Supplementary Figures

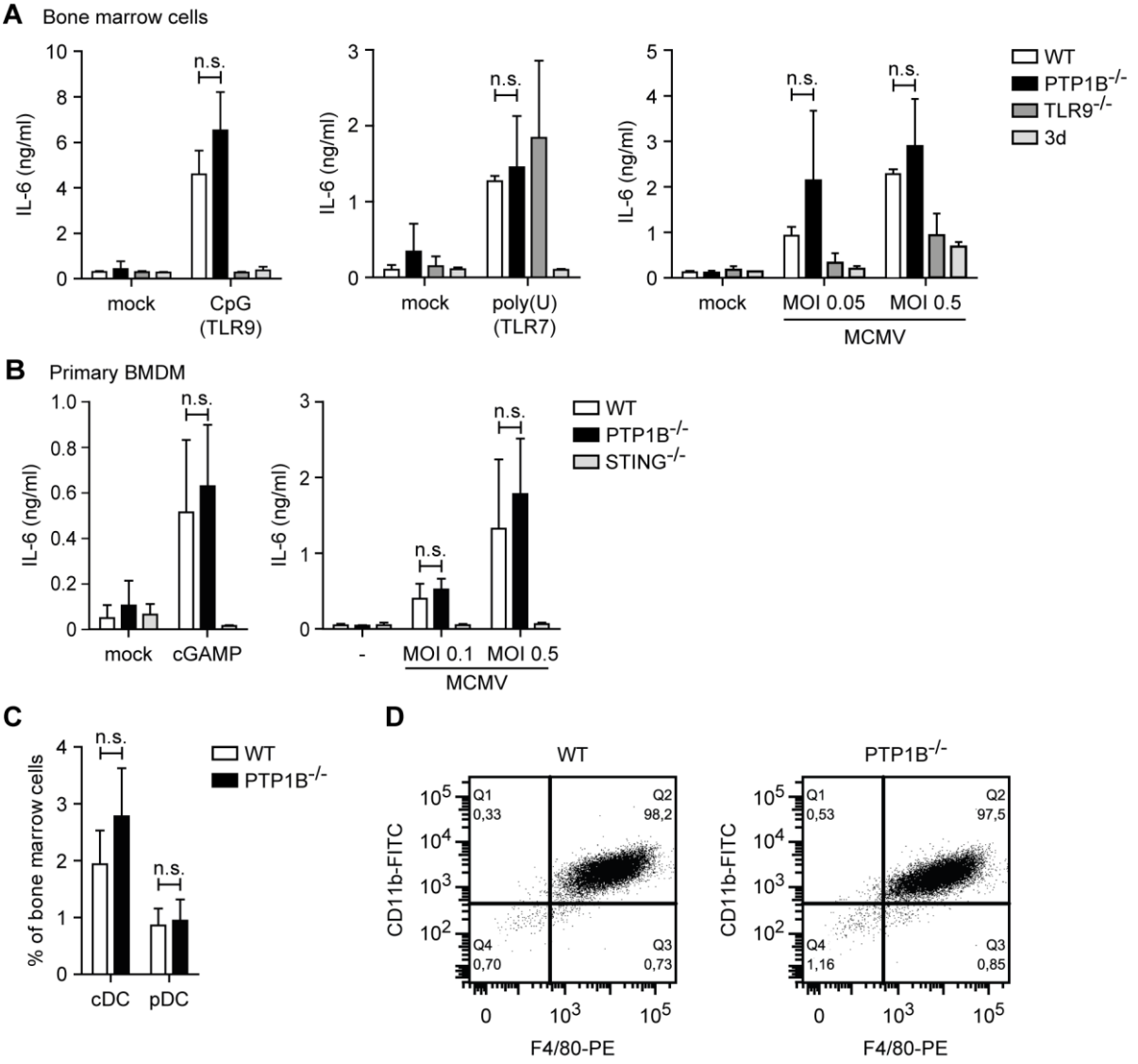

Figure S1: Bone marrow cells and BMDM from WT and PTP1B$^{-/-}$ mice secrete the same levels of IL-6 and express expected cell markers.

