SUPPORTING INFORMATION

Aspect Ratio Plays a Role in the Hazard Potential of CeO_2 Nanoparticles in Mice Lung and Zebrafish Gastrointestinal Tract

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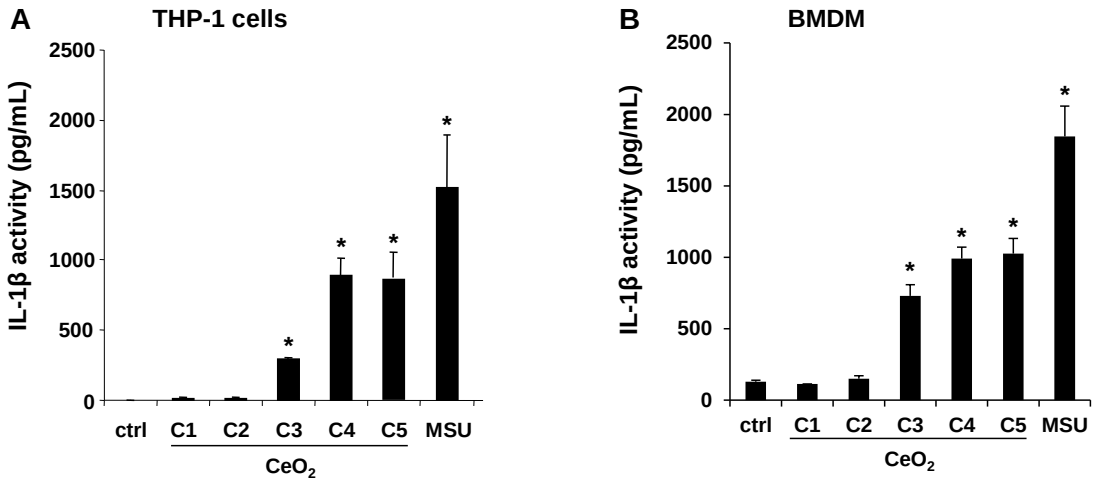


Figure S1. IL-1β production by THP-1 cells and bone marrow derived macrophages (BMDM) after exposure to CeO_2 nanoparticles. (A) THP-1 cells were differentiated by PMA treatment and then primed with 10 ng/mL LPS before addition of 100 μg/mL of each of the indicated CeO_2 nanoparticles for 24 hr. The supernatants were collected to measure the IL-1β production by ELISA (BD Biosciences, San Diego, CA), as described in Materials and Methods. (B) BMDMs derived from C57Bl/6 mice were primed with 500 ng/mL LPS for 5 hr before treatment with CeO_2 nanoparticles for 24 hr. The supernatants were collected for the measurement of IL-1β activity by ELISA. The * denote statistical significance at $p < 0.05$ compared to control. MSU: monosodium urinate.

