Figure S1. CTL activation and HLH-like phenotype in LCMV-infected C57BL/6J, Unc13d$^{jinx/jinx}$, and *Unc13d*$^{jinx/jinx}$; *Itgb2*$^{Joker/Joker}$ mice

7 days (A) and 12 days (B) following infection with the Armstrong strain of LCMV, splenocytes from mutant and wild type mice were stimulated *in vitro* for 5 hours in presence of the LCMV-derived GP33 peptide and brefeldin A, then stained for CD8α, CD3ε and intracellular IFNγ. Graphs represent percentages of LCMV GP33-specific IFNγ^{+}CD8^{+} T cells. Percentages of CD3ε^{+}CD8^{+} T cells in spleens of mutant and wild type mice (C), spontaneous production of IFNγ among CD8^{+} T cells as detected after a 5 hour incubation with brefeldin A (D), and surface expression of CD69 on CD8^{+} T cells (E) were measured at the indicated times after infection with LCMV. Blood samples were collected on day 12; hematocrit (F), lymphocytes (G), and neutrophils (H) were enumerated. Bars in graphs show the means. Dots represent individual mice. *jinx, Unc13d*$^{jinx/jinx}$ mice; *jinx*; *Joker, Unc13d*$^{jinx/jinx}$; *Itgb2*$^{Joker/Joker}$ double mutants.

Figure S2. Appearance of HLH-like disease in Unc13d$^{jinx/jinx}$, Unc13d$^{jinx/jinx}$; Tnf PanR1/PanR1, Unc13d$^{jinx/jinx}$; Ifngr$^{-/-}$ and wild type mice 12 days after LCMV infection

(A) Photographs of spleens of mutant and wild type mice. Spleen weights in gram are indicated (± SEM); n ≥ 3 per group of infected mice. Percentages of CD8^{+} T cells (B) and activated macrophages (C) in spleens of mutant and wild type mice. One representative experiment of 4 is shown for the analysis of *Unc13d*$^{jinx/jinx}$; *Ifngr*$^{-/-}$ (*jinx*; *Ifngr*$^{-/-}$) CD8^{+} T cells and macrophages. IFNγ (D) and TNF (E) concentrations in the sera of mutant and wild type mice were determined by ELISA on day 12 post infection; n ≥ 3 per group of infected mice. Serum IFNγ was also measured on day 7 post infection (F). Bars in graphs show the means. Dots represent individual mice. (G) LCMV viral titer as measured by FFU assay in kidneys of mice 12 days after LCMV infection. Means are indicated. *jinx, Unc13d*$^{jinx/jinx}$ mice; *jinx*; *Tnf PanR1, Unc13d*$^{jinx/jinx}$; *Tnf PanR1/PanR1 mice*; *jinx*; *Ifngr*$^{-/-}$, *Unc13d*$^{jinx/jinx}$; *Ifngr*$^{-/-}$; *jinx*; *Myd88 poc, Unc13d*$^{jinx/jinx}$; *Myd88*$^{poc/poc}$ mice. nd, non-detected. Error bars show standard error of the mean (SEM).

Figure S3. Complete blood counts of wild type, *Unc13d*$^{jinx/jinx}$, and *Unc13d*$^{jinx/jinx}$; *Myd88*$^{poc/poc}$ mice

Percentage of hematocrit (A), amount of hemoglobin (B), and absolute numbers of lymphocytes (C), neutrophils (D) and monocytes (E) enumerated in blood of wild type and mutant mice 12 days after LCMV infection. Representative data of 3 independent experiments are shown; n = 5 per group. *jinx, Unc13d*$^{jinx/jinx}$ mice; *jinx*; *Myd88*^{poc}, *Unc13d*$^{jinx/jinx}$; *Myd88*$^{poc/poc}$ mice. Error bars show standard error of the mean (SEM).

