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Targeted gene silencing for cancer treatment

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Cancer arises in the twenty-first century as one of the leading causes for mortality in the western civilization. In the last decades, several genes were identified as important players in the transformation of a normal cell into a tumor cell. Therefore, modulation of those genes is a promising strategy for cancer treatment. Gene downregulation can be mediated by small-interfering RNA (siRNA), 21-23 nucleotides long double strand of RNA, which has the potential to inhibit the expression of a target gene through specific cleavage of perfectly complementary mRNA. However, the clinical use of these molecules has been impaired by their unfavourable pharmacokinetics profile and low intracellular accumulation.

In order to address this issue, we have developed a novel targeted sterically stabilized lipid-based nanoparticle characterized by high siRNA encapsulation efficiency, efficient protection of siRNA, average size around 200 nm, and charge close to neutrality. Overall, these are nanoparticles that present adequate features for systemic administration.

Our results have shown that the targeted nanoparticles were specifically internalized by human cancer cells (MDA-MB-435 and MDA-MB-231) and endothelial cells (HMEC-1). In experiments performed with green fluorescent protein (GFP)-overexpressing human cancer cell lines, specific downregulation of GFP, both at the protein and mRNA levels, was further observed with the targeted nanoparticle but not with the non-targeted counterpart. As the developed nanoparticle is adequate for the encapsulation and delivery of any siRNA sequence, studies with a siRNA against a therapeutic molecular target are now ongoing.

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