Lyophilization approach to improve long-term stability of LGA-PEI nanoparticles for drug delivery

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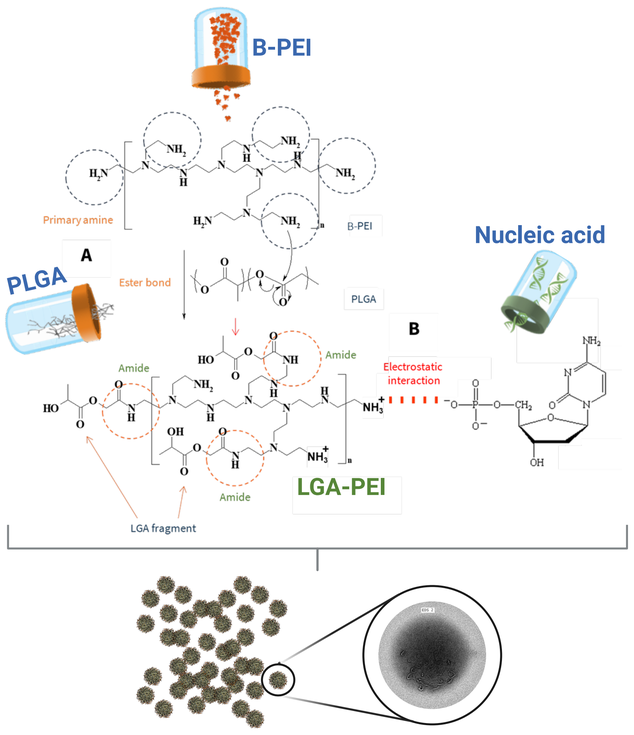
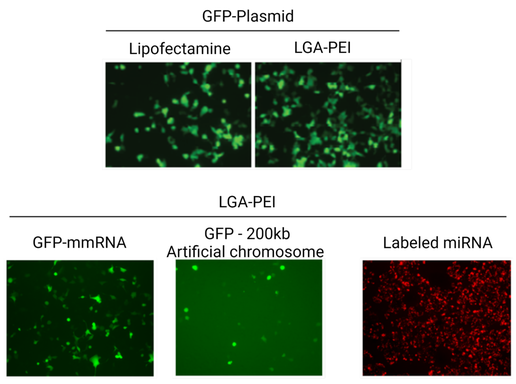
BACKGROUND

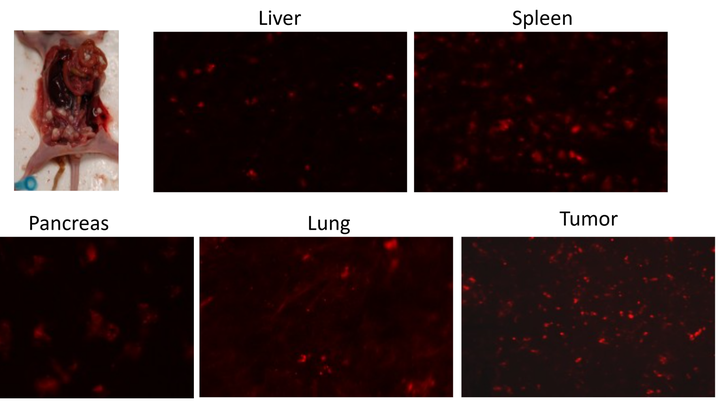
We developed **LGA-PEI**, a novel polymer in which **PLGA** is depolymerized into **LGA units** and covalently linked to **primary amines of PEI**. This combination creates a **potent, lower-toxicity nucleic acid delivery system**. LGA-PEI forms nanoparticles with nucleic acids via **electrostatic condensation** between remaining PEI amines and nucleic acid phosphate groups.



The nanotechnology has been optimized and thoroughly characterized, including its synthesis and interaction with nucleic acids. With diverse RNA or DNA payloads, it shows **strong transfection, effective delivery to major organs, and a favorable safety profile in mice**.



