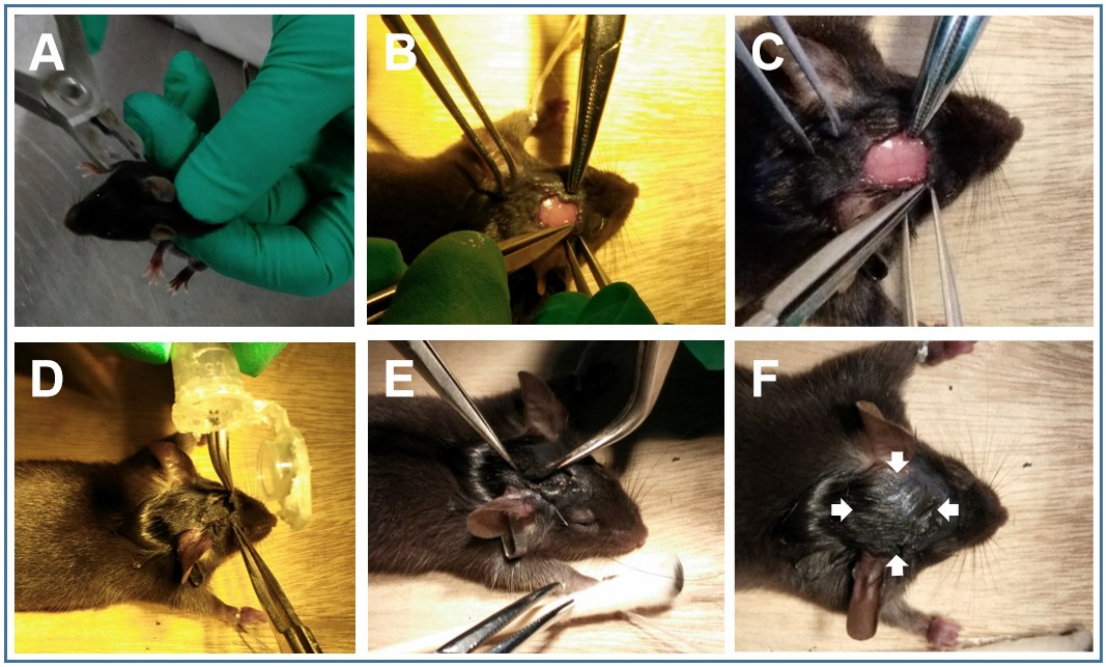
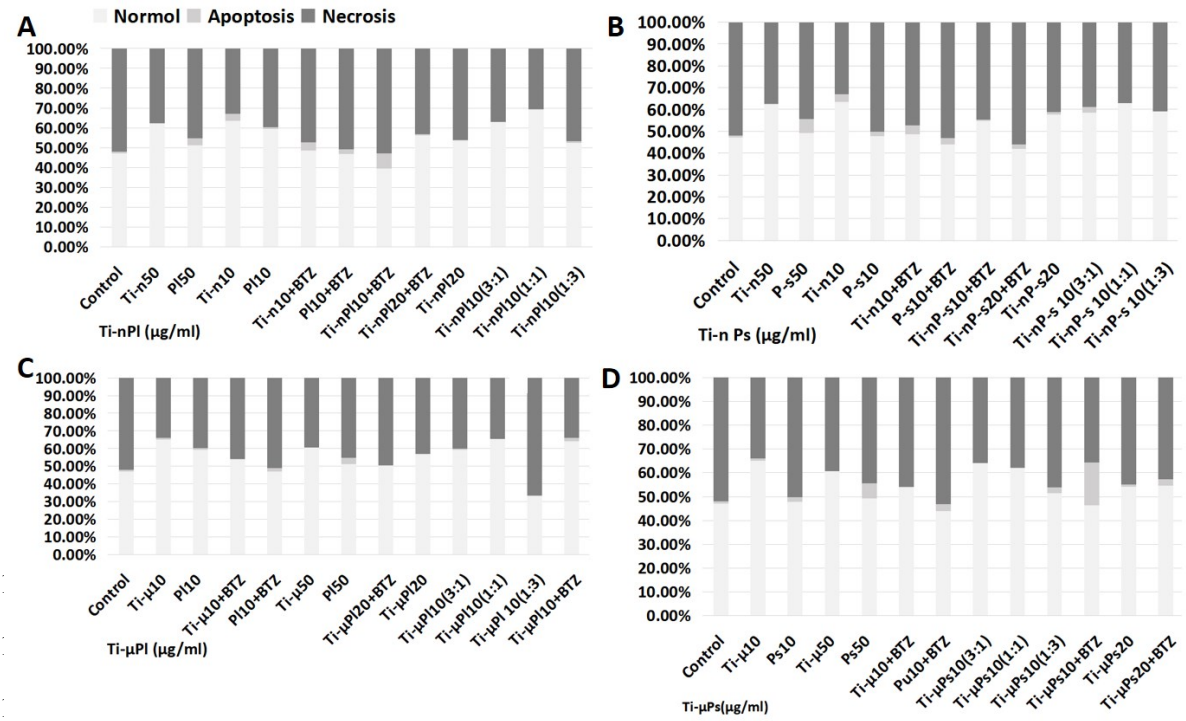


