

The behavior of antigen presenting cells can be altered upon a nanoparticle exposure

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In the past few years, nanoparticles (NP) have been increasingly used for therapeutic and diagnostic applications. From nanometric building blocks, further surface modifications and encapsulations allow developing smart drug carriers or contrast agents for imaging. This extensive use of NP has raised questions, about their potential toxicity and/or effects after natural exposures or medical administration.

The immune system, being specialized in the maintenance of body integrity, may engage responses in the presence of NP. Some of the immune cells, such as dendritic cells (DC) and macrophages, are part of the first line of defenses by their abilities to uptake external material/particles and to deliver signals to other components of the immune system.

We analyzed if NP exposures lead to the alteration of these cell functions by the measure of the phagocytosis and the synthesis of cytokines. Murine DC and J774 macrophage cell line were exposed at sub toxic concentrations to several NP: gold (15nm), Gd based silica (GdSi, 5nm) used as contrast agent, Poly Lactic-co-Glycolic Acid (150nm) and Lipidots® nanoemulsion (60nm) developed as bio carriers.

To study a possible alteration by NP of phagocytosis capacity, J774 macrophages were exposed or not to NP and then incubated with a fluorescein (FITC) stained dextran beads, which was used as probe for phagocytosis measured by flow cytometry. The data showed that NP impact on dextran internalization depended on particle nature: gold strongly altered the phagocytosis whereas GdSi did not.

To study the effects on cell activation, primary DC were cultured from murine bone marrow [1]. Exposure of DC to NP did not lead to their activation nor to the induction of cytokine secretions. However, their responses to known activators, such as bacterial lipopolysaccharide (LPS), were altered by some NP such as gold NP which reduced the production of IL-12 cytokine and increased IL-10 by LPS activated DC.

All together, these results show that analyzed NPs have only little direct effects on DC or macrophages. However, some could lead to alterations impacting on the innate immune system cell physiology. In the case of a gold NP exposure, both phagocytosis and IL-12/IL-10 productions by activated DC were modified. These changes could have consequences in the development of specific immune responses such as Th1, whose regulation is dependent on IL-12.

References.

[1] Villiers, C., H. Freitas et al (2010). "Analysis of the toxicity of gold nano particles on the immune system: effect on dendritic cell functions." *Nanopart Res* 12(1): 55-60