Project Title: Magnetic particles and nanowires for non-invasive cancer cell destruction by controlled magnetomechanical actuation
Project Acronym: MagneAct
Project Code: PN-III-P4-ID-PCE-2020-2381
Contract Number: PCE 20 / 2021
Host Institution: Institutul Național de Cercetare-Dezvoltare pentru Fizică Tehnică – IFT Iași
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Short Summary of the Final Report

The results obtained within this project have a particular impact on the application of magnetic particles in cancer therapy, highlighting a series of important new results in this area. We emphasize the novelty of these results both as new materials and as a new application.

Magnetic particles with the compositions $Fe_{68.2}Cr_{11.5}Nb_{0.3}B_{20}$, $Fe_{66.7}Ti_{13}$ $Nb_{0.3}B_{20}$, $Fe_{66.7}Mn_{13}$ $Nb_{0.3}B_{20,}$ were made by mechanical grinding of amorphous ribbons obtained by rapid quenching from the melt. Magnetic nanowires of CoFe, NiFe, Co and Ni were prepared by electrolytic deposition in porous alumina membranes.

Specific tests have shown that Fe-(Cr/Mn/Ti)-Nb-B type particles from the mentioned compositions as well as Ni, Co, Ni-Fe and especially Co-Fe nanowires are biocompatible in vitro with osteosarcoma (OS) cancer cells, adipose derived stem cells (ADSC) cells and normal fibroblast (FB) cells using different concentrations of nanoparticles/nanowires.

Specific tests of the viability of OS, ADSC and FB cells subjected to magnetic actuation in a rotating magnetic field showed that Fe-(Cr/ Mn/ Ti)-Nb-B type magnetic particles and magnetic nanowires (Co-Fe) can be used to achieve the destruction of cancer cells by means of magnetomechanical actuation without damaging healthy cells.

Starting from the known fact that STEM cells move by themselves to tumor areas or to areas presenting inflammation, we studied the possibility of using these cells to transport the particles produced by us to tumor areas where they are released by magnetomechanical actuation. In this sense, we determined the quantity of internalized particles inside ADSC cells, confirming that these cells can be used as a transport vehicle for MNP. We performed experiments to determine the mobility of particle-loaded and non-particle-loaded ADSC cells to tumor areas, establishing that the mobility of particle-loaded cells is higher and the cells can be used as carriers for the MNP. We evaluated the level of destruction induced to MNP loaded ADSC cells by magnetomechanical actuation, the release of particles in the area of cancer cells followed by their uptake and the destruction of OS by magnetomechanical actuation. Once these results were obtained, we pursued the possibility of associating the effect of destruction of cancer cells by magnetomechanical effect, with the delivery of anticancer drugs in the tumor area to increase the speed of destruction of cancer cells. We studied the ability of magnetic particles to adsorb antitumor drugs (7.45% w/w for mitoxantrone and 7.02% w/w for doxorubicin) and their subsequent release. We found that these particles adsorb significant amounts of the mentioned

drugs, especially due to a residual surface layer of oleic acid from the grinding process, and that they can release these drugs in the area of cancer cells. By combining magnetic actuation with the release of drugs, the speed of destruction of cancer cells is considerably increased. Final tests showed that drug-coated magnetic particles can be transported by STEM cells and released in a controlled manner into the tumor area.

Within this project we confirmed the possibility of actuating magnetic particles and magnetic nanowires in a rotating magnetic field, leading to the destruction of cancer cells by direct magnetomechanical effect or in association with other processes such as the use of STEM cells as transport vehicles for magnetic particles or magnetic nanowires, including coated with antitumor drugs.

These results represent important contributions to the identification of new methods of action in cancer therapy, using new magnetic materials and processes. The implementation of these results towards their actual use in the medical process depends essentially on how these results are brought to the attention of the scientific community. For this reason, we paid special attention to the dissemination of these results by presenting them at important international conferences, through direct discussions with specialists and by publishing them in prestigious international journals.

Thus, during the project, 10 scientific papers were presented at prestigious international conferences (5 planned).

Furthermore, 5 scientific papers were published in ISI indexed journals (4 planned), 1 paper was published in a journal indexed in international databases (unplanned), we registered an invention patent at OSIM, (1 planned), a book edited by two members of the project team was published in the Elsevier publishing house, in which 3 chapters were written by authors who are members of the project team (2 planned).