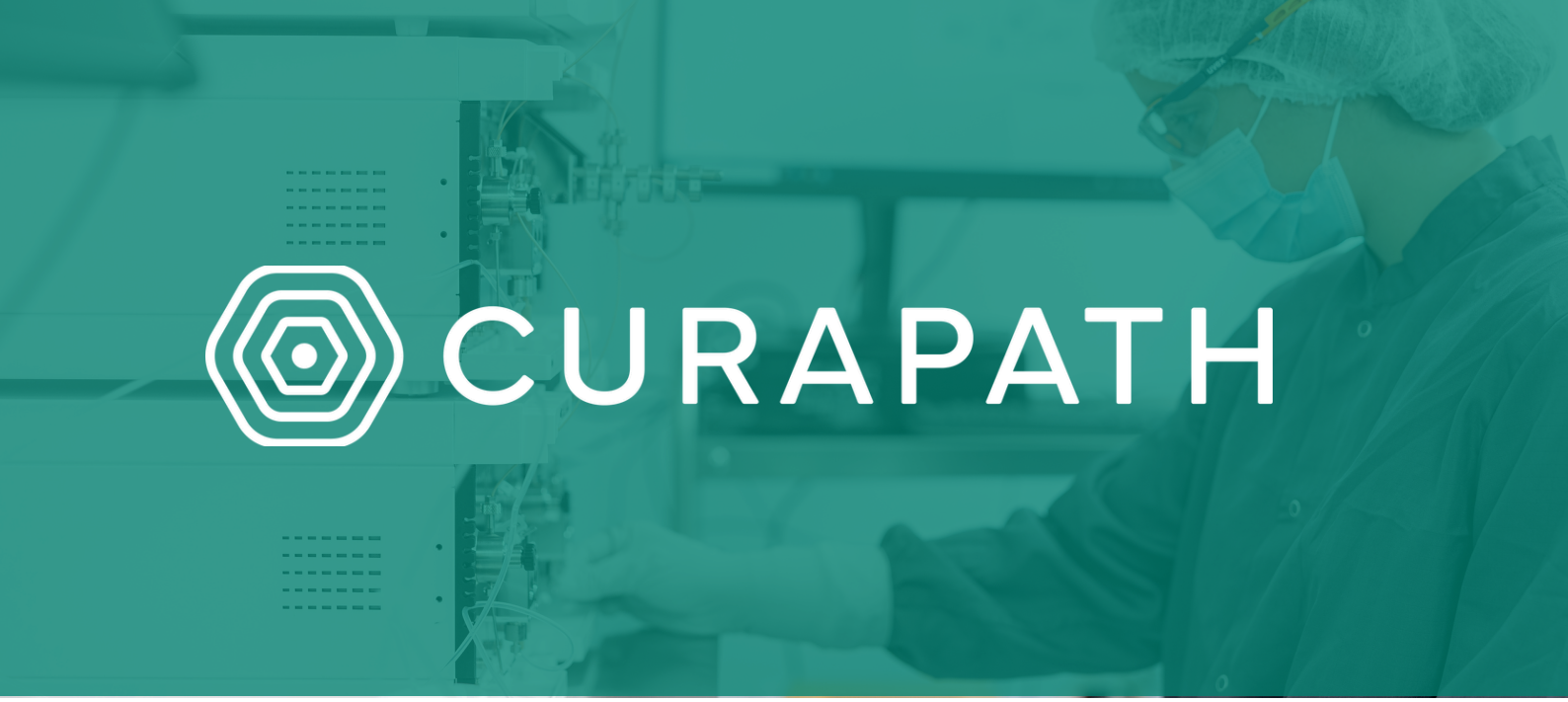
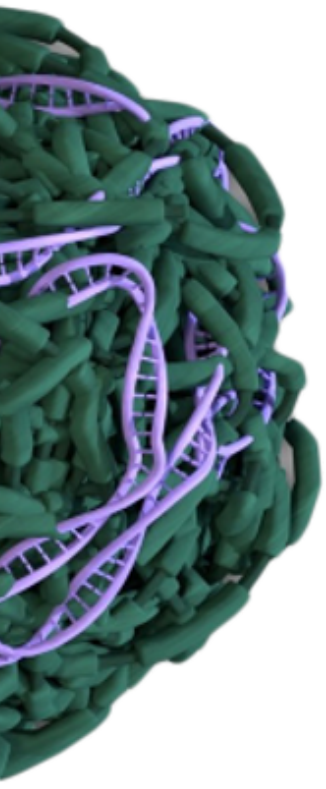


CURAPATH



Solutions For DNA Delivery

SCAN ME!

