

Supplementary Materials for

Confinement of Activating Receptors at the Plasma Membrane Controls Natural Killer Cell Tolerance

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Table S1. Lists of probe sets differentially expressed in NK cells from K^bD^bKO-TgKIR/HLA and K^bD^bKO-TgKIR mice.

Table S2. Lists of probe sets differentially expressed in NK cells from wild-type and K^bD^bKO mice.

Table S3. Lists of probe sets differentially expressed in NK cells from wild-type and β 2mKO mice.

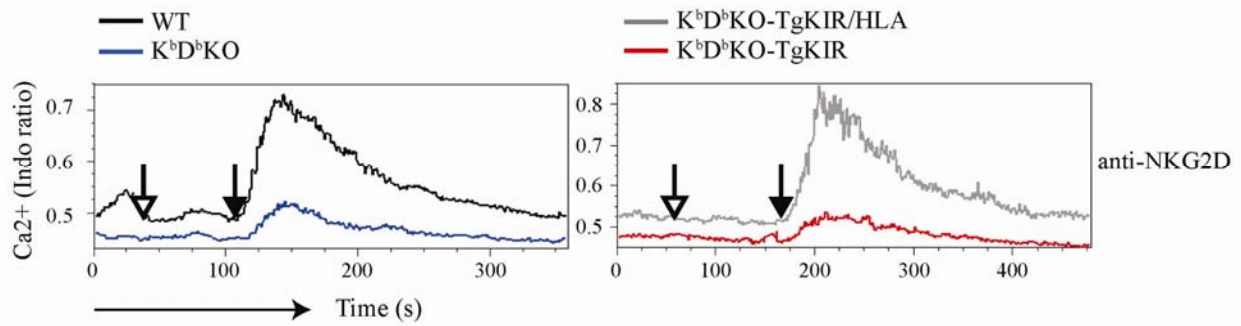


Fig. S1. NK cell education affects proximal signaling. Ca^{2+} flux changes were measured by flow cytometric analysis of freshly isolated NK cells. Biotinylated mAb against NKG2D (anti-NKG2D) was added to the cells when indicated (open-headed arrow), followed 1.5 min later by streptavidin (closed-headed arrow) to induce NKG2D cross-linking. NK cells were defined as $\text{CD49b}^+\text{CD3}^-$ cells. Changes in intracellular Ca^{2+} concentration over time are presented as the ratio of Indo-1 (violet) to Indo-1 (blue). Median values of kinetics are shown. Data are representative of four experiments for WT and $\text{K}^{\text{b}}\text{D}^{\text{b}}\text{KO}$ mice, and of three experiments for $\text{K}^{\text{b}}\text{D}^{\text{b}}\text{KO-TgKIR/HLA}$ and $\text{K}^{\text{b}}\text{D}^{\text{b}}\text{KO-TgKIR}$ mice.

