# How do nanoceria work? The metabolic control of the immunochemical potential.

**Victor Puntes**[1,2,3]
Lena Montaña[3]

*1 Institut Català de Nanociència i Nanotecnologia (ICN2), CSIC and BIST, Campus UAB, Bellaterra, 08193 Barcelona, Catalonia, Spain.*
*2 ICREA, Pg. Lluís Companys 23, 08010 Barcelona, Spain.*
*3 Vall d'Hebron Institut de Recerca (VHIR), 08035, Barcelona, Spain.*
*victor.puntes@vhir.org*

**Abstract.** Nanoceria, Cerium oxide (CeO2) nanoparticles, by buffering metabolic Reactive Oxygen Species (ROS), control the immunochemical potential, allowing to regulate the immune response by administering cellular power supply. To understand how nanoceria works inside a biological system, it is essential to know how immune cells employ different metabolic pathways to sustain their energetic demands. In this regard, macrophages have clearly shown different metabolic pathways regarding their polarization status (M0, M1 or M2), which are linked to their specific functions (quiescence, inflammation, resolution/repair). To understand that, we focus on the nanoceria effects on the mitochondria. Indeed, the mitochondria, considered the *powerhouse* of the cell, recently emerged as critical mediators of immune responses. They can control the energy requirements of cells through dynamic fission and fusion events, which are linked to Reactive Oxygen Species (ROS) production, a major player in immune response, disease and inflammation. Next, it is also necessary to understand how antioxidant substances work[1], and why they have recurrently failed to translate the promising preclinical results into clinical practice. In this context, new mineral antioxidant substances may overcome actual limitations, and thus open a new era for human Health management. Nanoceria, similar to other antioxidant substances, displays powerful anti-inflammatory effects. Nanoceria is indeed an antireducer (electrons sink), and act as heterogeneous catalytic free radical scavenger allowing both a long term activity with a single low dose, and the effective reduction of pathologic (excess of) ROS. Finally, nanoceria has shown to be safe to normal tissue and slowly biodegrade. In this paper, we focus on the chemical substrate that supports any biological system and state, allowing thus to understand the effects of antioxidant substances in the immune system without getting lost in the ultra-description of metabolism and immune responses.

[1] Note that biological oxidation is tuned by ROS, not oxygen concentration, which is more stable (constant) inside the body then ROS.