REACH OUT

RESOURCES

SOCIAL MEDIA

The Challenge

Non-viral transfection systems constitute a promising **alternative** to viral vectors **for in vivo DNA delivery**, particularly for applications requiring transient gene expression such as DNA vaccination and **in vivo CAR-T cell programming**. Their synthetic and modular nature enables flexible formulation design, accommodation of large DNA payloads, and scalable manufacturing, making them attractive platforms **for next-generation genetic medicines** and immunotherapies.

However, despite these advantages, current **non-viral DNA delivery systems** remain **limited** by several **barriers** to clinical translation, including cytotoxicity associated with highly cationic materials, suboptimal in vivo performance and poor biodegradability.



High Cytotoxicity & Poor Biocompatibility

Strong cationic polymers such as PEI can damage cell membranes, limiting safety and therapeutic dosing.



Limited In Vivo Performance

Hemolysis, complement activation, inflammation, and non-specific biodistribution reduce efficacy and tolerability after systemic administration.



Poor Biodegradability

Non-degradable polymers may accumulate in tissues, raising long-term safety concerns and restricting repeated dosing.



Limited Clinical & GMP Translation

Despite high in vitro transfection efficiency, challenges in safety, reproducibility, scalability, and GMP manufacturing have limited the clinical adoption of many non-viral DNA delivery systems.

Product Solutions

Curapath's Toolbox For Nucleic Acid Delivery

Curapath offers a **versatile DNA delivery platform based on** polymeric nanoparticles (**PNPs**) that can be tailored to the specific requirements of **different therapeutic applications**. Depending on the intended use, these nanoparticles can be provided in their native form or with protective surface modifications to enhance performance, stability, and biological compatibility. The platform also supports the **encapsulation and delivery of** a wide range of **DNA-based cargos**, including plasmid DNA (pDNA), while maintaining the flexibility to incorporate other nucleic acids and biomolecules.

Curapath's DNA delivery solutions are designed to **provide flexibility** in nanoparticle composition, **surface functionalization**, **and cargo encapsulation**, enabling the development of customized gene delivery systems adapted to diverse therapeutic needs.

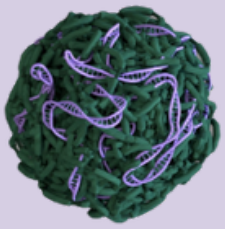
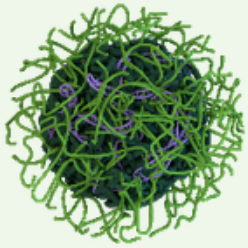
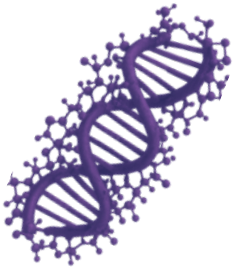
	Polymer nanoparticle (PNP)	**Shielded PNP**
		
SHELL	Naked	Polyanion: PGA-PSar PGA-PAOx PEG or custom alternative
CORE	Polycation: Polyethyleneimine (PEI) STAR-CXP – Family (polyaminoacids)	Polycation: Polyethyleneimine (PEI) STAR-CXP – Family (polyaminoacids)
CARGO	Nucleic acids, **peptides**, proteins	Nucleic acids, **peptides**, proteins
OPTIMAL CARGOS	**DNA**, e.g. pDNA., siRNA, saRNA, etc. **Peptides**	**DNA**, e.g. pDNA, siRNA, saRNA, etc. **Peptides**
BIODEGRADABILITY	Yes, for STAR-CXP PAsp family	Yes, for STAR-CXP PAsp family

Table 1. Curapath's toolbox for nucleic acid delivery

STAR-CXP Platform

The **STAR-CXP** Platform is a non-viral, targeted DNA delivery platform that offers a scalable alternative to viral vectors for in vivo gene transfer. Combining efficient DNA delivery with a favorable tolerability profile, STAR-CXP is designed to support next-generation genetic medicines, including DNA vaccines and gene therapies.

