Specific magnetic cell separation using receptor-mediated endocyted iron oxide nanoparticles

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Abstract

Medical applications of magnetic nanoparticles (MNPs) have attracted too much interest recently. This applications include magnetic cell separation, magnetic detection, magnetic resonance imaging (MRI) contrast agent, drug delivery and gene transfection[1]. The aim of the research in which this work is included is to design and develop a tumor cell detection method by means of magnetic nanoparticles sensing. The measurement method is based on the giant magneto-impedance (GMI) effect which consists of a change in the complex impedance of a ferromagnetic conductor induced by the variation of an applied magnetic field. A GMI-based sensor has already been proposed as a biosensor with high sensitivity to the weak field produced by magnetic nanoparticles[2]. Similar nanoparticles have been detected embedded inside human embryonic kidney cells[3].

Nanoparticles composed of a ferromagnetic core (Fe_3O_4) and a biocompatible surface coating including specific targeting ligands were used. The synthesis of the ferromagnetic core is performed using a modified Massart method[4], which allows obtaining 10-15 nm diameter particles. Surface functionalization of nanoparticles is necessary to assure that the nanoparticles attach exclusively to the desired area or cell target. This could be achieved if the MNPs are functionalized with a specific antibody. In this work, the nanoparticles were functionalized with human α-MICA, because of the relation of MICA receptor with antitumor immunity[5]. The process of functionalization consist of a three step streptavidin-biotin method: first, the nanoparticles are covered with streptavidin, second, the specific antibodies are tagged to biotin; and as the last step, the streptavidin and biotin are attached, resulting in functionalized particles.

Finally, two different cell cultures were infected by the nanoparticles, HeLa and HL60 cells. MICA is gently expressed on the cell surface in HeLa cells, but HL60 does not express MICA. Results shows that magnetic nanoparticles tags specifically the HeLa cells and can be concentrated by application of a magnetic gradient field, but does not tag to HL60. Separated HeLa cells were analyzed by transmission electron microscopy, showing that the nanoparticles were receptor-mediated endocyted by HeLa cells.

References

[1] Q A Pankhurst, J Connolly, S K Jones and J Dobson. *J. Phys. D: Appl. Phys.* **36** R167.

[2] G.V. Kurlyandskaya, M.L. Sánchez, B. Hernando, V.M. Prida, P. Gorria and M. Tejedor, Appl. Phys. Lett. **82**, (2003) 3053.

[3] A. Kumar, S. Mohapatra, V. Fal-Miyar, A. Cerdeira, J.A. García, H. Srikanthy, J. Gass and G.V. Kurlyandskaya, Appl. Phys. Lett. **91**, (2007) 143902.

[4] C. Massart, IEEE Trans. Mag., **MAG-17** (1981) 1247.

[5] S. González, A. López-Soto, B. Suárez-Álvarez, A. López-Vázquez and C. López-Larrea, Trends in Immunology 29 (2008) 397.

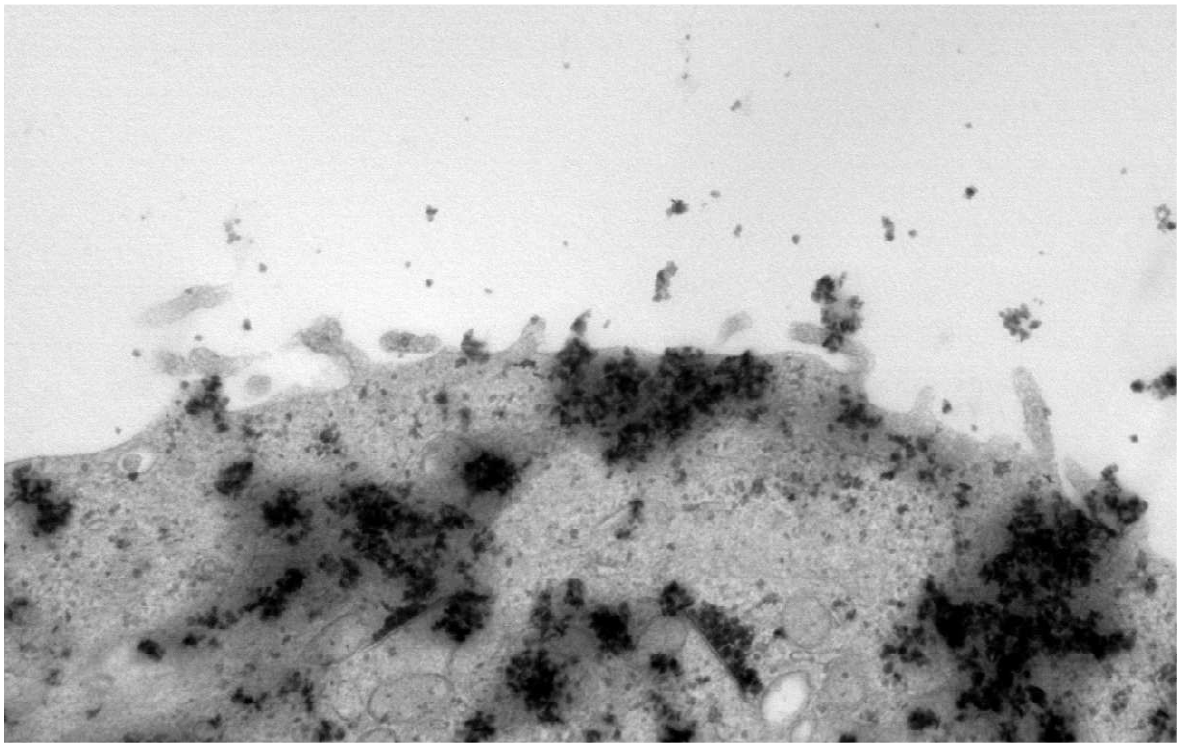

Figure 1: Transmision Electron Micrografy of HeLa cell with endocyted iron oxide nanoparticles.