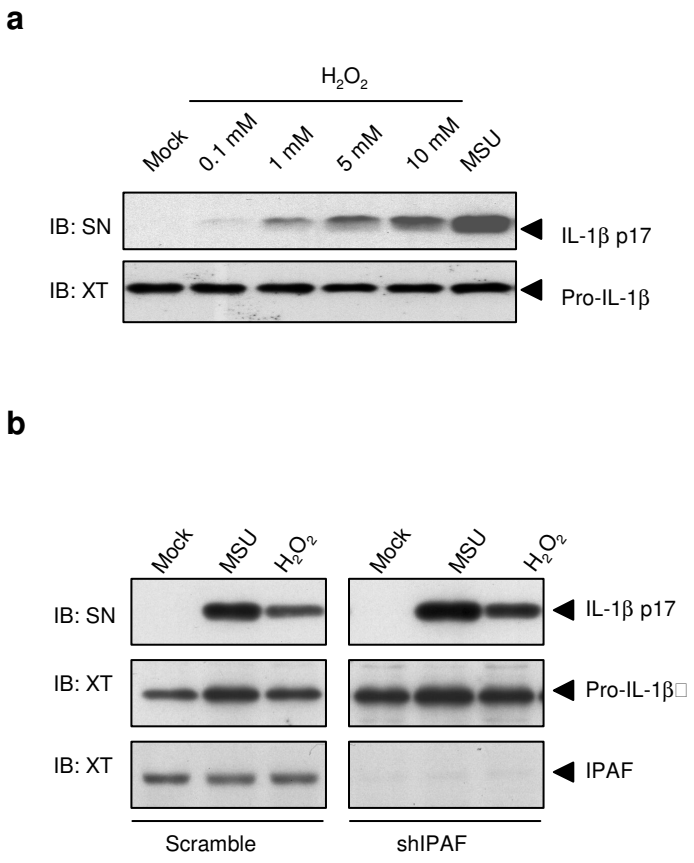
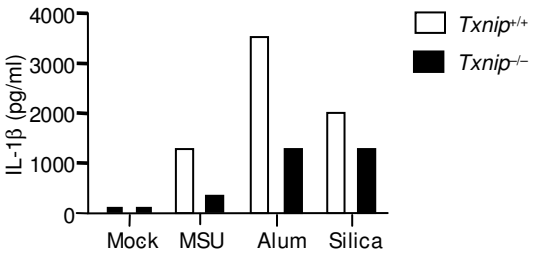


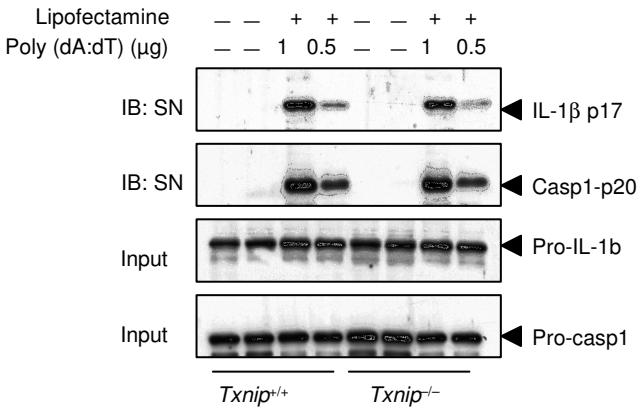
Supplementary Figure 1. H_2O_2 activates the NLRP3 inflammasome.

(a) THP-1 cells were treated with various doses of H_2O_2 for 6 h and supernatants and cell extracts analyzed by immunoblotting (IB) as indicated. MSU was used as a positive control. **(b**) THP-1 cells stably expressing shRNA against IPAF were stimulated for 6 h with MSU or H_2O_2. Media Supernatants (SN) and cell extracts (XT) were immunoblotted as indicated. All results are representative of at least three independent experiments.

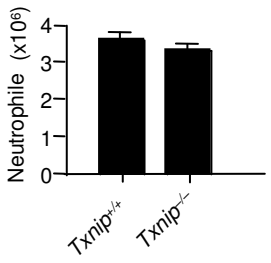
a



b



Supplementary Figure 2 TXNIP is crucial for NLRP3 inflammasome activation
(a) IL-1β release, triggered by MSU, Alum or silica was determined in BMDM from *Txnip*$^{-/-}$ mice by ELISA. **(b)** LPS-primed BMDMs were transfected with poly (dA:dT) at the indicated concentrations using lipofectamine. Supernatants (SN) and cell extracts (input) were immunoblotted (IB) as indicated.



