Fully biodegradable PEG-dendrimers for nucleic acid delivery

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Dendrimers are attractive carriers for several bioactives[1] due to their unique structural features: globular, well-defined, very branched and controllable nanostructure, low polydispersity and multivalency. Among such bioactives nucleic acids (NAs) are readily compacted into nanostructures named "dendriplexes", when complexed with positively charged dendrimers that are able to protect them from enzymatic degradation and rapid renal clearance after i.v. admistration.[2] However, one important disadvantage of the most commonly used dendrimers is their non-degradability under physiological conditions, that can lead to toxicity by bioaccumulation. Moreover, in the gene therapy field, vector stability can further hinder the intracellular release of the NA, consequently leading to low transfection efficiencies (TE). Therefore, recent interest has focused on the development of biodegradable dendrimers, but only few works report their biomedical applications.[3]

We have recently reported a new family of partially/hybrid biodegradable PEG-dendritic block copolymers for siRNA delivery.[4,5] Our systems showed a great ability to mediate siRNA cellular internalization,[5] yet a low transfection efficiency (TE) was observed due to the partial vector stability. Here, we present new fully biodegradable and biocompatible PEG-dendritic block copolymers,[4] as well as their function as siRNA vectors. Interestingly, the fully degradable character was crucial for a better nucleic acid release from the dendriplexes, contributing to an amazing improvement of the TE compared to their hybrid biodegradable counterparts.

Acknowledgments: This is supported by the grants PTDC/CTM-NAN/3547/2014 (FCT, Portugal); FIS-FIS-2015-01_CCV_20150630-88 (INFARMED); projects NORTE-01-0145-FEDER-000008 and NORTE-01-0145-FEDER-000012 (Norte Portugal Regional Operational Programme, NORTE 2020, under the PORTUGAL 2020 Partnership Agreement, through the European Regional Development Fund (ERDF) and FEDER - Fundo Europeu de Desenvolvimento Regional funds through the COMPETE 2020 - Operacional Programme for Competitiveness and Internationalisation (POCI), Portugal 2020), and by Portuguese funds through FCT/MCTES in the framework of the project "Institute for Research and Innovation in Health Sciences" (POCI-01-0145-FEDER-007274).

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