Nanographene oxide-cell interactions and its potential for tumor destruction

M.Vila[a,c,d], M.C.Matesanz[b], G.Gonçalves[a], M.J.Feito[b], J.Linares[b], P.A.A.P. Marques[a], M.T.Portolés[b], M.Vallet-Regi[c,d]

[a]Nanotechnology Research Division-TEMA, Mechanical Engineering Dpt, University of Aveiro, 3810-193 Aveiro, Portugal
[b]Department of Biochemistry and Molecular Biology I, Faculty of Chemistry, Universidad Complutense, 28040-Madrid, Spain
[c]Department of Inorganic and Bioinorganic Chemistry, Faculty of Pharmacy, Universidad Complutense, 28040-Madrid, Spain.
[d]Networking Research Center on Bioengineering, Biomaterials and Nanomedicine, CIBER-BBN, Spain,
mvila@ua.pt

Abstract

Many applications of graphene in the area of bio and nanomedicine have been proposed and it is important to review its potential with a fine-tooth comb with two main specific objectives: to evaluate if it could possess all the parameters that make a material suitable for its use on the human body, and to specify conditions, applications and materials modifications that could assure materials biocompatibility and a positive biological response.

For example, one of the most novel fields of nanomedicine applied to cancer research is using nanoparticles (NPs) but their application will not be feasible without a previous understanding of NPs-cell/tissue interactions, possible toxicity and accumulation risks. [1] These cancer therapies work through the NPs preferential accumulation in cancerous tissue after intravenous injection due to the combination of leaky vasculature and poor lymphatic drainage which results in what is known as the enhanced and permeability retention effect (EPR). Simultaneously, among the new arising therapies, the hyperthermia of tumours has been investigated as a minimally invasive alternative to surgery that can induce lethal damage to cellular components at temperatures above 40 ºC. Unfortunately, simple heating techniques have trouble discriminating between tumours and surrounding healthy tissues. Thus, by the combination of these two concepts, the localized nanoparticle-based hyperthermia raised as a powerful and potential treatment on its own.

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.[4] nGO cell exposure and its influence on both the innate and the adaptive immune responses was evaluated in murine lymphocytes and there was no stimulation of proinflammatory cytokine secretion assuring a good biocompatibility. [5] Moreover, the nGO incorporation kinetics and mechanisms 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 that it can also entry through clathrin-dependent mechanisms in hepatocytes and macrophages. [6] This fact gives light to which will be the key surface factors in a future design of targeted delivery of this NPs by means of active moieties.

Cell internalization kinetics 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.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 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.[7]

References

[1]. Day ES, Morton JG, West JL. J Biomed Eng 2009 ;131:074001.
[2]. Yang K, Wan J, Zhang et al. ACS Nano 2011;5:516-22.
[3] Gonçalves G, Vila M, et al. Adv. Healthcare Materials. 2013; 2(8):1072
[4] Vila M, Portolés MT, Marques PAAP, Feito et al. Nanotechnology 2012; 23:465103.
[5] MJ. Feito, M. Vila , MC. Matesanz et al J Colloid Interface Science 2014; 432, 221.
[6] J.Linares, M. C. Matesanz, M. Vila et al ACS applied materials & interfaces 2014; 27,13697.
[7] Vila M, Matesanz MC, Gonçalves G, et al. Nanotechnology 2014 (25) 035101.

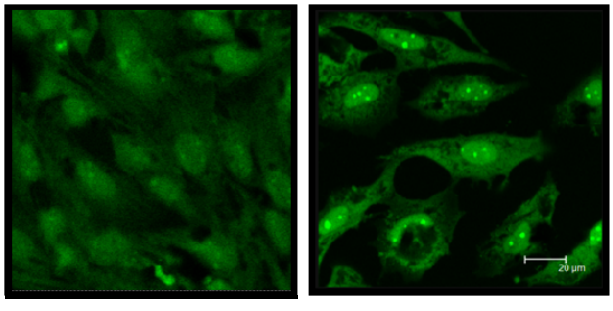

Fig. 1. Morphology evaluation by confocal microscopy of cultured human Saos-2 osteoblasts in the presence of GOs, before (left) and after 7 min of 1.5 W/cm^2 laser irradiation showing necrotic cells (right).