Figure S4. Disruption of IL-1R1-signaling does not rescue HLH-like disease

Mice were injected with LCMV and spleens were harvest 12 days later. (A) Mean of fluorescence intensity of CD86 expression on macrophages from wild type, *jinx* (*Unc13d*$^{jinx/jinx}$) and *jinx*; *Il1r1*$^{-/-}$ (*Unc13d*$^{jinx/jinx}$; B6.129S7-*Il1r1*^{tm1Imx}/J) mice. Cells were stained as in Figure 2. Splenocytes from LCMV-infected mice were left unstimulated for 5 hours in presence of brefeldin A, then stained for CD8α and intracellular IFNγ expression. Graphs report the percentages of CD8^{+} T cells (B) and the percentages of IFNγ^{+}CD8^{+} T cells (C). Serum IL-6 was measured by ELISA 7 days post infection (D). *jinx, Unc13d*$^{jinx/jinx}$ mice; *jinx*; *Ifng*$^{-/-}$, *Unc13d*$^{jinx/jinx}$; *Ifngr*$^{-/-}$; *jinx*; *Myd88*^{poc}, *Unc13d*$^{jinx/jinx}$; *Myd88*$^{poc/poc}$ mice. Bars in graphs show the means. Dots represent individual mice.

Figure S1

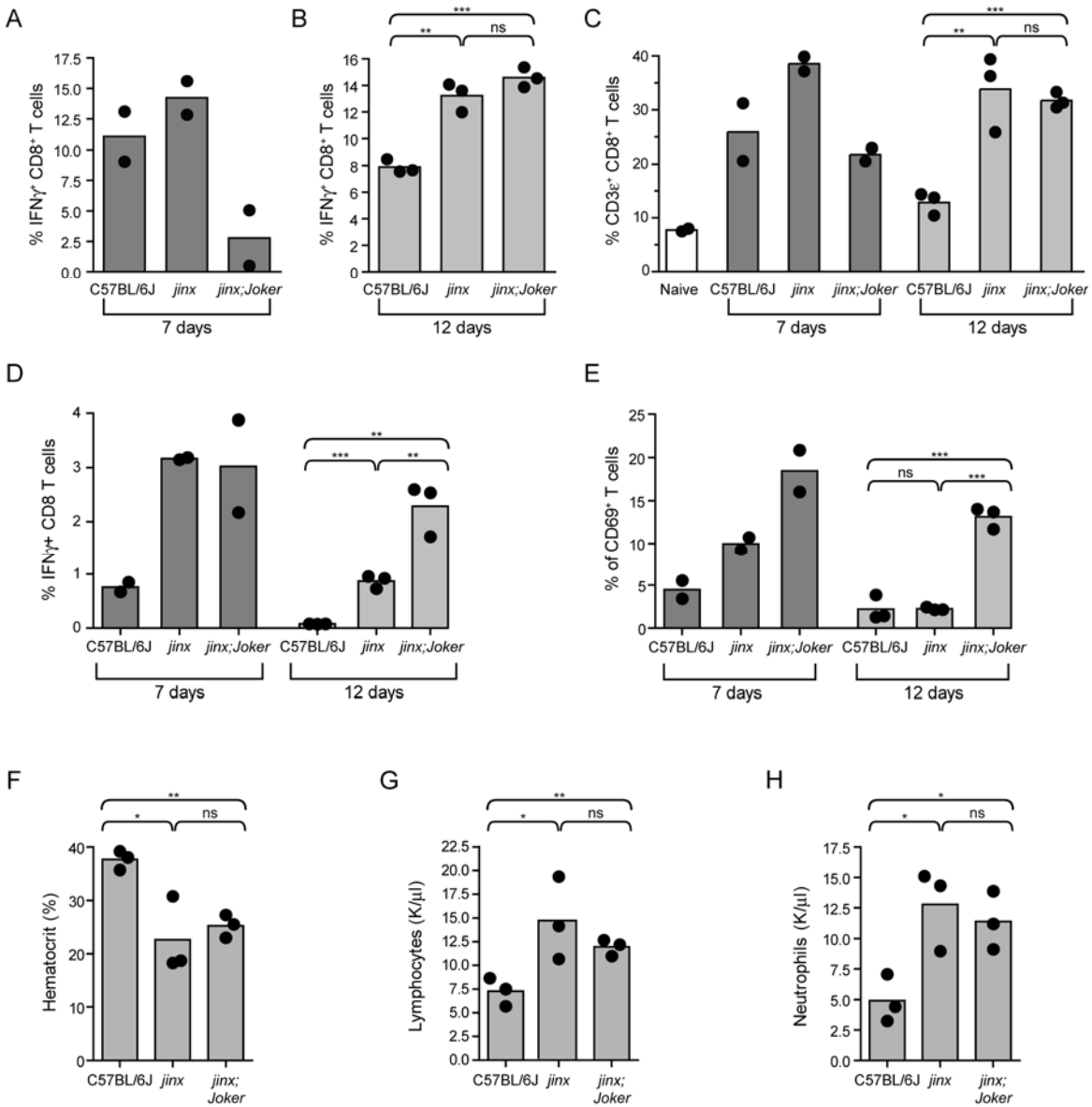

A
% IFNγ+ CD8+ T cells
C57BL/6J
jinx
jinx;Joker
7 days
B
% IFNγ+ CD8+ T cells
***
**
ns
C57BL/6J
jinx
jinx;Joker
12 days
C
% CD3ε+ CD8+ T cells
***
**
ns
Naive
C57BL/6J
jinx
jinx;Joker
7 days
C57BL/6J
jinx
jinx;Joker
12 days
D
% IFNγ+ CD8 T cells
**
***
**
C57BL/6J
jinx
jinx;Joker
C57BL/6J
jinx
jinx;Joker
7 days
12 days
E
% of CD69+ T cells
***
ns
***
C57BL/6J
jinx
jinx;Joker
C57BL/6J
jinx
jinx;Joker
7 days
12 days
F
Hematocrit (%)
**
*
ns
C57BL/6J
jinx
jinx;
Joker
G
Lymphocytes (K/µl)
**
*
ns
C57BL/6J
jinx
jinx;
Joker
H
Neutrophils (K/µl)
*
*
ns
C57BL/6J
jinx
jinx;
Joker

