

Supplemental Figure 1. Hepatic DX5⁻ NK cells preferentially traffic to the liver without further differentiation.

10⁵ DX5⁻ or DX5⁺ liver NK cells from GFP transgenic mice were adoptively transferred intraperitoneally to sublethally irradiated WT B6 mice. 3 days later, GFP⁺ NK cells were analyzed for DX5 expression in recipient liver and spleen.

Supplemental Table 1. Phenotypic analysis of DX5⁻ and DX5⁺ liver NK cells by FACS

	Adhesion Molecules	Chemokine Receptors	Activating/Inhibitory Receptors	Cytokine Receptors	Others
Higher on DX5⁻-NK	CD49a,CD51 CD11c,CD61 CD44,CD48	CXCR3 CXCR6	CD94/NKG2		TRAIL, LAG3, CD69, CD244
Higher on DX5⁺-NK	CD11b,CD49d CD62L,CD2		Ly49G2 Ly49C/I/F/H NKp46	IL4R α	KLRG1 CD43 CD29
High on both subsets	CD18, CD54		NKG2D	IL2R α	
Low on both subsets	CD103	CXCR4 CCR5 CCR6 CCR7 CX3CR1		IL2R α IL7R α IL12R α 1 IL21R	CD34 CD117

Expression of indicated surface markers was analyzed on DX5⁻ and DX5⁺ liver NK cells from WT B6 mice by flow cytometry.

Supplemental Table 2. Genes differentially expressed in DX5⁻ NK cells compared to DX5⁺ NK cells

Gene name	Full name	Probe ID	Fold change
GO:0050900 leukocyte migration			
Itga1	integrin alpha 1	1455251_at	22
Sele	selectin, endothelial cell	1421712_at	-8.7
Cx3cr1	chemokine (C-X3-C) receptor 1	1450020_at	-7.3
Itgam	integrin alpha M	1422046_at	-5.7
Il1b	interleukin 1 beta	1449399_a_at	-3.0
GO:0006955 immune response			
Lag3	lymphocyte-activation gene 3	1449911_at	17
Il2	interleukin 2	1449990_at	8.2
Cd7	CD7 antigen	1419711_at	5.9
Ltb	lymphotoxin B	1419135_at	5.4
Il4ra	interleukin 4 receptor, alpha	1423996_a_at	4.0
Csf2	colony stimulating factor 2 (granulocyte-macrophage)	1427429_at	3.8
Ctla4	cytotoxic T-lymphocyte-associated protein 4	1419334_at	3.1
Il6	interleukin 6	1450297_at	-10
Eomes	eomesodermin homolog (<i>Xenopus laevis</i>)	1435172_at	-8.1
Fcgr2b	Fc receptor, IgG, low affinity IIb	1451941_a_at	-7.9
Ccl9	chemokine (C-C motif) ligand 6	1448898_at	-5.4
Ccl6	chemokine (C-C motif) ligand 6	1417266_at	-5.2
Il18r1	interleukin 18 receptor 1	1421628_at	-4.1
Cd55	CD55 antigen	1418762_at	-3.6
Il18rap	interleukin 18 receptor accessory protein	1421291_at	-3.4
Irf8	interferon regulatory factor 8	1448452_at	-3.3

GO:0008219 cell death

Gzmc	granzyme C	1421256_at	12
Klk8	kallikrein related-peptidase 8	1419722_at	7.3
P2rx7	purinergic receptor P2X, ligand-gated ion channel, 7	1439787_at	6.1
Tnfsf10	tumor necrosis factor (ligand) superfamily, member 10	1439680_at	5.9
Mmp9	matrix metallopeptidase 9	1448291_at	5.0
Bcl11b	B-cell leukemia/lymphoma 11B	1450339_a_at	4.7
Gzmf	granzyme F	1418679_at	4.3
Traf4	TNF receptor associated factor 4	1460642_at	4.1
Serpinc9b	serine (or cysteine) peptidase inhibitor, clade B, member 9b	1422668_at	-9.8
Lyz1	lysozyme 1	1439426_x_at	-7.1
Eya1	eyes absent 1 homolog (Drosophila)	1443117_at	-5.4
Nuak2	NUAK family, SNF1-like kinase, 2	1429049_at	-4.1
Sgk1	serum/glucocorticoid regulated kinase 1	1416041_at	-3.5
Lyz2	lysozyme 2	1423547_at	-3.4