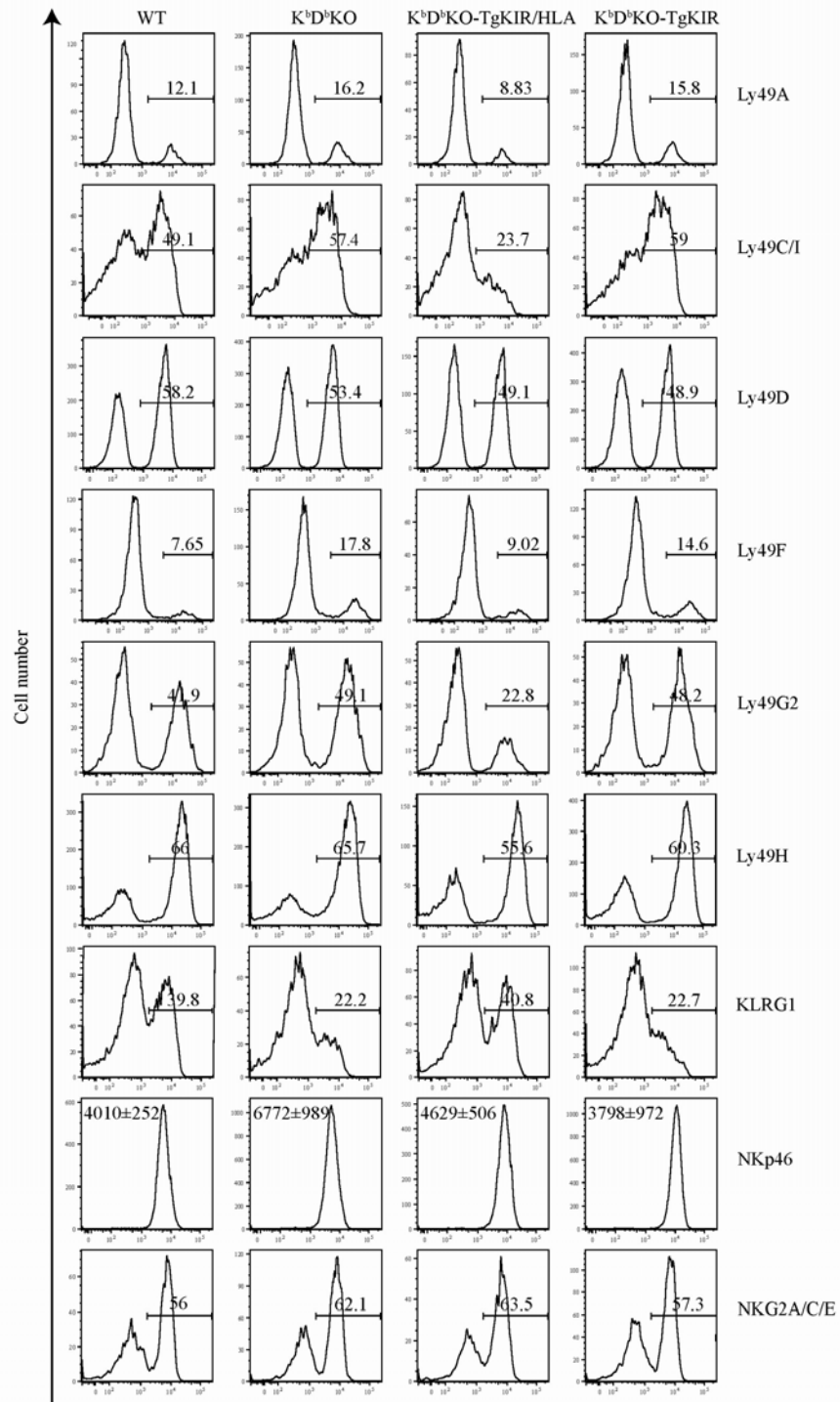


Fig. S2. Surface expression of NK cell receptors. Flow cytometric analysis of NK cell receptors on splenic NK cells from the indicated mice. The profiles represent the expression of the indicated markers on NK cells, which were defined as NK1.1⁺CD3⁻CD19⁻aquadead⁻ cells. Data show a representative experiment from at least two independent experiments (n = 3 mice per marker). The numbers represent percentages ± SEM, except for NKp46, for which the MFI ± SEM is shown.

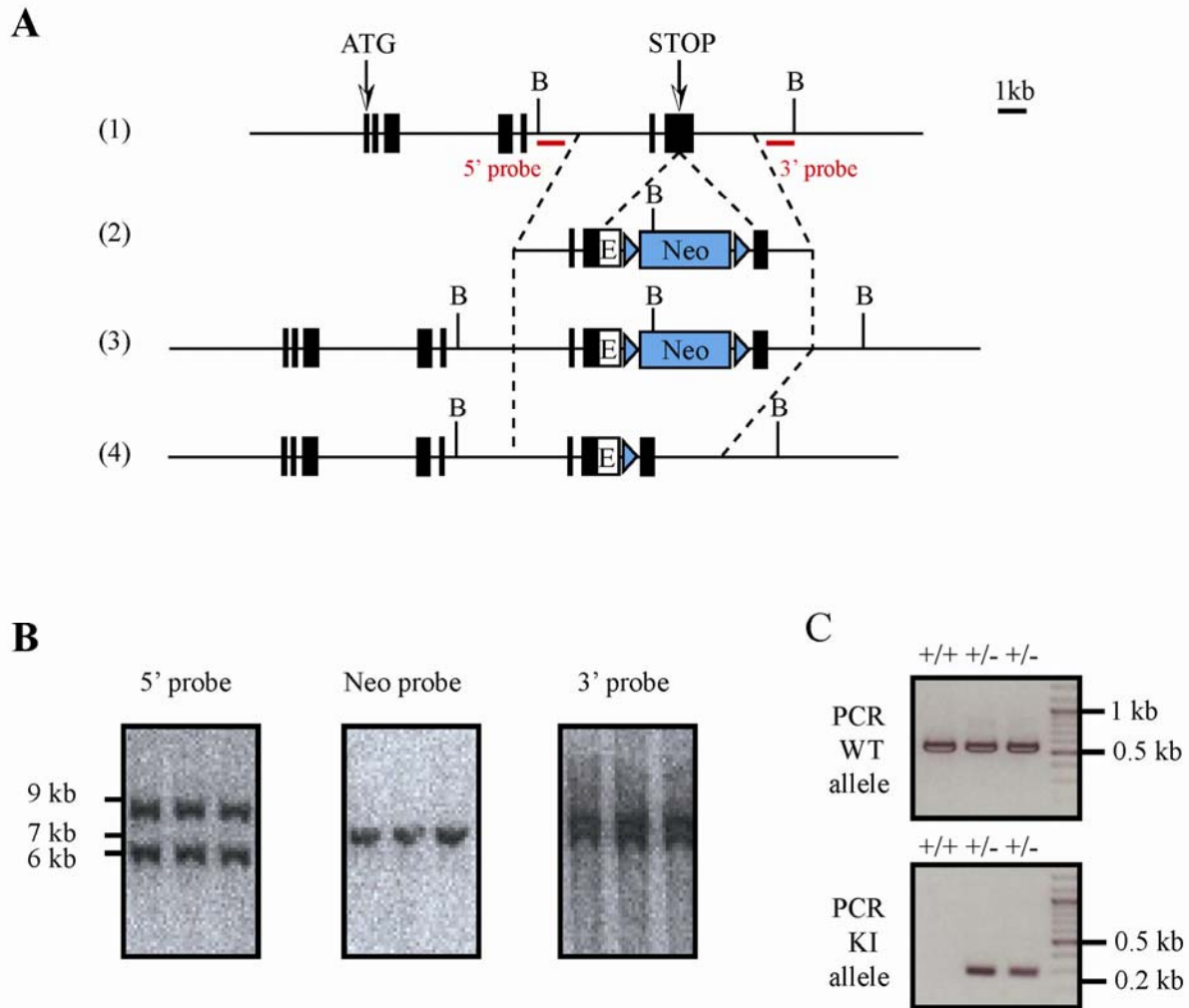


Fig. S3. Generation and identification of NKLT mice. **(A)** Strategy used to produce NKLT knock-in mice. (i) Partial restriction map of the *NCR1* gene. Exons are shown as filled black boxes. The initiation (ATG) and stop (STOP) codons are indicated. The 5'- and 3'-single copy probes used to verify proper homologous recombination events by Southern blotting analysis are shown in red. The selected homology arms are indicated by dotted lines. B: Bam HI. (ii) The targeting vector used for the introduction of the mutation into *NCR1*. The *Cre-neoR* auto-deleter cassette directs its own excision as it passes through the male germline and is shown flanked by loxP sites (triangles). (iii) Structure of the targeted *NCR1* allele following homologous recombination. (iv) Structure of the *NCR1* allele following homologous recombination and self-excision of the *Cre-neoR* cassette in male germinal cells. **(B)** Southern blotting analysis of three recombinant ES clones. DNA from ES cells was digested by Bam HI and hybridized to the indicated probes. **(C)** Genotyping of tail DNA of WT mice (lane 1) and of mice heterozygous (lanes 2 and 3) for the *NKLT* allele (KI) was performed by PCR analysis with primers in exon 7 and in the gene encoding EGFP.

