# Expanded View Figures

**Figure EV1. HIF1α is involved in tryptophan/NAD metabolism of splenic NK cells.**

A, B NK cell, defined as $CD45^+$ $CD3^-$ $NKp46^+$ $CD49b^+$, (A) count and (B) frequency in bone marrow of WT and HIF-1α KO mice ($n = 3$).

C, D NK cell (A) count and (D) frequency in liver of WT and HIF-1α KO mice ($n = 3$).

E Gene expression analysis of genes from the NAD—tryptophan pathway and key amino acid transporters from bulk RNA-sequencing performed on six samples of freshly isolated NK cells from WT and HIF-1α KO mice.

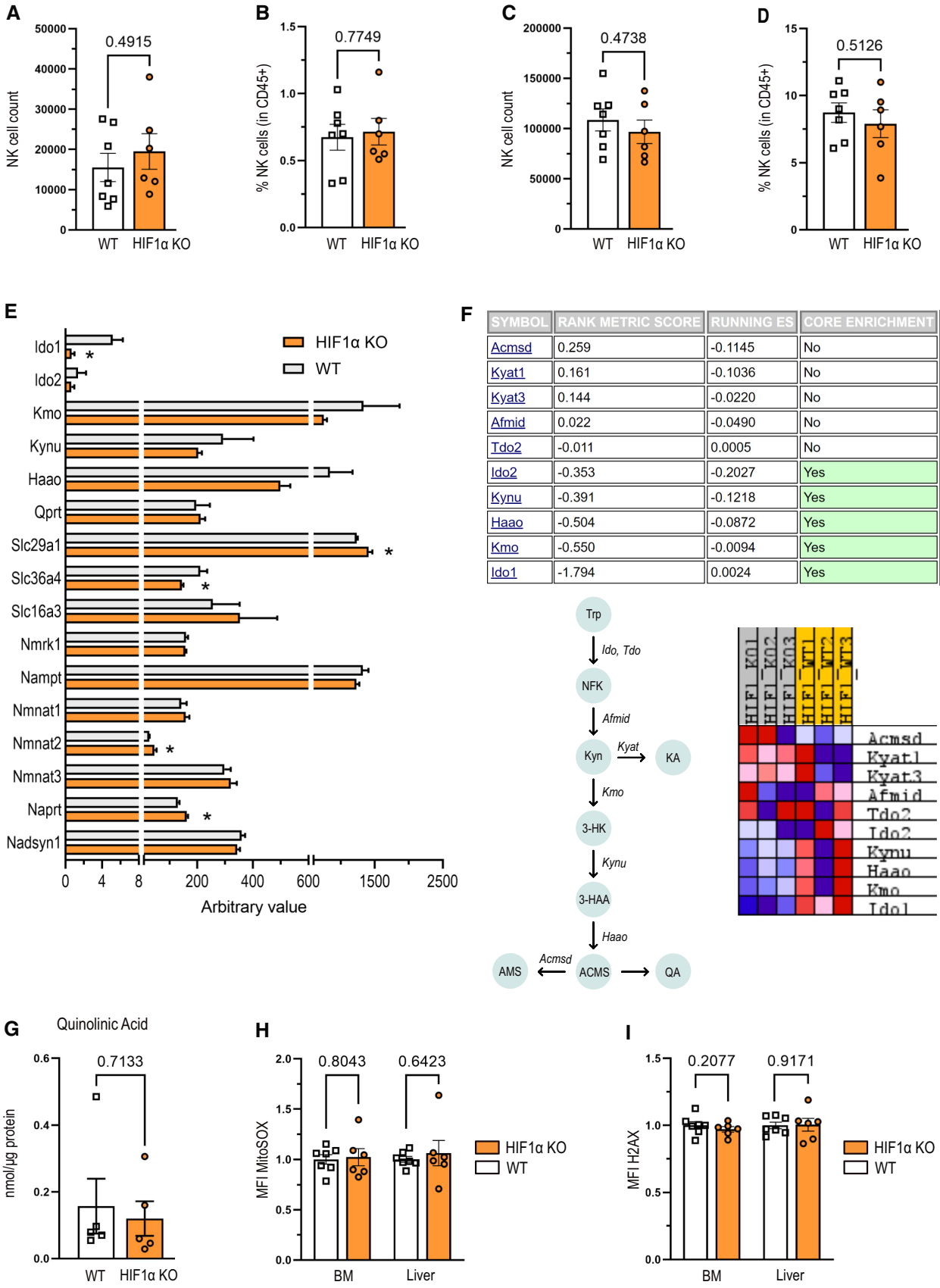
F The tryptophan pathway (Trp, tryptophan; NFK, N-formylkynurenine; Kyn, kynurenine; KA, kynurenic acid; 3-HK, 3-hydroxykynurenine; 3-HAA, 3-hydroxyanthranilic acid; ACMS, 2-amino-3-carboximuconate semialdehyde; AMS, aminomuconate semialdehyde; QA, quinolinic acid) and GSEA analysis of the RNA expression of its key enzymes (Ido, indoleamine-2,3-dioxygenase; Tdo, tryptophan-2,3-dioxygenase; Afmid, kynurenine formamidase; Kyat, kynurenine aminotransferase; Kmo, kynurenine 3-monooxygenase; Kynu, kynureninase; Haao, 3-hydroxyanthranilate 3,4-dioxygenase; Acmsd, ACMS decarboxylase).