GO:0008283 cell proliferation

Zeb1	zinc finger E-box binding homeobox 1	1446127_at	4.3
Cd38	CD38 antigen	1433741_at	4.2
Hbegf	heparin-binding EGF-like growth factor	1418350_at	3.5
Zeb2	zinc finger E-box binding homeobox 2	1422748_at	-7.3
S1pr1	sphingosine-1-phosphate receptor 1	1423571_at	-4.9
Pdgfa	platelet derived growth factor, alpha	1418711_at	-3.6
Vegfa	vascular endothelial growth factor A	1420909_at	-3.1

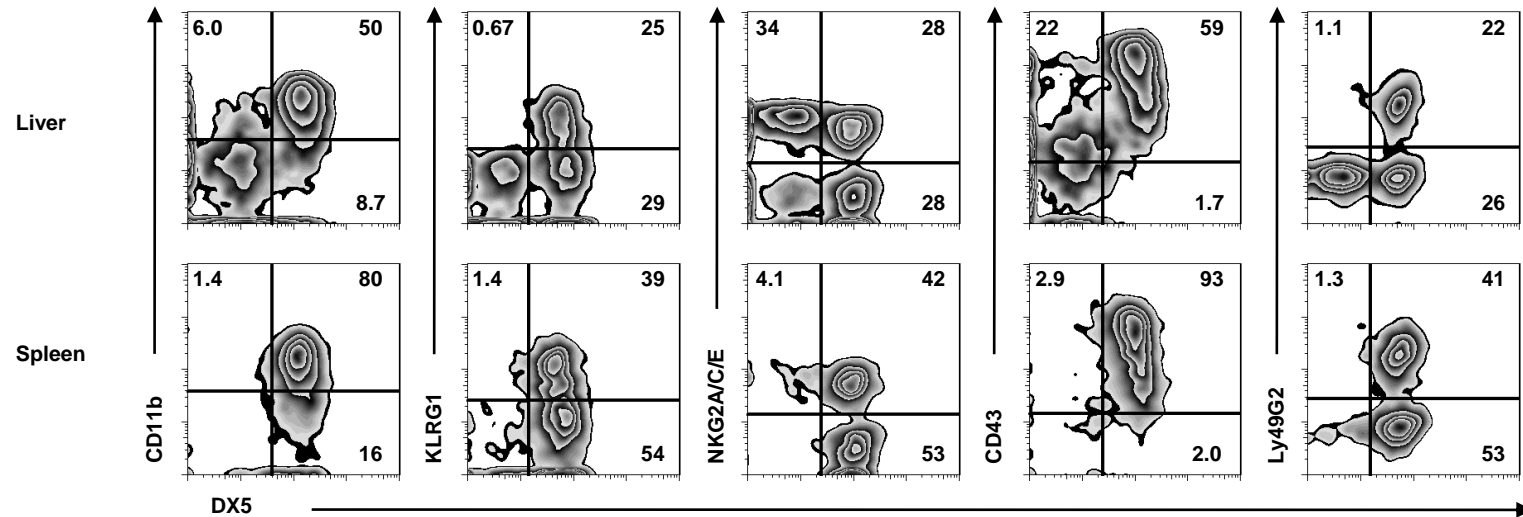
GO:0048469 cell maturation

Calca	calcitonin/calcitonin-related polypeptide, alpha	1452004_at	8.6
Ret	ret proto-oncogene	1436359_at	-11
Cdc25b	cell division cycle 25 homolog B (S. pombe)	1421963_a_at	-3.0

