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Supplemental Material

Quantitative Structure–Activity Relationship Models for Predicting Inflammatory Potential of Metal Oxide Nanoparticles

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Figure S2. Assessment of TNF-α and IL-6 production in THP-1 cells incubated with selected metal oxide nanomaterials (MeONPs). a. TNF-α and **b.** IL-6 production in THP-1 cells. MeONPs at 0, 25, 50, 100, 200 μg/mL were exposed to THP-1 cells in 96-well plates. After 24 h, the supernatants were collected to detect TNF-α and IL-6 production by ELISA.

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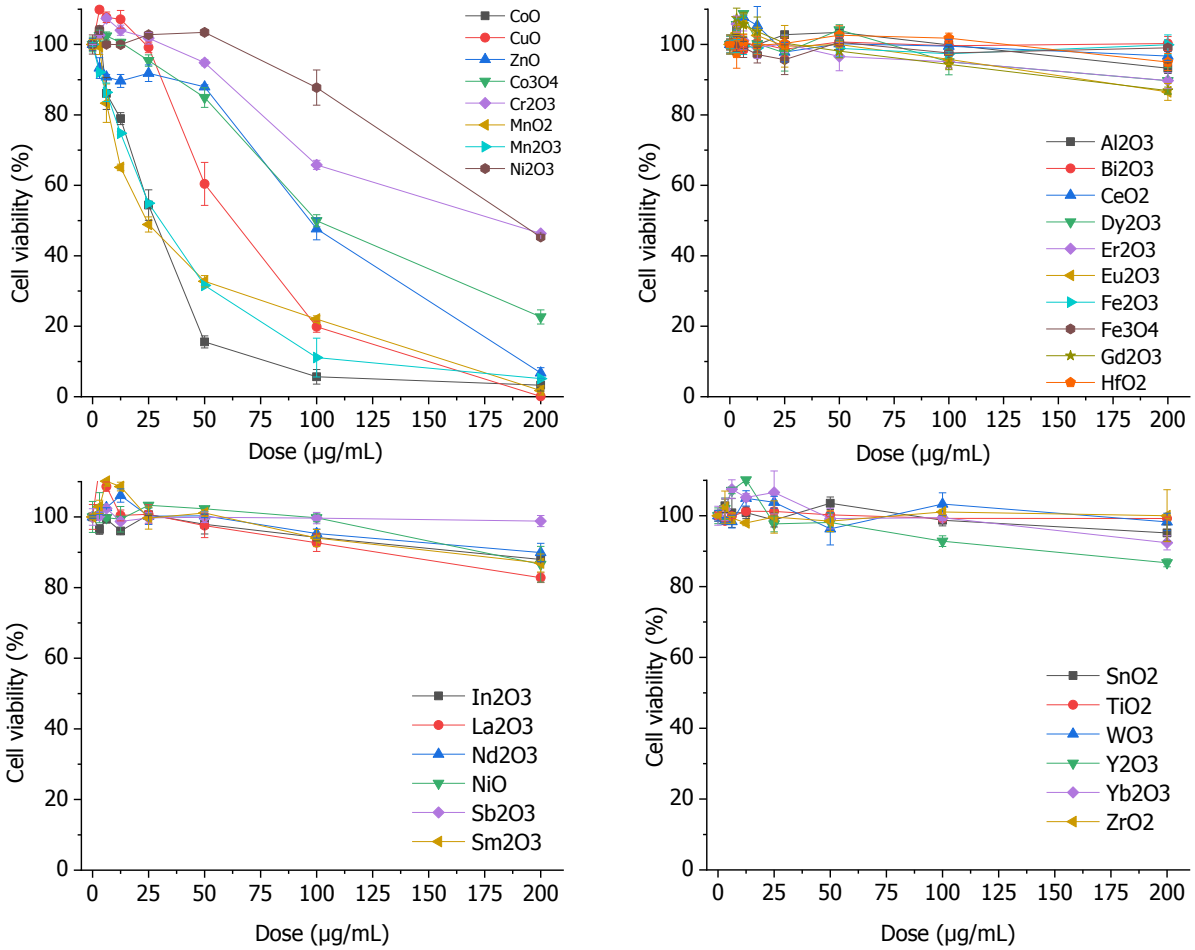
Figure S6. ICP-OES detection of cellular uptake of metal oxide nanomaterials (MeONPs). THP-1 cells seeded in six-well plates were exposed to 50 μg/mL metal oxide nanoparticles for 12 h. After thrice washing by PBS, the cell pellets were collected and lysed to measure protein concentration by Bradford assay. Then the cell lysis was digested to detect metal ions by ICP-OES (ICPE-9000, SHIMADZU, Japan). The metal contents were normalized by protein concentrations to determine the cellular uptake of MeONPs. ip-MeONPs: MeONPs with inflammatory potential; nip-MeONPs: MeONPs with non-inflammatory potential. *$p < 0.05$ compared to ip-MeONPs by two-tailed Student's t-test.