Supplementary figure 1. Schematic diagram of animal models. A. Preparing: Mouse anaesthesia, ear tag, skin preparing; B.Incision: A 1cm length incision along the mid-line by sharp dissection was maken and the periosteum over the calvarium was exposed; C: With blunt separating cranial periosteum, the surface of cranial bones was exposed, using periosteal elevator and hemostatic forceps and a 1cm × 1cm area around the mid-line crossing the front and bregma bone in the cranium of mouse was obtained in every mouse; D: Particle embedding; E: Closing the incision; F Botezomib (BTZ) administration: mice were locally subcutaneously injected with PBS or/and 0.1nM) of BTZ at each middle point of the edges of the surgical square area to make sure the drug cover the whole surgical area (arrow) three injections/week for two week.



Supplementary figure 2. Biological screens. The biological screens of the proportion of normal, early apoptosis, late apoptosis and death of RAW264.7 cells co-cultured with or without Ti, UHMWPE particles and 0.5umol/ml BTZ for 72 hours in flow cytometry assay. Different sizes of Ti and UHMWPE (A: Ti-n+P-l; B: Ti-n+P-s; C: Ti-μ+P-l; D: Ti-μ+P-s) were mixed and co-cultured with cells. (Ti-μ: 5μm; Ti-n: 21nm; P-s: 40-48μm; P-l: 155μm).

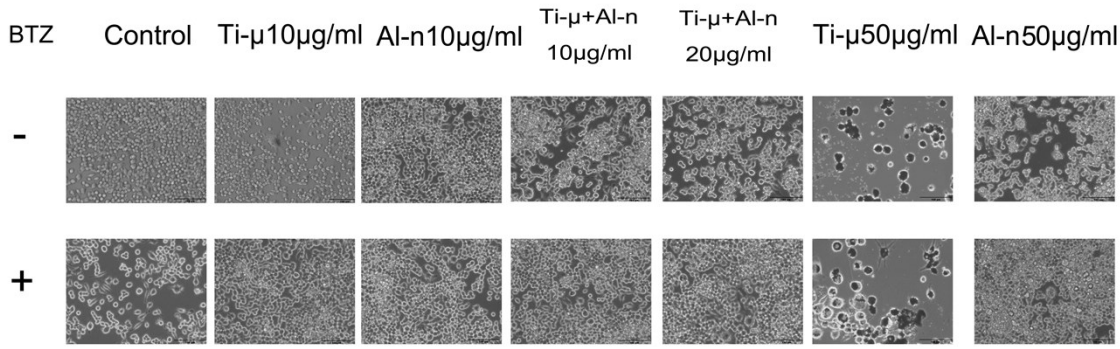
A: Ti-n+P-l groups: control, 50 μg/ml of Ti-n particles, 50 μg/ml of P-l particles,10 μg/ml of Ti-n particles; 10 μg/ml of P-l particles, 10 μg/ml of Ti-n mixed with P-l, (Ti:P-l=1:1), 10 μg/ml of Ti-n mixed with P-l(Ti:P-l=1:3), 10 μg/ml of Ti-n mixed with P-l (Ti:P-l=3:1) and 20 μg/ml of Ti-n mixed with P-l (Ti:P-l=1:1) with or without BTZ (0.5nmol/ml).

