Polymeric NPs as efficient tool for gene delivery

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Abstract

Gene therapy is described as the direct transfer of genetic material to cells or tissue for the treatment of inherited disorders and acquired diseases, such as cancer. The base of this therapeutic method is to introduce a gene encoding a functional protein altering the expression of an endogenous gene or possessing the capacity to cure or prevent the progression of a disease, or to introduce systems of gene silencing (such as siRNA, etc.) which has the ability to specifically silence target proteins that are crucial for modulating cellular pathways inducing an inhibitory effect on cancer proliferation. There are two types of gene delivery based on the carrier's nature: viral delivery and non-viral delivery. Gene delivery using viral vectors have long been proven to be the most efficient and stable transgene vectors into the cell. In addition, viruses are able to use the host cell machinery for protein synthesis, and some of them are able to stably insert into the host cell genome and provide a long-term transgene expression in transduced cells. Thus, viral gene carriers possess higher gene transfection efficiency than non-viral vectors. Despite some successes in clinic trials, viral vector gene transfer still has some safety issues. In order to limit the use of viral vectors, recent advances in vector technology have improved gene transfection efficiencies of non-viral carriers.
Nanoparticle (NP)-based therapeutic systems developed in recent years have shown efficient delivery of nucleic acids with low toxicity and sustained cargo release.
For gene delivery application, NPs can accommodate large DNA plasmids, RNA or proteins and may be produced at low cost on a large scale. NP-based systems overcome safety problems and limitations of viral vectors. FDA-approved polymers are particularly attractive for *in vivo* drug/gene delivery applications. Recently, we have developed a polymeric system for drug and gene based on pH-responsive and enzyme-responsive, core/shell NPs using the FDA approved PCL polymer [1-4].
Another, attractive polymer for gene delivery applications is polyglycolic acid (PGA), which has been approved by the FDA. PGA degradation is quicker *in vivo* and *in vitro*, and the degradation product, glycolic acid, is non-toxic and it can enter in the tricarboxylic acid cycle.
Our PGA NPs are obtained by nanoprecipitation and desolvation method, and are composed of a core loaded with the acid nucleic molecules and a PGA shell. Prior to particle assembly, active agent is complexed with a pH (as chitosan) or enzymatic (as protamine)-responsive polymer. By combining the sensitivity of the core polymer with the slow degradation of surface PGA, we obtained a simple and easy way to control the release of an active agent and improve its therapeutic efficiency.
The mean size of PGA nanoparticles is 100 nm, with a negative ζ-potential of -12 mV.
Our NPs have a regular spherical shape and no aggregation as observed by AFM and SEM analysis. No cytotoxicity is observed on different cell lines tested.
In addition, our PGA NPs have showed an efficient delivery of cDNA, observing relative numbers and mean fluorescence intensity of transfected GFP-positive cells comparable to those achieved with standard reagents used to promote transfection.
PGA NPs, thanks their properties, as biocompatibility, biodegradability and a good transfection efficacy, can be used as efficient tool of transfection overcome viral vector problems.

Acknowledgement
This study is supported by Tecnomed (FIRS project of nanotechnology, photonics and precision medicine) and AIRC through the grant MFAG n. 16803

References

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