Interaction of targeted of magnetoliposomes with Hela epithelial carcinoma and 3T3 fibroblasts cell lines.

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Abstract

In the last years, the development of iron oxide magnetic nanoparticles (IONPs) has significantly increased with respect to other nanosized particles because of their attractive properties as theranostic agents [1]. These systems combine both, therapeutic and diagnostic properties. In order to improve their versatility and biodisponibility, IONPs can be incorporated into liposomes, resulting in a new kind of nanoscale system, known as magnetoliposomes (MLs) [2]. MLs, which are biodegradable and highly versatile especially in composition, have opened great expectations for the development of personalized medicine [3]. Any biomedical use of MLs entails thorough understanding of their toxicology, establishment of principles and test procedures to ensure safe manufacture and usage, and comprehensive information about their safety and potential hazard [4]. In this way, we have designed MLs appropriate for theranostic applications. However, previously to any biomedical application, the lack of inherent toxicity must be checked. To this end, the following study has been performed according to the following steps: i) synthesis of IONPs; ii) incorporation of IONPs into liposomes of different lipid composition and, iii) analysis of the cytotoxicity and internalization of MLs in cell models. IONPs coated with polyethylene-glycol (PEG) were synthesized by the coprecipitation method according to the procedure described elsewhere [5]. As far as the lipid composition is concerned, three different lipid mixtures have been prepared, namely, a) bare liposomes: dimyristoylphosphatidylcholine (DMPC)/cholesterol (CHOL): 8:2; b) bare liposomes with PEG (DMPC/CHOL/PEG: 8:2:0.3) and; c) functionalized MLs or bare liposomes with the cyclic RGD peptide (DMPC/CHOL/PEG/RGD_c: 8:2:0.3:0.03). For internalization studies, MLs were decorated with the fluorescent label 0.05% Rhodamine-B.
The model cells chosen for the study were 3T3 fibroblasts and Hela epithelial carcinoma cell lines. Both cells are rich in integrin membrane proteins but they are different concerning which kind of ligand is recognized. In this way, 3T3 is rich in collagen-receptor integrins, whereas HeLa in RGD-receptor integrins. Therefore, the rationale of MLs compositions was the selective targeting of the functionalized MLs towards HeLa cells. Thus, bare and PEG-MLs are considered control MLs with no affinity for the above mentioned cells. Results obtained by confocal microscopy and flow cytometry were concordant with the possibility of the formation of the so called protein corona around the MLs [6].
Potser referenciar les figures 1 I 2 al text.

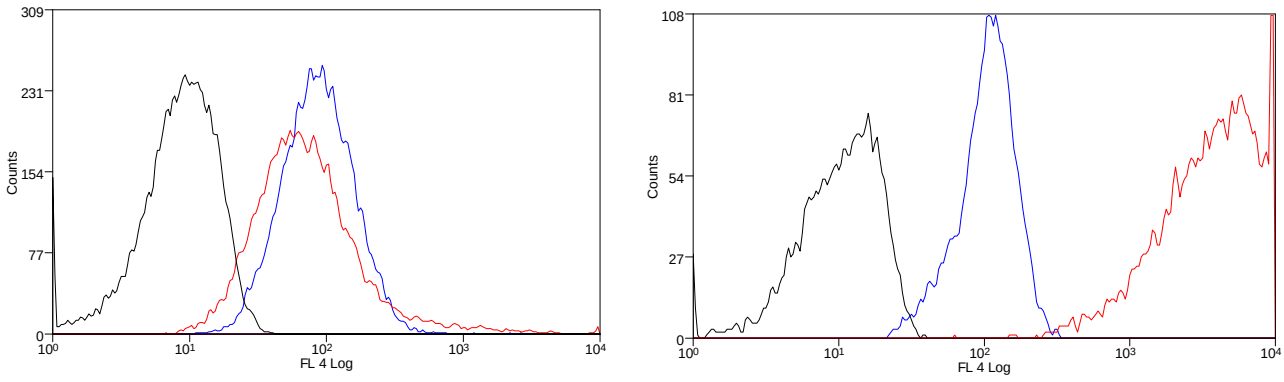

Figure 1. Flow cytometry of control (black); bare MLs of DMPC/CHOL/Rho-PE (80:20:0.05) (red) and, functionalized MLs DMPC/CHOL/PEG/RGD_c/Rho-PE (80:20:3: 0.3:0.05) incubated 4h with 3T3 cells (left) or Hela cells (right).

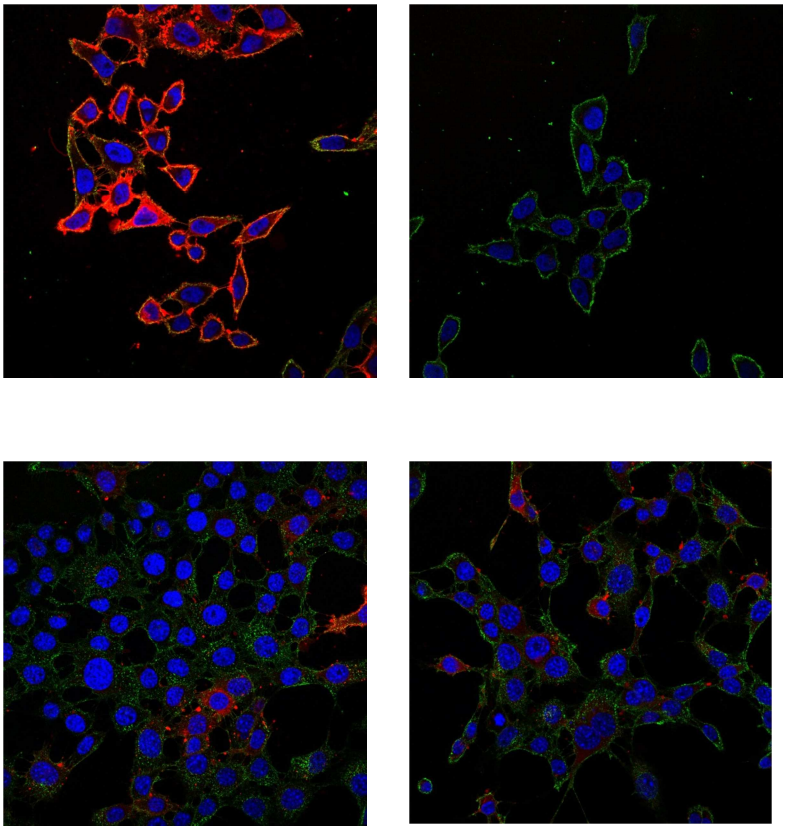

Figure 2. Laser confocal microscopy images of bare (left) and functionalized (right) MLs upon incubation for 4h with 3T3 cells (top) and Hela cells (bottom). Membrane cell was labeled with Alexa; the nucleus with DAPI and magnetoliposomes with Rhodamine B.

References

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