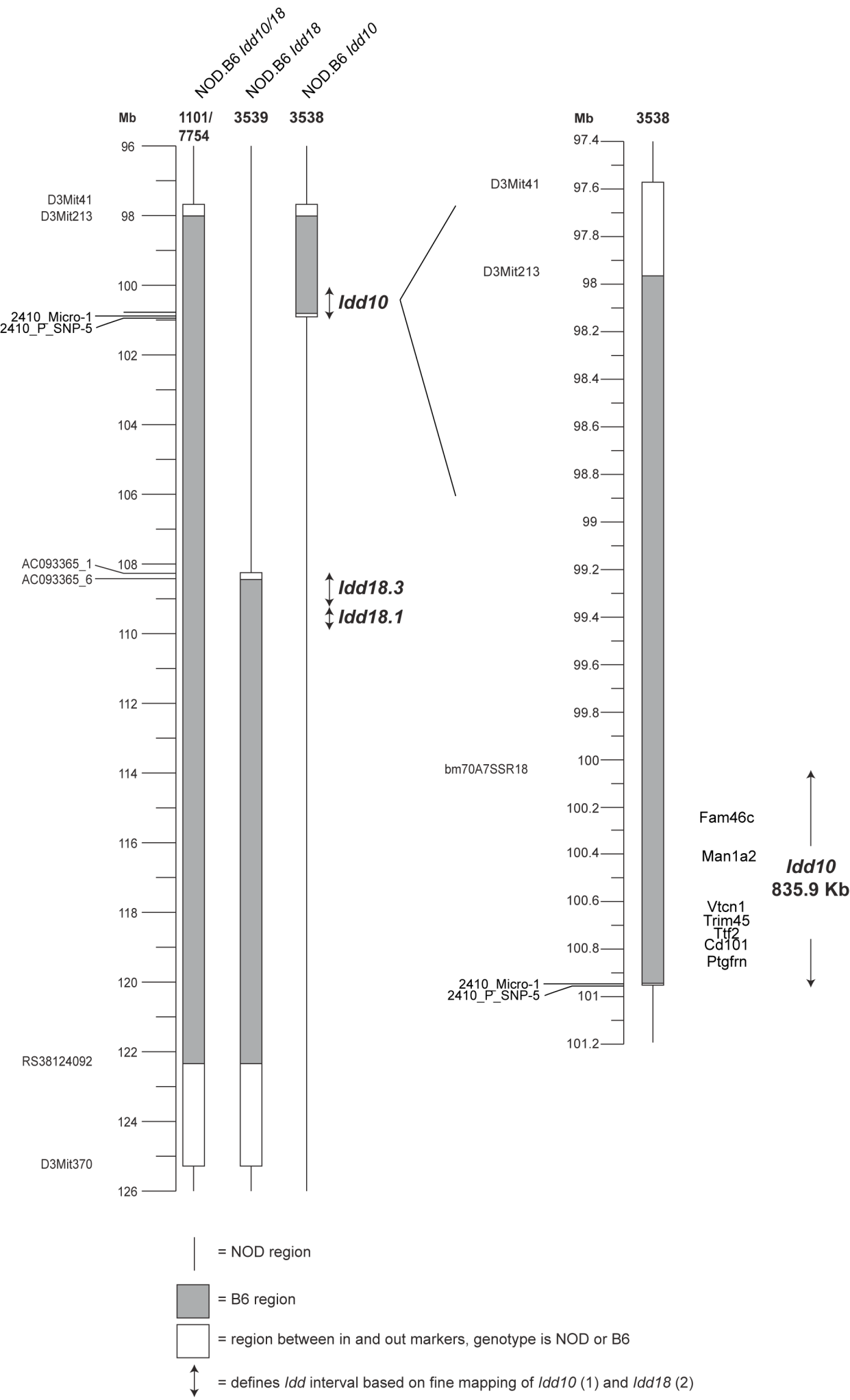
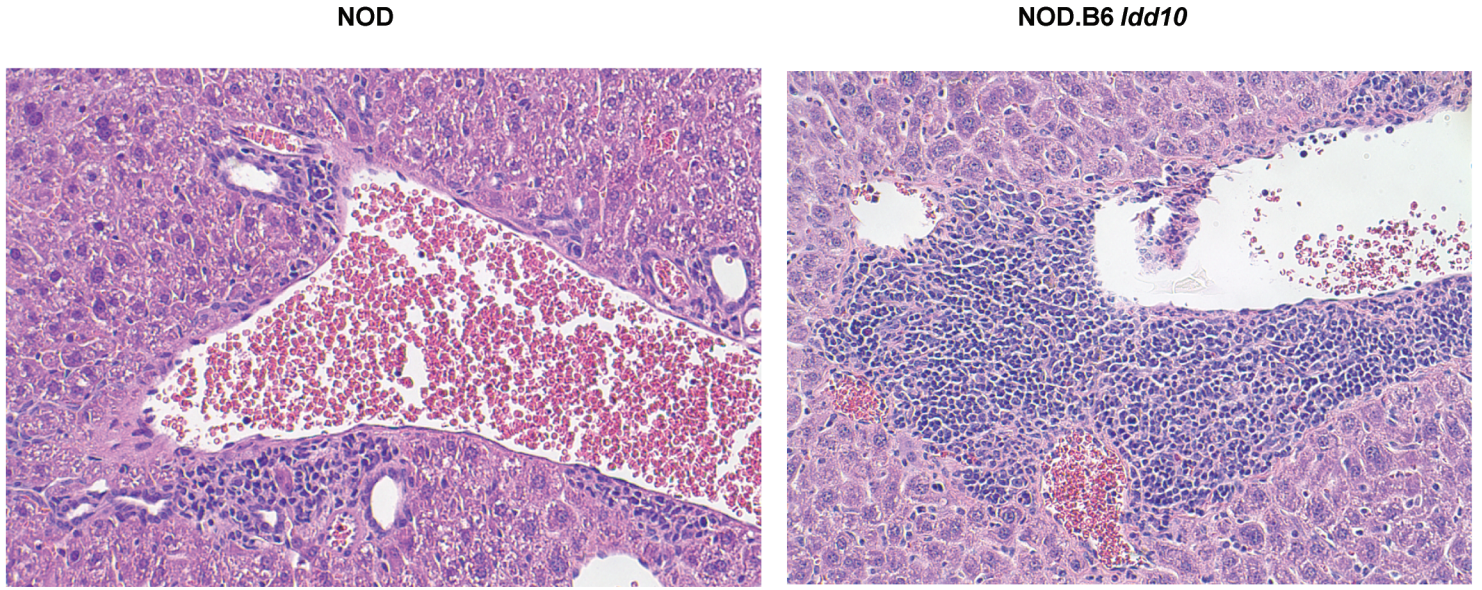
Supplementary Figure S1

