Oxaliplatin-loaded magnetoliposomes associated to LGR5 for targeted therapy of colorectal cancer

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Abstract

Introduction: Oxaliplatin (OXA) is one of the of the main chemotherapeutic drugs for colorectal cancer (CRC) treatment, the third most frequent cancer worldwide. In advanced stages, CRC has a five-year survival rate of 14%, with the appearance of multiple resistances being one of the main problems in treatment failure. In this context, colorectal cancer stem cells (CSCs), which are derived from intestinal stem cells positive for LGR5 marker, appear to be responsible for resistance to chemotherapy, radiotherapy and the development of metastases [1]. Thus, the development of new nanoformulations that selectively target colorectal CSCs appears as a promising strategy to improve the prognosis of these patients. In this context, magnetoliposomes (MLPs) are a type of nanocarriers with multiple properties, such as the controlled release of anti-tumor agents, active targeting through binding monoclonal antibodies and high bioavailability [2,3].
Materials and Methods: Protein expression of the LGR5 marker was analyzed by western blot in colorectal cancer cell lines MC38 and T84, in normal colon cell line CCD18, and in the hepatocellular carcinoma control line HepG2. MLPs loaded with OXA (MLP-OXA) (Fig.1) were synthesized, functionalized with anti-LGR5 (MLP-OXA-LGR5) and tested in the above cell lines. Cell proliferation percentages were analyzed using the Sulforhodamine B assay.
Results: LGR5 is expressed in MC38, T84, CCD18 and HepG2 cell lines. In MC38 and T84, treatment with MLPs-OXA-LGR5 showed greater cytotoxic effect than free drug and non-targeted nanoformulations. However, in CCD18 and the HepG2 control line, treatment with MLP-OXA-LGR5 produced the same antitumor effect as MLP-OXA.
Conclusions: MLP-OXA-LGR5 may be a promising strategy to selectively eliminate colon CSCs. Further in vitro and in vivo studies are needed to validate the antitumor effect of these nanocarriers.

References

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Figures

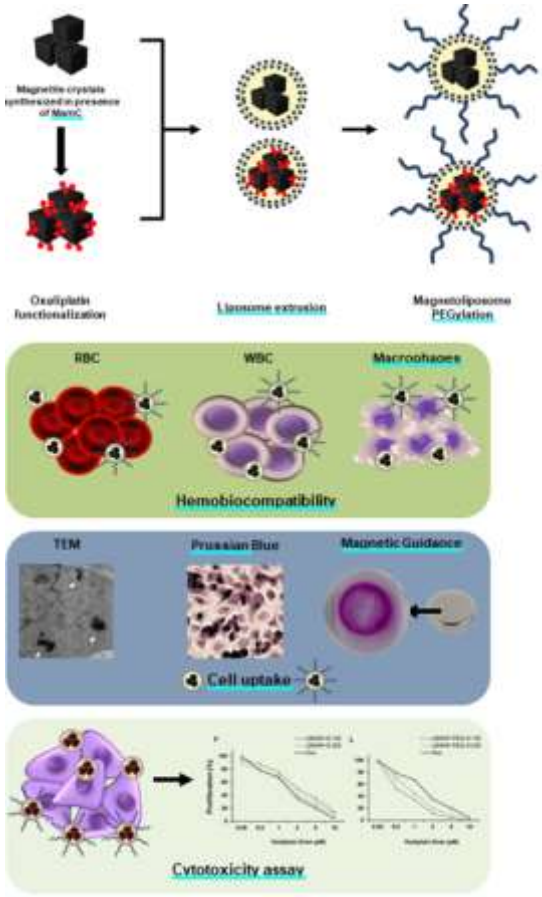

Figure 1: Representative image: magnetoliposome-OXA synthesis and in vitro analysis.