Supporting information

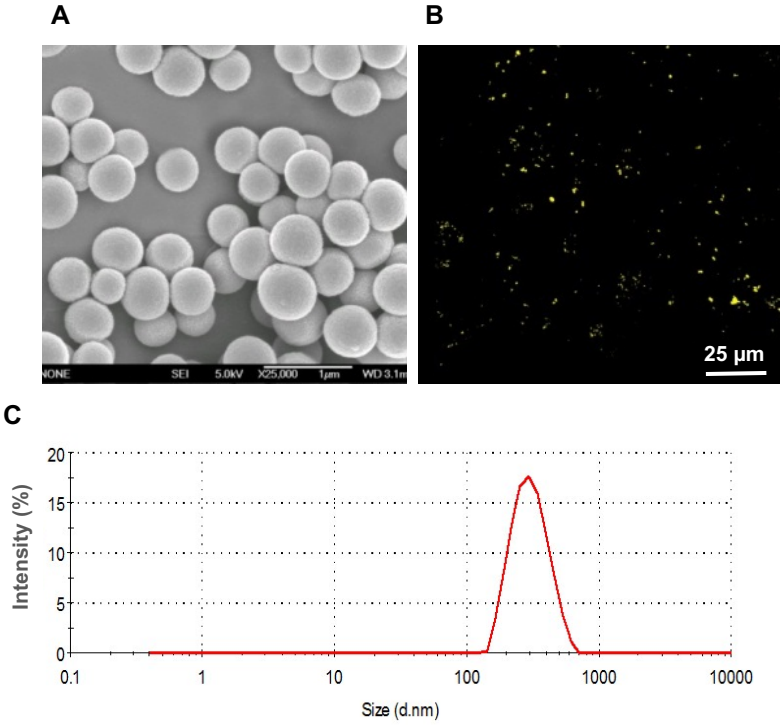

Figure S1. SEM image (A), confocal image (B) and the size distribution (C) of the nanoparticles (400 nm).

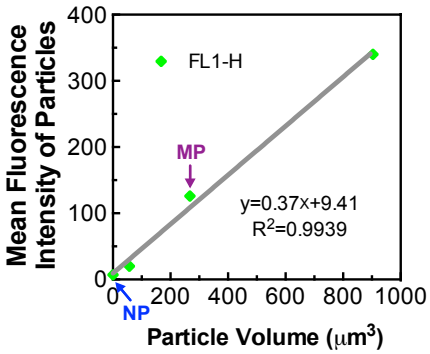

Figure S2. The linear relationship between the fluorescence intensity and the volume of chitosan particles. Particles at a size range from nano to micro were prepared and tested. Comparative data for NP (400 nm) and MP (8 µm) were highlighted by the arrows.

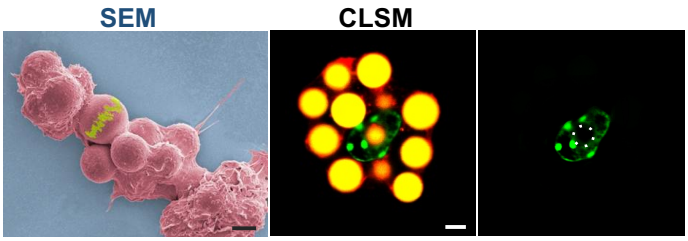

Figure S3. SEM and CLSM images of macrophage at high burden level of particles. Scale bars, 5 μm.

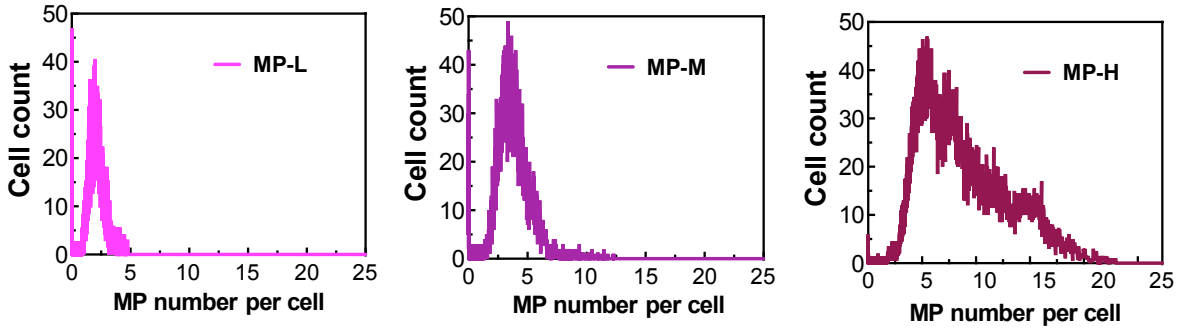

Figure S4. The distribution of MP number in each cell at three burden levels.