(A) Total BM cells were prepared from wild type (WT), PTP1B$^{-/-}$, TLR9$^{-/-}$, and 3d mice. Cells were stimulated with 1 µM CpG 2336 (left panel), transfected with poly(U) (center panel) or infected with MCMV at the indicated MOI (right panel) for 22 h. Levels of IL-6 in supernatants were determined by ELISA. Results are shown as mean ± S.D. of 2 independent experiments with biological duplicates.

(B) Primary MCSF-differentiated BMDM prepared from wild type (WT), PTP1B$^{-/-}$, and STING$^{-/-}$ mice were transfected with 3 µg/ml cGAMP (left panel) or infected with MCMV at the indicated MOI (right panel). 6 hours post stimulation or infection, levels of IL-6 in supernatants were determined by ELISA. Results are shown as mean ± S.D. of 2 independent experiments with biological duplicates.

(C) Single cell suspensions from the bone marrow of WT and PTP1B$^{-/-}$ mice were labeled with antibodies for CD11c, CD11b, B220, Siglec-H, and mPDCA-1 and analyzed by flow cytometry. Portions of cDC (CD11c^{+}CD11b^{+}B220^{-}) and pDC (CD11c^{+}Siglec-H^{+}mPDCA-1^{+}) were calculated relative to the amount of living cells. Results are shown as mean ± S.D. of bone marrow from n = 5 (WT) or n = 6 (PTP1B$^{-/-}$) mice.

(D) BMDM from WT and PTP1B$^{-/-}$ mice were labeled with antibodies for CD11b and F4/80 on day 8 of MCSF differentiation and analyzed by flow cytometry. Q1-Q4 show percentages of cells in respective quadrants. Results are shown from one representative experiment out of 2 independent experiments.

Statistical analysis: Student's t-test (unpaired, two-tailed), n.s. not significant

