

Supplementary Materials

Fig. S1. Protein levels of cytokine and transcription factors in ILC3s at different points of the circadian cycle.

Fig. S2. Acute SW model disrupts circadian rhythm without altering food intake or bodyweight.

Fig. S3. REV-ERB α deficiency results in reduced NKp46⁺ ILC3 in multiple tissues

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Fig. S5. Acute circadian disruption does not affect ILC3 mitochondria.

Fig. S6. Reduction of NKp46⁺ ILC3 in *Nr1d1*^{-/-} mice is not due to increase in plasticity.

Fig. S7. Accessibility of *Nfil3*, *Il17*, and *Tbp* loci in *Nr1d1*^{+/+} and *Nr1d1*^{-/-} ILC3s.

Table S1. Motif enrichment of known motifs by HOMER in *Nr1d1*^{+/+} NKp46⁻ ILC3s.

Table S2. *De novo* motif enrichment by HOMER in *Nr1d1*^{+/+} NKp46⁻ ILC3s.

Table S3. Motif enrichment of known motifs by HOMER in *Nr1d1*^{-/-} NKp46⁻ ILC3s.

Table S4. *De novo* motif enrichment by HOMER in *Nr1d1*^{-/-} NKp46⁻ ILC3s.

Table S5. Sequences of primers used for qPCR.

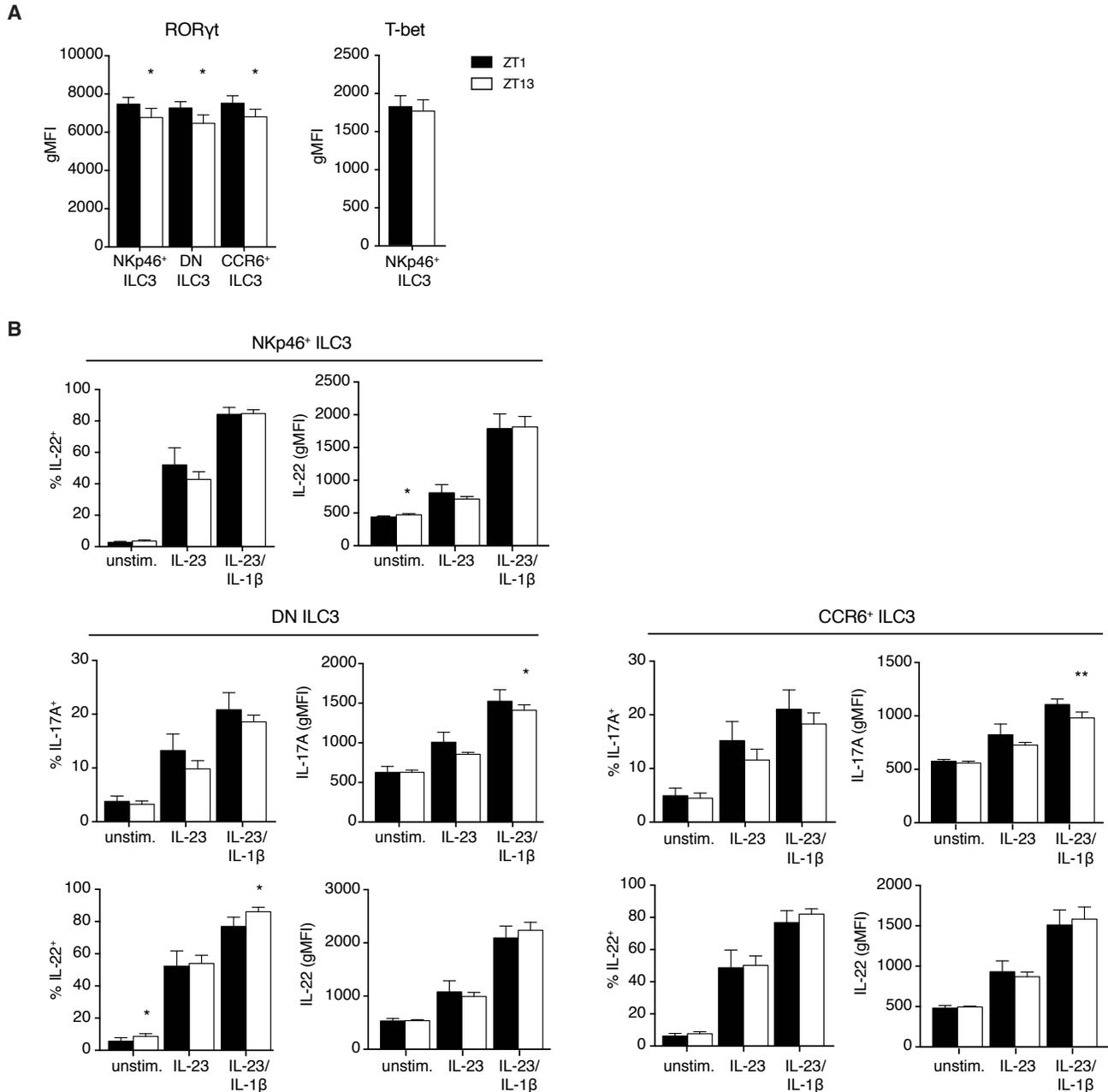


Figure S1. Protein levels of cytokine and transcription factors in ILC3s at different points of the circadian cycle.

C57Bl6/J mice were examined at ZT1 and ZT13. **A)** ROR γ t and T-bet expression by intracellular staining in ILC3 subsets. **B)** IL-17A and IL-22 production in ILC3 subsets in response to in vitro stimulation with 1 ng/mL IL-23 or 10 ng/mL IL-23/IL-1 β . Frequency of cytokine producing cells and amount of cytokine per cell (gMFI) are shown. Statistical analysis was performed using Student's t-test. Bars indicate mean (\pm SD). *, P<0.05; **, P<0.01; ***, P<0.001. Data are representative of two independent experiments, n=5 per group per experiment.

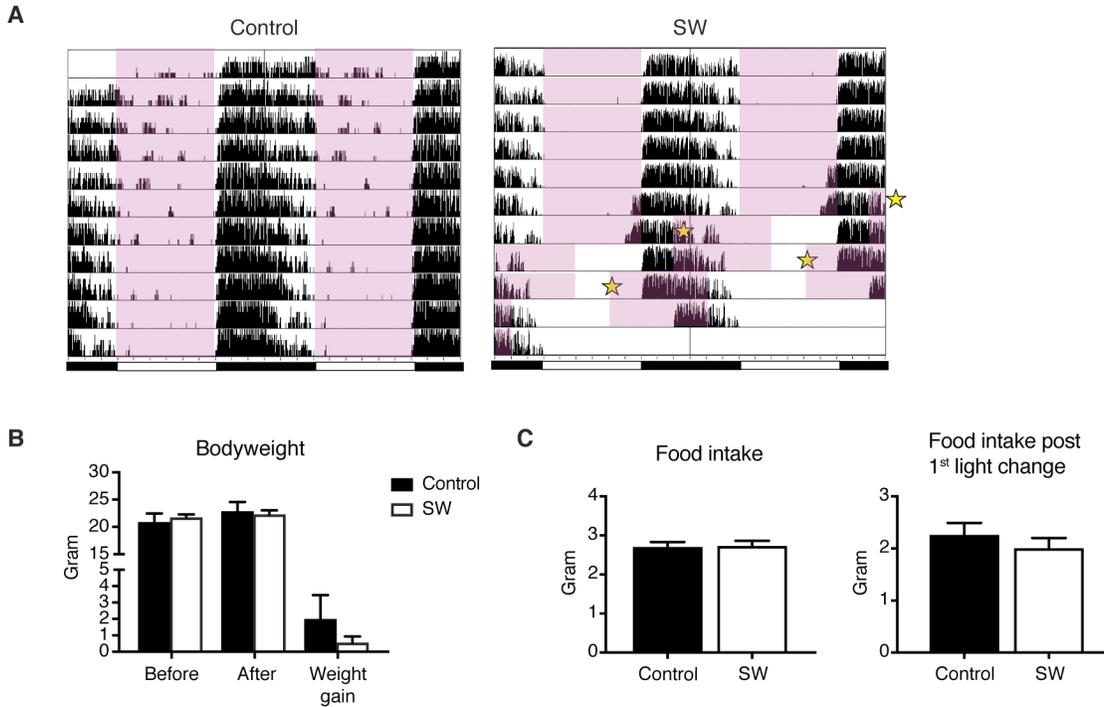


Figure S2. Acute SW model disrupts circadian rhythm without altering food intake or bodyweight.

A) Wheel-running activity of control and SW mice (colored blocks represent lighting schedule, stars indicate advance of light/dark cycle, double plotted for better visualization). **B)** Bodyweight and weight changes of control and SW mice. **C)** Average food intake per day during experiment (left) and food intake after first light change (right) of control and SW mice. Statistical analysis was performed using Student's t-test. Bars indicate mean (\pm SD). *, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.001$. Data are representative of two independent experiments (A-B), $n = 5$ per group per experiment.

