Expanded View Figures

Figure EV1. Peripheral T cell compartment characterization of *CD4cre Ptpn6$^{fl/fl}$* and *CD4cre Ptpn6$^{fl/fl}$/Ptpn11$^{fl/fl}$* mice.

A, B T cells from spleen (A) and inguinal lymph nodes (iLN) (B) of *CD4cre Ptpn6$^{fl/fl}$* and control mice were analyzed. Cellularity, CD4$^+$ and CD8$^+$ T cell numbers (gated as TCRβ$^+$ CD4$^+$ or CD8$^+$, respectively), percentages of CD44 high T cells are shown; regulatory T cell (Treg) numbers and frequency (gated as TCRβ$^+$ CD4$^+$ Foxp3$^+$) are illustrated for the spleen.

C Cellularity from thymus and number of CD4 and CD8 double-negative, double-positive, CD4 or CD8 single-positive thymocytes (gated on lineage$^-$; single-positives, an additional gate on TCRβ$^+$ was performed) of *CD4cre Ptpn6$^{fl/fl}$/Ptpn11$^{fl/flWbm}$* and control mice are depicted.

D Treg number and frequency (gated as TCRβ$^+$ CD4$^+$ Foxp3$^+$) are illustrated for the spleen of *CD4cre Ptpn6$^{fl/fl}$/Ptpn11$^{fl/flWbm}$* and control mice.

E Cellularity, CD4$^+$ and CD8$^+$ T cell numbers, as well as percentages of CD44 high T cells from the iLN of *CD4cre Ptpn6$^{fl/fl}$/Ptpn11$^{fl/flWbm}$* and control mice are shown.

F Survival curves of *CD4cre Ptpn6$^{fl/fl}$/Ptpn11$^{fl/flBgn}$* and control mice challenged with MC38.

G–I Ten to twelve days following MC38 tumor inoculation, isotype-treated *CD4cre Ptpn6/11$^{wt/wt}$* and *CD4cre Ptpn6$^{fl/fl}$/Ptpn11$^{fl/flWbm}$* mice were sacrificed. Graph depicts the frequencies of PD-1$^+$ CD8$^+$ T cells (gated as CD45$^+$ TCRβ$^+$ CD8$^+$) in the tumor (G). Frequencies of CD4$^+$ T cells (gated as CD45$^+$ TCRβ$^+$ CD4$^+$) expressing IFN-γ and TNFα upon re-stimulation (H) and percentages of CD4$^+$ T cells in the tumor are shown (I).

Data information: Results illustrate mean ± SEM of n = 7–8 mice/group (A, B), of n = 10–12 mice/group (C–E), or of n = 9–14 mice/group (G–I). Student's t-test (unpaired, two-tailed) was used to compare differences between experimental groups (A–E, G–I). Results depict n = 11 mice/group; statistical significance was calculated by log-rank (Mantel-Cox) test (F). *$P \leq 0.05$, **$P \leq 0.01$, ***$P \leq 0.001$, ****$P \leq 0.0001$.
Source data are available online for this figure.

