Immunity, Volume *55*

Supplemental information

Indoleamine 2,3-dioxygenase 1 activation in mature cDC1 promotes tolerogenic education of inflammatory cDC2 via metabolic communication

Marco Gargaro, Giulia Scalisi, Giorgia Manni, Carlos G. Briseño, Prachi Bagadia, Vivek Durai, Derek J. Theisen, Sunkyung Kim, Marilena Castelli, Chenling A. Xu, Gerd Meyer zu Hörste, Giuseppe Servillo, Maria A. Della Fazia, Giulia Mencarelli, Doriana Ricciuti, Eleonora Padiglioni, Nicola Giacchè, Carolina Colliva, Roberto Pellicciari, Mario Calvitti, Teresa Zelante, Dietmar Fuchs, Ciriana Orabona, Louis Boon, Alban Bessede, Marco Colonna, Paolo Puccetti, Theresa L. Murphy, Kenneth M. Murphy, and Francesca Fallarino

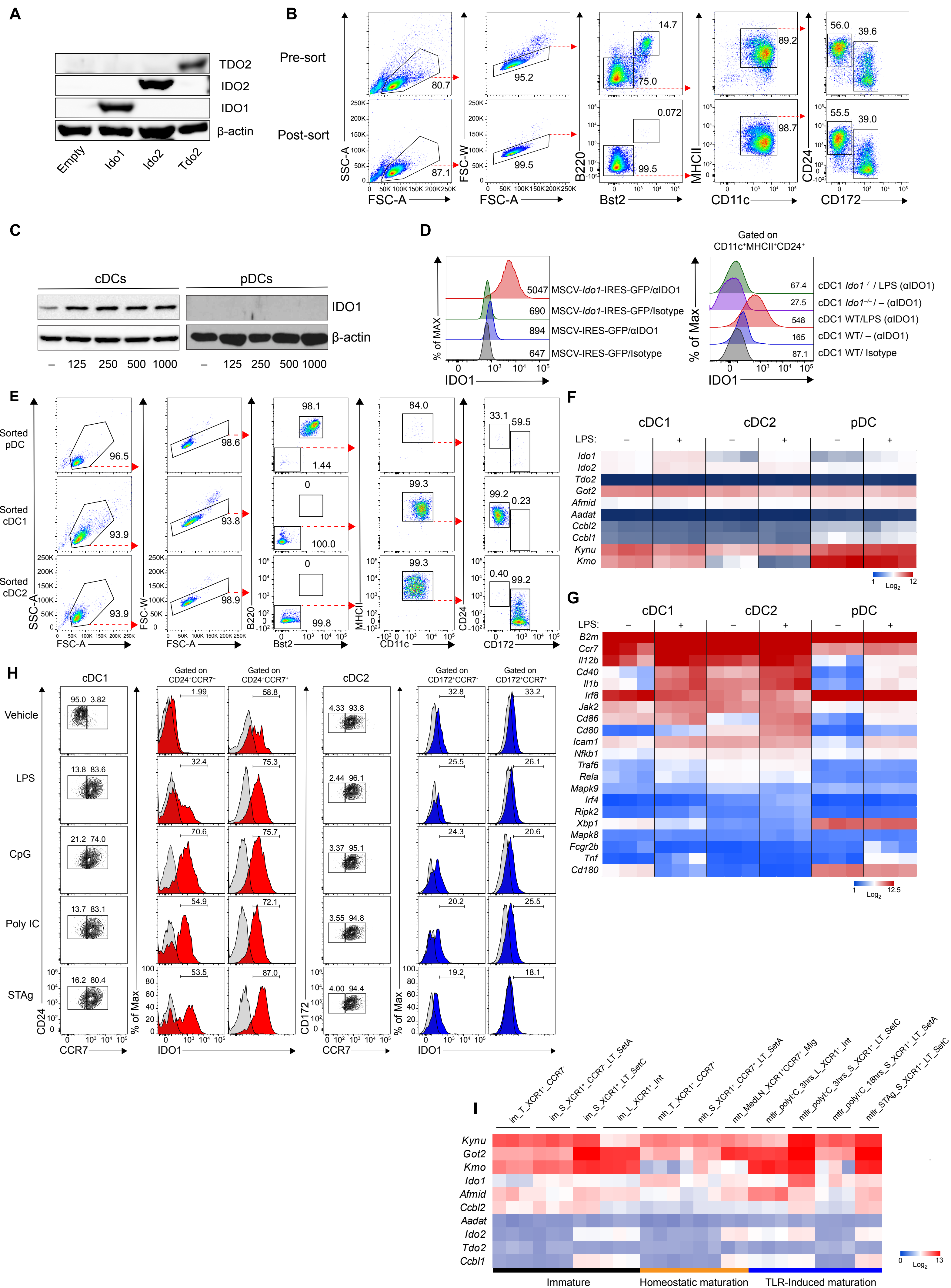


Figure S1 realted to Figure 1

Figure S1. Differential expression of IDO1 in BM derived DC subsets, related to Figure 1.

(**A**) RAW264.7 cells were stably transfected with a GFP retroviral vector expressing murine IDO1, IDO2 or TDO2. Mock transfected cells (empty GFP) were used as control. Sorted GFP^{+} cells were analyzed by Western blotting for the three enzymes using the corresponding reactive antibodies, to verify the IDO1 antibody specificity. IDO1, IDO2 and TDO2 were shown, and β-actin expression was used as loading control. One representative experiment (n = 3).

(**B**) BM cells were cultured for 9 days with Flt3L. Shown is the relative percentage of pDCs ($Bst2^{+}$ $B220^{+}$) and cDCs ($MHCII^{+}CD11c^{+}$) purity of indicated population before sorting (Pre-sort) and post sorting (Post-sort). Numbers represents the percentages of cells in the indicated gates. One representative experiment (n =3).

(**C**) Sorted cDCs and pDCs from BM cultures were left untreated or treated with the indicated concentrations of LPS (ng/ml) for 48 hours. Western analysis was carried out for IDO1 and β-Actin was used as loading control. One representative experiment (n = 3).

(**D**) Left: Transfected RAW264.7 cells described in (A) were analyzed by FACS to validate the use of IDO1-antibody in IS. IDO1 expression is shown as histogram. Mock transfected cells (MSCV- IRES-GPF) and isotype antibody were used as controls. Numbers in the histograms indicate the percentage of $IDO1^{+}$ cells. Right: Purified cDCs from BM cultures of indicated genotype were left untreated or treated with 250 ng/ml LPS for 48 hours and analyzed by IS for IDO1 expression. Shown are histograms of IDO1 expression of cells in the indicated gate. Isotype control is shown as grey histogram and numbers are the percentage of IDO1 positive cells. One representative experiment (n = 3).

(**E**) pDCs ($Bst2^{+}$ $B220^{+}$), cDC1 ($MHCII^{+}$ $CD11c^{+}$ $CD24^{+}$ $CD172^{-}$) and cDC2 ($MHCII^{+}$ $CD11c^{+}$ $CD24^{-}$ $CD172^{+}$), sorted from Flt3L-treated BM cultures, were analyzed by FACS to determine the purity of the indicated population after sorting. Numbers are the percent of cells in the indicated gates. Purity of sorted pDCs, cDC1 and cDC2 population was higher than 95%. One representative experiment (n = 4).

