CeO2NPs modulation 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. It causes a sever hypoxia in the mother's , causing a systemic inflammation and oxidative stress with elevated levels of reactive oxygen species (ROS).

Trophoblasts, as placental precursors, play a pivotal role. Hence, we utilize this immortalized cell line HTR-8/SVneo cultured in a hypoxic chamber at 0.5% oxygen (hypoxia) to replicate PE conditions in vitro.

Furthermore, our research focus on cerium oxide nanoparticles (CeO2NPs), renowned for their anti-inflammatory and antioxidant properties, as a potential treatment for PE. This effect relies on the nanoparticles capacity to scavenge ROS. To ascertain ceria's ability to modulate the hypoxic impact on trophoblasts, we have analyzed the gene expression of several key genes. These genes include those involved in vascular remodeling (MMP9 and MMP2), hypoxia-inducible factors 1/2α, angiogenesis (VEGF and PlGF), pro-inflammatory cytokines (IL-1β and IL-6), and metabolic genes related to anaerobic glycolysis (GLUT1) and fatty acid oxidation (PPAR-ɣ). Typically upregulated under hypoxia, we've observed ceria's ability to mitigate this effect, in most cases in a dose-dependent manner. Additionally, migration assays indicate ceria' s modulation of trophoblast behavior. This correlate with the MMPs gene expression results involved in vascular remodeling and migration.

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

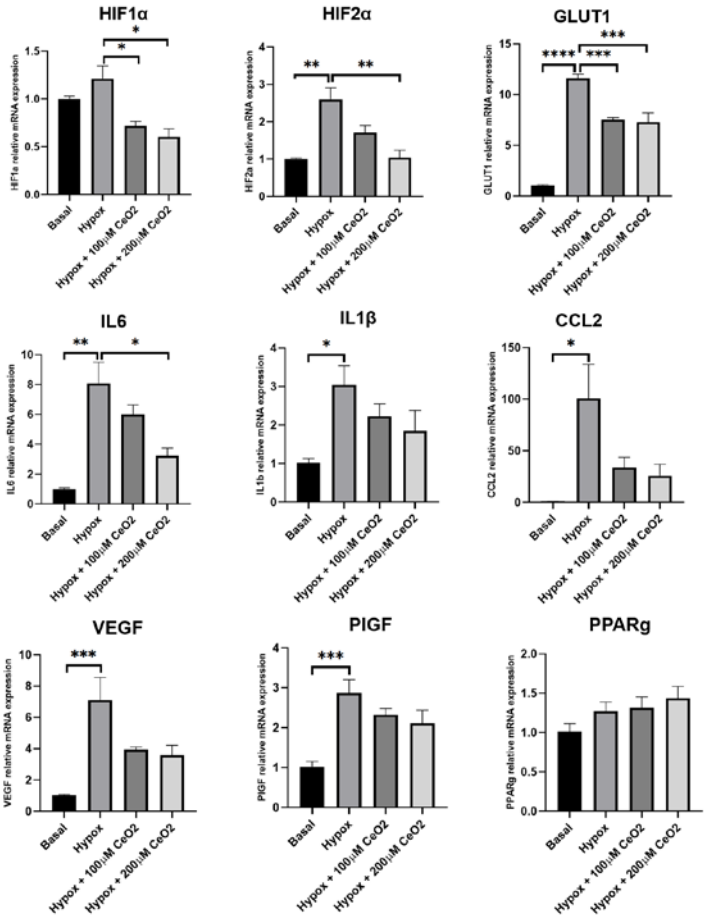

Figure1. Gene expression analysis of *HIF1α*, *HIF2α*, *GLUT1*, *IL6, IL1β*, *CCL2*, *VEGF*, *PlGF* and *PPARg* in HTR-8/Svneo cells. The expression of different genes were measured by real-time PCR. Data expressed as mean ± SEM and P-value ≤ 0.05.