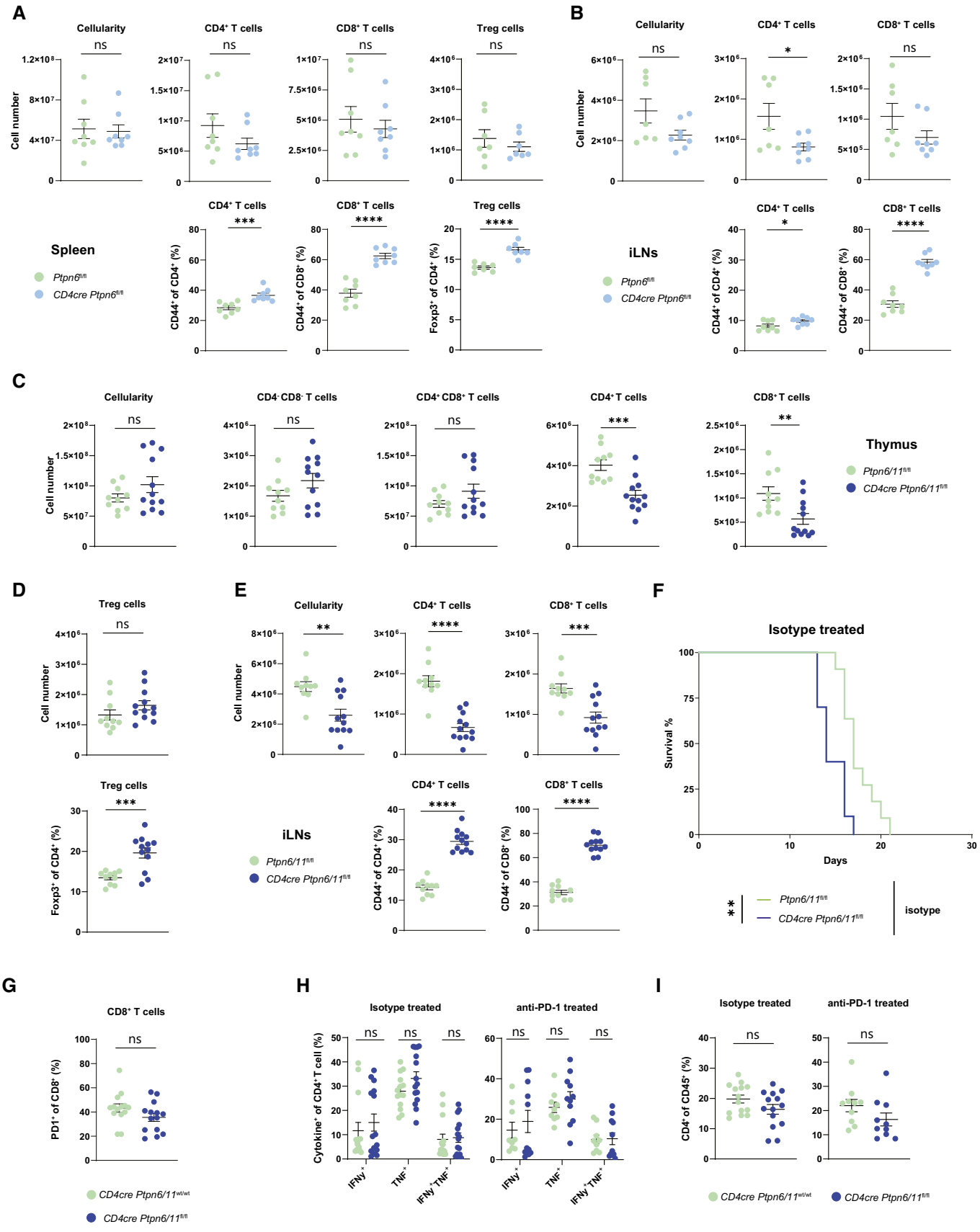
A
Cellularity
CD4+ T cells
CD8+ T cells
Treg cells
Cell number
Spleen
Ptpn6fl/fl
CD4cre Ptpn6fl/fl
CD44+ of CD4+ (%)
CD44+ of CD8+ (%)
Foxp3+ of CD4+ (%)
B
iLNs
C
CD4-CD8- T cells
CD4+CD8+ T cells
Thymus
Ptpn6/11fl/fl
CD4cre Ptpn6/11fl/fl
D
E
F
Isotype treated
Survival %
Days
isotype
G
CD8+ T cells
PD1+ of CD8+ (%)
CD4cre Ptpn6/11wt/wt
H
Isotype treated
anti-PD-1 treated
Cytokine+ of CD4+ T cell (%)
IFNγ+
TNF+
IFNγ+TNF+
I
CD4+ of CD45+ (%)

Figure EV1.