Figure S2

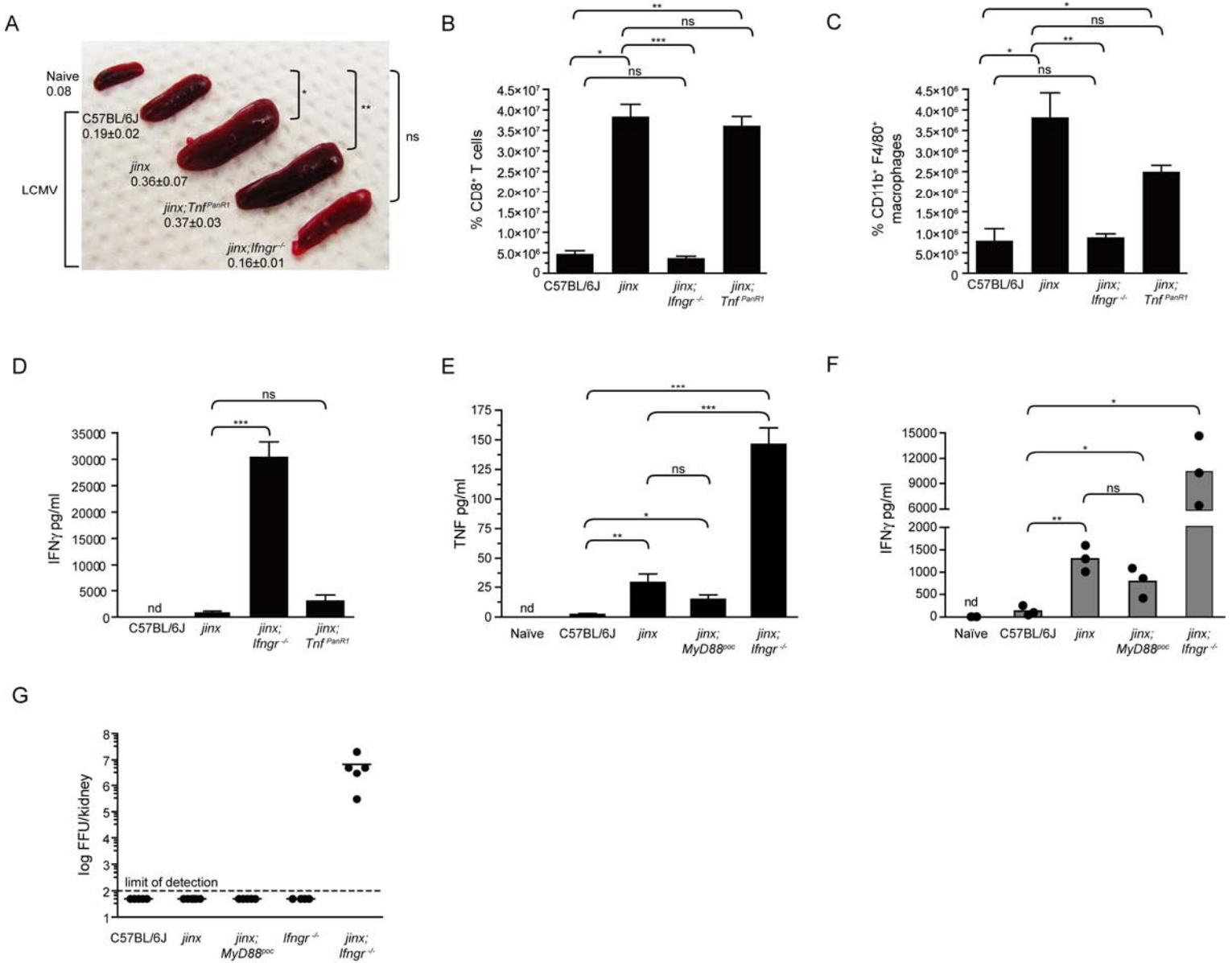

A
Naive
0.08
C57BL/6J
0.19±0.02
jinx
0.36±0.07
jinx;Tnf PanR1
0.37±0.03
jinx;Ifngr -/-
0.16±0.01
LCMV
*
**
ns
B
% CD8+ T cells
4.5×10^7
4.0×10^7
3.5×10^7
3.0×10^7
2.5×10^7
2.0×10^7
1.5×10^7
1.0×10^7
5.0×10^6
0
C57BL/6J
jinx
jinx; Ifngr -/-
jinx; Tnf PanR1
C
% CD11b+ F4/80+ macrophages
4.5×10^6
4.0×10^6
3.5×10^6
3.0×10^6
2.5×10^6
2.0×10^6
1.5×10^6
1.0×10^6
5.0×10^5
0
C57BL/6J
jinx
jinx; Ifngr -/-
jinx; Tnf PanR1
D
IFNγ pg/ml
35000
30000
25000
20000
15000
10000
5000
0
nd
C57BL/6J
jinx
jinx; Ifngr -/-
jinx; Tnf PanR1
E
TNF pg/ml
175
150
125
100
75
50
25
0
nd
Naïve
C57BL/6J
jinx
jinx; MyD88poc
jinx; Ifngr -/-
F
IFNγ pg/ml
15000
12000
9000
6000
2000
1500
1000
500
0
nd
Naïve
C57BL/6J
jinx
jinx; MyD88poc
jinx; Ifngr -/-
G
log FFU/kidney
8
7
6
5
4
3
2
1
limit of detection
C57BL/6J
jinx
jinx; MyD88poc
Ifngr -/-
jinx; Ifngr -/-

