

FIGURE S1. Gel condensation assays show that VIPER and sunflower polycations package both Luc mRNA and GFP mRNA. **(A)** As evidenced by the lack of free Luc mRNA in the polyplex lanes, Luc mRNA was readily packaged by VIPER and sunflower polycations at an N/P ratio of 5. **(B)** Similar packaging efficiency was observed with GFP mRNA polyplexes.

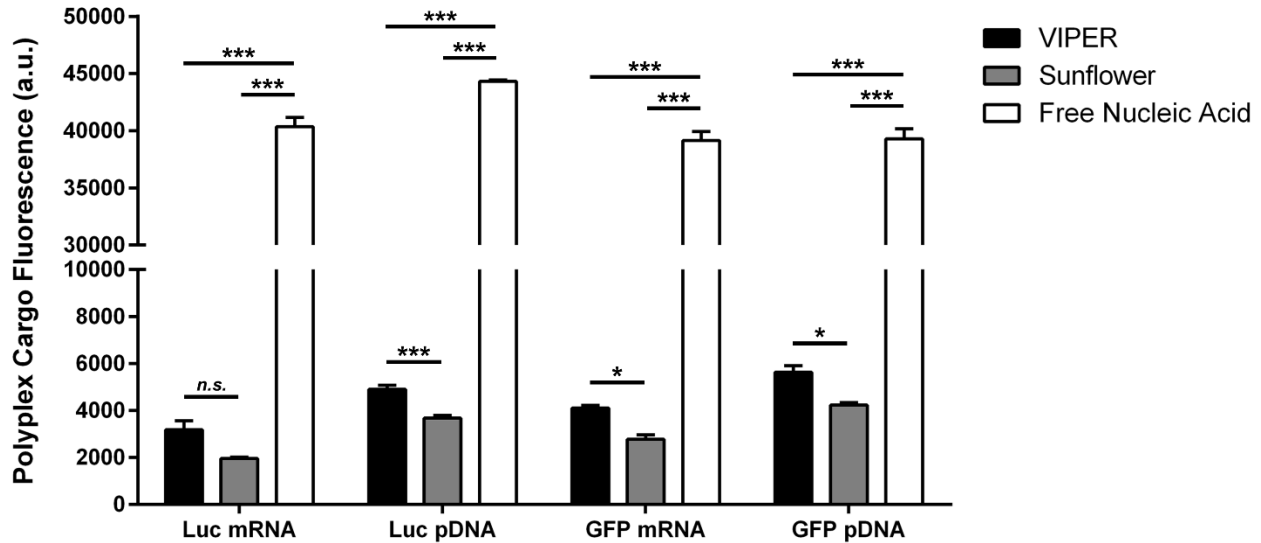


FIGURE S2. Fluorophore labeling of mRNA polyplex cargo confirms packaging of mRNA by VIPER and sunflower polycations. GFP mRNA and pDNA polyplexes were formulated with VIPER and sunflower polycations at an N/P ratio of 5, and were subsequently stained with RiboGreen nucleic acid dye. GFP mRNA cargo fluorescence of both VIPER and sunflower polyplexes was significantly decreased relative to that of free GFP mRNA, indicating successful packaging of free mRNA by polycations. Similarly, Luc mRNA cargo fluorescence of both VIPER and sunflower polyplexes was also significantly decreased relative to that of free Luc mRNA. Error bars are expressed as mean + SD, $n = 3$ (*p-value < 0.05; **p-value < 0.01; ***p-value < 0.001; *n.s.* = no significance; one-way ANOVA with post hoc Tukey HSD test).

