Supporting Information

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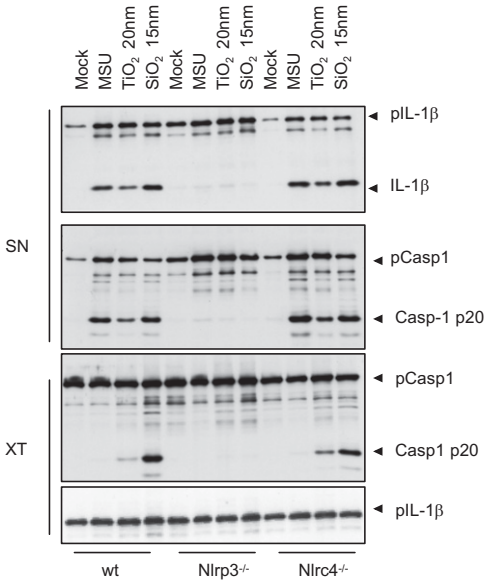

Fig. S1. Nano-TiO_2 and nano-SiO_2 activate the Nlrp3 inflammasome, but not the Nlrc4 inflammasome. Caspase-1 cleavage and IL-1β secretion was impaired in Nlrp3-deficient, but not in Nlrc4-deficient murine bone marrow-derived macrophages upon treatment with nano-TiO_2 (200 μg/mL) or nano-SiO_2 (200 μg/mL).

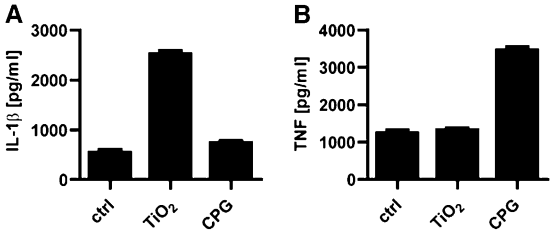

Fig. S2. Nano-TiO_2 activates IL-1β secretion in murine dendritic cells (DCs). (*A*) TiO_2 (200 μg/mL) exposure evoked robust secretion of IL-1β after LPS-priming (10 ng/mL) and (*B*) low levels of TNF in unprimed cells compared with the TLR9 ligand CpG (2.5 μg/mL).

