Dendritic cell uptake of magnetic nanoparticles for magnetic hyperthermia

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Dendritic cells (DCs) are the most important antigen presenting cells (APCs) and as its prime function play a key role in both innate and adaptive immune response. Dendritic cells and endothelial cells are closely related and *in vitro* studies have demonstrated that monocytes and dendritic cells transdifferentiate into endothelial cells in the presence of proangiogenic factors as vascular endothelial growth factor (VEGF). Vasculogenesis, which is the recruitment of endothelial progenitor cells circulating in peripheral blood, contribute to the neovascularization, a cardinal process for the tumor surviving.
Our main aim in this project is to vectorize dendritic cells, previously charged with magnetic nanoparticles (MNPs), to tumor microenvironment to become part of the new vessels by vasculogenesis. Once there, applying an alternate magnetic field we can rise the temperature of the cells causing their destruction and subsequently the damage of the vessels avoiding the nutrition of the tumor and its regression or death.
The particles used in these experiments consist of a magnetite core covered by dextran and functionalized with COOH- groups at the surface. A second type of NPs composed of a latex nucleus and fluorescent markers at the surface were used to verify the distribution within the cells using confocal microscopy (see figure). Both of them have the same hydrodynamic ratio of 250 nm and COOH- surface groups. We have investigated the internalization of magnetic nanoparticles (MNPs) into DCs and analyzed the viability of the cells after having been cultured with MNPs. After cheking that the particles have no toxic effect on the cells we have undergone the cells to an external alternate magnetic field and measure the cell viability using three different methods: Trypan Blue, MTT and Flow Cytometry. High levels of cell death (up to 90%) were observed after application of magnetic fields, only for those cells that were previously loaded with MNPs. The quantification of the MNPs into the DCs has been done using a SQUID (Superconducting Quantum Interference device).

Current projects and activities:

(1) Proyecto Multidisciplinario: “Vectorización de Nanoparticulas Magnéticas a través de células dendríticas y su utilización em Hipertermia Magnética para Terapia Oncológica.” Diputacion General de Aragon (DGA).
(2) Consolider-Ingenio2010. “Nanobiomed: Nanotechnologies in Medicine” MICINN.

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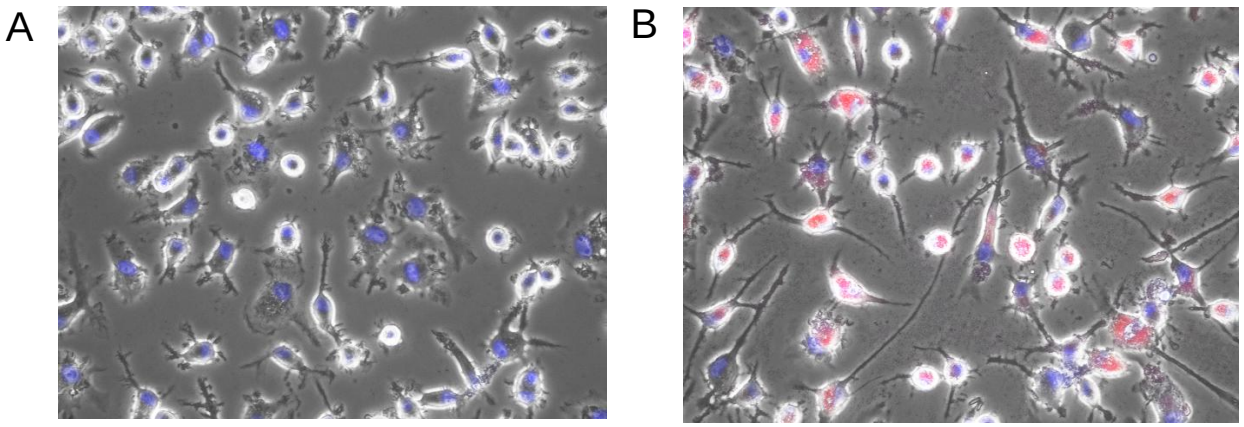
Figures:



Fluorescent microscopy of DCs seeded on fibronectin- coated coverslips and stained with DAPI (BLUE) which is a nucleus dye. **A**: DCs without NPs. **B**: DCs having been cultured overnight with fluorescent NPs-Rhodamine (RED).