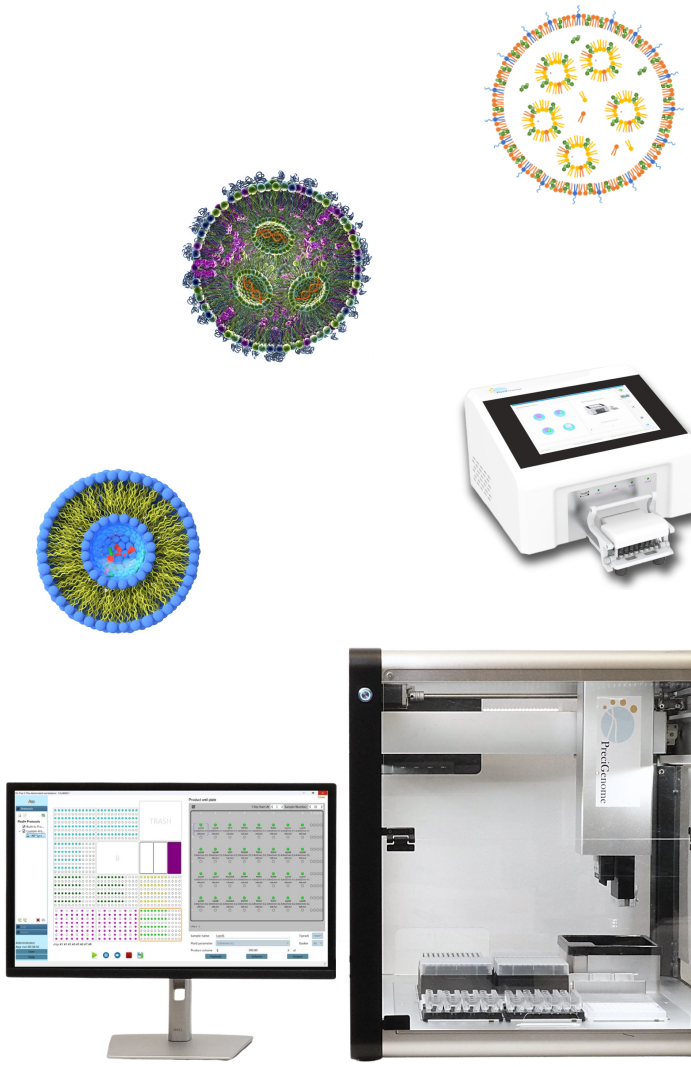
PreciGenome

NanoGenerator® Flex-S & Flex-S Plus System

High-throughput Discovery & Screening for Lipid Nanoparticle Formulations



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Version: v1.3.20250108

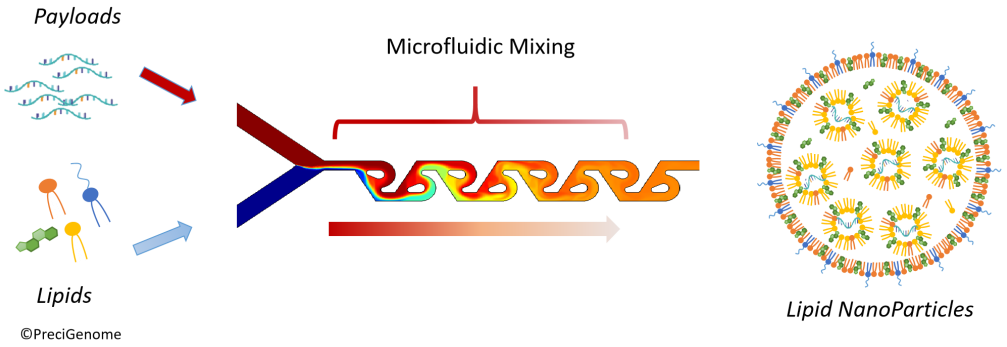
Advanced Microfluidic and Flow Control Technology

Microfluidic is an emerging technology that leverages precise manipulation of fluids at the microscale in the nanoparticle synthesis. Microfluidics offer superior control over LNP characteristics, such as size, surface charge, and drug loading, with low sample consumption, high reproducibility, and low-risk scalability.