GO:0001775 cell activation

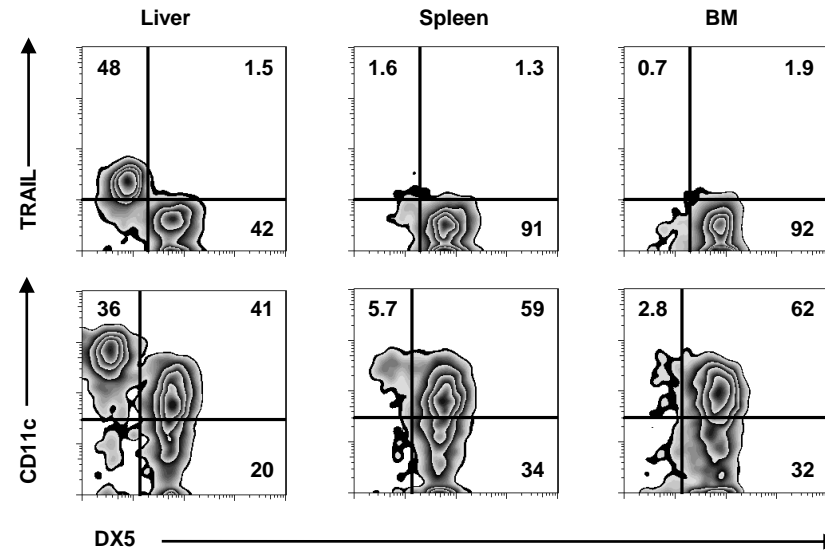
Evl	Ena-vasodilator stimulated phosphoprotein	1450106_a_at	4.5
Cd3d	CD3 antigen, delta polypeptide	1422828_at	3.3
Ndrp1	N-myc downstream regulated gene 1	1456174_x_at	-9.3
Sox4	SRY-box containing gene 4	1433575_at	-5.1

Genes with greater than or equal to 3-fold differences between DX5⁻ and DX5⁺ NK cells are listed according to their GO term functional classification. A positive value indicates higher expression in DX5⁻ NK cells.



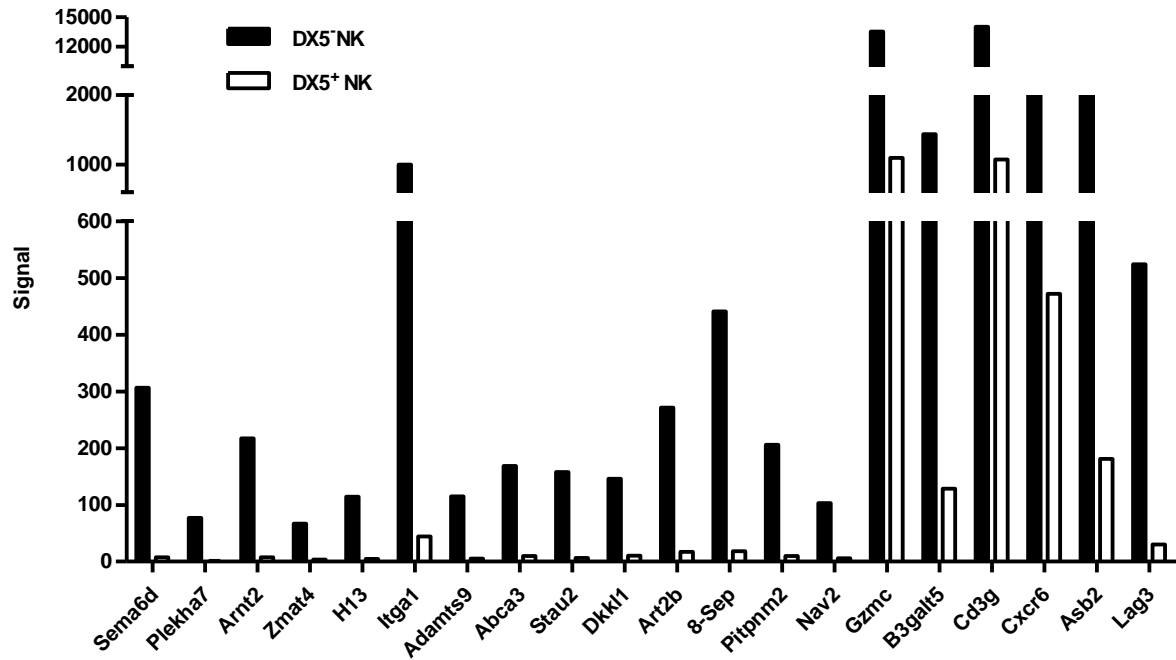
Supplemental Figure 2. DX5⁺ NK cells in the liver are phenotypically similar to those in the spleen.