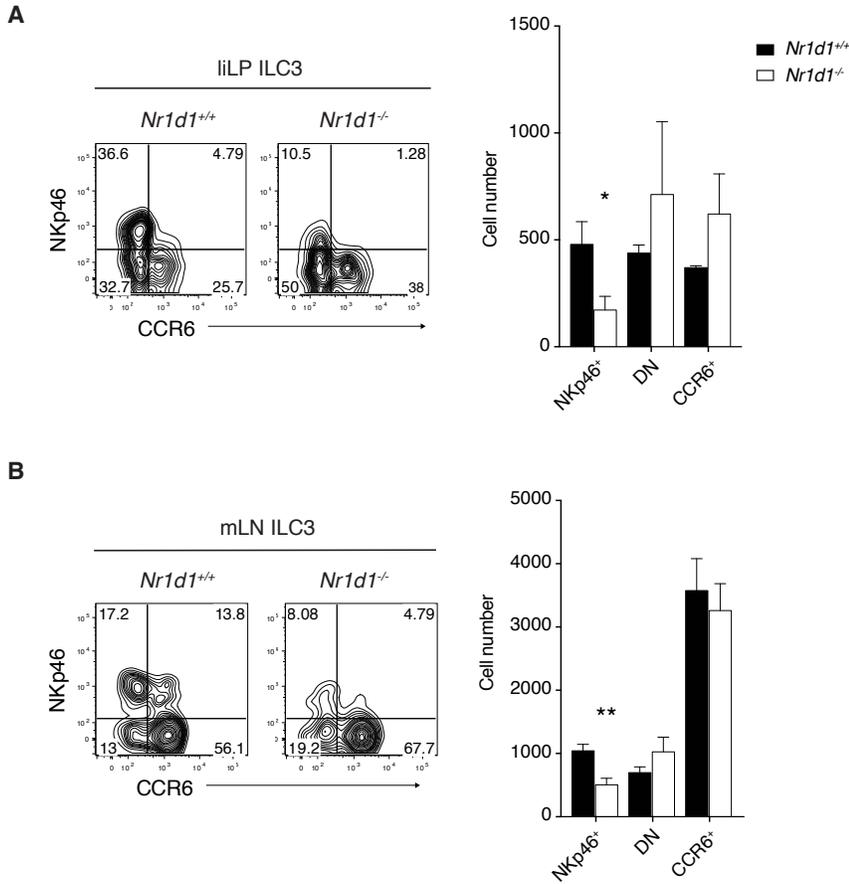


Figure S3. REV-ERB α deficiency results in reduced NKp46⁺ ILC3 in multiple tissues
 Representative plots (left) and numbers (right) of ILC3 subsets in: **A**) large intestine lamina propria (liLP), **B**) mesenteric lymph nodes (mLN). Statistical analysis was performed using Student's t-test. Bars indicate mean (\pm SD). *, P<0.05; **, P<0.01; ***, P<0.001. Data are representative of two independent experiments (A), n=3 per group per experiment.

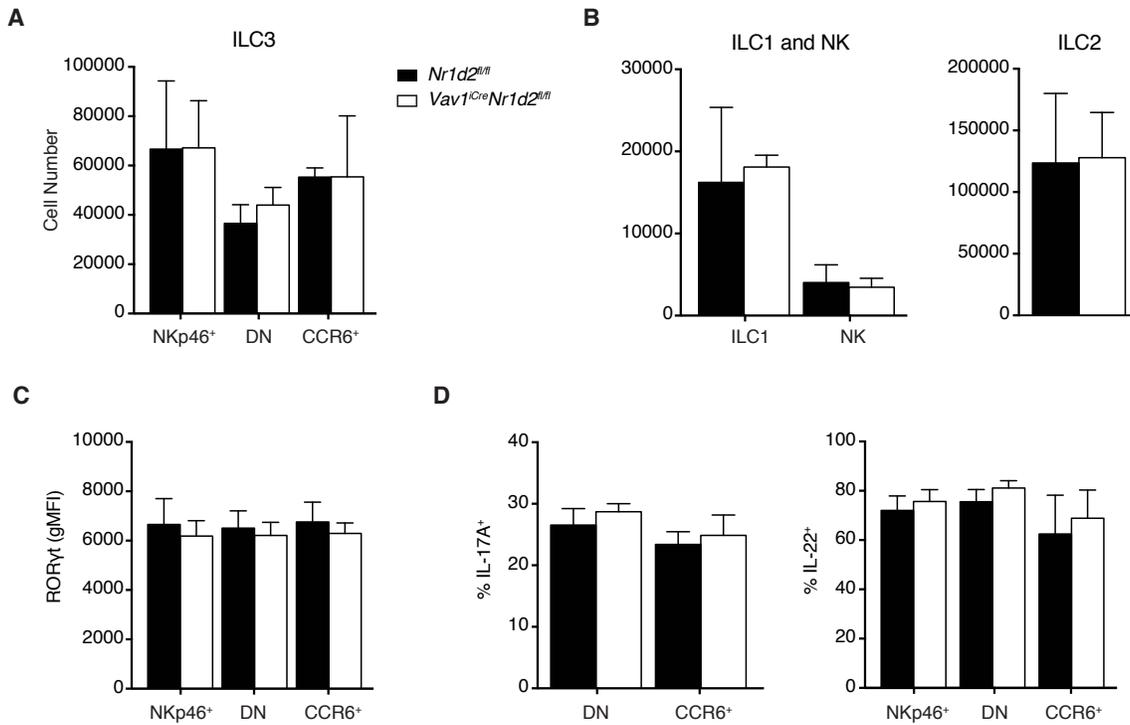


Figure S4. REV-ERB β deficiency alone does not affect ILC3s.

ILCs were isolated from *Nr1d2^{fl/fl}* and *Vav1^{iCre}Nr1d2^{fl/fl}* siLP. Cell counts of **A)** ILC3s, **B)** ILC1s, NKs, and ILC2s. **C)** Quantification of ROR γ t levels by intracellular staining in ILC3 subsets. **D)** Frequency of IL-17A⁺ and IL-22⁺ ILC3s after in vitro stimulation with 10 ng/mL of IL-23 and IL-1 β . Statistical analysis was performed using Student's t-test. Bars indicate mean (\pm SD). Data are representative of two independent experiments, n=3 per group per experiment.

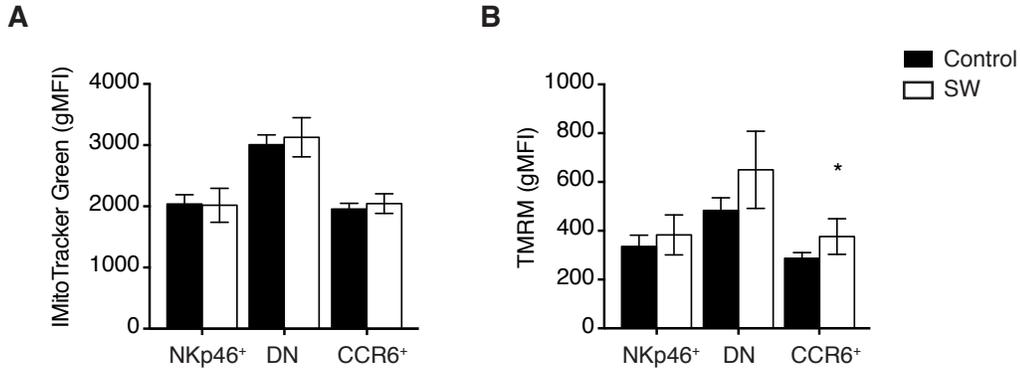


Figure S5. Acute circadian disruption does not affect ILC3 mitochondria.

Acute shift work model as in Fig. 2. Quantification of **A**) mitochondrial content by MitoTracker Green FM staining and **B**) mitochondrial potential by TMRM staining in ILC3 subsets. Statistical analysis was performed using Student's t-test. Bars indicate mean (\pm SD). *, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.001$. Data are representative of two independent experiments (A-B), $n = 5$ per group per experiment.

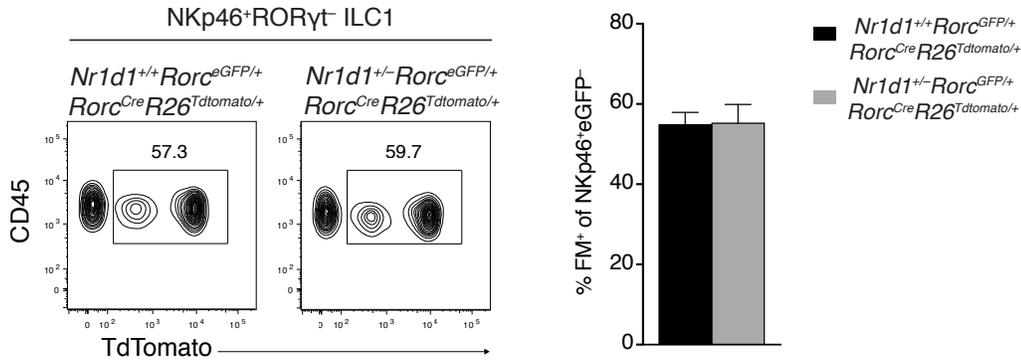


Figure S6. Reduction of NKp46⁺ ILC3 in *Nr1d1*^{-/-} mice is not due to increase in plasticity. Representative plot (left) and frequency (right) of RORyt-FM⁺ ILC1s (CD45⁺Lin⁻ (CD3/CD5/CD19)⁻RORyt-eGFP⁻NKp46⁺) from siLP of *Nr1d1*^{+/+} and *Nr1d1*^{-/-} RORyt-reporter-FM mice. Statistical analysis was performed using Student's t-test. Bars indicate mean (±SD). *, P<0.05; **, P<0.01; ***, P<0.001. Data are representative of two independent experiments, n=3-4 per genotype per experiment.