(**F-G**) Purified pDCs, cDC1 and cDC2 were left untreated (–) or treated with LPS 250 ng/ml (+) for 24 h and subjected to whole genome gene expression analysis. Shown are heatmaps with colored box representing differential gene expression (Log2) ranging from bright blue (lowest) to bright red (highest) showing expression of genes of the kynurenine pathway (**F**) and of inflammatory and costimulatory molecules (**G**). One representative experiment of two.

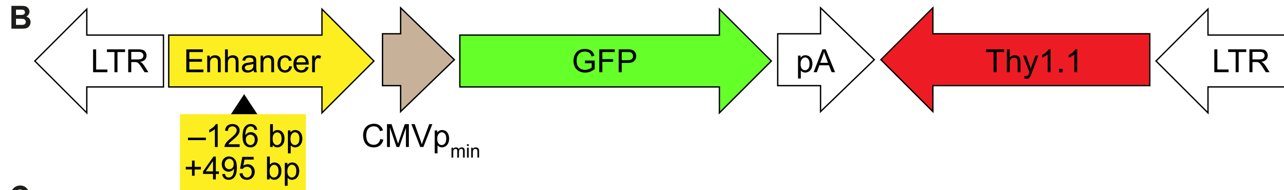
(H) Purified cDCs were left untreated (vehicle) or treated with LPS (250 ng/ml), CpG (10 μg/ml), Poli IC, (25 μg/ml) or STAg (1 μg/ml) for 48 hours. IDO1 expression was analyzed by IS in $CCR7^-$ and $CCR7^+$ cDC1 and cDC2. Shown are histograms of IDO1 expression in the indicated gates. Isotype control is shown as grey and IDO1 as red histogram. Numbers are the percentage of IDO1 positive cells (n = 3).
(I) Expression of selected genes of the kynurenine pathways across immature $XCR1^+$ $CCR7^–$ and mature $XCR1^+CCR7^+$ DCs from the thymus, spleen, lungs and mediastinal LNs. Data sets are described in (Ardouin et al., 2016). Abbreviations: im: immature; mh: matured under homeostatic conditions; mtlr: matured under TLR stimulation; T: thymus; S: spleen; L: lung; MedLN: mediastinal lymph nodes; LT: lymphoid-tissue resident; Mig: migratory; Int: intersticial

A

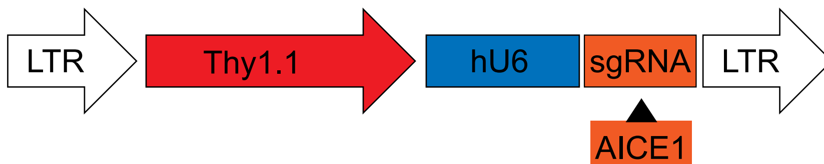
chr8:25,706,852-25,707,648

```
gggataaatctgataagaaacacaaatgtttagtttcttcatatgacgaagagagatcctttgtggtttggttgtttatc
aaattgcaaatacataaaacagaaaatgaaactgtcccaggtggaagccacttctccccgagtattacgtgtcagctgtg
gggtttggctaaaccctataagagatgctgggacattccttcagtggccaagtgggggtcagtggagtagacagcaatg
gcactcagtaaaatatctcctacagaaggttctagaaggatccttgaagaccaccacatagatgaagatgtgggctttgc
tctaccacatccactggtaagaaaagtgaaaatctgctttgtcctcattatttatctcgacagatgaatttctaagtaag
cagctctgtctcaggttctcttaagcgaatgagtgatgtcaaattcagagcccacttacaaaaagggagcctggctgctc
ttcagtgtttcttcttcttcttcttcctcaaaatccagcccttactttcttaacctggaaatgtgaagtggtgagggaag
gggcacatgagaagtctttttagtttcgtgaaggaaacgggctcatagaagggaagccagtttgtcacaatgacttttcc
agcacggtgtcctgaaacagcaacattcaaatgcccagagccatagaaacatttctcttctgaaccttatcaaatggatc
gatctgtgctcctcactgatttcagtatatgagatgatagatcaagcaacttttgtttcatactaataatgcttgtg
```