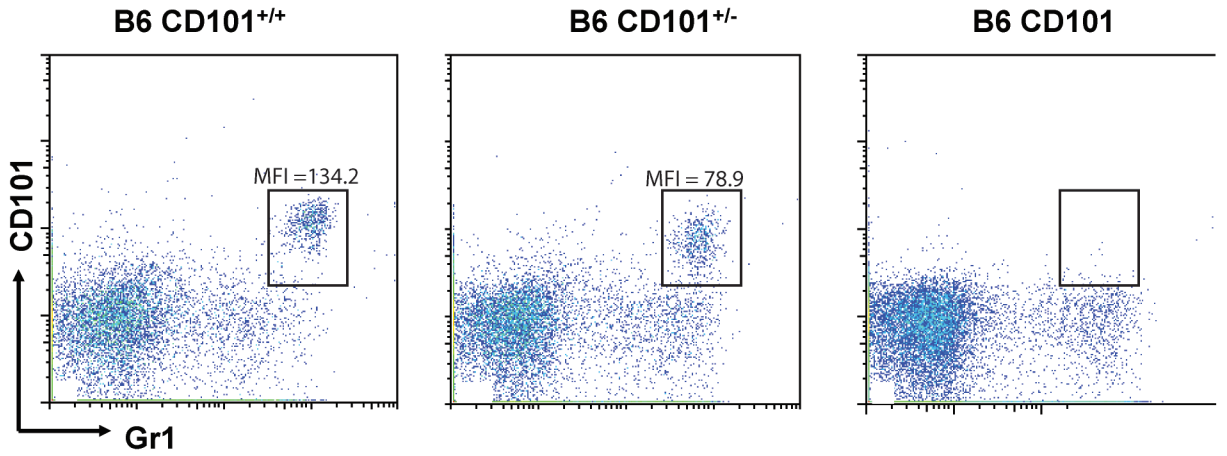


1 = Penha-Gonçalves *et al*. 2003. Diabetes. 52: 1551-1556.
2 = Fraser *et al*. 2010. J. Immunol. 184: 5075-5084.