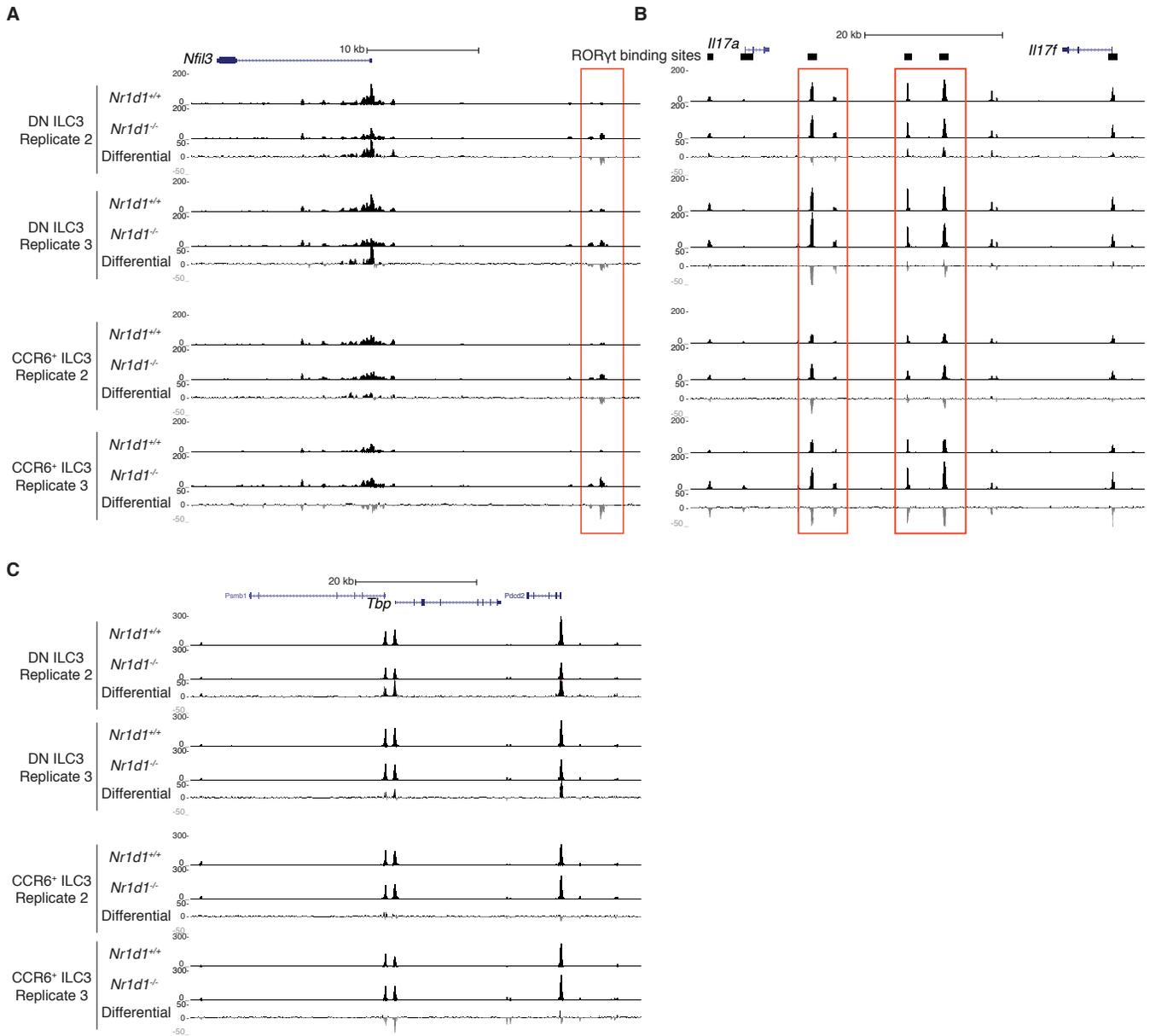


Figure S7. Accessibility of *Nfil3*, *Il17*, and *Tbp* loci in *Nr1d1*^{+/+} and *Nr1d1*^{-/-} ILC3s. UCSC genome browser view of ATAC-seq tracks at the **A)** *Nfil3*, **B)** *Il17*, and **C)** *Tbp* loci in biological replicates of *Nr1d1*^{+/+} and *Nr1d1*^{-/-} ILC3s.

| Motif Name | Consensus | P-value | Log P-value | q-value (Benjamini) | # of Target Sequences with Motif(of 1138) | % of Target Sequences with Motif | # of Background Sequences with Motif(of 48512) | % of Background Sequences with Motif |
|--|---------------|----------|-------------|---------------------|---|----------------------------------|--|--------------------------------------|
| RORgt(NR)/EL4-RORgt.Flag-ChIP-Seq(GSE56019)/Homer | AAYTAGGTCA | 1.00E-79 | -1.84E+02 | 0 | 208 | 18.28% | 1780.4 | 3.67% |
| RUNX1(Runt)/Jurkat-RUNX1-ChIP-Seq(GSE29180)/Homer | AAACCACARM | 1.00E-61 | -1.41E+02 | 0 | 617 | 54.22% | 14760.2 | 30.45% |
| RUNX(Runt)/HPC7-Runx1-ChIP-Seq(GSE22178)/Homer | SAAACCACAG | 1.00E-59 | -1.37E+02 | 0 | 500 | 43.94% | 10707.5 | 22.09% |
| RUNX2(Runt)/PCa-RUNX2-ChIP-Seq(GSE33889)/Homer | NWAACCACADNN | 1.00E-58 | -1.35E+02 | 0 | 556 | 48.86% | 12753.2 | 26.31% |
| RUNX-AML(Runt)/CD4+-PolII-ChIP-Seq(Barski_et_al.)/Homer | GCTGTGGTTW | 1.00E-54 | -1.26E+02 | 0 | 499 | 43.85% | 11056.3 | 22.81% |
| NFkB-p65(RHD)/GM12787-p65-ChIP-Seq(GSE19485)/Homer | WGGGGATTCCCC | 1.00E-52 | -1.21E+02 | 0 | 355 | 31.20% | 6563.7 | 13.54% |
| NFkB-p65-Rel(RHD)/ThioMac-LPS-Expression(GSE23622)/Homer | GGAAATTCCCC | 1.00E-44 | -1.03E+02 | 0 | 96 | 8.44% | 637 | 1.31% |
| NFkB-p50,p52(RHD)/Monocyte-p50-ChIP-Chip(Schreiber_et_al.)/Homer | GGGGGAATCCCC | 1.00E-18 | -4.19E+01 | 0 | 86 | 7.56% | 1210.6 | 2.50% |
| Tcf4(HMG)/Hct116-Tcf4-ChIP-Seq(SRA012054)/Homer | ASATCAAAGGVA | 1.00E-15 | -3.67E+01 | 0 | 253 | 22.23% | 6441.2 | 13.29% |
| Atf7(bZIP)/3T3L1-Atf7-ChIP-Seq(GSE56872)/Homer | NGRTGACGTCA Y | 1.00E-12 | -2.82E+01 | 0 | 235 | 20.65% | 6312.2 | 13.02% |
| Atf2(bZIP)/3T3L1-Atf2-ChIP-Seq(GSE56872)/Homer | NRRTGACGTCAT | 1.00E-11 | -2.73E+01 | 0 | 181 | 15.91% | 4514.4 | 9.31% |
| Atf1(bZIP)/K562-ATF1-ChIP-Seq(GSE31477)/Homer | GATGACGTCA | 1.00E-11 | -2.70E+01 | 0 | 297 | 26.10% | 8618.8 | 17.78% |
| c-Jun-CRE(bZIP)/K562-cJun-ChIP-Seq(GSE31477)/Homer | ATGACGTCATCY | 1.00E-11 | -2.67E+01 | 0 | 168 | 14.76% | 4116.1 | 8.49% |
| Etv2(ETS)/ES-ER71-ChIP-Seq(GSE59402)/Homer(0.967) | NNAYTTCCTGHN | 1.00E-10 | -2.51E+01 | 0 | 412 | 36.20% | 13142.3 | 27.12% |
| BATF(bZIP)/Th17-BATF-ChIP-Seq(GSE39756)/Homer | DATGASTCAT | 1.00E-10 | -2.39E+01 | 0 | 286 | 25.13% | 8442.9 | 17.42% |
| Egr2(Zf)/Thymocytes-Egr2-ChIP-Seq(GSE34254)/Homer | NGCGTGGGCGG R | 1.00E-10 | -2.38E+01 | 0 | 93 | 8.17% | 1890.4 | 3.90% |
| Jun-AP1(bZIP)/K562-cJun-ChIP-Seq(GSE31477)/Homer | GATGASTCATCN | 1.00E-10 | -2.38E+01 | 0 | 129 | 11.34% | 2995.3 | 6.18% |
| Fosl2(bZIP)/3T3L1-Fosl2-ChIP-Seq(GSE56872)/Homer | NATGASTCABNN | 1.00E-09 | -2.29E+01 | 0 | 168 | 14.76% | 4322.4 | 8.92% |

| | | | | | | | | |
|---|----------------|----------|-----------|---|-----|--------|---------|--------|
| ETS:RUNX(ETS,Runt)/Jurkat-RUNX1-ChIP-Seq(GSE17954)/Homer | RCAGGATGTGGT | 1.00E-09 | -2.29E+01 | 0 | 69 | 6.06% | 1239.3 | 2.56% |
| Fra1(bZIP)/BT549-Fra1-ChIP-Seq(GSE46166)/Homer | NNATGASTCATH | 1.00E-09 | -2.28E+01 | 0 | 245 | 21.53% | 7030.3 | 14.51% |
| PU.1(ETS)/ThioMac-PU.1-ChIP-Seq(GSE21512)/Homer | AGAGGAAGTG | 1.00E-09 | -2.21E+01 | 0 | 250 | 21.97% | 7264.3 | 14.99% |
| Atf3(bZIP)/GBM-ATF3-ChIP-Seq(GSE33912)/Homer | DATGASTCATHN | 1.00E-09 | -2.17E+01 | 0 | 283 | 24.87% | 8513.1 | 17.56% |
| Fra2(bZIP)/Striatum-Fra2-ChIP-Seq(GSE43429)/Homer | GGATGACTCATC | 1.00E-09 | -2.12E+01 | 0 | 215 | 18.89% | 6073.9 | 12.53% |
| Ets1-distal(ETS)/CD4+PolII-ChIP-Seq(Barski_et_al.)/Homer | MACAGGAAGT | 1.00E-09 | -2.11E+01 | 0 | 182 | 15.99% | 4915.7 | 10.14% |
| EWS:ERG-fusion(ETS)/CADO_ES1-EWS:ERG-ChIP-Seq(SRA014231)/Homer | ATTCCTGTN | 1.00E-08 | -2.01E+01 | 0 | 319 | 28.03% | 10010.7 | 20.65% |
| JunB(bZIP)/DendriticCells-Junb-ChIP-Seq(GSE36099)/Homer | RATGASTCAT | 1.00E-07 | -1.84E+01 | 0 | 239 | 21.00% | 7160.6 | 14.77% |
| ETS1(ETS)/Jurkat-ETS1-ChIP-Seq(GSE17954)/Homer | ACAGGAAGTG | 1.00E-07 | -1.69E+01 | 0 | 421 | 36.99% | 14339.8 | 29.59% |
| GABPA(ETS)/Jurkat-GABPa-ChIP-Seq(GSE17954)/Homer | RACCGAAGT | 1.00E-07 | -1.66E+01 | 0 | 376 | 33.04% | 12577 | 25.95% |
| TCFL2(HMG)/K562-TCF7L2-ChIP-Seq(GSE29196)/Homer | ACWTCAAAGG | 1.00E-07 | -1.64E+01 | 0 | 58 | 5.10% | 1140 | 2.35% |
| Tcf3(HMG)/mES-Tcf3-ChIP-Seq(GSE11724)/Homer | ASWTCAAAGG | 1.00E-07 | -1.63E+01 | 0 | 137 | 12.04% | 3672.6 | 7.58% |
| Gata2(Zf)/K562-GATA2-ChIP-Seq(GSE18829)/Homer | BBCTTATCTS | 1.00E-07 | -1.62E+01 | 0 | 277 | 24.34% | 8785 | 18.13% |
| Fli1(ETS)/CD8-FLI1-ChIP-Seq(GSE20898)/Homer | NRYTTCCGGH | 1.00E-06 | -1.54E+01 | 0 | 425 | 37.35% | 14670.3 | 30.27% |
| EWS:FLI1-fusion(ETS)/SK_N_MC-EWS:FLI1-ChIP-Seq(SRA014231)/Homer | VACAGGAAAT | 1.00E-06 | -1.45E+01 | 0 | 257 | 22.58% | 8188.1 | 16.89% |
| ERG(ETS)/VCaP-ERG-ChIP-Seq(GSE14097)/Homer | ACAGGAAGTG | 1.00E-06 | -1.43E+01 | 0 | 585 | 51.41% | 21425.3 | 44.21% |
| GATA(Zf),IR4/iTreg-Gata3-ChIP-Seq(GSE20898)/Homer | NAGATWNBATCTNN | 1.00E-06 | -1.41E+01 | 0 | 50 | 4.39% | 991.1 | 2.04% |
| AP-1(bZIP)/ThioMac-PU.1-ChIP-Seq(GSE21512)/Homer | VTGACTCATC | 1.00E-06 | -1.40E+01 | 0 | 296 | 26.01% | 9740.5 | 20.10% |
| JunD(bZIP)/K562-JunD-ChIP-Seq/Homer | ATGACGTCATCN | 1.00E-06 | -1.40E+01 | 0 | 58 | 5.10% | 1232.1 | 2.54% |
| COUP-TFII(NR)/Artia-Nr2f2-ChIP-Seq(GSE46497)/Homer | AGRGGTCA | 1.00E-06 | -1.39E+01 | 0 | 605 | 53.16% | 22327.3 | 46.07% |
| Gata6(Zf)/HUG1N-GATA6-ChIP-Seq(GSE51936)/Homer | YCTTATCTBN | 1.00E-05 | -1.37E+01 | 0 | 349 | 30.67% | 11856 | 24.46% |
| IRF2(IRF)/Erythroblasts-IRF2-ChIP-Seq(GSE36985)/Homer | GAAASYGAAASY | 1.00E-05 | -1.30E+01 | 0 | 57 | 5.01% | 1239.9 | 2.56% |