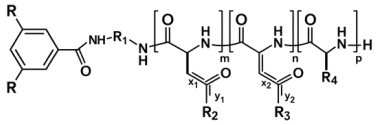
Reporter or customer's nucleic acid

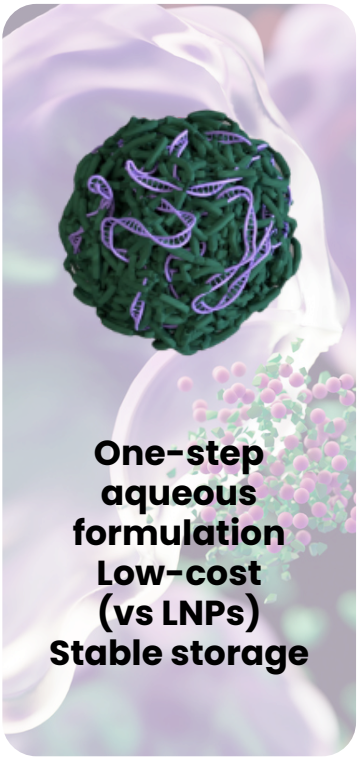


Polymer

STAR-CXP

PATENTED





One-step aqueous formulation
Low-cost (vs LNPs)
Stable storage

Cargo-Optimized

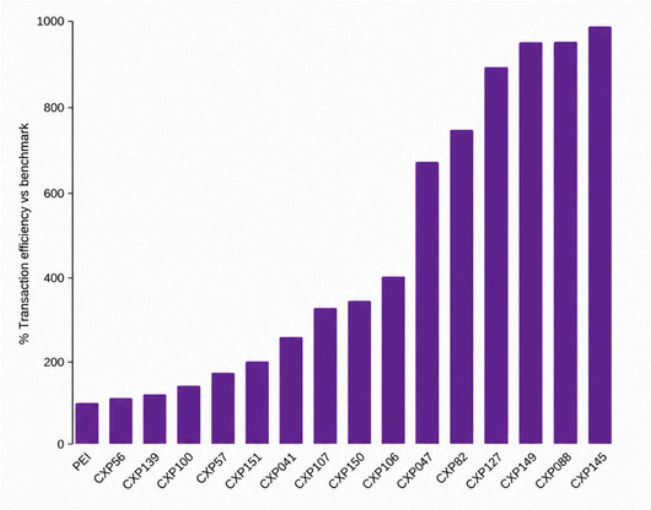
Improved Transfection

Biodegradable (Polyaminoacids)

Ideal For Peptides & Nucleic Acids

Curapath's STAR-CXP polymers outperform benchmarks in terms of transfection efficiency and reduced immunogenicity

Transfection Efficiency



C5 Activation

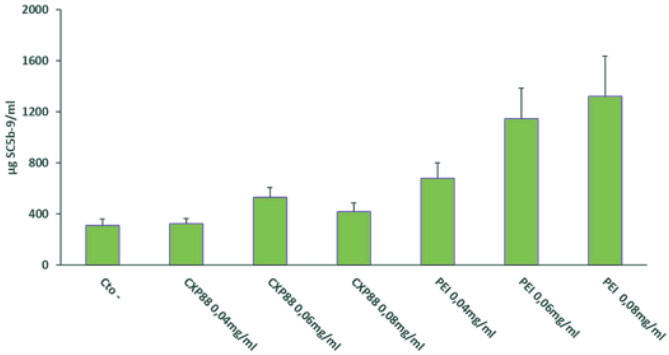


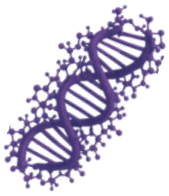
Figure 1. Left: Transfection efficiency normalized to the linear-PEI benchmark in a patient-derived primary cell line. Unshielded PXs were formulated in water at 150 ng DNA. STAR-CXP demonstrated superior performance, achieving up to 9× higher transfection efficiency than PEI. **Right: Complement C5 activation relative to benchmark.** Screening of the polymer library identified lead CXP candidates with substantially lower C5 activation than benchmark formulations, supporting their improved biocompatibility for non-viral *in vivo* delivery.