Expression of CD11b, KLRG1, NKG2A/C/E, CD43 and Ly49G2 versus DX5 was analyzed on NK1.1⁺CD3⁻CD19⁻ cells or NK1.1⁺CD3⁻ cells from liver and spleen of WT B6 mice. Numbers represent the percentages of cells in each quadrant. Plots are representative of at least four individual mice.

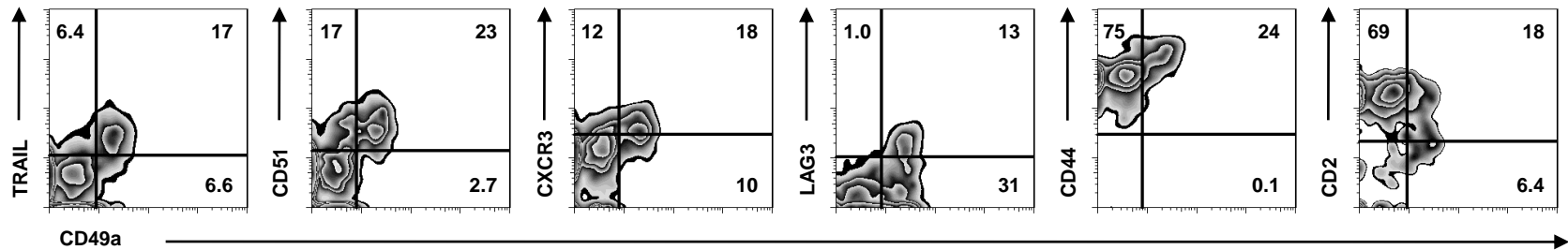


Supplemental Figure 3. Hepatic DX5⁻ NK cells are phenotypically different from BM DX5⁻ NK cells.

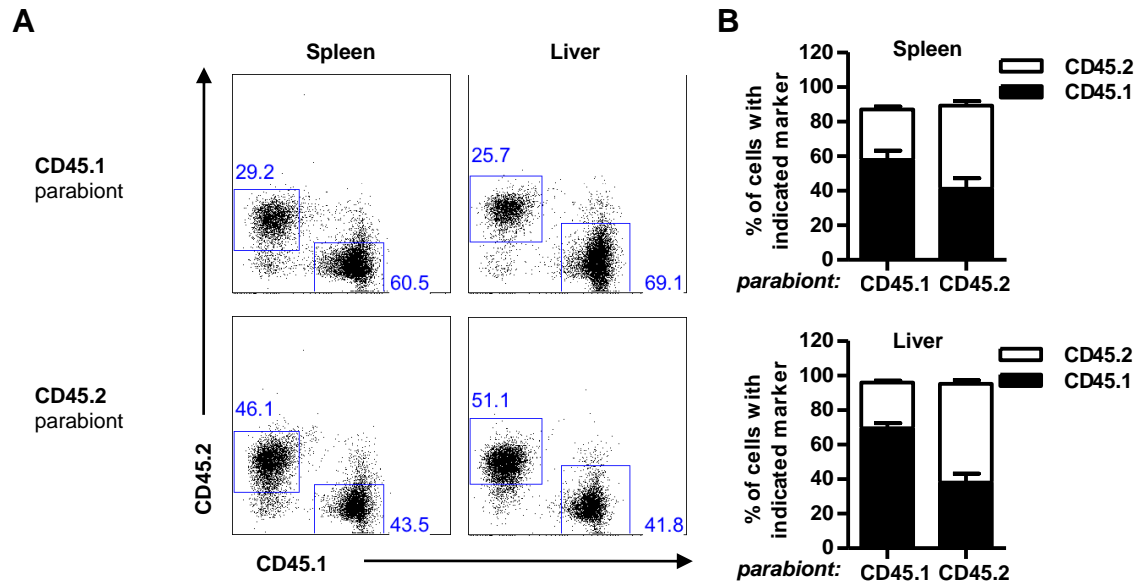
Expression of TRAIL and CD11c versus DX5 was analyzed on NK1.1⁺CD3⁻ cells from liver, spleen and BM of WT B6 mice. Plots are representative of six mice.