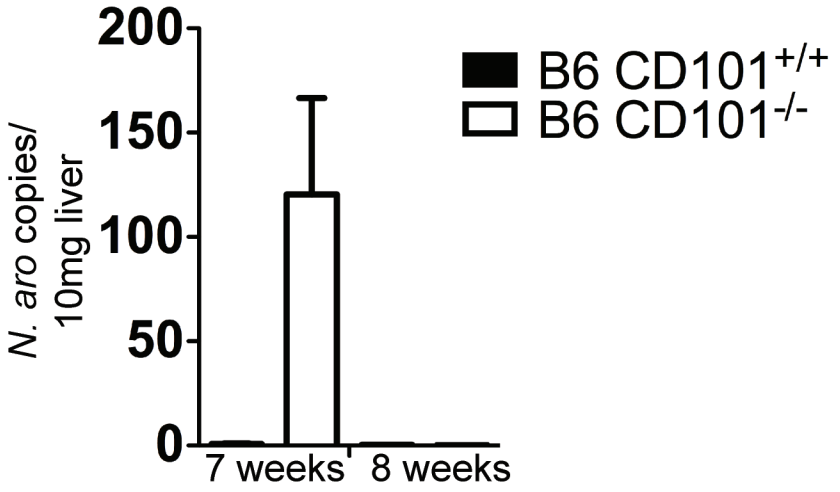
A

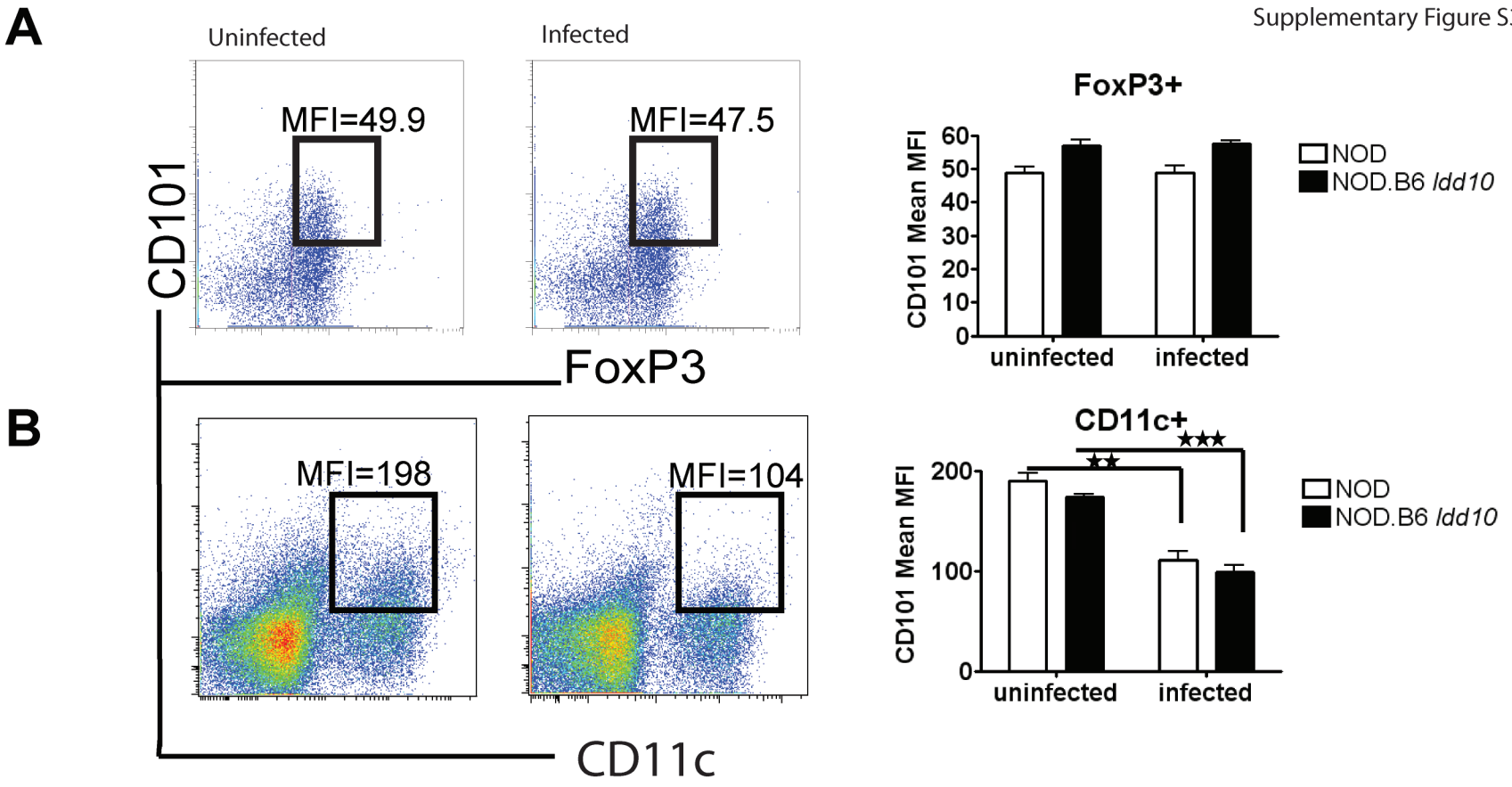

NOD
NOD.B6 Idd10

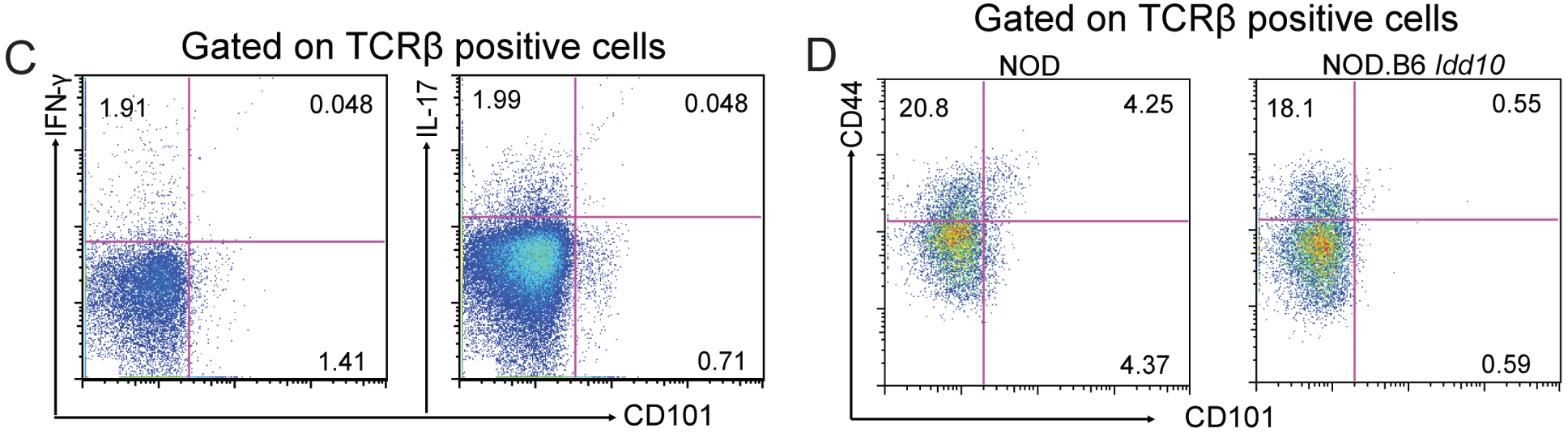
B