Polymer Nanoparticles

CURAPATH SHIELDING TECHNOLOGY BASED ON STEALTH POLYAMINO ACIDS

Shielding polymers can be incorporated into the **STAR-CXP** platform to reduce the toxicity associated with polycation-based polyplexes while enabling targeted delivery and enhancing transfection efficiency. This modular approach improves the overall safety and performance of non-viral gene delivery systems.

Reporter or customer's nucleic acid

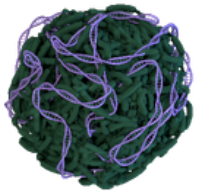


POLYMER

STAR-CXP



Polyplex

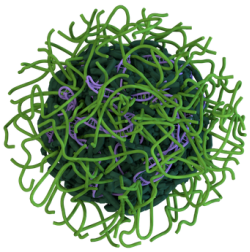


One-step aqueous formulation
Low-cost (vs LNPs)
Stable storage



SHIELDING POLYMER

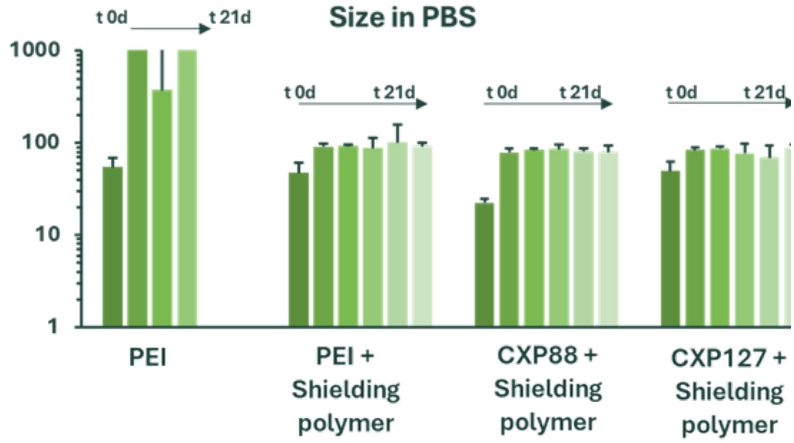
Shielded Polyplex



Increased stability
Reduced immunogenicity
Targeting possibilities

PSar Shielding Technology: Improved Safety and Performance

PSar shielding technology enhances the safety and performance of PEI-based polyplexes by reducing polymer-associated toxicity, enabling targetable delivery, boosting transfection efficiency, and maintaining long-term colloidal stability by preventing time-dependent particle aggregation. In contrast, unshielded PEI polyplexes exhibit a marked increase in particle size, consistent with particle aggregation over time.



tPNP Targeteability Potencial

Avoids Particle Aggregation

Enables i.v. administration

Figure 2. Hydrodynamic diameter of PEI polyplexes. PSar shielding maintains a stable hydrodynamic diameter over 21 days in PBS, preventing the progressive particle aggregation seen with unshielded PEI polyplexes. This shielding strategy also supports reduced toxicity, targetable delivery, and enhanced transfection performance.

Polymer Nanoparticles

Increasing Nuclear Delivery of pDNA with Curapath's PNPs

Efficient non-viral gene delivery requires not only cellular uptake but also successful transport of plasmid DNA (pDNA) to the nucleus, a critical step that remains a major barrier to transfection. To assess the performance of Curapath's polymeric nanoparticles (PNPs), cellular uptake and nuclear localization of Cy5-labeled pDNA were quantified by flow cytometry, providing a direct measure of intracellular trafficking and nuclear delivery efficiency across formulations.

