**[Comparison of cationic bottlebrush polymers for nucleic acid delivery](https://acs.digitellinc.com/acs/live/22/page/677/5?eventSearchInput=&eventSearchDateTimeStart=&eventSearchDateTimeEnd=&eventSearchTrack%5b%5d=201" \l "sessionCollapse394056)**

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Cationic polymer vehicles have emerged as promising platforms for nucleic acid delivery because of their scalability, biocompatibility, and chemical versatility. Advancements in synthetic polymer chemistry allow us to precisely tune chemical functionality with various macromolecular architectures to increase the efficacy of nonviral-based gene delivery. As various macromolecular architectures continue to be explored, this work demonstrates cationic bottlebrush polymer-mediated transgene expression and compare four unimolecular defined bottlebrush polymers to their linear analog. Poly *n*-dimethylamino ethylmethacrylate bottlebrushes were synthesized while, keeping the side chain degree of polymerization constant. Characterization of the physical and chemical properties were measured, while evaluating the toxicity and delivery efficiency of pDNA *in vitro*. Bottleplexes not only displayed vast increases in %EGFP+ cells in comparison to linear polymers, but also bottlebrushes increase transgene expression with respect to increasing molecular weight. Bottleplexes and polyplexes both displayed high pDNA internalization however, quantitative confocal analysis revealed higher levels of nuclear colocalization of pDNA payloads when delivered with bottleplexes compared to linear vehicles. This work was advanced to explore how bottlebrush end-group modification can alter the bottleplex stability, binding, and ultimately delivery of both pDNA and Cas9 protein therapeutics. A cationic bottlebrush polymer was altered to include a range of hydrophobicity/philicity as end-groups to explore the effect while binding pDNA and Cas9 protein. Overall, this work displays that macromolecular design of bottlebrush polymers serve as efficient polymer-based gene delivery vectors.