| | | | | | | | | |
|--|-----------------------|----------|-----------|--------|-----|--------|---------|--------|
| IRF1(IRF)/PBMC-IRF1-ChIP-Seq(GSE43036)/Homer | GAAAGTGAAAGT | 1.00E-05 | -1.30E+01 | 0 | 71 | 6.24% | 1677.8 | 3.46% |
| Brn1(POU,Homeobox)/NPC-Brn1-ChIP-Seq(GSE35496)/Homer | TATGCWAATBAV | 1.00E-05 | -1.25E+01 | 0 | 118 | 10.37% | 3275.6 | 6.76% |
| Reverb(NR),DR2/RAW-Reverba.biotin-ChIP-Seq(GSE45914)/Homer | GTRGGTCASTGGGTCA | 1.00E-05 | -1.25E+01 | 0 | 82 | 7.21% | 2060.2 | 4.25% |
| X-box(HTH)/NPC-H3K4me1-ChIP-Seq(GSE16256)/Homer | GGTTGCCATGGCAA | 1.00E-05 | -1.24E+01 | 0 | 67 | 5.89% | 1580.3 | 3.26% |
| Rfx2(HTH)/LoVo-RFX2-ChIP-Seq(GSE49402)/Homer | GTTGCCATGGCAACM | 1.00E-05 | -1.16E+01 | 0.0001 | 58 | 5.10% | 1334.7 | 2.75% |
| MafA(bZIP)/Islet-MafA-ChIP-Seq(GSE30298)/Homer | TGCTGACTCA | 1.00E-04 | -1.13E+01 | 0.0001 | 339 | 29.79% | 11764.9 | 24.27% |
| Rfx1(HTH)/NPC-H3K4me1-ChIP-Seq(GSE16256)/Homer | KGTTGCCATGGCAA | 1.00E-04 | -1.11E+01 | 0.0001 | 102 | 8.96% | 2824.1 | 5.83% |
| Gata1(Zf)/K562-GATA1-ChIP-Seq(GSE18829)/Homer | SAGATAAGR | 1.00E-04 | -1.10E+01 | 0.0001 | 237 | 20.83% | 7813.2 | 16.12% |
| ETV1(ETS)/GIST48-ETV1-ChIP-Seq(GSE22441)/Homer | AACCGGAAGT | 1.00E-04 | -1.10E+01 | 0.0001 | 503 | 44.20% | 18490.3 | 38.15% |
| GATA(Zf),IR3/iTreg-Gata3-ChIP-Seq(GSE20898)/Homer | NNNNNBAGATAWAYATCTVHN | 1.00E-04 | -1.07E+01 | 0.0002 | 72 | 6.33% | 1831.3 | 3.78% |
| RFX(HTH)/K562-RFX3-ChIP-Seq(SRA012198)/Homer | CGGTTGCCATGGCAAC | 1.00E-04 | -1.05E+01 | 0.0002 | 51 | 4.48% | 1169.4 | 2.41% |
| RAR:RXR(NR),DR5/ES-RAR-ChIP-Seq(GSE56893)/Homer | RGGTCADNNAGAGGTC | 1.00E-04 | -1.02E+01 | 0.0003 | 25 | 2.20% | 422.7 | 0.87% |
| Gata4(Zf)/Heart-Gata4-ChIP-Seq(GSE35151)/Homer | NBWGATAAGR | 1.00E-04 | -1.00E+01 | 0.0003 | 364 | 31.99% | 12945.3 | 26.71% |
| IRF3(IRF)/BMDM-Irf3-ChIP-Seq(GSE67343)/Homer | AGTTTCAKTTTC | 1.00E-04 | -9.45E+00 | 0.0005 | 135 | 11.86% | 4137.9 | 8.54% |
| IRF4(IRF)/GM12878-IRF4-ChIP-Seq(GSE32465)/Homer | ACTGAAACCA | 1.00E-04 | -9.30E+00 | 0.0006 | 178 | 15.64% | 5755 | 11.87% |
| GATA3(Zf),DR8/iTreg-Gata3-ChIP-Seq(GSE20898)/Homer | AGATSTNDNNDSAGATAASN | 1.00E-03 | -9.02E+00 | 0.0008 | 40 | 3.51% | 894.3 | 1.85% |
| Chop(bZIP)/MEF-Chop-ChIP-Seq(GSE35681)/Homer | ATTGCATCAT | 1.00E-03 | -9.00E+00 | 0.0008 | 84 | 7.38% | 2350.9 | 4.85% |
| CarG(MADS)/PUER-Srf-ChIP-Seq(Sullivan_et_al.)/Homer | CCATATATGGNM | 1.00E-03 | -8.60E+00 | 0.0012 | 124 | 10.90% | 3815.3 | 7.87% |
| Egr1(Zf)/K562-Egr1-ChIP-Seq(GSE32465)/Homer | TGCGTGGGYG | 1.00E-03 | -8.49E+00 | 0.0013 | 238 | 20.91% | 8164.3 | 16.84% |
| ISRE(IRF)/ThioMac-LPS-Expression(GSE23622)/Homer | AGTTTCASTTTC | 1.00E-03 | -8.39E+00 | 0.0014 | 33 | 2.90% | 708.7 | 1.46% |
| Elk1(ETS)/Hela-Elk1-ChIP-Seq(GSE31477)/Homer | HACTTCCGGY | 1.00E-03 | -8.37E+00 | 0.0014 | 206 | 18.10% | 6936.9 | 14.31% |
| Esrrb(NR)/mES-Esrrb-ChIP-Seq(GSE11431)/Homer | KTGACCTTGA | 1.00E-03 | -8.33E+00 | 0.0014 | 278 | 24.43% | 9762.6 | 20.14% |