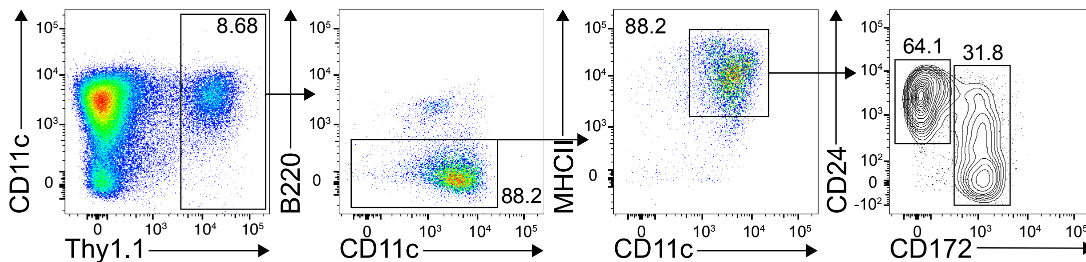
B



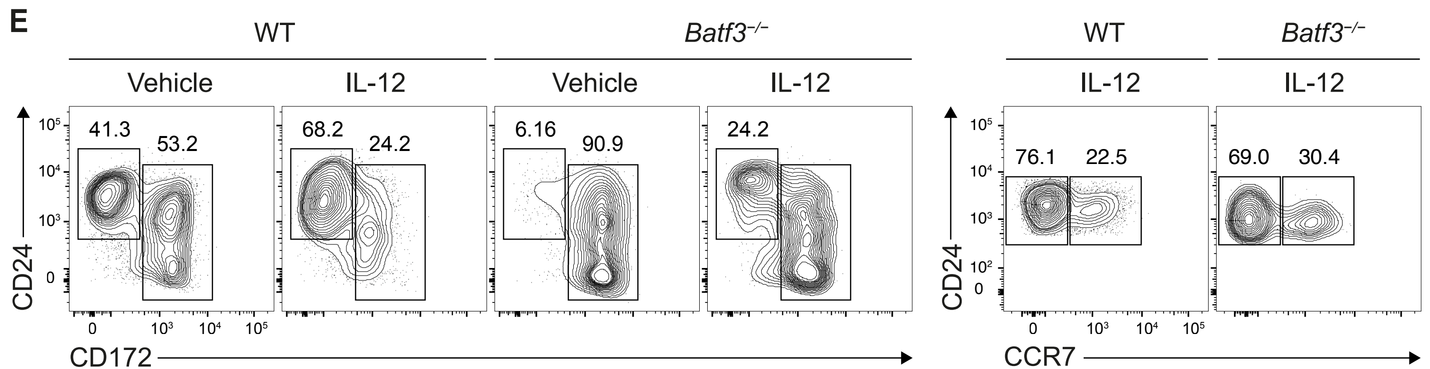
C



D



E



F

	WT		*Ido1*$^{-/-}$	
LPS	–	+	–	+
G-CSF	1	3,88	1	5,02
GM-CSF	30,26	49,6	42,73	57,71
IFN-γ	2,3	4,29	2,3	6,44
IL-10	49,29	66,62	55,47	72,06
IL-12p40	4710,13	9653,5	6406,96	13646,59
IL-12p70	16,28	43,64	22,61	45,1
IL-13	1	29,59	9,26	36,82
IL-17A	1,24	2,11	1,83	3,08
IL-1α	1,02	3,82	2,9	4,05
IL-1β	19,35	82,25	30,61	106,73
IL-2	3,58	7,2	4,22	7,76
IL-3	0,94	1,68	0,94	2,05
IL-4	0,76	1,8	0,82	1,69
IL-5	1,39	1,74	1,21	2,72
IL-6	7,99	99,42	11,19	107,54
IL-9	13,86	16,93	13,15	19,23
KC	7,45	26,12	11,68	37,31
MCP-1	112,94	162,96	119,11	177,59
MIP-1a	4,34	75,97	3,87	65,78
MIP-1b	5,28	113,4	4,79	67,88
RANTES	1486,56	5862,98	1336,82	5273,12
TNF-α	1	7,35	4,85	14,41
eotaxin	4,88	9,82	8,04	10,4

G

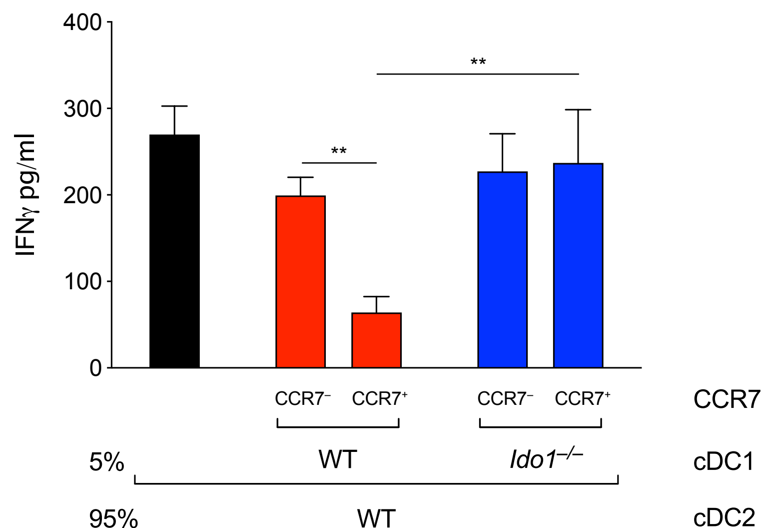


Figure S2 related to Figure 2

Figure S2. IRF8 allows constitutive IDO1 expression in cDC1, related to Figure 2.

(A) Nucleotide sequence containing AICEs (–126 bp and +495 bp) *Ido1* enhancer regions. The different regions are indicated by colored fonts. Shown is genomic sequence (black) surrounding AICE1 and AICE2 motif (green), 5' UTR region (orange) and exon 1 coding region (blue).
(**B**) A retroviral construct to assess integrated GFP-reporter activity driven by CMVpmin in combination with AICE1 or AICE2 enhancer elements.
(**C**) Schematic representation of sgRNA retroviral vector used in the study. Vector was made to express a sgRNA (orange) under control of an internal human U6 promoter (blue). This cassette is encoded on the sense strand downstream of the Thy1.1 marker (red).
(**D**) Gating strategy of infected cDCs after Flt3L culture. DCs were sorted as Thy1.1^{+} and analyzed by flow cytometry for expression of B220, CD11c, MHCII, CD24, and Sirpα to verify normal development after target knockout.
(**E**) Purified cDCs from BM cultures of indicated genotypes, treated as describe in **Figure 2G**, were analyzed by FACS to determine the cDC1 and cDC2 percentages and phenotypic markers. Shown are representative flow cytometry plots from one experiment (n =3). Numbers are the percentage cells in the indicated gates.
(**F**) Purified cDC1 from indicated genotypes were left untreated (–) or treated with LPS 250 ng/ml (+) for 48 hours. Cytokine profile was analyzed by means of multiplex cytokine analysis in culture supernatants. Shown is heatmap with colored boxes, representing cytokines amounts ranging from bright blue (lowest) to bright red (highest). Numbers represent cytokine concentrations (pg/ml).
(G) IFN-γ analysis was performed in culture supernatants of draining popliteal lymph nodes derived from mice treated as **Figure 2N,** collected 24 hours after the peptide challenge, and re-stimulated for 48 hours with HY peptide *in vitro*. Data are shown as mean ± S.D. ***$P < 0.01$, ****$P < 0.001$, two-way ANOVA followed by Bonferroni multiple comparison test.