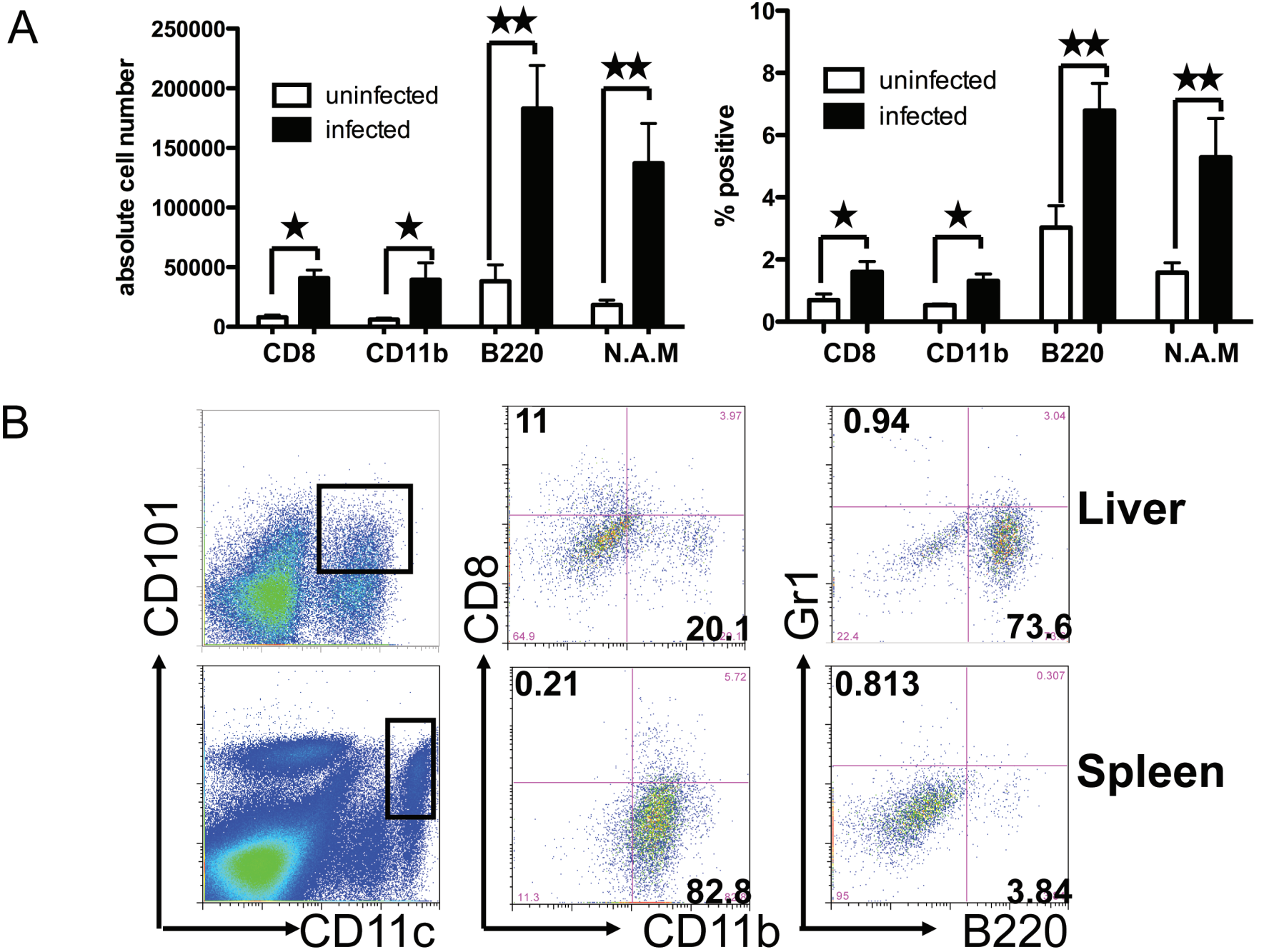

B6 CD101+/+
B6 CD101+/-
B6 CD101
MFI =134.2
MFI = 78.9
CD101
Gr1

C

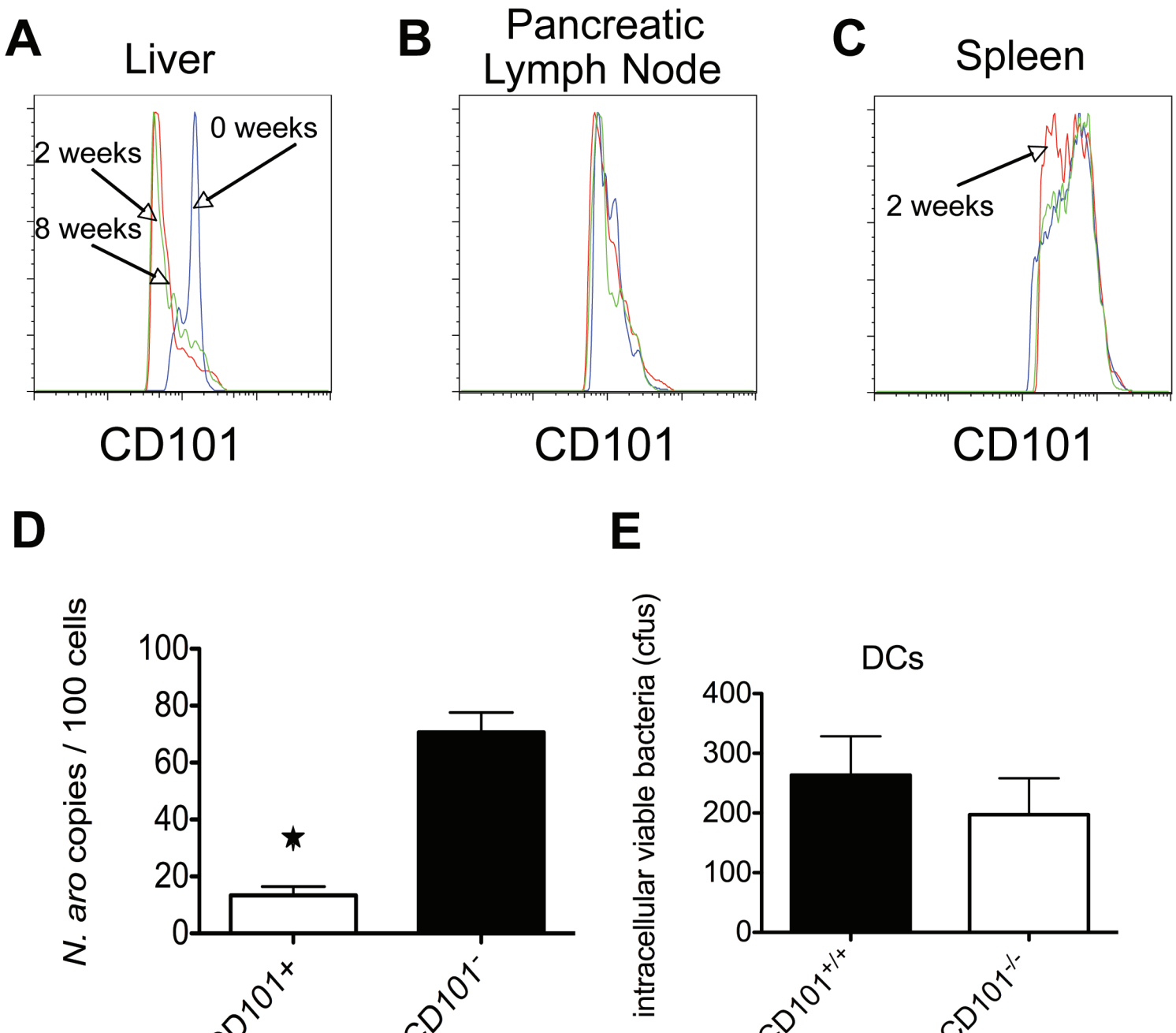

200
150
100
50
0
