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Pathway-dependent effects on the formation of bioreducible polycation-DNA polyplexes in saline media

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The delivery of genes for therapeutic applications requires advanced nanocarriers that can package and protect DNA, and then deliver it to ill cells or tissues. Polyplexes – soft nanoparticles resulting from the complexation of DNA with cationic polymers – are promising vehicles to achieve these goals, but further advances in the technology are needed to achieve the desired efficiency for use in gene therapy applications1. One promising approach to enhance the gene delivery efficiency of these particles makes use of polycations with disulfide bonds along their backbone that degrade in the reducing potential of the cytosol. This leads to an enhanced release of genes inside cells, and lowers the toxicity of the polymer2. In this work, we investigate the role of adding salt to the polyplex systems under different methodological order, up to physiological concentrations, on the structure, size and charge of conventional and bioreducible poly-L-lysine polyplexes. As a general trend, polyplexes assembled in water and transferred to physiological buffer afterwards display smaller sizes and enhanced colloidal stability when compared to polyplexes assembled in physiological buffer from start (figure 1). Since these parameters are key to the pharmacokinetics of nanocarriers, this approach can be used as a new tool to manipulate the properties of gene nanocarriers and enhance their transfection efficiency. Current live-cell imaging and transfection efficiency studies are focused on elucidating how these two methods of preparation influence cellular uptake and transfection efficiency.

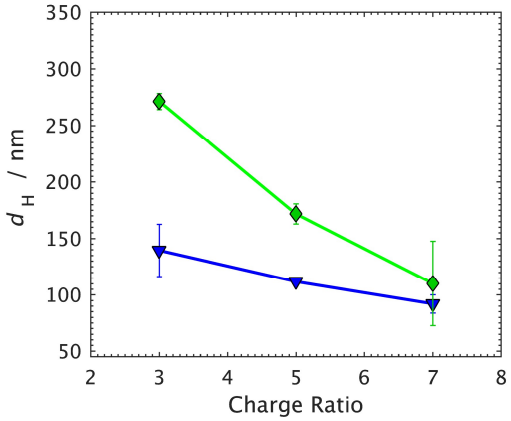

Figure 1: Influence of the order of salt addition (100 mM) on the size of polyplexes. As can be seen, polyplexes prepared in water and transferred to saline media after (▼) have a smaller size than polyplexes prepared in saline media from start (♦). The tendency is observed for the entire range of positive-to-negative charge ratios investigated.

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