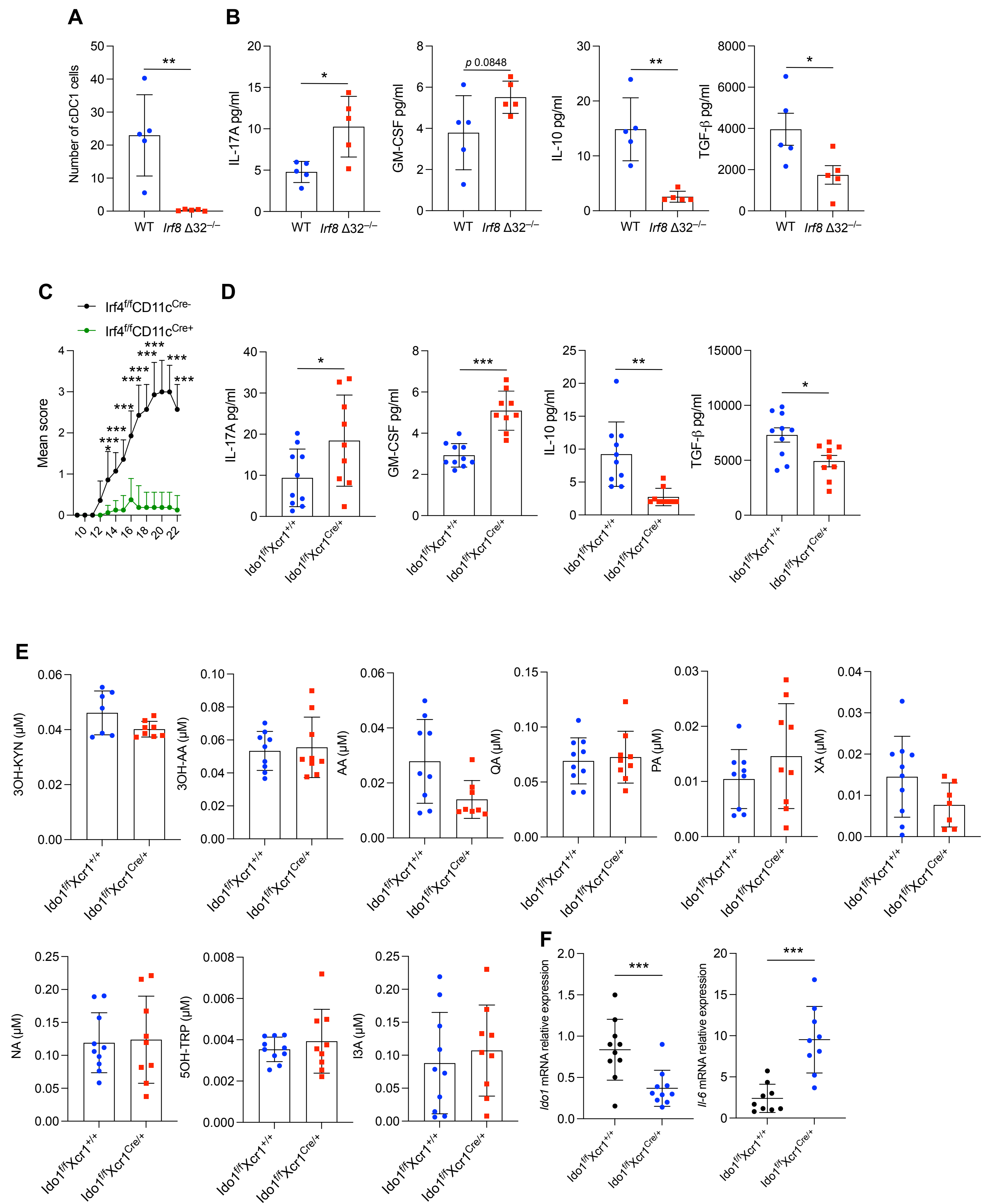


Figure S3 related to Figure 3

Figure S3. Ido1 in cDC1 is required for regulatory function in EAE, related to Figure 3

(A) cDC1 in spinal cord from EAE mice described in **Figure 3A**. Each dot represents an individual mouse. **P < 0.01, Unpaired t test.

(B) Levels of IL-17, GM-CFS, IL-10 and TGF-β in plasma of EAE mice described in **Figure 3A**. Each dot represents an individual value. *P < 0.05, **P < 0.01, Unpaired t test.

(C) EAE score in Irf4$^{f/f}$ CD11c$^{+/+}$ and Irf4$^{f/f}$ CD11c$^{cre/+}$ mice. Data are mean of daily EAE scores ± S.D. n = 3, with n = 5 mice per group. *P < 0.05, ***P < 0.001, two-way ANOVA followed by Bonferroni multiple comparison test.

(D) Measurement of IL-17, GM-CFS, IL-10 and TGF-β levels in plasma of EAE mice described in **Figure 3H**. Each dot represents an individual value. *P < 0.05, **P < 0.01, ***P < 0.001, Unpaired t test.

(E) Analysis of tryptophan metabolites in plasma from EAE mice as described in **Figure 3H**. Shown are 3 OH-KYN (3 OH- Kynurenine), 3OH-AA, AA (Anthranilic acid), QA (Quinolinic acid), PA (Picolinic acid), XA (Xanthurenic acid), 5OH-TRP (5 OH-Tryptophan) and I3A (indole-3-aldehyde). Each dot represents an individual value. Data are mean ± S.D. Unpaired t test.

(F) *Ido1* and *Il6* mRNA expression in cDC2 sorted from cervical lymph nodes of EAE mice described **in Figure 3H**. Data are represented as normalized transcript expression in the samples relative to normalized transcript expression in controls. Each dot represents an individual value. ***P < 0.001, Unpaired t test.

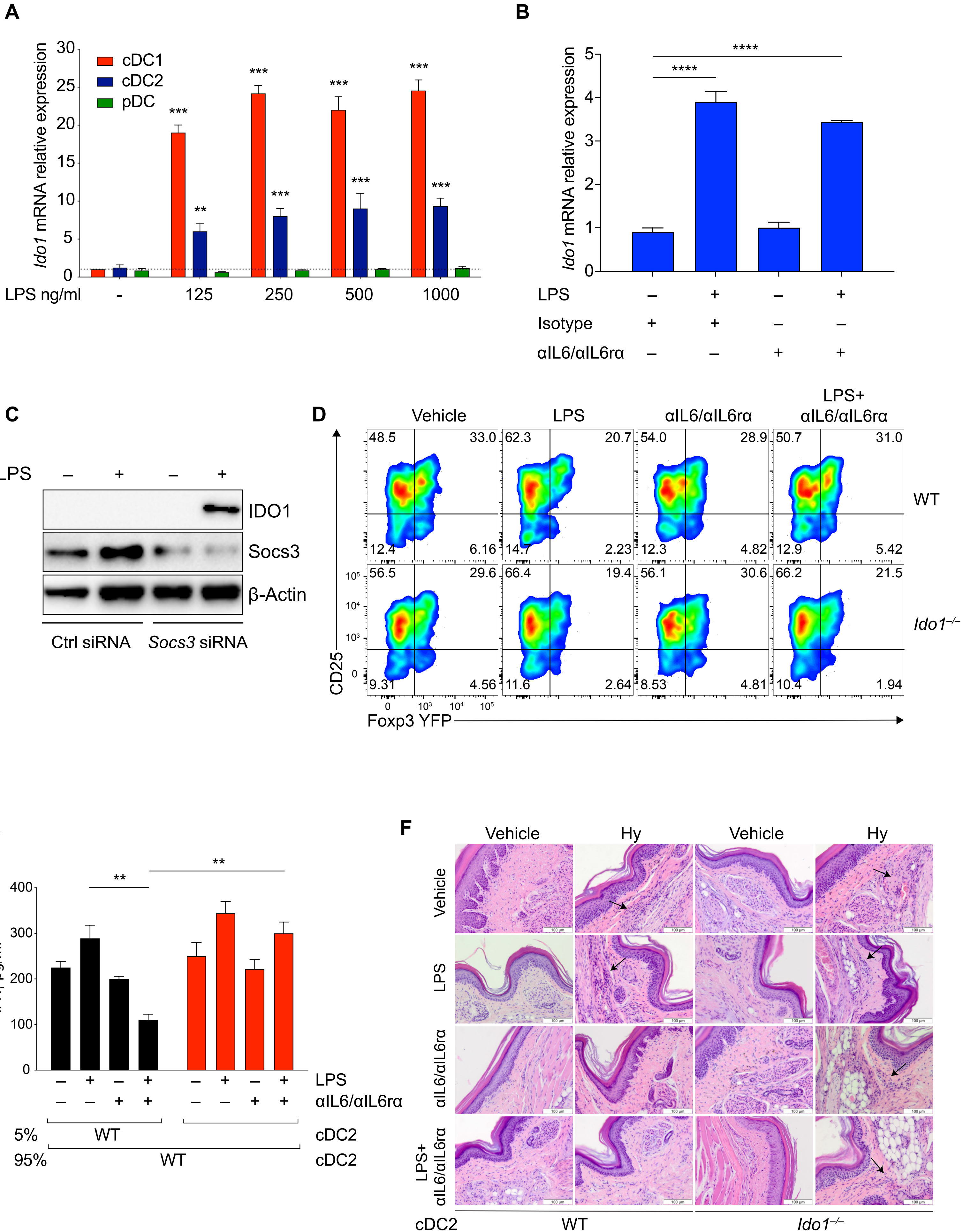


Figure S4 realted to Figure 4

Figure S4. IL-6 regulates IDO1 expression in cDC2, related to Figure 4.