Supplementary Figure 3. TXNIP is not essential for zymosan-mediated peritonitis. Wild type and *Txnip*$^{-/-}$ mice were injected intraperitoneally with 0.2 mg zymosan. Neutrophil influx was quantified 6 h later (values are mean ± SEM of 3-5 mice per group).

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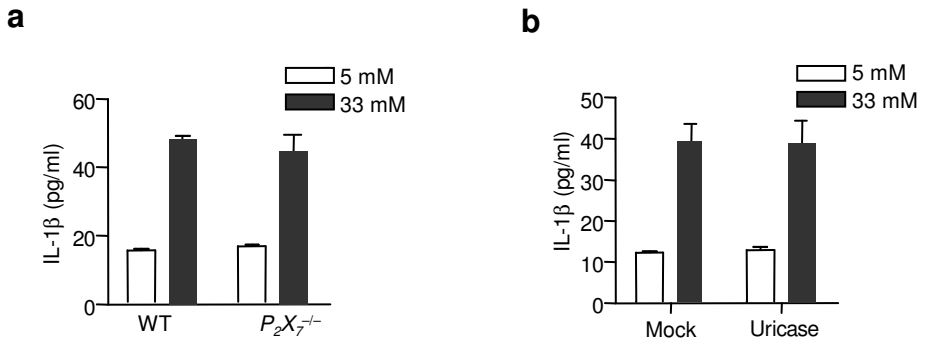
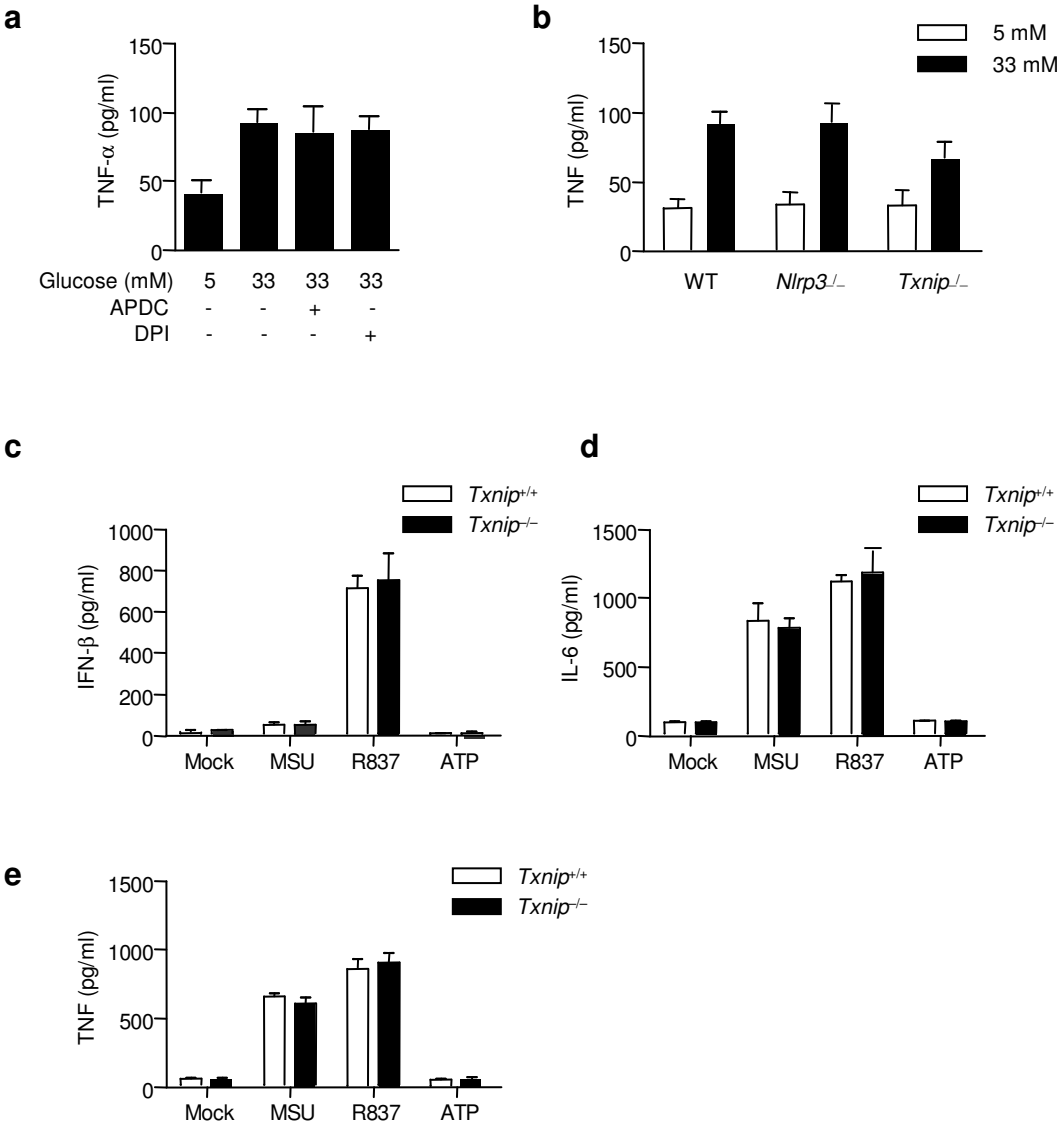
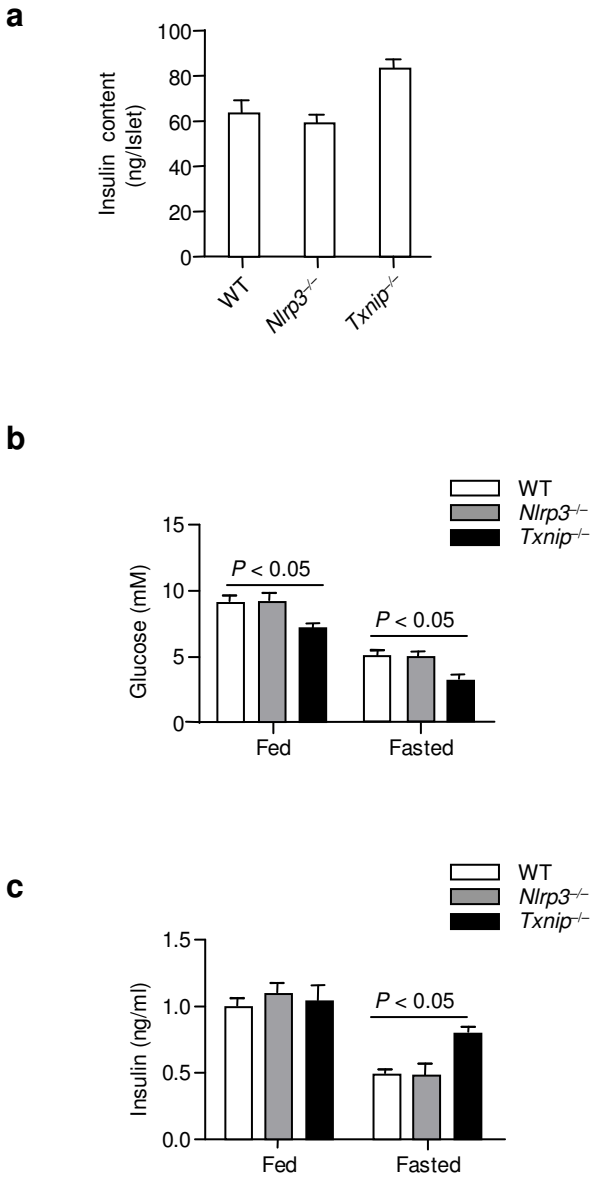


