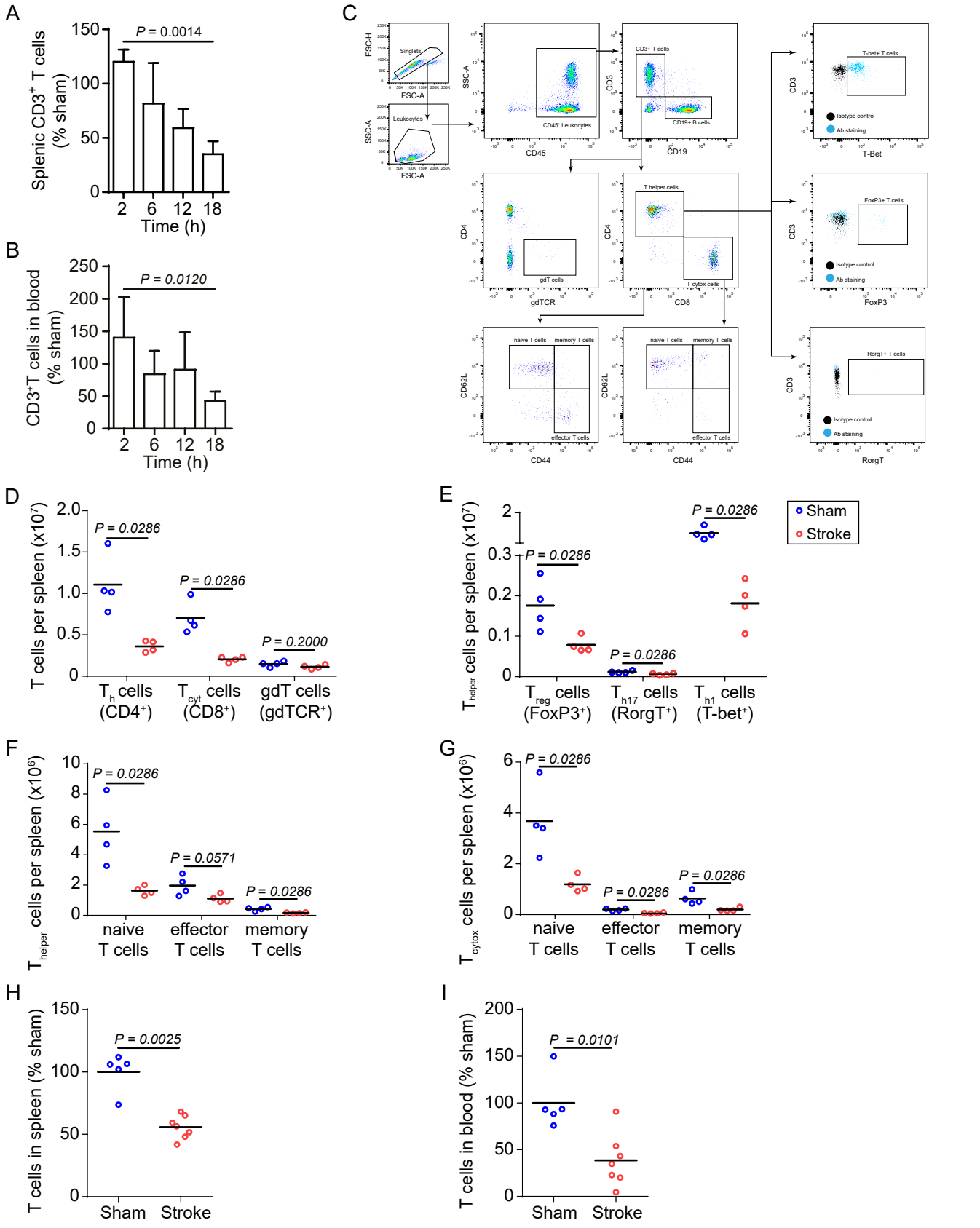
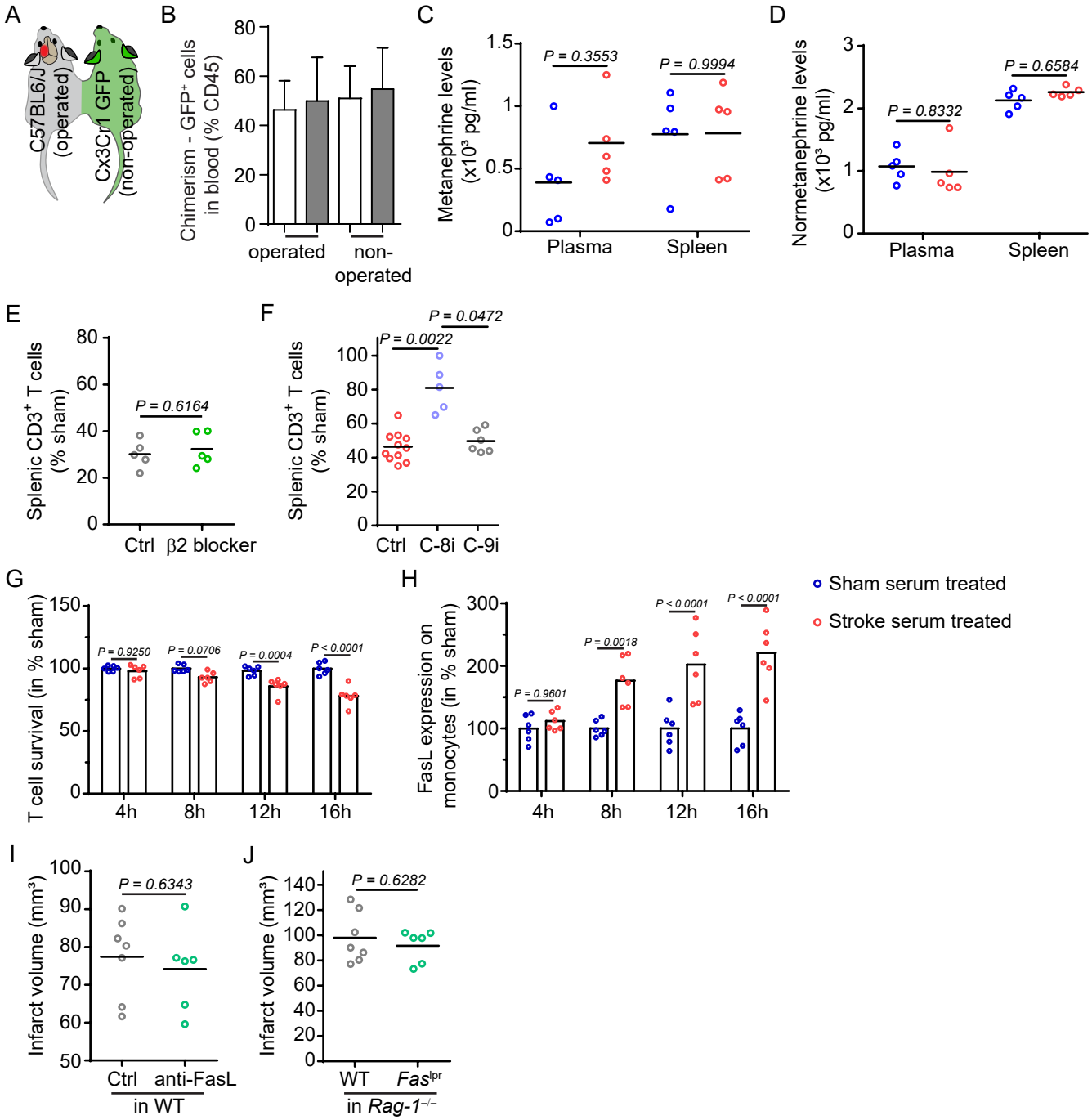
Supplementary Figure 1



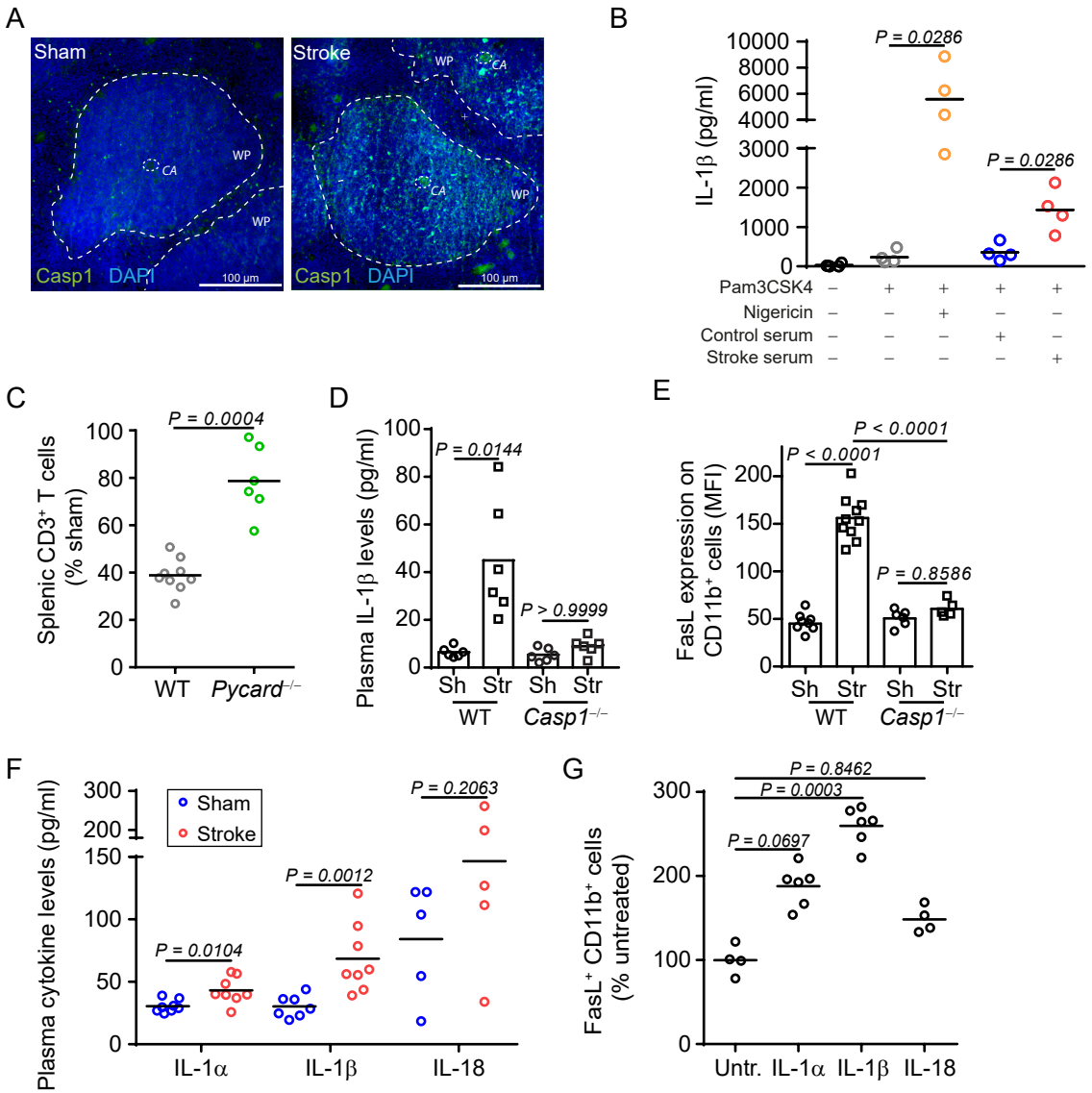
Supplementary Figure 1, related to Figure 1. Characterization of T cell subpopulations in spleen and blood after experimental stroke. (**A, B**) WT mice underwent sham or stroke surgery and were sacrificed 2, 6, 12 and 18h after operation. Blood and spleen were collected and analyzed by FACS for $CD3^+$ T cell counts in (A) spleens and (B) blood (n=6-9 per group; H-test). (**C**) Representative gating strategy for analysis of T cell subpopulations. (**D-G**) Flow cytometric analysis of splenic T cells, shown as $CD4^+$, $CD8^+$ $gdTCR^+$ (D), $CD3^+CD4^+$ $FoxP3^+$, $RorgT^+$ and $T\text{-}bet^+$ (E) and $CD4^+$ (F) or $CD8^+$ (G) naive, effector and memory T cells. (n= 4 per group; U-test for individual subset comparison). (**H, I**) GF mice underwent sham or stroke surgery and were sacrificed 18h after operation. CD3+ T cells from spleen (H) and blood (I) were quantified by FACS (n=5-7 per group; U-test).