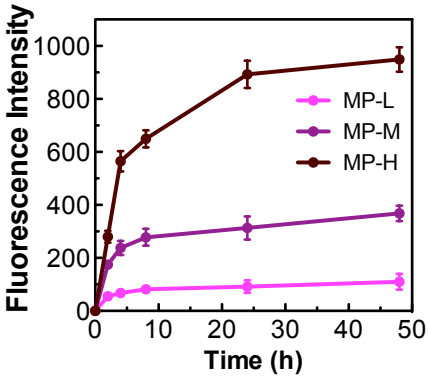

Figure S5. Kinetics of the cellular internalization at different MPs burden. Each experiment was performed in triplicate, and data were represented as means ± standard deviation.

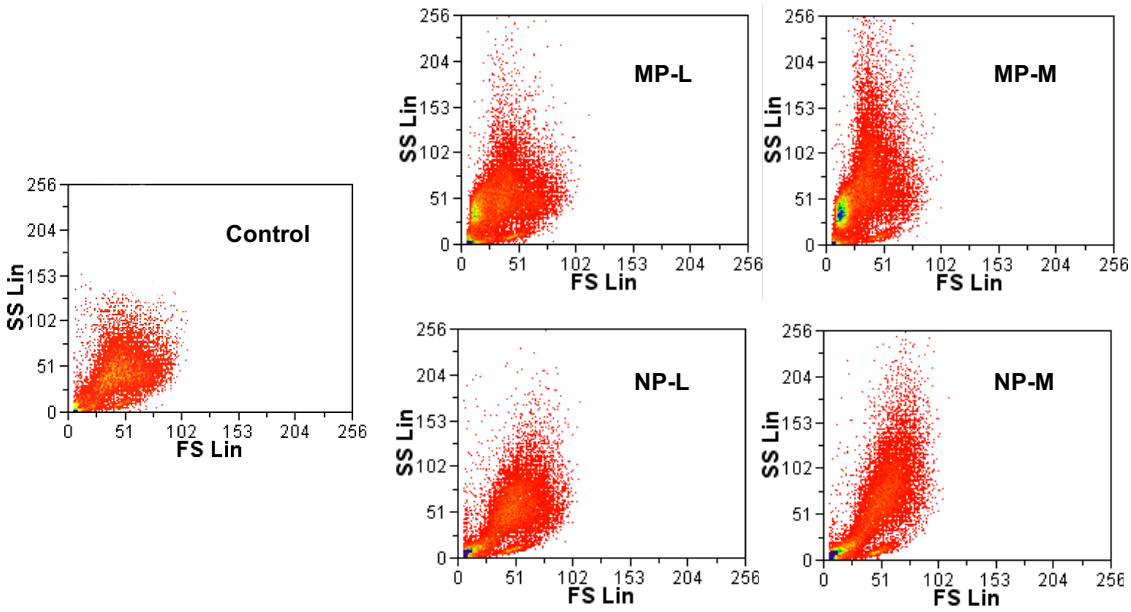

Figure S6. The scattered light signals (SS) of cells at different particles burden. SS were enhanced with the elevated extent of particle burden showing the increased internal complexity of cells.

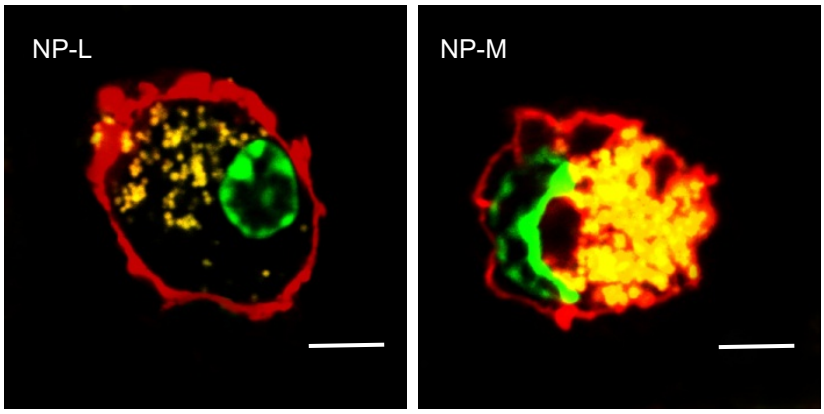

Figure S7. Confocal images showing the response of cell membrane and nucleus, upon the NPs at different burden. Scale bars: 5 μm.