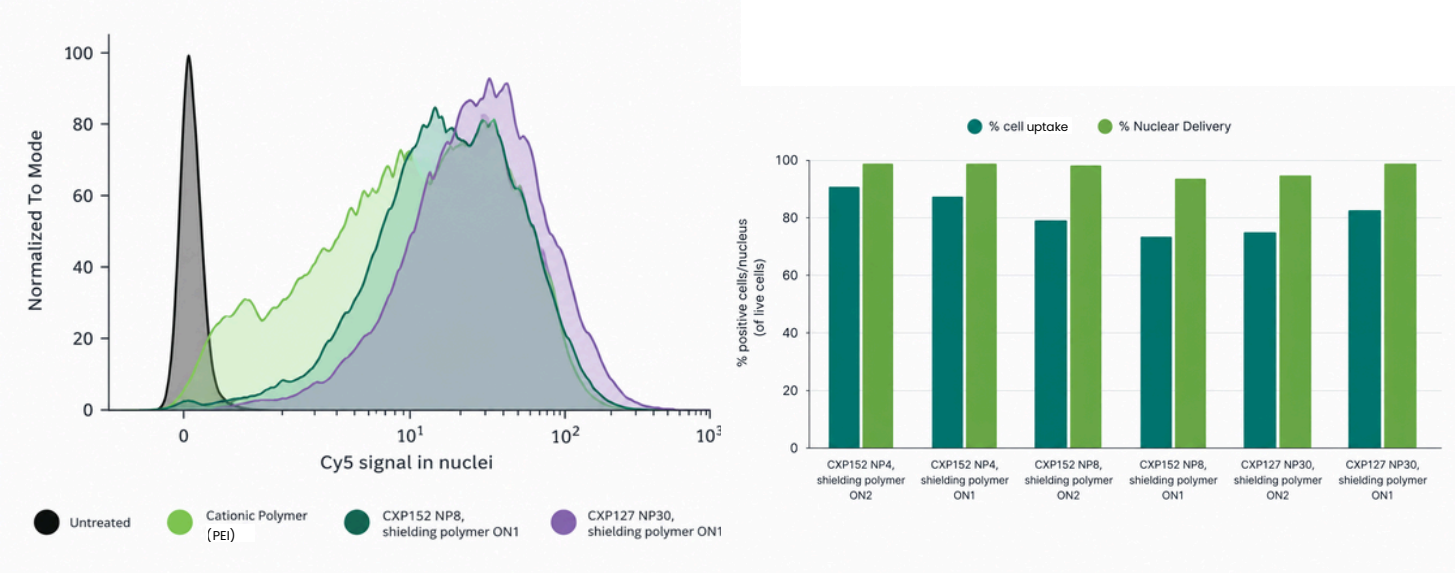


Figure 3. Flow cytometric analysis of Cy5-labeled plasmid DNA (pDNA) delivery following transfection with STAR-CXP formulations. **Left:** Histogram of nuclear Cy5 fluorescence intensity, illustrating the distribution of Cy5 signal within isolated nuclei for each formulation. **Right:** Percentage of Cy5-positive cells, representing cellular uptake across the different formulations, and percentage of Cy5-positive nuclei, representing nuclear delivery of pDNA across the different formulations.

Cellular uptake is maintained following the incorporation of the shielding polymer

Shielding does not compromise internalization efficiency

Curapath PNPs are ideal for DNA delivery into the nucleus

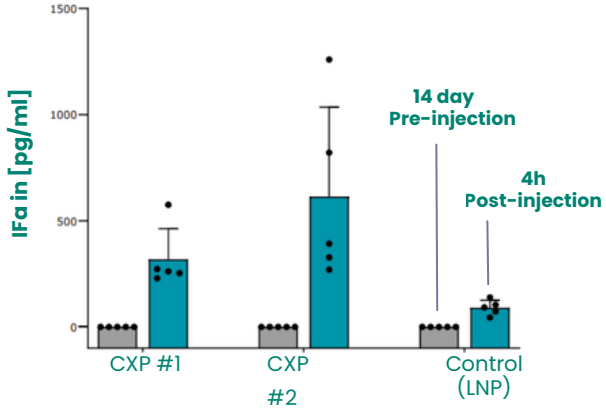
Polymers Nanoparticles
CXP in vivo

PSar-shielded PNPs with mRNA show good tolerability *in vivo*



Intravenous Injection (mice)