| | | | | | | | | |
|--|--------------------------|----------|-----------|--------|-----|--------|---------|--------|
| bZIP:IRF(bZIP,IRF)/Th17-BatF-ChIP-Seq(GSE39756)/Homer | NAGTTTCABTHT GACTNW | 1.00E-03 | -8.01E+00 | 0.0019 | 171 | 15.03% | 5639.1 | 11.63% |
| CRE(bZIP)/Promoter/Homer | CSGTGACGTCAC | 1.00E-03 | -7.85E+00 | 0.0022 | 99 | 8.70% | 2975.7 | 6.14% |
| EKLF(Zf)/Erythrocyte-Klf1-ChIP-Seq(GSE20478)/Homer | NWGGGTGTGGC Y | 1.00E-03 | -7.78E+00 | 0.0023 | 104 | 9.14% | 3163.7 | 6.53% |
| MafK(bZIP)/C2C12-MafK-ChIP-Seq(GSE36030)/Homer | GCTGASTCAGCA | 1.00E-03 | -7.68E+00 | 0.0026 | 105 | 9.23% | 3209.5 | 6.62% |
| Oct6(POU,Homeobox)/NPC-Pou3f1-ChIP-Seq(GSE35496)/Homer | WATGCAAATGAG | 1.00E-03 | -7.62E+00 | 0.0027 | 141 | 12.39% | 4549.3 | 9.39% |
| THRB(NR)/Liver-NR1A2-ChIP-Seq(GSE52613)/Homer | TRAGGTCA | 1.00E-03 | -7.36E+00 | 0.0034 | 962 | 84.53% | 39170 | 80.82% |
| Sp5(Zf)/mES-Sp5.Flag-ChIP-Seq(GSE72989)/Homer | RGKGGGCGGAG C | 1.00E-03 | -7.13E+00 | 0.0042 | 309 | 27.15% | 11196.3 | 23.10% |
| KLF6(Zf)/PDAC-KLF6-ChIP-Seq(GSE64557)/Homer | MKGGGYGTGGC C | 1.00E-03 | -7.06E+00 | 0.0045 | 346 | 30.40% | 12705.9 | 26.22% |
| Atf4(bZIP)/MEF-Atf4-ChIP-Seq(GSE35681)/Homer | MTGATGCAAT | 1.00E-03 | -7.04E+00 | 0.0045 | 98 | 8.61% | 3015.7 | 6.22% |
| Mef2a(MADS)/HL1-Mef2a.biotin-ChIP-Seq(GSE21529)/Homer | CYAAAAATAG | 1.00E-02 | -6.68E+00 | 0.0064 | 144 | 12.65% | 4774.7 | 9.85% |
| ELF3(ETS)/PDAC-ELF3-ChIP-Seq(GSE64557)/Homer | ANCAGGAAGT | 1.00E-02 | -6.66E+00 | 0.0064 | 292 | 25.66% | 10593.7 | 21.86% |
| E-box(bHLH)/Promoter/Homer | SSGGTCACGTGA | 1.00E-02 | -6.50E+00 | 0.0074 | 36 | 3.16% | 890.7 | 1.84% |
| ERE(NR),IR3/MCF7-ERa-ChIP-Seq(Unpublished)/Homer | VAGGTACNSTG ACC | 1.00E-02 | -6.30E+00 | 0.0089 | 121 | 10.63% | 3948.9 | 8.15% |
| KLF3(Zf)/MEF-Klf3-ChIP-Seq(GSE44748)/Homer | NRGCCCCRCCCH BNN | 1.00E-02 | -6.29E+00 | 0.0089 | 181 | 15.91% | 6252.6 | 12.90% |
| MITF(bHLH)/MastCells-MITF-ChIP-Seq(GSE48085)/Homer | RTCATGTGAC | 1.00E-02 | -5.97E+00 | 0.0121 | 353 | 31.02% | 13202.6 | 27.24% |
| Pdx1(Homeobox)/Islet-Pdx1-ChIP-Seq(SRA008281)/Homer | YCATYAATCA | 1.00E-02 | -5.66E+00 | 0.0163 | 312 | 27.42% | 11591.9 | 23.92% |
| GATA3(Zf)/iTreg-Gata3-ChIP-Seq(GSE20898)/Homer | AGATAASR | 1.00E-02 | -5.63E+00 | 0.0166 | 480 | 42.18% | 18536.9 | 38.25% |
| CEBP:AP1(bZIP)/ThioMac-CEBPb-ChIP-Seq(GSE21512)/Homer | DRTGTTGCAA | 1.00E-02 | -5.59E+00 | 0.017 | 253 | 22.23% | 9220.5 | 19.02% |
| Bach2(bZIP)/OCILy7-Bach2-ChIP-Seq(GSE44420)/Homer | TGCTGAGTCA | 1.00E-02 | -5.47E+00 | 0.019 | 83 | 7.29% | 2622.1 | 5.41% |
| Mef2d(MADS)/Retina-Mef2d-ChIP-Seq(GSE61391)/Homer | GCTATTTTAGC | 1.00E-02 | -5.44E+00 | 0.0194 | 65 | 5.71% | 1967.7 | 4.06% |
| IRF8(IRF)/BMDM-IRF8-ChIP-Seq(GSE77884)/Homer | GRAASTGAAAST | 1.00E-02 | -5.40E+00 | 0.0199 | 120 | 10.54% | 4022.7 | 8.30% |
| Elk4(ETS)/Hela-Elk4-ChIP-Seq(GSE31477)/Homer | NRYTTCCGGY | 1.00E-02 | -5.39E+00 | 0.0199 | 194 | 17.05% | 6904.6 | 14.25% |
| MafB(bZIP)/BMM-MafB-ChIP-Seq(GSE75722)/Homer | WNTGCTGASTCA GCANWTTY | 1.00E-02 | -5.17E+00 | 0.0243 | 163 | 14.32% | 5719.2 | 11.80% |

| | | | | | | | | |
|--|-------------------------------|----------|-----------|--------|-----|--------|---------|--------|
| Mef2b(MADS)/HEK293-Mef2b.V5-ChIP-Seq(GSE67450)/Homer | GCTATTTTTGGM | 1.00E-02 | -5.12E+00 | 0.0253 | 252 | 22.14% | 9269.1 | 19.12% |
| VDR(NR),DR3/GM1085 5-VDR+vitD-ChIP-Seq(GSE22484)/Homer | ARAGGTCANWGA GTTCANNN | 1.00E-02 | -5.04E+00 | 0.0271 | 96 | 8.44% | 3156.6 | 6.51% |
| ELF1(ETS)/Jurkat-ELF1-ChIP-Seq(SRA014231)/Homer | AVCCGGAAGT | 1.00E-02 | -5.00E+00 | 0.028 | 186 | 16.34% | 6654.6 | 13.73% |
| EHF(ETS)/LoVo-EHF-ChIP-Seq(GSE49402)/Homer | AVCAGGAAGT | 1.00E-02 | -5.00E+00 | 0.028 | 455 | 39.98% | 17642 | 36.40% |
| Srebp2(bHLH)/HepG2-Srebp2-ChIP-Seq(GSE31477)/Homer | CGGTCACSCCAC | 1.00E-02 | -4.98E+00 | 0.028 | 63 | 5.54% | 1938 | 4.00% |
| MafF(bZIP)/HepG2-MafF-ChIP-Seq(GSE31477)/Homer | HWWGTCAGCAW WTTT | 1.00E-02 | -4.94E+00 | 0.0287 | 97 | 8.52% | 3206.2 | 6.62% |
| ZNF136(Zf)/HEK293-ZNF136.GFP-ChIP-Seq(GSE58341)/Homer | YTKGATAHAGTAT TCTWGGTNGGCA | 1.00E-02 | -4.93E+00 | 0.0287 | 40 | 3.51% | 1122.3 | 2.32% |
| ELF5(ETS)/T47D-ELF5-ChIP-Seq(GSE30407)/Homer | ACVAGGAAGT | 1.00E-02 | -4.93E+00 | 0.0287 | 280 | 24.60% | 10441.5 | 21.54% |
| Nrf2(bZIP)/Lymphoblast-Nrf2-ChIP-Seq(GSE37589)/Homer | HTGCTGAGTCAT | 1.00E-02 | -4.74E+00 | 0.0337 | 24 | 2.11% | 595.7 | 1.23% |
| Rfx5(HTH)/GM12878-Rfx5-ChIP-Seq(GSE31477)/Homer | SCCTAGCAACAG | 1.00E-02 | -4.72E+00 | 0.0343 | 133 | 11.69% | 4619.7 | 9.53% |

Table S1. Motif enrichment of known motifs by HOMER in *Nr1d1*^{+/+} NKp46⁻ ILC3s.

| Rank | Motif | Best match | P-value | Log P-value | # of Target Sequences with Motif(of 1138) | % of Target Sequences with Motif | # of Background Sequences with Motif(of 48512) | % of Background Sequences with Motif |
|------|--------------|---|-----------|-------------|---|----------------------------------|--|--------------------------------------|
| 1 | AWBTAGGTCA | RORgt(NR)/EL4-RORgt.Flag-ChIP-Seq(GSE56019)/Homer(0.976) | 1.00E-108 | -250.39 | 495 | 43.50% | 7614.6 | 15.71% |
| 2 | GGAAATCCCC | MF0003.1_REL_class/Jaspar(0.976) | 1.00E-85 | -196.83 | 341 | 29.96% | 4498.2 | 9.28% |
| 3 | NNHRACCACA | RUNX2(Runt)/PCa-RUNX2-ChIP-Seq(GSE33889)/Homer(0.938) | 1.00E-67 | -155.98 | 464 | 40.77% | 8934.4 | 18.43% |
| 4 | AATCATAATAAC | PB0064.1_Sox14_1/Jaspar(0.712) | 1.00E-18 | -41.74 | 10 | 0.88% | 3.5 | 0.01% |
| 5 | CTTTGAWCTT | TCF7L2/MA0523.1/Jaspar(0.930) | 1.00E-17 | -40.78 | 212 | 18.63% | 4874.8 | 10.06% |
| 6 | GCCAAAGGGTTA | PB0191.1_Tcfap2c_2/Jaspar(0.625) | 1.00E-15 | -35.14 | 8 | 0.70% | 2.8 | 0.01% |
| 7 | AWTAGGACGG | 8- AWTAGGACGG,BestGuess:ZNF382(Zf)/HEK293-ZNF382.GFP-ChIP-Seq(GSE58341)/Homer(0.649) | 1.00E-15 | -34.66 | 161 | 14.15% | 3523 | 7.27% |
| 8 | TTCAAAAAGTGC | 13- TTCAAAAAGTGC,BestGuess:PB0146.1_Mafk_2/Jaspar(0.684) | 1.00E-13 | -30.17 | 81 | 7.12% | 1357.2 | 2.80% |
| 9 | AGTGA CTCAC | 10- AGTGA CTCAC,BestGuess:FOSL1/MA0477.1/Jaspar(0.850) | 1.00E-12 | -27.92 | 101 | 8.88% | 1978.9 | 4.08% |

Table S2. De novo motif enrichment by HOMER in *Nr1d1*^{+/+} NKp46⁻ ILC3s.