Supplementary Figure 2



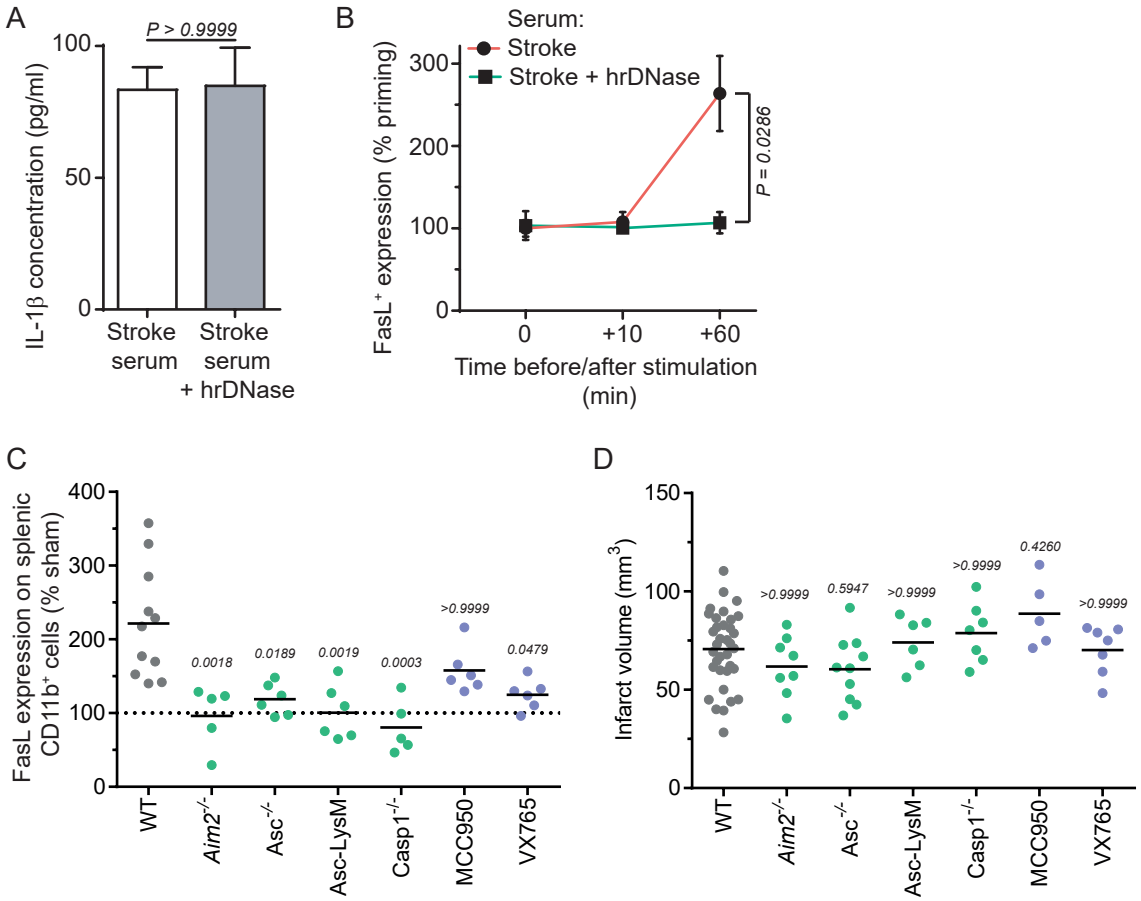
Supplementary Figure 2, related to Figure 1. Soluble mediators activate myeloid cells inducing FasL-Fas dependent T cell death after tissue injury. (**A**) Schematic of the parabionts showing the operated (C57Bl6/J) and non-operated (Cx3Cr1-GFP) mice sharing a common circulation. (**B**) FACS analysis for the percentage of GFP+ cells within the CD45+ population confirms full chimerim by shared circulation in all groups (n=10 per group; H-test). Quantification of (**C**) Metanephrine and (**D**) Normetanephrine levels in plasma and spleen 4h after stroke or sham surgery (n=5 per group, H-test). (**E**) ICI-118551 (β2-blocker) or control-treated WT mice underwent stroke or sham surgery and were euthanized 18h after surgery. Splenic T cells were analyzed by FACS (n=5 per group; U-test). (**F**) The role of intrinsic versus extrinsic apoptosis pathways for T cell death was tested by i.p. administration of either caspase-8 (C-8i) or caspase-9 (C-9i) inhibitor or vehicle control (Ctrl) after sham or stroke surgery (n=5-11 per group; H-test). (**G, H**) Whole splenocytes were cultured and treated with sham or stroke serum. For every time point after start of in vitro serum stimulation (4-16h) T cells (G) and FasL expression on CD11b+ splenocytes (H) were analyz-ed by FACS (n=6 per group; H-test). (**I**) Infarct volume from mice which were treated with anti-FasL prior to stroke surgery (corresponding to Fig. 1F, n= 7 per group; U-test). (**J**) Infarct volume from *Rag-1*$^{-/-}$ mice after WT or *Fas*^{lpr} T cells were transferred (corresponding to Fig. 1H).