Figure S7. Confocal imaging of cathepsin B release in THP-1 cells. THP-1 cells seeded in eight-well chamber were exposed to 25 μg/mL metal oxide nanoparticles for 12 h. The cells were stained by a Magic Red™ cathepsin B assay kit and hoechst 33342 for 1 h. After thrice washing by PBS, the cell images were captured by a confocal laser scanning microscope. Scale bar represents 10 μm.

Additional File- Excel Document



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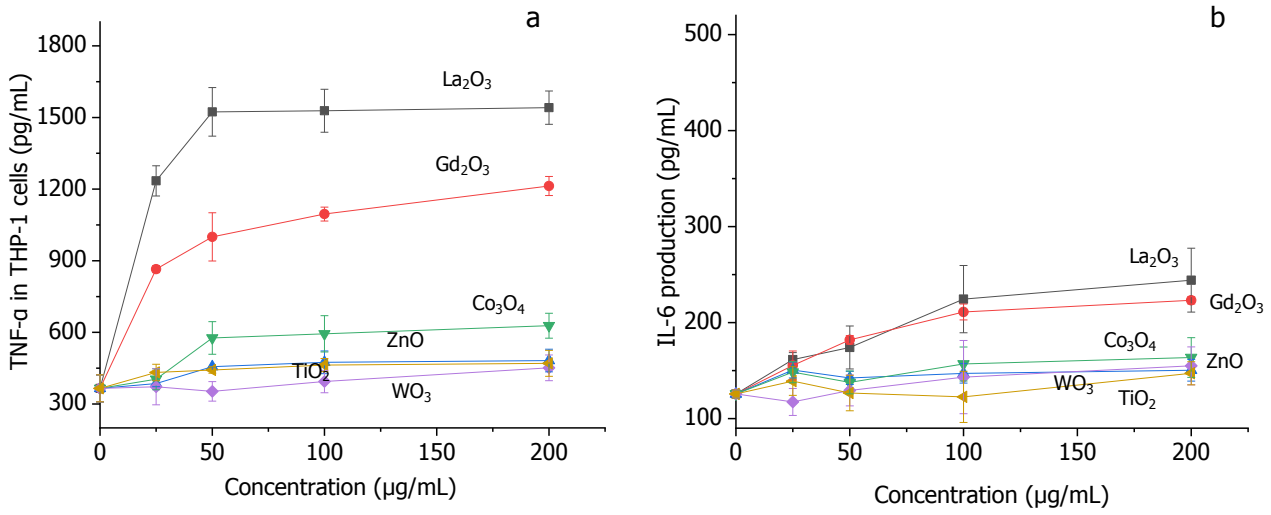
THP-1 cells were exposed to MeONPs at eight concentrations (0, 3.1, 6.2, 13, 25, 50, 100, 200 μg/mL). After 24 h incubation, the supernatants were aspirated and replaced by MTS assay solution for 3 h incubation. The absorbance of MTS solution was measured by micro-plate reader at 490 nm. The cell viability was calculated by formula 2.



