Probing the Molecular Mechanism of Cerium Oxide Nanoparticles in Protecting Against the Neuronal Cytotoxicity of Aß1-42 with Cu Ions

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Alzheimer’s disease (AD) is a progressive neurodegenerative disorder, which is characterized by the formation of senile plaques and neurofibrillary tangles in the brain. The pathological hallmark of AD is the cerebral amyloid beta peptide (Aß) deposits. The redox active metals involved in Aß peptides generally promote the aggregation of Aß peptides and produce reactive oxygen species (ROS) by Fenton-type and Harber-Weiss-type reactions, resulting in extensive impairment of cellular functions. Cerium oxide nanoparticles (CeO2NP), possess an astonishing pharmacological potential due to their antioxidant properties, deriving from a fraction of Ce3+ ions present in CeO2. Deriving from the Ce3+/Ce4+ ‘spontaneously’ recycle, CeO2NP has both superoxide dismutase (SOD) mimetic activity and catalase mimetic activity. By virtue to the ability of nanomaterials to cross the BBB, CeO2NP can be a promising candidate in the treatment of AD. The aim of this study is to probe the molecular mechanism for CeO2NP to protect against neural cytotoxicity from amyloid peptide and redox active metal ions. The systematic exploration of CeO2NP relieving AD related amyloid beta properties and neuronal cytotoxicity was carried out. Morphology of TEM revealed that CeO2NP may reduce Aß 1-42 aggregation. Cell viability assay indicated that CeO2NP protects neurotoxicity of Ab1-42 or Cu2+-Ab1-42 by scavenge ROS. CeO2NP can be administered in an amount sufficient to block production of hydroxyl or superoxide radicals, block free radical production or by Cu2+- Aß 1-42-induced ROS by Ce3+/Ce4+ catalytic cycles. All these results provide valuable insights into the molecular mechanism for CeO2NP as a therapeutic intervention to reduce oxidative and nitrosative damage.

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