Biocompatibility and antioxidant potential of nanoceria in human nervous cells

N. Fernández-Bertólez[1,2*], L. Ramos-Pan[1,2], A. Touzani[1,2], A. T. Reis[3,4,5], J. P. Teixeira[3,4,5], J. Mendez[1], B. Laffon[2,6], & V. Valdiglesias[1,2]

[1] Universidade da Coruña, Grupo NanoToxGen, CICA - Centro Interdisciplinar de Química e Bioloxía, Departamento de Biología, Facultad de Ciencias, Campus A Zapateira s/n, 15071, A Coruña, Spain
[2] Instituto de Investigación Biomédica de A Coruña (INIBIC), Complexo Hospitalario Universitario de A Coruña (CHUAC), Sergas, As Xubias, 15006, A Coruña, Spain
[3] Environmental Health Department, National Institute of Health, 4050-600 Porto, Portugal
[4] EPIUnit - Instituto de Saúde Pública, Universidade do Porto, 4050-600 Porto, Portugal
[5] Laboratório para a Investigação Integrativa e Translacional em Saúde Populacional (ITR), 4050-600 Porto, Portugal
[6] Universidade da Coruña, Grupo DICOMOSA, CICA - Centro Interdisciplinar de Química e Bioloxía, Departamento de Psicología, Facultad de Ciencias de la Educación, Campus Elviña s/n, 15071, A Coruña, Spain
** natalia.fernandezb@udc.es*

Cerium dioxide nanoparticles (CeO_2 NP), also known as nanoceria, have emerged as promising materials in biomedical and pharmacological applications due to their unique redox properties and antioxidant capacity. Due to these and other specific characteristics, they have raised high attention for their potential use in drug delivery, radioprotection, tissue regeneration or diagnostic imaging, particularly in neurological pathologies associated with oxidative stress. However, previous works have reported that nanoceria may also induce reactive oxygen species (ROS) production under certain conditions, leading to oxidative stress, cellular damage and cell death. This study aimed to investigate the CeO_2 NP effects on cell viability and morphology, as well as their influence on oxidative stress (both oxidizing and ROS scavenging activity) in human nervous cells (SH-SY5Y neurons and A172 glial cells) treated with different CeO_2 NP concentrations (1–100 µg/mL) for 3, 24 and 48 h. Results obtained showed that CeO_2 NP exhibited good biocompatibility, as there was no significant decrease in cell viability, morphological alterations or intrinsic acellular ROS production at any of the conditions tested, despite being stable over time and effectively internalized by both cell types. However, a significant increase in cellular ROS (mainly limited to the longest exposure period) and a slight induction of oxidative DNA damage (limited to the highest concentration after 3 h) was observed, predominantly affecting SH-SY5Y cells. Notably, nanoceria demonstrated a remarkable intrinsic capacity to scavenge H_2O_2-generated ROS, showcasing their antioxidant properties, more pronounced in neuronal cells. In conclusion, this study confirms the biocompatibility of CeO_2 NP within human nervous system cells and highlights their potential as therapeutic agents in neuroprotective strategies against oxidative stress-induced damage. These findings warrant further investigation into the applications of nanoceria in medical fields, especially for treating neurodegenerative diseases and as diagnostic tools in neurology.

Funding: This research was funded by Ministry of Science and Innovation: MCIN/AEI/10.13039/501100011033 (Grant PID2020-114908GA-I00), Xunta de Galicia (ED431B 2022/16), FCT - Fundação para a Ciência e Tecnologia, I.P. through UIDB/04750/2020 (https://doi.org/10.54499/UIDB/04750/2020) and LA/P/0064/2020 (https://doi.org/10.54499/LA/P/0064/2020). L.R.-P. was supported by a Ministry of Science and Innovation predoctoral fellowship (grant number FPU2023/03379).