| Motif Name | Consensus | P-value | Log P-value | q-value (Benjamini) | # of Target Sequences with Motif (of 926) | % of Target Sequences with Motif | # of Background Sequences with Motif (of 48705) | % of Background Sequences with Motif |
|---|------------------|----------|-------------|---------------------|---|----------------------------------|---|--------------------------------------|
| Etv2(ETS)/ES-ER71-ChIP-Seq(GSE59402)/Homer(0.967) | NNAYTTCCTGHN | 1.00E-61 | -1.41E+02 | 0 | 517 | 55.83% | 14392.3 | 29.55% |
| ETS1(ETS)/Jurkat-ETS1-ChIP-Seq(GSE17954)/Homer | ACAGGAAGTG | 1.00E-55 | -1.27E+02 | 0 | 529 | 57.13% | 15565.5 | 31.95% |
| Ets1-distal(ETS)/CD4+PolII-ChIP-Seq(Barski et al.)/Homer | MACAGGAAGT | 1.00E-53 | -1.22E+02 | 0 | 278 | 30.02% | 5475.8 | 11.24% |
| Fli1(ETS)/CD8-FLI-ChIP-Seq(GSE20898)/Homer | NRYTTCCGGH | 1.00E-51 | -1.18E+02 | 0 | 522 | 56.37% | 15647.7 | 32.12% |
| EWS:ERG-fusion(ETS)/CADO_ES1-EWS:ERG-ChIP-Seq(SRA014231)/Homer | ATTCCTGTN | 1.00E-50 | -1.16E+02 | 0 | 424 | 45.79% | 11333.1 | 23.27% |
| NF1(CTF)/LNCAP-NF1-ChIP-Seq(Unpublished)/Homer | CYTGGCABNSTGCCAR | 1.00E-48 | -1.13E+02 | 0 | 281 | 30.35% | 5857.2 | 12.02% |
| EWS:FLI1-fusion(ETS)/SK_N_MC-EWS:FLI1-ChIP-Seq(SRA014231)/Homer | VACAGGAAAT | 1.00E-44 | -1.03E+02 | 0 | 358 | 38.66% | 9103.4 | 18.69% |
| ERG(ETS)/VCaP-ERG-ChIP-Seq(GSE14097)/Homer | ACAGGAAGTG | 1.00E-40 | -9.26E+01 | 0 | 642 | 69.33% | 23169.8 | 47.57% |
| GABPA(ETS)/Jurkat-GABPa-ChIP-Seq(GSE17954)/Homer | RACCGGAAGT | 1.00E-38 | -8.96E+01 | 0 | 448 | 48.38% | 13609 | 27.94% |
| RUNX1(Runt)/Jurkat-RUNX1-ChIP-Seq(GSE29180)/Homer | AAACCACARM | 1.00E-38 | -8.96E+01 | 0 | 493 | 53.24% | 15713.9 | 32.26% |
| ETV1(ETS)/GIST48-ETV1-ChIP-Seq(GSE22441)/Homer | AACCGGAAGT | 1.00E-38 | -8.88E+01 | 0 | 576 | 62.20% | 19884.7 | 40.82% |
| RUNX(Runt)/HPC7-Runx1-ChIP-Seq(GSE22178)/Homer | SAAACCACAG | 1.00E-38 | -8.86E+01 | 0 | 398 | 42.98% | 11429.1 | 23.46% |
| Fra1(bZIP)/BT549-Fra1-ChIP-Seq(GSE46166)/Homer | NNATGASTCATH | 1.00E-37 | -8.54E+01 | 0 | 309 | 33.37% | 7874.5 | 16.17% |
| Fra2(bZIP)/Striatum-Fra2-ChIP-Seq(GSE43429)/Homer | GGATGACTCATC | 1.00E-36 | -8.38E+01 | 0 | 281 | 30.35% | 6847.9 | 14.06% |
| ETS:RUNX(ETS,Runt)/Jurkat-RUNX1-ChIP-Seq(GSE17954)/Homer | RCAGGATGTGGT | 1.00E-35 | -8.25E+01 | 0 | 108 | 11.66% | 1308 | 2.69% |
| Atf3(bZIP)/GBM-ATF3-ChIP-Seq(GSE33912)/Homer | DATGASTCATHN | 1.00E-35 | -8.13E+01 | 0 | 342 | 36.93% | 9389.4 | 19.28% |
| Jun-AP1(bZIP)/K562-cJun-ChIP-Seq(GSE31477)/Homer | GATGASTCATCN | 1.00E-34 | -8.05E+01 | 0 | 181 | 19.55% | 3423.2 | 7.03% |
| JunB(bZIP)/DendriticCells-Junb-ChIP-Seq(GSE36099)/Homer | RATGASTCAT | 1.00E-34 | -7.93E+01 | 0 | 303 | 32.72% | 7892.6 | 16.20% |
| Fosl2(bZIP)/3T3L1-Fosl2-ChIP-Seq(GSE56872)/Homer | NATGASTCABNN | 1.00E-33 | -7.82E+01 | 0 | 223 | 24.08% | 4912.4 | 10.08% |
| AP-1(bZIP)/ThioMac-PU.1-ChIP-Seq(GSE21512)/Homer | VTGACTCATC | 1.00E-32 | -7.44E+01 | 0 | 366 | 39.52% | 10746 | 22.06% |

| | | | | | | | | |
|--|---------------------|----------|-----------|---|-----|--------|---------|--------|
| BATF(bZIP)/Th17-BATF-ChIP-Seq(GSE39756)/Homer | DATGASTCAT | 1.00E-31 | -7.20E+01 | 0 | 330 | 35.64% | 9331.6 | 19.16% |
| RUNX2(Runt)/PCa-RUNX2-ChIP-Seq(GSE33889)/Homer | NWAACCACADN N | 1.00E-31 | -7.17E+01 | 0 | 425 | 45.90% | 13535.9 | 27.79% |
| PU.1(ETS)/ThioMac-PU.1-ChIP-Seq(GSE21512)/Homer | AGAGGAAGTG | 1.00E-30 | -6.92E+01 | 0 | 289 | 31.21% | 7779.1 | 15.97% |
| RORgt(NR)/EL4-RORgt.Flag-ChIP-Seq(GSE56019)/Homer | AAAYTAGGTCA | 1.00E-30 | -6.92E+01 | 0 | 123 | 13.28% | 1943 | 3.99% |
| Elk1(ETS)/Hela-Elk1-ChIP-Seq(GSE31477)/Homer | HACTTCCGGY | 1.00E-29 | -6.87E+01 | 0 | 274 | 29.59% | 7203.9 | 14.79% |
| RUNX-AML(Runt)/CD4+PolII-ChIP-Seq(Barski_et_al.)/Homer | GCTGTGGTTW | 1.00E-29 | -6.81E+01 | 0 | 386 | 41.68% | 11968.9 | 24.57% |
| Elk4(ETS)/Hela-Elk4-ChIP-Seq(GSE31477)/Homer | NRYTCCGGY | 1.00E-27 | -6.36E+01 | 0 | 263 | 28.40% | 6995.2 | 14.36% |
| ETS(ETS)/Promoter/Homer | AACCGGAAGT | 1.00E-27 | -6.30E+01 | 0 | 197 | 21.27% | 4523.1 | 9.29% |
| ELF3(ETS)/PDAC-ELF3-ChIP-Seq(GSE64557)/Homer | ANCAGGAAGT | 1.00E-25 | -5.91E+01 | 0 | 366 | 39.52% | 11600.9 | 23.82% |
| ELF1(ETS)/Jurkat-ELF1-ChIP-Seq(SRA014231)/Homer | AVCCGGAAGT | 1.00E-24 | -5.61E+01 | 0 | 252 | 27.21% | 6913.2 | 14.19% |
| Tlx?(NR)/NPC-H3K4me1-ChIP-Seq(GSE16256)/Homer | CTGGCAGSCTG CCA | 1.00E-23 | -5.41E+01 | 0 | 253 | 27.32% | 7050.8 | 14.47% |
| Bach2(bZIP)/OCILy7-Bach2-ChIP-Seq(GSE44420)/Homer | TGCTGAGTCA | 1.00E-21 | -5.04E+01 | 0 | 142 | 15.33% | 3045 | 6.25% |
| EHF(ETS)/LoVo-EHF-ChIP-Seq(GSE49402)/Homer | AVCAGGAAGT | 1.00E-20 | -4.81E+01 | 0 | 505 | 54.54% | 19024.8 | 39.06% |
| ELF5(ETS)/T47D-ELF5-ChIP-Seq(GSE30407)/Homer | ACVAGGAAGT | 1.00E-16 | -3.91E+01 | 0 | 331 | 35.75% | 11354.2 | 23.31% |
| SPDEF(ETS)/VCaP-SPDEF-ChIP-Seq(SRA014231)/Homer | ASWTCCTGBT | 1.00E-14 | -3.31E+01 | 0 | 414 | 44.71% | 15789.2 | 32.41% |
| USF1(bHLH)/GM12878-Usf1-ChIP-Seq(GSE32465)/Homer | SGTCACGTGR | 1.00E-10 | -2.35E+01 | 0 | 191 | 20.63% | 6321.2 | 12.98% |
| HLF(bZIP)/HSC-HLF.Flag-ChIP-Seq(GSE69817)/Homer | RTTATGYAAB | 1.00E-10 | -2.32E+01 | 0 | 287 | 30.99% | 10670.8 | 21.91% |
| c-Myc(bHLH)/LNCAP-cMyc-ChIP-Seq(Unpublished)/Homer | VCCACGTG | 1.00E-10 | -2.31E+01 | 0 | 164 | 17.71% | 5203.3 | 10.68% |
| SpiB(ETS)/OCILY3-SPIB-ChIP-Seq(GSE56857)/Homer | AAAGRGAAGT G | 1.00E-09 | -2.30E+01 | 0 | 122 | 13.17% | 3494.3 | 7.17% |
| bHLHE40(bHLH)/HepG2-BHLHE40-ChIP-Seq(GSE31477)/Homer | KCACGTGMCN | 1.00E-09 | -2.29E+01 | 0 | 132 | 14.25% | 3895.5 | 8.00% |
| CLOCK(bHLH)/Liver-Clock-ChIP-Seq(GSE39860)/Homer | GHCACGTG | 1.00E-09 | -2.11E+01 | 0 | 223 | 24.08% | 7927.4 | 16.27% |
| MafK(bZIP)/C2C12-MafK-ChIP-Seq(GSE36030)/Homer | GCTGASTCAGC A | 1.00E-08 | -2.02E+01 | 0 | 121 | 13.07% | 3623.7 | 7.44% |
| Bach1(bZIP)/K562-Bach1-ChIP-Seq(GSE31477)/Homer | AWWNTGCTGA GTCAT | 1.00E-08 | -1.85E+01 | 0 | 43 | 4.64% | 835.3 | 1.71% |
| MITF(bHLH)/MastCells-MITF-ChIP-Seq(GSE48085)/Homer | RTCATGTGAC | 1.00E-07 | -1.76E+01 | 0 | 350 | 37.80% | 14302 | 29.36% |