IFNα in mouse serum

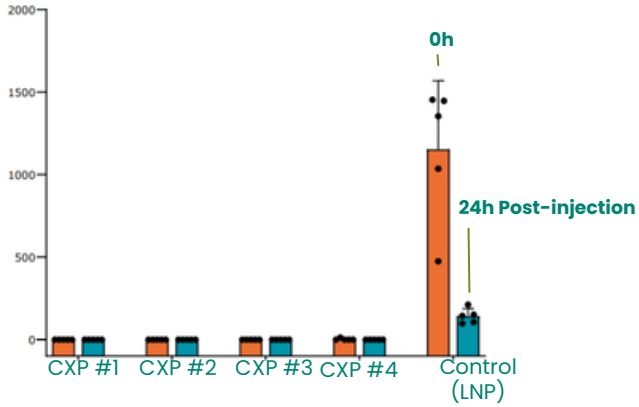


No indication of strong cytokine induction



Intramuscular Injection (mice)

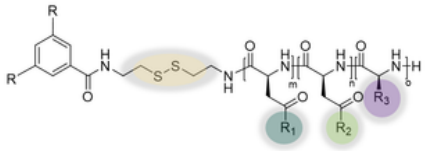
IFNα in mouse serum



IFa below detection limits

Figure 4. Serum IFNα levels measured in mice following administration of mRNA-loaded formulations. **Left**: IFNα concentrations quantified 14 days pre-injection and 4h post-injection. **Right:** IFNα concentrations measured at injection time and 24 h post-injection across the different formulations and the LNP control.

PSar shielded RNA-complexes are well tolerated in vivo, with no signs of strong cytokine induction, no elevation of liver enzymes and normal animal weight gain.



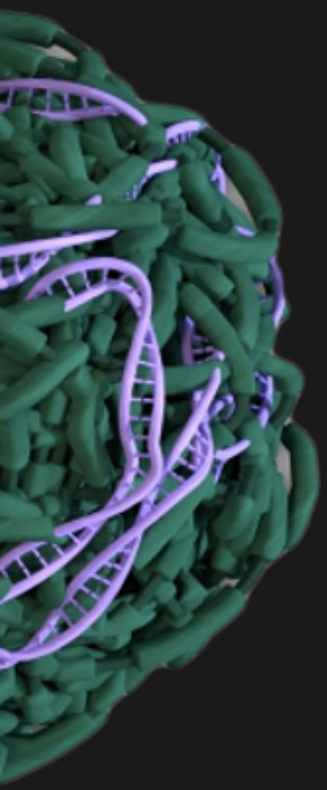
Complexing Polymers | **Shielding Polymer**

	CXP127	CXP088	CXP145	VLC3
Asp based and detachable arms	Biodegradability	Biodegradability	Biodegradability	PSar- based
Functionalization/ grafting	• Cationic/Ionizable moiety: Proton sponge effect for enhancing Endosomal Escape mechanism • Hydrophobic & ionizable moiety to enhance membrane fusion and EE	• Cationic/Ionizable moiety: Proton sponge effect for enhancing Endosomal Escape mechanism	• Cationic/Ionizable moiety: Proton sponge effect for enhancing Endosomal Escape mechanism	• Block copolymer • Systemic administration • Prevents off-target toxicity • Avoids particle aggregation enhanced stability • Non-immunogenic
Co-polymer backbone	• Random copolymer	• Random copolymer • Hydrophobic aromatic moiety to enhance membrane fusion and EE	• Block copolymer • Conformationally constrained cyclic moiety to facilitate membrane penetration by local structural disorder	• Block copolymer



CURAPATH

More than a CDMO



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