(**A**) *Ido1* mRNA expression in purified cDC1, cDC2 and pDCs left untreated (–) or treated with the indicated concentration of LPS for 24 hours. Data are represented as normalized transcript expression in the samples, relative to normalized transcript expression in control cultures. Data are shown as mean ± S.D. ***P < 0.001, ****P < 0.0001, two-way ANOVA followed by Bonferroni multiple comparison test (n =4).

(**B**) BM cells were treated as in **Figure 4D** and *Ido1* mRNA expression was analyzed by qRT-PCR. ****P < 0.001, one-way ANOVA followed by Bonferroni multiple comparison test (n =3).

(**C**) siRNA mediated knock-down of *Socs3* in purified cDC2. Cells were transfected with siRNA control (Ctrl siRNA) or *Socs3* siRNA and then left untreated (–) or treated with LPS (+) 250ng/ml for 48hrs. Western blotting were carried out for IDO1, SOCS3 and β-actin expression as control. One representative experiment (n =3).

(**D**) $CD4^+CD25^–$ cells were purified from the spleen of OVA TCR-transgenic OTII Foxp3 YFP mice and co-cultured with WT and *Ido1*$^{–/–}$ cDC2 treated as in **Figure 4D** and loaded with OVA protein. 3 days after Foxp3 expression was evaluated by flow. Shown are representative flow cytometry plots from one experiment (n =3). Numbers are the percentage cells in the indicated gates.

(**E**) Production of IFN-γ by leukocytes from draining lymph nodes of mice, sensitized with peptide-pulsed cDC2 combinations as in (**G**) and challenged with HY peptide 15 days later in the footpad. Leukocytes collected 24 hours later from draining popliteal lymph nodes (draining left hind footpads) were re-stimulated for 48 hours *in vitro* with HY peptide, followed by analysis of IFN-γ in culture supernatants. All data are shown as mean ± S.D. **P < 0.01, two-way ANOVA followed by Bonferroni multiple comparison test.

(F) H&E staining of mouse footpads of mice sensitized with peptide-pulsed cDC2 combinations as described in a **Figure 4G** and challenged with HY peptide 15 d later in the footpad. Footpads were collected 24hrs after peptide challenge and stained with H&E to identify inflammatory infiltrates.

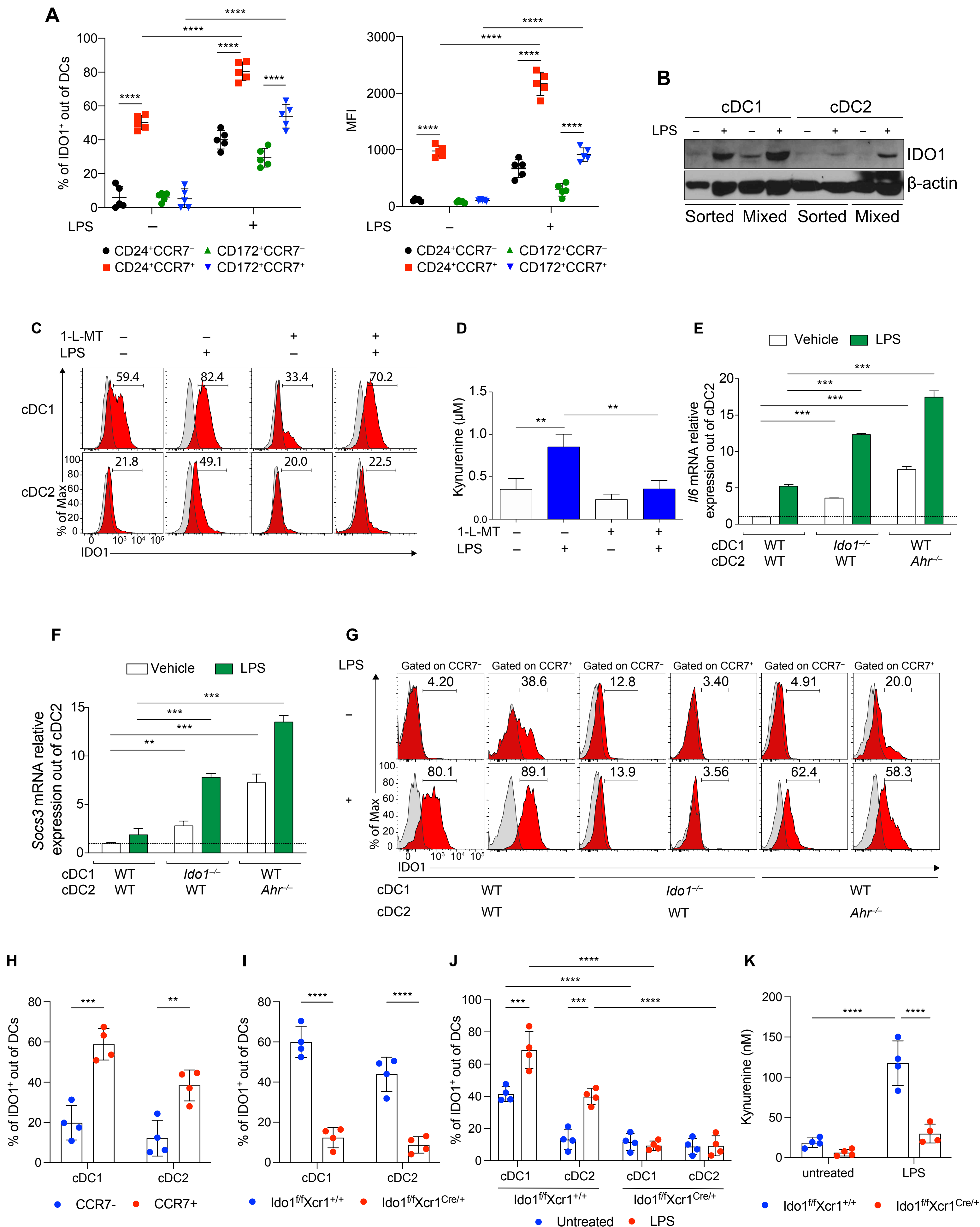


Figure S5 related to Figure 5

Figure S5. cDC2 cultured with cDC1 and treated with LPS exhibit conditional IDO1 expression, related to Figure 5.

(A) BM cells were cultured with FLT3L for 9 days and were either left untreated (–) or treated LPS 250 ng/ml (+) for 48 hours. Statistical analysis of IDO1 frequency (left) and MFI (right) by IS in the indicated cDCs gated populations. Each colored symbol represents an individual biological replicate. Data are shown as mean ± S.D. ****P < 0.0001, two-way ANOVA followed by Bonferroni multiple comparison test.

(**B**) BM cultures treated with Flt3L for 9 days were either left unsorted (mixed) or were first sorted into pure cDC1 and cDC2 populations (sorted), and either left untreated (–) or treated with 250 ng/ml LPS (+) for 48 hours. Following LPS treatment, mixed cultures were sorted to separate cDC1 and cDC2. Western analysis was performed on purified cDC1 and cDC2 from the indicated conditions for expression of IDO1 and β-Actin. One representative experiment (n = 3).

