

Shape engineered TiO₂ nanoparticles in *Caenorhabditis elegans*: a Raman imaging based approach to assist tissue-specific toxicological studies

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Titanium dioxide (TiO₂) nanoparticles (NPs) are one of the main sources of the nanoparticulate matter to which humans are directly exposed and several studies have demonstrated their potential toxic effects^{1,2}. The *in vivo* detailed spatial distribution of TiO₂ NPs is investigated herein for the first time, using a 2D chemical imaging analysis based on confocal Raman spectroscopy³. The invertebrate nematode *C. elegans* was employed as a prototypical model of living organisms. Rod, bipyramidal and quasispherical engineered TiO₂ NPs with different primary particle sizes and agglomeration states were prepared, characterized and then administered to nematodes. Exploiting the typical fingerprint of TiO₂ in the Raman spectrum, we monitored the biodistribution of NPs inside the worm using a non-invasive, label-free method. The high spatial resolution chemical imaging and the specificity of the Raman technique in the localization of TiO₂ NPs helped in the design of behavioral *C. elegans* studies aimed at elucidating the relationship among the size, shape, and agglomeration state of NPs and their ability to induce specific toxic effects. Rod-shaped NPs were the most toxic, greatly impairing pharyngeal function, reproduction and larval growth; this indicates that the rod shape, more than the bipyramidal and spherical shapes, enables NPs to interact with biological systems. These findings indicate that this Raman-nematode combined approach represents a step forward in the field of detection of NPs in living organisms, and being rapid and inexpensive enough, it can be applied as the first screening for the ability of NPs to biodistribute and exert toxicological properties *in vivo*.

[1] Weir A., Westerhoff P., Fabricius L. and Von Goetz N., *Environ. Sci. Technol* 2012; 46 (4): 2242–2250.

[2] Kuempel E. D. and Ruder A., *IARC Monograph* 2010; 93: 193-276.

[3] www.setnanometro.eu, FP7-NMP-2013 LARGE-7, 604577.

Acknowledgments

This work was supported by the SETNanoMetro Seventh Framework Programme project (project number 604577; call identifier FP7-NMP-2013_LARGE-7). C. elegans strains and E. coli OP50 were provided by CGC, which is funded by NIH Office of Research Infrastructure Program (P40 OD010440).