B: Ti-n+P-s groups: control, 50 μg/ml of Ti-n particles, 50 μg/ml of P-s particles, 10 μg/ml of Ti-n particles, 10 μg/ml of P-s particles, 10 μg/ml of Ti-n mixed with P-s (Ti:P-s=1:1), 10 μg/ml of Ti-n mixed with P-s (Ti:P-s=1:3), 10 μg/ml of Ti-n mixed with P-s (Ti:P-s=3:1) and 20 μg/ml of Ti-n mixed with P-s (Ti:P-s=1:1) with or without BTZ (0.5nmol/ml).

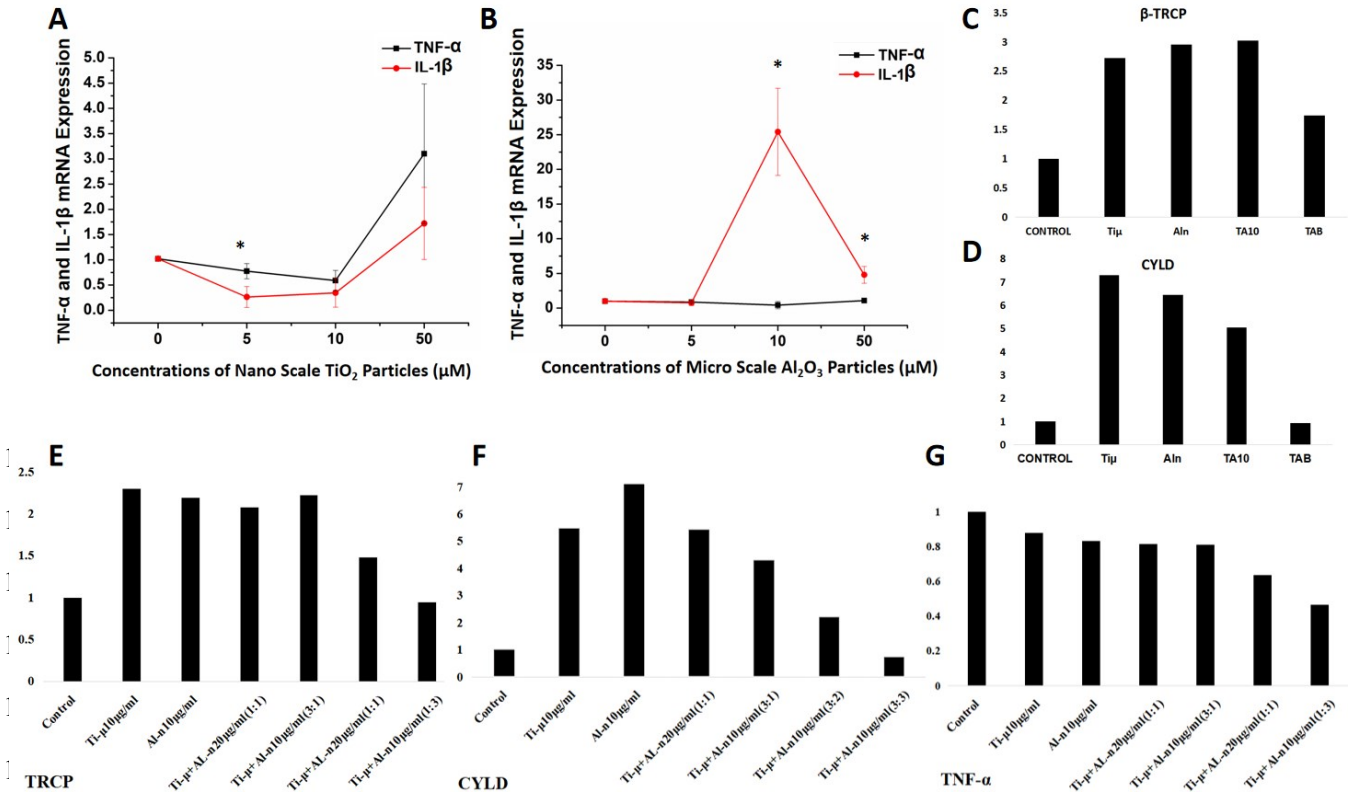
C: Ti-μ+P-l groups: control, 50 μg/ml of Ti-μ particles, 50 μg/ml of P-l particles,10 μg/ml of Ti-μ particles, 10 μg/ml of P-l particles, 10 μg/ml of Ti-μ mixed with P-l,

