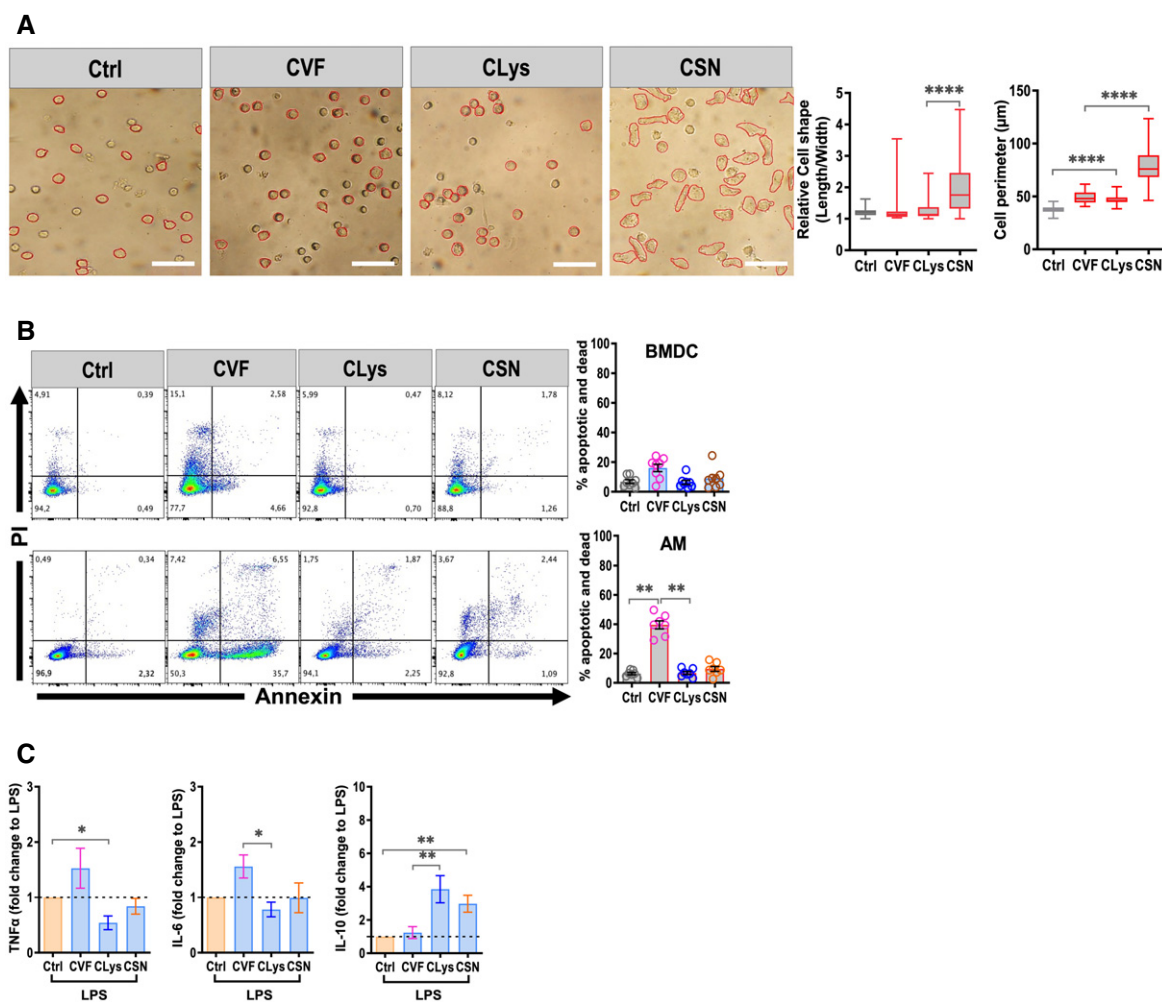


## Expanded View Figures



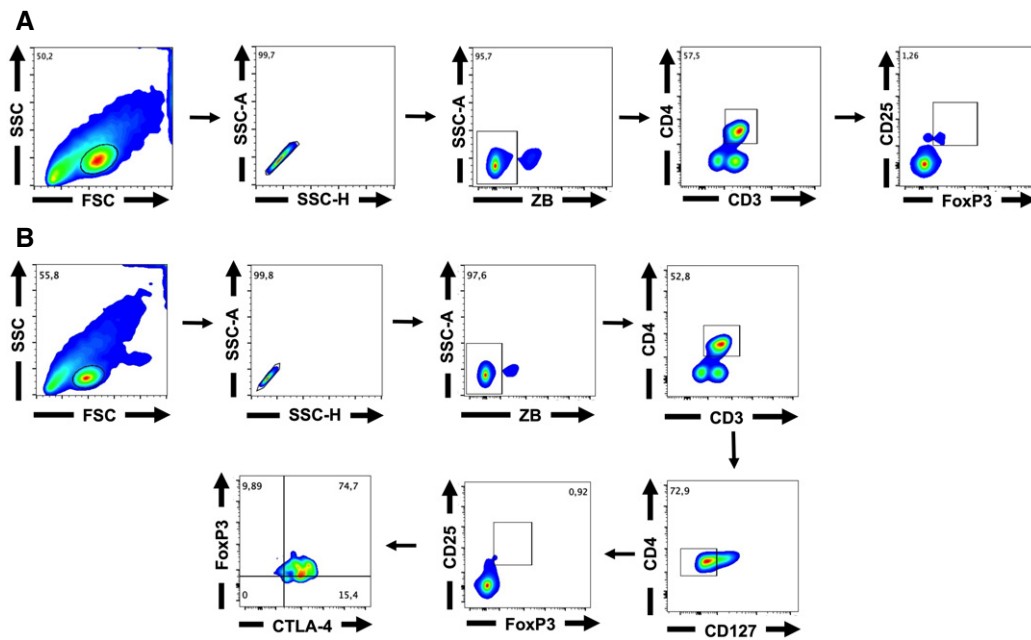
**Figure EV1.** In contrast to CLys and CSN, which impair LPS-induced  $\text{TNF}\alpha$ , CVF induces selective apoptosis in macrophages.

A Morphology, relative cell shape under light microscope, and measured perimeter of AM ( $n = 50$ ). Scale bar ( $50 \mu\text{m}$ ) applies to all images. Box and whisker plots represent the cell perimeter and relative shape (length/width) distribution. The middle line in the box shows the median cell dimensions (perimeter, shape) and the box indicates the range between the 25<sup>th</sup> and the 75<sup>th</sup> percentile. Whiskers above and below the box indicate the min and max cell dimensions respectively.

B FACS analysis for early (Annexin V<sup>+</sup>/PI<sup>-</sup>) and late (Annexin V<sup>+</sup>/PI<sup>+</sup>) apoptotic (necrotic) and dead (Annexin V<sup>+</sup>/PI<sup>+</sup>) BMDC (upper panel) and AM (lower panel) in presence of CVF, CLys, and CSN.

C Levels of  $\text{TNF}\alpha$ , IL-6, and IL-10 from BMDC preincubated with CVF, CLys, and CSN for 72 h before stimulation with LPS for 24 h.

Data information: Cytokine levels are expressed as fold change to LPS. Graphs are representative of 7–8 biological replicates ( $n = 7–8$ ). Results are expressed as means  $\pm$  SEM. Asterisks show significant statistical differences analyzed using Kruskal–Wallis one-way ANOVA followed by a Dunn's multiple comparison test. \* $P < 0.05$ ; \*\* $p < 0.01$ ; \*\*\*\* $p < 0.0001$ .