NanoGenerator® platform applies microfluidic approaches to synthesize varieties of nanoparticles in a continuous mode, from the small scale discovery & screening phase to the large scale GMP manufacturing.

Microfluidic Mixing System

- Controllable particle size
- Low PDI
- High encapsulation efficiency
- High reproducibility



System Specifications

Model	Flex-S	Flex-S Plus
Multi-sample per run	1 - 4	(1-12) × 4 per run Up to 96 samples per hour
Ful automation	N/A	Yes
Library preparation	N/A	Optional
Throughput	0.1-0.5 ml per sample	0.1-0.5 ml per sample
Total flow rate	3 ml/min, 4 ml/min	3 ml/min,
Flow rate ratio	3:1	3:1
Custom design flow rate	Yes	Yes
Size range	40 – 200 nm	40 – 200 nm
PDI	0.05 – 0.2	0.05 – 0.2
Encapsulation efficiency	Up to 99%	Up to 99%
Payload	DNA, mRNA, siRNA, Protein, small mo lecules, etc.	DNA, mRNA, siRNA, Protein, small m olecules, etc.

NanoGenerator® Flex-S Nanoparticle Synthesis System

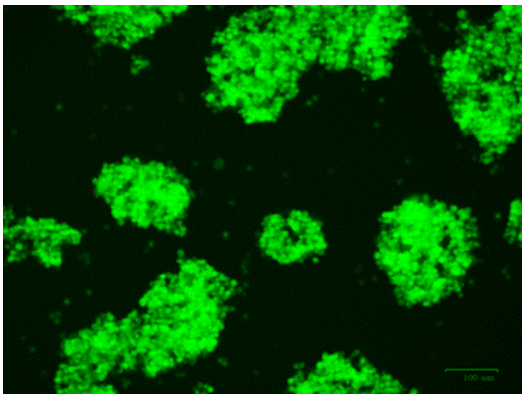
NanoGenerator® Flex-S

The NanoGenerator® Flex-S is designed for small scale production. It may run 1 to 4 samples at once, each sample from 0.1 to 0.5 ml. The throughput volume is therefore 0.1 to 2 ml per run, saving over 80% in reagent cost versus larger volumes and perfect for formulation screening and early discovery.

Even smaller output volumes (<0.1 ml per run), custom total flow rate, and custom flow rate ratio are attainable at special request by recipe optimization.

Model	NanoGenerator® Flex-S
Mixing Cartridge	CHP-MIX-4
Throughput	0.1 to 2 ml per run. 1 to 4 samples per run.
Total Flow Rate	3 ml/min, 4 ml/min
Flow Rate Ratio (W:O)	3:1
Size Range	40 to 200 nm
PDI	0.05 to 0.2
Encapsulation Efficiency	85-95%
Payloads	DNA, mRNA, siRNA, protein, small molecules

eGFP mRNA LNP Delivery to Jurkat Cells



Jurkat Cells transfected with Formulation #9. Green fluorescence image at 48 hours post transfection.

Example of Formulation Screening by Flex-S

Screening Panel			LNP Characterization			Cell Study
Formulation	Ionizable Lipid	N/P Ratio	Size (nm)	PDI	EE%	GFP expression
#1	40%	3.57	56.6	0.19	86%	+
#2	40%	5.35	79.9	0.246	84%	+
#3	40%	8	75.2	0.214	85%	++
#4	60%	5.35	128.5	0.13	81%	NA
#5	40%	5.35	62.8	0.186	90%	++
#6	40%	8	54.3	0.184	93%	++
#7	50%	8	79	0.155	88%	+
#8	50%	11	82.2	0.126	90%	NA
#9	50%	8	87.5	0.12	91%	+++