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|--|----------------------|----------|-----------|--------|-----|--------|---------|--------|
| NF1-halbsite(CTF)/LNCaP-NF1-ChIP-Seq(Unpublished)/Homer | YTGCCAAG | 1.00E-06 | -1.61E+01 | 0 | 537 | 57.99% | 24076.9 | 49.43% |
| IRF3(IRF)/BMDM-Irf3-ChIP-Seq(GSE67343)/Homer | AGTTTCAKTTTC | 1.00E-06 | -1.57E+01 | 0 | 134 | 14.47% | 4482.6 | 9.20% |
| Reverb(NR),DR2/RAW-Reverba.biotin-ChIP-Seq(GSE45914)/Homer | GTRGGTCASTG GGTCA | 1.00E-06 | -1.49E+01 | 0 | 82 | 8.86% | 2395.7 | 4.92% |
| NPAS2(bHLH)/Liver-NPAS2-ChIP-Seq(GSE39860)/Homer | KCCACGTGAC | 1.00E-06 | -1.46E+01 | 0 | 379 | 40.93% | 16146.6 | 33.15% |
| MafF(bZIP)/HepG2-MafF-ChIP-Seq(GSE31477)/Homer | HWWGTCAGCA WWTTC | 1.00E-06 | -1.41E+01 | 0 | 109 | 11.77% | 3549.8 | 7.29% |
| Max(bHLH)/K562-Max-ChIP-Seq(GSE31477)/Homer | RCCACGTGGYY N | 1.00E-05 | -1.36E+01 | 0 | 249 | 26.89% | 9936.6 | 20.40% |
| ETS:E-box(ETS,bHLH)/HPC7-Scl-ChIP-Seq(GSE22178)/Homer | AGGAARCAGCT G | 1.00E-05 | -1.36E+01 | 0 | 62 | 6.70% | 1696.4 | 3.48% |
| IRF4(IRF)/GM12878-IRF4-ChIP-Seq(GSE32465)/Homer | ACTGAAACCA | 1.00E-05 | -1.32E+01 | 0 | 167 | 18.03% | 6166.8 | 12.66% |
| Usf2(bHLH)/C2C12-Usf2-ChIP-Seq(GSE36030)/Homer | GTCACGTGGT | 1.00E-05 | -1.31E+01 | 0 | 132 | 14.25% | 4624.1 | 9.49% |
| Atf1(bZIP)/K562-ATF1-ChIP-Seq(GSE31477)/Homer | GATGACGTCA | 1.00E-05 | -1.28E+01 | 0 | 238 | 25.70% | 9510.8 | 19.52% |
| Atf2(bZIP)/3T3L1-Atf2-ChIP-Seq(GSE56872)/Homer | NRRTGACGTCA T | 1.00E-05 | -1.26E+01 | 0 | 140 | 15.12% | 5021.5 | 10.31% |
| NF-E2(bZIP)/K562-NFE2-ChIP-Seq(GSE31477)/Homer | GATGACTCAGC A | 1.00E-05 | -1.15E+01 | 0.0001 | 38 | 4.10% | 913.3 | 1.88% |
| Rfx5(HTH)/GM12878-Rfx5-ChIP-Seq(GSE31477)/Homer | SCCTAGCAACA G | 1.00E-04 | -1.14E+01 | 0.0001 | 137 | 14.79% | 5012.5 | 10.29% |
| n-Myc(bHLH)/mES-nMyc-ChIP-Seq(GSE11431)/Homer | VRCCACGTGG | 1.00E-04 | -1.12E+01 | 0.0001 | 239 | 25.81% | 9769.6 | 20.06% |
| Tcf4(HMG)/Hct116-Tcf4-ChIP-Seq(SRA012054)/Homer | ASATCAAAGGV A | 1.00E-04 | -1.06E+01 | 0.0002 | 182 | 19.65% | 7158.1 | 14.69% |
| E-box(bHLH)/Promoter/Home | SSGGTCACGTG A | 1.00E-04 | -1.05E+01 | 0.0002 | 36 | 3.89% | 885.9 | 1.82% |
| Nrf2(bZIP)/Lymphoblast-Nrf2-ChIP-Seq(GSE37589)/Homer | HTGCTGAGTCA T | 1.00E-04 | -1.05E+01 | 0.0002 | 32 | 3.46% | 747.8 | 1.54% |
| STAT5(Stat)/mCD4+-Stat5-ChIP-Seq(GSE12346)/Homer | RTTTCTNAGAAA | 1.00E-04 | -1.04E+01 | 0.0002 | 144 | 15.55% | 5430.6 | 11.15% |
| Atf7(bZIP)/3T3L1-Atf7-ChIP-Seq(GSE56872)/Homer | NGRTGACGTCA Y | 1.00E-04 | -1.04E+01 | 0.0002 | 175 | 18.90% | 6862.2 | 14.09% |
| FOXP1(Forkhead)/H9-FOXP1-ChIP-Seq(GSE31006)/Homer | NYYTGTTTACHN | 1.00E-04 | -1.03E+01 | 0.0002 | 165 | 17.82% | 6412.1 | 13.16% |
| MafA(bZIP)/Islet-MafA-ChIP-Seq(GSE30298)/Homer | TGCTGACTCA | 1.00E-04 | -1.01E+01 | 0.0002 | 305 | 32.94% | 13172.5 | 27.04% |
| NPAS(bHLH)/Liver-NPAS-ChIP-Seq(GSE39860)/Homer | NVCACGTG | 1.00E-04 | -9.60E+00 | 0.0004 | 477 | 51.51% | 22018 | 45.20% |

| | | | | | | | | |
|--|--------------------------|----------|-----------|--------|-----|--------|---------|--------|
| Gata2(Zf)/K562-GATA2-ChIP-Seq(GSE18829)/Homer | BBCTTATCTS | 1.00E-04 | -9.45E+00 | 0.0004 | 231 | 24.95% | 9648.8 | 19.81% |
| MafB(bZIP)/BMM-MafB-ChIP-Seq(GSE75722)/Homer | WNTGCTGASTC AGCANWTTY | 1.00E-04 | -9.38E+00 | 0.0005 | 166 | 17.93% | 6570 | 13.49% |
| BMAL1(bHLH)/Liver-Bmal1-ChIP-Seq(GSE39860)/Homer | GNCACGTG | 1.00E-03 | -9.05E+00 | 0.0006 | 527 | 56.91% | 24757.9 | 50.83% |
| PU.1-IRF(ETS:IRF)/Bcell-PU.1-ChIP-Seq(GSE21512)/Homer | MGGAAGTGAAA C | 1.00E-03 | -8.72E+00 | 0.0008 | 411 | 44.38% | 18773.1 | 38.54% |
| c-Jun-CRE(bZIP)/K562-cJun-ChIP-Seq(GSE31477)/Homer | ATGACGTCATC Y | 1.00E-03 | -8.50E+00 | 0.001 | 119 | 12.85% | 4515.6 | 9.27% |
| NFKB-p50,p52(RHD)/Monocyte-p50-ChIP-Chip(Schreiber_et_al.)/Homer | GGGGGAATCCC C | 1.00E-03 | -8.49E+00 | 0.001 | 42 | 4.54% | 1213.2 | 2.49% |
| ISRE(IRF)/ThioMac-LPS-Expression(GSE23622)/Homer | AGTTTCASTTTC | 1.00E-03 | -8.41E+00 | 0.0011 | 30 | 3.24% | 765.9 | 1.57% |
| GATA(Zf),IR4/iTreg-Gata3-ChIP-Seq(GSE20898)/Homer | NAGATWNBNA CTNN | 1.00E-03 | -8.37E+00 | 0.0011 | 41 | 4.43% | 1181.4 | 2.43% |
| PRDM1(Zf)/Hela-PRDM1-ChIP-Seq(GSE31477)/Homer | ACTTTCACTTTC | 1.00E-03 | -8.31E+00 | 0.0012 | 189 | 20.41% | 7806.4 | 16.03% |
| Gata1(Zf)/K562-GATA1-ChIP-Seq(GSE18829)/Homer | SAGATAAGRV | 1.00E-03 | -8.12E+00 | 0.0014 | 206 | 22.25% | 8653 | 17.76% |
| NFAT:AP1(RHD,bZIP)/Jurkat-NFATC1-ChIP-Seq(Jolma_et_al.)/Homer | SARTGGAAA AWRTGAGTCAB | 1.00E-03 | -8.03E+00 | 0.0015 | 74 | 7.99% | 2568.8 | 5.27% |
| PAX5(Paired,Homeobox)/GM12878-PAX5-ChIP-Seq(GSE32465)/Homer | GCAGCCAAGCR TGACH | 1.00E-03 | -7.96E+00 | 0.0016 | 136 | 14.69% | 5361.1 | 11.01% |
| Tcf3(HMG)/mES-Tcf3-ChIP-Seq(GSE11724)/Homer | ASWTCAAAGG | 1.00E-03 | -7.74E+00 | 0.002 | 108 | 11.66% | 4105.9 | 8.43% |
| ZNF322(Zf)/HEK293-ZNF322.GFP-ChIP-Seq(GSE58341)/Homer | GAGCCTGGTAC TGWGCCTGR | 1.00E-03 | -7.52E+00 | 0.0025 | 122 | 13.17% | 4771.2 | 9.79% |
| FOXP2(Forkhead)/U2OS-FOXP2-ChIP-Seq(E-MTAB-2204)/Homer | SCHTGTTTACAT | 1.00E-03 | -7.32E+00 | 0.003 | 221 | 23.87% | 9514.8 | 19.53% |
| Hoxc9(Homeobox)/Ainv15-Hoxc9-ChIP-Seq(GSE21812)/Homer | GGCCATAAATC A | 1.00E-03 | -7.18E+00 | 0.0034 | 157 | 16.95% | 6457.2 | 13.26% |
| TCFL2(HMG)/K562-TCF7L2-ChIP-Seq(GSE29196)/Homer | ACWTCAAAGG | 1.00E-03 | -7.15E+00 | 0.0035 | 43 | 4.64% | 1339.1 | 2.75% |
| TFE3(bHLH)/MEF-TFE3-ChIP-Seq(GSE75757)/Homer | GTCACGTGACY V | 1.00E-03 | -7.13E+00 | 0.0035 | 39 | 4.21% | 1179.7 | 2.42% |
| X-box(HTH)/NPC-H3K4me1-ChIP-Seq(GSE16256)/Homer | GGTTGCCATGG CAA | 1.00E-03 | -7.04E+00 | 0.0038 | 54 | 5.83% | 1802.4 | 3.70% |
| IRF8(IRF)/BMDM-IRF8-ChIP-Seq(GSE77884)/Homer | GRAASTGAAAST | 1.00E-03 | -6.96E+00 | 0.004 | 113 | 12.20% | 4429.5 | 9.09% |
| PU.1:IRF8(ETS:IRF)/pDC-Irf8-ChIP-Seq(GSE66899)/Homer | GGAAGTGAAS T | 1.00E-03 | -6.91E+00 | 0.0042 | 78 | 8.42% | 2852.8 | 5.86% |
| Pax8(Paired,Homeobox)/Thyroid-Pax8-ChIP-Seq(GSE26938)/Homer | GTCATGCHTGR CTGS | 1.00E-02 | -6.90E+00 | 0.0042 | 126 | 13.61% | 5040.4 | 10.35% |