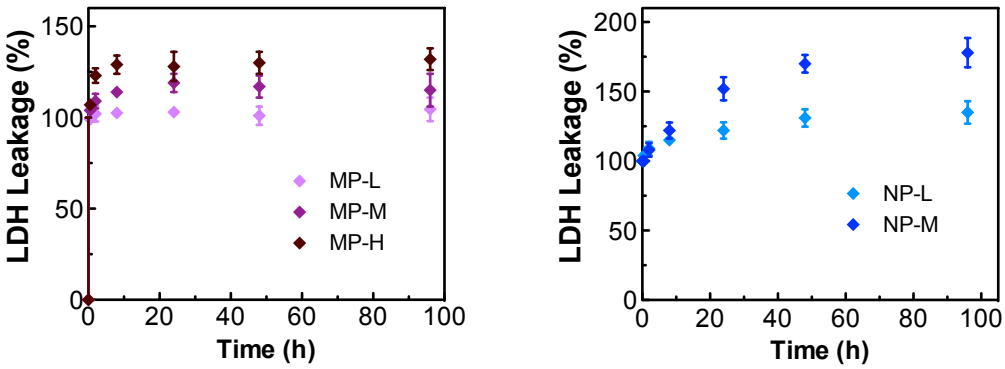

Figure S8. Lactic dehydrogenase (LDH) leakage at different cellular burden of MPs (left) and NPs (right). Each experiment was performed in triplicate, and data were represented as means ± standard deviation.

Figure S9. Schametic graphs of the conventianal surface topography method (left) and our "particle intake method" (right) for biophysical study.

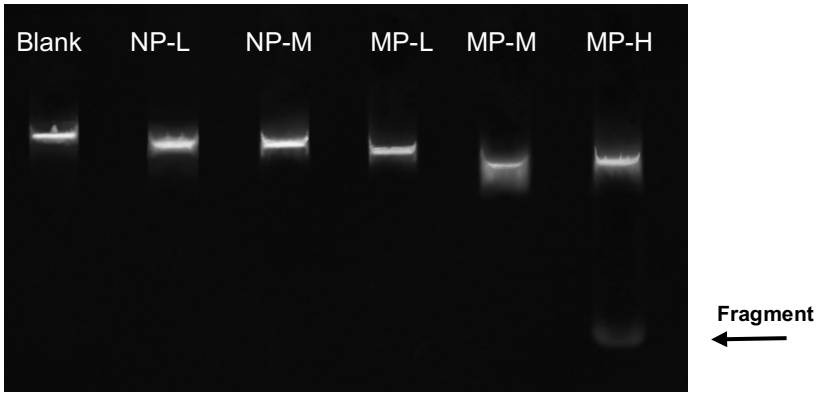

Figure S10. DNA fragment of the cells at different particle burden.

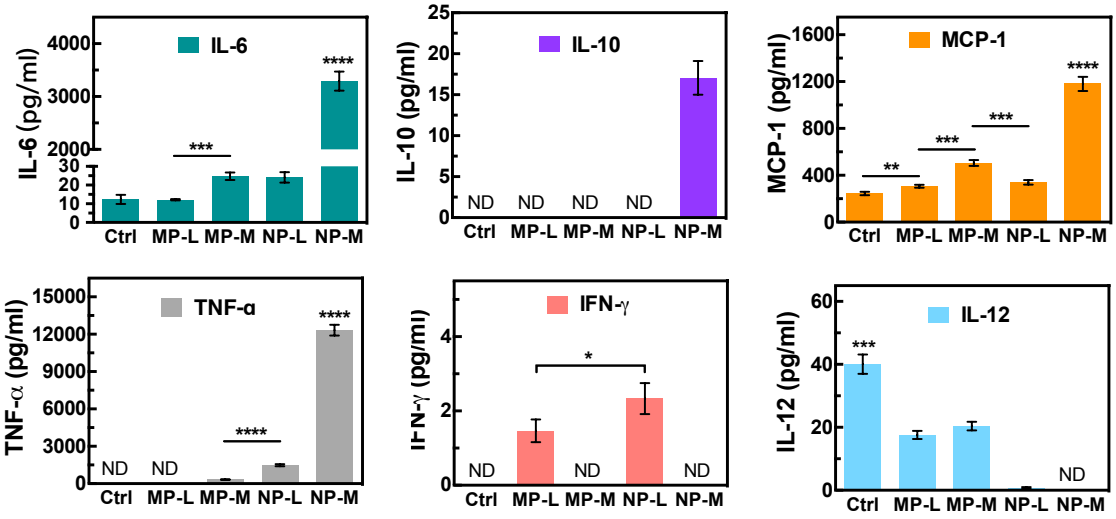

Figure S11. Cytokine profile of macrophages after exposure with MPs or NPs at different burden. Each experiment was performed in triplicate, and data were represented as means ± standard deviation. P*<0.05, P**<0.01, P***<0.001, P****<0.0001.