(**C**) Mixed cDCs were left untreated (–) or treated with 250 ng/ml LPS (+) in presence or absence of 1-L-MT (1 mM) for 48 hours and IDO1 expression were analyzed by IS. Shown are histograms for IDO1 in cDC1 and cDC2 in one representative experiment. Isotype control is shown in grey and numbers are the percentage of positive cells. (n = 3).

(**D**) Supernatants from cDCs prepared as in (B) were harvested 48 hrs after treatment and analyzed for L-kynurenine content by HPLC. Data are shown as mean ± S.D. **P < 0.01, one-way ANOVA followed by Bonferroni multiple comparison test.

(E-F) (**E**) *Il6* and (**F**) *Socs3* mRNA expression in cDC2 from transwell cDC1/cDC2 cocultures treated as described in **Figure 5F**. Data are represented as normalized transcript expression in the samples relative to normalized transcript expression in control cultures (untreated WT). Data are shown as mean ± S.D. **P < 0.01, ***P < 0.001, two-way ANOVA followed by Bonferroni multiple comparison test (n = 3).

(**G**) Purified cDC1 from trans-well cDC1/cDC2 co-cultures, treated as in **Figure 5F**, were analyzed for IDO1 expression by IS. Shown are representative histograms for IDO1 expression in cDC1. Numbers are the percentage of IDO1 positive cells. One representative experiment, (n = 3).

(**H**) $IDO1^{+}CCR7^{+}$ cDC1 and cDC2 frequency out of total cDCs by IS in mesenteric lymph node from WT mice. Each dot represents an individual mouse. Data are mean ± S.D. **P < 0.01, ***P < 0.001, two-way ANOVA followed by Bonferroni multiple comparison test (n = 3).

(I) Flow cytometric analysis of IDO1$^+$ cDC1 and cDC2 out of total cDCs by IS in total MLNs from Ido1$^{f/f}$ Xcr1$^{+/+}$ and Ido1$^{f/f}$Xcr1$^{cre/+}$. Each dot represents an individual mouse. ****P < 0.0001, two-way ANOVA followed by Bonferroni multiple comparison test (n = 3).

(J-K) Total splenocytes from mice in **(I)** were left untreated or treated with LPS 250 ng/ml LPS for 48h. **(J)** IDO1 expression were analyzed by IS. Shown are histograms for IDO1 in cDC1 and cDC2 out of total cDCs. **(K)** Supernatants from **J** were analyzed for L-Kyn. Each dot represents an individual mouse, ****P < 0.0001, ***P < 0.001, two-way ANOVA followed by Bonferroni multiple comparison test (n = 3).

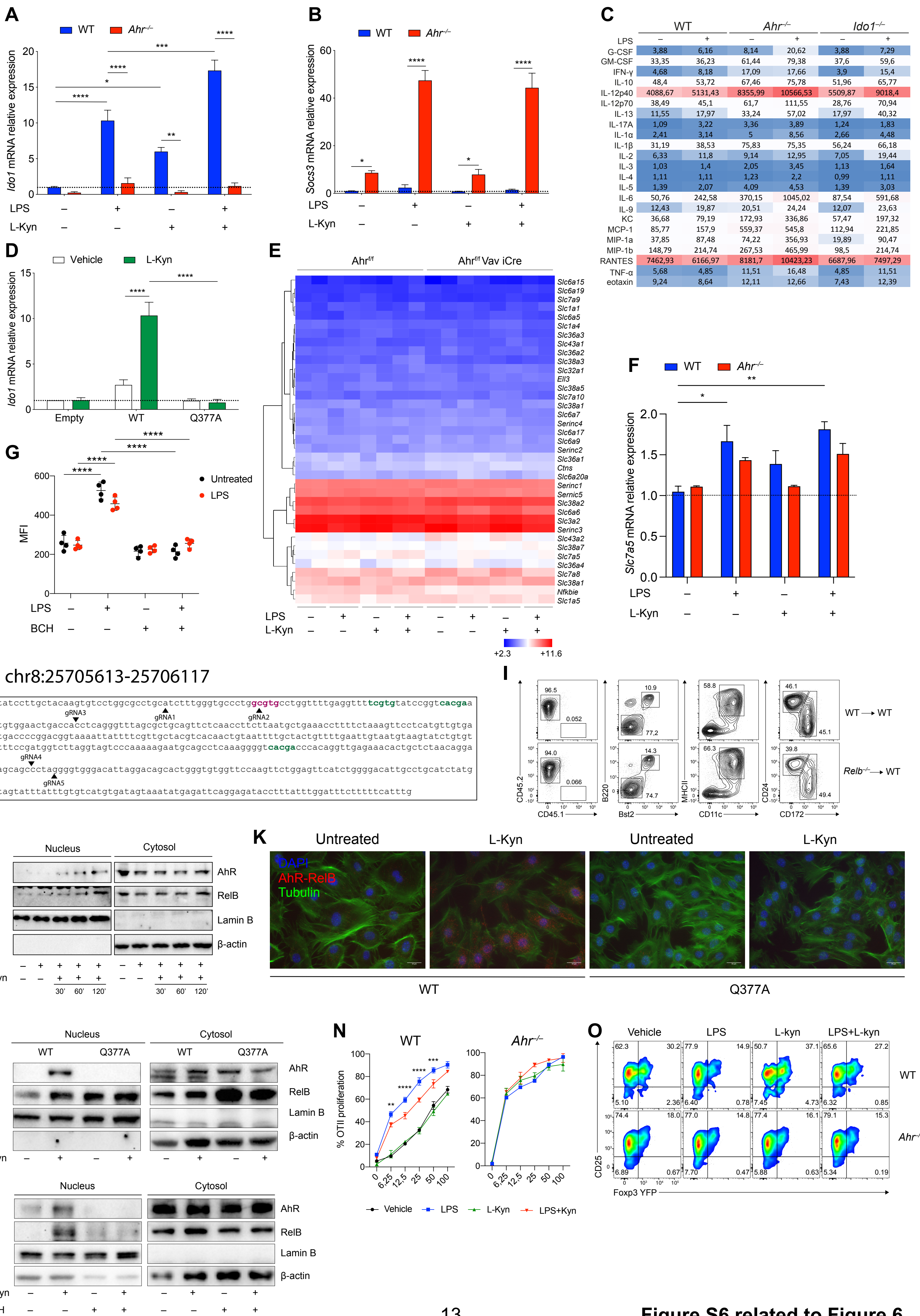


Figure S6 related to Figure 6

Figure S6. Isolated cDC2 treated with L-kynurenine downregulate IL-6 and acquire IDO1 expression through AhR and RelB cooperation, related to Figure 6.

(**A-B**) *Ido1* (**A**) and *Socs3* (**B**) mRNA expression in purified cDC2 treated as in **Figure 6B.** Data are represented as normalized transcript expression in the samples relative to normalized transcript expression in control (untreated WT) cultures. Data are shown as mean ± S.D. *P < 0.05, **P < 0.01, ***P < 0.001, ****P < 0.0001, two-way ANOVA followed by Bonferroni multiple comparison test, (n =4).

