

1 **Figure 5.** Titanium triggers inflammasome activation. Titanium particle internalization triggers  
2 the release of Cathepsin B from lysosomes, which together activate Nalp3. Activated Nalp3  
3 recruits ASC through PYD domain interactions. This complex triggers cleavage and recruitment  
4 of activated Caspase-1 through CARD domain interactions. This inflammasome complex then  
5 cleaves pro-IL-1 $\beta$  into its active, secreted form IL-1 $\beta$ , which can trigger downstream IL-1  
6 associated signaling, including neutrophil recruitment, through activation of the IL-1R. This  
7 acute inflammatory response can be inhibited with IL-1Ra treatment.

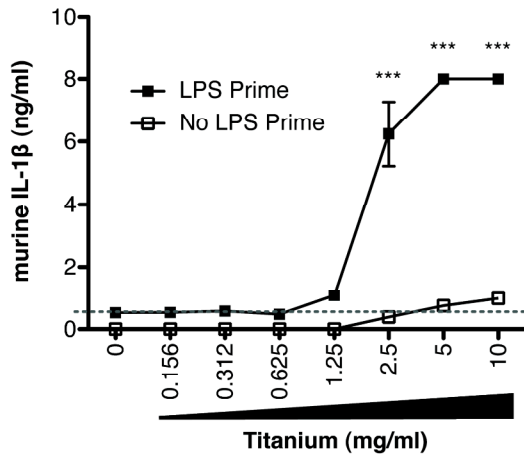
8 **Figure S1.** Cytokine responses to titanium-particle stimulation. **(a)** IL-1 $\beta$  secretion in WT  
9 immortalized mouse macrophages incubated with titanium particles only or titanium particles  
10 following an LPS prime for 6 h. Dashed line represents LPS prime only values. **(b)** IL-6  
11 secretion following incubation with titanium particles only or LPS only for 6 h. Secreted  
12 cytokine levels are mean  $\pm$  s.e.m. P-values are shown as \*\*\*  $\leq$  0.0001; \*  $<$  0.05

13

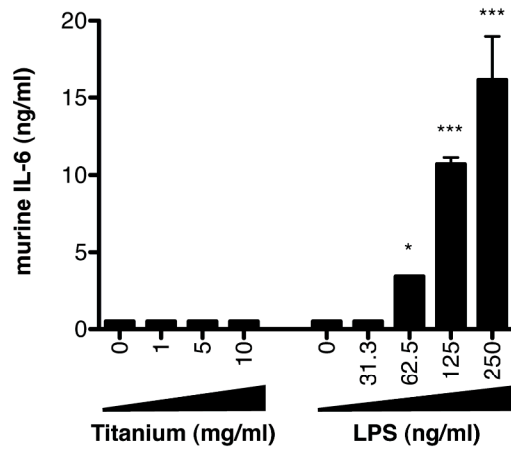
1 Supplemental Figure 1

2

a



b



3

4