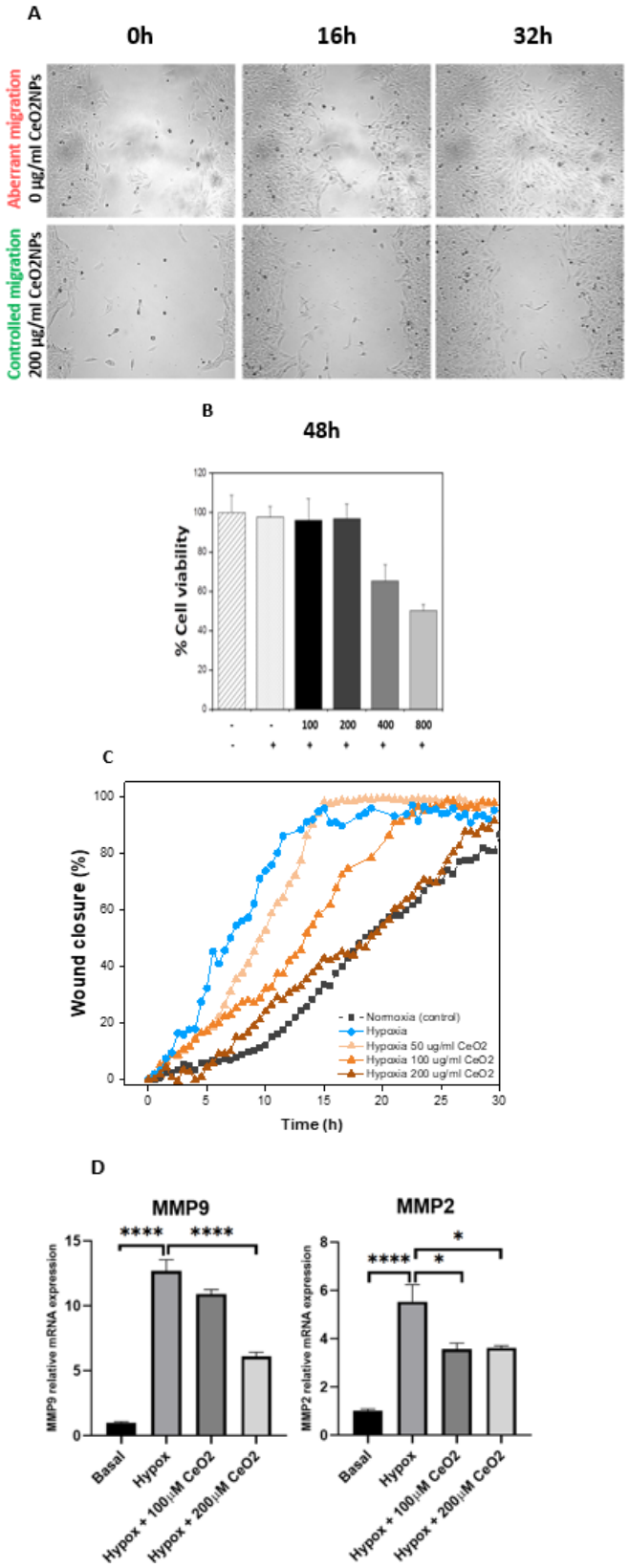

Figure2. Migration assay time-lapse confocal microscopy images. Untreated (above panels) and 200 µg/ml CeO2NPs treated (below panels) HTR-8/SVneo trophoblasts to 0.5% O2 at 0h, 16h and 32h (A). Cell viability in trophoblasts pre-treated with 100, 200, 400 and 800 µg/ml CeO2NPs and exposed to 0,5% O2 for 48h. Data expressed as mean ± SD (B). Evaluation of wound closure in % of untreated, 50, 100 and 200 µg/ml CeO2NPs treated HTR-8/Svneo trophoblasts (C). Gene expression analysis of *MMP9* and *MMP2* in HTR-8/Svneo cells. Measured by real-time PCR. Data expressed as mean ± SEM and P-value ≤ 0.05