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SIRNA Delivery Mediated By Inulin Based Polycations

Carla Sardo[1], Carmela Tommasino[1], Tiziana Esposito[1], Giulia Auriemma[1], Rita Patrizia Aquino[1]
[1] Department of Pharmacy, University of Salerno
via Giovanni Paolo II, 132, 84084 Fisciano, SA, Italy
csardo@unisa.it

Extended Abstract

RNA interference is a technique to induce specific gene silencing, mediated by siRNAs, double stranded RNA molecules (19–27 bp) that induce specific mRNA degradation in the cytoplasm [1]. Despite the immense therapeutic potentiality, siRNAs suffer of poor stability in vivo and almost zero uptake by cells due to high molecular weight, hydrophilicity and the presence of negative charges [2].

Polyplexes, colloidal systems originated from the electrostatic interaction between negative nucleic acids and positive charged polymers, emerged as one of the most versatile systems for nucleic acid delivery

Our current research focuses on the generation of libraries of graft semisynthetic polycations with multiple architectures and analogue composition, starting from Inulin (INU), a natural polysaccharide, to explore how the structure of the carrier influences the delivery process.

Inulin is constituted by a PEG backbone from which one fructose ring per repeating unit is hanging. It has already been investigated as scaffold for the design of siRNA vectors [3][4] and as PEG alternative in amphiphilic derivatives for nanocostruction [5]. Contrarily to PEG, INU has the advantage of being natural, non-immunogenic and functionalizable along its entire length, allowing the modulation of composition and architecture in a smooth way. In this contribution we present the first derivatives of the serie INU-PEI: Inulin-g-branched polyethyleneimine (INU-bPEI) and its amphiphilic analogue INU-bPEI-PLA. Derivatives with two different derivatization degree in PEI were tested to prepare copolymer/siRNA polyplexes by interpolyelectrolytic interactions. Agarose gel retardation assay showed that this new copolymers were able to stop the electrophoretic run of siRNA. Complexes were characterized by DLS studies and by stability studies in the presence of albumin. Our investigation showed the ability of this systems to resist to the anionic exchange. In addition, haemocompatibility of polyplexes was demonstrated. This early results encourage us to continue in this study to obtain efficient inulin based siRNA delivery systems.

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