## Supplementary Information

# Differential Effects of Surface-Functionalized Zirconium Oxide Nanoparticles on Alveolar Macrophages, Rat Lung, and a Mouse Allergy Model 

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Figure S1. In vitro effects of supernatants generated from particle $\mathrm{ZrO}_{2}$ NPs preparations. Particle stock suspensions of $\mathrm{ZrO}_{2}$-TODS, $\mathrm{ZrO}_{2}$-Acryl, $\mathrm{ZrO}_{2}-\mathrm{PGA}$, and $\mathrm{ZrO}_{2}$-APTS were subjected to centrifugation $(28,000 \mathrm{~g}, 8 \mathrm{~h})$ to obtain particle-free supernatants (SUP). Volumes equivalent to the $180 \mu \mathrm{~g} / \mathrm{mL}$ concentration (c.f. Figure 4) were then diluted in F-12K medium or KRPG buffer and applied to NR8383 macrophages. (ns) not significant, (CTL) untreated control cells.


Figure S2. Size distribution of rat serum albumin-coated $\mathrm{ZrO}_{2}$ particles as prepared for intratracheal administration in rats. Particles were buffered with $25 \mathrm{mM} \mathrm{HCO}_{3}{ }^{-}$and $5 \% \mathrm{CO}_{2}$. Measurements were carried out with optical particle tracking and NanoSight Software NTA 2.2 (Minton Park Amesbury, Wiltshire SP4 7RT, UK).


Figure S3. Size distribution of $\mathrm{ZrO}_{2}$ nanoparticles dispersed in $0.9 \% \mathrm{NaCl} / \mathrm{PBS}$ as used for an administration study in ovalbumin-sensitized mice. (a) $\mathrm{ZrO}_{2}-\mathrm{PGA}$, (b) $\mathrm{ZrO}_{2}-\mathrm{TODS}$, (c) $\mathrm{ZrO}_{2}$-APTS, and (d) $\mathrm{ZrO}_{2}$-Acryl. Measurements were carried out with optical particle tracking and NanoSight Software NTA 3.1 (Minton Park Amesbury, Wiltshire SP4 7RT, UK).

Table S1. Characteristics of zirconia nanoparticles as published by the NanoGEM consortium. Data are taken from references [23,24] cited in the main text.

|  | $\mathrm{ZrO}_{2}$-Acryl | $\mathrm{ZrO}_{2}$-PGA | ZrO 2 -APTS | $\mathrm{ZrO}_{2}$-TODS |
| :---: | :---: | :---: | :---: | :---: |
| Organic residue | polyacrylic acid | polyethylene glycol ( $600 \mathrm{~g} / \mathrm{mol}$ ) | aminopropyltrimethoxy silane | trioxadecanoic acid |
| Particle size TEM [nm\} | 9 | 9 | 10 | 9 |
| BET surface | 117 | 117 | 105 | 117 |
| Zeta potential (mV) | -29.2 | -25.2 | -20.5 | -25.1 |
| Structure |  |  |  |  |
| Formula | - | $\begin{gathered} \mathrm{HOOC}-\mathrm{CH}_{2}-\left(\mathrm{OC}_{2} \mathrm{H}_{4}\right) \mathrm{n}-\mathrm{O}-\mathrm{CH}_{2}- \\ \mathrm{COOH} \end{gathered}$ | $\begin{gathered} \mathrm{H}_{2} \mathrm{~N}-\mathrm{C}_{3} \mathrm{H}_{6}-\mathrm{Si}\left(\mathrm{OCH}_{3}\right)_{3} \\ \mathrm{SiC}_{6} \mathrm{H}_{15} \mathrm{O}_{3} \mathrm{~N} \end{gathered}$ | $\begin{gathered} \mathrm{HOOC}-\mathrm{CH}_{2}-\mathrm{O}-\mathrm{C}_{2} \mathrm{H}_{4}-\mathrm{O}- \\ \mathrm{C}_{2} \mathrm{H}_{2}-\mathrm{O}-\mathrm{CH}_{3} \\ \mathrm{C}_{7} \mathrm{O}_{5} \mathrm{H}_{14} \\ \hline \end{gathered}$ |

