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Potential impact of metal oxide nanoparticles on the immune system: The role of integrins, L-selectin and the chemokine receptor CXCR4

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The impact of metal oxide Nanoparticles (NPs) on the immune system has been studied in vitro using human peripheral blood lymphocytes (PBLs). Metal oxide NPs (ZnO, CeO_2, TiO_2 and Al_2O_3) induced changes in the expression levels of adhesion molecules and the C-X-C chemokine receptor type 4 (CXCR4) in these cells. Proliferation studies were carried out with CFSE in response to PHA, finding an increase in T cell proliferation upon cell exposure to TiO_2 and Al_2O_3 NPs. For ZnO NPs, a decrease in the chemotactic response to SDF-1α was observed. No changes were found in basophil activation and leukocyte oxidative burst after phagocytosis. Despite the absence of cytotoxicity, metal oxide NPs are not inert; they alter the expression levels of adhesion molecules and chemokine receptors, key actors in the immune response, and affect important cell functions such as T cell proliferative response to mitogens and chemotaxis.

Biography

Mercedes Rey is qualified as a specialist in Immunology in 2002 and gained her PhD from the Universidad Autónoma de Madrid (Madrid, Spain) in 2007, for her work on the chemokine receptors in T lymphocytes and their interaction with cytoskeletal proteins. In 2008, she moved to Institut Curie (Paris, France), where she worked on the molecular mechanisms underlying the extracellular matrix degradation associated with metastasis of breast cancer cells. From 2010 she has been working as an Immunologist at the Hospital Universitario Donostia (San Sebastián, Spain), where she combines her assistential duties (dignosing leukaemias and lymphomas by flow cytometry, among others) with research work, especially focusing on the potential adverse effects of the interactions between metallic nanoparticles and the immune cells.

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Antitumor and antioxidant activities of *Escherichia coli* are accompanied by changes in the metabolic pathways of L-arginine and creatine in Ehrlich ascites carcinoma

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A virulent strains of Escherichia coli isolated from healthy humans, exert antitumor and antioxidant activities and affect the subcellular metabolic pathways of L-arginine and creatine in peritoneal leucocyte following Ehrlich ascites carcinoma (EAC). Two days after EAC transplantation, a single non-invasive treatment the eyes and mouth of mice with alive cells of E. coli increases life span by 75 %, and on 11-th day of EAC development decreases thrice the volume of ascites fluid, and inhibits EAC-induced lipid peroxidation (LPO) processes in the peritoneal leucocyte. The level of malondialdehyde (MDA) and its in vitro formation are decreased by 3.2 and 1.8 times in cytoplasm and mitochondria respectively, thus ameliorating deleterious effects of oxidative stress and immunosuppression. EAC caused alterations in the L-arginine metabolism are corrected by bacterial treatment. E. coli-treatment reduces twice the content of L-arginine in the cytoplasm of peritoneal leucocyte which was elevated by 4.4 times in EAC, as well as causes a decrease of arginase and NOS activities in the leucocyte cytoplasm and mitochondria that were increased during EAC. The correlated changes were observed in the peritoneal leucocyte basal levels of ornithine (produced partially by arginase), and generated mainly by NOS reactive nitrogen species and L-citrulline. E. coli-treatment completely suppresses the arginase activity in the EAC-cells and could diminish their proliferation due to inhibition of the synthesis of polyamines. At the same time E. coli-treatment up-regulates the NOS in tumor cells there through stimulates both nitrosation stress and suppression of intracellular antioxidant system. Moreover, E. coli-treatment cancels completely the EAC-induced stimulation of the cytoplasmic creatine kinase (CK) and restores the mitochondrial CK activity in the peritoneal leucocyte (dropped in EAC) stabilizing their structure. Simultaneously, the level of creatine significantly decreased in EAC-cells, disrupting the energy metabolism. In conclusion, it was demonstrated for the first time that E. coli antitumor effects are accompanied by changes in the L-arginine and creatine pathways and oxidative stress processes in the peritoneal leucocyte and tumor cells and should be taken into account in E. coli application in adjuvant cancer therapy.

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