Ferromagnetic nanoparticles as delivery system of antitumor drugs for targeting breast cancer cells

Ana Lazaro-Carrillo[*1,2], Macarena Calero[1,2], Pierre Couleaud[2], Antonio Aires[2], Alfonso Latorre[2], Álvaro Somoza[2], Aitziber L. Cortajarena[2], Rodolfo Miranda[2,3] and Angeles Villanueva[1,2]

[1] Universidad Autónoma de Madrid, Departamento de Biología, Darwin 2, 28049 Madrid, Spain.
[2] Instituto Madrileño de Estudios Avanzados en Nanociencia (IMDEA Nanociencia), Faraday 9, 28049 Madrid, Spain.
[3] Universidad Autónoma Madrid, Departamento de Física de la Materia Condensada, Francisco Tomás y Valiente 7, 28049 Madrid, Spain.
ana.lazaro@imdea.org / ana.lazaro@uam.es

In the last century there has been a spectacular development of chemotherapeutic drugs against cancer. Nowadays a huge amount of cancer types are treated with different antitumor agents, however they produce multiple side effects. Nanotechnology-based approaches hold substantial potential for improving the care of patients with cancer.
In this work we have used biocompatible magnetic nanoparticles (MNPs) coated with dimercaptosuccinic acid (DMSA) called MF66. Anti-neoplastic drug doxorubicin (DOX) and pseudopeptide Nucant (N6L) have been immobilized onto DMSA coating by electrostatic interactions.
After 24 h incubation MNP-DOX were efficiently internalized by human breast cancer cells (MDA-MB-231). This fact was confirmed by fluorescence microscopy and Prussian blue staining, producing an increased uptake by MNP-N6L. We assessed DOX linked to MNPs was more efficiently retained into cells than free DOX. Up to 48 h after MNP-DOX incubation aberrant mitosis were appeared and later, 72 h after treatment, apoptosis and mitotic catastrophe cell death were triggered. We confirmed these results by α-tubulin (see Fig. 1) and caspase 3 immunofluorescence and flow cytometry and in addition this process was filmed by time-lapse video microscopy. Finally Alamar blue assay and Trypan blue were carried out to evaluate cytotoxicity of these formulation, showing a great pharmacological activity of the drug reducing cell viability approximately to 50% and many of the remaining cells enter senescence state.
In summary, these multifunctionalized magnetic nanoparticles seems a promising tool as therapeutic agent, due their ability to produce efficient drug delivery and cancer cells inactivation.

* This work was partially supported by grants from EU-FP7 (no 262943) and Spanish Ministry of Economy and Competitiveness (CTQ2013-48767-C3-3-R)

References

[1] Calero, M.; Gutiérrez, L.; Salas, G.; Luengo, Y.; Lázaro, A.; Acedo, P.; Morales, MP.; Miranda, R.; Villanueva, A. Nanomedicine **10** [2014] 733-43.

Figures

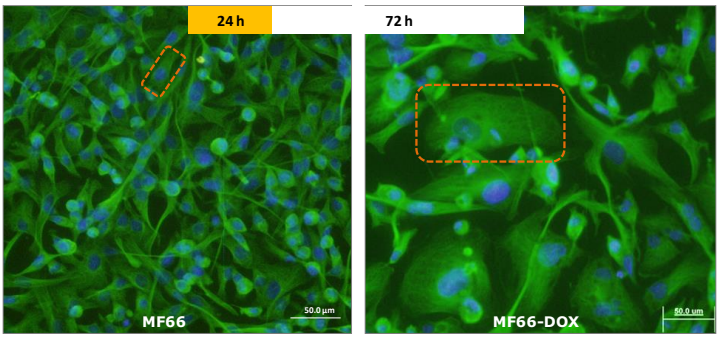

Figure 1. Immunofluorescence for α-tubulin (green) and DNA counterstained with Hoechst-33258 in MDA-MB-231 cells. Left image: cells incubated with MF66 without functionalization. Right image: cells incubated with MF66-DOX at the same magnification, where doxorubicin induced increased cell size.