

## Genotoxicity assessment of silica-coated iron oxide nanoparticles in human astrocytes

**Natalia Fernández-Bertólez<sup>a,b</sup>, Gözde Kiliç<sup>c</sup>, Carla Costa<sup>d,e</sup>, Fátima Brandão<sup>d,e</sup>, Sonia Fraga<sup>d,e</sup>, Joao Paulo Teixeira<sup>d,e</sup>, Eduardo Pásaro<sup>a</sup>, Blanca Laffon<sup>a</sup>, Vanessa Valdiglesias<sup>a</sup>**

<sup>a</sup>DICOMOSA Group, Department of Psychology, Area of Psychobiology, Universidade da Coruña, Edificio de Servicios Centrales de Investigación, Campus Elviña s/n, 15071-A Coruña, Spain.

<sup>b</sup>Department of Cell and Molecular Biology, Universidade da Coruña, Facultad de Ciencias, Campus A Zapateira s/n, 15071-A Coruña, Spain.

<sup>c</sup>Division of Molecular Toxicology, Institute of Environmental Medicine, Karolinska Institutet, 171 77 Stockholm, Sweden.

<sup>d</sup>Department of Environmental Health, Portuguese National Institute of Health, Rua Alexandre Herculano, 321, 4000-055 Porto, Portugal.

<sup>e</sup>EPIUnit - Institute of Public Health, University of Porto, Rua das Taipas, 135, 4050-600 Porto, Portugal.

Iron oxide nanoparticles (ION) have great potential for various biomedical and neurobiological applications such as magnetic resonance neuroimaging agents, heating mediators in hyperthermia-based cancer therapy, and molecular cargo in targeted drug/gene delivery across blood-brain barrier. For all these applications, ION must be introduced in the human body and be in contact with cells and tissues, so it is imperative to know the potential risks associated to this exposure, especially in the nervous system. ION surface may be modified by coating with a number of materials to enhance their desirable properties, biocompatibility and biodegradability. Nevertheless, surface covering can alter cellular internalization and other toxicity endpoints. Even though ION seem to be biocompatible and present low toxicity, current data on their effects on the human nervous system are scarce. Thus, the main objective of this work was to examine possible genotoxic effects of ION (silica-coated magnetite) on human glioblastoma (A172) cell line. To this aim, two treatment times (3 and 24 h), a range of ION concentrations (5-100 µg/ml), and different outcomes were tested: the standard alkaline comet assay to analyze primary DNA damage, H2AX histone phosphorylation to assess the induction of DNA double-strand breaks, and micronucleus (MN) test to determine chromosome alterations. Flow cytometry uptake analysis indicated that ION were not effectively internalized by the cells, but induced a dose- and time-dependent increase in primary DNA damage which, according to the results of H2AX assay, were not related to double strand breaks excepting for the highest concentrations and longest exposure time. Negative results in MN test indicate (i) no aneugenic effects and (ii) that the previously mentioned DNA strand breaks were not fixed upon cell division. Further research is necessary to determine the cause of the genotoxicity events detected in absence of nanoparticle uptake.

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