N. aro copies/ 10mg liver
B6 CD101+/+
B6 CD101-/-
7 weeks
8 weeks

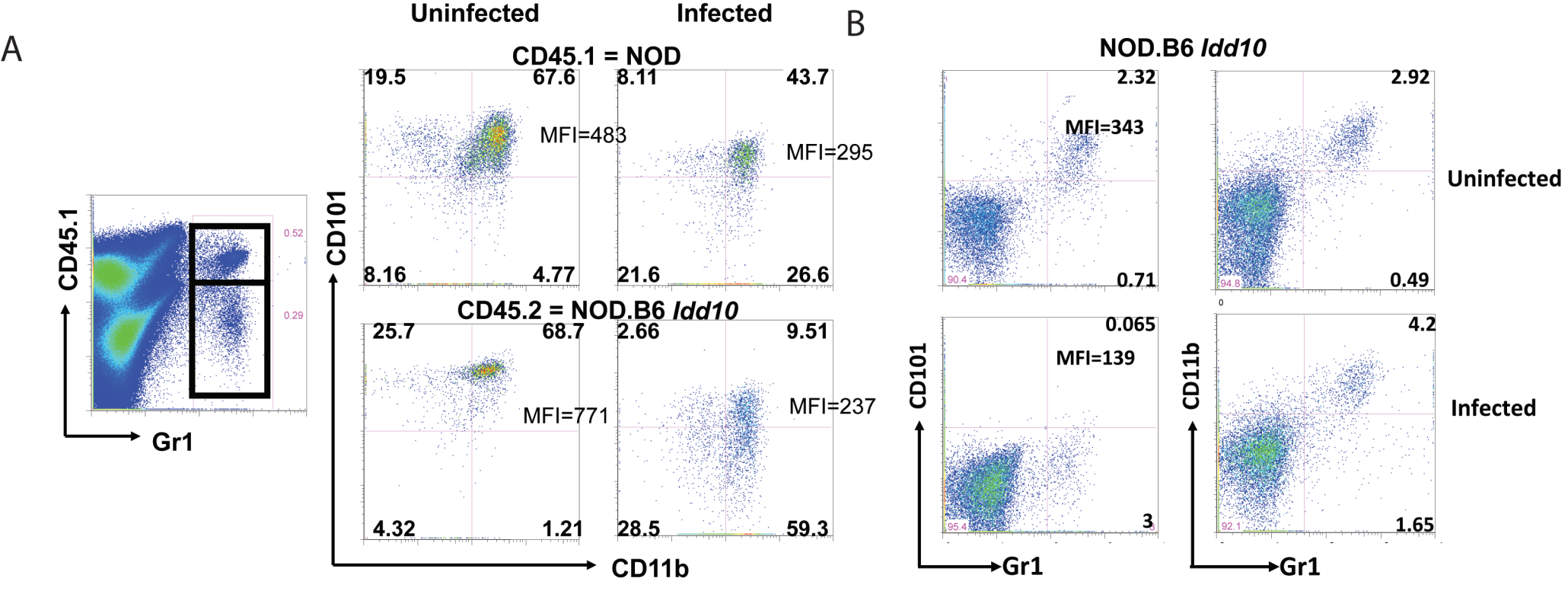

A
Uninfected
Infected
MFI=49.9
MFI=47.5
CD101
FoxP3
B
MFI=198
MFI=104
CD11c
FoxP3+
CD101 Mean MFI
60
50
40
30
20
10
0
uninfected
infected
NOD
NOD.B6 Idd10
CD11c+
CD101 Mean MFI
200
100
0
uninfected
infected
NOD
NOD.B6 Idd10