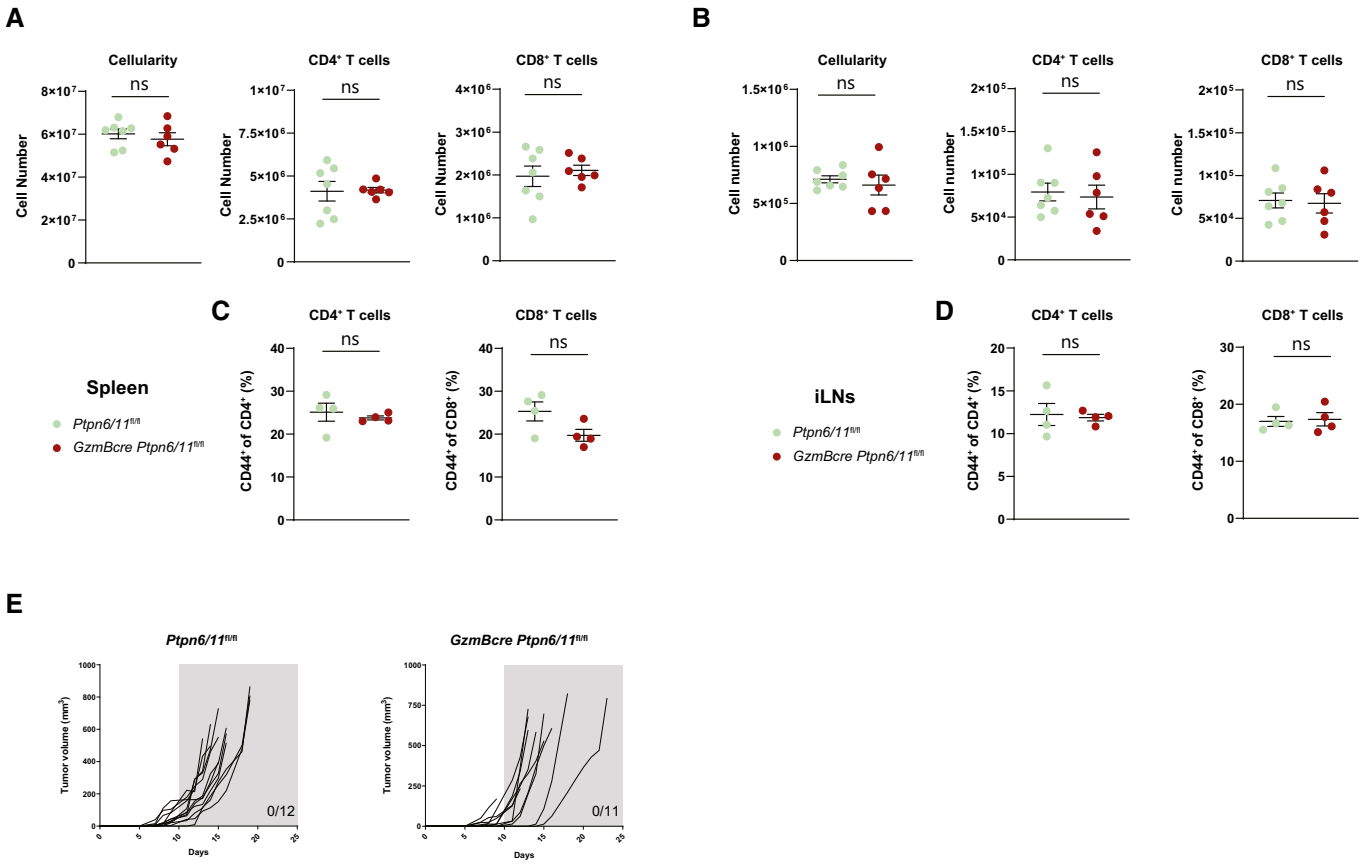

Figure EV2. Peripheral T cell compartment characterization of *GzmBcre Ptpn6/11$^{fl/fl}$* mice.

A–D Spleen and iLN of *GzmBcre Ptpn6/11$^{fl/fl}$* mice and control mice were analyzed. Cellularity, CD4$^+$ and CD8$^+$ T cell numbers are depicted for spleen (A) and iLN (B). Percentages of CD44 high of CD4$^+$ and CD8$^+$ T cells are shown for spleen (C) and iLN (D). Results depict n = 6–7 mice/group (A, B) and n = 4 mice/group for percentages of CD44 high cells (C, D). Student's t-test (unpaired, two-tailed) was used to compare differences between experimental groups.