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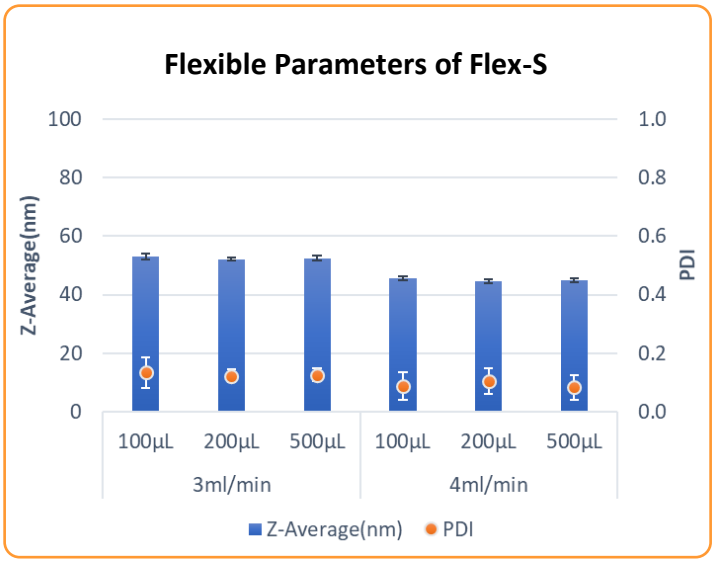


New features of NanoGenerator® Flex-S:

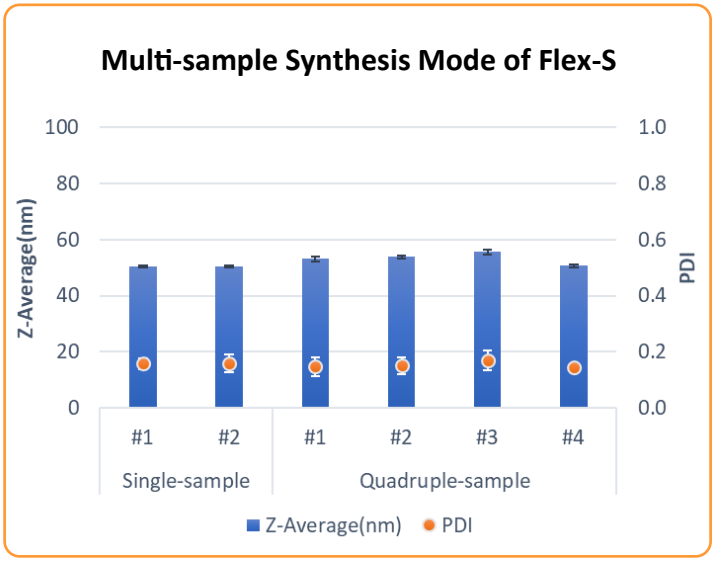
- **More total flow rate settings.** Users can choose 3 or 4 ml/min to conduct LNP synthesis. Higher total flow rate generates smaller LNPs. Other total flow rate and flow rate ratio are attainable at special request. *LNP size and PDI also depend on other factors such as the payload and formulation choice.*

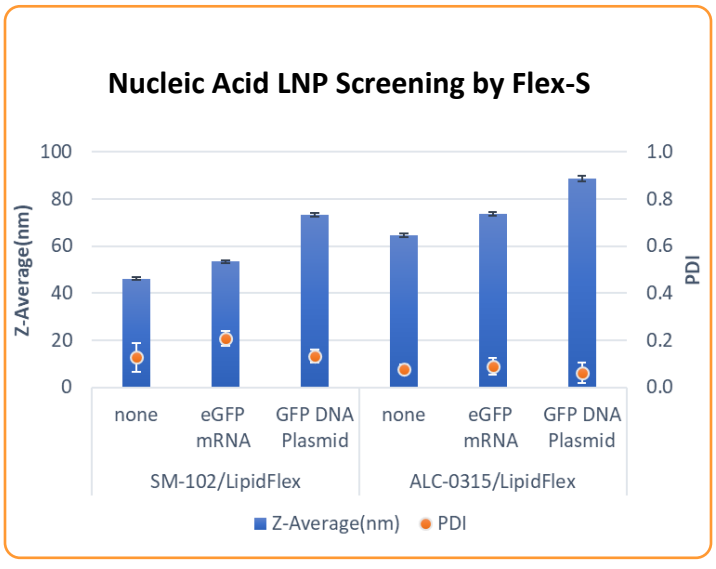
- **Output volume as low as 100 µl** is attainable by loading 75 µl aqueous samples (e.g. mRNA samples) and 25 µl lipid formulation.