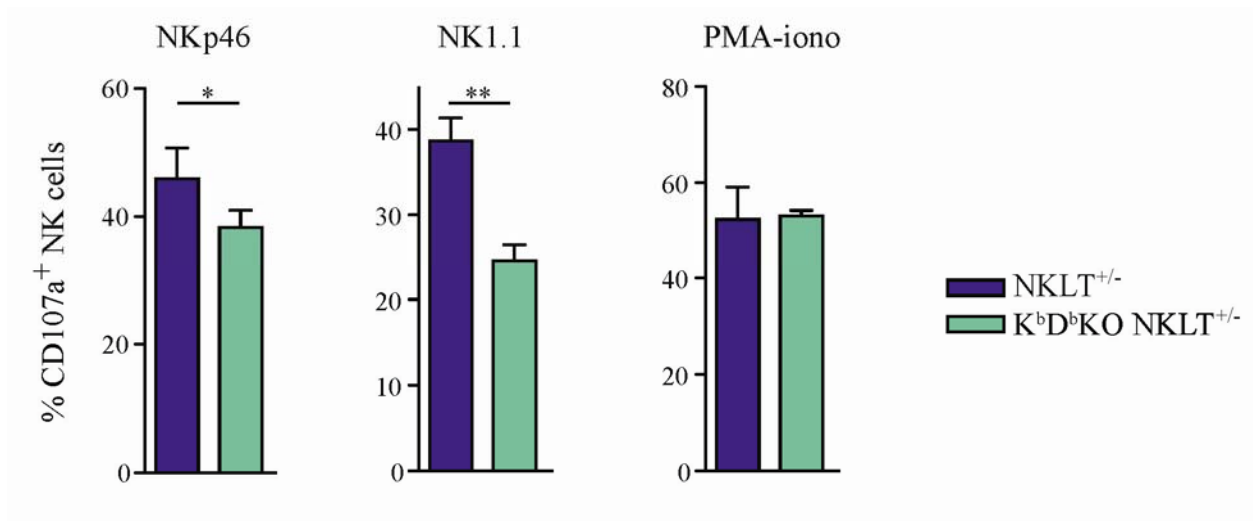


Fig. S4. Responsiveness of NKLT^{+/-} NK cells. Splenocytes from NKLT^{+/-} or K^bD^bKO NKLT^{+/-} mice were stimulated for four hours in vitro on plates coated with NKp46 or NK1.1 mAbs. Maximal cell responsiveness was assessed by stimulation with PMA and ionomycin. Cells were activated in presence of monensin and PE-conjugated antibody against CD107a (1D4B) in complete medium. Data show the frequencies of CD107a⁺ NK cells (NK1.1⁺quadead⁻ or NKp46⁺quadead⁻).

Table S1. Lists of probe sets differentially expressed in NK cells from K^bD^bKO-TgKIR/HLA and K^bD^bKO-TgKIR mice. Lists of probesets that were differentially expressed when comparing splenic NK cells from K^bD^bKO-TgKIR/HLA mice with those from K^bD^bKO-TgKIR mice, with an unpaired *t* test ($P \leq 0.05$) and a fold-change filter with a 1.7-fold cut-off. Affymetrix probset ID, fold change values, type of regulation, and gene symbols are shown for each probeset.

Affymetrix Probe Set ID	Fold-change	Regulation in K ^b D ^b KO-TgKIR	Gene Symbol
1415810_at	3.6699352	down	<i>Uhrf1</i>
1415811_at	3.2239454	down	<i>Uhrf1</i>
1415849_s_at	2.6403003	down	<i>Stmn1</i>
1415860_at	2.3476803	down	<i>Kpna2</i>
1415878_at	1.7028017	down	<i>Rrm1</i>
1415935_at	1.7117351	down	<i>Smoc2</i>
1415993_at	3.2291582	down	<i>Sqle</i>
1416076_at	5.058836	down	<i>Ccnb1</i> /// EG434175 /// EG667005
1416105_at	1.7650491	up	<i>Nnt</i>
1416107_at	3.695695	up	<i>Nsg2</i>
1416118_at	1.9391941	down	<i>Trim59</i>
1416120_at	4.808488	down	<i>Rrm2</i>
1416258_at	4.0869503	down	<i>Tk1</i>
1416299_at	6.9863477	down	<i>Shcbp1</i>
1416309_at	7.61813	down	<i>Nusap1</i>
1416416_x_at	1.7599665	up	<i>Gstm1</i>
1416492_at	1.7323813	down	<i>Ccne1</i>
1416503_at	1.8822169	down	<i>Lxn</i>
1416544_at	1.7501012	down	<i>Ezh2</i>
1416558_at	4.70689	down	<i>Melk</i>
1416575_at	2.391847	down	<i>Cdc45l</i>
1416592_at	1.7472541	down	<i>Glrx</i>
1416664_at	2.1035497	down	<i>Cdc20</i>
1416698_a_at	4.2456	down	<i>Cks1b</i>
1416746_at	2.1884964	down	<i>H2afx</i>
1416757_at	1.9212471	down	<i>Zwilch</i>
1416802_a_at	6.314643	down	<i>Cdca5</i>
1416868_at	1.8681884	down	<i>Cdkn2c</i>
1416871_at	1.8164266	down	<i>Adam8</i>
1416882_at	2.3070579	up	<i>Rgs10</i>
1416961_at	3.8082814	down	<i>Bub1b</i>
1416962_at	1.7104387	down	<i>Rcc1</i>
1417019_a_at	5.257899	down	<i>Cdc6</i>
1417185_at	2.5570245	down	<i>Ly6a</i>
1417299_at	2.1505325	down	<i>Nek2</i>
1417300_at	1.9616288	down	<i>Smpdl3b</i>
1417445_at	2.5237653	down	<i>Ndc80</i>
1417450_a_at	3.5064354	down	<i>Tacc3</i>
1417506_at	2.1935265	down	<i>Gmn</i>
1417541_at	2.0526695	down	<i>Hells</i>
1417644_at	1.7166264	down	<i>Sspn</i>
1417656_at	1.8011323	down	<i>Mybl2</i>