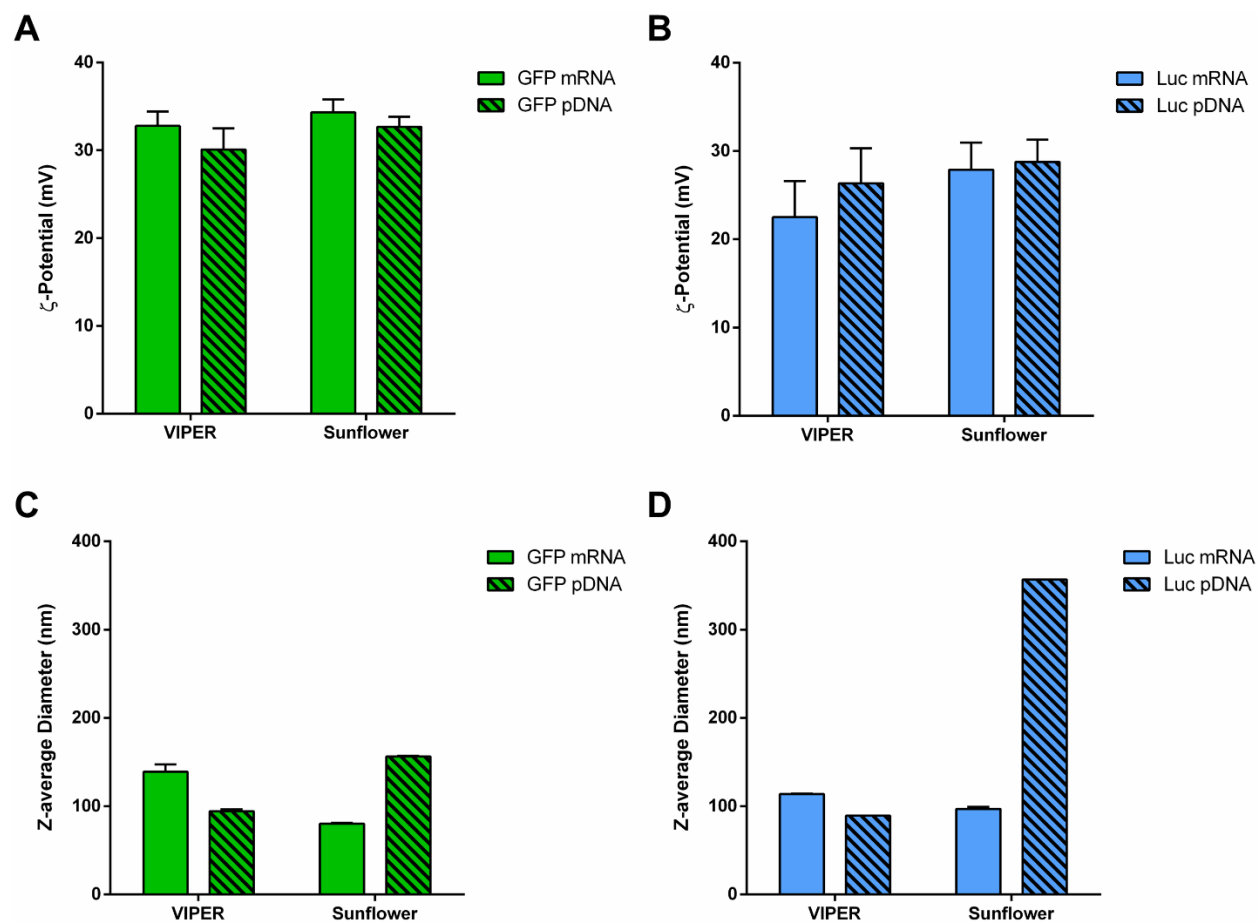


FIGURE S3. VIPER and sunflower polycations form mRNA polyplexes with defined ζ -potentials and hydrodynamic diameters. (A-B) VIPER and sunflower mRNA polyplexes were characterized by mean ζ -potentials between 20-40 mV. These ζ -potentials were comparable to those of VIPER and sunflower pDNA polyplexes. (C-D) VIPER and sunflower mRNA polyplexes were characterized by z-average hydrodynamic diameters between 80-140 nm. These hydrodynamic diameters were comparable to those of VIPER and sunflower pDNA polyplexes. Error bars are expressed as mean + SD, $n = 3$.

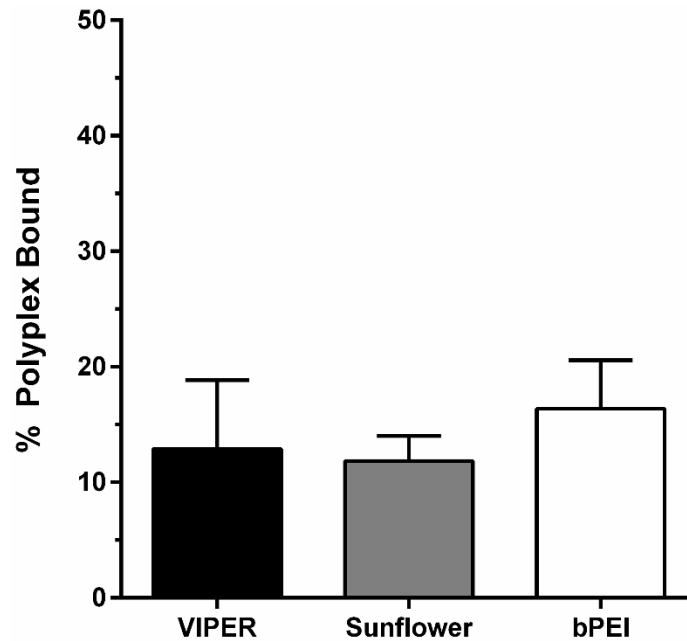


FIGURE S4. VIPER, sunflower, and bPEI mRNA polyplexes bind to HeLa cells. HeLa cells were incubated with polyplexes packaging Cy5-labeled GFP mRNA for 30 minutes under serum-free conditions. After 30 minutes, the amount of polyplex remaining in the transfection media was measured and the percentage of polyplexes bound to cells was calculated. Approximately 13% of VIPER mRNA polyplexes, 12% of sunflower mRNA polyplexes, and 16% of bPEI mRNA polyplexes were bound to HeLa cells after 30 minutes of exposure to serum-free transfection media. Error bars are expressed as mean + SD, $n = 3$.

TABLE S1. Polyplex Formulations for *In Vitro* Reporter mRNA Transfections

Parameter	Serum-free OptiMEM	Complete Media
Quantity of mRNA per well	1 μ g	2 μ g
VIPER N/P	3	5
Sunflower N/P	5	5
bPEI N/P	5	5
Duration of Transfection	1 hour	4 hours