Multi-sample Synthesis by NanoGenerator® Flex-S:

- **10 seconds, 4 samples!** Users can enable multi-sample synthesis mode to conduct formulation screening. The screening time is as low as 10 seconds

- **Reliable screening results.** Using PreciGenome's advanced air-flow control technology, users can obtain reliable LNP results on both single- and multi-sample synthesis modes.





- **Affordable formulation screening.** With the NanoGenerator® Flex-S, users can conduct formulation screening with minimal reagent consumption and reduced reagent cost.

- **Excellent batch-to-batch consistency.** Ease of operation and reliable components ensure consistent performance.

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NanoGenerator® Flex-S Plus Nanoparticle Synthesis System

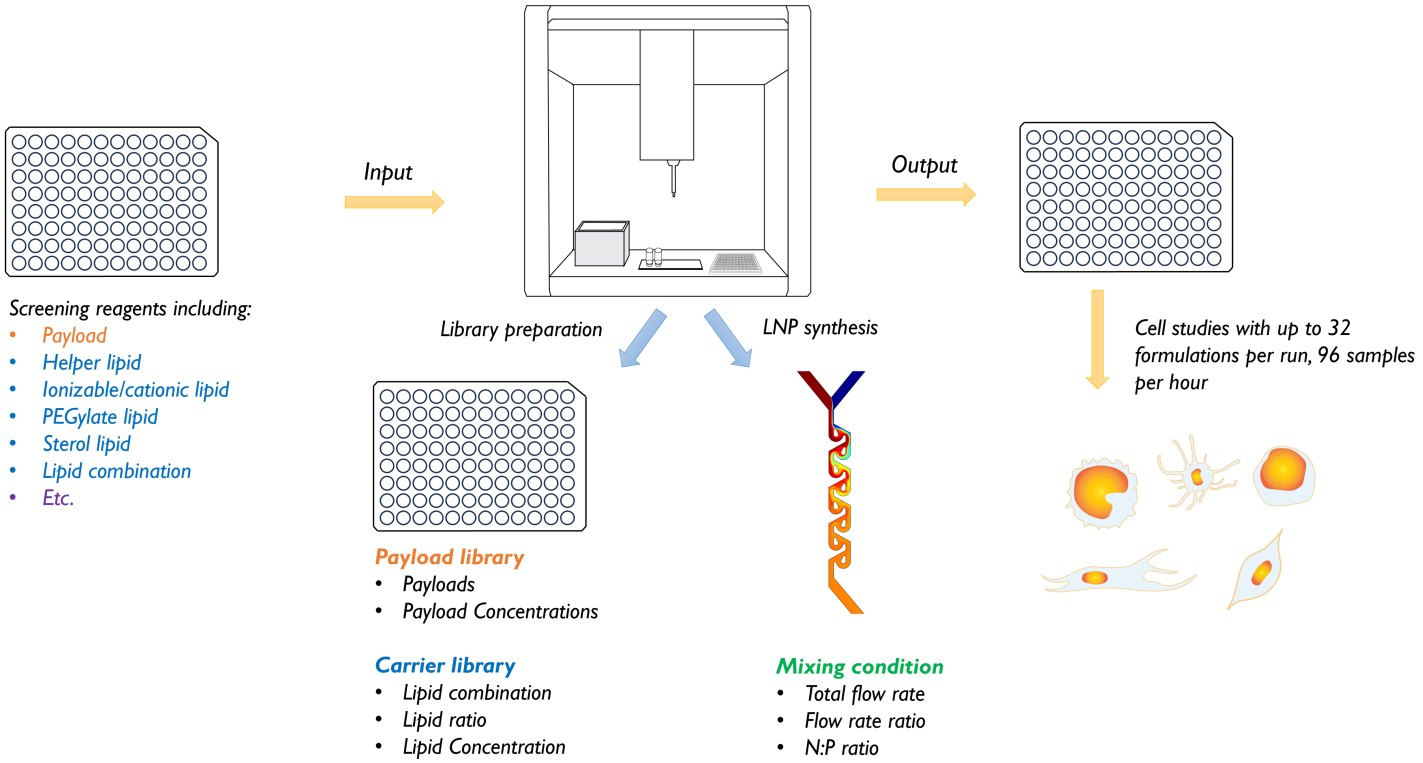
NanoGenerator® Flex-S Plus