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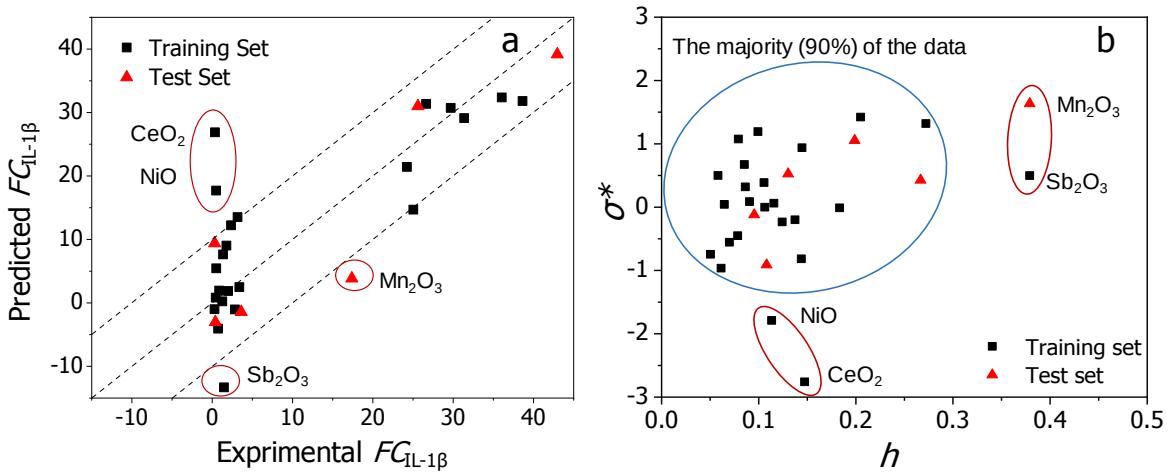

$$FC_{(IL\text{-}1\beta)} = 23.4 - 16.2\chi_{me} + 0.227\zeta\text{-}potential + 0.0229D_{water} \qquad \text{(Equation S1)}$$

$$N_{Training\ set} = 24,\ R^2 = 0.629,\ RMSE_{CV} = 9.41,\ Q^2_{CV} = 0.613,$$

$$N_{Test\ set} = 6,\ Q^2_{EXT} = 0.698,\ RMSE_P = 8.57$$

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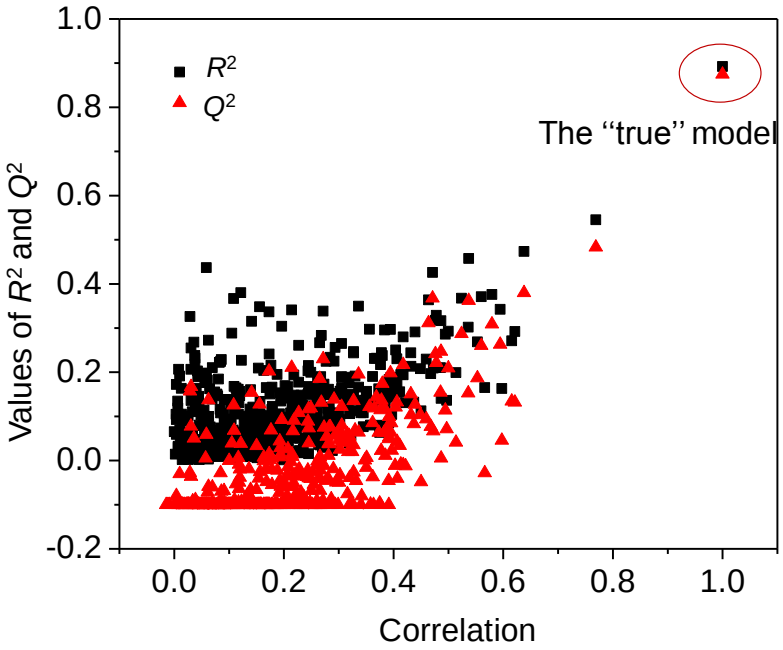
a. Plot of experimentally determined (observed) versus predicted $FC_{(IL\text{-}1\beta)}$ values of 30 data points. **b.** Williams Plot of standardized residuals (σ^*) versus leverage values (h_i) for $FC_{(IL\text{-}1\beta)}$.



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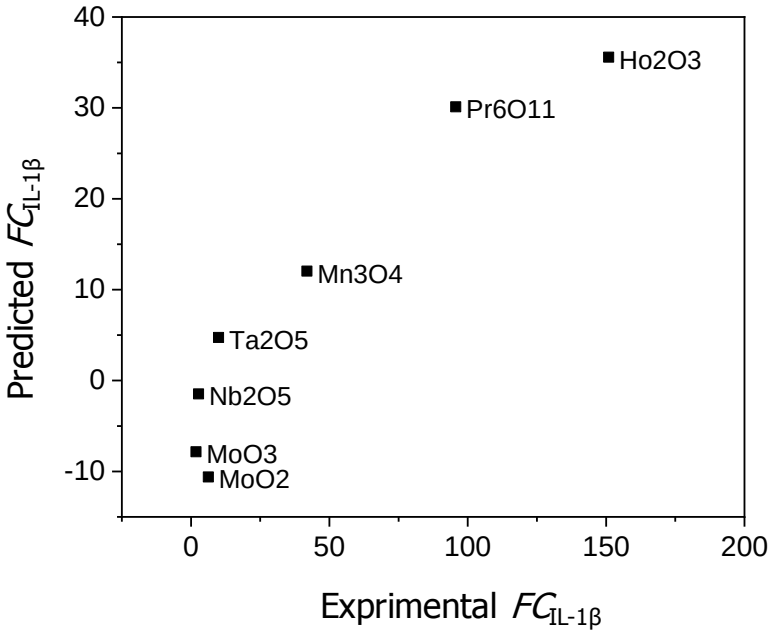