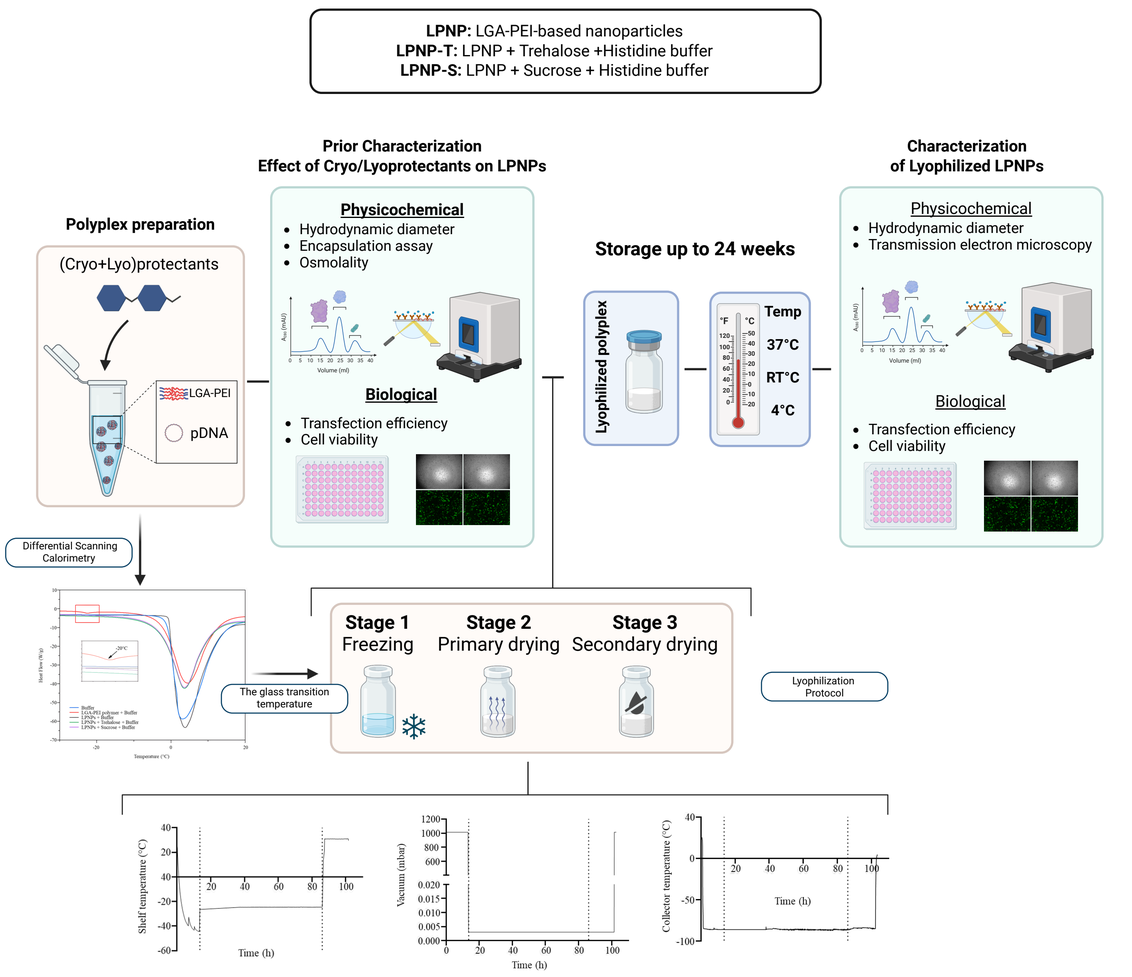
Parameter (Units)	Group (Expressed in Mean ± S.D., n = 4)	
	Untreated (Saline Solution)	LPNP-pCtrl (2.5 mg/kg)
Albumin (g/dL)	2.4 ± 0.1	2.2 ± 0.2
Globulin (g/dL)	2.6 ± 0.3	2.5 ± 0.1
Albumin/Globulin (ratio)	0.94 ± 0.07	0.88 ± 0.12
Total protein (g/dL)	5.0 ± 0.5	4.6 ± 0.1
Alkaline phosphatase (U/L)	42 ± 7	49 ± 10
Alanine transaminase (U/L)	56 ± 21	53 ± 8
Lipase (U/L)	848 ± 103	845 ± 81
Amylase (U/L)	1565 ± 164	1557 ± 77
Creatine (mg/dL)	0.08 ± 0.1	0.10 ± 0.08
Urea nitrogen (mg/dL)	0.20 ± 0.14	0.18 ± 0.1
Total bilirubin (mg/dL)	21 ± 2	20 ± 1
Glucose (mg/dL)	171.3 ± 29.3	156.8 ± 7.7



LGA-PEI provides a safer, scalable alternative to viral and lipid-based delivery systems, but its clinical translation is limited by aggregation during prolonged storage and transport.

METHODS

LPNP: LGA-PEI-based nanoparticles
LPNP-T: LPNP + Trehalose +Histidine buffer
LPNP-S: LPNP + Sucrose + Histidine buffer



This study shows that LPNPs can be stabilized long-term in aqueous and lyophilized forms without losing functionality, supporting their potential as clinically viable, scalable, and logistically flexible nucleic acid delivery platforms.

References

Lü, J. M. *et al.Nanomedicine***11**, 1971–1991 (2016)
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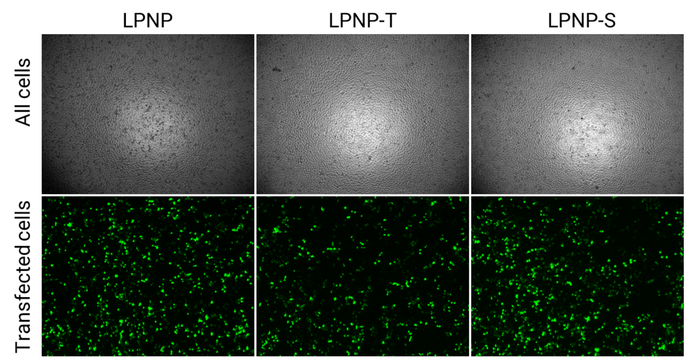
RESULTS OF LPNPs PRIOR CHARACTERIZATION

Adding trehalose or sucrose cryo/lyoprotectants in histidine buffer preserved LPNPs physicochemical and functional properties while increasing osmolality toward physiological levels.



Formulation	Hydrodynamic diameter (nM)	Osmolality (mOsmol/kg)	Transfection efficiency (%)	Cell viability (%)
LPNP	159±19	45±2.5	54±11	90±3
LPNP-T	186±22	267±3.5	51±4	90±2
LPNP-S	146±7	335±3.2	48±3	91±6

RESULTS OF LYOPHILIZED LPNP CHARACTERIZATION

Lyophilized, histidine-buffered LPNPs with trehalose or sucrose showed significantly enhanced long-term stability, maintaining physicochemical integrity, transfection efficiency, and low cytotoxicity even after 24 weeks at 37 °C.