Nanographene-oxide mediated hyperthermia for cancer treatment

Mercedes Vila

[a]TEMA-NRD, Mechanical Engineering Department and Aveiro Institute of Nanotechnology (AIN), University of Aveiro, 3810-193 Aveiro, Portugal mvila@ua.pt

Abstract

One of the new trends of nanomedicine is the application of nanoparticles for targeting tumors to achieve localized tumor cell destruction while producing minimal side effects on healthy cells, but their application will not be feasible without a previous understanding of vector-cell/tissue interactions, possible toxicity and accumulation risks. [1]

The enhanced permeability and retention effect (EPR), provoked by the angiogenesis process of tumors, allows preferential concentration of nanosystems on the tumor periphery, making hyperthermia mediated by these systems a potential efficient therapy for producing confined tumoral cell death. [2] It can induce lethal damage to cellular components at temperatures above 40 ºC and cancerous cells are subsequently removed by macrophages, causing the tumor to diminish. Although hyperthermia is a well-known concept, little is known about the type of damage, cell death and secondary effects that these nanosystems mediated therapies can provoke locally.

Amongst hyperthermia potential agents, nano graphene oxide (nGO) has been proposed due to its strong Near-Infrared (NIR 700-1100 nm range) optical absorption ability and its unique 2-dimensional aspect ratio. [3] Restricting all dimensions at nanoscale could allow unique performing when compared to any other nanoparticle, but it is mandatory to deeply study the hyperthermia route and the kind of nGO-cell interactions induced in the process.

By optimizing the nGO synthesis, it is possible to diminish the initial cell-particle interactions to reduce possible future toxicity in healthy cells.[3,4] Cell internalization kinetics (specifically for targeting tumoral osteoblasts on a bone cancer model) were established for producing a safe and efficient tumor cell destruction avoiding damage on untreated cells as well as an evaluation of the nature of tumor destruction that could be produced by this hyperthermia treatment.[5,6] The type of cell damage and toxicity produced by NIR laser irradiation was evaluated as a function of exposure time and laser power in order to control the temperature rise and consequent damage in the nGO containing cell culture medium. The results showed that cell culture temperature (after irradiating cells with internalized nGO) increases preferentially with laser power rather than with exposure time. Moreover, when laser power is increased, necrosis is the preferential cell death (Fig. 1). The results suggested that controlling the type of cell death, the threshold for producing soft or harmful damage could be precisely controlled and so, the increase of cytokine release to the medium, having this a direct impact on immune system reactions. Moreover, nGO cell exposure did not stimulate proinflammatory cytokine secretion [7] and nanoparticles incorporation by different cell types either in the absence or in the presence of eight endocytosis inhibitors, showed that macropynocitosis is the general mechanism of nGO internalization, but it can also entry through clathrin-dependent mechanisms in hepatocytes and macrophages. [8]

References

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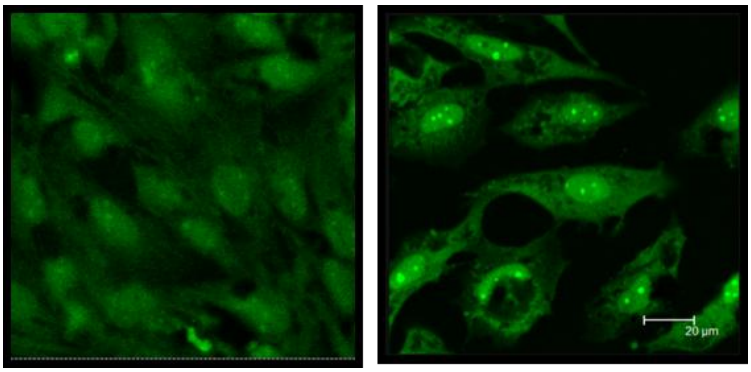

Fig. 1. Morphology evaluation by confocal microscopy of cultured human SAOS-2 osteoblasts in the presence of GOs, before (left) and after 7 min of 1.5 W/cm^2 laser irradiation showing necrotic cells (right).