1417732_at	2.0154784	down	<i>Anxa8</i>
1417741_at	2.302543	up	<i>Pygl</i>
1417878_at	2.0178015	down	<i>E2f1</i>
1417910_at	6.1874447	down	<i>Ccna2</i>
1417911_at	8.2588005	down	<i>Ccna2</i>
1417926_at	3.9417481	down	<i>Ncapg2</i>
1417938_at	4.476496	down	<i>Rad51ap1</i>
1417976_at	1.8559239	down	<i>Ada</i>
1418026_at	2.3705127	down	<i>Exo1</i>
1418049_at	1.9176909	down	<i>Ltbp3</i>
1418058_at	1.7311714	up	<i>Eltf1</i>
1418059_at	2.0101335	up	<i>Eltf1</i>
1418184_at	2.0365424	down	<i>Cenpm</i>
1418206_at	2.4504	down	<i>Sdf2l1</i>
1418264_at	2.5437813	down	<i>Cenpk</i>
1418281_at	2.6889772	down	<i>Rad51</i>
1418355_at	2.185466	down	<i>Nucb2</i>
1418455_at	1.8533355	down	<i>Copz2</i>
1418497_at	2.393315	up	<i>Fgf13</i>
1418509_at	2.151511	down	<i>Cbr2</i>
1418612_at	2.9556298	up	<i>Slfn1</i>
1418762_at	2.2166145	up	<i>Cd55</i>
1418778_at	2.0802956	down	<i>Ccdc109b</i>
1418843_at	1.9389781	up	<i>Slc30a4</i>
1418919_at	3.2414906	down	<i>Sgoll</i>
1419042_at	1.9802169	down	<i>Iigp1</i>
1419103_a_at	1.808803	up	<i>Abhd6</i>
1419148_at	1.8353237	down	<i>Avil</i>
1419152_at	4.774165	down	<i>2810417H13Rik</i>
1419153_at	8.623594	down	<i>2810417H13Rik</i>
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1419838_s_at	1.7380689	down	<i>Plk4</i>
1419943_s_at	4.0136366	down	<i>Ccnb1</i>
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1420388_at	1.7522465	up	<i>Prss12</i>
1420398_at	2.0206907	down	<i>Rgs18</i>
1420688_a_at	3.3398173	up	<i>Sgce</i>
1420692_at	1.7637686	down	<i>Ii2ra</i>
1420703_at	1.7015269	up	<i>Csf2ra</i>
1420788_at	3.1588125	down	<i>Klrg1</i>
1420907_at	1.8367591	up	<i>Cd2ap</i>
1420913_at	2.2405622	down	<i>Slco2a1</i>
1420928_at	3.1910813	up	<i>St6gal1</i>
1421223_a_at	1.7956824	down	<i>Anxa4</i>
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1421344_a_at	2.407495	up	<i>Jub</i>
1421375_a_at	1.856265	down	<i>S100a6</i>
1421407_at	1.7383016	down	<i>F2rl2</i>

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1421923_at	1.9535877	up	<i>Sh3bp5</i>
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1422189_x_at	3.1890974	up	<i>Tcrg-V4</i>
1422280_at	3.0925083	down	<i>Gzmk</i>
1422430_at	3.9316213	down	<i>Figl1</i>
1422460_at	1.8706846	down	<i>Mad2l1</i>
1422462_at	1.7663914	down	<i>Ube2t</i>
1422533_at	1.8291037	down	<i>Cyp51</i>
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1422573_at	1.7000344	up	<i>Ampd3</i>
1422751_at	2.0853505	up	<i>Tle1</i>
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1424099_at	2.9248135	down	<i>Gpx8</i>
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1424478_at	1.7007077	up	<i>Bbs2</i>
1424511_at	2.628545	down	<i>Aurka</i>

1424542_at	2.4068608	down	<i>S100a4</i>
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1424971_at	2.4299216	down	<i>Ccdc99</i>
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1425213_at	2.2393517	down	<i>Fam81a</i>
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1427655_a_at	1.8374404	up	<i>A630038E17Rik</i>
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1429295_s_at	2.1283958	down	<i>Trip13</i>
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1433892_at	3.737253	down	<i>Spag5</i>
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1434099_at	1.861647	up	
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1434437_x_at	6.8953204	down	<i>Rrm2</i>
1434695_at	4.0848002	down	<i>Dtl</i>
1434748_at	2.8975642	down	<i>Ckap2</i>
1434767_at	3.4847662	down	<i>C79407</i>

