Stimuli responsive PGA Nanoparticles as safe agents for non viral gene delivery

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Abstract

Nanoparticle (NP)-based therapeutic systems developed in recent years have shown efficient delivery of drugs and/or nucleic acids with low toxicity and sustained cargo release.

Recently, more attention has been paid to stimuli sensitive delivery systems that are promising strategies for active agent release. Many techniques have been developed to produce systems that could be used for effective encapsulation of active agents, as drugs or genes. External and internal stimuli, such as temperature, [1] pH, [2] light, [3] and protease, [4] could be utilized to control the active agent release in delivery systems. Among all these strategies, release systems based on pH variation have obtained more attention, because the pH difference between different intracellular compartments could be used for targeting systems design.

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, core/shell NPs using the FDA approved PCL polymer. [5-8]

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.

For gene delivery, we have developed pH-responsive core-shell polymeric NPs showing that they mediate efficient cDNA delivery. Our PGA NPs (Figure 1) with size about 300 nm, obtained by the emulsion-diffusion-evaporation method, are composed of a core with DNA molecules and a PGA shell. Using PGA NPs loaded with GFP cDNA in different cell lines, we observed 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.

References

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Figures

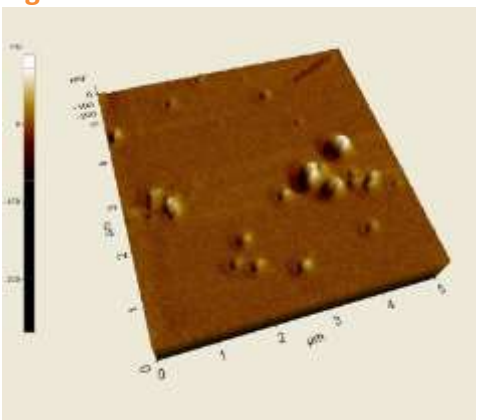

Figure 1. AFM image of PGA NPs.

Acknowledgement

This study are supported by Tecnomed (FIRS project of nanotechnology, photonics and precision medicine) and partially by Italian Association for Cancer Research (AIRC) through the grant MFAG n. 16803