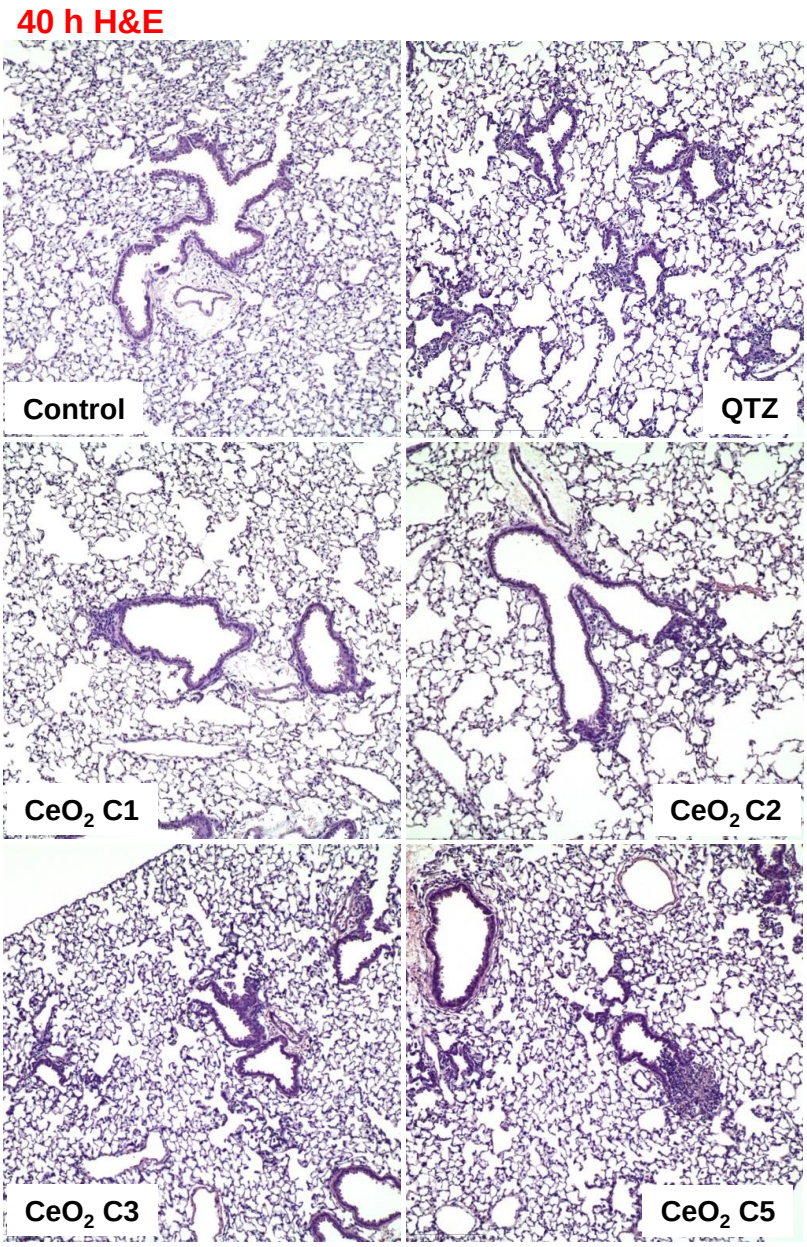


Figure S2. H&E stained lung section (100× magnification) from mice exposed to CeO_2 nanoparticles for 40 hr. Mice were exposed to C1, C2, C3 and C5 nanoparticles at 2.0 mg/kg. QTZ at 5.0 mg/kg was used as a control.

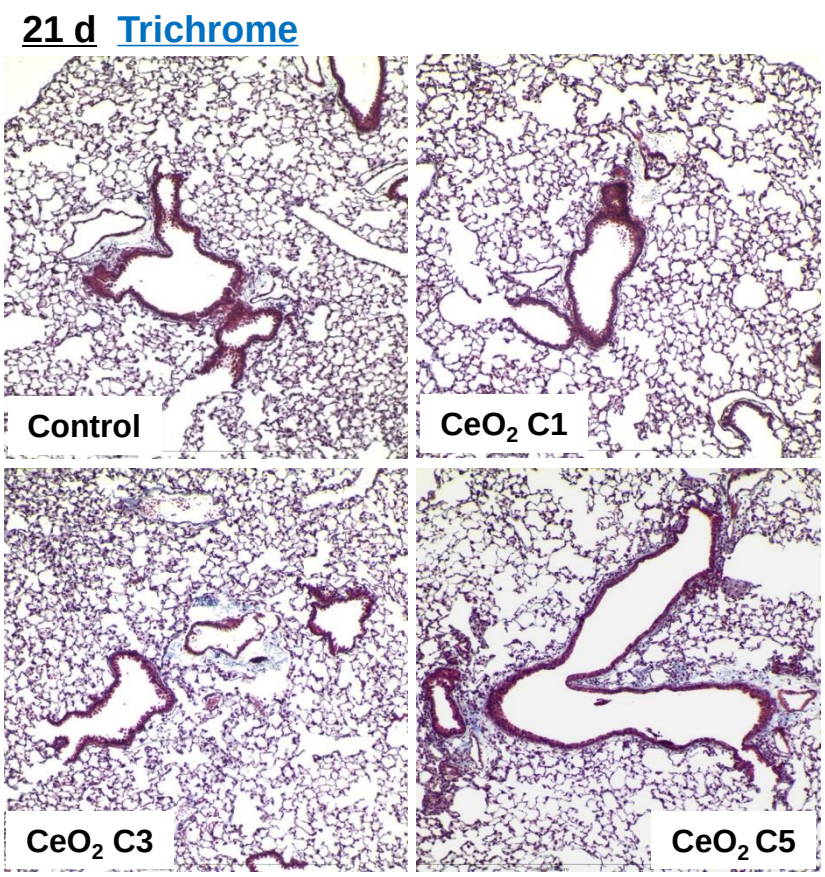


Figure S3. Masson's trichrome stained images (100 × magnification) of the animal lungs treated with CeO_2 nanoparticles for 21 days. Mice were exposed to 2 mg/Kg CeO_2 nanoparticles (C1, C3 and C5) by oropharyngeal aspiration. QTZ was used as a positive control. The concentrated blue color development represents collagen staining.