The Flex-S Plus System facilitates the rapid screening of nanoparticle formulations and early-stage mRNA candidates, offering a substantial increase in project efficiency.

With a max throughput of 48 samples per run, 96 samples per hour, the Flex-S Plus greatly streamlines screening processes. It offers comprehensive automation of complex protocols, enabling users to concentrate on other laboratory duties.

The system also permits experimentation with as little as 75 µl of payload reagent (e.g. mRNA) while providing control over collection volumes. This allows users to optimize the use of valuable materials.

Automated Screening Workflow



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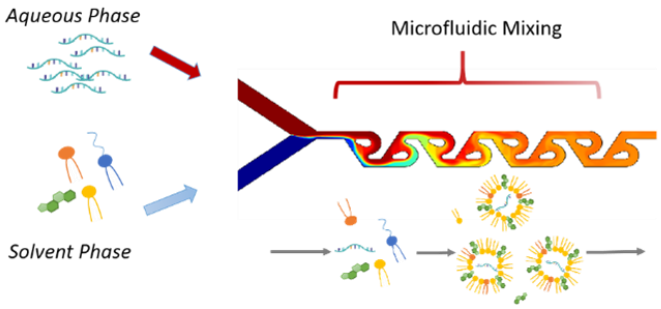
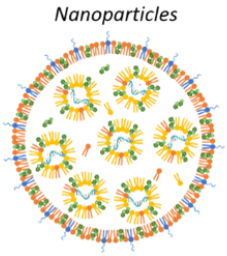
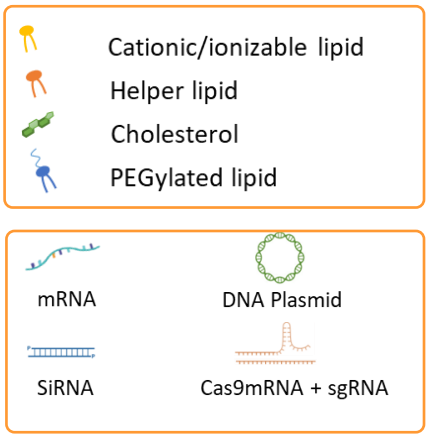
Formulation Screening & Discovery with High-throughput