1435054_at	1.930674	down	<i>Eme1</i>
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1435494_s_at	2.6861942	up	<i>Dsp</i>
1436186_at	3.2120006	down	<i>E2f8</i>
1436213_a_at	1.8416955	up	<i>1110028C15Rik</i>
1436707_x_at	3.2214992	down	<i>Ncaph</i>
1436845_at	1.7439119	up	<i>Axin2</i>
1436922_at	2.8578634	down	<i>Ppil5</i>
1437270_a_at	1.7400428	up	<i>Clcf1</i>
1437611_x_at	7.396423	down	<i>Kif2c</i>
1437716_x_at	4.4824457	down	<i>Kif22</i>
1438312_s_at	2.0903513	down	<i>Ltbp3</i>
1438675_at	1.7243843	up	<i>Sfrs8</i>
1438847_at	1.7100003	down	<i>Mxd3</i>
1439040_at	4.888544	down	<i>Cenpe</i>
1439377_x_at	3.272107	down	<i>Cdc20</i>
1439389_s_at	2.1845	down	<i>Myadm</i>
1448113_at	2.806064	down	<i>EG623112 /// Stmn1</i>
1448127_at	1.7800418	down	<i>Rrm1</i>
1448191_at	3.0735369	down	<i>Plk1</i>
1448205_at	5.358721	down	<i>Ccnb1</i>
1448226_at	7.2358866	down	<i>Rrm2</i>
1448259_at	1.714419	up	<i>Fstl1</i>
1448314_at	6.3794737	down	<i>Cdc2a</i>
1448330_at	1.752065	up	<i>Gstm1</i>
1448441_at	4.3068047	down	<i>Cks1b</i>
1448466_at	4.1243987	down	<i>Cdca5</i>
1448501_at	2.1220877	up	<i>Tspan6</i>
1448502_at	1.9645599	up	<i>Slc16a7</i>
1448562_at	2.75959	down	<i>Upp1</i>
1448627_s_at	7.70986	down	<i>Pbk</i>
1448635_at	1.7019736	down	<i>Smc2</i>
1448650_a_at	1.9476362	down	<i>Pole</i>
1448676_at	3.2789478	up	<i>Camk2b</i>
1448834_at	1.9243475	down	<i>Foxm1</i>
1448878_at	1.7082483	down	<i>Mxd3</i>
1448898_at	1.7899119	down	<i>Ccl9</i>
1448899_s_at	4.7233415	down	<i>Rad51ap1</i>
1448956_at	1.8855348	up	<i>Stard10</i>
1449060_at	2.1769445	down	<i>Kif2c /// LOC631653</i>
1449171_at	4.3270426	down	<i>Ttk</i>
1449207_a_at	4.7409267	down	<i>Kif20a</i>
1449254_at	4.3465514	down	<i>Spp1</i>
1449670_x_at	1.9227343	up	<i>Gpr137b /// LOC100044979</i>
1449699_s_at	3.4634364	down	<i>C330027C09Rik</i>
1449708_s_at	3.0089135	down	<i>Chek1</i>
1449799_s_at	3.128915	up	<i>Pkp2</i>
1449856_at	2.2517307	down	<i>Rgs18</i>

1450019_at	3.0367515	down	<i>Cx3cr1</i>
1450020_at	4.3806167	down	<i>Cx3cr1</i>
1450033_a_at	1.875821	down	<i>Stat1</i>
1450156_a_at	4.3182034	down	<i>Hmmr</i>
1450330_at	1.8066626	down	<i>Il10</i>
1450389_s_at	1.7740113	up	<i>Pip5k1b</i>
1450496_a_at	3.9996424	down	<i>2810433K01Rik</i>
1450521_a_at	4.8612256	up	<i>Tcrg-V4</i>
1450646_at	1.9766742	down	<i>Cyp51</i>
1450677_at	2.8197803	down	<i>Chek1</i>
1450692_at	3.118905	down	<i>Kif4</i>
1450789_at	2.5151844	down	<i>Rhpn1</i>
1450813_a_at	5.9507065	down	<i>Tnni1</i>
1450842_a_at	1.9260871	down	<i>Cenpa</i>
1450862_at	2.6161468	down	<i>Rad54l</i>
1450896_at	2.124586	up	<i>Arhgap5</i>
1450920_at	8.814886	down	<i>Ccnb2</i>
1451122_at	1.8682183	down	<i>Idi1</i>
1451128_s_at	5.0005484	down	<i>Kif22</i>
1451246_s_at	6.149014	down	<i>Aurkb</i>
1451281_at	1.7668197	up	<i>Zscan12</i>
1451335_at	5.015263	down	<i>Plac8</i>
1451358_a_at	1.8644638	down	<i>Racgap1</i>
1451721_a_at	2.3514323	down	<i>H2-Ab1</i>
1451910_a_at	3.6180365	up	<i>Cd6</i>
1452040_a_at	4.3466187	down	<i>Cdca3</i>
1452073_at	1.8996198	down	<i>6720460F02Rik</i>
1452210_at	1.9247924	down	<i>Dna2</i>
1452242_at	5.595585	down	<i>Cep55</i>
1452251_at	2.1241186	up	<i>Nbea</i>
1452305_s_at	2.7722244	down	<i>Cenpn</i>
1452314_at	4.919814	down	<i>Kif11</i>
1452331_s_at	1.701591	up	<i>Qser1</i>
1452432_at	1.8442512	up	<i>Tfpi</i>
1452458_s_at	5.179815	down	<i>Ppil5</i>
1452492_a_at	2.105308	up	<i>Slc37a2</i>
1452597_at	1.7088486	down	<i>2310061C15Rik</i>
1452679_at	2.5449023	down	<i>Tubb2b</i>
1452754_at	1.7157662	down	<i>Creld2</i>
1452843_at	1.9724172	up	<i>Il6st</i>
1452878_at	1.7346901	up	<i>Prkce</i>
1452954_at	6.1309295	down	<i>Ube2c</i>
1453107_s_at	3.9483368	down	<i>4933413G19Rik /// Foxm1 ///</i>
			<i>Pebp1</i>
1453678_at	1.7055153	up	<i>Mbd1</i>
1453851_a_at	2.3376431	down	<i>Gadd45g</i>
1454694_a_at	6.6915174	down	<i>Top2a</i>
1455040_s_at	2.127514	down	<i>Nhs12</i>
1455602_x_at	1.7299461	up	<i>1110028C15Rik</i>
1455730_at	2.0139458	down	<i>Dlgap5</i>