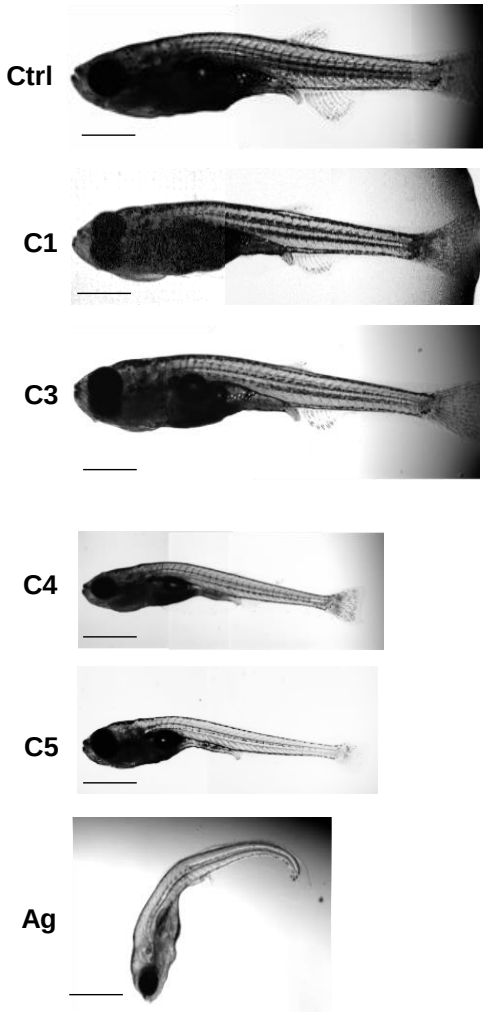


Figure S4. Representative microscopic images of 14 dpf larvae in the control group as well as larvae exposed to CeO_2 C1, C3, C4, C5, and AgNPs. Larvae were anesthetized using 0.02 % Tricaine solution and embedded in low-melt agarose gel for positioning. The images were captured in lateral view using an optical inverted microscope equipped with a 2.5 × objective (Zeiss Observer D1). Three images were captured and blended together to cover the total body length. Scale bars: 1 mm. The total body length of the control and C1/C3 exposed larvae were 9-10 mm long. These larvae also expressed recognizable dorsal and anal fins. In contrast, C4 and C5 exposed larvae showed reduced body lengths (~ 6-7 mm long) and failed to develop dorsal and anal fin structures. AgNPs induced significant developmental abnormalities such as a bent spine or pericardial edema, in addition to a reduced length.

