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Facile Synthesis of Semi-Library of Low Charge Density Cationic Polyesters from Poly(alkylene maleate)s for Efficient Local Gene Delivery

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Abstract

Cationic polymers are one of the main non-viral vectors for gene therapy, but their applications are hindered by the toxicity and inefficient transfection, particularly in the presence of serum or other biological fluids. While rational design based on the current understanding of gene delivery process has produced various cationic polymers with improved overall transfection, high-throughput parallel synthesis of libraries of cationic polymers seems a more effective strategy to screen out efficacious polymers. Herein, we demonstrate a novel platform for parallel synthesis of low cationic charge-density polyesters for efficient gene delivery. Unsaturated polyester poly(alkylene maleate) (PAM) readily underwent Michael-addition reactions with various mercaptamines to produce polyester backbones with pendant amine groups, poly(alkylene maleate mercaptamine)s (PAMAs). Variations of the alkylens in the backbone and the mercaptamines on the side chain produced PAMAs with tunable hydrophobicity and DNA-condensation ability, the key parameters dominating

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