Bio-functionalized nanoconstructs for gene editing and therapy

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Although many approaches for the treatment of diseases with chemical drug, some disease such as cancer remains a leading cause of death worldwide. Various strategies including small molecules, inhibitors, and chemotherapeutic reagents can be used to care the patients. However, drug resistance and tolerance may result in uncontrolled diseases. To overcome this challenge, gene therapeutics may be employed, this approach minimizes side effects caused by non-selective drug mechanisms. Among of nucleic acid materials, mRNA and gene editing materials offer several advantages over DNA including minimized genomic integration risk, controlled expression, and correction of gene mutations.

Key to the widespread and application of therapeutic gene materials is the safe and effective delivery of multiple gene components into single cells. Additionally, the increase of stability of nucleic acid materials and ribonucleoproteins (RNPs) is critical factor to enhance the therapeutic efficiency. To address this issue, we report the robust mRNA and RNP delivery platform based on a biocompatible nanoconstruct with an absorptive structure for packing and directly delivering therapeutic materials, including mRNA, Cas9 nuclease RNP (Cas9-RNP) and base editor RNP (BE-RNP). Compared to commercial material (Lipid)-based methods, our nanocontruct could effectively protect the therapeutic materials and show the high-efficiency expression of mRNA and gene editing in vitro and in vivo models. Moreover, low toxicity and high biodegradability of nanoconstruct assure organ function. By engineering the nanoconstruct to overcome practical challenges in therapeutic gene application, we expect this platform to be a modular therapeutic gene delivery system and a game-changer for *in vivo* gene expression and editing.

References Times New Roman 10 pt Bold; references themselves Times New Roman 10 pt

[1] H.Lee et.al *Adv. Healthcare. Mater.* **2023**, *12*, 2201825.