Figure S3

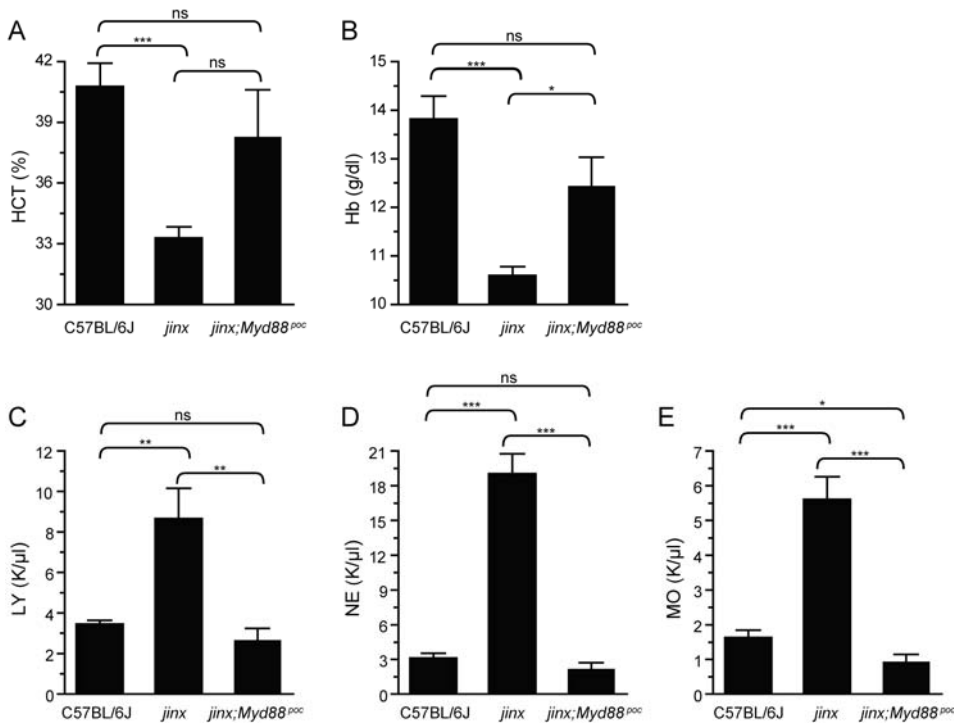
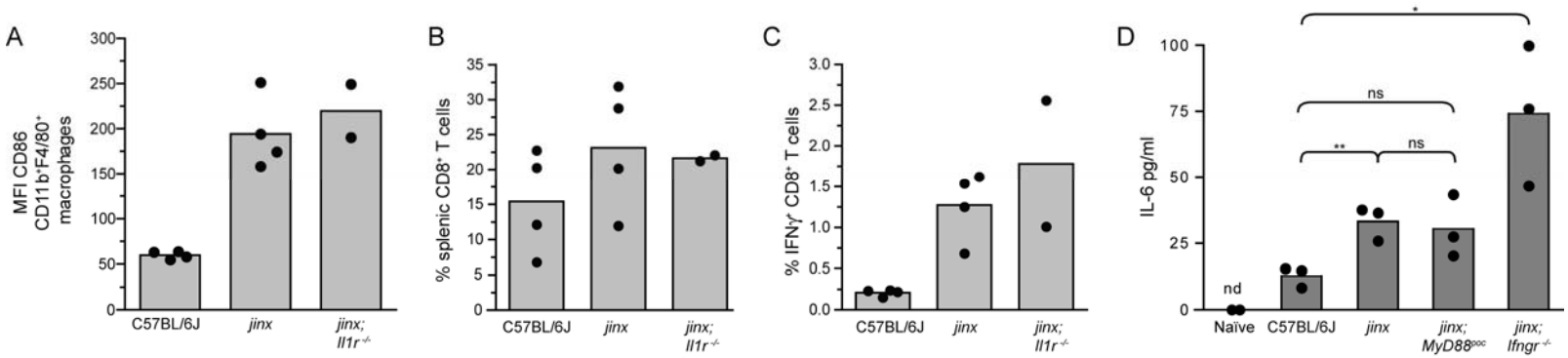

A
ns
***
ns
HCT (%)
42
39
36
33
30
C57BL/6J
jinx
jinx;Myd88poc
B
ns
***
*
Hb (g/dl)
15
14
13
12
11
10
C57BL/6J
jinx
jinx;Myd88poc
C
ns
**
**
LY (K/µl)
12
10
8
6
4
2
0
C57BL/6J
jinx
jinx;Myd88poc
D
ns
***
***
NE (K/µl)
21
18
15
12
9
6
3
0
C57BL/6J
jinx
jinx;Myd88poc
E
*
***
***
MO (K/µl)
7
6
5
4
3
2
1
0
C57BL/6J
jinx
jinx;Myd88poc

Figure S4


A
MFI CD86 CD11b+F4/80+ macrophages
300
250
200
150
100
50
0
C57BL/6J
jinx
jinx; Il1r-/-
B
% splenic CD8+ T cells
35
30
25
20
15
10
5
0
C57BL/6J
jinx
jinx; Il1r-/-
C
% IFNγ+ CD8+ T cells
3.0
2.5
2.0
1.5
1.0
0.5
0.0
C57BL/6J
jinx
jinx; Il1r-/-
D
IL-6 pg/ml
100
75
50
25
0
*
ns
**
ns
nd
Naïve
C57BL/6J
jinx
jinx; MyD88poc
jinx; Ifngr-/-