(**C**) Purified cDC2 from indicated genotypes were left untreated (–) or treated with LPS 250 ng/ml (+) for 48 hours. Cytokines were analyzed by means of multiplex ELISA. Shown is heatmap with colored boxes representing cytokines amount, ranging from bright blue (lowest) to bright red (highest). Numbers represent cytokine concentrations (pg/ml).

(**D**) *Ido1* mRNA expression in purified cDC2 treated as in **Figure 6E**. Data are represented as normalized transcript expression in the samples relative to normalized transcript expression in control (untreated) cultures. Data are shown as mean ± S.D. ****P < 0.0001, two-way ANOVA followed by Bonferroni multiple comparison test (n = 3).

(**E**) Heat map representation of large neutral amino acid transporters (LATs) solute carrier family gene expression in cDC2 from *Ahr*$^{f/f}$ mice *versus Ahr*$^{f/f}$ *Vav1* iCre mice, with no conditioning (–) or conditioned with LPS 250 ng/ml (+) in presence or absence of exogenous L-kynurenine. Color from red to blue indicates highest to lowest expression.

(**F**) *Slc7a5* mRNA expression in cDC2 stimulated as in (F). Data are represented as normalized transcript expression in the samples relative to normalized transcript expression in controls. Each dot represents an individual value. *P<0.05 **P < 0.01, two-way ANOVA followed by Bonferroni multiple comparison test (n = 3).

(**G**) Shown are MFI in different groups as in **Figure 6G** of four independent experiments. Data are mean ± S.D. ****P < 0.0001, two-way ANOVA followed by Bonferroni multiple comparison test.

(**H**) Nucleotide sequences contain XRE (+1340 bp) and AhREIIIs (+1361 bp, +1374 bp and +1601 bp) *Ido1* enhancer regions described in **Figure 6H**. Shown are genomic sequence surrounding +1340 bp XRE motif (purple) and +1361 bp, +1374 bp and +1601 bp AhREIIIs

motif (green). Black arrows indicate the sgRNAs sequences used for CRISPR/Cas9-mediated deletion.

(**I**) WT CD45.1 mice were lethally irradiated and reconstituted with WT or *Relb*$^{-/-}$ CD45.2 BM as described in **Figure 6M**. BM cultures from those mice were treated with Flt3L and analyzed by FACS after 9 days to evaluate the differentiation of DC subsets. Shown are representative FACS plots of DC subsets, of indicated chimeras, gated as the following: pDCs (B220^{+}Bst2^{+}), cDC1 (CD11c^{+}MHCII^{+}CD24^{+}CD172^{-}), cDC2 (CD11c^{+}MHCII^{+}CD172^{+}). Numbers indicate the percent of cells in the indicated gates. One representative experiment (n = 3).

(**J**) Purified cDC2 were treated as in **Figure 6K** and nuclear and cytosolic extracts were performed and analyzed by Western blotting. β-actin and Lamin B are purity controls of cytoplasmic and nuclear fraction, respectively. Immunoblotting representative experiment of n = 3.

(**K**) AhR and RelB interaction was analyzed by PLA in MEF cells expressing WT or Q377A AhR either untreated (–) or conditioned with L-kynurenine (+). Red spots show a single AhR/RelB interaction. DNA counterstaining was performed with DAPI. α-Tubulin-FITC antibody was used to identify the cellular edge. Background control was performed according to the manufacturer's instruction. Scale bars, 10 μm. One representative experiment of n = 3 cultures.

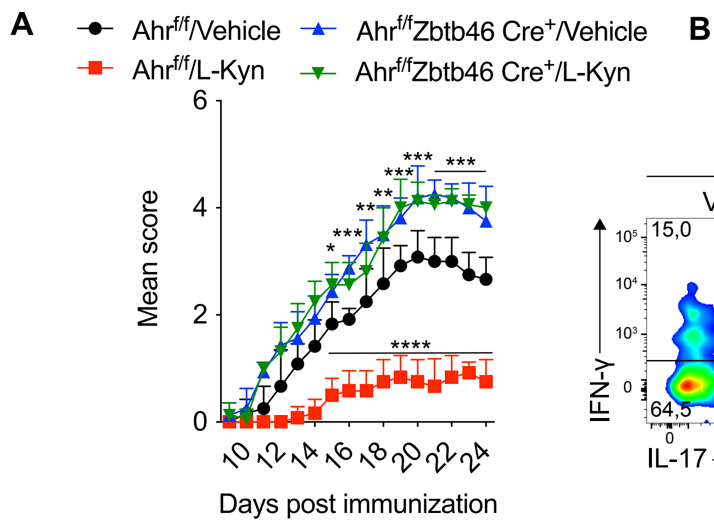
(**L**) MEF cells expressing WT or Q377A AhR were left untreated (–) or treated with L-kynurenine (+). Nuclear and cytosolic extracts were performed and AhR and RelB were analyzed by immunoblotting. β-actin and Lamin B are purity controls of cytoplasmic and nuclear fraction, respectively. Immunoblotting representative experiment of n = 3.

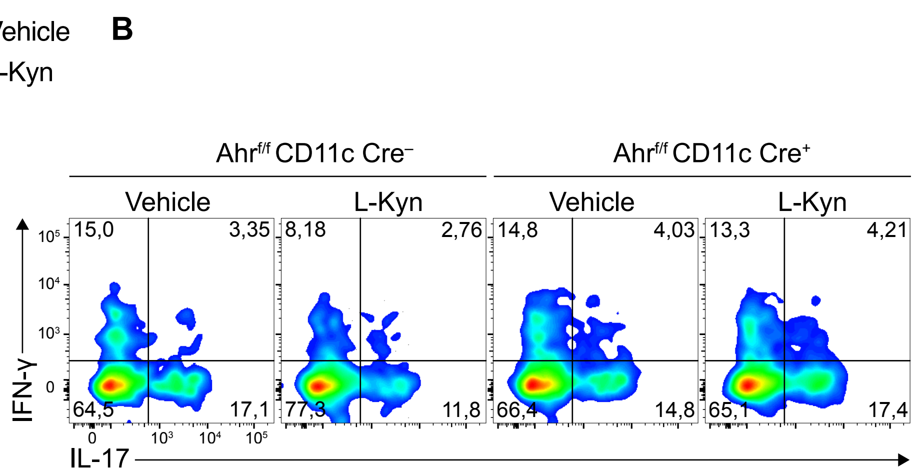
(**M**) MEF cells expressing WT AhR were treated with L-kyn alone in combination with BCH (10 mM). Nuclear and cytosolic extracts were performed and AhR and RelB were analyzed by immunoblotting. β-actin and Lamin B are purity controls of cytoplasmic and nuclear fraction, respectively. Immunoblotting representative experiment of n = 3.