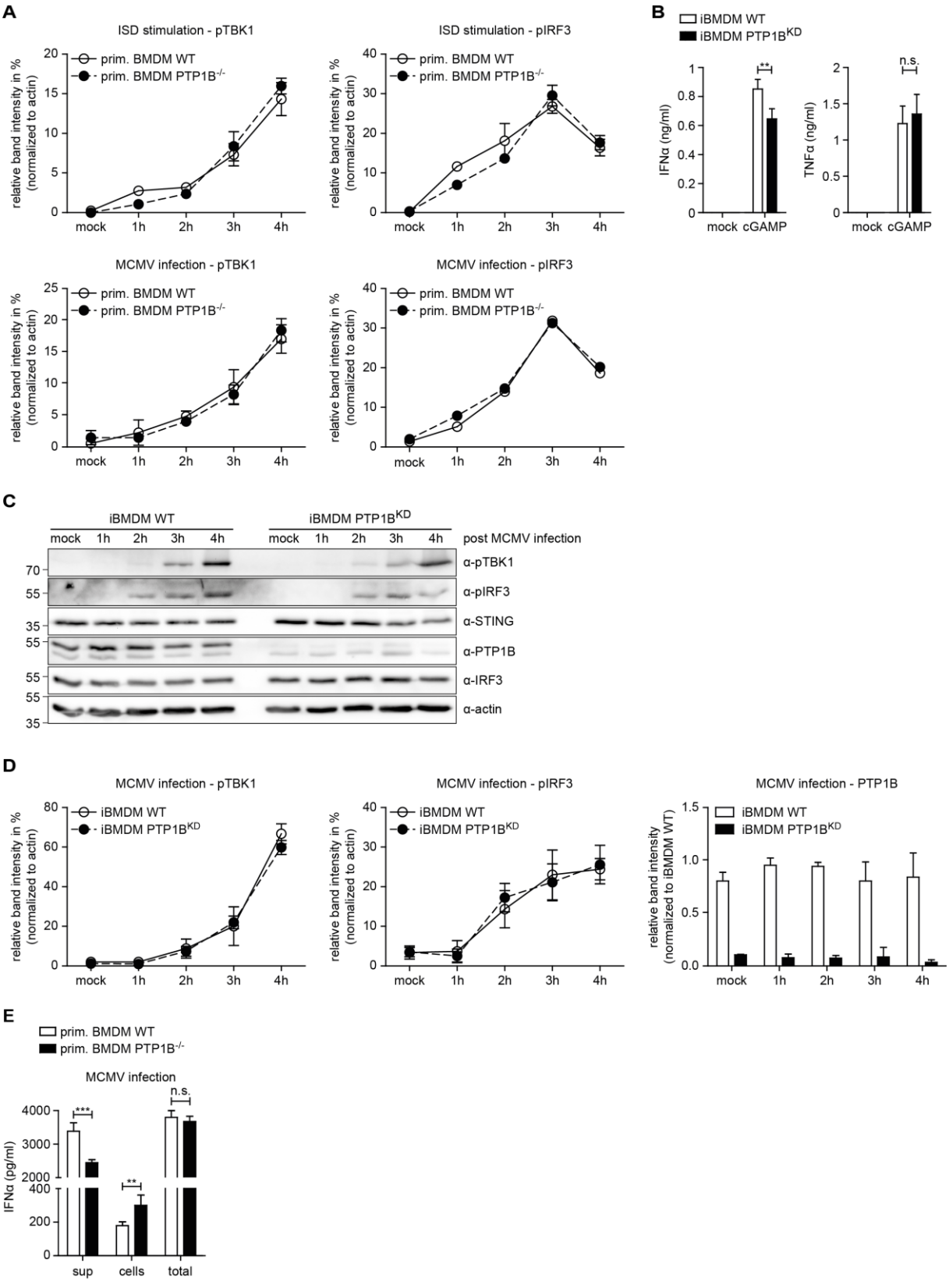

Figure S2: cGAS-STING-mediated signalling and induction of type I IFN transcription is not affected in iBMDM PTP1B^{KD}.

(A) Quantification of immunoblots shown in Figure 3A. Band intensities of pTBK1 (left panels) and pIRF3 (right panels) upon stimulation with ISD (upper panels) or infection with MCMV

(lower panels) were normalized to the respective actin loading control. Data is combined from two independent experiments and shown as mean ± S.D, except for pIRF3 levels upon MCMV infection which are shown from one representative experiment.

(B) WT or PTP1B^{KD} iBMDM were stimulated by addition of 10 µg/ml cGAMP. 6 hours post stimulation, levels of IFNα (left panel) and TNFα (right panel) in supernatants were determined by ELISA. Data is shown as mean ± S.D. of two combined experiments performed with biological duplicates.

(C) iBMDM WT or iBMDM PTP1B^{KD} were left untreated or infected with MCMV (MOI 0.5) for 1, 2, 3, or 4 hours. Cells were lysed and phospho-TBK1, phospho-IRF3, STING, PTP1B, total IRF3, and actin protein levels were analyzed by immunoblotting with respective antibodies. One representative experiment out of two independent experiments is shown.

(D) Quantification of immunoblots shown in C. Band intensities of pTBK1 (left panel) and pIRF3 (middle panel) upon infection with MCMV were normalized to the actin loading control. Band intensity of PTP1B (right panel) was analysed to confirm Cas9-mediated knockdown of PTP1B. Data is combined from two independent experiments and shown as mean ± S.D.

(E) BMDM from WT or PTP1B$^{-/-}$ mice were infected with MCMV (MOI 2). 4 hours post infection, the supernatant (1), cells (2) or both combined (3) as described in Figure 4D were harvested, and IFNα levels were determined by ELISA. Data is shown as mean ± S.D. of two combined experiments performed with biological duplicates.

Statistical analysis: Student's t-test (unpaired, two-tailed), n.s. not significant, **p<0.01, ***p<0.001. Differences between datasets were n.s. if not stated otherwise.