G Analysis of quinolinic acid quantification from targeted metabolomics.

H Analysis of mitochondrial ROS amount of freshly isolated NK cells from bone marrow (BM) and liver of WT and HIF-1α KO mice ($n = 3$).

I Analysis of DNA damage in bone marrow (BM) and liver NK cells from WT and HIF-1α KO mice by FACS measurement of γ-H2AX ($n = 3$).

Data information: Statistical significance was determined by an unpaired Student's *t*-test. Bars represent mean values, error bars indicate the s.e.m., (*n*) represents the number of independent experiments, and each data point represents a biological sample from a mouse.
Source data are available online for this figure.




| SYMBOL | RANK METRIC SCORE | RUNNING ES | CORE ENRICHMENT |
|---|---|---|---|
| Acmsd | 0.259 | -0.1145 | No |
| Kyat1 | 0.161 | -0.1036 | No |
| Kyat3 | 0.144 | -0.0220 | No |
| Afmid | 0.022 | -0.0490 | No |
| Tdo2 | -0.011 | 0.0005 | No |
| Ido2 | -0.353 | -0.2027 | Yes |
| Kynu | -0.391 | -0.1218 | Yes |
| Haao | -0.504 | -0.0872 | Yes |
| Kmo | -0.550 | -0.0094 | Yes |
| Ido1 | -1.794 | 0.0024 | Yes |

**Figure EV1.**

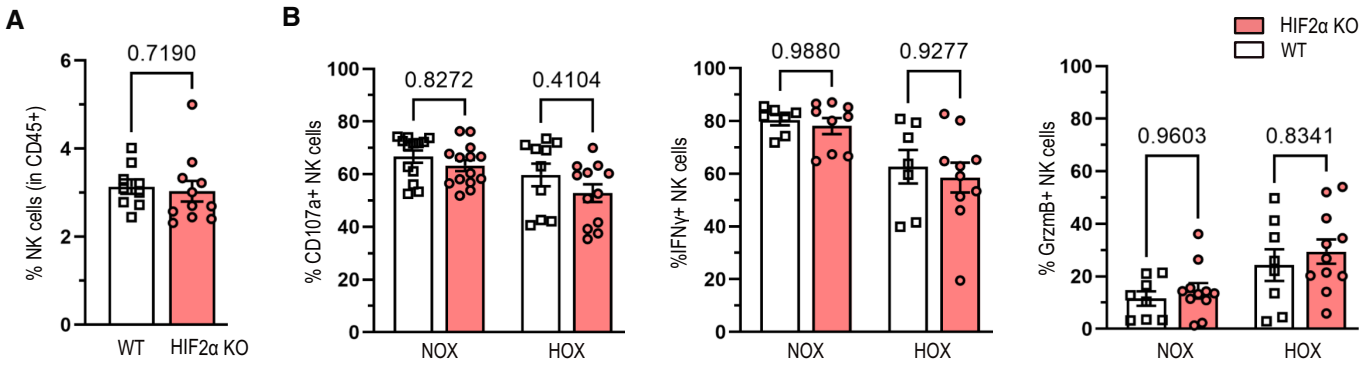



**Figure EV2. HIF2α does not play a major role for homeostasis and activation of NK cells.**

A NK cell frequency, defined as $CD45^+$ $CD3^-$ $NK1.1^+$ $NKp46^+$, in spleens from WT and HIF-2α KO mice ($n = 3$).

B Splenocytes of WT and HIF-2α KO mice were stimulated with PMA (200 ng/ml) and ionomycin (1 μg/ml) for 6 h at 37°C, 5% $CO_2$ and 20% $O_2$ (NOX) or 2% $O_2$ (HOX) in complete RPMI medium. Degranulation (CD107a) ($n = 3$), IFN-γ ($n = 2$) and granzyme B ($n = 4$) expression were analyzed by flow cytometry.

Data information: Statistical significance was determined by an unpaired Student's *t*-test, one-sample *t*-test or one-way ANOVA where appropriate. Bars represent mean values, error bars indicate the s.e.m., (*n*) represents the number of independent experiments, and each data point represents a biological sample from a mouse.
Source data are available online for this figure.