The use of metal oxide nanoparticles as third generation immunotherapy: Phenotypic changes follow changes in the chemical potential.

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Recently, nanomaterials have been proposed for use in the treatment of certain cancers and other human diseases. Among those, Cerium oxide nanoparticles (CeO2NCs) have emerged in biomedical applications due to their multienzymatic character that buffers oxidative stress and Reactive OxygenSpecies (ROS). This material has shown to have both anti-inflammatory and antitumoral behaviour [1]. Previous studies have shown that CeONP is cytotoxic to cancer cells, inducing oxidative stress and causing lipid peroxidation and cell membrane leakage. It is also reported to protect normal cells but not cancer cells from ROS damage. This may be attributed to cancer cells having a more acidic cytosolic pH than normal cells because of higher glycolysis and significantly higher production of lactate. As previously mentioned, in acidic conditions, the antioxidant ability of CeONP is lost and it behaves as a strong oxidant, which may facilitate the oxidation of intracellular and extracellular components to induce cell apoptosis. Besides, more recently superparamagnetic iron oxide (magnetite) NPs have been also shown to play a role with oxidative stress altering the tumour microenvironment, inducing macrophages M1 polarization and resulting into benefitial anti-tumoral effects [2].

It is well known that the ROS can drive both the initial development and progression of cancer, as well as down regulate antioxidant enzymes that normally combat radical production. In cancer, ROS account for its genomic instability, resistance to apoptosis, proliferation, and angiogenesis. Importantly, ROS trigger cancer cell invasion as well as extravasation into distant metastasis sites. In normal, healthy cells, the cellular levels of ROS are tightly controlled. The ability to modulate the redox status of cells has applications in cancer where ROS levels have become deregulated or are altered by treatment. Some studies have shown CeO2NCs to possess innate cytotoxicity to cancer cells, anti-invasive properties, and the ability to sensitize cancer cells to radiation-induced cell death (due to the generation of free radicals by the ionizing radiation), while protecting the surrounding normal tissues. This could be reproduced with Fe3O4 inducing the generation of free radicals in a Fenton like raction and the CeO2 amplifying it.

References

[1] https://www.nature.com/articles/am201388]
[2] https://www.nature.com/articles/nnano.2016.168