EFFECTS OF NANOPARTICLES LOADED WITH THE EPIGENETIC DRUG JQ1AGAINST TRIPLE NEGATIVE BREAST CANCER CELLS

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There are no current targeted therapies available for the treatment of triple negative breast cancer (TNBC), and the traditional cytotoxic chemotherapy is not effective to improve the poor prognosis of this disease. Recently, inhibition of bromo- and extra-terminal domain (BET) proteins, regulators of the transcription of genes involved in cell cycle progression, viability and apoptosis, is being highlighted as an important therapeutic strategy for several types of cancer. An anticancer effect against TNBC cells has been shown in vitro by JQ1, a selective BET-inhibitor which *in vivo* is neutralized by the endosomal proton pumps. In this study, to protect the drug from premature degradation, we developed, characterized and investigated the effects of PEGylated nanoparticles containing JQ1(nano-JQ1) on two TNBC cell lines, MDA-MB 157and 231. The nanoparticles containing various amounts of JQ1were prepared following the nanoprecipitation method of preformed PLGA in an aqueous solution of poloxamer 188(1.5% w/v) used as a stabilizer. Mean size, size distribution and the Z-potential of nanosystems were investigated with a Zetasizer Nano ZS. The amount of JQ1retained by the colloidal structure was evaluated by a spectrophotometric analysis. The anticancer effect of this formulation was analyzed by MTT, adhesion and migration assays with respect to the free drug.
The nanoparticles presented a mean diameter of ~100-150 nm, a very low polydispersity index (~0.1) and a negative surface charge. The drug did not influence the physico-chemical properties of the system and was efficiently retained in the colloidal structure. In both TNBC cell lines, the treatment for 48h with JQ1at different concentrations determined a significant dose dependent decrease of cell proliferation. In particular, the maximum effect was observed at concentration 5μM (~90% and ~70%, $p<0.001$vs untreated cells, for MDA-MB 157and 231, respectively). Better effects were obtained when the drug was encapsulated. Nano-JQ1determined a reduction of cell viability of 50% ($p<0.001$vs untreated cells) even at concentrations 0.05μM in MDA-MB 231and at 0.5μM in MDA-MB 157cells. At these concentrations, the treatment also reduced significantly cell adhesion (~40%, $p< 0.01$vs untreated cells) and migration (~40%, $p< 0.01$vs untreated cells) properties in MDA-MB 231cells. Similar results were obtained in MDA-MB 157cells.
These findings demonstrate that the encapsulation of JQ1in nanoparticles promotes a significant increase of the anticancer efficacy of the drug with respect to its free form. If confirmed even *in vivo*, the described nanomedicine may represent an innovative formulation for the treatment of TNBC.