cell types in which each gene is specifically expressed based on the Immunological Genome (ImmGen) database.

Figure S8. *Gene Enrichment Analysis of CLD-Dependent Genes from Microarray Measurements of Whole Lymph Node, Related to Figure 3A*. Shown are the Gene Ontology (GO) terms and canonical pathways (KEGG database) (rows) statistically enriched among the 217 genes with at least a 2-fold decrease in expression at 0 and 8 hours (columns) after VSV infection in CLD-treated mice compared to control (PBS). Enriched GO term categories include BP: biological process, and CC: cellular component. Green: p value < 10^{-15}; white: p value < 10^{-4}; grey: no enrichment.

Figure S9. *mRNA Expression Profiles of Genes Increased upon CLD Treatment in Whole Lymph Node Before Infection, Related to Figure 3A*. Shown are expression profiles for 29 differentially expressed genes (rows) with at least a 2-fold increase in expression in CLD-treated mice compared to controls (PBS). The right-most column indicates the cell types in which each gene is specifically expressed based on the Immunological Genome (ImmGen) database.

Figure S10. *mRNA Expression Profiles of Genes Increased upon CLD Treatment in Whole Lymph Node After Infection, Related to Figure 3A*. Shown are expression profiles for 127 differentially expressed genes (rows) with at least a 2-fold increase in expression in CLD-treated mice compared to controls (PBS) at 8 hours after VSV infection. The right-most column indicates the cell types in which each gene is specifically expressed based on the Immunological Genome (ImmGen) database.

Figure S11. *CLD Increases Ab Responses Independently of pDCs or NK Cells, Related to Figure 3A.* (**a**) VSV nAb titers 7 days p.i. in the serum of C57BL/6 mice that received PBS or were depleted of pDCs via anti-PDCA-1 (α–PDCA1) injection 24 hours prior to VSV infection. These mice were described in Fig. 3j and Suppl. Fig. 8b from ref. (Iannacone et al., 2010). (**b**) VSV nAb titers 7 days p.i. in the serum of C57BL/6 mice that were injected (or not) with anti-Asialo-GM1 depleting Ab (α–Asialo-GM1, see Methods for details) and were subsequently footpad injected with PBS or CLD immediately

prior to VSV infection in the same footpad. n = 5; results are representative of 2 independent experiments.

**: $P < 0.01$; *: $P < 0.05$; n.s.: non statistically significant

Supplementary Table 1 Title and Legend.

Table S1. *List of Genes Differentially Regulated upon CLD Treatment, Related to Figure 3A.* List of 6869 probe sets with expression values > 40 after RMA normalization. Shown are normalized data for duplicate microarrays on whole popliteal lymph node from mice treated with PBS or CLD before (0h) and 8h after VSV infection.

Table S2. *Characteristics (Treatment, Gender, Age and Diagnosis) of Patients with Osteoporosis or Paget's Disease of Bone That Were Treated with Neridronate or Zoledronate, Related to Figure 3I,J*.

TREATMENT	GENDER	AGE	DIAGNOSIS
Neridronate 200 mg	Female	52	Paget's disease of bone
Neridronate 200 mg	Female	56	Paget's disease of bone
Neridronate 200 mg	Female	67	Paget's disease of bone
Neridronate 200 mg	Female	68	Paget's disease of bone
Neridronate 200 mg	Female	73	Paget's disease of bone
Neridronate 200 mg	Male	54	Paget's disease of bone
Neridronate 200 mg	Male	55	Paget's disease of bone
Neridronate 200 mg	Male	56	Paget's disease of bone
Neridronate 200 mg	Male	64	Paget's disease of bone
Neridronate 200 mg	Male	68	Paget's disease of bone
Neridronate 200 mg	Male	77	Paget's disease of bone
Zoledronate 5mg	Female	56	Osteoporosis
Zoledronate 5mg	Female	68	Osteoporosis
Zoledronate 5mg	Female	70	Osteoporosis
Zoledronate 5mg	Female	76	Osteoporosis
Zoledronate 5mg	Female	76	Osteoporosis
Zoledronate 5mg	Female	78	Osteoporosis
Zoledronate 5mg	Male	53	Paget's disease of bone
Zoledronate 5mg	Male	61	Paget's disease of bone
Zoledronate 5mg	Male	72	Paget's disease of bone