C
Gated on TCRβ positive cells
IFN-γ
1.91
0.048
1.41
IL-17
1.99
0.048
0.71
CD101
D
Gated on TCRβ positive cells
NOD
NOD.B6 Idd10
CD44
20.8
4.25
4.37
18.1
0.55
0.59
CD101


A
absolute cell number
250000
200000
150000
100000
50000
0
uninfected
infected
CD8
CD11b
B220
N.A.M
% positive
10
8
6
4
2
0
B
CD101
CD11c
CD8
CD11b
Gr1
B220
11
3.97
64.9
20.1
0.94
3.04
22.4
73.6
Liver
0.21
5.72
11.3
82.8
0.813
0.307
95
3.84
Spleen

Supplementary Figure S5




A
Uninfected
Infected
CD45.1 = NOD
19.5
67.6
MFI=483
8.11
43.7
MFI=295
8.16
4.77
21.6
26.6
CD45.2 = NOD.B6 Idd10
25.7
68.7
MFI=771
2.66
9.51
MFI=237
4.32
1.21
28.5
59.3
CD101
CD11b
CD45.1
Gr1
0.52
0.29
B
NOD.B6 Idd10
2.32
MFI=343
0.71
2.92
0.49
Uninfected
0.065
MFI=139
3
4.2
1.65
Infected
CD101
CD11b
Gr1
Gr1

Supplemental Figures:

Figure S1: Genetic map of the *Idd10* and *Idd18* regions on chromosome 3.

The NOD congenic strains used in this study and their respective introgressed regions are displayed. The NOD.B6 *Idd10/18* congenic strain (lines 1101 and 7754) has two noncontiguous, introgressed B6 regions encompassing *Idd10* and *Idd18*, whereas the NOD.B6 *Idd10* (line 3538) and NOD.B6 *Idd18* congenic strain (line 3539) have single introgressed B6 regions at *Idd10* and *Idd18*, respectively. The *Idd10* region consists of seven genes, five pseudogenes and one non-coding RNA (44, 47).

Figure S2: The severity of liver disease and the duration of bacterial persistence correlate with the level and extent of CD101 expression after infection

(A) Chronic liver disease in NOD and NOD.B6 *Idd10* mice.

Portal inflammation in 10-week-old (20x) NOD (left panel) and NOD.B6 *Idd10* (right panel) mice infected with *N. aro* at the age of 1 month.

(B) Reduction of CD101 protein expression on Gr1+ cells from heterozygous $CD101^{+/-}$ mice.

Expression levels of CD101 on Gr1+ liver cells from 8-week-old B6 $CD101^{+/+}$, B6 $CD101^{+/-}$ and B6 $CD101^{-/-}$ mice. Respective FACS dot plots for large granular cells and the mean MFI for CD101 are displayed. Similar results were obtained for CD11c+ and TCRβ+ FoxP3+ cells (not shown).

(C) Prolonged bacterial persistence in B6 $CD101^{-/-}$ compared to B6 $CD101^{+/+}$ mice.

Copy numbers of *N. aro* in individual livers of the indicated mouse strains were analyzed by a *N. aro*-specific 16S rRNA qPCR. *N. aro* copies in the livers of B6 $CD101^{+/+}$ and B6 $CD101^{-/-}$ mice were compared and analyzed at the indicated weeks after infection. Statistical significance for two combined independent experiments was calculated with organs from 3 individual mice for each strain using a student's t-test. The p-value was <0.01 for the comparison at week 7. At week 8 the infection was completely cleared from the livers of both mouse strains.

Figure S3: Downregulation of CD101 expression on DCs upon infection and inverse correlation between CD101 expression and the expression of activation markers on T cells

(A+B) CD101 expression levels on regulatory T cells and DCs before and after infection.

The mean fluorescence intensity (MFI) of CD101 on TCRβ+ Foxp3+ (A) and CD11c+ (B) cells from the livers of uninfected and infected NOD and NOD.B6 *Idd10* mice was determined. 8-week-old, female mice of each strain were infected with $5x10^7$ *N. aro* cfus or received PBS 2 days before FACS analysis. Note the decreased CD101 expression levels in CD11c+ cells, while the MFIs remain unaffected on TCRβ+ cells upon infection (respective data are displayed for the FoxP3 positive T cell population, but also the FoxP3 negative population (that consisted mainly of CD44+ T cells) did not reveal any change in CD101 expression levels (41.1 in uninfected mice vs 42.3 in infected mice). Respective dot plot samples for TCRβ+ Foxp3+ (A) and CD11c+ (B) cells from uninfected (left column) and infected (middle column) NOD mice as well as the summary (right column) for 4 individual NOD and NOD.B6 *Idd10* mice are displayed. *In vivo* data for the suppression of CD101 expression on Gr1+ cells are shown in the bone marrow chimera studies in Fig. S6A.