(Ti:P-l=1:1), 10 μg/ml of Ti-μ mixed with P-l (Ti:P-l=1:3), 10 μg/ml of Ti-μ mixed with P-l (Ti:P-l=3:1) and 20 μg/ml of Ti-μ mixed with P-l (Ti:P-l=1:1) with or without BTZ (0.5nmol/ml).

D: Ti-μ+P-s groups: control, 50 μg/ml of Ti-μ particles, 50 μg/ml of P-s particles, 10 μg/ml of Ti-μ particles, 10 μg/ml of P-s particles, 10 μg/ml of Ti-μ mixed with P-s, (Ti:P-s=1:1), 10 μg/ml of Ti-μ mixed with P-s (Ti:P-s=1:3), 10 μg/ml of Ti-μ mixed with P-s (Ti:P-s=3:1) and 20 μg/ml of Ti-μ mixed with P-s (Ti-μ:P-s=1:1) with or without BTZ (0.5nmol/ml).



Supplementary figure 3. Effects of BTZ and Ti Particles on Raw 264.7. RAW264.7 cells co-cultured with or without Ti-μ, Al-n particles and 0.5umol/ml BTZ for 3 days. (Bar = 0.1 mm. Group: control, Ti-μ (10μg/ml), Al-n (10μg/ml), 10 μg/ml of Ti-μ mixed with Al-n (Ti-μ:Al-n=1:1), 20 μg/ml of Ti-μ mixed with Al-n (Ti-μ:Al-n=1:1), Ti-μ 50μg/ml with or without 0.5 nmol/ml BTZ, and Al-n 50μg/ml with or without 0.5 nmol/ml BTZ.



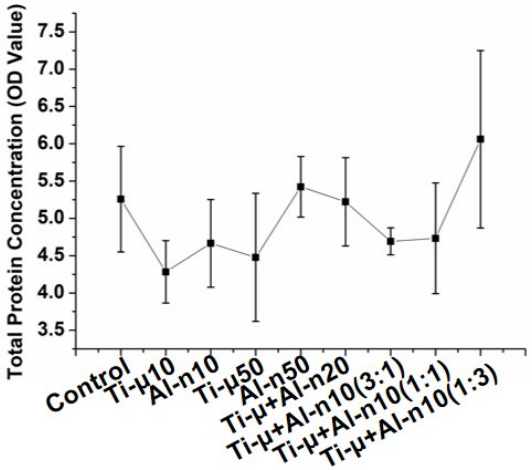
Supplementary figure 4. mRNA screen of TNF-α and IL-1β expression

A: A mRNA screen of TNF-α and IL-1β expression of macrophage under the stimulation of different concentrations of nano scale TiO_2 particles.