| | | | | | | | | |
|---|-----------------|----------|-----------|--------|-----|--------|---------|--------|
| Foxa3(Forkhead)/Liver-Foxa3-ChIP-Seq(GSE77670)/Homer | BSNTGTTTACWYWGN | 1.00E-02 | -6.78E+00 | 0.0046 | 120 | 12.96% | 4777.2 | 9.81% |
| IRF2(IRF)/Erythroblastic-IRF2-ChIP-Seq(GSE36985)/Homer | GAAASYGAAASY | 1.00E-02 | -6.71E+00 | 0.0049 | 42 | 4.54% | 1329.1 | 2.73% |
| JunD(bZIP)/K562-JunD-ChIP-Seq/Homer | ATGACGTCATCN | 1.00E-02 | -6.63E+00 | 0.0053 | 42 | 4.54% | 1335.8 | 2.74% |
| E2F4(E2F)/K562-E2F4-ChIP-Seq(GSE31477)/Homer | GGCGGGAAAH | 1.00E-02 | -6.23E+00 | 0.0078 | 76 | 8.21% | 2837.6 | 5.83% |
| c-Myc(bHLH)/mES-cMyc-ChIP-Seq(GSE11431)/Homer | VVCCACGTGG | 1.00E-02 | -6.13E+00 | 0.0085 | 172 | 18.57% | 7346.4 | 15.08% |
| Gata6(Zf)/HUG1N-GATA6-ChIP-Seq(GSE51936)/Homer | YCTTATCTBN | 1.00E-02 | -6.00E+00 | 0.0096 | 286 | 30.89% | 13003.2 | 26.69% |
| CEBP(bZIP)/ThioMac-CEBPb-ChIP-Seq(GSE21512)/Homer | ATTGCGCAAC | 1.00E-02 | -5.79E+00 | 0.0117 | 184 | 19.87% | 7991.7 | 16.41% |
| Stat3+il21(Stat)/CD4-Stat3-ChIP-Seq(GSE19198)/Homer | SVYTTCCNGGAR | 1.00E-02 | -5.75E+00 | 0.012 | 241 | 26.03% | 10806.5 | 22.18% |
| STAT1(Stat)/HelaS3-STAT1-ChIP-Seq(GSE12782)/Homer | NATTTCCNGGAAT | 1.00E-02 | -5.69E+00 | 0.0126 | 111 | 11.99% | 4512.2 | 9.26% |
| Tbox:Smad(T-box,MAD)/ESCd5-Smad2_3-ChIP-Seq(GSE29422)/Homer | AGGTGHCAGACA | 1.00E-02 | -5.48E+00 | 0.0156 | 87 | 9.40% | 3428.6 | 7.04% |
| CHR(?)/Hela-CellCycle-Expression/Homer | SRGTTTCAAA | 1.00E-02 | -5.44E+00 | 0.016 | 191 | 20.63% | 8402.6 | 17.25% |
| STAT6(Stat)/Macrophage-Stat6-ChIP-Seq(GSE38377)/Homer | TTCKNAGAA | 1.00E-02 | -5.37E+00 | 0.0169 | 192 | 20.73% | 8464.9 | 17.38% |
| CEBP:AP1(bZIP)/ThioMac-CEBPb-ChIP-Seq(GSE21512)/Homer | DRTGTTGCAA | 1.00E-02 | -5.30E+00 | 0.018 | 225 | 24.30% | 10109.9 | 20.75% |
| ZNF264(Zf)/HEK293-ZNF264.GFP-ChIP-Seq(GSE58341)/Homer | RGGGCACTAAC | 1.00E-02 | -5.25E+00 | 0.0187 | 210 | 22.68% | 9376 | 19.25% |
| Foxa2(Forkhead)/Liver-Foxa2-ChIP-Seq(GSE25694)/Homer | CYTGTTTACWY | 1.00E-02 | -5.19E+00 | 0.0197 | 266 | 28.73% | 12184.7 | 25.01% |
| E2F1(E2F)/Hela-E2F1-ChIP-Seq(GSE22478)/Homer | CWGGCGGGAA | 1.00E-02 | -5.17E+00 | 0.0198 | 39 | 4.21% | 1324.4 | 2.72% |
| NFAT(RHD)/Jurkat-NFATC1-ChIP-Seq(Jolma et al.)/Homer | ATTTTCCATT | 1.00E-02 | -5.16E+00 | 0.02 | 269 | 29.05% | 12343.9 | 25.34% |
| Gata4(Zf)/Heart-Gata4-ChIP-Seq(GSE35151)/Homer | NBWGATAAGR | 1.00E-02 | -5.13E+00 | 0.0204 | 305 | 32.94% | 14170.4 | 29.09% |
| p53(p53)/Saos-p53-ChIP-Seq(GSE15780)/Homer | RRCATGYCYRGR | 1.00E-02 | -5.03E+00 | 0.0221 | 44 | 4.75% | 1552 | 3.19% |
| p53(p53)/Saos-p53-ChIP-Seq/Homer | RRCATGYCYRGR | 1.00E-02 | -5.03E+00 | 0.0221 | 44 | 4.75% | 1552 | 3.19% |
| CEBP:CEBP(bZIP)/MEF-Chop-ChIP-Seq(GSE35681)/Homer | NTNATGCAAYM | 1.00E-02 | -5.01E+00 | 0.0224 | 49 | 5.29% | 1771.7 | 3.64% |
| FOXP1(Forkhead)/HEK293-FOXP1-ChIP-Seq(GSE51673)/Homer | NVWTGTTTAC | 1.00E-02 | -4.88E+00 | 0.0251 | 315 | 34.02% | 14742 | 30.26% |
| Stat3(Stat)/mES-Stat3-ChIP-Seq(GSE11431)/Homer | CTTCCGGGAA | 1.00E-02 | -4.79E+00 | 0.0273 | 169 | 18.25% | 7456.8 | 15.31% |

Table S3. Motif enrichment of known motifs by HOMER in *Nr1d1*^{-/-} NKp46⁻ ILC3s.

| Rank | Motif | Best match | P-value | Log P-value | # of Target Sequences with Motif(of 1138) | % of Target Sequences with Motif | # of Background Sequences with Motif(of 48512) | % of Background Sequences with Motif |
|------|--------------|--|----------|-------------|---|----------------------------------|--|--------------------------------------|
| 1 | RACAGGAAGY | Ets1-distal(ETS)/CD4+-PoIII-ChIP-Seq(Barski et al.)/Homer(0.967) | 1.00E-69 | -160.02 | 334 | 36.07% | 6378 | 13.09% |
| 2 | TGTGGTTT | RUNX1(Runt)/Jurkat-RUNX1-ChIP-Seq(GSE29180)/Homer(0.981) | 1.00E-48 | -111.56 | 292 | 31.53% | 6284.1 | 12.90% |
| 3 | VTGASTCAKN | Atf3(bZIP)/GBM-ATF3-ChIP-Seq(GSE33912)/Homer(0.985) | 1.00E-39 | -91.68 | 251 | 27.11% | 5457.5 | 11.20% |
| 4 | TGGCACNVWGCC | Tlx?(NR)/NPC-H3K4me1-ChIP-Seq(GSE16256)/Homer(0.907) | 1.00E-38 | -88.04 | 225 | 24.30% | 4665 | 9.58% |
| 5 | GTTATGTAAC | NFIL3/MA0025.1/Jaspar(0.920) | 1.00E-34 | -79.06 | 75 | 8.10% | 636.2 | 1.31% |
| 6 | AACTAGGTCA | RORgt(NR)/EL4-RORgt.Flag-ChIP-Seq(GSE56019)/Homer(0.970) | 1.00E-33 | -76.48 | 136 | 14.69% | 2154 | 4.42% |
| 7 | CTGGCAGCCA | NF1-halfsite(CTF)/LNCaP-NF1-ChIP-Seq(Unpublished)/Homer(0.722) | 1.00E-15 | -35.35 | 296 | 31.97% | 10046.2 | 20.62% |
| 8 | DTGACCTCATTT | JUND(var.2)/MA0492.1/Jaspar(0.767) | 1.00E-13 | -31.55 | 21 | 2.27% | 113.3 | 0.23% |
| 9 | CACGTGAC | Arntl/MA0603.1/Jaspar(0.982) | 1.00E-13 | -30.55 | 219 | 23.65% | 7012.8 | 14.40% |

Table S4. De novo motif enrichment by HOMER in *Nr1d1*^{-/-} NKp46⁻ ILC3s.

| Primer | Forward | Reverse |
|------------------------|---------------------------|---------------------------|
| <i>Nr1d1</i> | TGGCATGGTGCTACTGTGTAAGG | ATATTCTGTTGGATGCTCCGGCG |
| <i>Nr1d1</i> | GTCTCTCCGTTGGCATGTCT | CCAAGTTCATGGCGCTCT |
| <i>Nr1d2</i> | GGAGTTCATGCTTGTGAAGGCTGT | CAGACACTTCTTAAAGCGGCACTG |
| <i>Clock</i> | CACTCTCACAGCCCCACTGTAC | CCCCACAAGCTACAGGAGCAGT |
| <i>Per1</i> | TGAAGCAAGACCGGGAGAG | CACACACGCCATCACATCAA |
| <i>Dbp</i> | AATGACCTTTGAACCTGATCCCGCT | GCTCCAGTACTTCTCATCCTTCTGT |
| <i>Nfil3</i> | CTTTCAGGACTACCAGACATCCAA | GATGCAACTTCCGGCTACCA |
| <i>Bmal1</i> | TGACCCTCATGGAAGGTTAGAA | GGACATTGCATTGCATGTTGG |
| <i>Rorc</i> | TTCACCCACCTCCACTG | GTGCAGGAGTAGGCCACATT |
| Eubacteria 16s rDNA | CGGCAACGAGCGCAACCC | CCATTGTAGCACGTGTGTAGCC |
| <i>Actb</i> | GACGGCCAGGTCATCACTATTG | AGGAAGGCTGGAAAAGAGCC |
| <i>Il17a</i> | CCAAGGACTTCTCCAGAATG | CCCAGATCACAGAGGGATATCTA |
| <i>Il22</i> | TCCTGACCAAACCTCAGCAATC | CTTGATCTCTCCACTCTCTCCA |

Table S5. Sequences of primers used for qPCR