

## **THERMALLY RESPONSIVE, POLYPEPTIDE-BASED COPOLYMERS AS NON-VIRAL VECTORS FOR TRANSPORT OF BIOLOGICAL MOLECULES**

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The modern trends in diagnosis, targeted transfer of drugs, and regenerative medicine are mainly directed to find new, efficient to storage and delivery vehicles [1-2]. The polymeric nanoparticle carriers as non-viral vectors have been a promising candidate due to their low cytotoxicity, biocompatibility and ability to impart different functionality and possibility of good control of their properties [3]. It is well established that the cationic polymers such poly(L-lysine) are positively charged at physiological conditions and are capable to complex various oppositely charged biomacromolecules such DNA and RNA [4]. The major drawback of such types of homopolymers is their toxicity, as well as the fast recognition by the reticulo-endothelial cells and blood clearance of the polyplexes, which strongly reduces the gene transportation efficiency. To overcome the drawbacks new synthetic strategies are being developed. Recently block copolymers based on thermoresponsive poly(N-isopropylacrylamide), poly(oxyethylene) and polypeptide (Z-L-lysine) (PZLLys) containing segments received a high scientific attention [5]. Because of the different chemical nature of the selected block segments, the copolymers meet several basic requirements which are a good precondition for obtaining of well-defined and effective polymeric-nanocarriers. The objective of present contribution is the synthesis of a series peptide-based thermoresponsive copolymers containing biodegradable poly(L-lysine) cationic block with increasing 10 to 65 degrees of polymerization and thermally responsive PNIPAM-g-PEG block used as macroinitiator for ZLLys-NCA polymerization. Detailed copolymers characterization and evaluation of their capability to condense DNA and/or RNA into a polyplexes were performed.

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[1] Gene delivery by lipoplexes and polyplexes, Conchita Tros de Parduya et. al, European Journal of Pharmaceutical Sciences, 2010, 40(3), pp 159.

[2] Partially Hydrolyzed Poly(n-propyl-2-oxazoline): Synthesis, Aqueous Solution Properties, and Preparation of Gene Delivery Systems, Maarten Mees, et.al, Biomacromolecules, 2016, 17, pp 3580.

[3] A mild and versatile approach for DNA encapsulation, Ivaylo Dimitrov et.al, Soft Matter, 2011, 7, pp 8002.

[4] Thermally sensitive polypeptide-based copolymer for DNA complexation into stable nanosized polyplexes, Emilya Ivanova et.al Nanopart Res, 2013, 15, pp 1358.

[5] Temperature-Switchable Control of Ligand Display on Adlayers of Mixed Poly(lysine)-g-(PEO) and Poly(lysine)-g-(ligand-modified poly-N-isopropylacrylamide), C. Tribe et.al., 2016, 17, pp 1727.