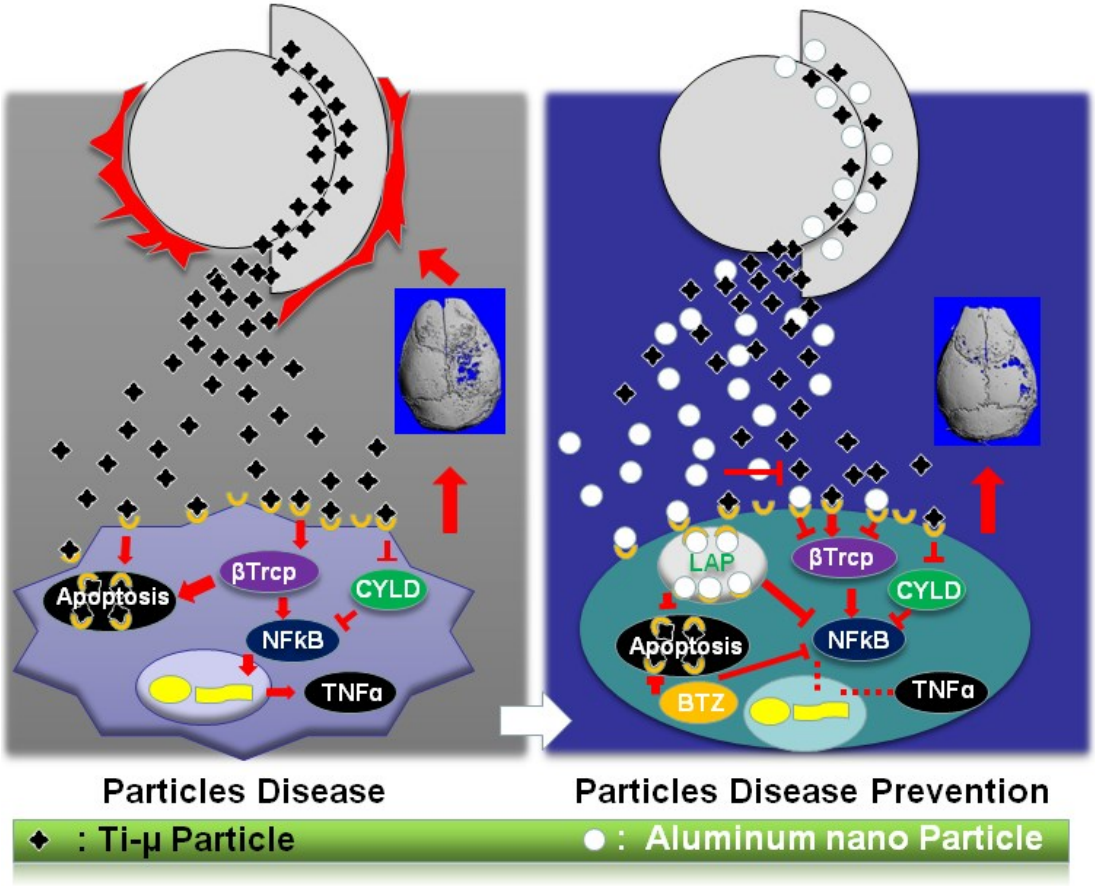
B: A mRNA screen of TNF-α and IL-1β expression of macrophage under the stimulation of different concentrations of micro scale of Al_2O_3 particles.

C-D: Quantification of the Figure 5 C.

E-G: Quantification of the Figure 5 F.



Supplementary figure 5. BCA assay: RAW 264.7 cells were co-cultured with pure or mixed particles as the following groups such as Control, Ti-μ 10, Al-n 10, Ti-μ 50, Al-n 50, Ti-μ+Al-n 20 (1:1), Ti-μ+ Al-n 10 (3:1), Ti-μ+ Al-n 10 (1:1), Ti-μ+ Al-n 10 (1:3) for three day. And the cells were then harvested with lysed in cold RIPA buffer with protease inhibitors (Beyotime, Shanghai, China) to extract proteins. Then, The whole cell protein concentration in the lysates were centrifuged 4℃. The lysates from each sample were detected with a BCA Protein Assay Kit (Biyotime Biotechnology, P0012).



Supplementary figure 6. The mimic mechanism of Al-n particles and BTZ could reduce the inflammatory and aseptic absorption caused by Ti-μ particles.