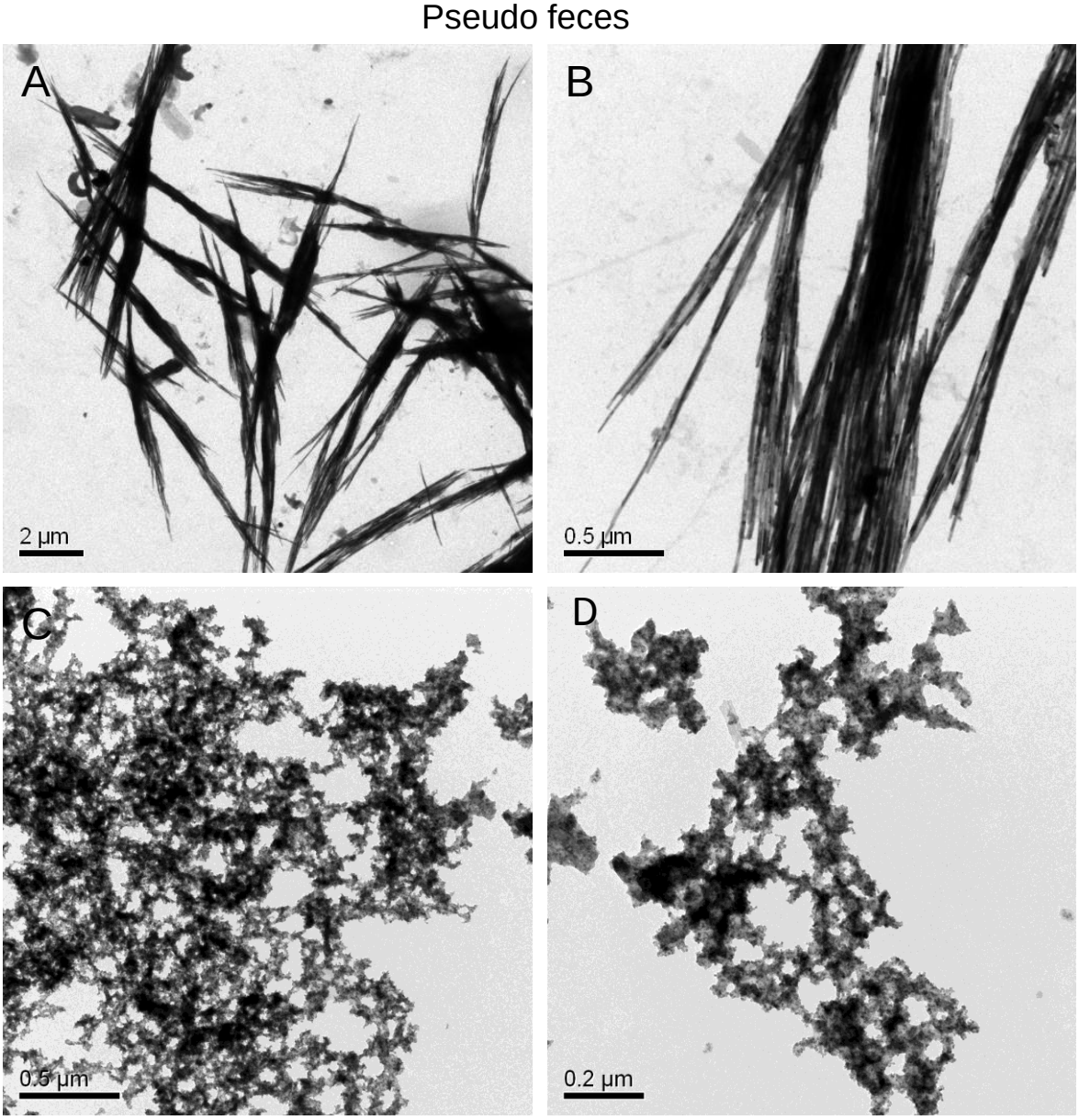


Figure S5. Representative TEM images on the pseudo-feces collected 24 hr after larval exposure to C1 and C5 nanoparticles (A) and (B) Representative images of C5 found in the larval pseudo-feces. (C) and (D) Representative images of C1 found in the larval pseudo-feces. The TEM images clearly show that CeO_2 retained their sizes, shapes, and aspect ratios after passage through the GIT.

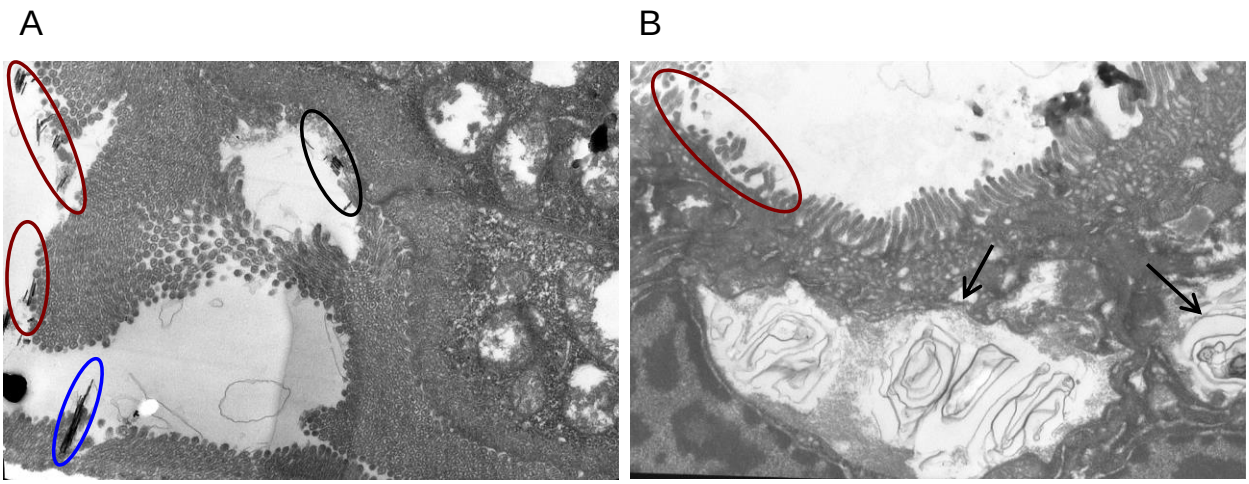


Figure S6. Representative TEM images of the interaction of C5 nanorods with microvilli in the GIT. (A) Besides adsorbing to the tips of the microvilli (red circles), bundles of C5 can be found disrupting (black circle) and piercing the microvilli (blue circle). (B) Blunted microvilli, loss of microvilli (red circle) and prominent vacuolization of the endothelial cells (black arrows) were frequently observed in the GIT of C5 exposed larvae.