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Solvent-induced size reduction of self-assembled siRNA/copolymer nanoparticles WEI QU, Northwestern University, JUAN WU, HAI-QUAN MAO, Johns Hopkins University, ERIK LUIJTEN, Northwestern University — Small interfering RNA (siRNA) therapeutics has a demonstrated potential for treating numerous liver diseases. However, traditional polycation vectors used for siRNA delivery typically produce siRNA-containing particles of large size (> 100 nm), along with high cytotoxicity and low colloidal stability. Inspired by earlier work on nanoparticles for plasmid DNA delivery [1], we graft hydrophilic and biocompatible polyethylene glycol (PEG) blocks to the polycation vector to overcome these limitations. We find that the PEG-grafted polycations result in slightly larger particle size, even though the hydrophilic PEG blocks are expected to hinder the formation of larger aggregates. To explain this observation, we investigate siRNA/copolymer self-assembly via computer simulations of coarse-grained polymer and siRNA models. Our calculations suggest that hydrogen bonding between PEG and the polycation leads to the increased particle size, and that smaller particles can be obtained by inhibiting hydrogen bonding in such system. Subsequent experiments employing solvents of lower polarity indeed lead to particles with smaller size.

[1] X. Jiang *et al.*, Adv. Mater., doi: 10.1002/adma.201202932

Wei Qu
Northwestern University

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