Supplementary Figure 4. ATP and uric acid crystals (MSU) are not intermediates of glucose-mediated NLRP3 inflammasome activation.
(a) Islets from wild type or $P_2X_7^{-/-}$ mice were stimulated with glucose as indicated for 24 h. **(b)** Islets were stimulated with glucose as indicated in the presence or absence of uricase (0.1 U/ml). The concentration of IL-1β was determined by ELISA . All values are mean ± SEM and all results are representative of at least three independent experiments



Supplementary Figure 5 The absence of TXNIP does not affect secretion of inflammatory cytokines other than IL-1β.
(a) Islets were stimulated with glucose in the presence of APDC (100 nM) or DPI (25 μM) (**b)** Islets from *Nlrp3*$^{-/-}$ or *Txnip*$^{-/-}$ mice were treated with glucose (5mM or 33mM) for 24 h. TNF-α secretion was then determined by ELISA. . **(c-e)** LPS-primed, murine BMDMs from *Txnip*$^{-/-}$ mice were stimulated with MSU, ATP or R837 and IFN-β, IL-6 and TNF concentrations were measured in the supernatant by ELISA. All values are mean ± SEM and all results are representative of at least three independent experiments.



Supplementary Figure 6 Insulin and glucose levels are not affected in *Nlrp3*$^{-/-}$ mice.

(a) Isolated islets from chow fed wild type, *Nlrp3*$^{-/-}$ and *Txnip*$^{-/-}$ mice were tested for insulin content by ELISA. All values are mean ± SEM. **(b,c)** Chow fed wild type, *Nlrp3*$^{-/-}$ and *Txnip*$^{-/-}$ mice were fed or fasted overnight and then serum glucose and insulin levels were examined (values are mean ± SEM of 3-5 mice per group).