Supplementary Figure 3



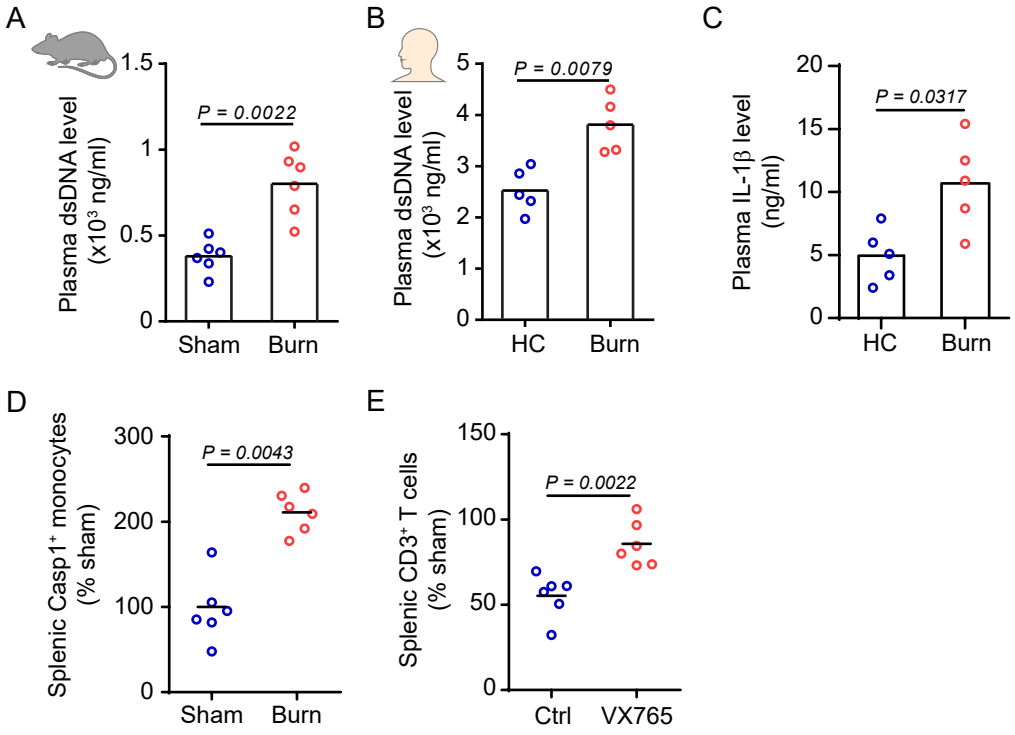
Supplementary Figure 3, related to Figure 3. Myeloid FasL expression after injury is IL-1β dependent. (**A**) Representa- tive histology images of the white pulp from murine spleen 6h after sham or stroke surgery. Active caspase-1⁺ (FAM FLICA) regions are labelled green (CA = central artery; WP = white pulp). (**B**) Monocytes from human blood were isolated and stimulated with either healthy control or stroke patients' serum (Pam3CSK4 for priming, Nigericin as positive control). Monocyte culture supernatant levels of IL-1β were measured by ELISA (n=4 different monocyte donors; H-test). (**C**) ASC-deficient (*Pycard*$^{-/-}$) and WT mice underwent a stroke or sham surgery and were euthanized 18h after surgical procedure. Splenic T cells were analyzed by FACS (n=5 per group; U-test). (**D**) Plasma of WT and *Casp1*$^{-/-}$ mice was collected 18h after sham or stroke surgery. IL-1β levels in the plasma were acquired by ELISA (n=6 per group; H-test). (**E**) Analysis of the mean fluorescent intensity (MFI) for FasL (geometric mean of APC fluorescence) on CD11b⁺ monocytes of WT and *Casp1*$^{-/-}$ mice 18h after sham or stroke surgery (n= 5-10 per group; H-test). (**F**) Plasma of mice was collected 4h after sham or stroke surgery. IL-1a, IL-1b and IL-18 levels were acquired by ELISA (n= 5-8 per group, U-test per individual cytokine). (**G**) BMDMs were treated with 100 ng of either cytokine for 4h. FasL+ expression was acquired and normalized to the untreated (Untr.) control (n= 4-6 per group; H-test).

Supplementary Figure 4



