

31st Nano Congress for Future Advancements &

13th Edition of International Conference on Nanomedicine and Advanced Drug Delivery

August 29-30, 2019 London, UK

Efficient gene delivery promoted by PEGylated poly(2-aminoethyl methacrylate hydrochloride)-based nanosystems

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Pegylation of cationic polyplexes is a promising approach to enhance their stability and reduce unwanted interactions with biomolecules. However, this process generally has a negative effect on cellular uptake and transfection to target cells. In this work, we evaluate the impact of PEGylation on biological and physicochemical properties of poly (2-aminoethyl methacrylate) (PAMA)-based polyplexes. For this purpose, different PEG-b-PAMA block copolymers, and the respective homopolymers, were synthesized varying the molecular weight of the cationic segment. The obtained data show that PEG-b-PAMA-based polyplexes exhibited much better transfection activity/cytotoxicity relationship than the corresponding non-PEGylated nanocarriers. The best formulation, prepared with the largest block copolymer (PEG45-b-PAMA168) at the 25/1 N/P ratio, presented a 350-fold higher transfection activity than that obtained with polyplexes generated with gold standard bPEI. The highest transfection activity of the best formulation was not only associated to a higher cellular uptake but most notably to a more efficient escape from the endolysosomal pathway. Moreover, these nanosystems present suitable physicochemical properties for gene delivery namely reduced sizes and high DNA protection. Overall, these findings demonstrate the high potential of the PEG45-b-PAMA168 block copolymer as gene delivery system.

Biography

Henrique Faneca is principal investigator at Centre for Neuroscience and Cell Biology, and invited assistant professor at University of Coimbra. He received is PhD degree in Biochemistry from Coimbra University in 2005. The main focus of his research are the development of lipid- and polymer-based nanosystems for gene and drug delivery into target cells and the generation of new antitumor strategies, involving different gene therapy approaches either per se or in combination with chemotherapeutic agents. Henrique Faneca is author of more than 45 scientific papers corresponding to over 1500 citations and to an h-index of 19.

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