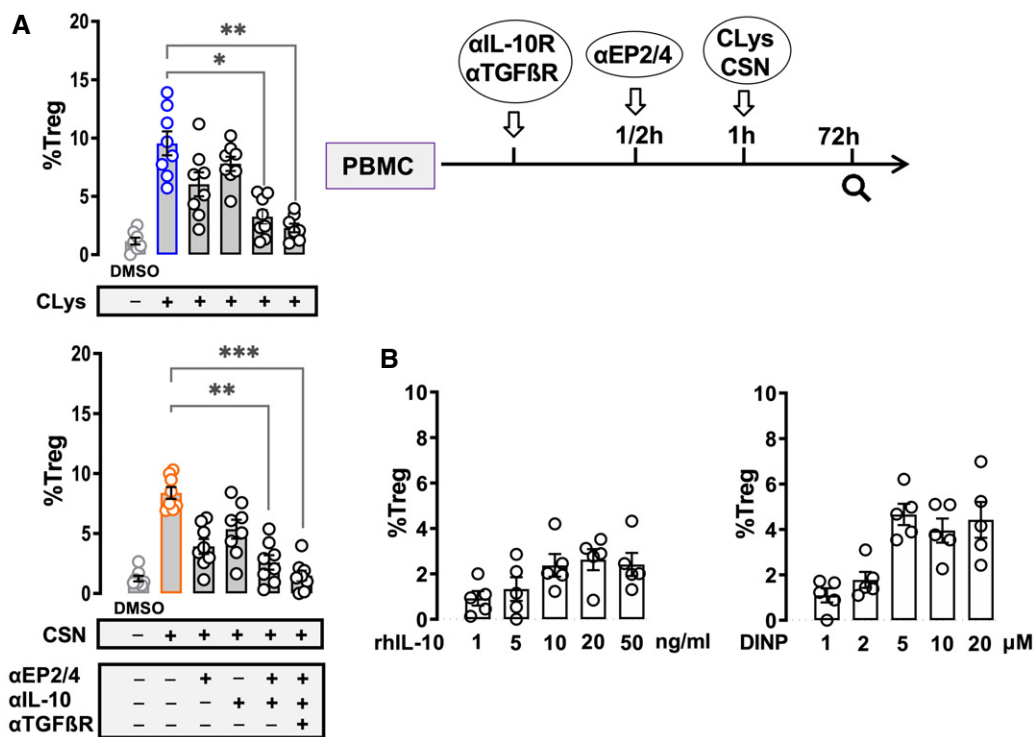


**Figure EV2. Phenotypic characterization of murine and human Tregs.**

A Murine Tregs were characterized from spleen as  $CD4^+CD25^+FoxP3^+$  cells.

B Tregs were characterized from human PBMCs as  $CD4^+CD127^-CD25^{hi}FoxP3^+CTLA4^+$  cells.

Data information: Plots show an example of characterization using a control sample.

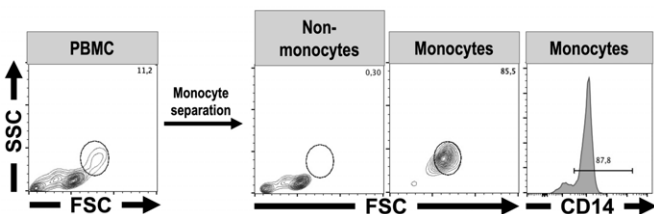


**Figure EV3. Titration of the effect of rhIL-10 and PGE<sub>2</sub> and receptor blockade on Treg induction.**

A Treg induction by CLys or CSN following PBMC preincubation with TGF-βR and/or IL-10R inhibitors, and PGE<sub>2</sub> receptor (EP<sub>2</sub> and EP<sub>4</sub>) antagonists (or DMSO as a control).

B Treg induction from PBMCs with increasing concentrations of rhIL-10 and PGE<sub>2</sub> analog dinoprostone (DINP).

Data information: Graphs are representative of 8 biological replicates ( $n = 8$ ) for (A) and 5 biological replicates ( $n = 5$ ) for (B). Results are expressed as means  $\pm$  SEM. Asterisks show significant statistical differences analyzed using Kruskal–Wallis one-way ANOVA followed by a Dunn’s multiple comparison test. \* $P < 0.05$ ; \*\* $P < 0.01$ ; \*\*\* $P < 0.001$ .



**Figure EV4. Monocyte purification.**

Monocytes were purified from peripheral blood of healthy donors ( $n = 5-7$ ) using a RosetteSep Human Monocyte Enrichment Cocktail kit, and the purity was assessed by FACS staining with FSC/SSC gate and CD14 staining. A representative plot and gating is shown.