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Author: Mr. Attilio Marino
Italian Institute of Technology (IIT), Italy, attilio.marino@iit.it

Ms. Antonella Rocca
Italian Institute of Technology (IIT), Italy, antonella.rocca@iit.it
Ms. Veronica Rocca
University of Pisa, Italy, vero9988@hotmail.it
Dr. Stefania Moscato
University of Pisa, Italy, s.moscato@med.unipi.it
Mr. Giuseppe de Vito
Italian Institute of Technology (IIT), Italy, giuseppe.devito@iit.it
Dr. Vincenzo Piazza
Italian Institute of Technology (IIT), Italy, vincenzo.piazza@iit.it
Dr. Barbara Mazzolai
Italian Institute of Technology (IIT), Italy, barbara.mazzolai@iit.it
Dr. Virgilio Mattoli
Italian Institute of Technology (IIT), Italy, virgilio.mattoli@iit.it
Dr. Jennifer Ngo-Anh
European Space Agency (ESA), The Netherlands, jennifer.ngo-anh@esa.int
Dr. Gianni Ciofani
Italian Institute of Technology (IIT), Italy, gianni.ciofani@iit.it

HYPERGRAVITY ENHANCES NANOPARTICLE UP-TAKE BY STEM CELLS: IMPLICATIONS IN BIOMEDICINE

Abstract

The control of proliferation and differentiation of mesenchymal stem cells (MSCs) represents a key issue in tissue engineering and regenerative medicine. Among different strategies raised in the latest years, nanomaterials not only represent a powerful tool for fostering the expansion and the differentiation of MSCs [1], but also an innovative system for drug and gene delivery [2]. Another efficient physical cue, shown to be able to modulate muscle [3] and bone [4] cell differentiation, is the application of altered gravitational forces. Aiming at synergistically combining these two approaches, in this work we propose for the first time to take advantage of hypergravity stimulation in order to enhance nanoparticle internalization inside cells. At this purpose, we investigated the internalization of ceramic nanovectors, barium titanate nanoparticles (BTNPs), inside MSCs both in altered gravity (20 g) and normal gravity (1 g) conditions. Simulation of hypergravity was performed by using the Large Diameter Centrifuge (LDC) of the European Space Agency (ESA, Noordwijk, The Netherlands) during the “Spin Your Thesis!” 2013 campaign. Cells were incubated for 3 hours with 20 μg/ml of nanoparticles, both at 20 g and at 1 g, as control. Assessment of BTNP internalization was carried out thanks to two different imaging approaches, based on confocal fluorescence microscopy and Coherent Anti-Stokes Raman Spectroscopy (CARS). Interestingly, the results shown as this short-time of hypergravity stimulation significantly increased the BTNP up-take by MSCs in terms of percentage of cytoplasmatic area occupied by nanoparticles (1.5 $\pm$ 0.2 % at 1 g conditions vs. 2.7 $\pm$ 0.3 % at 20 g; $p < 0.05$). This increment was detected not only

immediately after the hypergravity treatment, but also after two days since the stimulation in samples undergone to osteogenic differentiation (3.7 $\pm$ 0.4 % at 1 g conditions vs. 6.6 $\pm$ 0.9 % at 20 g; $p < 0.05$). Obtained findings are, in our opinion, extremely interesting for an improved exploitation of nanomaterials in biomedicine, for example aiming at increasing the drug delivery and DNA transfection efficiency, and open new perspectives in the field of tissue engineering and regenerative medicine.

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