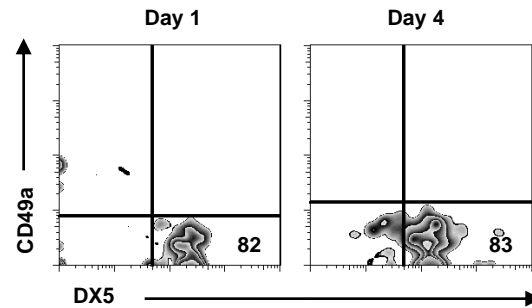
Supplemental Figure 4. Top 20 most highly up-regulated genes in hepatic DX5⁻ NK cells. Gene expression of DX5⁻ and DX5⁺ liver NK cells was assayed using Affymetrix GeneChip Mouse Genome 430 2.0 arrays, and the top 20 most up-regulated genes in DX5⁻ NK cells are shown.



Supplemental Figure 5. The phenotype of CD49a⁺ and CD49a⁻ liver NK cells from BALB/c mice. Expression of TRAIL, CD51, CXCR3, LAG3, CD44 and CD2 versus CD49a was analyzed on hepatic DX5⁺CD3⁻ cells from WT BALB/c mice. Plots are representative of three individual mice.

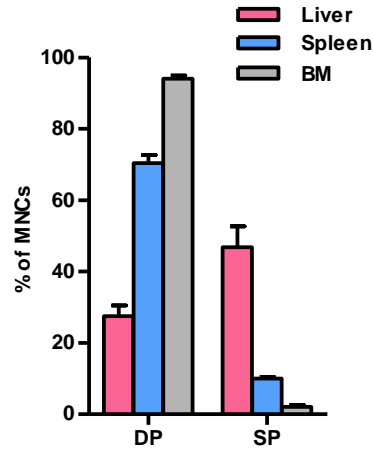


Supplemental Figure 6. Lymphocyte exchange in the spleen and liver of parabiotic mice. WT B6 (CD45.2) mice were parabiosed to congenic B6-CD45.1 mice. Day 14 post parabiosis surgery the spleen and liver were harvested and stained for CD45.2 and CD45.1. **(A)** Representative dot plot of the percentage of gated live cells expressing CD45.1⁺ and CD45.2⁺ in the indicated parabiont in the spleen and liver. **(B)** The percentages from **(A)** are depicted in stacked bar graph. The stacked bar graph represents a summary of n=7 parabiotic pairs.



Supplemental Figure 7. Ear NK cells are predominantly CD49a⁻DX5⁺ after challenge.

WT B6 mice were sensitized on two consecutive days by painting of 5% OXA on the shaved abdomen; 5 days later, their ears was challenged with 1% OXA. One day or four days after challenge, their ears were havested and the expression of CD49a and DX5 was analyzed on ear NK1.1⁺CD3⁻CD19⁻ cells.



Supplemental Figure 8. Transferred liver MNCs preferentially found in the liver.

As described in Figure 7C, 1 month post-transfer, the percentages of DP and SP cells among total lymphocytes of indicated organs were respectively analyzed. Means \pm SEM are shown (n=3 per group).