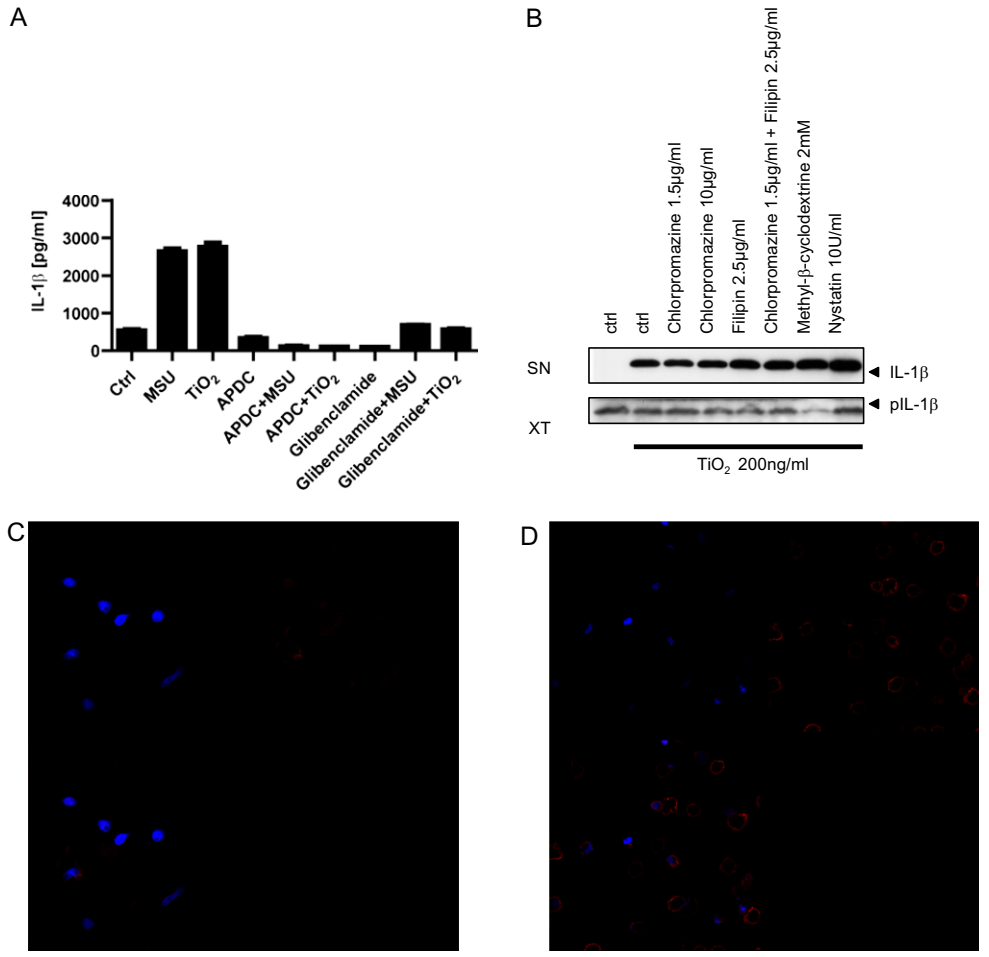

Fig. S3. ROS scavengers and glibenclamide, but not endocytosis-inhibitors block nano-TiO_2–induced IL-1β secretion. (*A*) Pretreatment with the ROS scavenger APDC (100 μM) and the ATP-sensitive potassium inhibitor glibenclamide (50 μM) impairs nano-TiO_2 (200 μg/mL)-induced IL-1β release from bone marrow-derived DCs, whereas (*B*) lipid-raft extraction by methyl-β-cyclodextrin (MBCD; 2× 10 mM wash, 2 mM during treatment), blocking clathrin-mediated endocytosis by chlorpromazine-hydrochloride (1.5 μg/mL or 10 μg/mL) and blocking caveolin-dependent endocytosis by either filipin (2.5 μg/mL or 2.5 μg/mL in combination with chlorpromazine-hydrochloride, 1.5 μg/mL) or nystatin (10 U/mL) did not alter TiO_2-induced IL-1β secretion in THP1 cells. The effective lipid-raft depletion was demonstrated by the lack of membranous cholera toxin B staining (*C*) after treatment with MBCD, (*D*) compared with the untreated control.

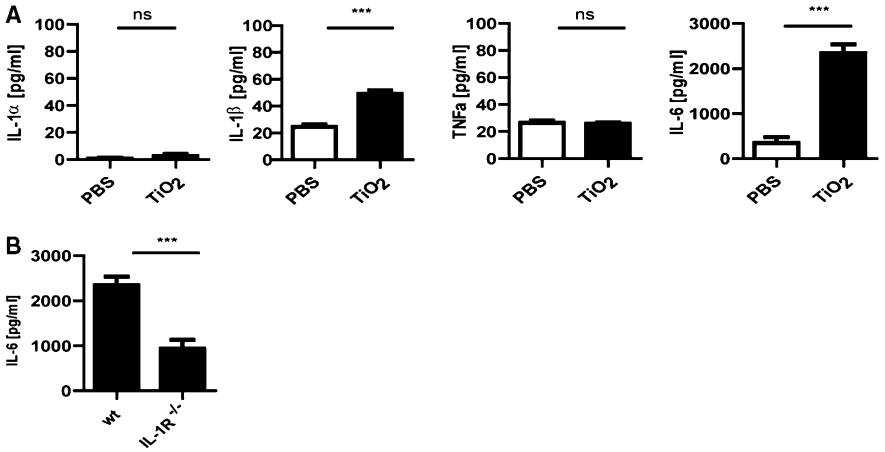

Fig. S4. TiO_2 i.p. injection induces IL-1β and IL-1 receptor-dependent IL-6 secretion. (*A*) I.p. injection of 1.5 mg TiO_2 into the peritoneal cavity led to significant IL-1β and IL-6 secretion, whereas IL-1α and TNF remained unchanged. (*B*) IL-6 release into the peritoneal cavity was drastically dimished in IL-$1R^{-/-}$ mice compared with wild-type controls, indicating the dependence of IL-6 secretion on IL-1 signaling (*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$; NS, nonsignificant, $n = 6–7$ mice per group).