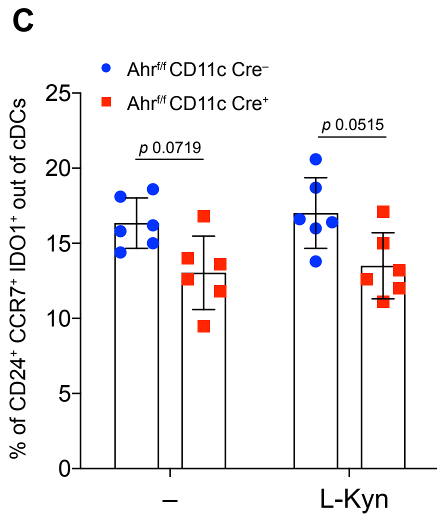
(**N**) WT and *Ahr*$^{-/-}$ cDC2 treated as in **Figure 6B** were assayed for presentation to OT-II T cells (CFSE^{-} CD4^{+}CD44^{+} TCRVα2^{+}) in response to indicated concentrations of soluble OVA protein. Data are shown as mean ± S.D. **P < 0.001, ***P < 0.001, ****P < 0.0001, two-way ANOVA followed by Bonferroni multiple comparison test (n = 3).

(**O**) CD4^{+}CD25^{-} T cells were purified from the spleen of OVA TCR-transgenic OTII Foxp3 YFP

mice and co-cultured with WT and *Ahr*$^{-/-}$ cDC2 treated as in **Figure 6B** and loaded with OVA protein. 3 days after Foxp3 expression was evaluated by flow. Shown are representative flow cytometry plots from one experiment (n =3). Numbers are the percentage cells in the indicated gates.







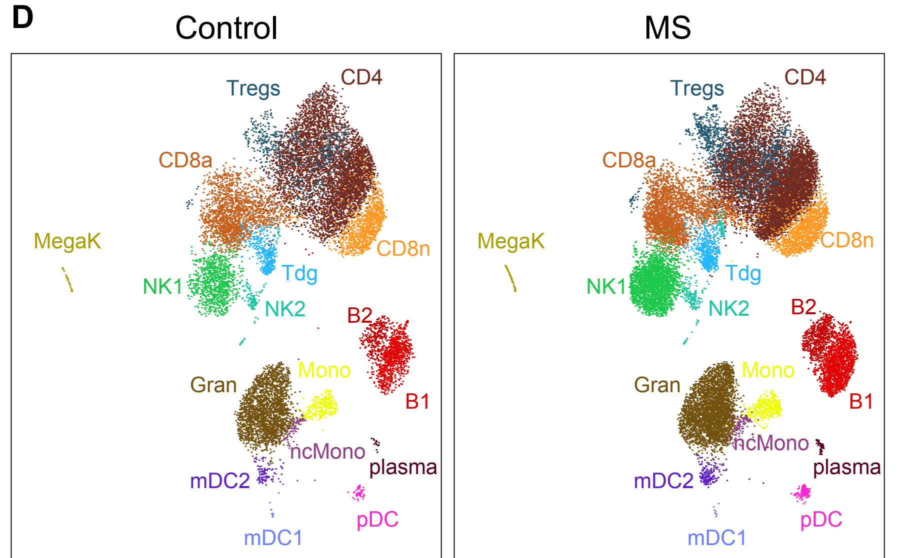


Figure S7 related to Figure 7

Figure S7. L-kynurenine suppresses EAE, related to Figure 7.

(**A**) EAE score in Ahr$^{f/f}$ Zbtb46 Cre^{-} or Ahr$^{f/f}$ Zbtb46 Cre^{+} mice orally treated with L-kyn 2.5 mg/mouse or PBS as vehicle, from day 3 to 22 after MOG immunization. Data are mean of daily EAE scores ± S.D. n = 3, with n = 5 mice per group. **P < 0.01, ****P < 0.001, two-way ANOVA followed by Bonferroni multiple comparison test.

(B) CD4^{+} T cells derived from dLN of mice treated as in **Figure 7A** were assessed for cytokine production after ex *vivo* re-stimulation with PMA/ionomycin. Representative flow cytometry plots, six mice per group (n =3).

(**C**) Statistical analysis of the frequency of IDO1^{+}CCR7^{+} cDC1 out of total cDCs by IS from cervical LNs from EAE mice in **Figure 7A.** Each dot represents an individual mouse. Data are mean ± S.D. two-way ANOVA followed by Bonferroni multiple comparison test (n = 3).

(**D**) Comparative UMAP plots depicting blood cells from control and MS donors. Color coding and cluster names are as in **Figure 7N.**

Table S2, related to figure 2N, 3C, 3I, 5K, 7J, S4F. Histology sections quantification.

Figure	Biological Replicates	Sample	Count	P value
2N	3	WT $CCR7^-$/Vehicle	373	
		WT $CCR7^-$/HY	730	
		Ido1$^{-/-}$ $CCR7^-$/Vehicle	329	
		Ido1$^{-/-}$ $CCR7^-$/HY	545	
		WT $CCR7^+$/Vehicle	500	
		WT $CCR7^+$/HY	401	0,0011
		Ido1$^{-/-}$ $CCR7^+$/Vehicle	270	
		Ido1$^{-/-}$ $CCR7^+$/HY	418	
3C	3	WT	168	
		Irf8 $\Delta32^{-/-}$	354	0,0114
3I	3	$Ido1^{f/f}$ $XCR1^{+/+}$	390	
		$Ido1^{f/f}$ $XCR1^{cre/+}$	549	0,0163
5K	3	*Ido1*$^{-/-}$ + *Irf4*$^{f/f}$ → WT	385	
		Ido1$^{-/-}$ + *Irf4*^{cKO} → WT	740	0,0006
7J	3	$Ahr^{f/f}$ CD11c Cre^-/Vehicle	258	
		$Ahr^{f/f}$ CD11c Cre^-/L-Kyn	98,3	0,0033
		$Ahr^{f/f}$ CD11c Cre^+/Vehicle	279	
		$Ahr^{f/f}$ CD11c Cre^+/L-kyn	326	
S4F	3	cDC2 WT/− (Vehicle)	339	
		cDC2 WT/LPS (Vehicle)	198	
		cDC2 WT/αIL6-αIL6ra (Vehicle)	184	
		cDC2 WT/LPS+αIL6-αIL6ra (Vehicle)	332	
		cDC2 WT/− (HY)	526	
		cDC2 WT/LPS (HY)	575	
		cDC2 WT/αIL6-αIL6ra (HY)	311	0,0002
		cDC2 WT/LPS+αIL6-αIL6ra (HY)	397	0,0043
		cDC2 *Ido1*$^{-/-}$ /− (Vehicle)	362	
		cDC2 *Ido1*$^{-/-}$/LPS (Vehicle)	326	
		cDC2 *Ido1*$^{-/-}$ /αIL6-αIL6ra (Vehicle)	574	
		cDC2 *Ido1*$^{-/-}$/LPS+αIL6-αIL6ra (Vehicle)	256	
		cDC2 *Ido1*$^{-/-}$/− (HY)	551	
		cDC2 *Ido1*$^{-/-}$/LPS (HY)	358	
		cDC2 *Ido1*$^{-/-}$ /αIL6-αIL6ra (HY)	646	
		cDC2 *Ido1*$^{-/-}$ /LPS+αIL6-αIL6ra (HY)	615	

* P value is calculated on sample control.