Towards understanding the CeO_2NPs effect in an *in vitro* preeclampsia model

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Preeclampsia (PE) is a potentially lethal orphan-drug disease that affects 5-8% of pregnant women globally. PE is characterized by high blood pressure and endothelial damage, causing a systemic inflammation and oxidative stress with elevated levels of reactive oxygen species (ROS).

Trophoblasts are cells that develop as part of the placenta. They also provide nutrients and help the embryo adhere to the uterus. In this study, we employ immortalized trophoblasts (HTR8/SVneo) exposed to 1% O2 hypoxia to mimic a preeclampsia-like phenotype. Trophoblast under hypoxia tend to migrate aberrantly causing inflammation and ROS.

Our research focuses on the use of cerium oxide nanoparticles (CeO2NPs) known for their antiinflammatory and antioxidant properties as a possible treatment for PE. This effect could be achieved through its ROS scavenging capacity.

No changes in cell viability are observed when trophoblasts are exposed to 1% O2 (hypoxic conditions). CeO2NPs have no cytotoxic effect in trophoblasts exposed to 1% O2. An excess of trophoblast migration is associated with preeclampsia (hypoxic environment). CeO2NPs reduce migration in trophoblast exposed to 1% O2. Thus, CeO2NPs may be promising candidates for treating preeclampsia.

References

[1] Ernst LM, Puntes V. How Does Immunomodulatory Nanoceria Work? ROS and Immunometabolism. Front Immunol. 2022. Mar 17;13:750175.

[2]. Casals, E., Gusta, M.F., Montana, L., Mendoza, M., Maiz, N., Carreras, E., Puntes, V. Nanotechnology for Maternal Foetal Medicine. 2018. International Journal of Pediatrics and Neonatal Health, 2:5, 57-66.

Figures

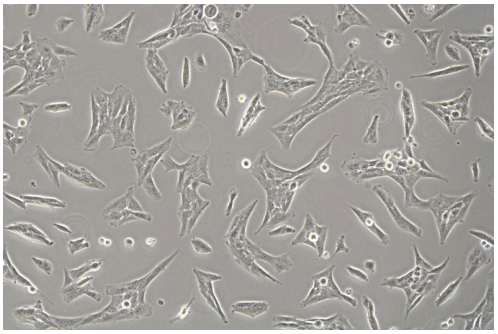
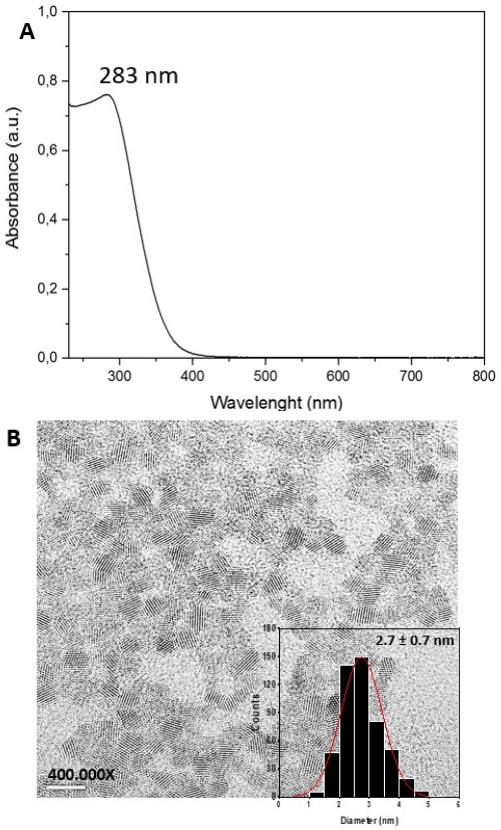


Figure 1. HTR-8/SVneo trophoblasts 40X



C

pH	8.3
Size by number (DLS)	4.2±0,9 nm
Z-pot	-17±3.4 mV

Figure 2. CeO2NPs UV-visible spectroscopy and size distribution (A). 2.5 nm CeO2NPs by high-resolution transmission electron microscopy (B). pH, size by dynamic light scattering (DLS), zeta potential (C).