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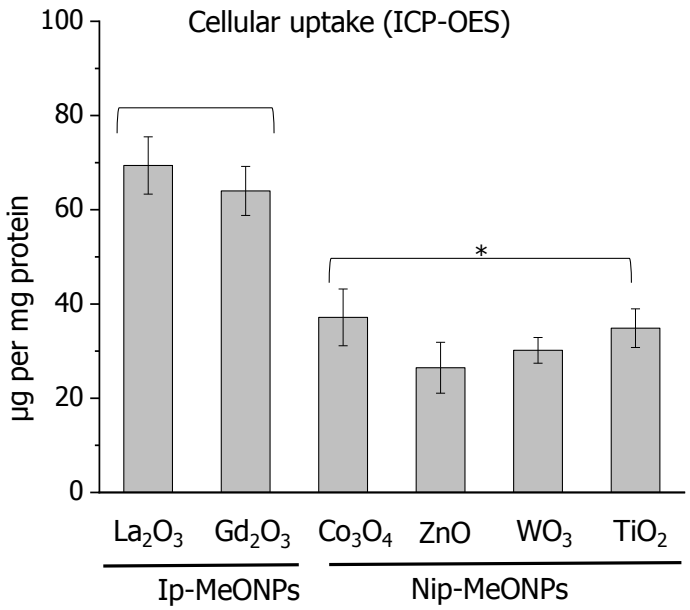

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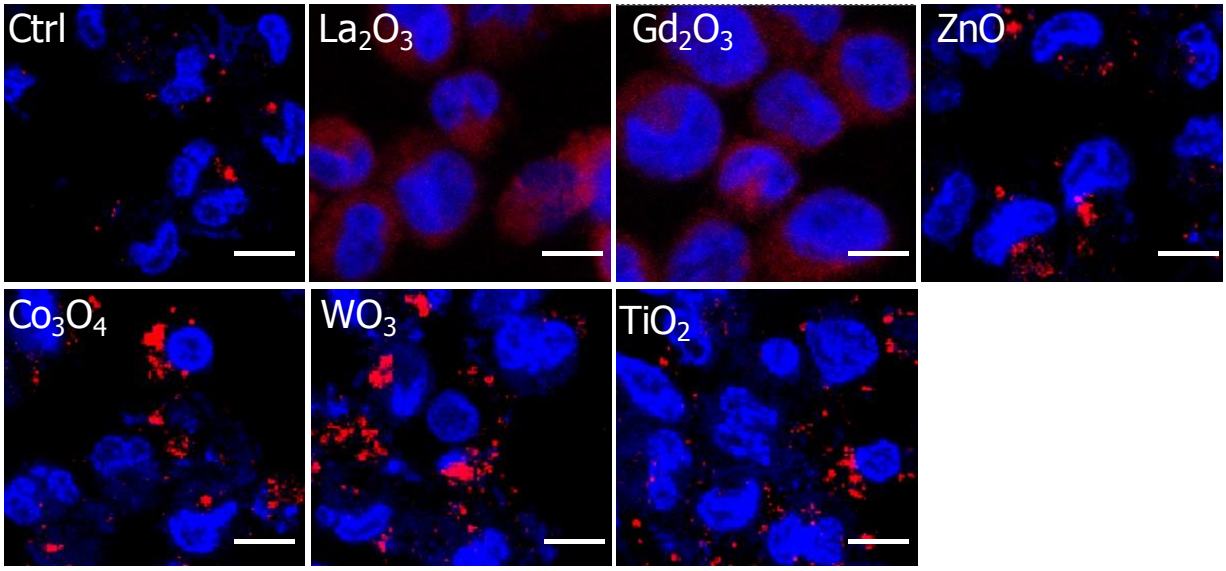

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