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5. The **closing date** for all submissions is **15 September 2017.**

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**Multifunctional Gene Carrier System Self-Assembled from Redox-Sensitive and Zwitterionic Polymer Blocks via Host-Guest Interaction**

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INTRODUCTION: Although methodologies are existing to address individual hurdle in polymeric gene delivery processes, incorporation of multiple features into one single system to overcome multiple barriers during gene delivery is still a big challenge. Herein, a supramolecular approach is established to construct a multifunctional DNA delivery system with the functions of zwitterionic phosphorylcholine based extracellular stabilization and favorable cellular uptake, and disulfide bond based reduction-responsive intracellular DNA release.

METHODS: The multifunctional gene delivery system composed of two LEGO-like molecular building blocks: host polymer, which is a redox-sensitive β-cyclodextrin based cationic star polymer, and guest polymer, which is adamantyl-capped biomemetic phosphorylcholine based zwiterionic polymer. Both host and guest polymer are synthesized via ATRP method. The host and guest polymers self-assemble to integrate multiple functions into one system, based on the host-guest interaction between β-cyclodextrin and adamantyl moieties in the host and guest. The cellular uptake capacity and gene transfection ability of the system, functions of biomemetic shell and disulfide bond are evaluated. Additionally, the gene delivery ability of system is evaluated by delivering therapeutic p53 anti-cancer gene in MCF-7 cells.

RESULTS AND CONCLUSIONS: With rational design, the multifunctional supramolecular gene delivery system is proven to possess supreme serum tolerance, which is due to the shielding properties of guest polymer, high cellular uptake efficiency which is ascribed to the membrane-mimic structure of guest polymer and intracellular DNA release properties, which is owing to the redox-induced degradation of disulfide bonds in the host polymer. These features work simultaneously to achieve high transfection efficiency. Finally, the supramolecular delivery system is applied to deliver p53 anti-cancer gene in MCF-7 cells, showing great potential for cancer gene therapy application. In summary, the design serves as an example for developing customized gene carriers that can overcome multiple hurdles via the convenient “Molecular LEGO” strategy.