An International Journal Specializing in Environmental Mutagenesis

Volume 63
Number S1
August 2022

Environmental and Molecular Mutagenisis

Epigenomics
In Vivo Mutagneisis
Applied Genetic Toxicology
Genomics and Data Sciences
Germ Cell and Heritable Effects
DNA Repair and Mutagenic Mechanisms
Genotoxicity Risk Assessment and Public Health

In this issue: Abstracts from the 13th International Conference on Environmental Mutagens and 53rd Annual Meeting of the Environmental Mutagenesis and Genomics Society, August 27 - September 1, 2022 - Ottawa, Canada, Maintaining Genomic Health in a Changing World
Program Chairs: Dr. Francesco Marchetti, Paul White, PhD, and Carole Yauk, PhD

Platform 7: Risk Assessment

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Cellular, Molecular and Genotoxic Effects of Digested Titanium Dioxide Nanomaterials

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Human exposure to titanium dioxide nanomaterials(TiO_2NMs) occurs particularly by ingestion, due to food/food contact materials and consumer products. However, the possibility of adverse effects in gastrointestinal tract is unclear. Aiming to study the impact of digestion on the NMs' properties and their cellular/molecular effects, two human intestinal cell lines were used, Caco-2 and HT29-MTX-E12. After exposure to TiO_2NMs(NM-102, NM-103, NM-105), undigested or subjected to standardized static *in vitro* digestion method (mimicking human digestion), the cells were analyzed for toxicity, genotoxicity, reactive oxygen species, NM uptake and intestinal translocation.

We showed that *in vitro* digestion of TiO_2NMs may increase their toxicity and DNA-damaging effect, depending on the NM, more relevant for the rutile/anatase NM-105, possibly due to its smaller hydrodynamic size in the cellular medium. Effects on chromosomal integrity were seen in HT29-MTX-E12 cells, for all tested TiO_2NMs, especially after digestion. Internalization into early endosomes was confirmed for NM-103 and NM-105, before and after digestion, in monolayers of both cell lines, and at the apical membrane of polarized Caco-2 cells. The internalized NMs accumulated in late endosomes/multivesicular bodies, partially transversing the basolateral membrane of polarized Caco-2 cells without changing transepithelial electrical resistance or epithelial marker abundance. These results suggest that part of the TiO_2NMs can be transcytosed through colonic epithelia without disrupting intestinal barrier integrity.

Overall, the biological outcomes from TiO_2NMs interaction with intestinal cells were more pronounced after digestion, highlighting its relevance in the hazard assessment of ingested NMs.

Funded by FCT/MCTES: PTDC/SAU-PUB/29481/2017, UIDB/00009/2020; UIDP/00009/2020;UIDP/50017/2020+UIDB/50017/2020+LA/P/0094/2020; CEECIND/03143/2017 (LG), 2020.07168.BD (NV).

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Deriving an Optimal Transcriptomic Metric to Establish Protective and Relevant Transcriptomic Points of Departure for Risk Assessment Application

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The expanding number and complexity of substances used in products on the Canadian market presents a major challenge for evaluators assessing the health or ecological risks posed by these chemicals. The increasing demand and general paucity of available safety data for these substances provides the opportunity to implement novel, more efficient strategies using in vitro and in silico based methods.