1455990_at	4.0997715	down	<i>Kif23</i>
1456302_at	1.8800787	up	<i>Pex6</i>
1456573_x_at	2.101338	up	<i>Nnt</i>
1460242_at	1.8240907	up	<i>Cd55</i>
1460336_at	2.090758	up	<i>Ppargc1a</i>
1460370_at	1.8570069	down	<i>Top1mt</i>
1460373_a_at	1.7659694	up	<i>Setd4</i>
1420081_s_at	1.771288	down	<i>D2Ertd750e</i>
1428304_at	5.0267115	down	<i>Esco2</i>
1428480_at	4.712276	down	<i>Cdca8</i>
1428481_s_at	4.9399967	down	<i>Cdca8</i>
1428527_at	1.8353298	down	<i>Snx7</i>
1428638_at	2.3568962	up	<i>Efhc2</i>
1428694_at	2.0931973	up	<i>Mirhg1</i>
1428713_s_at	2.0018868	down	<i>Gins2</i>
1428861_at	1.7950603	up	<i>Filip1l</i>
1428967_at	1.7983817	up	<i>Igflr</i>
1429058_at	1.9567873	down	<i>Tmem107</i>
1429095_at	2.7306604	down	<i>Cenpp</i>
1429156_at	1.7358754	down	<i>2610036L11Rik</i>
1429268_at	2.1312642	down	<i>2610318N02Rik</i>
1429284_at	1.90603	up	<i>Mobkl2b</i>
1429404_at	1.7480247	down	<i>2010317E24Rik</i>
1429499_at	2.5959148	down	<i>Fbxo5</i>
1430574_at	3.4583254	down	<i>Cdkn3</i>
1430834_at	1.9613096	up	<i>Gprin3</i>
1431087_at	2.678833	down	<i>Spc24</i>
1432361_a_at	3.386116	down	<i>Cenpp</i>
1433104_at	1.7160046	up	<i>Pus3</i>
1433557_at	1.8194237	up	<i>Cbx7</i>
1433862_at	4.8701005	down	<i>Espl1</i>
1434111_at	1.8161925	down	<i>LOC100048050 /// Lphn2</i>
1434112_at	1.9742806	down	<i>LOC100048050 /// Lphn2</i>
1434404_at	1.7558609	up	<i>Fam73a</i>
1434559_at	1.7903675	up	<i>Stx3</i>
1434729_at	1.7062457	up	<i>Zc4h2</i>
1434789_at	3.6614337	down	<i>Depdc1b</i>
1434911_s_at	2.1400468	down	<i>Arhgap19</i>
1435005_at	4.0388136	down	<i>Cenpe</i>
1435092_at	1.7197586	up	<i>Arl4a</i>
1435190_at	4.1909614	up	<i>Chl1</i>
1435198_at	1.990056	up	<i>545228</i>
1435207_at	4.222042	down	<i>Dixdc1</i>
1435264_at	4.0703387	down	<i>Emilin2</i>
1435267_at	1.8124915	up	<i>A430108E01Rik</i>
1435497_at	1.9858732	down	<i>5730590G19Rik ///</i> <i>LOC100047683</i>
1435575_at	4.483588	down	<i>Kntc1</i>
1435671_at	1.706612	up	<i>Mipol1</i>
1435746_at	1.9118053	up	<i>Srpk2</i>

1435773_at	2.42903	down	<i>4930547N16Rik</i>
1435938_at	1.9604104	down	<i>Ckap2l</i>
1436039_at	1.9973412	up	<i>Cmah</i>
1436200_at	2.079435	up	<i>Lonrf3</i>
1436434_at	4.0388093	down	<i>E2f2</i>
1436447_at	1.792074	up	<i>A630026N12Rik</i>
1436509_at	1.8294306	down	<i>Mlec</i>
1436654_at	1.7182603	down	<i>Gen1</i>
1436723_at	2.2498891	down	<i>Cenpi</i>
1436847_s_at	6.5186496	down	<i>Cdca8</i>
1436865_at	1.7418985	up	<i>Slc26a11</i>
1437128_a_at	1.9530666	up	<i>A630033E08Rik</i>
1437181_at	1.848429	up	<i>Peli2</i>
1437187_at	3.764946	down	<i>E2f7</i>
1437244_at	2.2247336	down	<i>Gas2l3</i>
1437245_at	2.0512862	down	<i>Tmem154</i>
1437251_at	3.1912405	down	<i>Cdca2</i>
1437370_at	2.077413	down	<i>Sgol2</i>
1437486_at	1.8438734	down	<i>Gprc5a</i>
1437580_s_at	4.0154705	down	<i>Nek2</i>
1437935_at	2.3777363	up	<i>4930486G11Rik</i>
1438310_at	2.3652496	up	
1438434_at	3.0574372	down	<i>Arhgap11a</i>
1438593_at	2.9732475	up	
1438811_at	1.7035422	down	<i>Dlgap5</i>
1438833_at	3.7219927	down	<i>Casc5</i>
1439066_at	2.1956315	up	<i>Angpt1</i>
1439510_at	2.9392688	down	<i>Sgol1</i>
1439622_at	2.3745222	up	<i>Rassf4</i>
1439768_x_at	1.9736015	up	<i>Sema4f</i>
1439855_at	2.2424247	down	<i>Tmtc1</i>
1440184_at	1.7140757	up	
1440200_at	1.7976784	down	<i>Fam184b</i>
1440298_at	2.6768088	up	<i>Trem12</i>
1441241_at	2.3885815	down	<i>9630013D21Rik</i>
1441579_at	5.004844	up	<i>Dmrta1</i>
1441789_at	2.160578	up	
1441971_at	2.537943	up	
1441972_at	1.8148069	down	<i>6230424C14Rik</i>
1442134_at	1.7195443	down	<i>Prr11</i>
1442190_at	1.7807344	up	
1442291_at	1.7419935	up	<i>Lpar2</i>
1442414_at	1.8463026	up	<i>Rnf103</i>
1442445_at	3.4532437	up	<i>2610027H17Rik</i>
1442556_at	1.9888262	up	
1442590_at	1.9144484	up	<i>Tnfrsf22 /// Tnfrsf23</i>
1442773_at	2.0036526	up	
1443777_at	2.9657211	up	
1443906_at	1.8499986	up	<i>Cd55</i>

