Breast cancer cell death induced by magnetic nanoparticles subjected to AC magnetic fields

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Iron oxide nanoparticle-based platforms have been investigated extensively for their potential applications on oncology and other biomedical fields.[1] Their magnetic properties have opened the possibility to develop more efficient and selective cancer diagnostic and therapeutic approaches than the current-ones. Coating these nanoparticles with polyester and polysaccharide materials renders biocompatibility, high charge levels and stabilisation against agglomerations and opsonisation under physiological conditions. This combination of properties favours cell internalization[2] and therefore promising perspectives on biomedical applications. Magnetic nanoparticles into a cell allow thermal treatment approach when subjected to AC magnetic fields at high frequencies (in the range of hundreds of kHz). The magnetic energy dissipation into heat and/or the Brownian motion of the nanoparticles into the cell may induce apoptotic mechanisms and consequently lead to cell death.

Here, we report on *in vitro* studies to determine the cell death mechanisms in cancer cells induced by internalized iron oxide nanoparticles subjected to AC magnetic fields up to 600 G in intensity and 500 kHz in frequency. We employ the cell line, in particular, human breast cancer (MDA-MB-231 cells). Iron oxide nanoparticles with sizes around 10 nm were synthesized by thermal decomposition method in organic media.[3] In a second step, the nanoparticles were coated with dimercaptosuccinic acid (DMSA) to remove the oleic acid in an aqueous solution where nanoparticles aggregate forming colloids with a hydrodynamic radius smaller than 100 nm.[4] Standard methyl thiazol tetrazolium bromide (MTT) assays were carried out in MDA-MB-231 cells incubated 24 h with DMSA (0.5 mg Fe/ml) and subsequently subjected under different exposure times to AC magnetic fields with different strength and frequency conditions. Cancer cells without internalized nanoparticles were also subjected to similar AC magnetic fields conditions as control. Optical microscopy was used to evaluate the effect of the applied AC magnetic fields on the morphology of the different samples.

MTT assays showed that cell survival was not affected by the nanoparticle internalization into the cells or by the electromagnetic field on cells without nanoparticles. As an example, Figure 1 shows an optical microscopy image of the magnetic nanoparticles internalized inside the MDA-MB 231 cells. However, the application of the alternating electromagnetic field to cells preincubated with DMSA-nanoparticles led to a significant cell death. Figure 2b shows the morphological changes observed by optical microscopy in these preincubated cells induced by application of an AC magnetic field at high frequency, in comparison with a control sample constituted by MDA-MB-231 cells (Fig. 2a). Furthermore, we have observed that cell death rate increases with magnetic field strength and frequency which might be due to a heat transfer effect from the iron oxide nanoparticles into the cells under application of AC magnetic fields.

References

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Figures

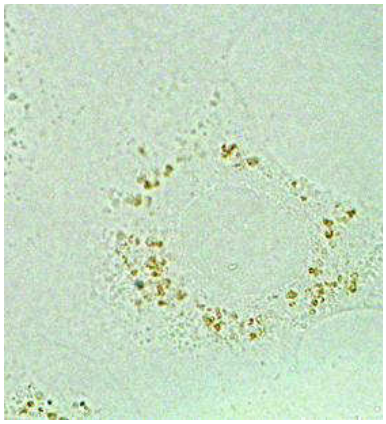

Figure 1. *Nanoparticles internalized inside living MDA-MB 231 cells after 24 h incubation with DMSA (0.5 mg Fe/ml). The intracellular pattern distribution consists in brown cytoplasmic spots of different sizes.*

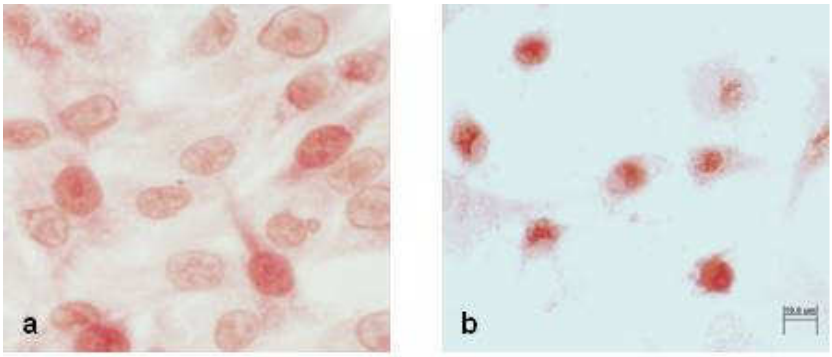

Figure 2. *MDA-MB 231 cells fixed and stained with neutral red. a) Control cells. b) Morphological changes induced by application of an AC magnetic field on cells preincubated with DMSA-nanoparticles.*