Supplementary Figure 4, related to Figure 4. Post-stroke inflammasome activation induces myeloid FasL upregulation but does not affect acute infarct volume. (**A**) BMDMs were stimulated with serum (± hrDNase) from stroke mice. IL-1β concentrations did not differ between the two stroke serum groups. (**B**) BMDMs were stimulated for 10 minutes with the post-stroke serum (± hrDNase) and FasL expression of the BMDMs was aquired before stimulation, 10 and 60 minutes after the stimulation by FACS (n=4 per group, U-test). (**C**) FasL expression on splenic $CD11b^+$ cells and (**D**) infarct volume of brains were analyzed 18h after stroke in WT mice, the indicated genetic inflammasome knockout models and the pharmacological inflammasome inhibition using MCC950 (NLRP3 inhibitor) and VX765 (Caspase-1 inhibitor). H-test; p-values (post-hoc test) in comparison to WT group.

Supplementary Figure 5



Supplementary Figure 5, related to Figure 4. Post-burn injury T cell death is also driven by caspase-1 activation in monocytes. (**A**) Plasma dsDNA levels of burn injury mice are increased compared to mice which underwent a control surgery (n=6 per group; U-test). (B, C) Plasma of burn injury patients show significantly increased dsDNA levels (**B**) and IL-1β (**C**) compared to age-matched healthy controls (HC) (n=5 per group; U-test). (D, E) Mice underwent an experimental burn injury or control surgery and were euthanized 18h after surgery. Splenic caspase-1 activity (**D**) and T cell numbers, from burn injury mice treated with control or VX765 treatment (**E**) were analyzed by FACS (n=6 per group;