“Organocatalytic Polymerization: From Chemistry to Biology”

We have developed a family of selective organic catalysts for ring-opening polymerization reactions, and have integrated these catalysts into flow reactors for the programmed synthesis of block copolymer libraries. In parallel efforts, we have developed aerobic alcohol oxidation catalysts that generate new monomers which were then enchained using organocatalytic polymerization to generate functional materials that proved useful agents for the delivery of messenger RNA into living animals. Functional delivery of messenger RNA (mRNA) in-vivo is key to implementing potentially transformative strategies for vaccination, protein replacement therapy and genome editing. The step-economical synthesis and evaluation of a new, tunable and effective class of synthetic biodegradable materials: Charge-Altering Releasable Transporters (CARTs) will be described for mRNA delivery. CARTs are structurally unique and operate through an unprecedented mechanism, serving initially as oligo(α-amino ester) cations that complex, protect and deliver mRNA, and then change physical properties through a degradative, charge-neutralizing intramolecular rearrangement, leading to intracellular release of functional mRNA and highly efficient protein expression.

Fig. 1 Organocatalytic Synthesis of Degradable CARTs for the delivery of mRNA.