Do nanoparticles induce neurodegenerative diseases? Understanding the origin of reactive oxidative species and protein aggregation and mis-folding phenomena in the presence of nanoparticles (NEURONANO)

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Title of project or programme

Do nanoparticles induce neurodegenerative diseases? Understanding the origin of reactive oxidative species and protein aggregation and mis-folding phenomena in the presence of nanoparticles (NEURONANO)

Principal Investigators of project/programme grant

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Source of funding information

European Commission

Total sum awarded (Euro)

2498000

Start date of award

01-02-2009

Total duration of award in months

The project/programme is most relevant to

- Alzheimer’s disease and other dementias
- Neurodegenerative disease in general

Keywords

risk assessment,health effects of nanoparticles,blood-brain barrier,nanoparticle surface characteristics,nanoparticle-biomolecule corona,nanoparticle safety,cellular and molecular mechanisms

Research abstract in English

As the use of nanoparticles becomes more prevalent, it is clear that human exposure will inevitably increase. Considering the rapidly ageing European population and the resulting increase in the incidence of neurodegenerative diseases, there is an urgent need to address the risk presented by nanoparticles towards neurodegenerative diseases. It is believed that nanoparticles can pass through the blood-brain barrier. Once in the brain, nanoparticles have two potential major effects. They can induce oxidative activity (production of Reactive Oxygen Species), and can induce anomalous protein aggregation behaviour (fibrillation). There are multiple disease targets for the nanoparticles, including all of the known fibrillation diseases (e.g. Alzheimer s and Parkinson s diseases).

The factors that determine which nanoparticles enter the brain are not known. Nanoparticle size, shape, rigidity and composition are considered important, and under physiological conditions, the nature of the adsorbed biomolecule corona (proteins, lipids etc.) determines the biological responses. The NeuroNano project will investigate the detailed mechanisms of nanoparticle passage through the blood-brain barrier using primary cell co-cultures and animal studies. Using nanoparticles that are shown to reach the brain, we will determine the mechanisms of ROS production and protein fibrillation, using state-of-the-art approaches such as redox proteomics and isolation/characterisation of the critical pre-fibrillar species. Animal models for Alzheimer s diseases will confirm the effects of the nanoparticles in vivo. At all stages the exact nature of the nanoparticle biomolecule corona will be determined.

Lay Summary