1443978_at	1.7739942	down	<i>Ankle1</i>
1444248_at	1.7622756	up	<i>Rcn2</i>
1444257_at	1.7941667	down	<i>Prr11</i>
1444299_at	2.4450178	up	<i>A430093F15Rik</i>
1444525_at	1.849573	up	
1444552_at	1.8341651	up	
1445298_at	2.2777479	down	
1445680_x_at	1.7630373	down	<i>F2rl2</i>
1446731_at	1.7837094	up	<i>Fancf</i>
1446835_at	1.7745968	up	
1447363_s_at	5.179759	down	<i>Bub1b</i>
1447502_at	1.7951344	up	
1452881_at	2.258692	down	<i>Gins2</i>
1452980_at	1.8403064	down	<i>2810468N07Rik</i>
1453067_at	1.798755	down	<i>Aptid1</i>
1453119_at	2.003339	up	<i>Otud1</i>
1453188_at	1.8352824	down	<i>6230424C14Rik</i>
1453226_at	2.9994128	down	<i>3000004C01Rik</i>
1453416_at	2.758219	down	<i>Gas2l3</i>
1454685_at	2.587664	up	<i>Gpr146</i>
1454744_at	1.8541728	down	<i>F630043A04Rik</i>
1455251_at	2.1320436	down	<i>Itga1</i>
1455609_at	2.456802	down	<i>Cit</i>
1455790_at	4.5962663	down	<i>E2f2</i>
1455962_at	1.787973	up	<i>Hhat</i>
1455980_a_at	3.9753745	down	<i>Gas2l3</i>
1455983_at	2.6746798	down	<i>Cdca2</i>
1456077_x_at	1.8364053	down	<i>Cdc25c</i>
1456229_at	2.0827067	up	<i>Hoxb3</i>
1456280_at	5.5093117	down	<i>Clspn</i>
1456475_s_at	1.938659	down	<i>Prkar2b</i>
1456685_at	3.1535633	up	<i>Nsg2</i>
1456720_at	2.0132613	up	
1456765_at	3.1624365	down	<i>6430511F03</i>
1456795_at	2.3691146	up	<i>D330027G24Rik</i>
1456821_at	1.917048	up	
1456843_at	1.8022252	up	<i>Yes1</i>
1457434_s_at	1.9517447	down	<i>Ptpla</i>
1457796_at	1.7485873	up	<i>Ubr1</i>
1457813_at	2.2312589	up	
1458341_x_at	2.0436935	down	
1458374_at	3.4601495	down	<i>C79407</i>
1458427_at	1.8437926	down	<i>Brip1</i>
1459400_at	1.9165465	up	<i>A630038E17Rik</i>
1459838_s_at	1.9174937	up	<i>Btd11</i>
1459839_x_at	1.8215778	up	<i>Btd11</i>
1459864_at	1.753582	up	<i>Gpr146</i>
1460628_at	2.3678231	up	<i>Eme2</i>

Table S2. Lists of probe sets differentially expressed in NK cells from wild-type and K^bD^bKO mice. Lists of probesets that were differentially expressed when comparing splenic NK cells from WT mice with those from K^bD^bKO mice, with an unpaired *t* test ($P \leq 0.05$) and a fold-change filter with a 1.7-fold cut-off. Affymetrix probset ID, fold change values, type of regulation, and gene symbols are shown for each probeset.

