Effect of silver doped nanostructured titanium dioxide (TiO_2) on breast cancer epithelial cells

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Abstract

The scientific community approaches the multivariate condition of cancer disease in many ways. There are still aspects of the research field of alternative cancer treatments that remains to be discovered, focusing on minimize the undesirable consequences of the conventional treatment methods. It is now well established that when TiO_2 nanoparticles are photo-excited, the photon energy generates pairs of electrons and holes which react with water and oxygen to yield reactive oxygen species (ROS) which can damage cancer cells. Therefore, TiO_2 is a promising photosensitizer against cancer.

The aim of this study is the development of TiO_2 nanoparticles with the potential to photo-induce anticancer effect via the mechanism of oxidative stress upon irradiation with visible light. Surface modification by doping with metal ions improves TiO_2 photocatalytic activity. This process leads to reduction of electron-hole recombination, resulting in efficient separation and stronger photocatalytic reactions. Particularly, silver is an important dopant, which up-regulates TiO_2 biological activity.

Thus, Ag-doping of TiO_2 was undergone, followed by detailed characterization (XRD, micro-Raman, SEM). Cultured MCF-7 and MDA-MB-468 breast cancer epithelial cells were irradiated, using visible light, in the presence of Ag-doped TiO_2 aqueous dispersion. Cell viability was estimated, by MTT colorimetric assay. Western blot analysis of protein expression and characterization, as well as DNA laddering assay were used to investigate the existence of cell apoptosis.

We demonstrated that Ag-doped TiO_2 nanoparticles induced apoptosis specifically in the highly malignant MDA-MB-468 cancer cells. MCF-7 cells were still unaffected, under the same circumstances. The molecular mechanism of TiO_2 nanoparticles cytotoxicity was associated with increased pro-apoptotic Bax expression and caspase-mediated poly (adenosine diphosphate (ADP)-ribose) polymerase (PARP) activation thus resulting in DNA fragmentation and programmed cell death.

Further studies are already in progress, focalizing at the development of visible-light-excited co-doped TiO_2 nanoparticles with silver and nitrogen, for targeted cancer therapy.

Image

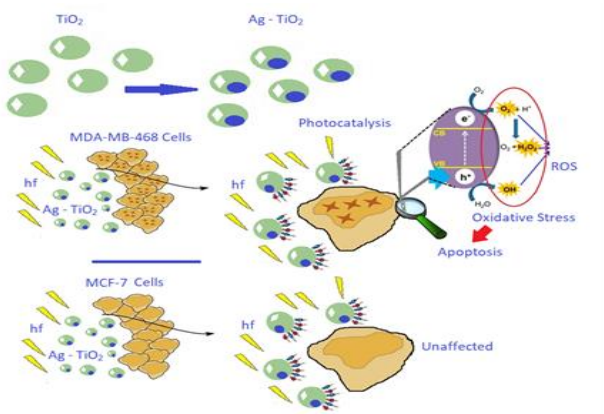

Figure 1. Schematic representation of photokilling effect of Ag-doped TiO_2 on breast cancer epithelial cells. Ag-doped TiO_2 nanoparticles induced apoptosis specifically in the highly malignant MDA-MB-468 cancer cells. MCF-7 cells were still unaffected, under the same circumstances.

Recent publications

1. Yin Z. F., et al. (2013) Recent progress in biomedical applications of titanium dioxide. Phys. Chem. Chem. Phys. 15(14): 4844-4858.
2. Fagana R. et al. (2016) A review of solar and visible light active TiO_2 photocatalysis for treating bacteria, cyanotoxins and contaminants of emerging concern. Mat. Sci. Semicon. Proc. 42: 2–14.
3. Lagopati N., et al. (2014) Effect of nanostructured TiO_2 crystal phase on photoinduced apoptosis of breast cancer epithelial cells. Int. J. Nanomedicine. 9: 3219-3230.
4. Li Z., et al., (2-11) Study on the visible-light-induced photokilling effect of nitrogen-doped TiO_2 nanoparticles on cancer cells. Nanoscale Res Lett. 6 (366): 1-7.
5. Ahamed M. et al. (2017) Ag-doping regulates the cytotoxicity of TiO2 nanoparticles via oxidative stress in human cancer cells. Sci. Reps. 7(1):17662
6. Murugan K et al. (2016) Hydrothermal synthesis of titanium dioxide nanoparticles: mosquitocidal potential and anticancer activity on human breast cancer cells (MCF-7). Parasitol Res.115 (3): 1085-1096.

Biography

Dr. Nefeli Lagopati studied Physics (BSc), Medical Physics (MSc), Advanced Materials (MSc) and Biology (PhD). She works as a postdoc researcher at the National Technical University of Athens, School of Chemical Engineering, and at Molecular Carcinogenesis Group, School of Medicine, University of Athens, where she additionally works as an adjunct lecturer, teaching “Cancer Biology”. Her research interests include the multidisciplinary field of nanomedicine in cancer treatment. Specifically, she focuses on the possible apoptotic effect of nanomaterials on breast cancer cells (IKY Scholarship). In the past, she had worked on (European) research projects, related to dosimetry in nuclear medicine, radiobiology - investigation of chromosomal alterations due to radiation, biochemistry of ROS-induced glutathionylation and evaluation of the role of iron ions, development of drug delivery systems and biomaterials, based on hydroxyapatite and chitosan, Monte Carlo Simulation etc. She is also a classical guitarist (BSc) and loves art and travelling.

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