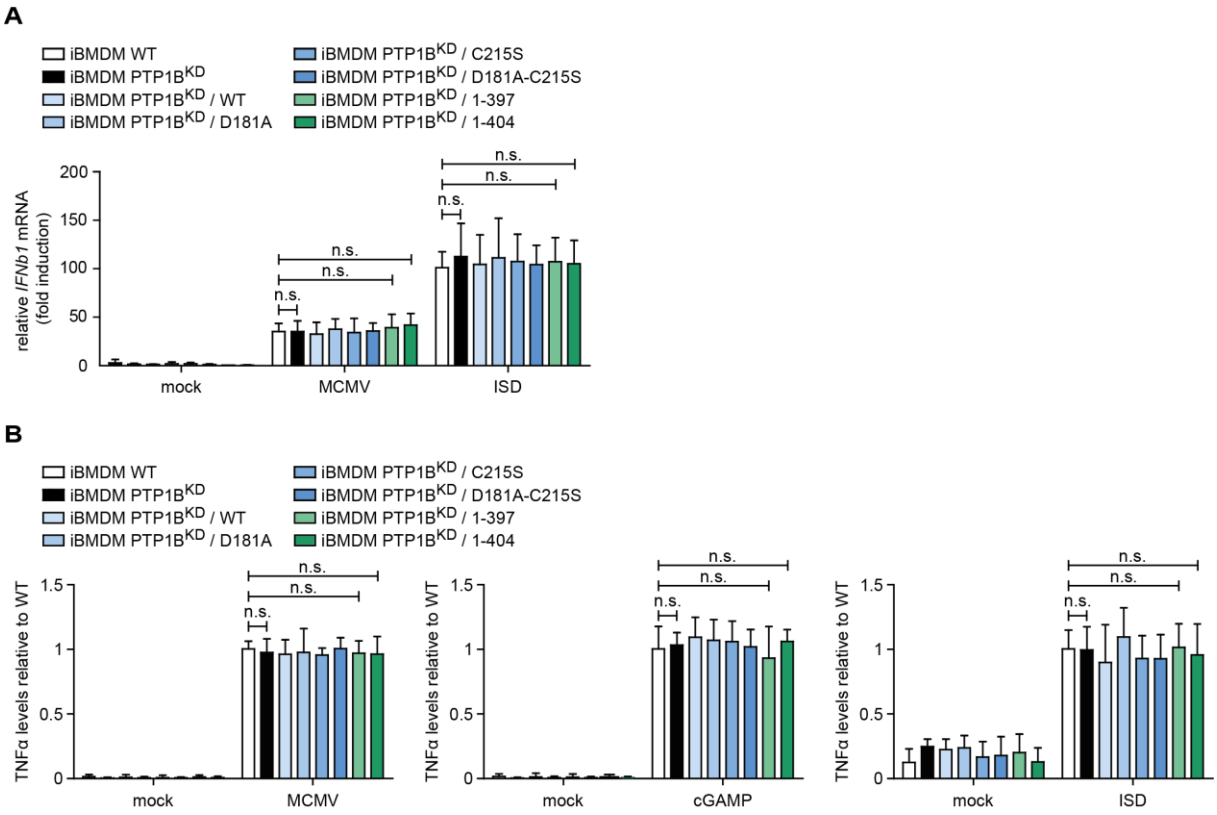

Figure S3: TNFα secretion upon cGAS-STING stimulation is not affected in iBMDM PTP1B^{KD}.

(A) WT iBMDM, PTP1B^{KD} iBMDM, or PTP1B^{KD} iBMDM stably expressing either HA-tagged PTP1B WT, phosphatase mutants (D181A, C215S, D181A-C215S) or membrane anchor mutants (1-397 or 1-404) were infected with MCMV at an MOI of 2 or stimulated by transfection with 3 µg/ml ISD. 4 hours post infection or stimulation, total RNA was extracted to determine *IFNb1* mRNA transcripts by qRT-PCR. Data shown as mean ± S.D. of one representative out of two independent experiments performed with biological duplicates.

(B) Immortalised WT BMDM, iBMDM PTP1B^{KD}, or iBMDM PTP1B^{KD} stably expressing either HA-tagged PTP1B WT, D181A, C215S, D181A-C215S, 1-397, or 1-404 were infected with MCMV at an MOI of 2 (left panel), or stimulated by addition of 10 µg/ml cGAMP (center panel), or transfection of 3 µg/ml ISD (right panel). 16 hours post infection or stimulation, levels of TNFα in supernatants were determined by ELISA. Results are shown as mean ± S.D. of one representative out of three experiments performed with biological duplicates.

