Functionalized and targeted nanoformulations: combined therapy against colorectal cancer tumor cells

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Introduction. Oxaliplatin (OXA) is one of the most widely used chemotherapy drugs, both alone and in combination [1], for the treatment of colorectal cancer (CRC). However, OXA induces many side effects, such as peripheral neuropathy [2]. Therefore, it is necessary to develop new strategies that allow greater targeting of treatments. In this context, CRC cancer stem cells (CSCs) may show high expression of LGR5 which has been related to the initiation of tumor growth, the resistance to chemotherapy and radiotherapy, and aggressiveness [3]. The synthesis of nanoformulations to selectively target CSCs or CRC cells through specific markers constitutes a new research field with a promising future [4]. Specifically, magnetoliposomes (MLPs) are a type of nanocarrier with multiple properties, such as controlled release of antitumor agents, active targeting by monoclonal antibody binding, and high bioavailability. Our objetive was to analyse in vitro effect of OXA-loaded MLPs directed against LGR5 (MLPs-OXA-LGR5).

Methods. OXA-loaded MLPs directed against LGR5 (MLPs-OXA-LGR5) were generated and characterizated. Protein expression of the LGR5 was analyzed by western blot in CRC cell lines. CCR CSCs were generated and their markers analyzed by q-PCR. Cytotoxicity experiments were performed using the sulforhodamine B assay. All methods were carried out following our own experience [5].

Results and conclusion. The MLP-OXA-LGR5 nanoformulations showed high stability and could be tested in vitro using different CRC cell cultures. Analysis of LGR5 in T-84 and MC38 CRC cell lines showed high expression. CRC CSCs, classically associated with chemoresistance, showed controversial results. Specifically, MLP-OXA-LGR5 showed a greater cytotoxic effect than the OXA-free drug in T84 and MC38 CRC cell lines. The control (empty MLP) showed no effect on cell culture. MLP-OXA-LGR5 may be a promising strategy to selectively eliminate LGR5+ cells from CRC. Further in vitro and in vivo studies are needed to validate the selective antitumor effect.

References

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