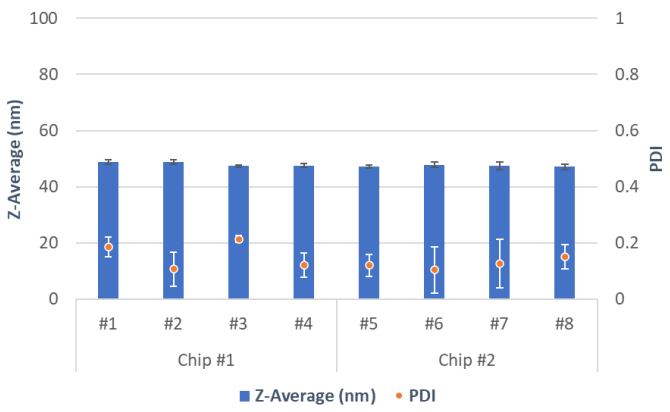


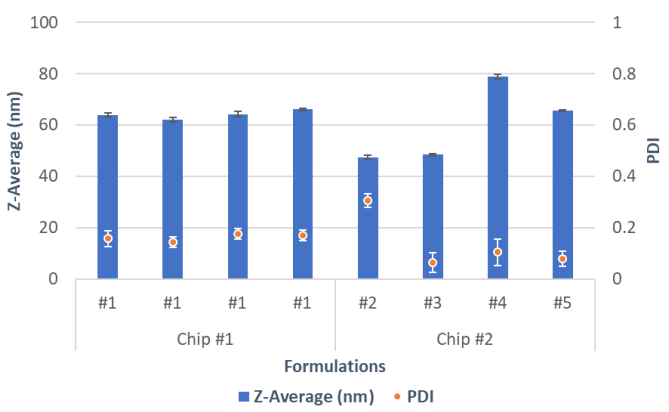


Model	NanoGenerator® Flex-S Plus
Mixing Cartridge	CHP-MIX-4
Throughput	0.1 to 0.5 ml per sample.
Sample per run	(1 - 12) × 4 per run Up to 96 samples per hour
Library Preparation	Optional
Total Flow Rate	3 ml/min, 4 ml/min
Flow Rate Ratio (W:O)	3:1
Size Range	40 to 200 nm
PDI	0.05 to 0.2
Encapsulation Efficiency	85-95%
Screening factors	Lipids, Payloads, N:P ratio, etc.

Multi-sample Screening by NanoGenerator® Flex-S Plus:

Example screening factors with the Flex-S Plus include payloads, carrier formulation, total flow rate, flow rate ratio, N:P ratio, Lipid concentration, and payload concentration. Precise control of parameters ensures consistent CQAs, guaranteeing speed, cost-effectiveness, and reliability at every stage of the experiment.





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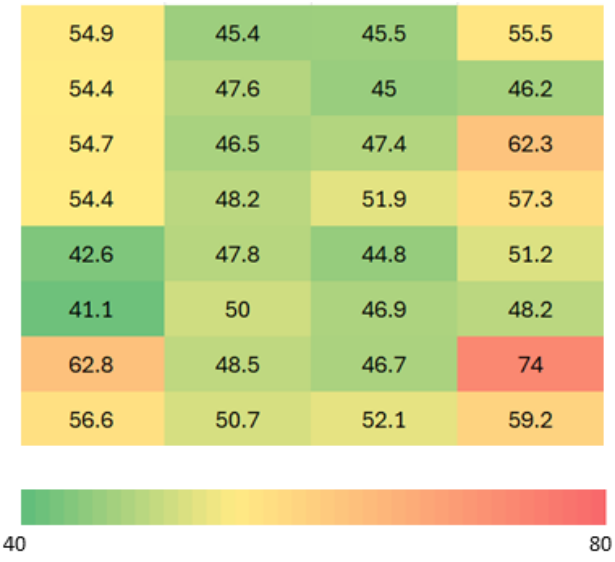
Formulation Screening & Discovery with High-throughput

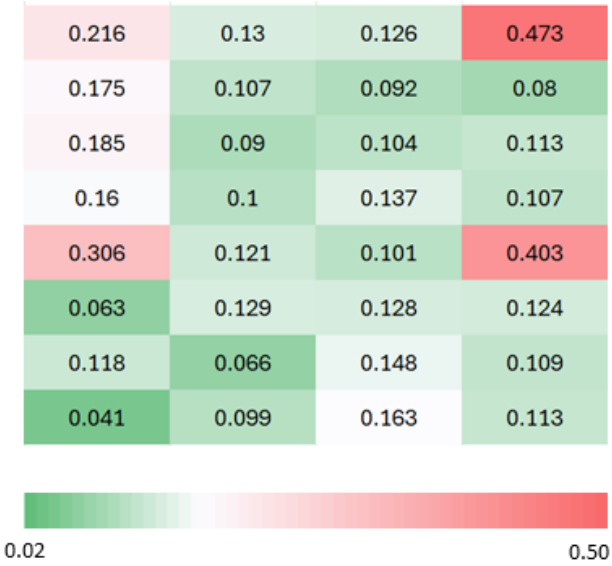
Application — 32 sample Screening by NanoGenerator® Flex-S Plus:

