



Theresa Reineke

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Theresa M. Reineke is the Prager Endowed Chair in Macromolecular Science and a Distinguished McKnight University Professor in the Department of Chemistry at the University of Minnesota. She received her B.S. in Chemistry and Physics from the University of Wisconsin–Eau Claire. She then received an M.S. from Arizona State University and a Ph.D. from the University of Michigan in the laboratory of Professor Omar Yaghi. She subsequently completed an NIH Postdoctoral Fellowship at the California Institute of Technology with Professor Mark Davis. Theresa began her independent career at the University of

Cincinnati, later moving to Virginia Tech, before joining the University of Minnesota. Her research pioneers polymeric materials at the chemistry–biology interface, enhanced by high-throughput screening and modern data science and machine learning tools. The Reineke Lab seeks to discover fundamental and applied advancements in the fields of macromolecules for nucleic acid delivery and gene editing, oral delivery of therapeutics, and sustainability. Theresa is a cofounder of two current biotechnology companies in nucleic acid delivery, Nanite, Inc. and LiberateBio, Inc., and is Editor-in-Chief of Bioconjugate Chemistry (American Chemical Society Publications). She is a Fellow of the American Chemical Society, the Royal Society of Chemistry, and the American Institute for Medical and Biological Engineering, and has been further recognized by awards from the Sloan, Beckman, and Dreyfus Foundations. She is also a recipient of the American Chemical Society's Arthur C. Cope Scholar Award and Carl S. Marvel Creative Polymer Chemistry Award.

Abstract: “Designer Macromolecules: From Combinatorial Synthesis to Organ-Targeted Therapeutics”

Multifunctional macromolecules are transforming nucleic acid delivery, gene editing, and sustainable formulation science, yet the vast chemical and architectural space of polymer systems still defies rational design. Our group meets this challenge by designing macromolecules from the bottom up; we unite combinatorial synthesis, high-throughput characterization, and predictive modeling to discover high-performance materials and reveal the structure–function principles that govern them. In one effort, we synthesized libraries of statistical copolymers and systematically mapped their physicochemical and biological behavior, from size, charge, molecular weight, and encapsulation to cellular uptake, editing efficiency, and cytotoxicity. These datasets exposed distinct design rules for mRNA, DNA, and CRISPR delivery and identified architectures that outperform commercial reagents in genome editing. In a complementary effort, we engineered ternary mixed micelles from cationic, anionic, and PEG-bearing amphiphilic block copolymers. Systematic blending tuned the surface chemistry and morphology that govern mRNA complexation, stability, and biodistribution. Increasing anionic content drove a transition from spherical to wormlike micelles while preserving high zeta potential and efficient complexation. Top formulations achieved over 95% transfection efficiency and viability across cell types (twice that of homomimetic controls) and, in vivo, redirected mRNA expression from lung to spleen. This morphology-driven organ selectivity departs from charge-centric targeting and establishes a composition-based route to organ-specific delivery. Together, these studies show how the deliberate design of macromolecules, guided by quantitative characterization and data-driven analysis, can unlock hidden structure–function relationships and yield next-generation materials that deliver therapeutics to defined organs and advance sustainable nucleic acid drug discovery.