E Tumor growth in individual mice challenged with MC38 is shown for the indicated genotypes; number of mice eradicating the tumor is shown within the graphs.

Source data are available online for this figure.

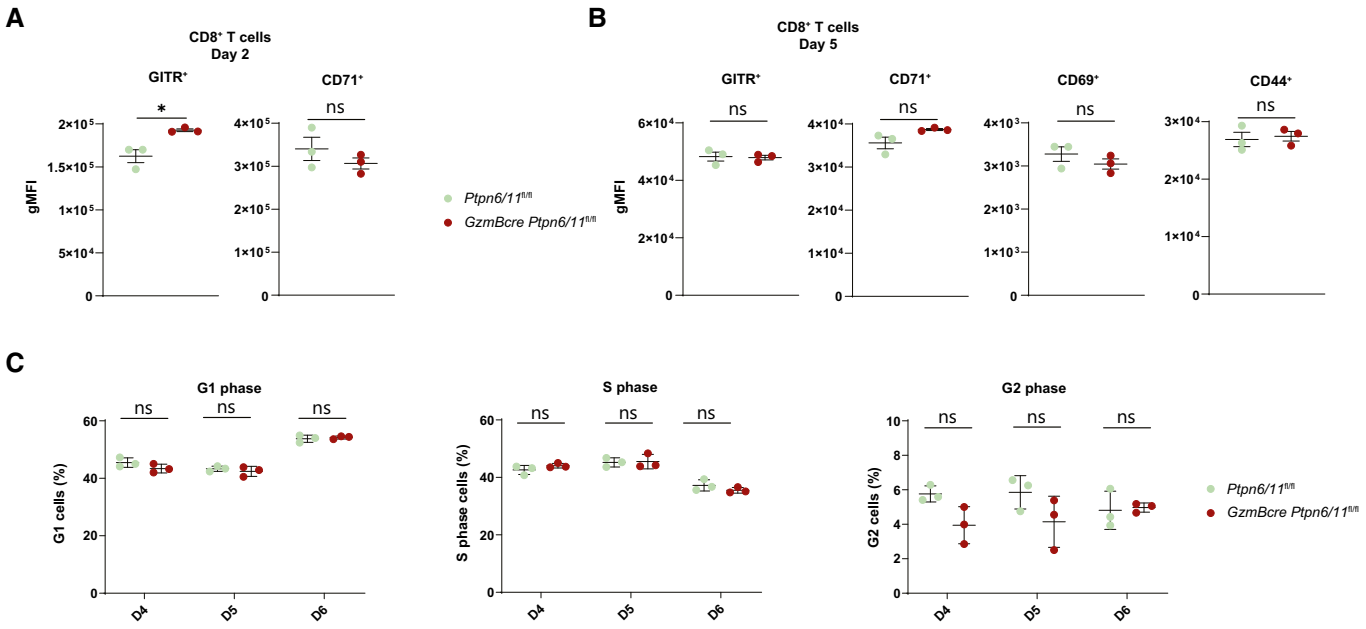

Figure EV3. Characterization of CTLs from *Ptpn6/11$^{fl/fl}$* and *GzmBcre Ptpn6/11$^{fl/fl}$* mice.

$CD8^+$ cytotoxic lymphocytes were generated from splenocytes of the indicated mice by anti-CD3, anti-CD28, and IL-12 stimulation and maintained in IL-2.

A, B $CD8^+$ T cells were analyzed by flow cytometry for surface expression of GITR and CD71 after 2 days (A) and for surface expression of GITR, CD71, CD69, and CD44 after 5 days (B); a quantification of these parameters is shown in the graphs (A and B).

C Graphs depict the percentages of cells in G1, S, and G2 phase as measured by flow cytometry-based cell cycle analysis of *Ptpn6/11$^{fl/fl}$* and *GzmBcre Ptpn6/11$^{fl/fl}$* CTLs (gated on $CD8^+$ T cells) at the indicated days.

Data information: Results depict mean ± SD of $n = 3$ biological replicates and Student's *t*-test (unpaired, two-tailed) was used to compare differences between experimental groups (A–C). *$P \leq 0.05$.
Source data are available online for this figure.