Statistical analysis: Student's t-test (unpaired, two-tailed), n.s. not significant

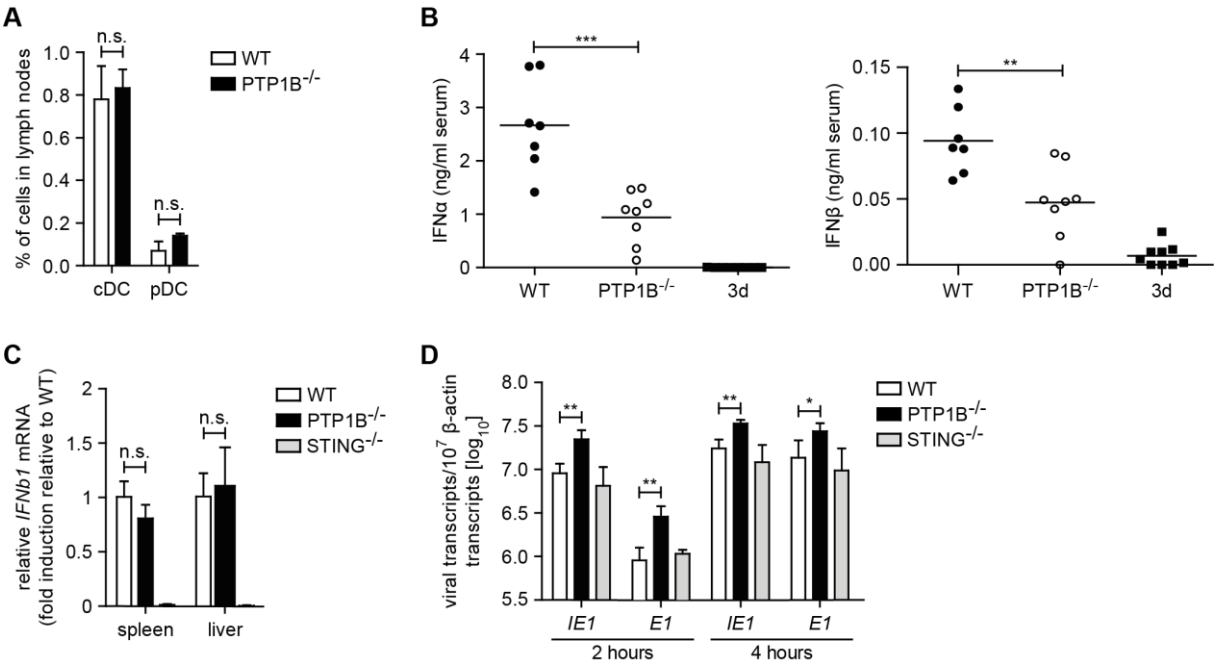

Figure S4: Levels of secreted type I IFN, but not of type I IFN transcripts, are reduced in PTP1B$^{-/-}$ mice upon MCMV infection, which leads to enhanced transcription of MCMV genes.

(A) Single cell suspensions from inguinal lymph nodes of WT and PTP1B$^{-/-}$ mice were labeled with antibodies for CD11c, CD11b, B220, Siglec-H, and mPDCA-1 and analyzed by flow cytometry. Portions of cDC (CD11c^{+}CD11b^{+}B220^{-}) and pDC (CD11c^{+}Siglec-H^{+}mPDCA-1^{+}) were calculated relative to the amount of living cells. Results are shown as mean ± S.D. of lymph nodes from three mice per group.

(B) Wild type (WT), PTP1B$^{-/-}$, and 3d mice were intravenously infected with 4 x 10^{5} PFU MCMV. Levels of IFNα (left panel) and IFNβ (right panel) in serum 36 hours post infection were determined by ELISA. Results are from two independent experiments with each data point representing one individual mouse.

(C) Wild type (WT), PTP1B$^{-/-}$, and STING$^{-/-}$ mice (n=3 per group) were intravenously infected with 4 x 10^{5} PFU MCMV. 6 hours post infection, total RNA from spleen and liver was extracted and transcript levels of *IFNb1* mRNA were determined by qRT-PCR. Fold induction was normalized to *IFNb1* mRNA transcripts in WT mice. Results are shown as mean ± S.D.

(D) Primary BMDM of wild type (WT), PTP1B$^{-/-}$, and STING$^{-/-}$ mice were infected with MCMV at an MOI of 0.01. Two and 4 hours post infection, total RNA was extracted and transcript levels of MCMV *IE1* and MCMV *E1* were determined by qRT-PCR. Results are combined from two independent experiments and shown as mean ± S.D.

Statistical analysis: Student's t-test (unpaired, two-tailed), n.s. not significant, **p<0.01, ***p<0.001.