Sub-5nm silica-coated superparamagnetic iron oxide fluorescent nanoparticles for application in stem cell-based therapy through magnetic targeting of human mesenchymal stromal cells

Ledda M.[a*], Fioretti D.[a*], Lolli M.G.[a], Mecchia A.[a], Papi M.[b,c], Di Gioia C.[d], Carletti R.[d], Ciasca G.[b,c], Foglia S.[e], Marchese R.[f], Grimaldi S.[a], Rinaldi M. [a#], Lisi A.[a#]

[a] Institute of Translational Pharmacology (IFT), National Research Council (CNR), Rome, 00133, Italy.
[b] Fondazione Policlinico Universitario A.Gemelli IRCSS, Rome, 00168, Italy.
[c] Institute of physics, Cattolica del Sacro Cuore University, Roma, Italy
[d] Sapienza University, Department of Radiological Sciences, Oncology and Pathology, Rome, 00161, Italy.
[e] Institute of Materials for Electronics and Magnetism (IMEM), National Research Council (CNR), Parma, 43124, Italy
[f] Research Center FBF S. Peter Hospital, Rome, 00189, Italy.
*These authors shared first authorship.
#These authors shared senior authorship.
e-mail: antonella.lisi@ift.cnr.it - monica.rinaldi@ift.cnr.it

Keywords: Superparamagnetic Iron oxide nanoparticles; stem cell therapy; magnetic targeting; biocompatibility; human amniotic mesenchymal stromal cells

Over the last decade, the attention on biotechnological nanomaterials has largely increased and in this field, iron oxide nanoparticles (IONPs) have attracted a great interest for their intriguing properties and biomedical applications [1].
One of the main limitations of the stem cell-based therapy is the cell delivery to the site of interest and the low efficiency of engraftment. One promising application of IONPs is the magnetic delivery of stem cells to target tissues that promotes their engraftment through the application of an external magnetic field at the site of interest [1] [2].
In this study, we used new-synthesized ultrafine 3nm Fe_3O_4 superparamagnetic water-dispersible nanoparticles, named-5nm silica-coated magnetic iron oxide fluorescent (sub-5 SIO-Fl) [3].
The aim of this work was to assess cellular uptake and biocompatibility, of sub-5 SIO-Fl nanoparticles in human amniotic mesenchymal stromal cells (hAMSCs). Phase contrast and fluorescence microscopy analyses were performed to study nanoparticles internalization whereas their up-take was evaluated through the iron assay. hAMSCs growth, viability and distribution of cell cycle phases resulted unaffected following nanoparticles internalization. At last, the possible nanoparticles influence on hAMSC stemness and differentiation capability was analyzed revealing that sub-5 SIO-Fl do not induce effects on stemness and differentiation marker expression after their internalization.

[1] N.V.S. Vallabani and S. Singh, 3 Biotech. 8 (2018)
[2] L.H. Silva et al., Stem cell research & therapy 8 (2017).
[3] S. Foglia et al., Sci Rep. 7 (2017)

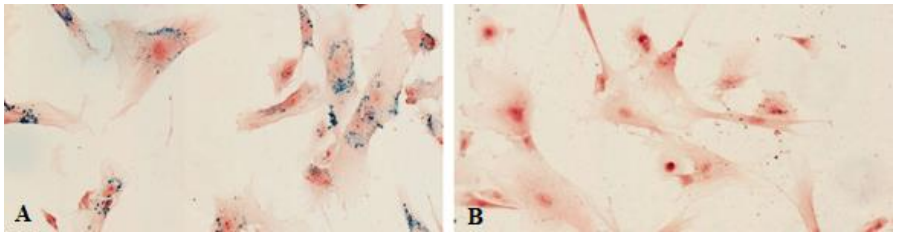

Figure 1. Blue Prussian staining used to detect the internalization of iron in hAMSC after 48h of exposure at 50μg/ml of sub-5 SIO-Fl nanoparticles (A) in comparison with the untreated control cells (B).

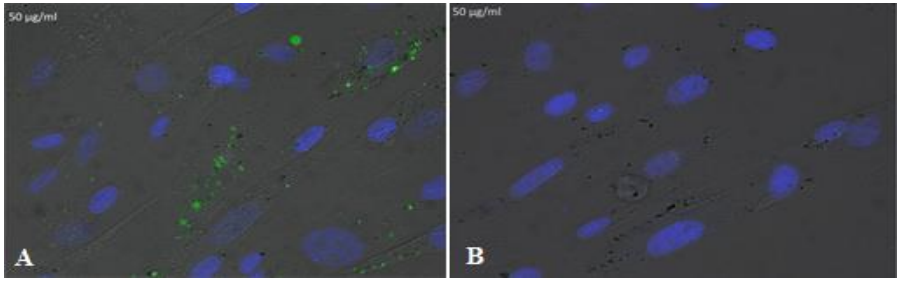

Figure 2. A phase contrast microscopy image and a fluorescence microscopy image have been overlapped to detect the cellular internalization of sub-5 SIO-Fl nanoparticles functionalized with FITC (green) after 48h of exposure at a concentration of 50μg/ml (A), in comparison with the untreated control cells (B).

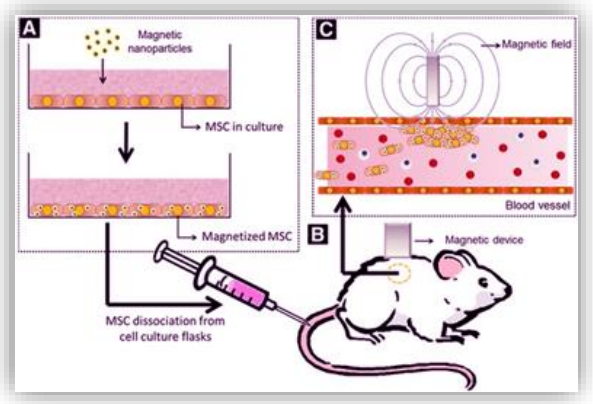

Figure 3. Magnetic targeting of Mesenchymal stromal cells (MSC) representation. (A) MSC are expanded in culture and exposed to magnetic nanoparticles which are internalized by the cells. (B) Magnetized MSC are transplanted into animals, which are exposed to static magnetic field to lead the stem cells to the target tissue. (C) MSC delivery and engraftment into site of interest through magnetic delivery.