(C+D) Inverse correlation between CD101 expression and the expression of activation markers on T cells

(C) CD101-negative T cells express IFN-γ and IL-17 during early stages after infection.

Ex vivo FACS analysis and intracellular cytokine staining (ICS) of liver T cells 60 hours after infection with $5x10^7$ *N. aro* cfus. Dot plots are representative for three NOD.B6 *Idd10* mice tested individually.

(D) CD44 expressing T cells in NOD.B6 *Idd10* mice are CD101-negative. *Ex vivo* FACS analysis of liver T cells two weeks after the second infection. Dot plots are representative for three NOD and NOD.B6 *Idd10* mice tested individually.

Figure S4: DC subpopulations in uninfected and infected NOD and NOD.B6 *Idd10* mice

(A) DCs were divided by FACS analysis into lymphoid (CD8+), myeloid (CD11b+) and plasmacytoid (B220+) subpopulations as well as CD11c positive cells expressing none of these additional markers (N.A.M.). Their recruitment was determined before and 5 days after infection in the livers of 8-week-old NOD and NOD.B6

Idd10 mice. Summaries for the absolute number (left panel) and the relative distribution (right panel) of each subpopulation are displayed for uninfected and infected NOD.B6 *Idd10* mice. In NOD mice, there was also an increase in all of these DC subpopulations upon infection without a significant change in the proportion of the subpopulations compared to NOD.B6 *Idd10* mice.

(B) Expression of CD101 on different DC subpopulations

CD11b+, B220+ and CD8+ DC populations were analyzed for their CD101 expression. Note that B220+ (plasmacytoid) DCs form the DC population that preferentially express CD101 in the liver, while the main CD101+ DC population in the spleen consists of CD11b+ CD11c+ cells.

Figure S5: Decreased CD101 expression correlates with increased numbers of *N. aro*.

(A-C) Long-term suppression of CD101 on DCs is liver-specific

Analysis of CD101 expression on DCs from the livers (A), pancreatic lymph nodes (B) and spleens (C) in 14 week-old NOD.B6 *Idd10* mice. Uninfected animals (0 weeks) and mice infected with *N. aro* 2 and 8 weeks before were compared. One representative histogram of three individual livers (A) and spleens (C) and an average of pancreatic lymph nodes of five individual mice (B) are displayed.

(D+E) DCs infected with *N. aro* exhibit reduced expression of CD101.

(D) CD11c+ cells were purified from the livers of three individual NOD mice three days after infection with $5x10^7$ *N. aro* cfus and separated into CD101+ and CD101- cells by cell sorting. DNA of $1x10^6$ CD101+ and CD101- DCs was extracted and tested for the presence of *N. aro* copies using a 16S rRNA specific qPCR. Data are displayed as number of *N. aro* copies of 100 CD101+ or CD101- DCs each. Statistical significance was calculated using a student's t-test and indicated as $*$ for $p<0.05$.

(E) CD101-deficiency does not affect bacterial uptake

Bone marrow-derived DCs from wild-type B6 and B6 $CD101^{-/-}$ mice were exposed to *N. aro* for 12 hours and 100 μg/ml gentamicin for an additional hour followed by 10 μg/ml gentamicin for the duration of the assay. Viable intracellular bacteria were quantitated by gentle lysis of the macrophages and subsequent plating on LB

agar. Experiments were performed two times.

Figure S6: Allele-intrinsic downregulation of CD101 expression on Gr1+ cells upon infection.

(A) CD101 expression on Gr1+ cells from NOD CD45.2/NOD.B6 *Idd10* bone marrow chimeras after infection *in vivo*.

CD101 expression was analyzed on Gr1+ cells from uninfected or infected - 2 days after infection - NOD CD45.2/NOD.B6 *Idd10* bone marrow chimeras. Note the enhanced CD101 expression in Gr1+ cells expressing the B6 CD101 allele from naïve chimeras and the reduced CD101 expression in Gr1+ cells expressing the B6 CD101 allele from infected chimeras.

(B) CD101 expression on Gr1+ cells after infection *in vitro*.

Liver mononuclear cells from 3 individual NOD.B6 *Idd10* mice were depleted of B and NK cells using MACS. The remaining cells were infected at a MOI of 10 with *N. aro* or left untreated and analyzed two days later for CD101 expression. Respective FACS dot plots for Gr1+ cells are displayed. While the expression of CD101 on Gr1+ cells decreased, CD11b expression remains unchanged.