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# Delivery of shNupr1 plasmid by solid lipid nanoparticles reduces the expression of *Nupr1* gene in hepatocellular carcinoma cells.

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Hepatocellular carcinoma (HCC) is one of the most frequent cancers worldwide. Effective therapy to this cancer is currently lacking, creating an urgent need for new therapeutic strategies. Gene therapy approach, that implies any procedure intended to treat a disease by genetically modifying the cell of a patient (transferring genes, gene segments, or oligonucleotides), may provide a promising strategy.
To obtain therapeutic effects, nucleic acids need to cross several biological barriers and be protected from the degradation by nucleases, gaining access to their intracellular targets. Therefore, it is necessary to use biocompatible carriers to facilitate their translocation across the cell membranes protecting them from being degraded while circulating in the bloodstream. At this purpose, cationic solid lipid nanoparticles (cSLN),

able to bind nucleic acids by electrostatic interactions, have emerged as promising vectors due to their versatility and low toxicity. Nupr1 is a small multifunctional protein whose expression is induced by several stresses. It interacts with numerous partners to regulate cell cycle, programmed cell death, autophagy, chromatin accessibility and transcription. For all these reasons *Nupr1* might be a protein whose blockade would prevent cancer progression and metastasis development. In the present study, we aimed to develop cSLN able to efficiently bind, protect and deliver shNupr1 plasmid for the treatment of hepatocellular carcinoma. The cSLN were prepared, characterized in terms of size, polydispersity index and zeta potential, and complexed with shNupr1 plasmid, in presence or absence of trehalose, at different weight ratios. The physical binding between SLN and the nucleic acids was confirmed by zeta potential measurements and electrophoretic mobility studies. Finally, *in vitro* biological assays confirmed that these nanosystems were not cytotoxic and efficiently knockdown *Nupr1* expression in Hep3B cells. The obtained data suggest that these nanosystems may be useful for in vivo applications as nonviral vectors for the treatment of HCC.