Affymetrix Probe Set ID	Fold change	Regulation K ^b D ^b KO	Gene Symbol
1416529_at	8.829441	up	<i>Emp1</i>
1416666_at	2.557019	down	<i>Serpine2</i>
1418102_at	1.7885547	down	<i>Hes1</i>
1419417_at	1.8529904	down	<i>Vegfc</i>
1419647_a_at	2.6330945	up	<i>Ier3</i>
1419658_at	2.000851	up	<i>C920025E04Rik</i>
1420908_at	1.9490643	up	<i>Cd2ap</i>
1420909_at	2.1038	down	<i>Vegfa</i>
1421358_at	2.162965	down	<i>H2-M3</i>
1423006_at	1.9229474	up	<i>Pim1</i>
1424108_at	2.003114	up	<i>Glo1</i>
1424109_a_at	1.8268915	up	<i>Glo1</i>
1424936_a_at	1.9320046	up	<i>Dnahc8</i>
1424948_x_at	5.2096744	down	<i>H2-D1 /// H2-K1 /// LOC100044874</i>
1425336_x_at	3.2939978	down	<i>H2-K1</i>
1425545_x_at	10.032284	down	<i>H2-D1</i>
1425702_a_at	2.6343858	down	<i>Enpp5</i>
1426140_x_at	1.7905974	up	<i>Klra19</i>
1426324_at	2.1418061	down	<i>H2-D1</i>
1427243_at	1.8361837	down	<i>Rell1</i>
1427651_x_at	1.9934055	down	<i>H2-D1 /// H2-L /// LOC636948</i>
1427746_x_at	3.704592	down	<i>H2-K1</i>
1427820_at	3.7564974	up	
1428891_at	1.8094653	down	<i>9130213B05Rik</i>
1434280_at	4.2996387	down	
1448676_at	2.5413916	down	<i>Camk2b</i>
1449048_s_at	3.6467059	up	<i>Rab4a</i>
1450534_x_at	6.3028607	down	<i>H2-K1</i>
1451240_a_at	2.3555243	up	<i>Glo1</i>
1451683_x_at	69.202736	down	<i>H2-D1</i>
1451784_x_at	9.646849	down	<i>H2-D1</i>
1451931_x_at	9.361458	down	<i>H2-L</i>
1452359_at	1.9530272	down	<i>Rell1</i>
1452639_at	2.1677158	down	<i>Enpp4</i>
1456573_x_at	1.8502339	up	<i>Nnt</i>
1429452_x_at	1.7274002	up	<i>4933439C20Rik</i>
1430221_at	1.7209109	down	<i>9130008F23Rik</i>
1434580_at	2.505162	down	<i>Enpp4</i>
1437467_at	1.8163551	down	<i>Alcam</i>
1437904_at	2.0019093	up	<i>Rbm45</i>
1438239_at	2.3373804	down	<i>Mid1</i>
1438732_at	2.345159	down	<i>RP23-448C18.1</i>

1439766_x_at	1.809566	down	<i>Vegfc</i>
1440739_at	1.881122	down	<i>Vegfc</i>
1442166_at	2.514879	up	<i>Cpne5</i>
1453144_at	2.563195	up	<i>4933439C20Rik</i>
1455342_at	1.9412179	up	<i>A230083H22Rik</i>
1457717_at	1.7204499	down	<i>AI987986</i>
1458719_at	9.841171	up	
1459171_at	2.2728	up	<i>Emp1</i>
1459601_at	2.9079165	down	<i>Sik1</i>

Table S3. Lists of probe sets differentially expressed in NK cells from wild-type and β 2mKO mice. Lists of probesets that were differentially expressed when comparing splenic NK cells from WT mice with those from β 2mKO mice, with an unpaired t test ($P \leq 0.05$) and a fold-change filter with a 1.7-fold cut-off. Affymetrix probset ID, fold change values, type of regulation, and gene symbols are shown for each probeset.

Affymetrix Probe Set ID	Fold change	Regulation in β 2mKO	Gene Symbol
1416666_at	2.7589548	down	<i>Serpine2</i>
1418544_at	1.8058175	down	<i>Kcnip3</i>
1420788_at	2.0527008	down	<i>Klrg1</i>
1423571_at	1.831654	up	<i>Slpr1</i>
1424454_at	5.3136406	up	<i>Tmem87a</i>
1425045_at	2.5987358	down	<i>Jmjd7</i>
1426140_x_at	1.7325664	up	<i>Klra19</i>
1427347_s_at	1.8196455	down	<i>Tubb2a</i>
1430447_a_at	5.1968164	down	<i>Lair1</i>
1430989_a_at	1.700448	down	<i>1700020114Rik</i>
1431232_a_at	1.7325331	down	<i>Mga</i>
1433428_x_at	1.796557	down	<i>Tgm2</i>
1438177_x_at	1.7114209	down	<i>Entpd4 /// LOC100048085</i>
1448899_s_at	1.7679436	down	<i>Rad51ap1</i>
1449001_at	1.9001516	down	<i>Ivd</i>
1449129_a_at	2.0935707	down	<i>Kcnip3</i>
1449289_a_at	5.697256	down	<i>B2m</i>
1450639_at	2.0732577	down	<i>RP23-357114.1 / Slc28a2</i>
1452359_at	1.8440537	down	<i>Rell1</i>
1452428_a_at	42.329067	down	<i>B2m</i>
1452679_at	1.970879	down	<i>Tubb2b</i>
1460300_a_at	2.5210006	up	<i>Ltk</i>
1428371_at	2.1017413	up	<i>Tibk2</i>
1429345_at	1.952076	down	<i>Tubgcp4</i>
1430577_at	5.202535	down	<i>Haus2</i>
1433681_x_at	1.8048913	down	<i>Capn3</i>
1438732_at	2.1205072	down	<i>RP23-448C18.1</i>
1438833_at	2.3899975	down	<i>Casc5</i>
1439067_at	17.247318	down	<i>Lair1</i>
1442074_at	2.2238128	up	
1442316_x_at	2.1255512	down	<i>Trp53bp1</i>
1442424_at	7.273943	down	
1442466_a_at	3.9354877	down	<i>Hisppd2a</i>
1443484_at	1.8003345	down	<i>Rpap1</i>
1444040_at	18.90525	down	<i>Lair1</i>
1445191_at	2.982918	up	<i>Exdl</i>
1447900_x_at	1.8850272	down	<i>Entpd4 /// LOC100048085</i>
1454112_a_at	2.3646243	down	<i>Haus2</i>
1454880_s_at	5.397154	down	<i>Bmf</i>
1455863_at	6.4252095	down	<i>Spata511</i>
1456047_at	2.5467615	down	<i>Pla2g4b</i>
1457088_at	6.9635987	up	<i>Pldn</i>
1457796_at	2.0248196	down	<i>Ubr1</i>

1457812_at	2.3993654	down	<i>Trp53bp1</i>
1460470_at	2.9812536	down	<i>Acox1</i>
