June 8, 2016

The Japan Society of Mechanical Engineers
Hokkaido Branch
"Biomechanics Research Meeting"
23rd Seminar

Chairman: Toshiro Ohashi

The Biomechanics Research Meeting will sponsor a presentation by Prof. M. Ricardo Ibarra from University of Zaragoza, Spain. Faculty members, graduate students, and undergraduates are encouraged to participate in the seminar.

Date&Time: June 24, 2016, 11:00-12:00

Place: Room#A1-17, Faculty of Engineering, Hokkaido University
http://www.eng.hokudai.ac.jp/building/?place=outer

Speaker: **Prof. M. Ricardo Ibarra, Ph.D.**
University of Zaragoza, Spain

Title: **Magnetic nanoparticles for new therapies and diagnosis**

Magnetic nanoparticles (MNPs) constitute nowadays a vast field of research due to the current and expected application in nanobiomedicine. The potential MNPs stems from the intrinsic properties of their magnetic cores, combined with the functionality acquired under an appropriate coating. The capability for loading and targeted controlled release of drugs is one of the main issues in cancer therapy (for recent reviews see [1,2]). The biofunctionalization of the nanoparticles surface make them suitable for magnetic separation based on the biomolecular recognition of biological moieties. New inmunomagnetic assays using magnetic nanoparticles provides a new route to quantize the results in biosensors. The presence of MNPs also perturb locally the hydrogen proton relaxation, this phenomenon is on the bases of the enhance MRI diagnostic using contrast agents. Targeting of these contrast agents could detect angiogenesis processes at early stages.

In this talk a brief review of all these different applications will be depicted emphasizing the application of electromagnetic waves in new therapies based on magnetic hyperthermia. The case of dendritic cells (DCs) as main candidate for magnetic hyperthermia will be reported. Magnetic hyperthermia (MH) is based on the use of MNPs to selectively increase the temperature of MNP-loaded target tissues when applying an alternating magnetic field (AMF) in the range of radiofrequency. To date, all MH research has focused on heat generation in an attempt to elucidate the mechanisms for the death of MNP-loaded cells submitted to AMF. However, recent in vitro studies have demonstrated the feasibility of inducing dramatic cell death without increasing the macroscopic temperature during AMF exposure. Here, we show that the cell death observed following AMF exposure, specifically that of MNPs loaded dendritic cells (DCs) in culture, was caused by the release of toxic

agents into the cell culture supernatants and not due to a macroscopic temperature increase[3]. We performed MH in vitro experiments to demonstrate that the supernatant of the cell culture following AMF exposure was highly toxic when added to control unloaded DCs, as this treatment led to nearly 100% cell death. Therefore, our results demonstrate that heat is not the only agent responsible for triggering cell death following MH treatment. This finding offers new perspectives for the use of DCs as the proverbial Trojan horse to vectorise MNPs to the target tumour area and these results further support the use of DCs as therapeutic agents against cancer when submitted to AMF. Furthermore, this discovery may help in understanding the mechanism of cell death mediated by exposure to AMF.

[1] "Magnetic nanoparticles for drug delivery" M. Arruebo, R. Fernandez-Pacheco, M.R. Ibarra and J. Santamaría. Nanotoday 2 (2007) 22

[2] "Magnetic nanoparticles for cancer therapy" G.F: Goya, V. Grazu and M.R. Ibarra. Current Nanoscience 4 (2008) 1-16

[3] "Induced cell toxicity originates dendritic cell death following magnetic hyperthermia treatment" L Asín, G F Goya, A Tres & M R Ibarra. Cell Death and Disease 4, e596 doi:10.1038/cddis.2013.121 (http://www.nature.com/cddis)

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