The following shows an application study of 32 sample screening by NanoGenerator® Flex-S Plus with total flow rate of 3ml/min and flow rate ratio of 3:1. Each cell in the heatmap indicates a unique LNP sample with a specific lipid formulation or a specific N:P ratio. The following heatmap offers an insight of the physical properties (size & PDI) of 32 kinds of different LNPs

32 sample screening — Size (nm)



32 sample screening — PDI



System Benefits

High Throughput & Efficiency

- Multiple sample (1/4/32) per run.
- Runtime <5 min for 4 samples, 48/96 samples per hour.

Automation

- Automated workflow
- Real-time data monitoring & recording
- Electronic batch records

High Yield

- Small reagent volume (minimum 100 µl) for each sample.
- Save up to 80% of RNA/lipid cost

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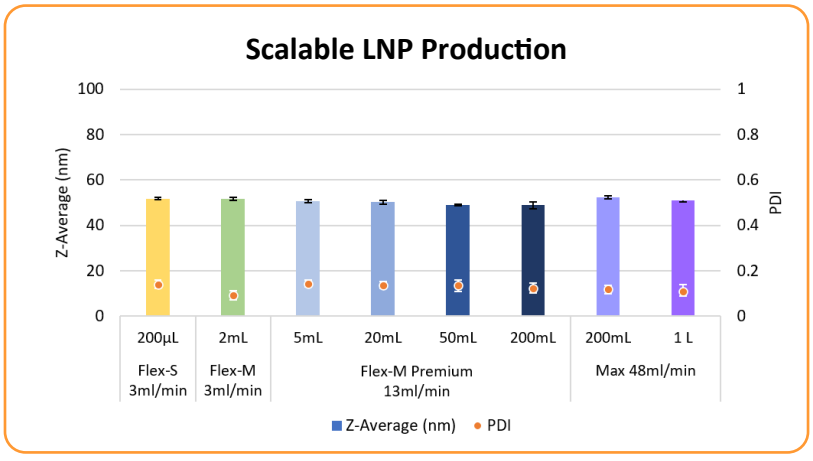
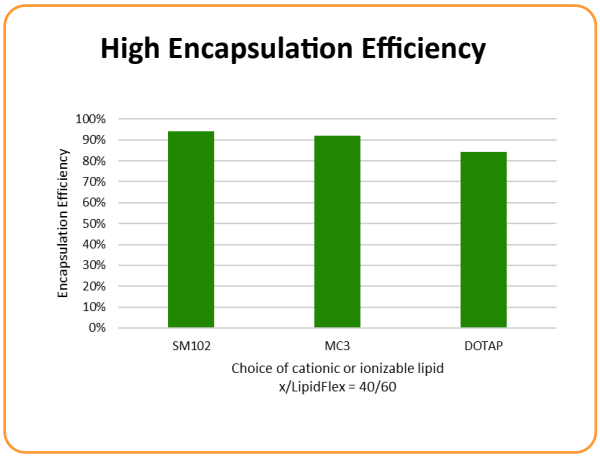
Cost-effective, Scalable, and Reproducible Formulation Screening

PreciGenome NanoGenerator® platform's precise control of parameters ensures consistent critical quality attributes, such as particle size, throughout the entire development and manufacturing process. This guarantees speed, cost-effectiveness, and reliability at every stage.