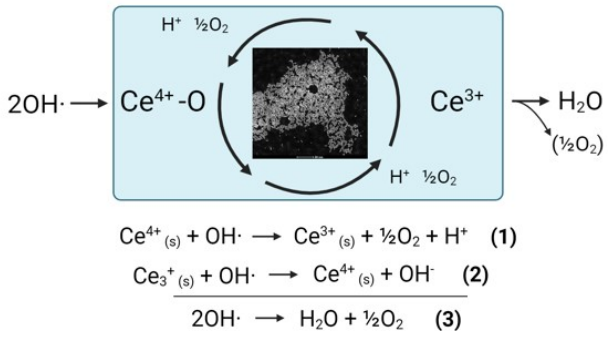


Figure 3. Schema of CeO2NPs possible bio-catalysis mechanism. Adapted from: Ernst LM, Puntes V. How Does Immunomodulatory Nanoceria Work? ROS and Immunometabolism. (doi: 10.3389/fimmu.2022.750175)

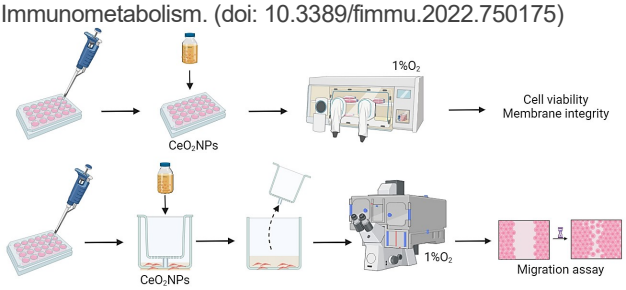


Figure 4. Schema of the methodology used to perform cell viability and membrane integrity assays (A), and the migration assay (B) under hypoxia conditions (1%O2).

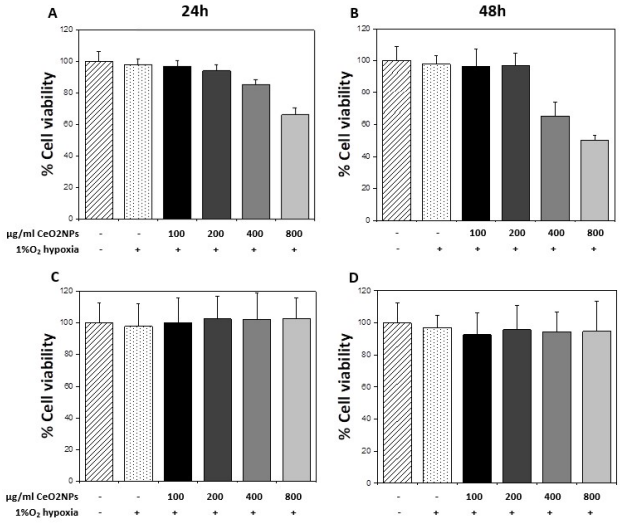


Figure 5. Cell viability by PrestoBlue assay (A,B) and membrane integrity by Lactate Dehydrogenase assay (C,D) in HTR-8/SVneo trophoblasts pre-treated with 0, 100, 200, 400 and 800 µg/ml CeO2NPs and exposed to 1% O2 for 24h and 48h. Data expressed as mean ± SD.

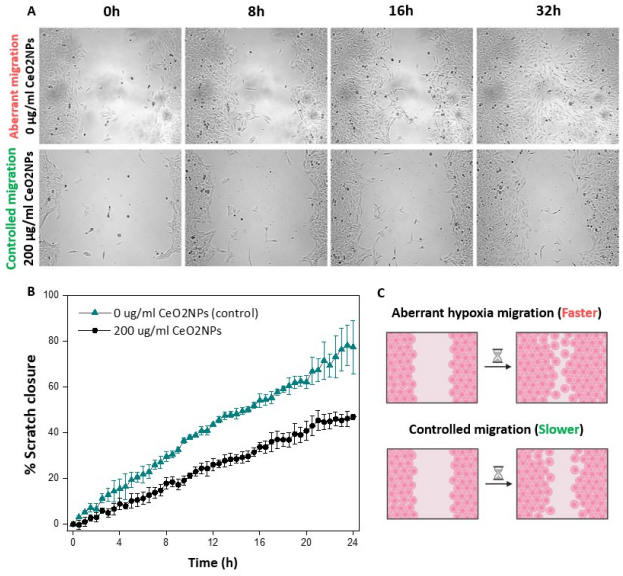


Figure 6. Migration assay time-lapse confocal microscopy images. Untreated (above panels) and 200 µg/ml CeO2NPs treated (below panels) HTR-8/SVneo trophoblasts exposed to 1% O2 at 0h, 8h, 16h and 32h after insert removal (A). Evaluation of scratch wound closure in % of untreated and 200 µg/ml CeO2NPs treated HTR-8/SVneo trophoblasts exposed to 1% O2. Measures performed continuously for 24h. Data expressed as mean ± SD (B). Schema of the aberrant migration that take place under hypoxia (PE in vitro mimic conditions) versus a normal controlled migration (C).