Reagents Cost Comparison

	NanoGenerator Flex-S/Flex-S Plus	Syringe Pump Systems	Tubing Connection Systems
Dead volume per sample	< 20ul	0.5 mL	0.5 - 1 mL
Source of dead volume	Micro-channel in the mixing Chip	Syringe, connector, and/ or mixing chip	Tubing, connector, and mixing chip
Typical production volume	100 uL – 0.5 mL per sample	1 – 10 mL	1 – 10 mL
Minimum input volume (Aqueous :Lipid = 3:1)	Aqueous : 75ul Lipid: 25ul	Aqueous: 1 mL Lipid: 0.5 mL	Aqueous: 1 mL Lipid: 0.5 mL
Estimated minimum mRNA cost	$50	$660	$660





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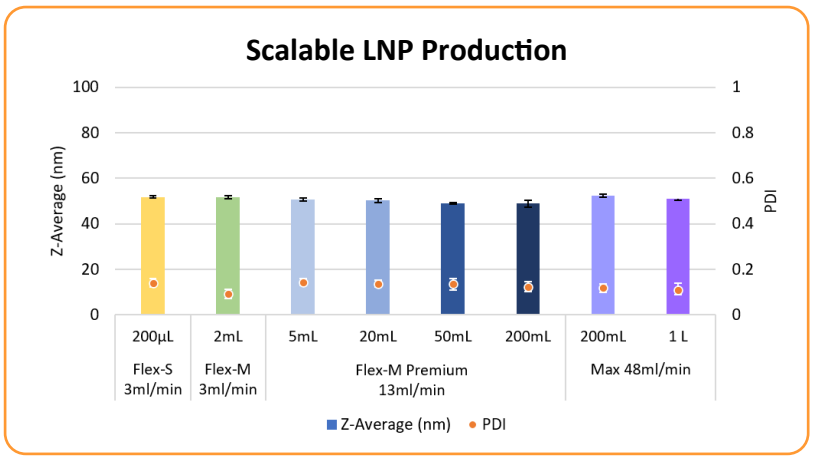
Path from Discovery to Commercialization

NanoGenerator® offers controllable and reproducible mixing conditions, ensuring the accurate synthesis of LNPs through its scalable architecture found in the entire NanoGenerator® product line. Options are available for all production stages, allowing seamless transfer of crucial process parameters and guaranteeing consistent critical quality attributes (CQAs). LNPs produced from NanoGenerator® may be used for a wide range of applications, such as vaccine development, gene therapy, cell therapy, etc.

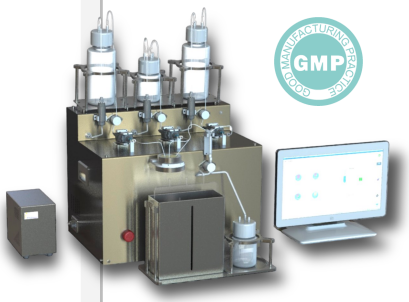


Discovery & Screening | Pre-Clinical | Clinical | Commercial

Flex-S
0.1 - 2mL per run
1 - 4 samples per run

Flex-M
1 - 12mL per run

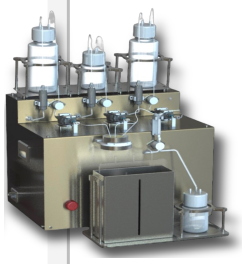
Flex-M Premium
1 - 200 mL per run



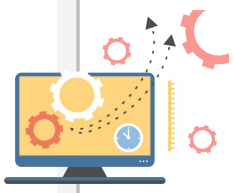
MAX cGMP
50mL - 1L per run

MAX cGMP (40L/h)
>20L per run

Flex-S Plus
0.1 - 0.5mL per sample
48 samples per run
96 samples per hour



MAX (RUO)
50mL - 1L per run



Custom design and
OEM solutions

>200 L throughput

Target Validation
API Identification
Excipient Identification

Formulation Development
& Optimization
Candidate Selection

Clinical Development
Approved Medicine
Customized GMP Solution

PreciGenome is located in the heart of Silicon Valley, San Jose, California, USA. We have been focusing on developing nanoparticle synthesis systems and solutions for our customers. Our technology enables nanoparticle synthesis with high quality and reliable performance for lipid nanoparticles, liposomes, PLGA, etc.

HEADQUARTER

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